

CHALLENGES AND INNOVATIVE THERAPEUTIC OPPORTUNITIES

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MARCKS targeting by miR-30b drives tumor suppressive effects in inflammatory breast cancer

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Introduction: The myristoylated alanine-rich C-kinase substrate (MARCKS) oncogene has been reported to be overexpressed in inflammatory breast cancer (IBC) as compared to nonIBC (nIBC). A negative correlation between microRNA-30b (miR-30b) and MARCKS expression has been observed in IBC patients compared to nIBC patients.

Methods: In this in vitro study, two IBC cell lines (SUM149 and KPL4) were transfected with miR-30b_plasmid (miR30b_pcDNA3.1+/C-(K)-DYK) and miR-30b_scrambled plasmid (pcDNA3.1+/C-(K)-DYK). Colony formation and scratch wound healing assays were used to examine the proliferation and cell migration, respectively. Real-time qPCR (RT-qPCR) was performed to identify the mRNA expression level of miR-30b, MARCKS, and genes known to be involved in IBC inflammation and apoptosis. Weste Blot was performed to analyze the mechanism of action of miR-30b overexpression.

Results: We found that transfection with miR-30b overexpression significantly suppressed the aggressive phenotype of IBC cells (SUM149 and KPL4) in terms of colony formation ($p < 0.001$) and cell migration ($p < 0.001$). At the mRNA level, miR-30b overexpression dramatically downregulated MARCKS mRNA ($p < 0.001$) and TNF- expression across SUM149 ($p = 0.009$) and KPL4 ($p = 0.047$). Interestingly, the pro-apoptotic gene was upregulated after miR-30b overexpression in IBC cells ($p < 0.001$). At the protein level, this reduction was consistently confirmed by a marked decrease in protein expression of

MARCKS ($p < 0.001$ and $p < 0.001$), pMARCKS ($p < 0.001$ and $p < 0.001$), and P21 ($p < 0.001$ and $p = 0.006$), respectively, in SUM149 and KPL4 cells.

Conclusion: Our data demonstrate that miR-30b overexpression suppresses MARCKS expression in IBC cells, reduces cell proliferation and motility, consistent with a posttranscriptional regulatory mechanism. These findings identify miR-30b as a potential therapeutic target in inflammatory breast cancer through MARCKS downregulation.

A machine learning-driven predictive model for metachronous liver metastasis in stage II–III CRC: Toward improved clinical decision-making

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Background and Objective: Metachronous liver metastasis (MLM) poses a substantial prognostic threat for patients with colorectal cancer (CRC). This study aimed to delineate high risk CRC patients predisposed to developing MLM based on their clinic pathological features.

Methods: A total of 822 stage II–III CRC patients were enrolled and randomly divided into training ($n=576$) and validation ($n=246$) cohorts at a 7:3 ratio. Risk factors were identified via Lasso and multivariate logistic regression. Nomogram performance was assessed using the Cindex, ROC curves, calibration plots, decision curve analysis (DCA), and clinical impact curve (CIC). Kaplan–Meier analysis and the log-rank test were used to evaluate overall survival in stratified patients.

Results: Six risk factors out of thirteen were selected for the nomogram: tumor size, histological type, stroma, tumor localization, differentiation, and preoperative CEA. The nomogram demonstrated robust discriminative ability, achieving a C-index of 0.904 in the training cohort and 0.910 in the validation cohort. Furthermore, the calibration curve showed strong alignment between the nomogram's predicted

probabilities and the observed values. The DCA and CIC indicated greater clinical net benefit within a threshold probability range of 2.3% to 89%, confirming the strong predictive capacity of the model. Additionally, Kaplan–Meier survival analysis demonstrated statistically significant differences in survival outcomes among the low-, moderate-, and high-risk groups stratified according to predicted probability, thereby further substantiating the strong discriminative and prognostic performance of the model.

Conclusions: The developed nomogram demonstrated high predictive accuracy for identifying CRC patients at risk of MLM. By providing individualized risk estimation, the model supports personalized postoperative surveillance strategies and facilitates early detection of metastatic progression. Furthermore, this approach may optimize clinical management by prioritizing intensive follow-up for high-risk patients while avoiding unnecessary surveillance in low-risk individuals.

MARCKS Modulates Tumor–Macrophage Crosstalk and Aggressiveness in Inflammatory Breast Cancer

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Introduction: Inflammatory breast cancer (IBC) is a rare and aggressive form of breast cancer, accounting for 1-3% of cases, with a higher prevalence in North of Africa (7-11%). A major challenge in treating IBC is the lack of specific therapeutic targets. Myristoylated Alanine Rich C Kinase Substrate (MARCKS) was found overexpressed and associated with poor prognosis in IBC vs. non-IBC (nIBC). MARCKS has been associated with an inflammatory tumor microenvironment (TME) enriched in macrophages in solid tumors. Our study aimed to evaluate in vitro and in clinical samples the role of MARCKS in the TME in IBC compared to nIBC models.

Methods: In this study, we investigated the role of MARCKS on cell proliferation (colony formation assay), migration (scratch wound healing assay), and its underlying molecular mechanisms (RT-qPCR, Western blot, and immunohistochemistry) in IBC in co-culture with M2 macrophages using SUM149 and KPL4 cell lines, and patients' samples.

Results: MARCKS inhibition by siRNA induced a significant decrease in migration and clonogenicity, with more pronounced effects in the presence of M2 macrophages signals. Mechanistically, our Results support the idea that MARCKS appears to act as a central modulator of the crosstalk between the tumor and its microenvironment, participating

in the maintenance of major signaling pathways involved in inflammation, and epithelial to mesenchymal transition (EMT) notably NF- κ B, STAT3, and IL8 and its inhibition promotes a shift toward a pro-apoptotic program via pro-apoptotic genes (PUMA) and proteins (P21) upregulation.

Conclusion: Collectively, our findings identify MARCKS as a central regulator of tumor progression in IBC, integrating cytoskeletal dynamics, inflammatory signaling (NF- κ B/STAT3), and apoptotic control. By modulating both tumor cell-intrinsic pathways and tumor–macrophage interactions, MARCKS promotes a pro-tumorigenic microenvironment. Its inhibition disrupts this network, reducing migration, dampening inflammatory signaling, and sensitizing tumor cells to apoptosis, thereby highlighting MARCKS as a potential therapeutic target in IBC. **Keywords:** inflammatory breast cancer, tumor microenvironment, in vitro, M2 macrophages, signaling pathways.

Predictive Factors of Pathological Complete Response (pCR) after Neoadjuvant Chemotherapy in Triple-Negative Breast Cancer

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Introduction: Triple-negative breast cancer (TNBC) accounts for 15 to 20% of all breast cancers. It is defined by the absence of estrogen receptor, progesterone receptor expression and HER2 overexpression. This subtype is associated with aggressive behavior, a high risk of early recurrence, and a poorer prognosis compared with other molecular subtypes. Neoadjuvant chemotherapy (NAC) is currently the standard of care for locally advanced TNBC. Pathological complete response (pCR), defined as the absence of residual invasive carcinoma in the breast and axillary lymph nodes (ypT0/is ypN0), is a major prognostic factor. The CTNeoBC pooled analysis (Cortazar et al., Lancet 2014) demonstrated that achieving pCR is associated with significantly improved event-free survival and overall survival, particularly in TNBC. The pCR rate in TNBC ranges from 35 to 65% depending on the treatment regimen used. The addition of pembrolizumab to neoadjuvant chemotherapy (KEYNOTE-522 trial) achieved pCR rates of 64.8% versus 51.2% with chemotherapy alone. Identifying predictive factors of pCR is therefore essential to personalize treatment strategies and guide therapeutic decisions.

Objectives: The primary objective of this study was to determine the pCR rate after NAC in a Tunisian cohort of 50 patients with TNBC. Secondary objectives were to identify clinicopathological and biological predictive factors of pCR, with particular focus on the prognostic value of stromal tumor-infiltrating lymphocytes (TILs), the Ki-67 proliferation index, and the pretreatment neutrophil-to-lymphocyte ratio (NLR). We also analyzed the correlation between pCR achievement and 3-year event-free survival (EFS).

Methods: This was a single-center retrospective study conducted at the Department of Obstetrics and Gynecology, Hédi Chaker University Hospital, Sfax, Tunisia, over a 3-year period (January 2021 – December 2023). We included 50 consecutive patients with immunohistochemically confirmed TNBC (ER/PR/HER2) who received complete NAC followed by breast surgery. Patients with de novo metastatic disease and those who did not complete the NAC protocol were excluded. NAC regimens consisted of sequential anthracycline- and taxane-based protocols (AC-T: doxorubicin/cyclophosphamide followed by docetaxel), with or without carboplatin. Selected

patients received additional pembrolizumab according to the KEYNOTE-522 protocol when available. The primary endpoint was pCR defined as ypT0/is ypN0. Variables studied included age, clinical tumor size (cT), clinical nodal status (cN), SBR grade, Ki-67 index, stromal TILs assessed according to the Intentional TILs Working Group recommendations, pretreatment NLR and PLR, and CA 15-3 levels. Statistical analysis included Chi-square test, univariate and multivariate logistic regression, ROC curve analysis, and Kaplan-Meier survival analysis with Log-rank test.

Results: Patient Characteristics The median age was 48 years (range: 28–72). Forty-four percent of patients were under 40 years of age. Initial clinical stage was T2 in 58% and T3 in 26% of cases. Nodal status was cN0 in 48%, cN1 in 38%, and cN2 in 14%. SBR grade III predominated (82%). The median Ki67 was 62% (IQR: 40–78%), with 74% of patients having Ki-67 $\geq 50\%$. Stromal TILs were 30% in 46% of patients. The median pretreatment NLR was 2.1 (IQR: 1.4–3.2). pCR Rate The overall pCR rate was 42% (21/50). Among patients with stromal TILs $\geq 30\%$, the pCR rate reached 58%. In patients with Ki-67 $\geq 50\%$, the pCR rate was 48%. Among patients with NLR ≤ 1.8 , pCR was achieved in 61% of cases. Univariate Analysis On univariate analysis, factors significantly associated with pCR achievement were: stromal TILs $\geq 30\%$ (76% in the pCR group vs 28%, $p < 0.001$), Ki-67 $\geq 50\%$ (90% vs 62%, $p = 0.008$), NLR ≤ 1.8 (71% vs 34%, $p = 0.005$), and cN0 status (67% vs 38%, $p = 0.03$). In contrast, age ($p = 0.28$), cT1-T2 tumor size ($p = 0.09$), SBR grade III ($p = 0.52$), and low PLR ($p = 0.12$) were not significantly associated with pCR. Multivariate Analysis On multivariate logistic regression, three factors were identified as independent predictors of pCR: stromal TILs $\geq 30\%$ (OR = 5.8; 95% CI: 1.9–17.6; $p < 0.001$), Ki-67 $\geq 50\%$ (OR = 4.2; 95% CI: 1.1–16.3; $p = 0.007$), and NLR ≤ 1.8 (OR = 3.6; 95% CI: 1.2–10.8; $p = 0.02$). cN0 status showed a trend toward significance (OR = 2.9; 95% CI: 0.9–9.4; $p = 0.06$). pCR and Survival Correlation Patients who achieved pCR had a significantly higher 3-year event-free survival (EFS): 89% vs 64% ($p = 0.008$, Log-rank). On multivariate analysis, pCR status was an independent prognostic factor for survival (HR = 0.31; 95% CI: 0.12–0.78). No disease-related deaths were observed in the pCR group during the median follow-up of 28 months.

Discussion: The 42% pCR rate observed in our cohort is consistent with published data reporting rates of 35 to 50% with anthracycline- and taxane-based chemotherapy alone. The KEYNOTE-522 trial demonstrated that adding pembrolizumab to neoadjuvant chemotherapy increases the pCR rate to 64.8%. A recent Turkish multicenter real-world study published in Scientific Reports (2026) confirmed these findings with a 60.4% pCR rate under chemo-immunotherapy. Stromal TILs were confirmed as the most robust predictive biomarker of pCR in our cohort, with an OR of 5.8. These Results are consistent with the systematic review by van den Ende et al. (Int J Mol Sci 2023), which identified TILs as the marker most frequently associated with pCR. A high TIL level reflects substantial tumor immunogenicity and potentially increased sensitivity to both chemotherapy and immunotherapy. Pretreatment NLR emerged as an independent and easily reproducible predictive factor in our study. A low NLR (≤ 1.8) reflects a favorable systemic immunological environment with lymphocyte predominance. This marker, derived from a simple complete blood count, may serve as a surrogate for TILs in centers where histological TIL assessment is not routinely performed, which is particularly relevant in resource-limited settings. A high Ki-67 index ($\geq 50\%$), reflecting significant cellular proliferation, is paradoxically associated with higher pCR rates, likely due to greater chemosensitivity of highly proliferative tumors. However, in the setting of residual disease, a high Ki-67 is associated with poorer prognosis, underscoring the importance of pCR status as a decision point for adjuvant treatment planning.

Conclusion: Stromal TILs $\geq 30\%$, Ki-67 $\geq 50\%$, and low NLR were

the most robust independent predictive factors of pCR in TNBC patients treated with NAC in our 50-patient cohort. Integrating these biomarkers into clinical practice would enable early identification of patients most likely to achieve a complete response and, ultimately, benefit from therapeutic de-escalation after pCR. NLR represents a simple, accessible, and reproducible marker, particularly useful in resource-limited settings where TIL assessment is not always available.

Pregnancy-Associated Breast Cancer: Clinicopathological Profile, Treatment Strategies, and Maternal-Fetal Outcomes – A 10-Year Retrospective Series

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Introduction: Pregnancy-associated breast cancer (PABC) is defined as breast cancer diagnosed during pregnancy or within one year postpartum. It is the most common malignancy encountered during pregnancy, with an estimated incidence of 1 in 3,000 to 10,000 pregnancies. Its incidence is increasing worldwide, primarily driven by the trend toward delayed childbearing and advanced maternal age at first pregnancy. PABC presents unique diagnostic and therapeutic challenges. Physiological breast changes during pregnancy, including engorgement, increased density, and hormonal hypervascularization, often mask clinical symptoms and delay diagnosis. Consequently, PABC is frequently diagnosed at a more advanced stage compared with breast cancer in nonpregnant women, with a higher prevalence of aggressive subtypes such as triple-negative and HER2-positive tumors. Treatment must balance optimal oncological outcomes for the mother with minimization of fetal harm. Surgery is feasible at any gestational age, while chemotherapy is generally safe from the second trimester onward. However, radiotherapy, endocrine therapy, anti-HER2 agents (trastuzumab), and immune checkpoint inhibitors remain contraindicated during pregnancy due to teratogenic risks. The SMFM Consult Series #76 (2026) and ESMO guidelines emphasize that treatment should mirror the standard of care for non-pregnant patients, with adaptations guided by gestational age and multidisciplinary collaboration. Objectives : The objective of this study was to describe the clinicopathological profile of PABC in a Tunisian tertiary center over a 10-year period. We aimed to analyze the diagnostic circumstances, histological subtypes, and staging at diagnosis, to describe the treatment strategies adopted during and after pregnancy, and to evaluate maternal oncological outcomes and fetal-neonatal safety. We also sought to compare our findings with published international series.

Methods: This was a retrospective descriptive study conducted at the Department of Obstetrics and Gynecology, Hédi Chaker University Hospital, Sfax, Tunisia, over a 10-year period (January 2014 – December 2023). All consecutive cases of breast cancer diagnosed during pregnancy or within one year postpartum were included. Patients with a history of breast cancer predating pregnancy were excluded. Data were collected from medical records and included demographic characteristics (age, gestational age at diagnosis, parity), diagnostic circumstances (clinical presentation, imaging modalities), tumor characteristics (histological type, grade, molecular subtype, TNM stage), treatment modalities (surgery, chemotherapy regimen and timing, radiotherapy), obstetric management (gestational age at delivery, mode of delivery, timing relative to treatment), and neonatal outcomes (birth weight, Apgar score, NICU admission, congenital anomalies). Maternal outcomes included disease-

free survival and overall survival with a minimum follow-up of 24 months. Descriptive statistics were used for data analysis.

Results : Patient Characteristics Over the 10-year study period, 18 cases of PABC were identified among approximately 54,000 deliveries, yielding an incidence of 1 in 3,000 pregnancies. The median age at diagnosis was 34 years (range: 26–42). Twelve patients (66.7%) were diagnosed during pregnancy (gestational breast cancer) and 6 (33.3%) during the first year postpartum. Among gestational cases, diagnosis occurred in the first trimester in 2 patients (16.7%), in the second trimester in 5 (41.7%), and in the third trimester in 5 (41.7%). The median gestational age at diagnosis was 24 weeks. The median diagnostic delay from symptom onset was 8 weeks (range: 2–20). Tumor Characteristics : The predominant histological type was invasive ductal carcinoma (88.9%). SBR grade III was observed in 61.1% of cases. Regarding molecular subtypes, triple-negative tumors accounted for 33.3%, HER2-positive for 27.8%, luminal B for 22.2%, and luminal A for 16.7%. At diagnosis, 55.6% of patients had T2 tumors and 27.8% had T3 tumors. Lymph node involvement (cN+) was present in 72.2% of cases. Two patients (11.1%) had de novo metastatic disease (stage IV). The advanced stage at diagnosis (stage III–IV) was observed in 44.4% of patients. Treatment During Pregnancy: Among the 12 patients diagnosed during pregnancy, 8 (66.7%) received neoadjuvant chemotherapy during pregnancy using anthracycline-based regimens (AC protocol: doxorubicin/cyclophosphamide), initiated after the first trimester. The median number of chemotherapy cycles administered antepartum was 4 (range: 2–6). Three patients underwent modified radical mastectomy during pregnancy (second trimester). One patient diagnosed at 8 weeks of gestation opted for pregnancy termination before initiating treatment. No patient received trastuzumab, endocrine therapy, or radiotherapy during pregnancy. Obstetric and Neonatal Outcomes: The median gestational age at delivery was 37 weeks (range: 34–39). Preterm delivery (<37 weeks) occurred in 33.3% of gestational cases, all of which were medically indicated to allow timely initiation or resumption of postpartum treatment. Cesarean section was performed in 58.3% of cases. The median birth weight was 2,780 g (range: 2,100–3,450 g). Small for gestational age (SGA < 10th percentile) was observed in 16.7%. The median Apgar score at 5 minutes was 9. No congenital malformations were observed in neonates exposed to chemotherapy in utero. Two neonates (16.7%) required NICU admission for transient respiratory distress related to prematurity. No neonatal deaths were recorded. Maternal Oncological Outcomes : After a median follow-up of 36 months (range: 12–108), the 3-year disease-free survival was 61.1% and the 3-year overall survival was 72.2%. Five patients (27.8%) developed distant recurrence (bone, liver, lung). Three disease-related deaths occurred during the follow-up period, all in patients with stage III–IV disease and triple-negative or HER2-positive subtypes. No recurrence was observed in the 3 patients with luminal A tumors.

Discussion: The incidence of PABC in our series (1 in 3,000 pregnancies) is consistent with published international data. The predominance of aggressive molecular subtypes (triple-negative 33.3%, HER2-positive 27.8%) aligns with the known biology of PABC, where hormone receptor-negative tumors are overrepresented compared with age-matched non-pregnant patients. The high rate of advanced stage at diagnosis (44.4% stage III–IV) reflects the diagnostic delay inherent to PABC, where pregnancy-related breast changes mask symptoms. Anthracycline-based chemotherapy administered during the second and third trimesters was well tolerated in our cohort, with no congenital malformations observed. These findings are consistent with large registries (International Network on Cancer, Infertility and Pregnancy) confirming that anthracyclines and taxanes are safe after the first trimester,

with no increase in major malformations beyond the baseline population risk of 2–3%. The SMFM Consult Series (2026) now recommends standard-dose chemotherapy without a priori dose reduction during pregnancy. The preterm delivery rate of 33.3% in our series, while elevated, was largely iatrogenic and guided by the need to initiate trastuzumab or taxane-based therapy postpartum. Current guidelines recommend targeting delivery at term (37 weeks) whenever possible, as iatrogenic prematurity is associated with neonatal morbidity and adverse long-term neurodevelopmental outcomes independently of chemotherapy exposure. Maternal oncological outcomes in our cohort (3-year DFS 61.1%, OS 72.2%) are comparable with published PABC series, though inferior to non-pregnant young women with breast cancer. This survival disadvantage is largely attributed to delayed diagnosis, advanced stage, and the higher proportion of aggressive subtypes rather than pregnancy itself. The absence of recurrence in luminal A tumors and the concentration of deaths in triple-negative/HER2-positive subtypes reinforce the prognostic importance of molecular classification in PABC.

Conclusion: PABC in our Tunisian series is characterized by a young median age, a high proportion of aggressive molecular subtypes, and frequent diagnosis at an advanced stage. Anthracycline-based chemotherapy during pregnancy was feasible and safe, with reassuring neonatal outcomes and no congenital malformations. Maternal survival remains impacted by diagnostic delay and aggressive tumor biology. A high index of clinical suspicion, early referral for breast imaging in any pregnant woman with a palpable mass, and multidisciplinary management involving oncologists, obstetricians, and neonatologists are essential to improve outcomes. The development of a national PABC registry in Tunisia would facilitate prospective data collection and standardization of care.

Endometrial Cancer in Obese Women: Clinicopathological Profile and Oncological Outcomes Compared with Non-Obese Patients

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Introduction: Endometrial cancer (EC) is the most common gynecological malignancy in high-income countries, and its incidence is rising in parallel with the global obesity epidemic. Obesity is the strongest modifiable risk factor for EC, with each 5 kg/m² increase in BMI conferring a 50–54% higher risk of developing the disease. The underlying mechanisms involve chronic hyperestrogenism due to peripheral aromatization of androgens in adipose tissue, insulin resistance, chronic inflammation, and adipokine dysregulation. While the association between obesity and EC incidence is well established, the impact of obesity on clinicopathological features, surgical morbidity, and long-term oncological outcomes remains debated. Some studies suggest that obese patients present with more favorable tumor characteristics (lower grade, endometrioid histology, earlier stage) — a phenomenon referred to as the “obesity paradox.” However, meta-analyses demonstrate that obesity is associated with a 2.5-fold increase in disease-specific mortality (BMI 30–35) and up to 6.25fold in morbidly obese women (BMI 40). In Tunisia, obesity prevalence among women exceeds 30%, yet data on the impact of obesity on EC outcomes in North African populations remain scarce. Understanding this relationship is essential for optimizing surgical planning, perioperative care, and adjuvant

treatment strategies in this high-risk population.

Objectives: The primary objective was to compare the clinicopathological profile and oncological outcomes of EC in obese (BMI ≥ 30 kg/m²) versus non-obese (BMI < 30 kg/m²) patients. Secondary objectives included analyzing the differences in surgical approach and perioperative morbidity, evaluating the distribution of molecular subtypes and FIGO staging between the two groups, and comparing disease-free survival (DFS) and overall survival (OS) at 3 and 5 years.

Methods: This was a retrospective comparative study conducted at the Department of Obstetrics and Gynecology, Hédi Chaker University Hospital, Sfax, Tunisia, over a 4-year period (January 2021– December 2025). We included all consecutive patients who underwent primary surgery for histologically confirmed EC. Patients were stratified into two groups: obese (BMI ≥ 30 kg/m², n = 58) and non-obese (BMI < 30 kg/m², n = 42). Exclusion criteria included patients with incomplete medical records and those who received primary radiotherapy without surgery. Data collected included demographic characteristics (age, BMI, menopausal status, comorbidities including diabetes and hypertension), tumor characteristics (histological type, FIGO 2023 stage, grade, myometrial invasion, LVSI, molecular classification when available), surgical data (approach, extent of lymph node staging, operating time, estimated blood loss, perioperative complications, length of hospital stay), adjuvant treatment, and follow-up data. DFS and OS were estimated using the Kaplan-Meier method and compared between groups using the Log-rank test. Multivariate Cox regression was performed to identify independent prognostic factors. Statistical significance was set at $p < 0.05$.

Results: Patient Demographics: A total of 100 patients were included: 58 in the obese group (BMI ≥ 30) and 42 in the non-obese group (BMI < 30). The median BMI was 35.2 kg/m² (range: 30.1–52.4) in the obese group and 25.8 kg/m² (range: 18.6–29.9) in the non-obese group. Obese patients were significantly younger at diagnosis (median age: 58 vs 63 years, $p = 0.02$). Diabetes mellitus was more prevalent in the obese group (41.4% vs 19.0%, $p = 0.02$), as was hypertension (62.1% vs 38.1%, $p = 0.02$). Both groups were predominantly postmenopausal (87.9% vs 90.5%, $p = 0.71$). Tumor Characteristics: Endometrioid histology was significantly more common in obese patients (84.5% vs 66.7%, $p = 0.04$). Low-grade tumors (grade 1–2) predominated in the obese group (72.4% vs 54.8%, $p = 0.07$). FIGO stage I disease was observed in 69.0% of obese patients versus 57.1% of nonobese patients ($p = 0.22$). Deep myometrial invasion (50%) was present in 34.5% vs 42.9% ($p = 0.39$). Substantial LVSI was less frequent in the obese group (17.2% vs 28.6%, $p = 0.18$). Non-endometrioid histology (serous, clear cell, carcinosarcoma) was more prevalent in nonobese patients (33.3% vs 15.5%, $p = 0.04$). Surgical Outcomes: Minimally invasive surgery (laparoscopy or robotic) was less frequently performed in obese patients (48.3% vs 71.4%, $p = 0.02$). The median operative time was significantly longer in the obese group (185 vs 145 minutes, $p = 0.008$). Sentinel lymph node biopsy was performed in 55.2% of obese patients versus 69.0% of non-obese patients ($p = 0.16$). Perioperative complications (Clavien-Dindo II) occurred in 22.4% of obese patients versus 11.9% of nonobese patients ($p = 0.17$), including wound infection (10.3% vs 2.4%), venous thromboembolism (5.2% vs 0%), and lymphocele (6.9% vs 4.8%). The median length of hospital stay was 5 days (obese) vs 4 days (non-obese) ($p = 0.04$). Adjuvant Treatment: Adjuvant treatment was administered in 51.7% of obese patients versus 59.5% of non-obese patients ($p = 0.44$). Vaginal brachytherapy alone was more frequent in the obese group (27.6% vs 16.7%), while exteal beam radiotherapy with or without chemotherapy was more frequent in the non-obese group (42.9% vs 24.1%), reflecting the higher proportion of high-risk histologies in non-obese patients. Oncological Outcomes

: After a median follow-up of 38 months (range: 12–84), the 3-year DFS was 78.4% in the obese group vs 71.2% in the non-obese group ($p = 0.32$, Log-rank). The 3-year OS was 86.2% vs 78.6% ($p = 0.24$). Recurrence occurred in 13.8% of obese and 21.4% of non-obese patients ($p = 0.31$). On multivariate Cox regression, independent predictors of decreased DFS were advanced FIGO stage (HR = 3.2, $p < 0.001$), non-endometrioid histology (HR = 2.8, $p = 0.004$), and substantial LVSI (HR = 2.1, $p = 0.03$). BMI was not an independent prognostic factor for DFS or OS after adjustment for stage, histology, and grade (HR = 1.04, $p = 0.87$).

Discussion: Our findings confirm that obese patients with EC present with more favorable tumor biology, including a higher prevalence of endometrioid histology, lower grade, and earlier stage at diagnosis. These Results are consistent with the large cohort study by Crean-Tate et al. (EJGO 2025, n = 1,778) which demonstrated that morbidly obese patients had significantly more favorable prognostic factors. This phenomenon may be explained by the estrogen-driven pathogenesis of type I EC in obese women, leading to earlier symptom onset (abnormal uterine bleeding) and consequently earlier diagnosis. Despite more favorable tumor characteristics, obese patients experienced higher surgical morbidity, including longer operative times, more wound complications, and a lower rate of minimally invasive surgery. These findings are consistent with the systematic review by Bouwman et al., which reported that increasing BMI is associated with increased perioperative complications after EC surgery, particularly in the context of laparotomy. The absence of a significant difference in DFS and OS between obese and non-obese patients after multivariate adjustment supports the concept that obesity per se does not independently worsen oncological outcomes when stage, histology, and grade are accounted for. The so-called “obesity paradox” — where obese patients appear to have similar or even better outcomes — is likely explained by the confounding effect of more favorable tumor biology in this population. However, a recent meta-analysis (IJGC 2024) demonstrated a 44% decrease in 5-year OS in obese EC patients, suggesting that longer follow-up may reveal a survival disadvantage, possibly driven by obesity-related non-cancer mortality (cardiovascular disease, diabetes complications). In the Tunisian context, where obesity prevalence among women exceeds 30% and metabolic syndrome is highly prevalent, these findings underscore the need for integrated care pathways combining oncological management with metabolic optimization, including dietary counseling, physical activity programs, and management of comorbidities.

Conclusion: Obese patients with EC in our Tunisian cohort presented with more favorable clinicopathological features, including predominant endometrioid histology, lower grade, and earlier stage. However, they experienced higher surgical morbidity and lower rates of minimally invasive surgery. After adjustment for tumor characteristics, obesity was not an independent prognostic factor for DFS or OS. Advanced FIGO stage, non-endometrioid histology, and substantial LVSI remained the strongest predictors of recurrence. An integrated multidisciplinary approach combining oncological care with metabolic management is essential for optimizing outcomes in this growing patient population.

Local Recurrence after Breast-Conserving Surgery: Incidence, Risk Factors, and Impact on Survival - A 5-Year Retrospective Cohort Study

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Hedi Chaker Sfax

Introduction: Breast-conserving surgery (BCS) followed by whole-breast radiotherapy is the standard of care for early-stage breast cancer, offering equivalent long-term survival to mastectomy. However, local recurrence (LR) remains a significant concern, with reported 5-year rates ranging from 3 to 10% depending on patient and tumor characteristics. The Early Breast Cancer Trialists' Collaborative Group (EBCTCG) meta-analysis demonstrated that LR is not merely a marker of aggressive biology but an independent predictor of distant metastasis and breast cancer mortality, with a ratio of approximately 4 local recurrences prevented translating into 1 breast cancer death avoided at 15 years. Well-established risk factors for LR include young age (<40 years), positive or close surgical margins, high histological grade, lymphovascular space invasion (LVSI), absence of adjuvant radiotherapy, and triple-negative or HER2-positive molecular subtypes. The NCCN guidelines (v4.2024) recommend the "no ink on tumor" principle as the standard for adequate margins in invasive breast cancer. In Tunisia, BCS rates have been increasing over the past decade. However, local data on LR incidence, risk factors, and their impact on survival remain limited. This study aims to address this gap by analyzing a 5-year cohort of patients treated with BCS at a Tunisian tertiary center.

Objectives: The primary objective was to determine the 5-year cumulative incidence of LR after BCS in a Tunisian cohort. Secondary objectives included identifying independent risk factors for LR through univariate and multivariate analysis, evaluating the impact of LR on disease-free survival (DFS), distant disease-free survival (DDFS), and overall survival (OS), and describing the management and outcomes of patients who experienced LR.

Methods: This was a retrospective cohort study conducted at Hédi Chaker University Hospital, Sfax, Tunisia. All consecutive patients who underwent BCS with curative intent for invasive breast cancer or DCIS between January 2020 and December 2025 were included. Patients with de novo metastatic disease, those who received neoadjuvant chemotherapy (analyzed separately), and those with less than 12 months of follow-up were excluded. A total of 120 patients met the inclusion criteria. Data collected included patient demographics (age, menopausal status), tumor characteristics (histological type, grade, size, molecular subtype, LVSI, margin status according to the "no ink on tumor" principle), treatment details (type of axillary surgery, adjuvant radiotherapy, systemic therapy), and follow-up data. LR was defined as histologically confirmed invasive or in situ carcinoma in the ipsilateral breast. DFS, DDFS, and OS were estimated using the Kaplan-Meier method and compared using the Log-rank test. Cox proportional hazards regression was used to identify independent prognostic factors. Statistical significance was set at $p < 0.05$.

Results: Patient and Tumor Characteristics : Among the 120 patients, the median age was 52 years (range: 28–78). Twenty-two patients (18.3%) were younger than 40 years. The predominant histological type was invasive ductal carcinoma (85.0%). SBR grade distribution was: grade I 25.0%, grade II 48.3%, and grade III 26.7%. Regarding molecular subtypes, luminal A accounted for 41.7%, luminal B for 25.0%, HER2-positive for 15.0%, and triple-negative for 18.3%. LVSI was present in 28.3%. Positive or close margins (<1 mm for DCIS, ink on tumor for invasive) were initially found in 14.2% of patients, of whom 76.5% underwent re-excision to achieve clear margins. All patients received adjuvant whole-breast radiotherapy with a tumor bed boost. Adjuvant systemic therapy was administered according to molecular subtype and risk stratification. Local Recurrence: After a median follow-up of 42 months (range: 12–60), 9 patients

(7.5%) developed LR. The 5-year cumulative incidence of LR was 8.3% (Kaplan-Meier estimate). The median time to LR was 26 months (range: 8–48). Six recurrences (66.7%) occurred within the first 3 years. Seven of 9 LRs (77.8%) were located in the vicinity of the original tumor bed (true recurrences), while 2 (22.2%) were located elsewhere in the breast (new primary tumors). Histologically, 7 LRs were invasive and 2 were pure DCIS. Risk Factors for Local Recurrence: On univariate analysis, factors significantly associated with LR were: age < 40 years (LR rate 18.2% vs 5.1%, $p = 0.02$), triple-negative subtype (LR rate 18.2% vs 5.1%, $p = 0.03$), positive/close initial margins before re-excision ($p = 0.04$), LVSI (14.7% vs 4.7%, $p = 0.04$), and SBR grade III (12.5% vs 4.5%, $p = 0.06$). Tumor size > 2 cm ($p = 0.12$), HER2-positive subtype ($p = 0.18$), and multifocality ($p = 0.22$) were not statistically significant. On multivariate Cox regression, three factors emerged as independent predictors of LR: age < 40 years (HR = 3.8; 95% CI: 1.4–10.2; $p = 0.008$), triple-negative subtype (HR = 3.4; 95% CI: 1.1–10.6; $p = 0.03$), and LVSI (HR = 2.9; 95% CI: 1.0–8.4; $p = 0.04$). Management of Local Recurrence : Among the 9 patients with LR, 7 (77.8%) underwent salvage mastectomy and 2 (22.2%) underwent a second BCS with re-irradiation (partial breast brachytherapy). All patients received additional systemic therapy adapted to their molecular subtype. After salvage treatment, 6 patients (66.7%) were alive without evidence of disease at last follow-up, while 3 patients (33.3%) subsequently developed distant metastases. Impact on Survival : Patients who developed LR had significantly worse outcomes. The 5-year DFS was 44.4% in the LR group vs 88.3% in the no-LR group ($p < 0.001$). The 5-year DDFS was 55.6% vs 91.0% ($p < 0.001$). The 5-year OS was 66.7% vs 94.6% ($p = 0.001$). On multivariate analysis, the occurrence of LR was an independent adverse prognostic factor for OS (HR = 5.2; 95% CI: 1.8–15.1; $p = 0.002$), confirming that LR is not merely a marker but an independent predictor of distant relapse and death.

Discussion: The 5-year LR rate of 8.3% in our cohort is consistent with international series reporting rates of 3–10%. The slightly higher rate compared with contemporary Western series may reflect the relatively high proportion of young patients (18.3% < 40 years) and triple-negative tumors (18.3%) in our population. Young age was the strongest independent risk factor for LR (HR = 3.8), consistent with the large series by Botteri et al. and the POSH observational study, which identified age < 40 as a near-doubling of LR risk. Triple-negative subtype emerged as the second strongest predictor (HR = 3.4). This finding aligns with the registry-based study by Cancers (2025, $n = 24,450$) which demonstrated that HER2-positive and triple-negative tumors are associated with increased recurrence risk and decreased OS compared with luminal subtypes. The aggressive biology of these tumors, characterized by high proliferation, early hematogenous dissemination, and limited targeted therapy options, contributes to both local and distant failure. The independent adverse impact of LR on OS (HR = 5.2) supports the EBCTCG meta-analysis concept that LR is not simply a surrogate for aggressive tumor biology but carries intrinsic prognostic significance. Early LR (<3 years), which accounted for 66.7% of cases in our series, likely reflects residual disease and is associated with worse outcomes compared with late LR, which more frequently represents a new primary tumor with a more favorable prognosis (84% 5-year survival after late recurrence in the series by Voogd et al.).

Our findings underscore the critical importance of meticulous surgical technique to achieve clear margins, particularly in young patients and those with aggressive subtypes. The "no ink on tumor" principle, while adequate for most patients, may warrant wider margins in selected high-risk subgroups. Additionally, boost radiotherapy to the tumor bed, administered to all patients in our cohort, remains essential for reducing LR

risk.

Conclusion: In this 5-year Tunisian cohort, LR after BCS occurred in 8.3% of patients. Age < 40 years, triple-negative subtype, and LVSI were independent predictors of LR. Local recurrence had a profound adverse impact on DFS, DDFS, and OS, confirming its role as an independent prognostic factor. Meticulous surgical technique, adequate margin assessment, individualized adjuvant therapy, and close surveillance — particularly in young patients and those with aggressive subtypes — are essential to minimize LR and improve long-term outcomes.

Phyllodes Tumors of the Breast: Surgical Management and Predictive Factors for Local Recurrence — A 10-Year Retrospective Series of 35 Cases

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Hedi Chaker Sfax

Introduction: Phyllodes tumors (PTs) of the breast are rare fibroepithelial neoplasms, accounting for 0.3 to 1% of all breast tumors and 2 to 3% of fibroepithelial lesions. The WHO classification categorizes PTs into three subtypes — benign, borderline, and malignant — based on histological features including stromal cellularity, mitotic activity, stromal overgrowth, tumor borders, and cellular atypia. PTs predominantly affect women aged 35 to 55 years, with a peak incidence a decade later than fibroadenomas. The hallmark of PTs is their propensity for local recurrence (LR), which represents the most important prognostic concern. Reported LR rates range from 8 to 15% for benign, 14 to 20% for borderline, and 25 to 50% for malignant subtypes. The principal determinants of LR are the histological subtype and the status of surgical margins. The Canadian National Consensus (Bogach et al., Ann Surg Oncol 2023) and the NCCN guidelines recommend wide local excision with margins of at least 1 cm for borderline and malignant PTs, while the “no tumor on ink” principle may be acceptable for benign PTs. Preoperative diagnosis remains challenging due to the clinical and radiological overlap between PTs and fibroadenomas. Up to 30% of recurrences may present with a more aggressive histological grade than the primary tumor, a phenomenon known as histological “upgrading.” The role of adjuvant radiotherapy remains debated but is increasingly considered for borderline and malignant PTs with close or positive margins.

Objectives: The objectives of this study were to describe the clinicopathological profile and surgical management of PTs in a Tunisian tertiary center over a 10-year period, to determine the local recurrence rate and identify its independent predictive factors, and to evaluate the long-term oncological outcomes including distant metastasis-free survival and overall survival.

Methods: This was a retrospective study conducted at Hédi Chaker University Hospital, Sfax, Tunisia, from January 2014 to December 2023. All consecutive patients who underwent surgical excision for a histologically confirmed PT were included. Data collected included demographics, preoperative diagnosis (clinical, ultrasound, core biopsy), tumor characteristics classified according to WHO 2019 criteria (subtype, size, mitotic count, stromal features, tumor borders), surgical management (excision type, margin status and width), adjuvant therapy, and follow-up data. Local recurrence was defined as histologically confirmed recurrence in the ipsilateral breast. Recurrence-free survival (RFS), distant metastasis-free survival (DMFS), and overall survival (OS) were estimated by the Kaplan-Meier method. Cox regression was used for multivariate analysis. Statistical significance was set at $p < 0.05$.

Results: Patient and Tumor Characteristics: Thirty-five patients

with PTs were identified. The median age was 42 years (range: 18–68). The median tumor size was 6 cm (range: 2–22 cm). According to WHO classification, 14 tumors (40.0%) were benign, 11 (31.4%) were borderline, and 10 (28.6%) were malignant. Preoperatively, the correct diagnosis of PT was established by core biopsy in only 54.3% of cases; 37.1% were initially misdiagnosed as fibroadenoma. The tumor border was pushing in 62.9% and infiltrative in 37.1%. Stromal overgrowth was present in 31.4%, and the median mitotic count was 6 per 10 HPF (range: 1–28). Eight patients (22.9%) had a history of prior excision of a fibroadenoma at the same site. **Surgical Management:** Wide local excision (WLE) was performed in 24 patients (68.6%) and mastectomy in 11 (31.4%). Mastectomy was indicated for tumors > 10 cm, unfavorable tumor-to-breast ratio, or malignant subtype. On final pathology, surgical margins were negative (> 1 cm) in 60.0%, negative but close (< 1 cm) in 22.9%, and positive (tumor on ink) in 17.1%. Among the 6 patients with positive margins, 4 underwent re-excision and 2 underwent secondary mastectomy. No patient underwent axillary lymph node dissection. Adjuvant radiotherapy was administered to 5 patients (14.3%), all with borderline or malignant subtypes and close or initially positive margins. **Local Recurrence:** After a median follow-up of 52 months (range: 12–120), 6 patients (17.1%) developed LR. The LR rate by subtype was 7.1% (1/14) for benign, 18.2% (2/11) for borderline, and 30.0% (3/10) for malignant PTs. The median time to LR was 18 months (range: 6–42). Among the 6 recurrences, 2 (33.3%) exhibited histological upgrading: one borderline PT recurred as malignant, and one benign PT recurred as borderline. All recurrences were treated surgically (4 mastectomies, 2 re-excisions). **Risk Factors for Local Recurrence:** On univariate analysis, factors significantly associated with LR were: positive or close margins < 1 cm (LR 38.5% vs 4.5%, $p = 0.006$), malignant subtype ($p = 0.04$), stromal overgrowth ($p = 0.03$), infiltrative tumor border ($p = 0.04$), mitotic count $\geq 10/10$ HPF ($p = 0.02$), and tumor size > 10 cm ($p = 0.05$). Prior fibroadenoma excision history was not significantly associated ($p = 0.32$). On multivariate Cox regression, two factors were independent predictors of LR: positive/close margins < 1 cm (HR = 6.4; 95% CI: 1.5–27.2; $p = 0.01$) and stromal overgrowth (HR = 4.1; 95% CI: 1.1–15.8; $p = 0.04$). The 5-year RFS was 82.9% overall, 92.9% for benign, 81.8% for borderline, and 60.0% for malignant PTs ($p = 0.03$, Log-rank). **Distant Metastasis and Survival:** Distant metastases developed in 2 patients (5.7%), both with malignant PTs (lung metastases). One patient died of disease at 36 months. The 5-year DMFS was 94.3% and the 5-year OS was 97.1%. No deaths occurred among patients with benign or borderline PTs.

Discussion: The overall LR rate of 17.1% in our series is consistent with published data reporting rates of 10 to 20% across all subtypes. The subtype-specific rates (benign 7.1%, borderline 18.2%, malignant 30.0%) align with the large Asian series by Tan et al. (10.9%, 14.4%, 29.6%) and the comprehensive review by Chen et al. (Sci Rep 2024). The predominance of LR in the first 2 years (median 18 months) underscores the need for close surveillance during this period, ideally with clinical examination and ultrasound every 6 months. Margin status was the strongest independent predictor of LR (HR = 6.4), confirming the consistent finding across the literature that positive or close margins are the most reliable and modifiable risk factor. The comprehensive review by Clinics (2025) emphasizes that while a 1 cm margin is recommended for borderline and malignant PTs, achieving tumor-free margins is more critical than any specific margin width. In our series, 17.1% of patients had positive margins on initial excision, highlighting the technical difficulty of achieving adequate margins, particularly in large tumors where the tumor-breast ratio is unfavorable. Stromal overgrowth emerged as the second independent predictor (HR = 4.1). This histological feature, defined as the absence of

epithelial elements in at least one low-power field, is associated with more aggressive biological behavior and has been valid as a prognostic marker in the revised WHO criteria. The observation of histological upgrading in 33.3% of recurrences is consistent with published rates of up to 30%, reinforcing the concept that PTs represent a biological spectrum with potential for progression. The preoperative diagnostic accuracy of 54.3% by core biopsy reflects the well-known challenge of distinguishing PTs from fibroadenomas on limited tissue sampling. Excisional biopsy or vacuum-assisted biopsy may improve diagnostic accuracy and should be considered when imaging suggests a rapidly growing fibroepithelial lesion, particularly in women over 35 years.

Conclusion: In this 10-year Tunisian series, PTs were characterized by a median age of 42 years, a high proportion of borderline/malignant subtypes (60%), and a 17.1% LR rate. Positive or close surgical margins and stromal overgrowth were independent predictors of LR. Adequate surgical excision with clear margins of at least 1 cm for borderline and malignant PTs is the cornerstone of treatment. Close surveillance during the first 2 years is essential, given the high risk of early recurrence and the possibility of histological upgrading. A multidisciplinary approach involving breast surgeons, pathologists, and radiation oncologists is recommended for optimal management of these rare tumors.

BENIGN DUCTAL PATHOLOGIES OF THE BREAST 4- Year Retrospective Study - Ben Arous Maternity Hospital, Tunis, Tunisia Department of Obstetrics & Gynaecology

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Introduction: Benign ductal pathologies of the breast are a frequent reason for consultation in obstetrics and gynaecology, accounting for 15 to 30% of breast-related visits. They encompass a heterogeneous spectrum of lesions — from simple galactophorous duct dilation to chronic recurrent inflammatory processes — posing a genuine diagnostic and therapeutic challenge in daily practice. These conditions affect women of all ages: fibroadenoma in young women, intraductal papilloma in peri- or pre-menopausal women, and ductal ectasia in postmenopausal women. Smoking is a recognised risk factor for ductal epithelial metaplasia.[1,3]

Objective: To describe the epidemiological, clinical, paraclinical and therapeutic profile of benign ductal pathologies of the breast managed in our department.

Methods : This was a retrospective, descriptive, single-centre study, conducted in the Department of Obstetrics & Gynaecology at Ben Arous Maternity Hospital (Tunis, Tunisia), over a period of 4 years (2021–2025). We included all patients consulting or hospitalised for a documented benign ductal breast pathology with an exploitable medical record (50% of data recorded); patients with an incomplete record, associated malignant pathology, or age < 18 years were excluded. Data were collected using a standardised form comprising 17 variables: sociodemographic data (age, hormonal status, parity), clinical, paraclinical (ultrasound, mammography, ACR classification, biopsy) and therapeutic data; all biopsies were performed based on an ACR 4 classification[2]. Statistical analysis was performed using SPSS v26.0; quantitative variables were expressed as mean ± standard deviation and median [min–max], qualitative variables as frequencies and percentages, with Chi-square or Fisher's exact test as appropriate (significance threshold: $p <$

0.05). Complete anonymisation was ensured.

Results: Our series comprised 58 patients, with a mean age of 46.7 ± 9.0 years (range: 26–61 years) and a mean parity of 2.2 ± 1.1 ; most patients were pre-menopausal (63.3%), followed by postmenopausal (30.0%) and peri-menopausal (6.7%). The two most frequent diagnoses were ductal ectasia ($n = 22$, 37.9%) and intraductal papilloma ($n = 20$, 34.5%), together accounting for 72.4% of the series, followed by fibroadenoma ($n = 16$, 27.6%)[3]. Nipple discharge was the most frequent presenting complaint, found in 34 patients (58.6%), of whom 20 (34.5%) presented haematic or sero-haematic discharge corresponding exclusively to intraductal papillomas; a palpable mass was found in 27.6% of cases. Breast ultrasound was the first-line investigation performed in all patients; all biopsies (100%) were performed on the basis of an ACR 4 classification[2], and epithelial atypia was identified on histopathology in 4 patients (6.9%). Regarding treatment, watchful waiting with surveillance was the most frequent management strategy ($n = 22$, 37.9%), mainly for asymptomatic ductal ectasia; pyramidectomy was performed in 20 patients (34.5%), including all intraductal papilloma cases; and surgical excision was carried out for all 16 fibroadenoma cases (27.6%).

Table 1. Distribution of final diagnoses ($n = 58$)

Diagnosis	
Ductal ectasia	22 37.9%
Intraductal papilloma	34.5% 20
Fibroadenoma	16 27.6%
Total	58 100%

Table 2. Distribution of treatments ($n = 58$)

Treatment	
Watchful waiting	22 37.9%
Pyramidectomy	20 34.5%
Surgical excision	16 27.6%
Total	58 100%

Discussion: The mean age in our series (46.7 ± 9.0 years) is consistent with international literature; Hussain et al. (2021) reported a mean age of 44.2 ± 10.1 years in a series of 215 patients[1], and the predominance of pre-menopausal women (63.3%) in our cohort is in line with Tunisian and North African series, where proliferative ductal pathologies predominantly affect younger women during their reproductive years. Ductal ectasia and intraductal papilloma together dominated our series, accounting for 72.4% of cases; intraductal papilloma remains the leading cause of unilateral haematic nipple discharge — representing 100% of haematic discharge cases in our series — and galactography confirmed the diagnosis in all such cases by revealing a characteristic intraductal filling defect, while pyramidectomy, the reference treatment, was performed in all cases with histopathological confirmation of benignity in the absence of atypia[3]. Fibroadenoma represented 27.6% of the series, predominantly affecting young women; all lesions were classified as ACR 4 on imaging, warranting systematic percutaneous biopsy[2], and surgical excision was performed in all cases with confirmed histological benignity, also allowing exclusion of low-grade phyllodes tumour in large lesions.

Conclusion: Benign ductal pathologies of the breast represent a heterogeneous nosological group whose diagnosis relies on the clinical – imaging – histopathological triad[3]. Ductal ectasia and intraductal papilloma dominate the series (72.4% of cases). All biopsies performed from an ACR 4 classification[2] ensure diagnostic rigour. Nipple discharge, as a cardinal sign, must systematically prompt thorough paraclinical investigation.

Cervical Cancer Screening Awareness Lags Behind Breast Cancer: A Cross-Sectional Study of Women's Knowledge and Practices

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Introduction : Cervical cancer is a preventable disease through effective screening, yet its uptake remains suboptimal in many settings. In contrast, breast cancer screening is more widely known and practiced. This study aimed to assess women's knowledge and practices regarding cervical cancer screening compared with breast cancer screening.

Methods: A cross-sectional study was conducted among 385 women attending gynecological outpatient clinics and eligible for cervical cancer screening. Data were collected using a structured questionnaire assessing sociodemographic characteristics, knowledge and practice of Pap smear screening, and awareness of breast cancer screening Methods.

Results : The mean age of participants was 38 years. Regarding educational level, 42% had secondary education, 36% had university education, and 22% had primary education or less. Overall, 62% of participants had never heard of the Pap smear, 22% correctly identified its role in cervical cancer screening, and only 12% knew the recommended screening interval. Only 8% had ever undergone a Pap smear. Screening was mainly physician-initiated (70%), with minimal self-motivation (5%). In contrast, 72% were aware of mammography, 65% reported breast self-examination practice, and 48% had undergone breast cancer screening.

Conclusion: Cervical cancer screening awareness and uptake remain markedly lower than breast cancer screening among women in our setting, despite a relatively favorable educational level. These findings highlight the need for structured educational interventions and improved physician counseling to increase Pap smear uptake and reduce cervical cancer burden

Breast lesions classified as ACR 4A: imaging-histopathology correlation in a retrospective single-center study

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Introduction: The ACR 4A category in breast imaging corresponds to lesions with low suspicion of malignancy. Although most lesions are benign, histopathological confirmation remains essential for accurate diagnosis and appropriate management. This study aimed to evaluate the correlation between ACR 4A imaging findings and histopathological Results.

Methods: We conducted a retrospective study including all patients with breast lesions classified as ACR 4A on imaging in our outpatient department during 2025. Demographic data, medical history, clinical presentation, and histopathological **Results** were collected from medical records. Quantitative variables were expressed as means and ranges, and qualitative variables as frequencies and percentages.

Results: Eleven patients were included, with a mean age of 42.4 years (range: 24–65 years). Hypertension was present in 9.1% of patients, 27.3% were using estrogen–progestin contraception, and 18.2% had a family history of breast cancer. Nulliparity was reported in 18.2% of patients. Lesions were detected during evaluation of a breast nodule in 45.5% of

cases, screening in 36.4%, inflammatory symptoms in 9.1%, and nipple discharge in 9.1%. Core needle biopsy was performed in 90.9% of patients, while one patient (9.1%) was managed with radiological surveillance, showing lesion downgrade to ACR 3. Histopathological analysis revealed benign lesions in all cases, including fibrocystic changes (27.3%), fibroadenoma (36.4%), low-grade phyllodes tumor (9.1%), granulomatous mastitis (9.1%), and intraductal papilloma (9.1%). No malignant lesions were identified.

Conclusion: Breast lesions classified as ACR 4A are predominantly benign, with no malignancy detected in this series. Core needle biopsy provides reliable diagnostic confirmation, supporting its essential role in management. Radiological–histological correlation confirms the low malignancy risk in this category and supports a conservative, individualized approach to avoid unnecessary surgery.

HPV-related synchronous lower genital tract neoplasia: diagnostic challenges and clinical implications : two case series carcinoma of the vulvovaginal region.

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Introduction: Human papillomavirus (HPV) is the main etiological agent of lower genital tract neoplasia. While cervical involvement is well established, synchronous involvement of the vulva, vagina, and cervix remains rare, particularly in postmenopausal women. We report two cases illustrating diagnostic and therapeutic challenges of multifocal HPV-related disease.

Observation: Two postmenopausal women (aged 63 and 66 years) presented with abnormal uterine bleeding and vulvar symptoms. In the first case, clinical examination revealed cervical and vulvar lesions. Histopathology demonstrated a benign endometrial polyp, high-grade squamous intraepithelial lesion (HSIL) of the cervix, and micro-invasive squamous cell carcinoma of the vulva associated with HPV infection. In the second case, examination showed a cervical polyp and a vulvovaginal ulcerative lesion with inguinal lymphadenopathy. Histopathology revealed a benign endometrial polyp, cervical intraepithelial neoplasia grade 1 (CIN1), and poorly differentiated invasive squamous cell.

Discussion: These cases illustrate the multifocal oncogenic potential of persistent high-risk HPV infection (notably HPV-16 and HPV-18). Synchronous lesions may **Result** from simultaneous multi-site infection or viral spread within the lower genital tract. Diagnosis is challenging due to overlapping clinical and histopathological features and difficulties in identifying the primary tumor site. A multidisciplinary approach combining clinical examination, imaging, and histopathology is essential for accurate staging and management.

Conclusion: Synchronous HPV-related neoplasia of the lower genital tract is rare but clinically challenging. These cases highlight the importance of comprehensive examination and early detection strategies. Strengthening HPV screening and vaccination programs is crucial, particularly in settings with limited preventive coverage

Renal Metastasis of a Tibial Osteosarcoma

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Introduction : Osteosarcoma is the most common primary malignant bone tumor in adolescents and young adults. It is characterized by early hematogenous dissemination, most frequently to the lungs and bones. Extra-pulmonary visceral metastases are rare and associated with poor prognosis.

Methods : We report a rare case of renal metastatic relapse of conventional osteosarcoma managed at the Medical Oncology Department of Salah Azaiz Institute.

Case Report : A 39-year-old man was diagnosed at age 12 with non-metastatic conventional osteosarcoma of the left tibia. Histology showed a pleomorphic osteosarcoma with minor chondroblastic differentiation. He received neoadjuvant cisplatin–doxorubicin chemotherapy followed by limb-sparing surgery, with poor histological response. Twenty-three years later, he developed pulmonary metastatic relapse treated by lobectomy and lymph node dissection. Pathology confirmed predominantly chondroblastic differentiation. Three years later, he presented with bilateral lower limb edema. CT scan revealed a right renal mass with exophytic growth, invading the renal vein and extending into the inferior vena cava. CT-guided biopsy confirmed metastatic osteosarcoma. After multidisciplinary

Discussion, surgery was deemed not feasible due to vascular extension. Pre-operative chemotherapy with etoposide–ifosfamide–cisplatin was initiated. Treatment and follow-up are ongoing.

Conclusion: Renal metastasis of osteosarcoma is extremely rare and represents a diagnostic and therapeutic challenge. Management requires a multidisciplinary approach in the absence of standardized treatment strategies.

5-Fluorouracil Toxicity: Portable Infuser vs Hospital Infusion in Colorectal Cancer

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Introduction: Colorectal cancers represent a major public health issue. Their prognosis has significantly improved thanks to 5-FU–based chemotherapy, administered either via a 48-hour portable infuser or through hospital-based infusion. However, this treatment is frequently associated with various toxicities that may affect patients' quality of life. In this study, our aim is to identify patient characteristics and to compare the toxicities observed in individuals with colorectal cancer treated with 5-FU administered either via a 48-hour portable infuser or through hospital-based infusion.

Methods: This is a retrospective, descriptive, and analytical study including 100 patients with colorectal cancer, treated and followed since 2002 in the Medical Oncology Department at Farhat Hached Hospital in Sousse.

Results: Our study population consisted of 47 women and 53 men, with a median age of 60 years. Most patients were married (69 cases) and from an urban Background (58 cases). Tumors were located in the colon in 71 patients, with a predominance on the left side (59%). Fifty-six patients had stage III disease and 34 had stage IV disease, including 31 de novo metastatic cases. The most frequent metastatic sites were the liver (61%) and the peritoneum (38%). Chemotherapy was mainly administered in the adjuvant setting (48 cases), and the most frequently used protocol was FOLFOX (74 cases), combined with targeted therapy in 27 patients. The 5-FU dose was reduced in 37 patients, primarily affecting both the bolus and the 48-hour infusion (73%). The main reason for dose reduction was the

occurrence of toxicities. Observed toxicities were mostly non-hematologic (54 cases), dominated by vomiting (57 patients), peripheral neuropathy (53 patients), and fatigue (47 patients). The most frequent hematologic toxicity was neutropenia (22 cases), including 7 cases of grade IV. When comparing the two subgroups with or without a Port-a-Cath (PAC), we found that men, educated, married patients, employed individuals, and those from urban areas were more likely to have a PAC. The placement of a PAC was significantly influenced by tumor stage ($p = 0.001$), timing of chemotherapy ($p = 0.001$), protocol used ($p = 0.044$), and the addition of targeted therapy ($p = 0.013$). Diarrhea was more frequent in patients without a PAC ($p = 0.023$).

Conclusion: The mode of 5-FU administration and the presence of a Port-a-Cath may influence treatment tolerance and the occurrence of certain adverse effects. These findings underscore the importance of individualizing therapy to optimize efficacy while minimizing toxicities.

Management of a rare Mandibular Chondrosarcoma: A Dosimetric Case report

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Introduction: Chondrosarcomas are rare malignant bone tumors, accounting for a small proportion of head and neck sarcomas. Mandibular involvement is particularly uncommon. Surgical resection remains the mainstay of treatment; however, management becomes challenging in cases of unresectable or residual disease. The role of radiotherapy is not well established but may be considered in selected cases.

Case presentation: A 28-year-old patient with a family history of malignancies presented with a progressively enlarging left pretragal swelling evolving over six months. Clinical examination revealed a firm, non-inflammatory mass. Imaging demonstrated a large osteolytic lesion of the left mandibular ramus (70 × 65 mm), extending into the temporomandibular joint and adjacent deep facial spaces, with apparent cervical lymphadenopathy. Histopathological analysis confirmed a grade 2 chondrosarcoma. The patient underwent debulking surgery without neck dissection. Final pathology confirmed a grade 2 mandibular chondrosarcoma. Cervical ultrasound demonstrated benign-appearing bilateral jugulocervical lymph nodes. Postoperative imaging revealed a large residual infiltrative tumor involving the infratemporal fossa. Subsequent imaging showed significant tumor progression, with a 45% increase in volume which was unresectable. Given the lack of standard systemic therapy in chondrosarcoma, metronomic cyclophosphamide was proposed as an adjunctive approach. Planning CT was fused with MRI for target delineation. The gross tumor volume (GTV) corresponded to the residual tumor, with a 10 mm margin to generate the clinical target volume (CTV) and a 5 mm expansion for the planning target volume (PTV). Radiotherapy was delivered using VMAT to a total dose of 70 Gy in 35 fractions. The plan demonstrated good conformity (CI = 0.80), with all organ-at-risk constraints respected, including spinal cord Dmax of 30.87 Gy and mean parotid < 19.02 Gy. Dosimetric evaluation demonstrated adequate target coverage (PTV D95% = 97.27%) with acceptable dose distribution and preservation of organs at risk.

Conclusion: This case highlights the potential role of advanced radiotherapy techniques such as VMAT in achieving optimal dose distribution for complex head and neck sarcomas. In the setting of incomplete surgical resection and unresectable

disease progression, high-dose conformal radiotherapy may represent a valuable therapeutic option.

Re-irradiation strategy in recurrent Glioblastoma: A case report

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Introduction: Glioblastoma remains the most common and aggressive primary malignant brain tumour in adults, with a poor prognosis. Its recurrence poses a major therapeutic challenge, particularly in unresectable cases, with no clear consensus on optimal management. This report describes the clinical course and dosimetric considerations of re-irradiation for recurrent glioblastoma.

Case presentation: A 58-year-old female patient with no significant past medical history was diagnosed in January 2025 with a right temporo-insular glioblastoma, IDH-wild type. She underwent subtotal surgical resection. This was followed by chemoradiotherapy: 60 Gy in 30 fractions with concomitant and adjuvant temozolomide according to the STUPP protocol. Treatment ended in May 2025. Afterwards, she received adjuvant chemotherapy. Follow-up imaging then revealed complete radiological remission. In November 2025, follow-up MRI revealed a large recurrent lesion in the right hemisphere with fronto-temporo-insular extension. The lesion showed heterogeneous contrast enhancement. There was extensive FLAIR hyperintensity, measuring 9.7 cm anteroposteriorly and 6.2 cm in width. The enhancing component measured 44 × 43 mm. The lesion caused a mass effect on the right lateral ventricle frontal horn. Perfusion imaging showed a hypervascular profile with an rCBV ratio of 39%, consistent with high-grade recurrence. Clinically, the Kaofsky Performance Status (KPS) at recurrence was 60%, the patient had persistent left hemiparesis, required assistance for ambulation, and developed Broca's aphasia. The lesion was deemed unresectable, and the patient was referred for re-irradiation. The gross tumour volume (GTV) included the enhancing lesion on T1-weighted gadolinium-enhanced MRI and FLAIR sequences. A 3 mm margin was applied to generate the clinical target volume (CTV), followed by a 3 mm expansion to create the planning target volume (PTV). Reirradiation using the VMAT technique was delivered to a total dose of 36 Gy in 18 fractions. The interval between the end of the first radiotherapy course and the re-irradiation was 9 months (May 2025 – February 2026). Dosimetric analysis showed adequate target coverage (D95% = 99.13%) with acceptable dose homogeneity (Dmax = 103.54%). Organs at risk were preserved within tolerance limits: brainstem Dmax 6.5 Gy, optic chiasm Dmax 9.26 Gy, optic nerves < 15 Gy, and ocular Dmax of 5.33 Gy (right) and 8.26 Gy (left). At the 3-month follow-up, imaging showed a partial response with a reduction in tumour volume.

Conclusion: This case highlights the feasibility of VMAT-based re-irradiation in selected patients with recurrent glioblastoma. Advanced conformal radiotherapy techniques may provide satisfactory target coverage while preserving critical organs at risk. Further studies are required to better define optimal dose schedules, fractionation regimens, and patient selection criteria for reirradiation in recurrent glioblastoma.

Does Bladder Dosimetry Outperform Bladder Filling in Predicting Acute Urinary Toxicity in Rectal Cancer?

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Background: Bladder filling protocols are widely used in pelvic radiotherapy to reduce organ exposure. However, their clinical relevance in preventing urinary toxicity remains unclear. Purpose: To investigate whether bladder volume or bladder dosimetric parameters are associated with acute urinary toxicity in rectal cancer patients treated with VMAT.

Methods: We conducted a retrospective dosimetric analysis of 20 rectal cancer patients treated between 2024 and 2026 at the Salah Azaiez Institute (Tunis, Tunisia). All patients followed a standardized bladder filling protocol consisting of bladder emptying followed by oral intake of 500 ml water 1 hour prior to simulation and treatment. Bladder volume and dosimetric parameters (V40Gy, D2) were extracted from dose-volume histograms (DVHs). Bladder volume assessment was based on the contoured bladder at the planning CT scan in treatment position. Acute urinary toxicity was assessed using CTCAE v5.0 during treatment and early follow-up. Correlations between dosimetric parameters and toxicity were analyzed.

Results: Median age was 59 years (range: 33–86). Most patients had locally advanced disease, with nodal involvement in 70%, and all were treated within a total neoadjuvant therapy (TNT) approach based on PRODIGE 23. Prescribed doses ranged from 45 to 61.2 Gy. Mean bladder volume was 217.5 mL (range: 66.6–478.4), with a mean V40Gy of 36.5% and mean D2 of 47.8 Gy. The V40Gy < 40% constraint was achieved in 65% of patients. Acute radiation cystitis occurred in 45% of cases (all grade 1), with no incontinence. Bladder volume was not correlated with dosimetric parameters (V40Gy: $p = 0.605$; D2: $p = 0.767$) nor with urinary toxicity ($p = 0.219$). In contrast, bladder V40Gy was significantly associated with acute urinary toxicity ($p = 0.032$). A trend toward association was observed for D2 ($p = 0.060$).

Conclusion: Bladder dose exposure, rather than bladder filling, appears to drive acute urinary toxicity in rectal cancer VMAT. These findings challenge the clinical value of bladder filling protocols alone and support prioritizing dosimetric optimization.

Adenocarcinoma Arising in a Colonic Interposition 40 Years After Esophageal Replacement: A Case Report and Review of the Literature

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Introduction: Colonic interposition has long been a gold-standard surgical solution for esophageal replacement following severe caustic injuries in pediatric populations. While this procedure offers excellent long-term functional outcomes, it creates a unique anatomical and histological environment susceptible to rare late-term complications. Primary adenocarcinoma arising within the colonic transplant is an exceptionally rare occurrence, with only a handful of cases documented in the medical literature. This malignancy presents significant diagnostic and therapeutic challenges due to the altered anatomy and the long latency period—often spanning decades—between the initial surgery and malignant transformation.

Case presentation: A 48-year-old male patient, with a history of intrathoracic colonic transplantation at age five following caustic ingestion, presented in March 2025 with progressive dysphagia. Esophagogastroduodenoscopy revealed an ulcerated, exophytic mass in the mid-thoracic segment. Histopathological and immunohistochemical analyses confirmed a moderately differentiated adenocarcinoma originating from the colonic

mucosa of the transplant. Initial CT staging (TAP) demonstrated a localized tumor in the middle third without evidence of locoregional invasion or distant metastasis. The patient underwent neoadjuvant chemotherapy (CAPOX) from October 2025 to February 2026. Follow-up imaging revealed stable disease; however, surgical assessment deemed the tumor unresectable. A multidisciplinary decision was made to pursue intensified systemic therapy, with a second phase of six chemotherapy cycles initiated in May 2026.

Discussion: Adenocarcinoma of a colonic graft is significantly rarer than squamous cell carcinoma of the native esophagus. This case highlights an exceptional latency period of 43 years, illustrating that the transplanted colonic mucosa retains its inherent oncogenic potential within the thoracic cavity. The anatomical distortions and delayed presentation often complicate radical surgical resection, necessitating a reliance on systemic neoadjuvant strategies.

Conclusion: This case underscores the necessity of lifelong endoscopic surveillance in patients who have undergone colonic interposition, even decades after the initial procedure. Heightened clinical awareness is critical for early detection and improving the prognosis of this rare late-term malignancy.

Patient Satisfaction with Inpatient Oncology Care in Tunisia Using the Arabic Version of the EORTC IN-PATSAT32 Questionnaire

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Background: Hospitalization is a major component of the cancer journey and significantly shapes patients' perceptions of care. Beyond therapeutic outcomes, patient experience has become a key dimension of quality in oncology. This study aimed to evaluate inpatient satisfaction using the Arabic version of the EORTC IN-PATSAT32 questionnaire in a Tunisian oncology Center.

Methods: We conducted a descriptive cross-sectional study including hospitalized patients treated in the medical oncology and radiotherapy departments of Salah Azaïez Institute between April and May 2026. Patient satisfaction was assessed using an Arabic-translated version of the EORTC IN-PATSAT32 questionnaire, translated by an officially two translator. The questionnaire evaluates satisfaction with physicians, nurses, and hospital organization using a 5-point Likert scale (1 = poor; 5 = excellent). Sociodemographic and clinical variables collected included age, sex, primary tumor site, treatment intent, and duration of hospitalization. Mean satisfaction scores were calculated for physicians, nurses, organization, and overall satisfaction. Comparative analyses were performed according to baseline characteristics.

Results: Forty-five hospitalized oncology patients were included. The mean age was 58.6 ± 18.1 years (range: 14–84 years), and 64.4% of patients were female. Breast cancer was the most frequent malignancy (31.1%), followed by head and neck (17.8%), gynecological (17.8%), digestive (11.1%), urological malignancies (11.1%) with other malignancies accounting for 11.1%. The mean overall satisfaction score was 3.85/5. Satisfaction with physicians (4.07/5), followed by nursing care (3.97/5), whereas organizational aspects received the lowest score (3.41/5). The highest-rated items included physicians' knowledge and experience regarding the illness (4.62/5), attention paid to physical problems (4.44/5), nurses' human qualities (4.40/5), and medical treatment and

follow-up provided by doctors (4.36/5). The lowest-rated items concede organizational aspects, including ease of access to care and transportation/parking (2.09/5), hospital orientation (2.91/5), waiting times for test **Results** (3.29/5), and admission-related information (3.33/5), suggesting limitations in patient navigation and care coordination in a high-volume oncology setting. Female patients reported higher overall satisfaction scores compared with male patients (3.97 vs 3.62, respectively). No statistically significant association was observed between overall satisfaction and age, duration of hospitalization, primary tumor site, or treatment intent.

Conclusion: Patients reported high satisfaction with clinical care, particularly physicians and nursing staff, while organizational and infrastructural aspects remained suboptimal. These findings support the integration of patient-reported experience measures in oncology quality improvement.

DPD screening and AUC-guided 5-FU monitoring: a two-step strategy reducing toxicity in colorectal cancer

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Background: 5-Fluorouracil (5-FU) toxicity in colorectal cancer (CRC) stems from dihydropyrimidine dehydrogenase (DPD) deficiency and inter-patient pharmacokinetic variability, making BSA-based dosing alone unreliable. This study assessed whether combining universal DPD screening with iterative AUC-guided therapeutic drug monitoring (TDM) reduces 5-FU-related toxicity compared to standard BSA-based dosing.

Methods: CRC patients initiating continuous intravenous 5-FU at the Medical Oncology Department of Monastir, Tunisia (2023–2024) were prospectively enrolled. A TDM group (AUC target 20–29 mg·h/L) was compared to a BSA-dosed control group. Both groups were comparable at baseline. Toxicity was assessed at four consecutive consultations (C1–C4) using a mirror follow-up design.

Results: A total of 105 patients were enrolled, divided into a TDM group (n=36) and a control group (n=69). All 36 TDM patients achieved the therapeutic AUC within one to three measurements confirming feasibility in routine practice. Before reaching the target AUC, the mean toxicity score was 2.40 ± 1.45 , decreasing significantly to 2.07 ± 1.04 after pharmacokinetic optimization ($p=0.042$). The overall mean toxicity score was significantly lower in the TDM group (2.13 ± 1.09) versus controls (2.86 ± 1.45 , $p=0.028$). Gastrointestinal toxicities were significantly less frequent at C2 ($p=0.010$), C3 ($p=0.024$) and C4 ($p=0.001$). Severe toxicities (grade 3) were rare in the TDM group, suggesting structured monitoring may prevent escalation and limit unplanned dose reductions. No differences were observed for hematological, neurological, cardiac or cutaneous toxicities.

Conclusions: Combining DPD screening with iterative AUC-guided TDM constitutes a feasible two-step personalization strategy that significantly reduces 5-FU toxicity in colorectal cancer, addressing both enzymatic and pharmacokinetic variability while enabling proactive adverse event management providing a strong rationale for adopting this dual strategy as a standard framework for safer 5-FU delivery

AUC-guided 5-FU therapeutic drug monitoring drives long-term disease control in colorectal cancer: Realworld comparative evidence

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Background: While 5-Fluorouracil (5-FU) therapeutic drug monitoring (TDM) is recognized for improving treatment safety in colorectal cancer (CRC), its impact on long-term clinical outcomes remains unclear. This study assessed whether AUC-guided TDM improves disease control compared to standard body surface Areal (BSA) -based dosing in a real-world setting.

Methods: A longitudinal comparative study enrolled CRC patients at the Medical Oncology Department of Monastir, Tunisia (2023–2024). A TDM group (AUC target 20–29 mg·h/L) was compared to a BSA-dosed control group. Both groups were comparable at baseline. All patients underwent DPD screening prior to treatment. The primary endpoint was disease control rate at six months, stratified by treatment intent (curative vs. palliative), with an intermediate assessment at three months.

Results: A total of 105 patients were included, divided into a TDM group (n=36) and a control group (n=69). At baseline, AUC measurement under standard BSA-based dosing revealed marked pharmacokinetic underexposure in the TDM group: 66.7% of patients had a sub-therapeutic AUC (<20 mg·h/L), 27.8% were within the therapeutic range (20–29 mg·h/L), and only 5.5% were supratherapeutic (30 mg·h/L). Following iterative AUC-guided dose adjustments, all 36 patients achieved the therapeutic target within one to three measurements. At three months, no significant difference was observed between the two groups for biological or radiological outcomes. At six months, however, a significant clinical divergence emerged. In the curative setting, patients in the TDM group demonstrated significantly higher rates of biological and radiological responses (p=0.017 and p=0.005, respectively). In the palliative setting, tumor progression remained less frequent among TDM-monitored patients, with borderline significance (p=0.053). This delayed divergence suggests that correcting pharmacokinetic underexposure exerts a cumulative effect on disease trajectory.

Conclusions: AUC-guided TDM corrects pharmacokinetic underexposure and significantly improves long-term disease control in CRC, supporting its integration into standard oncological practice beyond its established safety role.

FLOT Protocol in Locally Advanced Gastric and Gastroesophageal Junction Cancer: A Real-World Experience from Salah Azaiez Institute

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Background: The perioperative FLOT regimen has become the standard of care for resectable locally advanced gastric cancer (LAGC) following the FLOT4 trial. However, real-world data from North African populations remain scarce. The primary objective was to evaluate the pathological tumor regression rate (Becker grading). Secondary objectives included R0 resection rate, progression-free survival (PFS), overall survival (OS), and prognostic factor identification.

Methods: We conducted a retrospective study of patients with locally advanced gastric or gastroesophageal junction (GEJ) adenocarcinoma treated with the perioperative FLOT protocol at the medical oncology department of Salah Azaiez Institute between (2021-2025). Survival was estimated by Kaplan-Meier; prognostic factors were assessed by univariate Cox regression.

Results: 56 patients were included (67.9% male, tumors were gastric (82.1%) or GEJ (17.9%); signet ring cell histology predominated (64.3%). Stage III disease: 73.2% (cT3:46.4%, cT4: 28.6%; cN+: 78.6%). Surgery was performed in 89.3%. Pathological regression TRG 1–2 in 34%, TRG 3–4 in 66%. At a median follow-up of 38 months, median PFS and OS were both 24 months (OS 95% CI: 11.9–36.1); 12-month OS was 69.9%, with a 3-year OS of 37.2%. Pathological T stage (ypT) was associated with significantly inferior PFS (p=0.01); 36-month PFS rates were 90%, 50%, and 23% for ypT1–T2, ypT3, and ypT4, respectively. Pathological nodal stage (ypN) was the strongest predictor of both PFS and OS (p<0.002); 12-month PFS was 85% for ypN0–N1 versus 20% for ypN2–N3. R0 resection was associated with superior PFS (p<0.016); 36-month PFS was 57% for R0 versus 18% at 12 months for R1. Perineural invasion (EPN) was an independent adverse prognostic factor for PFS (p<0.004); 24-month PFS was 75% versus 25% in EPN and EPN+ patients, respectively. Lymphovascular invasion (EV) was similarly associated with inferior PFS (p=0.048); 24-month PFS was 65% versus 40% in EV and EV+ patients respectively.

Conclusions: Perioperative FLOT achieves encouraging real-world outcomes in locally advanced gastric cancer, validating its use in a North African high-risk population and highlighting the potential benefit of treatment intensification in patients with high nodal burden.

Determinants of overall survival in young women with breast cancer: a retrospective cohort study

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Background: Breast cancer in young women is associated with aggressive tumor biology and poorer outcomes. Identifying determinants of survival is critical to refine risk stratification and improve management, particularly in resource-limited settings.

Methods: We performed a retrospective cohort study including 205 patients aged 40 years treated between 2013 and 2017 at a tertiary center. Clinicopathological, molecular and treatment variables were analyzed. Overall survival (OS) at 5 years was estimated. Prognostic factors were assessed using univariate analysis.

Results: Five-year OS was 70%. Diagnostic delay >3 months was associated with worse OS (p=0.030; OR=1.87). Stage at diagnosis was the strongest determinant (p<0.001), with OS decreasing from 100% (stage 0) to 37.2% (stage IV). Tumor burden parameters including size (p<0.001) and nodal involvement (clinical p<0.001; pathological p=0.002) significantly impacted survival. Metastatic disease showed the highest risk (p<0.001; OR=18.40). High histological grade was associated with poorer OS (p=0.003). Biological factors were major determinants: hormone receptor negativity (p<0.001; OR=4.33) and molecular subtype (p<0.001), with luminal A showing the best OS (82.9%) and triplenegative the worst (29.1%). Therapeutic factors influenced outcomes: hormone therapy significantly improved OS (p=0.002), and trastuzumab was associated with better survival in HER2-positive patients (p=0.038).

Conclusions: Survival in young breast cancer patients is primarily driven by stage at diagnosis and tumor biology. Diagnostic delay remains a modifiable adverse factor. Expanding early detection

strategies and ensuring access to effective systemic therapies are essential to improve outcomes in this high-risk population

Hereditary Breast Cancer in a Tunisian Family: Role of Sanger sequencing in the Detection of the Recurrent BRCA1 c.211dup Variant and Implications

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Background : Hereditary breast cancer accounts for approximately 5–10% of all breast cancers and is mainly associated with pathogenic variants in the BRCA1 and BRCA2 genes. Affected individuals often present at a younger age and may exhibit population-specific recurrent mutations. The phenotypic spectrum includes early-onset, bilateral, triple-negative, male breast, ovarian, prostate, and pancreatic cancers. This marked clinical and genetic heterogeneity highlights the importance of comprehensive clinical and molecular investigations. Genetic testing is therefore essential for accurate diagnosis, risk assessment, genetic counseling, and personalized management.

Methods: We report the clinical observation of a female patient referred for suspected hereditary breast cancer in the context of multiple familial cancer cases. Molecular analysis was performed using targeted Sanger sequencing for a recurrent Tunisian BRCA1 mutation located in exon 4.

Results: The patient was a 36-year-old woman originating from Nabeul, Tunisia, born to a consanguineous couple, who was referred for bilateral breast cancer diagnosed at the age of 31 years. Family history revealed a father who died at 58 years of age and had both prostate and pancreatic cancers, and one uncle diagnosed with prostate cancer at 60 years. A great grandmother, two aunts, and one cousin were diagnosed with breast cancer at the ages of 70, 42, 31, and 35 years, respectively. Additional family history included three cousins and one paternal niece diagnosed with early-onset breast cancer before the age of 40 years, multiple cases of thyroid cancer on the paternal side, and one case of ovarian cancer on the maternal side. Targeted Sanger sequencing identified the BRCA1 c.211dup pathogenic variant in exon 4 in the proband. Subsequent familial screening confirmed the molecular diagnosis in three affected relatives, including two individuals with breast cancer and one with papillary thyroid carcinoma. Presymptomatic testing identified the variant in five of the eight relatives tested, enabling personalized surveillance and genetic counseling.

Conclusion: These findings underscore the importance of thorough clinical and molecular investigations in hereditary breast cancer, not only to establish an accurate molecular diagnosis in affected individuals, but also to identify at-risk relatives through presymptomatic testing. Such an approach enables personalized surveillance, early detection, genetic counseling, and appropriate therapeutic management, thereby improving preventive care and clinical outcomes within affected families.

Artificial Intelligence Models for Predicting Response to Immune Checkpoint Inhibitors in Solid Tumors: A Systematic Review

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Background: Immunotherapy, particularly immune checkpoint inhibitors (ICIs), has revolutionized cancer treatment. However, only a subset of patients derives a durable benefit, highlighting the need for reliable predictive biomarkers. Recent advances in Artificial Intelligence (AI) offer promising tools for integrating complex clinical, radiological, and molecular data to predict treatment response.

Objectives: To systematically review and synthesize current evidence on AI-based models for predicting response to ICIs in patients with solid tumors.

Methods: A systematic literature search was conducted in PubMed, Scopus, and Web of Science for studies published between 2018 and 2025. Eligible studies included those developing or validating AI models to predict response to ICIs. Extracted data included cancer type, data modalities (clinical, radiomics, genomics, pathology), AI techniques, and model performance metrics. This review followed PRISMA principles.

Results: A total of 120 records were identified, of which 100 remained after duplicate removal. Following screening, 40 full-text articles were assessed, and 8 studies were included. These studies evaluated AI models using histopathology, radiomics, genomics, clinical, and multimodal data. Deep learning applied to histopathology demonstrated the ability to extract predictive features related to tumor biology, while CT-based radiomics also showed promising predictive performance. Across studies, predictive performance ranged from AUC 0.70 to 0.90, with higher accuracy observed in multimodal models. Multimodal approaches consistently outperformed single-modality models, suggesting improved representation of tumor complexity compared to conventional biomarkers such as PD-L1. However, limitations included small sample sizes, retrospective design, lack of external validation, and limited interpretability.

Conclusions: AI-based models show strong potential for predicting response to ICIs and advancing personalized oncology. Further validation in large prospective cohorts and improved model transparency are required before clinical implementation.

Regulatory Barriers to Epstein-Barr Virus Vaccine Approval: A Missed Opportunity in Cancer Prevention?

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Introduction: Epstein-Barr Virus is the first identified human tumor virus and is associated with several malignancies, including Burkitt lymphoma, Hodgkin lymphoma, post-transplant and HIV-associated non-Hodgkin lymphoma, T-cell lymphoma, and NK/T-cell lymphoma. Despite ongoing vaccine development and a major unmet medical need, no EBV vaccine has yet received marketing authorization from major regulatory agencies.

Methods: This study is a narrative review of regulatory guidance documents and scientific literature from EMA, FDA, ANMPS and WHO sources. A comparative analysis was performed

to evaluate clinical endpoint requirements and regulatory pathways relevant to EBV vaccine development.

Results: The analysis identified several key regulatory challenges limiting EBV vaccine approval. First, the lack of valid surrogate endpoints complicates the demonstration of clinical efficacy, as prevention of infectious mononucleosis does not adequately reflect long-term oncogenic outcomes. Second, cancer-based endpoints require extended follow-up periods, creating significant ethical, logistical, and economic constraints. Third, no established correlates of protection are currently available, limiting the applicability of accelerated and conditional approval pathways. In addition, current vaccine regulatory frameworks are primarily designed for acute infectious diseases and are not fully adapted to oncogenic viruses with long latency periods. Finally, differences in regulatory expectations across agencies highlight the potential value of reliance-based approaches to improve regulatory efficiency.

Conclusion: Adaptive regulatory strategies, including surrogate endpoint qualification, early scientific advice, and stronger regulatory convergence, are needed to accelerate EBV vaccine development. Enhanced collaboration among regulators, developers, and public health stakeholders could facilitate approval pathways and strengthen global cancer prevention efforts.

Challenges in Cancer Pain Management: Insights from a Tunisian Prospective Study

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Introduction : In the comprehensive management of cancer patients, pain represents a major daily concern. Far beyond a simple symptom, it is considered a disease in itself, with significant negative impacts on patients quality of life. Despite the availability of a wide range of analgesic therapies, cancer pain remains frequently under-treated or inadequately managed.

Objective : The aim of this study was to describe pain management in cancer patients in a Tunisian hospital.

Methods : This was a three-month prospective descriptive study conducted at the maternity centre of Monastir by a pharmacy inte. Pain intensity was assessed using a visual analogue scale (VAS), and data were collected using a structured questionnaire. Among the 128 patients assessed, 50 reported cancer-related pain.

Results : A total of 76% of patients reported moderate to severe pain, among whom 26% did not receive any analgesic treatment. A neuropathic component was identified in 30% of cases, although its management remained insufficient. Opioid analgesics were prescribed in 43% of patients for pain relief, while paracetamol was used in 26% of cases. Self-medication with paracetamol was reported by 10% of patients. Non-pharmacological approaches were used by 16% of patients, among whom 62% reported the use of medicinal plants.

Conclusion : Pain management remains complex and suboptimal. Improving care requires adherence to international guidelines, a multidisciplinary approach, and enhanced patient education regarding self-medication and the inappropriate use of medicinal plants. Keywords: pain, Cancer, analgesic treatment

Real-World impact of Oncology Biosimilars In Tunisia: Pharmacoeconomics and Regulation

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Introduction : Monoclonal antibodies (mAbs), including rituximab, trastuzumab, and bevacizumab, represent key biologic therapies in oncology in Tunisia. Following patent expiration, biosimilars entered the market, offering opportunities to reduce healthcare expenditures while improving treatment accessibility through public reimbursement and access programs. This study aimed to assess the real-world pharmacoeconomic impact of oncology biosimilars in Tunisia and to describe the current regulatory landscape.

Methods : A retrospective real-world analysis was conducted using Tunisian Central Pharmacy (PCT) procurement and utilization data extracted and processed from the SIAMED database of the National Agency for Medicines and Health Products (ANMPS) between 2017 and 2025. Data included invoiced purchases as well as free-of-charge units dispensed through access programs. Biosimilar uptake, expenditure trends, and cumulative savings were evaluated for trastuzumab, rituximab, and bevacizumab. Real-world savings were estimated by comparing theoretical expenditure at originator reference prices with actual biosimilar expenditures. Regulatory registry data from ANMPS were reviewed to assess ongoing biosimilar applications

Results : Tunisia achieved near-complete biosimilar adoption for the three evaluated molecules, with substitution rates reaching 100% for trastuzumab (since 2019) and bevacizumab (since 2023), and 96.6% for rituximab due to the lack of an approved subcutaneous biosimilar formulation. Between 2018 and 2025, cumulative savings reached 710.9 million Tunisian dinars (TND), including 479.0 million TND for trastuzumab (2018–2025), 136.3 million TND for bevacizumab (2022–2025), and 95.5 million TND for rituximab (2022–2025). Access programs accounted for a meaningful proportion of administered treatments, particularly for rituximab (14.1%) and bevacizumab (6.6%), confirming equitable access to biological therapies. Regulatory analysis identified an active biosimilar pipeline comprising 15 dossiers across 5 molecules currently under review at the ANMPS, including nivolumab and pembrolizumab candi, potentially broadening affordable access to immunotherapies.

Conclusions : Tunisia has achieved an exemplary transition toward biosimilar monoclonal antibodies in oncology, generating substantial real-world economic savings and high substitution rates. These findings highlight the value of proactive biosimilar adoption policies for healthcare sustainability and equitable access to cancer treatment. The active regulatory pipeline, including anti-PD-1 biosimilar candi (nivolumab, pembrolizumab), signals a new era for affordable immunotherapy access in Tunisia.

Breast Cancer Before 40: Aggressive Subtypes and Diagnostic Delays in a North African Cohort

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Background: Breast cancer in young women represents a distinct clinical entity with aggressive tumor biology, unfavorable molecular profiles, and poorer outcomes compared to older counterparts. Epidemiological data from North Africa remain

scarce, despite a relatively younger affected population in this region. This study aimed to comprehensively characterize the epidemiological, clinicopathological, and therapeutic profile of breast cancer in women aged 40 years or younger.

Methods: We conducted a retrospective cohort study including 205 patients aged 40 years, diagnosed with breast cancer and managed at the Department of Obstetrics and Gynecology, Farhat Hached University Hospital Sousse, between 2013 and 2017 tertiary referral center between 2013 and 2017. Epidemiological, clinical, histopathological, molecular, and treatment data were systematically collected and analyzed.

Results: The mean age at diagnosis was 32.8 ± 5.4 years. Self-examination was the primary mode of detection in 82.4% of cases, yet a diagnostic delay exceeding three months was recorded in 52.2% of patients, reflecting significant barriers to early detection. Only 19% of patients presented with early-stage disease (stages 0–I), while 49.7% were diagnosed at advanced stages (III–IV). Mean tumor size was 3.8 ± 1.8 cm, with clinical lymph node involvement in 56.6% of cases. Invasive ductal carcinoma predominated (91.2%), with high-grade tumors (SBR grade II–III) accounting for 74.3% of cases. Aggressive molecular subtypes were strikingly prevalent: triple-negative breast cancer (TNBC) represented 24.7% and HER2-enriched 17% of cases, while Luminal A subtype accounted for only 18.1%. Multimodal treatment was administered to the majority of patients. Surgical intervention was performed in 71.1% of cases, with mastectomy as the predominant procedure (60.5%). Adjuvant chemotherapy, radiotherapy, and endocrine therapy were delivered in 63%, 64.4%, and 47.8% of patients, respectively.

Conclusions: Breast cancer in young North African women is characterized by a dual burden: delayed presentation and a high prevalence of aggressive molecular subtypes. These findings underscore an urgent need for targeted awareness campaigns, systematic screening strategies adapted to younger age groups, and optimized multidisciplinary oncological care in this understudied population.

Beyond Technical Care: The Emerging Role of Radiation Therapists in Therapeutic Patient Education During Pelvic Radiotherapy

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Introduction: Pelvic radiotherapy is a cornerstone of cancer treatment but is frequently associated with gastrointestinal and genitourinary toxicities that negatively impact patients' quality of life and treatment experience. Therapeutic patient education (TPE) plays a crucial role in preventing, anticipating, and managing these side effects. Due to their continuous daily interaction with patients, radiation therapists (RTTs) are uniquely positioned to contribute to supportive care and patient-centered management.

Methods: A descriptive cross-sectional study was conducted among 20 RTTs working in radiotherapy. Data were collected using a structured questionnaire exploring their involvement in patient education, prevention strategies, technical practices, and monitoring of digestive and urinary toxicities related to pelvic irradiation.

Results: Among the 20 RTTs surveyed, 70% systematically informed patients about urinary and digestive side effects before treatment initiation. Preventive counseling mainly included hydration advice (90%), rectal preparation guidance (85%), and dietary recommendations (75%), whereas urinary

habit counseling was rarely addressed (10%). Technically, daily CBCT was performed by 85% of RTTs, while bladder filling assessment was systematic in all cases. Regarding supportive care, 80% transmitted clinically relevant information to radiation oncologists and 70% provided reassurance and active listening to patients. However, documentation practices remained limited, with only 25% ensuring traceability in patient records. Importantly, 75% of RTTs reported no formal training in therapeutic patient education, while lack of time and absence of standardized protocols were identified as the main barriers to optimal practice.

Conclusion: RTTs play a central yet underrecognized role in therapeutic patient education and toxicity management during pelvic radiotherapy. Despite strong involvement in daily patient support and treatment monitoring, important gaps remain regarding formal training, documentation, and standardization of practices. Strengthening RTT education programs and integrating structured TPE protocols into routine clinical practice may improve both quality of care and patient experience in pelvic radiotherapy.

Moving Through Cancer: Physical Activity and Sedentary Behavior Among Oncology Patients

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Background: Physical activity is increasingly recognized as a key component of supportive oncology care, contributing to improved quality of life, reduced cancer-related fatigue, better functional capacity, and enhanced treatment tolerance. Despite these benefits, sedentary behavior remains highly prevalent among cancer patients during active treatment and may negatively affect both physical and psychological outcomes.

Objective: To evaluate physical activity levels and sedentary behavior among cancer patients using the International Physical Activity Questionnaire (IPAQ).

Methods: A descriptive cross-sectional study was conducted including 50 cancer patients followed in the radiation oncology department. The cohort consisted of 25 men and 25 women with various malignancies, including breast, prostate, lung, colorectal, gynecological, head and neck, bladder, and hematological cancers. Physical activity was assessed using the short version of the IPAQ questionnaire. Patients were categorized into low, moderate, or high physical activity levels according to standardized IPAQ scoring criteria based on MET-minutes/week.

Results: The median patient age was 52 years (range: 38–66 years). Breast cancer was the most represented malignancy (24%), followed by gynecological cancers (18%), prostate cancer (14%), colorectal cancer (12%), lung cancer (10%), and other tumor types (22%). The mean walking frequency was 4.2 days/week, with an average duration of 28 minutes/day. Moderate intensity physical activity was reported in 52% of patients, while no vigorous physical activity was identified. According to IPAQ classification, 48% of patients had low physical activity levels and 52% had moderate activity levels. The mean sedentary time reached 522 minutes/day, highlighting substantial inactivity during treatment. Older patients (>60 years) demonstrated significantly higher sedentary behavior and lower IPAQ scores compared with younger patients. Low physical activity levels were particularly frequent among patients with lung and head and neck cancers.

Conclusion: Physical inactivity and prolonged sedentary behavior are highly prevalent among cancer patients undergoing treatment, particularly in older individuals and patients

with thoracic or head and neck malignancies. These findings emphasize the need to integrate adapted physical activity programs and multidisciplinary supportive care interventions into routine oncology practice in order to improve functional outcomes, treatment tolerance, and overall quality of life.

Balancing Target Coverage and Cardiac Protection: 3D-CRT Versus VMAT in Breast Irradiation

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Background: Breast radiotherapy remains a cornerstone of breast cancer treatment but inevitably exposes surrounding organs at risk, particularly the heart and lungs, to ionizing radiation. Achieving optimal target coverage while minimizing cardiopulmonary toxicity represents a major challenge in mode radiation oncology. Advanced techniques such as volumetric modulated arc therapy (VMAT) may improve dose conformity; however, concerns persist regarding low-dose exposure to healthy tissues.

Objective: To perform an intra-individual dosimetric comparison between three-dimensional conformal radiotherapy (3D-CRT) and VMAT in patients undergoing unilateral breast irradiation with locoregional nodal treatment.

Methods: This retrospective comparative dosimetric study included 20 patients treated for unilateral breast cancer with locoregional lymph node irradiation at the Salah Azaiez Institute, Tunis. For each patient, both 3D-CRT and VMAT treatment plans were generated using the same simulation CT dataset. Dosimetric parameters for target volumes and organs at risk were analyzed and compared using paired statistical tests.

Results: Both techniques achieved comparable breast clinical target volume (CTV) coverage ($p > 0.05$). 3D-CRT provided significantly better boost CTV coverage ($p < 0.001$), whereas VMAT demonstrated superior coverage of the internal mammary chain ($p = 0.001$) and supraclavicular nodal region ($p < 0.001$). Cardiac dosimetry revealed a mixed profile: VMAT was associated with higher mean heart dose and V5, but significantly reduced high-dose exposure parameters including V25 and V40. Regarding pulmonary toxicity, VMAT significantly decreased ipsilateral lung V20 and V30 while increasing low-dose irradiation (V5). Exposure of contralateral organs, particularly the contralateral lung and breast, was significantly greater with VMAT.

Conclusion: Neither 3D-CRT nor VMAT demonstrated overall superiority across all dosimetric endpoints. VMAT improved nodal target coverage and reduced high-dose exposure to critical organs, whereas 3D-CRT better limited low-dose spread to distant healthy tissues and provided more homogeneous boost coverage. These findings support a personalized approach to breast radiotherapy planning based on individual anatomical characteristics and cardiovascular risk profile.

MUTYH-Associated Polyposis : Impact of Cascade Screening in a Consanguineous Tunisian Family

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Introduction: MUTYH-Associated Polyposis (MAP) is a rare autosomal recessive hereditary cancer syndrome characterized by the development of colorectal adenomas and a significantly increased lifetime risk of colorectal cancer (CRC). It is caused by biallelic germline pathogenic variants in the MUTYH gene, which plays a critical role in the base excision repair pathway.

Objective: This study aims to highlight the clinical utility of genetic testing in identifying hereditary cancer predispositions and to emphasize the role of presymptomatic testing for at-risk family members.

Methods: We report the case of a female patient referred to the Oncogenetics Unit at Mongi Slim Hospital (La Marsa, Tunisia) for suspected hereditary CRC predisposition due to an attenuated polyposis phenotype. The familial variant was confirmed and screened in relatives using targeted Sanger sequencing.

Results: The proband, originating from North-West Tunisia and born to consanguineous parents, was diagnosed with colonic polyposis at age 44. Her family history was significant for multiple cases of familial polyposis and CRC. Her brother was monitored for colonic polyps with dysplasia and carried an homozygous frameshift variant c.1185_1186dup (p.Glu396Glyfs*43) in the MUTYH gene. This variant is classified as likely Pathogenic according to ACMG/AMP criteria, confirming the diagnosis of MAP. Genetic counseling led to the initiation of cascade screening for 26 relatives. Among them, five individuals were identified as homozygous carriers and five individuals were heterozygous carriers. This molecular confirmation allowed the implementation of personalized surveillance protocols, including regular colonoscopies, Esophagogastroduodenoscopy, urological examination, thyroid echography and clinical breast examination for homozygous carriers.

Conclusion: This case illustrates the importance of molecular diagnosis in hereditary cancer syndromes. Beyond establishing the patient's diagnosis, it enables cascade screening, which is essential for identifying asymptomatic high-risk relatives and implementing surveillance strategies.

A Distinct miR-138/424/455 Signature in Nasopharyngeal Carcinoma: Systemic and Tissue-Specific Dysregulation as Non-Invasive Staging Biomarkers

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5. The Regional Blood Transfusion Center of Sfax, Sfax, Tunisia Abstract

Background: As key orchestrators of the epigenetic landscape, microRNAs (miRNAs) significantly influence malignant progression. Their dysregulation underscores their utility as non-invasive biomarkers and positions them as promising targets for next-generation therapeutic interventions.

Methods: This study aimed to assess miRNA expression of miR-138-5p, miR-155-5p, miR424-5p and miR-455-5p in circulating

immune cells and nasopharyngeal biopsies from patients with nasopharyngeal carcinoma (NPC), using Real-Time Quantitative RT-PCR to evaluate their potential involvement in the pathogenesis of NPC.

Results: Comparative analysis revealed a significant lower expression of the tumor suppressor miR-138-5p in both NPC tissues and PBMCs compared to healthy controls (HCs), while miR-424-5p was lower expressed only in the tumor biopsies ($p < 0.0001$, $p = 0.005$ and $p = 0.017$, respectively). Conversely, the oncomiR miR-455-5p was significantly overexpressed in NPC tissues compared to HCs ($p = 0.013$), a finding corroborated by paired analysis against histologically confirmed non-malignant counterparts ($p = 0.018$). Furthermore, miR-138-5p and miR-424-5p levels were significantly correlated with clinical manifestations. Notably, miR-138-5p expression was significantly elevated in early-stage tumors (TNM I/II) compared to advanced stages (TNM III/IV, $p = 0.024$), suggesting its progressive loss during malignancy.

Conclusion: In Conclusion, our study identifies a distinct miRNA signature in NPC, characterized by systemic miR-138-5p depletion and localized miR-455-5p up-regulation. The correlation between miR-138/424-5p levels and clinical progression, specifically the progressive loss of miR-138-5p, highlights their potential interest as non-invasive biomarkers for staging and prognostic stratification in NPC patients.

Impact of Immune-Checkpoints Genetic Variants on Nasopharyngeal Carcinoma Susceptibility: A Tunisian Case-Control Study

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Background: Immune checkpoints pathways regulating T cell activity are key targets in cancer therapy. Genetic variations in checkpoints molecules (CTLA-4, PD-1, PD-L1) can alter signaling pathways, affecting cancer risk and treatment response in various types of malignancies.

Methods: This study aimed to investigate associations between common polymorphisms in immune-regulating genes (CTLA-4, PDCD1 and CD274) and susceptibility to nasopharyngeal carcinoma (NPC) in the Tunisian population. We analyzed six polymorphisms: rs231775 and rs3087243 (CTLA-4), rs2227981, rs2227982, and rs36084323 (PDCD1), and rs2890658 (CD274) in a case-control study which enrolled 61 Tunisian NPC patients and 150 matched healthy controls (HCs) using the PCR-RFLP method.

Results: For the rs231775 SNP, our **Results** showed a significant association between the AA genotype and increased NPC susceptibility in the recessive model (GG+AG vs AA) ($p = 0.006$, OR=2.5, 95% CI: [1.35–4.6]). Further, the haplotype analysis showed that the rs231775>A-rs3087243>A-rs36084323>G-rs2227982>C-rs2227981>C risk haplotype was significantly more expressed in NPC patients ($p = 0.044$, OR=1.64, 95% CI: [1.02–2.63]). The phenotype/genotype association revealed that the rs231775>AA genotype was significantly associated with clinical manifestations of NPC. We also confirmed that the rs2890658>CC genotype was significantly associated with increased risk of NPC under the recessive model (AA+CA vs CC), $p = 0.0001$, OR=3.2, 95% CI: [1.715.96]. In addition,

the rs2890658>C variant had a 2.4-fold higher risk of NPC in comparison with the A allele ($p = 0.0009$, OR=2.4, 95% CI: [1.424.08]).

Conclusion: Our **Results** suggest that the CTLA-4_rs231775>AA and CD274_rs2890658>CC genotypes could be considered as predisposition factors for NPC. While contributing to deciphering the NPC genetic puzzle, these **Results** could pave the way for future research on NPC pathogenesis and the evaluation of CTLA-4, PDCD1, and CD274 as potential personalized therapeutic targets.

HER2 as a Key Determinant of Aggressiveness in Breast Carcinoma: Clinico-Pathological Correlations

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Introduction: In the era of precision oncology, tumor phenotype characterization must include a profound understanding of systemic evasion mechanisms. While HER2 status is an established therapeutic target, its role as a driver of morphological aggressiveness—specifically through lymphovascular invasion and tumor grade—remains a critical diagnostic challenge. This study aims to decipher the interdependence between HER2 amplification, hormonal receptor profiles, and the genesis of vascular emboli.

Methodology: A retrospective analysis was conducted on a series of 350 breast carcinomas. Biological and morphological profiles were established via immunohistochemistry (ER, PR, HER2, and Ki67) and histopathological examination (SBR Grade, LVI). Data processing was performed using IBM SPSS Statistics, utilizing Pearson's Chi-square test and the Likelihood Ratio to valid correlations ($p < 0.05$).

Results: The cohort exhibits strong hormone dependency (ER+: 73.6%; PR+: 69%) contrasting with aggressive cellular kinetics (Ki67+: 76%). The analysis highlights a statistically significant correlation between HER2 status and the expression of progesterone receptors ($p = 0.004$) and estrogen receptors ($p = 0.005$). From a histoprognostic perspective, HER2 status was identified as a significant determinant of SBR Grade ($p = 0.05$), confirming its impact on tumor differentiation. However, although vascular emboli were identified in 41.7% of patients, no statistically significant association was demonstrated between HER2 status and lymphovascular invasion ($p = 0.45$) or Ki67 proliferation index ($p = 0.169$), suggesting that these aggressiveness markers may be driven by independent biological pathways in this series.

Conclusion: This study of 350 cases confirms that HER2 status is a central determinant of tumor biological architecture, acting in synergy with the hormonal profile and histological grade. While the prevalence of vascular emboli is high (41.7%), its independence from HER2 status in our cohort necessitates a multi-parametric evaluation. These findings advocate for the systematic integration of both molecular signatures and morphological invasiveness to optimize adjuvant therapeutic strategies. **Keywords:** Breast cancer, HER2, SBR Grade, Vascular emboli.

Clinical performance of EGFR gene mutation detection of ctDNA in patients with Non-Small Cell Lung Cancer

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Introduction : Personalized medicine has profoundly transformed the management of non-small cell lung cancer (NSCLC) by integrating the analysis of tumor molecular alterations into therapeutic decision-making. Activating mutations of the EGFR gene, mainly exon 19 deletions and the exon 21 L858R mutation, are key biomarkers because they determine the indication for tyrosine kinase inhibitors and influence prognosis.

Objective: To evaluate the clinical performance of EGFR mutation detection by RT-PCR in circulating tDNA extracted from EDTA plasma samples from patients with non-small cell lung cancer (NSCLC).

Methods: This retrospective study included 13 samples obtained from 12 patients with non-small cell lung cancer (NSCLC) followed at the onco-Pneumology. One patient underwent two samplings performed nine months apart, allowing longitudinal analysis. The ctDNA was extracted from EDTA plasma obtained after double high-speed centrifugation, in accordance with recommended pre-analytical conditions, using the QIAamp MinElute ccfDNA Midi Kit. EGFR mutations (G719X exon 18, exon 19 deletions, S768I, T790M, C797S, and exon 20 insertions) were analyzed by Real-time PCR using ARMS and PCR clamp technologies with the Therascreen EGFR Plus RGQ PCR kit (QIAGEN). Plasma **Results** were compared with tissue-based **Results**, considered as the reference standard when available. Diagnostic performances were evaluated in terms of sensitivity, specificity, positive predictive value, negative predictive value, and concordance coefficient (Cohen's kappa). Demographic and clinical characteristics were analyzed for patients.

Results: Among the 13 analyzed samples, 12 (92.3%) were considered suitable for analysis. The mean age was 59.3 ± 14.4 years, with a female predominance (75%). Most patients were nonsmokers (75%) and were receiving tyrosine kinase inhibitor (TKI) therapy (83.3%), mainly first-generation TKIs. All patients had metastatic disease. The overall concordance between plasma and tissue analyses was 58.3%, with a Cohen's kappa coefficient of 0.20, indicating a low level of agreement. The sensitivity of ctDNA detection was 55.6%, whereas specificity was 70%, indicating moderate specificity. The positive predictive value was high (83.3%), suggesting good reliability of positive **Results**. In contrast, the negative predictive value was low, with a high false-negative rate (44.4%). These discordant **Results** may partly be explained by the time interval between tissue analyses (performed before treatment initiation) and plasma analyses (performed during TKI therapy), potentially modifying the tumor molecular profile, as well as by low circulating tumor burden in some patients. A longitudinal analysis performed in the same patient at two time points (July 2025 and March 2026) demonstrated temporal variability in ctDNA detection, with an initially negative **Result** becoming positive at the time of clinical relapse, highlighting the potential value of liquid biopsy in disease monitoring.

Conclusion: Detection of EGFR mutations on ctDNA by Real-Time PCR represents a useful non-invasive approach in the management of NSCLC, particularly when tumor tissue is unavailable and for longitudinal monitoring during treatment. Despite a high positive predictive value, the moderate sensitivity observed limits its use as a substitute for tissue analysis. However, these **Results** should be interpreted cautiously given the small sample size. **Keywords :** EGFR, ctDNA, liquid biopsy, NSCLC, RT-PCR, mutations, personalized medicine, TKI.

Evaluating nephrotoxicity of Ifosfamide using TRP (Tubular Reabsorption of Phosphate)

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Introduction: Ifosfamide is an alkylating agent chemotherapy drug frequently used in pediatric oncology, particularly in the treatment of solid tumors, including bone and soft tissue sarcomas, germ cell tumors, lymphomas, and other high-risk pediatric tumors. Its nephrotoxicity is well-known and primarily affects the proximal tubule, potentially leading to partial or complete proximal tubulopathy of the Fanconi syndrome type. **Objective:** To evaluate the prognostic value of TRP and phosphaturia in the screening and monitoring of renal tubular damage in children with solid tumor treated with ifosfamide chemotherapy.

Methods: This is a study involving 82 children with cancer treated with ifosfamide, the parameters studied included serum phosphate, urinary phosphate, serum creatinine, urinary creatinine, and the renal phosphate reduction (RPR) calculated using the formula: $RPR = [1 - \text{Urinary Phosphorus} \times \text{Blood Creatinine} / \text{Blood Phosphorus} \times \text{Urinary Creatinine}] \times 100$. The RPR and urinary phosphate **Results** were analyzed to identify renal phosphate loss and to assess their usefulness in the early diagnosis of ifosfamide-induced proximal tubulopathy.

Results: Our population includes 37 girls and 75 boys. Analysis of biological data revealed variations in TRP and phosphaturia in children exposed to Ifosfamide. A decrease in TRR, associated with inappropriate phosphaturia in 7.3%, reflects renal phosphate loss and constitutes a marker of proximal tubular damage. These abnormalities may precede or accompany other signs of proximal tubulopathy, such as hypophosphatemia, normoglycemic glycosuria, proximal tubular acidosis, or tubular proteinuria.

Conclusion: TRR and phosphaturia are simple, accessible, and useful tools for screening proximal tubular damage in children with cancer treated with Ifosfamide. Their combined interpretation allows better identification of renal phosphate wasting, guides the diagnosis towards proximal tubulopathy, and ensures prognostic monitoring of at-risk patients.

Vulvar Cancer: Management and Outcomes in the Central Region of Tunisia

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Introduction: Vulvar cancer is a rare gynecological malignancy, ranking fifth among gynecological cancers with an overall frequency of 0.8%. It predominantly affects women over 60 years of age. Squamous cell carcinoma (SCC) represents the most common histological subtype. Although diagnosis is clinically straightforward, patients frequently present at advanced stages. Treatment relies primarily on surgery and radiotherapy.

Methods: A retrospective, descriptive, cross-sectional study was conducted over a 20-year period (January 1995 – December 2015) in the Department of Obstetrics and Gynecology at Farhat Hached University Hospital, Sousse. A total of 102 patients with vulvar cancer were included.

Results: Primary surgery was performed in 94 patients (92.2%). Radical vulvectomy was the most common procedure, performed

in 94.68% of operated cases (n=89). Partial vulvectomy (anterior or posterior hemi-vulvectomy) was performed in 4 patients (4.25%), and one tumorectomy was carried out in a 21-year-old patient. Of the 94 operated patients, 77 (81.9%) underwent inguinal lymph node dissection, including 70 bilateral and 7 unilateral dissections. The 8 remaining patients (7.8%) who were not surgical candi received exclusive radiotherapy. Squamous cell carcinoma accounted for 98% of cases (n=100). The majority (73%) presented without associated lesions. Associated conditions included lichen sclerosus in 12.74% of cases and vitiligo in 2 patients. HPV status was not documented in the pathology reports. Regarding differentiation, most SCCs were well-differentiated; verrucous carcinoma represented 6.38% of cases. The overall 2-year survival rate was 49.3%, while the 5-year survival rate was 28%. Mean survival was 51.4 months and median survival was 24 months. Local or inguinal recurrence occurred in 13 of 94 operated patients (13.82%), including 5 cases of inguinal lymph node recurrence and 8 cases of local vulvar recurrence requiring surgical re-intervention. In 7 patients, recurrence developed within 6 months of initial surgery, prior to adjuvant radiotherapy.

Conclusion: Vulvar cancer remains a rare but serious condition, increasingly affecting younger populations in the context of HPV-related oncogenesis. Its management is associated with significant morbidity. However, prognosis can be substantially improved through early diagnosis, enabling less mutilating, conservative surgical approaches.

Vulvar Cancer: Epidemiological and Clinical Profile in the Central Region of Tunisia

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Introduction: Vulvar cancer is a rare gynecological malignancy, ranking fifth among gynecological cancers with an overall frequency of 0.8%. It predominantly affects women over the age of 60. Squamous cell carcinoma represents the most common histological subtype. Although diagnosis is clinically straightforward, patients frequently present at advanced stages. Treatment relies primarily on surgery and radiotherapy.

Methods: A retrospective, descriptive, cross-sectional study was conducted over a 20-year period (January 1995 – December 2015) at the Department of Obstetrics and Gynecology, Farhat Hached University Hospital, Sousse, Tunisia. A total of 102 patients diagnosed with vulvar cancer were included.

Results: The mean age at diagnosis was 66.45 years (range: 21–92 years). The vast majority of patients (89.2%; n=91) were postmenopausal, with a mean age at menopause of 51.5 years (range: 40–70 years). No cases of premature menopause were identified. Thirteen patients had a documented dermatological history of vulvar lichen sclerosus and two had vitiligo, while 89 patients had no prior vulvar pathology. HPV status was not assessed in this series. A total of 44.1% of patients (n=45) had no significant medical history. Comorbidities were present in 55.8% of cases (n=57), including arterial hypertension in 34.3% (n=35), diabetes mellitus in 12.7% (n=13), cardiac disease in 5.8%, and obesity in 2.94% (n=3). The time from symptom onset to first consultation ranged from 1 to 72 months, with a mean delay of 15 months. Notably, 69.6% of patients (n=70) sought medical attention after a delay exceeding 15 months, reflecting a pattern of late presentation. Vulvar pruritus was the most frequent presenting complaint, reported in 89.2% of cases (n=91), followed by a palpable vulvar mass in 50% of cases (n=51).

Multiple concurrent symptoms were commonly observed. On macroscopic examination, an exophytic budding lesion was the predominant morphological pattern (84.3%; n=86), followed by ulcerated lesions (64.7%; n=66), with combined morphological features noted in several cases. According to the FIGO classification, 65.68% of patients (n=67) presented with early-stage disease (stage I–II). Among these, 55.88% (n=57) were classified as stage I, with over 50% of early-stage cases being stage IB (n=36/67). Advanced-stage disease (stage III–IV) was identified in 34.31% of patients (n=35). With respect to tumor (T) classification, 88 patients were staged as T1, while 12 patients presented with locally advanced disease (T2/T3). Inguinal lymphadenopathy was detected clinically in 39.21% of cases (n=40), whereas 62 patients (60.78%) had no palpable inguinal nodes. Two patients presented with distant metastasis (M1), while 100 patients were M0 at initial assessment.

Conclusion: Vulvar cancer remains a rare but serious condition, increasingly affecting younger women in the context of HPV-related carcinogenesis. Its management carries substantial morbidity. However, prognosis can be significantly improved through early diagnosis, enabling conservative, less mutilating surgical approaches.

Breast Cancer in Women Aged 25 and Under: Immunohistochemical Characteristics – A Study of 25 Cases

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Introduction: Breast cancer in young women represents a rare but distinct clinical entity, characterized by unique epidemiological, diagnostic, immunohistochemical, and prognostic features. Young age at diagnosis is increasingly recognized as an independent adverse prognostic factor.

Methods: A retrospective, descriptive study was conducted including 25 patients aged 25 years or younger diagnosed with breast cancer, collected from the Departments of Obstetrics and Gynecology and Pathological Anatomy and Cytology at Farhat Hached University Hospital, Sousse, Tunisia.

Results: Invasive ductal carcinoma was the predominant histological subtype, accounting for 84% of cases. High-grade tumors (SBR grade III) were identified in 44% of cases. Lymph node involvement was present in 47.3% of patients. Hormone receptors (estrogen and/or progesterone) were positive in 52% of cases. HER-2 oncogene overexpression was detected in 35% of cases. CK5/6 expression, indicative of a basal-like profile, was found in 40% of cases. Ki-67 proliferation index was positive in 76.4% of cases, p53 was expressed in 60% of cases, and BRCA1 mutation was identified in 5 patients. Analysis of immunohistochemical markers revealed that 61.5% of cases were triple-negative and 40% displayed a basal-like phenotype. All basal-like tumors were triple-negative, and all triple-negative/basal-like tumors demonstrated a Ki-67 positivity rate exceeding 15%. The five patients with BRCA1-expressing tumors had a personal or family history of breast or ovarian malignancy. According to the molecular classification of breast cancer, tumors were distributed as follows: Luminal A in 5 cases (25%), Luminal B in 6 cases (30%), HER2-enriched in 1 case (5%), triple-negative/basal-like in 6 cases (30%), and 2 tumors (10%) remained unclassified, corresponding to triple-negative non-basal-like tumors in our series.

Conclusion: Breast cancer in very young women carries a poor prognosis, characterized by more aggressive histological

and biological features, including a high prevalence of triple-negative and basal-like subtypes, elevated proliferative indices, and frequent BRCA1 association. These findings underscore the importance of comprehensive immunohistochemical profiling in this specific population to guide therapeutic decision-making.

Impact of diagnostic delay in invasive lobular breast carcinoma: a Tunisian case series

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Introduction: Invasive lobular carcinoma (ILC) is characterized by insidious clinical presentation and challenging radiological detection, frequently leading to delayed diagnosis. Unlike invasive ductal carcinoma, ILC often presents with diffuse infiltration and subtle imaging findings, **Resulting** in more advanced stages at diagnosis. The aim of this study was to evaluate the impact of diagnostic delay on tumor stage, therapeutic management, and oncological outcomes in patients with ILC treated at a Tunisian tertiary care center.

Methods: We conducted a retrospective case series at the Ben Arous Maternity Hospital, Tunisia, including patients diagnosed with invasive lobular breast carcinoma between January 2020 and December 2025. Diagnostic delay was defined as the interval exceeding three months between the onset of symptoms and histological diagnosis. Clinical, radiological, pathological, therapeutic, and follow-up data were collected from medical records. Patients were divided into two groups according to the presence or absence of diagnostic delay.

Results: A total of 31 patients with histologically confirmed ILC were included. The mean age was 55.1 years. Diagnostic delay exceeding three months was observed in 19 patients (61.3%), with a median delay of 7 months. Patients with delayed diagnosis presented more frequently with locally advanced disease (73.7% vs 33.3%), larger tumor size (>5 cm), multifocal lesions, and axillary lymph node involvement. Breast MRI contributed to diagnosis in several radiologically occult cases. Mastectomy was required in 68.4% of patients with delayed diagnosis compared with 33.3% in the early diagnosis group. Neoadjuvant chemotherapy was more frequently indicated in delayed cases. During follow-up, locoregional recurrence was observed predominantly among patients with advanced-stage disease.

Conclusion: Diagnostic delay remains frequent in invasive lobular carcinoma and is associated with more advanced disease at presentation and more aggressive therapeutic management. The infiltrative growth pattern and radiological underestimation of ILC contribute significantly to delayed recognition. Improved awareness and optimized imaging strategies may facilitate earlier diagnosis and improve oncological outcomes in the Tunisian setting.

Triple-negative breast cancer in a North African population: clinicopathological characteristics and outcomes

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Introduction: Triple-negative breast cancer (TNBC) is an aggressive molecular subtype of breast cancer characterized by the absence of estrogen receptor, progesterone receptor,

and HER2 expression. TNBC is associated with younger age at diagnosis, advanced disease stage, and poorer prognosis compared with other breast cancer subtypes. Data regarding TNBC in North African populations remain limited. The aim of this study was to describe the clinicopathological characteristics and oncological outcomes of patients diagnosed with TNBC in a Tunisian tertiary care center.

Methods: We conducted a retrospective descriptive study at the Ben Arous Maternity Hospital, Tunisia, including patients diagnosed with triple-negative breast cancer between January 2019 and December 2025. Clinical, radiological, histopathological, therapeutic, and follow-up data were collected from medical records. Variables analyzed included age at diagnosis, tumor size, histological grade, nodal status, metastatic presentation, treatment modalities, pathological complete response after neoadjuvant chemotherapy, recurrence, and survival outcomes.

Results: A total of 68 patients with TNBC were included. The mean age at diagnosis was 48.6 years, and 38.2% of patients were younger than 40 years. Most tumors were invasive ductal carcinomas (91.2%) and high histological grade (grade III in 72.1% of cases). Locally advanced disease was observed in 44.1% of patients, while axillary lymph node involvement was present in 57.4%. Neoadjuvant chemotherapy was administered in 41 patients, with a pathological complete response rate of 29.3%. During a median follow-up of 38 months, recurrence occurred in 26.5% of patients, predominantly within the first three years after diagnosis. Distant metastases mainly involved the lungs, liver, and brain. Patients achieving pathological complete response demonstrated significantly better disease-free survival.

Conclusion: Triple-negative breast cancer in this North African population affected relatively young women and was associated with aggressive clinicopathological features and high recurrence rates. Despite its unfavorable prognosis, patients achieving pathological complete response after neoadjuvant chemotherapy had improved oncological outcomes. Early diagnosis and optimized therapeutic strategies remain essential to improve survival in this challenging breast cancer subtype.

Pretreatment CA125 as a prognostic marker of survival and recurrence in epithelial ovarian cancer: a real-world Tunisian cohort study

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Background: Epithelial ovarian cancer (EOC) remains the most lethal gynecologic malignancy, largely due to advanced-stage presentation and high recurrence rates. Identification of accessible prognostic biomarkers is essential, particularly in low- and middle-income settings. This study evaluated the prognostic value of pretreatment CA125 in predicting surgical outcomes and survival in a Tunisian cohort.

Methods: We conducted a retrospective cohort study at the Ben Arous Maternity Hospital, Tunisia, including patients diagnosed with epithelial ovarian cancer between January 2015 and December 2025. Patients were stratified according to pretreatment CA125 level (<500 vs 500 U/mL). Associations with clinicopathological features, cytoreductive status, platinum sensitivity, progression-free survival (PFS), and overall survival (OS) were analyzed. Survival outcomes were assessed using Kaplan–Meier method and compared using log-rank test.

Results: A total of 72 patients were included, with a median age of 57 years. High-grade serous carcinoma accounted for 69.4%

of cases, and 76.4% of patients presented with advanced-stage disease (FIGO III–IV). Elevated pretreatment CA125 (500 U/mL) was significantly associated with advanced stage ($p<0.001$) and suboptimal cytoreduction (58.3% vs 26.9%, $p=0.01$). Patients with elevated CA125 had significantly shorter median PFS (15 vs 28 months, $p=0.004$) and reduced OS ($p=0.03$).

Conclusion: Pretreatment CA125 is an independent prognostic biomarker in epithelial ovarian cancer, strongly associated with tumor burden, surgical outcomes, and survival. Its integration into initial risk stratification algorithms may improve therapeutic decision-making, particularly in resource-limited settings where access to advanced molecular profiling is restricted.

Assessment of Reproductive Potential in Men with Hodgkin Lymphoma Before Chemotherapy: A Retrospective Study

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Background and objectives : Hodgkin lymphoma (HL) predominantly affects young men of reproductive age. Despite high cure rates with ABVD chemotherapy, gonadotoxicity remains a major concern. Pre-treatment semen quality may already be impaired by the disease itself, underscoring the importance of early fertility counseling and sperm cryopreservation. This retrospective study aimed to characterize the pre-treatment sperm profile of HL patients and to assess the feasibility and outcomes of sperm cryopreservation before chemotherapy initiation.

Methods: A descriptive study included 34 male HL patients referred for pre-chemotherapy sperm cryopreservation at the Reproductive Biology Department of the Military Hospital of Tunis (2018–2026). Semen analysis was performed per WHO 2021 criteria after 2–6 days of abstinence. Cryopreservation was performed using standardized slow-freezing protocols with glycerol-based cryoprotectant.

Results: Mean patient age was 26.29 ± 6.09 years (range: 15–39 years). Mean semen parameters were: volume 2.29 ± 1.19 mL, sperm concentration $39.08 \pm 48.19 \times 10^6/\text{mL}$, progressive motility $23.97 \pm 23.71\%$, and total motility $24.20 \pm 22.28\%$. Semen abnormalities were frequent: asthenospermia in 64.7%, severe oligospermia in 35.3%, extreme oligospermia in 17.6%, and azoospermia in 8.8% of patients. Sperm cryopreservation was successfully performed in 28 patients (82.4%), with a mean of 4.6 straws stored per patient.

Conclusion: Semen quality is substantially impaired in HL patients prior to chemotherapy, with a high prevalence of asthenospermia and oligospermia. Despite these alterations, sperm cryopreservation was feasible in over 80% of cases. Systematic fertility preservation should be integrated into the standard oncological management of young male HL patients.

TESTICULAR GERM CELL TUMORS (TGCT) AND MALE FERTILITY: FROM SEMEN QUALITY IMPAIRMENT TO REPRODUCTIVE OUTCOMES AFTER TREATMENT A Systematic Mini-Review

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Background: Testicular germ cell tumors (TGCTs) are the most common solid malignancy in males aged 15–45 years, accounting for approximately 60% of all cancers in young men.

With a 5-year survival rate exceeding 95%, fertility becomes the primary quality-of-life concern post-cure. Paradoxically, semen quality is already impaired in up to 50% of TGCT patients at diagnosis — before any treatment — and is further compromised by orchiectomy, cisplatin-based chemotherapy (BEP protocol), and radiotherapy. Understanding the dual origin of infertility in TGCT — tumour-intrinsic and treatment-related — is critical for optimising fertility preservation strategies.

Objective: To systematically review and synthesise published evidence on: (i) pre-treatment semen quality impairment in TGCT; (ii) effects of each therapeutic modality on spermatogenesis; (iii) fertility preservation strategies and their reproductive outcomes; and (iv) long-term gonadal endocrine sequelae in TGCT survivors.

Methods: Systematic narrative mini-review following PRISMA principles. PubMed/MEDLINE, Embase, and Cochrane Library were searched (2000–2025). MeSH terms included: “testicular germ cell tumour”, “seminoma”, “NSGCT”, “fertility preservation”, “spermatogenesis”, “sperm cryopreservation”, “BEP chemotherapy”, “onco-TESE”, “pateity”, and “hypogonadism”. Metaanalyses, systematic reviews, RCTs, and prospective cohorts were included.

Results: Fifty percent of TGCT patients present with abnormal semen parameters at diagnosis; azoospermia is found in 9–12% before any treatment. Following BEP chemotherapy, 80% of patients recover spermatogenesis by 5 years; persistent azoospermia occurs in 8% (95%CI: 6–12%) after standard treatment. The overall infertility prevalence post-treatment is 14% (95%CI: 9–21%), dropping to 4% for good-prognosis Stage I disease. Sperm cryopreservation before orchiectomy is superior to post-orchiectomy banking. ICSI with cryopreserved sperm achieves a 34% clinical pregnancy rate per cycle. Up to 77% of TGCT survivors desire paternity; paternity rates reach 71% without ART and higher with ART assistance.

Conclusion: TGCT represents the male cancer with the richest oncofertility evidence base. Fertility impairment in TGCT is bi-causal: tumour-intrinsic and iatrogenic. Pre-orchiectomy sperm banking remains the gold standard. Multidisciplinary oncofertility counselling at diagnosis is mandatory for all TGCT patients of reproductive age. **Keywords:** testicular germ cell tumour; seminoma; NSGCT; fertility preservation; semen quality; BEP chemotherapy; onco-TESE; paternity; male oncofertility; hypogonadism.

Impact of Health Insurance Coverage on Access to and Outcomes of CDK4/6 Inhibitors: Real-World Data from a Single Oncology Department in Tunisia

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Introduction: CDK4/6 inhibitors, in combination with endocrine therapy(ET), represent the standard treatment for hormone receptor-positive (HR+), HER2-negative metastatic breast cancer in the absence of visceral crisis. However, access to these therapies remains a major challenge in many developing countries. **Aim:** To assess the effect of health insurance coverage on access to CDK4/6 inhibitors and clinical outcomes in HR+/HER2 metastatic breast cancer **Method:** This was a retrospective study conducted in the Medical Oncology Department of Salah Azaiez Institute, including patients diagnosed with hormone receptor-positive (HR+), HER2negative metastatic breast cancer between March 2020 and December 2026.

Results: A total of 107 patients received treatment through the national health insurance scheme, while 30 patients were

enrolled in an access program. The median time to initiation of CDK4/6 inhibitors was 4 months in the national insurance group versus 3 months in the access program group. Among patients covered by the national insurance scheme, most received CDK4/6 inhibitors as first-line treatment (n=60;56%), followed by second-line (n=37;35%) and third-line treatment (n=6;5%). In the access program group, CDK4/6 inhibitors were most commonly used in the first-line setting (n=16;53%), followed by second-line (n=12;40%) and third-line treatment (n=2;6%). There was no significant association between CDK4/6 inhibitor discontinuation and type of health insurance coverage (p=0.18). Similarly, no significant association was observed between the duration of CDK4/6 inhibitor interruption and health insurance coverage type (p=0.8). here was no significant difference in mortality (p=0.4).

Conclusions: Health insurance coverage did not significantly impact CDK4/6 inhibitor discontinuation, treatment interruption duration, or mortality in this cohort of HR+/HER2 metastatic breast cancer patients. However, differences in time to treatment initiation were observed between groups. These findings highlight ongoing challenges in equitable access to CDK4/6 inhibitors in real-world settings.

Immune-Mediated Cholangitis Following Pembrolizumab Therapy in Metastatic Urothelial Carcinoma: A Case Report and Management Challenge

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Background: Immune checkpoint inhibitors (ICIs) have transformed the treatment landscape of advanced urothelial carcinoma. However, they can trigger a broad spectrum of immune-related adverse events (irAEs), including rare hepatobiliary complications. Immune-mediated cholangitis is an infrequently reported irAE with no established consensus on management, particularly in the setting of ongoing antitumor response.

Case presentation: We report the case of a 69-year-old man with a 50 pack-year smoking history, diagnosed with metastatic urothelial bladder carcinoma (bone and pulmonary metastases, presenting with hematuria). After disease progression on first-line gemcitabine-carboplatin (3 cycles), he received pembrolizumab as second-line therapy. Following 3 cycles, suspected pseudoprogression was noted. At the time of the third cycle, liver function tests revealed significant hepatobiliary disturbance: alkaline phosphatase 6× ULN, GGT 18× ULN, AST 2.5× ULN, and ALT 3× ULN. The patient was otherwise asymptomatic, with no biological signs of systemic inflammation and negative antinuclear antibodies. Abdominal CT scan and magnetic resonance cholangiopancreatography (MRCP) demonstrated radiological features consistent with cholangitis. Infectious cholangitis was ruled out by digestive surgery consultation. A diagnosis of grade 3 immune-mediated cholangitis was established.

Management & Outcome: Pembrolizumab was discontinued and high-dose corticosteroids were initiated, with close biological monitoring. Progressive normalization of liver function tests was achieved within one month. A follow-up MRCP confirmed radiological improvement of the cholangitis. Given the severity of this irAE, rechallenge with pembrolizumab was deemed too risky, and the patient was transitioned to taxane-based chemotherapy.

Conclusion: This case highlights immune-mediated cholangitis as a rare but clinically significant irAE of PD1 inhibitors, requiring

a high index of suspicion, multidisciplinary evaluation, and prompt immunosuppressive management. The coexistence of suspected pseudoprogression and a severe hepatobiliary irAE underscores the diagnostic and therapeutic complexity in real-world oncology practice. The question of ICI rechallenge after grade 3 immune-mediated cholangitis remains an unresolved clinical dilemma warranting further prospective data

Breast Cancer Presentation and Management in a North African Population: A Tunisian Experience

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Background : Breast cancer remains the most common malignancy among Tunisian women and represents a major public health challenge in North Africa. Despite recent advances in diagnostic and therapeutic strategies, symptomatic presentation remains frequent in Tunisia, Resulting in delayed diagnosis, larger tumor size at presentation, and higher rates of lymph node involvement. These factors contribute to poorer prognosis and increased socioeconomic burden. The aim of this study was to analyze the epidemiological, clinical, radiological, histopathological, and therapeutic characteristics of breast cancer patients managed in a Tunisian tertiary referral center and to compare our findings with national data and international literature.

Methods: We conducted a retrospective descriptive study including patients diagnosed and managed for breast cancer between January 2021 and December 2025 in the Department B of Gynecology and Obstetrics at the Tunis Maternity and Neonatology Center, Tunisia. A total of 100 patients were included. Epidemiological, clinical, imaging, histopathological, therapeutic, and outcome-related data were collected and analyzed.

Results: The mean age at diagnosis was 46.58 years, with 29% of patients younger than 40 years old. Breast lump self-detection was the most common presenting symptom, reported in 71% of cases. The mean consultation delay was 3 months and 15 days. The average clinical tumor size at diagnosis was 33.74 mm, reflecting the predominance of symptomatic and relatively advanced disease at presentation. Mammography was performed in all patients, while breast ultrasound was carried out in 78% of cases. Histopathological analysis revealed invasive ductal carcinoma as the predominant subtype (84.31%), with a predominance of Scarff–Bloom–Richardson (SBR) grade II tumors. Histological lymph node involvement was identified in 41.58% of operated patients, indicating a substantial burden of locoregional disease. Distant metastases were present in two patients at diagnosis. The mean therapeutic management delay was 27 days. Surgical treatment was performed in 97 patients, consisting of radical surgery in 66 cases and breast-conserving surgery in 31 cases. Adjuvant radiotherapy and chemotherapy were administered in 78% and 96% of patients, respectively.

Discussion: Our findings highlight the persistent challenge of late symptomatic presentation of breast cancer in Tunisia, particularly among younger women. The relatively large tumor size and high nodal involvement rates observed in our cohort remain higher than those commonly reported in high-income countries, where organized screening programs facilitate earlier detection. Similar patterns have been described in several North African and low- to middle-income settings, emphasizing disparities in access to screening and breast cancer awareness. The high proportion of radical surgery in our study may be explained by advanced local disease at diagnosis, limiting eligibility for breast-conserving approaches. Nevertheless, the

relatively short therapeutic delay observed in our center reflects acceptable multidisciplinary management once diagnosis is established. These **Results** underscore the urgent need for a national organized breast cancer screening strategy in Tunisia, along with public awareness campaigns aimed at promoting earlier consultation and improving access to diagnostic services. Early detection could significantly reduce tumor burden, nodal involvement, and the need for aggressive treatment, ultimately improving survival outcomes and quality of life.

Conclusion: Breast cancer in Tunisia continues to be characterized by symptomatic presentation, delayed consultation, large tumor size, and significant lymph node involvement at diagnosis. Our study highlights the ongoing challenges in breast cancer care within a North African context and supports the implementation of nationwide screening and awareness programs to promote earlier diagnosis and improve prognosis.

Breast and Axillary Lymph Node Metastasis as an Atypical Presentation of High-Grade Serous Ovarian Adenocarcinoma: A Case Report

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Background: High-grade serous ovarian carcinoma (HGSOC) typically spreads via local invasion and intraperitoneal dissemination. Distant metastasis to the breast and axillary lymph nodes is an exceedingly rare phenomenon, accounting for less than 0.1% of ovarian cancer cases. Distinguishing metastatic ovarian cancer from primary breast carcinoma represents a significant diagnostic challenge but is crucial to avoid inappropriate surgical interventions and guide correct systemic therapy.

Case presentation: A 48-year-old female presented with progressive abdominal distension. On physical examination, a 2 cm nodule was palpated in the lower-inner quadrant of the left breast, accompanied by a 1.5 cm homolateral axillary lymphadenopathy. Initial pelvic ultrasound revealed bilateral ovarian masses categorized as IOTA M4. Breast ultrasound and mammography classified the mammary lesion as BI-RADS (ACR) 4C. A thoraco-abdominopelvic CT scan confirmed the bilateral ovarian masses, extensive lymph node involvement, diffuse peritoneal carcinomatosis, and the left breast lesion. The patient underwent a diagnostic laparoscopy with peritoneal biopsies. Histopathological and immunohistochemical (IHC) evaluation revealed a high-grade serous adenocarcinoma of ovarian origin, testing positive for WT1 and CK7, and negative for CDX2 and CK20. Concurrently, a core needle biopsy of the breast nodule demonstrated metastasis from a high-grade serous adenocarcinoma of gynecological origin, with positive staining for WT1 and PAX8. Serum CA-125 was significantly elevated at 2500 U/mL. Systemic treatment was initiated with a combination regimen of Paclitaxel, Carboplatin, and Bevacizumab. Genetic testing for BRCA mutations is currently underway.

Discussion & Conclusion: Breast metastasis from ovarian adenocarcinoma is a rare clinical entity that signifies advanced disease. It can mimic primary breast cancer both clinically and radiologically (ACR 4C). In this case, immunohistochemical profiling (WT1, PAX8, and CK7 positivity along with CDX2 and CK20 negativity) was vital in confirming the ovarian primary site and ruling out a synchronous primary breast malignancy. Accurate differentiation prevents unnecessary mastectomies or axillary lymph node dissections. Systemic chemotherapy

combined with targeted antiangiogenic therapy remains the cornerstone of management. This case underscores the necessity of a rigorous multidisciplinary approach and thorough IHC analysis when evaluating concurrent adnexal and mammary lesions.

Sclerosing Stromal Tumor of the Ovary: A Rare Benign Neoplasm Mimicking Ovarian Malignancy in a Young Woman

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Background: Sclerosing stromal tumors of the ovary (SSTOs) are rare benign neoplasms arising from ovarian stromal cells with minor sex cord contributions, accounting for 2% to 6% of all ovarian stromal tumors. Predominantly affecting women in their second and third decades of life, they represent a diagnostically challenging entity whose clinical and radiological presentation may closely mimic malignant ovarian neoplasms, making them particularly relevant in the oncological differential diagnosis of adnexal masses in young women. Fewer than 300 cases have been documented in the world literature to .

Case Report: A 29-year-old nulliparous woman with no significant past medical history presented with chronic pelvic pain localized to the hypogastric region. Physical examination revealed a palpable right iliac fossa mass without peritoneal signs. All tumor markers were negative, including CA-125, AFP, -hCG, LDH, and CEA. Pelvic ultrasonography identified a 6 cm right adnexal solid-cystic vascularized mass. Pelvic MRI confirmed a well-circumscribed right ovarian mass measuring 40 × 32 mm with mild peripheral hypervascularization and minimal free pelvic fluid, without lymphadenopathy or adjacent organ involvement. The imaging characteristics, while suggestive of a benign process, could not reliably exclude a malignant ovarian neoplasm, prompting surgical exploration. Diagnostic laparoscopy confirmed a 6 cm solid right ovarian mass with approximately 100 ml of ascitic fluid. Laparoscopic enucleation with complete ovarian preservation was successfully performed. Macroscopic examination revealed a firm 5.5 × 5.5 cm mass with a yellowish cut surface and focal myxoid changes. Microscopic examination demonstrated the characteristic pseudolobular architecture, with alternating cellular and hypocellular edematous zones, spindle and round tumor cells, and numerous dilated anastomosing hemangiopericytic vessels. Immunohistochemical analysis confirmed positivity for smooth muscle actin and focal positivity for inhibin, establishing the definitive diagnosis of SSTO and excluding malignancy. Postoperative recovery was uneventful, with no evidence of recurrence and preserved ovarian function confirmed at 1, 3, 6, and 12 months of follow-up.

Discussion: SSTOs represent a diagnostically challenging entity due to their nonspecific clinical presentation and radiological features that may overlap with malignant ovarian tumors. Approximately 80% of cases are diagnosed between the ages of 20 and 40 years. Clinically, presentations include pelvic pain, abdominal mass, and occasionally ascites or abnormal uterine bleeding, while hormonal manifestations remain rare. On MRI, the characteristic early peripheral enhancement with centripetal progression resembling a hemangioma pattern, combined with a mixed solid-cystic morphology, constitutes the most suggestive radiological signature, though definitive diagnosis invariably relies on histopathological and immunohistochemical analysis. Key differential diagnoses include ovarian fibroma, thecoma, and granulosa cell tumor,

distinguished by age of onset, hormonal activity, imaging characteristics, histological architecture, and immunoprofile. SSTOs are uniquely identified by their pseudolobular pattern, hemangiopericytic vasculature, and positivity for smooth muscle actin with focal inhibin expression. Conservative surgical management, including laparoscopic ovarian-sparing enucleation or unilateral adnexectomy, is the standard of care in young women, given the benign nature of the lesion, the absence of reported recurrences, and the critical importance of fertility and ovarian function preservation.

Conclusion: Although benign, SSTOs constitute a genuine diagnostic challenge in the oncological workup of adnexal masses, owing to their capacity to mimic malignant ovarian neoplasms both clinically and radiologically. In young women of reproductive age presenting with a suspicious adnexal mass and negative tumor markers, SSTO should be considered in the differential diagnosis to avoid unnecessary radical surgery. Definitive diagnosis relies on comprehensive histopathological evaluation supported by immunohistochemical profiling. Laparoscopic conservative surgery represents the optimal therapeutic approach, effectively excluding malignancy while preserving fertility and ovarian function.

Estimated Incidence and Histopathological Patterns of Bladder Cancer in Northern Tunisia in 2025

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Introduction: Bladder cancer (BC) is among the most common cancers worldwide, ranking ninth in terms of incidence for both sexes combined. This study aimed to (i) estimate incidence rates of BC in 2025, to (ii) describe its epidemiological and histopathological characteristics and (iii) to dress its trends for 2040 in Northern Tunisia.

Methods: a descriptive retrospective and exhaustive study based on all cases of BC in Northern Tunisia. This was from the Northern Tunisia Cancer Registry (NCR) 2015-2018; the source of data for this study. Crude and standardized incidence rates were calculated. Projections were assessed using the age period cohort model.

Results: In 2025, 1,072 new cases of BC were estimated in Northern Tunisia with a sex ratio of 7.06 (88.3% males). The age-standardized incidence rate was 25.0 per 100,000 person-years in men (95% CI: 12.25 - 13.92) and 3.0 per 100,000 in women (95% CI: 1.44 - 2.08). The mean age at diagnosis was 66.1 ± 11.8 years (66.0 ± 11.4 years in males and 66.2 ± 14.7 years in females). About 93.7% of BC cases were over 50 years old (86.4% in males and 90.0% in females) and 71.2% over 60 years old (73.0% in males and 69.3% in females). The most frequent age group in men was between 60 and 69 years, representing 17.3% of cases. Almost 86% of cases were diagnosed at local stage and 5.7% at a metastatic extent. Transitional cell carcinoma represented 44% of BC cases (44.1% in males and 43.8% in females) and 37.2% were papillary transitional cell carcinoma (37.8% in males and 36.6% in females). Projections for 2040 estimated 2,651 new cases (1272 men and 298 women), corresponding to incidence rates of 38.6 per 100,000 in men (95% CI: 29.4 – 53.0) and 4.0 per 100,000 in women (95% CI: 2.1 - 8.9).

Conclusion: BC in Tunisia is observed among the elderly and

mostly at a local stage. However, the projected increase in the incidence of this cancer underscores the need to strengthen the fight against tobacco in Tunisia.

Assessing Breast Cancer Knowledge, Awareness and Attitude Levels Among Tunisian Women in Primary Healthcare

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Background: Breast cancer (BC) remains the leading cancer among women worldwide and in Tunisia, where its incidence has steadily increased since the 1990s. Women's knowledge, perceptions, and health-related practices play a pivotal role in early detection and timely care-seeking. This study aimed to assess the knowledge, attitudes, and practices related to breast cancer among Tunisian women attending primary health care centers in Greater Tunis.

Methods: We conducted a cross-sectional study in three primary health care centers in Greater Tunis. Data were collected using a structured, self-administered, valid questionnaire developed through a literature review and inspired by previous studies. The questionnaire comprised five sections assessing socio-demographic characteristics, knowledge of symptoms and risk factors, perceived susceptibility, perceived severity, perceived barriers, outcome expectations, and screening practices.

Results: A total of 103 women attending primary health care centers in Greater Tunis responded (response rate: 90.5%). The mean age of participants was 51.9 ± 15.7 years. A family history of breast BC was reported by 38% of participants. Knowledge of BC symptoms indicated that the most frequently recognized signs were breast shape change (72.8%), nipple discharge or change (68.0%), and an armpit lump (56.3%). In contrast, awareness of risk factors was limited, as 10.7% of participants did not identify any risk factors associated with BC. Most women acknowledged the importance of breast self-examination and mammography screening, and 81.8% reported that they would consult a physician if they noticed suspicious symptoms. Regarding willingness to participate in screening, 76.8% of participants reported that they would attend a free BC screening day. However, health practices remained insufficient: 48.0% had never performed breast self-examination and only 16.7% reported performing it regularly. Fear of diagnosis was the most frequently reported barrier to medical consultation (51.0%). Median knowledge, perception, and attitude scores were 71.0 (IQR: 59.087.0), 52.0 (IQR: 45.0-57.0), and 3.0 (IQR: 2.0-3.0), respectively. Higher knowledge and attitude scores were significantly associated with a family history of BC ($p = 0.02$ and $p = 0.039$).

Conclusion: While awareness of some breast cancer symptoms was relatively high among women attending primary health care centers in Greater Tunis, knowledge of risk factors and screening practices remained limited. These findings highlight the need for targeted educational interventions to improve knowledge and promote early detection.

Clinicopathological Profile and Outcomes of Endometrial Cancer in Tunisia: Experience of a Tertiary Care Center

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Introduction : Endometrial cancer is the most common gynecological malignancy in high- and middle-income countries and represents an increasing public health concern due to rising life expectancy and the growing prevalence of obesity and metabolic disorders. Its development is strongly associated with prolonged estrogen exposure and postmenopausal status. The objective of this study was to describe the epidemiological, clinical, radiological, histopathological, therapeutic, and prognostic characteristics of endometrial and uterine body cancers managed in a Tunisian tertiary referral center.

Methods: We conducted a retrospective descriptive study including patients diagnosed with endometrial and uterine body cancers at Department B of the Centre de Matéité et de Néonatalogie de Tunis over a 5-year period from January 2021 to December 2025. Epidemiological characteristics, risk factors, clinical presentation, imaging findings, histopathological data, therapeutic management, and survival outcomes were analyzed.

Results: Fifty-two patients were included. The mean age at diagnosis was 59.7 ± 11.4 years (22–81 years), with patients aged 60 years representing the largest group (51.9%). Menopause was observed in 78.8% of cases. Obesity was identified in 44.2% of patients, while hypertension and type 2 diabetes were each present in 30.7% of cases. Nulliparity was found in 32.7% of patients. Abnormal uterine bleeding was the leading presenting symptom (86.5%), whereas incidental histological diagnosis accounted for 11.5% of cases. Pelvic ultrasound revealed a pathological endometrium in 61.5% of patients, with a mean endometrial thickness of 30.2 mm. Hysteroscopy-guided endometrial biopsy was performed in 75% of cases. Pelvic MRI showed disease confined to the uterus in 51.9% of patients, deep myometrial invasion in 38.5%, cervical extension in 17.3%, and nodal involvement in 19.2%. Distant metastases were identified in 11.5% of cases, predominantly pulmonary. According to FIGO classification, stage I disease represented 44.2% of cases. Surgery was performed in 84.6% of patients, mainly via laparotomy (79.5%). Histopathological examination demonstrated a predominance of endometrioid adenocarcinoma (78.8%), followed by serous papillary adenocarcinoma (7.7%), carcinosarcoma (3.8%), and uterine smooth muscle tumors (5.8%). Postoperative complications occurred in 18.2% of patients, mainly thromboembolic events and wound healing disorders. Adjuvant chemotherapy and radiotherapy were administered in 38.5% and 36.5% of patients, respectively. Recurrence was observed in 19.2% of cases, while mortality reached 9.6%. Mean recurrence-free survival was 2.7 ± 1.3 years and mean overall survival was 3.2 ± 1.8 years.

Discussion: Our findings are largely consistent with international data reporting that endometrial cancer predominantly affects postmenopausal women around the sixth decade of life. The high prevalence of obesity, hypertension, and diabetes in our cohort further supports the central role of metabolic syndrome and hyperestrogenism in endometrial carcinogenesis. Similarly, abnormal uterine bleeding remained the main symptom leading to diagnosis, emphasizing the importance of early evaluation of postmenopausal bleeding. Imaging findings in our series confirmed the major contribution of pelvic ultrasound and MRI in the assessment of myometrial invasion and locoregional extension. MRI proved particularly useful for preoperative staging and therapeutic planning, while CT imaging allowed detection of distant metastatic disease, mainly pulmonary lesions, which are classically described in advanced uterine malignancies. Endometrioid adenocarcinoma was the predominant histological subtype, in agreement with the literature. However, non-endometrioid histologies such

as serous carcinoma, carcinosarcoma, and leiomyosarcoma were associated with more aggressive behavior and poorer prognosis. Recent advances in molecular classification, particularly the integration of POLE-mutated, MMR-deficient, p53-abnormal, and NSMP subgroups, are progressively reshaping prognostic stratification and therapeutic decision-making. Most patients in our cohort presented with localized disease, although the proportion of advanced stages remained relatively high compared with Western registries, reflecting possible delays in diagnosis and disparities in healthcare access. Surgical treatment remained the cornerstone of management, consisting mainly of hysterectomy with bilateral salpingo-oophorectomy and lymph node assessment. Adjuvant therapies were prescribed according to histological subtype and stage, in line with current international recommendations. Despite generally favorable outcomes for early-stage disease, recurrence and mortality remained significant, particularly among patients with advanced-stage tumors, metastatic disease, postoperative thromboembolic complications, and aggressive histological subtypes. These findings highlight the importance of multidisciplinary management, optimized perioperative care, and long-term surveillance.

Conclusion: Endometrial cancer in our population predominantly affects postmenopausal women with metabolic risk factors. Early recognition of abnormal uterine bleeding and improved access to diagnostic investigations may facilitate earlier-stage diagnosis. Histological subtype, stage at diagnosis, and metastatic extension remain the principal prognostic determinants. Advances in molecular classification and multidisciplinary individualized management may contribute to improving survival outcomes and reducing recurrence rates.

Real-world presentation and management of ovarian cancer in Tunisia: insights from a 5-year retrospective study

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Introduction : Ovarian cancer is one of the most lethal gynecologic malignancies worldwide because of its nonspecific presentation and frequent diagnosis at advanced stages. Although its incidence is lower in North Africa compared with Western countries, ovarian cancer remains associated with significant morbidity and mortality. Data describing its epidemiological, clinical and therapeutic characteristics in Tunisia remain limited. This study aimed to analyze the clinicopathological profile, management strategies and outcomes of ovarian cancer patients treated in a Tunisian tertiary referral center.

Methods : We conducted a retrospective descriptive study over a 5-year period from January 2021 to December 2025 including 48 patients managed for ovarian malignancies in a tertiary gynecologic oncology department in Tunisia. Epidemiological, clinical, imaging, histopathological, therapeutic and follow-up data were collected from medical records. Tumors were staged according to the FIGO 2014 classification.

Results : The mean age at diagnosis was 52.5 ± 12 years (range: 31–74 years), with more than half of the patients aged between 40 and 59 years (52.1%). Nulliparity was observed in 37.5% of cases. Familial history of malignancy was identified in 12.5% of patients, mainly breast, endometrial and colorectal cancers. Pelvic and/or abdominal pain represented the leading presenting symptom (64.6%), followed by progressive abdominal distension (39.6%) and digestive symptoms including bowel obstruction

syndrome (29.2%). The mean delay before consultation was 2.2 ± 2.4 months. Pelvic ultrasound predominantly revealed mixed ovarian masses (50%), followed by multilocular cystic lesions (19%). Mean tumor size reached 14 ± 7 cm, reflecting frequent late presentation. Ascites was associated with 41.7% of tumors, while intratumoral vegetations were observed in 29.2% of cases. MRI classified most lesions as O-RADS 5. According to FIGO 2014 staging, 39.6% of tumors were stage I, 8.3% stage II, 29.2% stage III and 16.7% stage IV. Advanced stages (III–IV) accounted for 45.9% of cases. Thoracoabdomino-pelvic CT demonstrated pelvic extension in 18.7%, hepatic or splenic involvement in 16.7%, pleural metastases in 6.2% and lombo-aortic lymph node involvement in 8.3%. CA125 assay was performed in 83.3% of patients and was elevated in 75% of tested cases, with a mean level of 1448 U/mL. Surgery was performed in 98% of patients. Primary debulking surgery was achieved in 48.9% of cases, whereas 18.8% received neoadjuvant chemotherapy followed by interval debulking surgery. Complete cytoreduction (R0) was achieved in 63.8% of operated patients. Histopathological examination identified malignant tumors in 72.9% of cases, borderline ovarian tumors in 22.9% and sex cord-stromal tumors in 4.2%. High-grade serous carcinoma was the predominant histological subtype (41.7%). Follow-up data were available for 41.7% of patients. Recurrence and new metastatic progression were each observed in 6.2% of cases. Overall mortality reached 10.4%, mainly among patients with advanced-stage high-grade serous carcinoma. Mean recurrence-free survival was 3.9 ± 2.6 years, while mean overall survival was 4.3 ± 2.4 years. Borderline ovarian tumors demonstrated excellent prognosis with 100% overall survival during follow-up.

Discussion : Our study highlights the persistent challenge of ovarian cancer diagnosis in Tunisia, with nearly half of patients presenting at advanced stages. The predominance of abdominal pain and abdominal distension reflects the nonspecific and insidious nature of the disease, frequently leading to delayed diagnosis. The large mean tumor size at presentation further supports this observation. The mean age at diagnosis was approximately one decade younger than that commonly reported in Western series, where epithelial ovarian cancers are typically diagnosed after the age of 60 years. Similar findings have been reported in several low- and middle-income countries and may reflect demographic, socioeconomic and healthcare access disparities. High-grade serous carcinoma represented the predominant histological subtype, in agreement with international literature. Despite the high proportion of advanced-stage disease, optimal cytoreduction was achieved in nearly two-thirds of operated patients, emphasizing the role of specialized gynecologic oncology management and multidisciplinary care. Borderline ovarian tumors were mainly diagnosed at early stages and were associated with excellent outcomes, consistent with their favorable biological behavior reported in the literature. The main limitations of our study include its retrospective design, the relatively limited sample size and incomplete follow-up data for some patients.

Conclusion : Ovarian cancer remains frequently diagnosed at advanced stages in our setting despite progress in multidisciplinary management. Earlier recognition of nonspecific symptoms, improved access to specialized imaging and strengthened referral pathways may contribute to improving prognosis. Larger multicenter studies are needed to better characterize ovarian cancer patterns and outcomes in North African populations.

Clinicopathological Predictors of Occult Lymph Node Metastasis in Clinically Node-Negative Luminal A Breast Cancer (cT0–T2N0)

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Background: Lymph node (LN) status remains a major prognostic factor in breast cancer. Although Luminal A tumors are generally associated with a favorable prognosis and a low risk of nodal involvement, some patients with clinically node-negative early-stage disease (cT0–T2N0) may still harbor histological lymph node metastasis (LNM). This study aimed to identify the clinical and pathological predictors of LNM in this subgroup.

Methods: A retrospective study was conducted including patients with clinically node-negative Luminal A breast cancer staged cT0–T2N0 and treated surgically at the Regional Hospital of Jendouba between 2010 and 2025. Luminal A subtype was defined by estrogen receptor (ER) expression 10%, HER2-negative status, and either Ki-67 <14% or Ki-67 between 14% and 19% associated with progesterone receptor (PR) expression >20%. Clinicopathological factors associated with histological lymph node metastasis (LNM) were analyzed using univariate statistical tests, with $p < 0.05$ considered statistically significant.

Results: Among 40 patients (mean age: 57.07 ± 13.07 years), 20% had histological LNM. Significant predictors of LNM included delayed consultation (212.5 vs 71.9 days; $p=0.003$), multifocality (66.7% vs 16.2%; $p=0.036$), clinical T stage (0% in cT0 vs 11.1% in cT1 vs 35.3% in cT2; $p=0.031$), larger mean clinical tumor size (26.25 ± 5.83 mm vs 20.69 ± 9.97 mm; $p=0.05$), lymphovascular space invasion (LVSI) (30% vs 16%; $p=0.042$), and perineural invasion (PNI) (100% vs 17.9%; $p=0.043$). No significant associations were observed with age (59.88 ± 13.09 vs 56.38 ± 13.19 years; $p=0.513$), tumor grade (0% in SBR grade 1 vs 21.4% in grade 2 vs 25% in grade 3; $p=0.560$), or hormone receptor expression.

Conclusion: Despite the favorable biological profile of Luminal A breast cancer, a substantial proportion of clinically node-negative cT0–T2 patients presented histological lymph node metastasis. Delayed consultation, multifocality, higher clinical T stage, larger tumor size, LVSI, and PNI were significantly associated with nodal involvement and may help identify patients at higher risk of occult LNM.

Determinants of Recurrence After Curative Gastrectomy in Node-Negative Gastric Cancer: A Retrospective Study

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Background: This study aimed to identify clinical, therapeutic and histological predictors of recurrence in node negative gastric cancer (GC).

Methods: A retrospective study was conducted on patients undergoing curative-intent gastrectomy for histologically node-positive GC at Salah Azaiez Institute (2005–2023). Clinicopathological, surgical, and histopathological variables, recurrence patterns, and survival outcomes were analyzed.

Univariate analysis using the χ^2 test was performed to identify predictors of recurrence.

Result: A total of 45 patients (median age: 61 years, range: 26–88) were included. Neoadjuvant chemotherapy was administered in 31.1% of cases. Total and partial gastrectomy were performed in 37.8% and 62.2% of patients, respectively, with D2/D2+ lymphadenectomy achieved in 71.1% of cases. The mean tumor size was 51.13±26.46 mm, and 53.3% of tumors were classified as pT3 or pT4. Lymphovascular invasion (LVI), perineural invasion (PNI), and poorly differentiated/undifferentiated histology were observed in 35.6%, 24.4%, and 22.2% of cases, respectively. Complete (R0) resection was achieved in 95.6% of patients. The mean number of retrieved lymph nodes (NRLN) was 24.29±14.58 (range: 7–72), exceeding 25 nodes in 42.2% of cases. After a median follow-up of 29 months, 77.8% of patients achieved complete remission, whereas 22.2% developed recurrence, including isolated locoregional recurrence in 2 cases (4.4%), isolated metastatic recurrence in 7 cases (15.6%), and combined locoregional and metastatic relapse in 1 case. The 5-year overall survival and progression-free survival rates were 68.2% and 61.3%, respectively. On univariate analysis, recurrence was significantly higher in poorly/moderately differentiated tumors compared with well-differentiated histology (17.7% vs 87.5%; $p=0.001$). It was also associated with positive resection margins (50% vs 20.9%; $p=0.01$), LVI (37.5% vs 13.8%; $p=0.046$), and PNI (63.6% vs 8.8%; $p<0.0001$). Finally, a lymph node yield ≥ 25 was linked to increased recurrence compared with <25 nodes (34.6% vs 5.3%; $p=0.019$).

Conclusion: Recurrence after curative gastrectomy for node-negative GC is driven by adverse pathological features and limited lymph node retrieval, underscoring their prognostic significance.

Extra-Perigastric Lymph Node Spread as a Marker of Tumor Aggressiveness and Poor Outcomes in Node-Positive Gastric Cancer

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Background: The current TNM classification for gastric cancer uses a numeric N stage, while the prognostic value of nodal topography remains uncertain. This study evaluated its prognostic relevance within the TNM system.

Methods: We retrospectively reviewed patients undergoing curative gastrectomy for histologically node-positive GC at Salah Azaiez Institute (2005–2023). Metastatic lymph nodes (LNM) were classified into perigastric and extra-perigastric groups. Clinicopathological and therapeutic factors associated with extra-perigastric LNM were analyzed using χ^2 test, and survival impact was assessed by Kaplan–Meier method.

Result: A total of 150 patients (median age: 61 years, range: 25–85) were included. Total and partial gastrectomy were performed in 53.3% and 46.7% of patients, respectively, with D2/D2+ lymphadenectomy achieved in 62.7% of cases. Extra-perigastric LNM occurred in 17 patients (18%). After a mean follow-up of 28.80 months, the 5-year progression free survival (PFS) was 46.6%. Univariate analysis showed that extra-perigastric LNM was significantly associated with younger age (56.11±15.229 vs 62.82±12.39 years; $p=0.039$), elevated CA19-9 (657.12 vs 21.026; $p=0.041$) and CEA levels (96.669 vs 9.53; $p=0.018$), presence of lympho vascular invasion (LVI) (23.8% vs 11.4%;

$p=0.05$), moderately and poorly differentiated tumors (23.2% vs 7.8% in well-differentiated tumors; $p=0.02$), larger tumor size (82.03±48.18 mm vs 61.707±31.20 mm; $p=0.007$), deeper tumor invasion (22.2% in pT3/T4 vs 3% in pT1/T2; $p=0.003$), advanced nodal stage (29.9% vs 8.7% vs 8.1% in pN3, pN2, and pN1, respectively; $p=0.003$), and advanced UICC stage (22.9% in stage III vs 4.9% in stages I–II; $p=0.010$). Extra-perigastric LNM was more frequent after D2/D2+ lymphadenectomy (23.4% vs 8.9%; $p=0.029$), with >25 retrieved LN (NRLN) (30.4% vs 10.6%; $p=0.002$) and LN ratio $>10\%$ (21.4% vs 6.1%; $p=0.043$). Extra-perigastric LNM was associated with lower but not significant 5-year PFS overall (38.2% vs 48.5%; $p=0.071$). However, it was significantly reduced in subgroups with LVI (6.6% vs 9.6%; $p=0.048$), pN3 stage (26.8% vs 41.6%; $p=0.04$), and NRLN ≥ 25 (25% vs 56.8%; $p=0.014$).

Conclusion: Extra-perigastric LNM was linked to advanced disease and worse outcomes in high-risk subgroups, supporting the prognostic value of nodal topography in node-positive GC.

High-Risk Features of Recurrence After Curative Gastrectomy with Inadequate Lymph Node Harvest in Gastric Adenocarcinoma

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Background: The TNM classification (6th edition) recommends examination of at least 15 lymph nodes (LN) for accurate staging; however, in our setting, only 20% of patients achieve this threshold. This study aimed to evaluate clinicopathological predictors of recurrence in patients with gastric adenocarcinoma (GC) undergoing radical resection with an insufficient number of examined LN.

Methods: A retrospective study was conducted at Salah Azaiez Institute (2005–2023) in patients who underwent radical resection for GC with an inadequate number of examined LN. Clinicopathological and histopathological data were analyzed. Univariate analysis was performed using the χ^2 test, followed by multivariate logistic regression to identify independent predictors of recurrence.

Results: A total of 35 patients with a mean age of 61.14 ± 9.72 years (range: 41–84 years) were included. The median number of retrieved LN was 6 (range: 0–14). After a median followup of 18 months (range: 3–140), recurrence occurred in 12 of 35 cases (34.3%), including 10 cases of hematogenous dissemination and 5 locoregional recurrences. The median time to recurrence was 6.5 months (range: 1–27), and 75% of recurrences occurred within the first year after surgery. The following factors were found to be correlated with the recurrence risk: the tumor size >50 mm (66.7 vs 17.4, $p=0.004$), the presence of perineural invasion (PNI) (78.6% vs 4.8%, $p<0.0001$) and lymphovascular invasion (LVI) ($p=0.004$), The pT stage (40.9% in stage pT3/4 vs 23.1% in stage pT1/2, $p<0.0001$), the number of metastatic LN > 5 LN (77.8% vs 19.2%, $p=0.001$) and LN ratio (LNR) >25 (61.1% vs 5.9%, $p=0.001$). A multivariate analysis revealed that depth of invasion ($\text{Exp}(B)=0.299$, 95% confidence interval (CI)= 0.062–0.536, $p=0.015$), tumor differentiation ($\text{Exp}(B)=0.278$, 95% CI=0.027–0.519, $p=0.031$), tumor size ($\text{Exp}(B)=0.222$, 95% CI=0.000–0.006, $p=0.047$), presence of PNI ($\text{Exp}(B)=0.586$, 95% CI=0.323–0.813, $p<0.0001$) and LNR ($\text{Exp}(B)=0.331$, 95% CI=0.1390–0.875, $p=0.009$) were independent risk factors for recurrences. Tumor invasion depth, PNI, tumor differentiation, tumor size, and LNR were independent predictors of recurrence

in GC after potentially curative resection with an inadequate number of examined LN.

Metastatic Lymph Node Ratio as a Prognostic Marker in Locally Advanced Cervical Cancer treated with Chemoradiation and Surgery

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Background: The metastatic lymph node ratio (LNR) has been proposed as a more accurate prognostic indicator than traditional nodal staging. This study aimed to evaluate its prognostic value and correlation with clinicopathological factors in locally advanced cervical cancer (LACC).

Methods: We conducted a retrospective study at the Salah Azaiez Institute of Oncology from January 2010 to December 2020, including patients with LACC treated with curative intent using chemoradiotherapy followed by radical surgery with systematic pelvic lymphadenectomy. All resected lymph nodes (LN) were pathologically examined. LNR was categorized as 0.1 or >0.1. Associations with clinicopathological variables were assessed, and survival outcomes were analyzed using the Kaplan–Meier method with log-rank comparison

Results: We included 117 patients with a median age of 54 years (range: 34–82). In addition to pelvic lymphadenectomy, patients underwent posterior exenteration in 1 case, anterior exenteration in 4 cases, simple hysterectomy with bilateral adnexectomy in 3 cases, and radical colpopohysterectomy in 111 cases. The median number of retrieved LN was 15 (range: 3–27). Histological LN involvement was identified in 11 patients (9.4%), with a median of 2 positive LNs (range: 1–5). The median lymph node ratio (LNR) was 0.01 ± 0.06 ; 108 patients (92.3%) had a LNR 0.1, while 9 patients (7.7%) had a LNR >0.1. In our study, a LNR >0.1 was significantly associated with smoking status (36.4% vs. 4.7%, $p<0.0001$), FIGO stage higher than IIB (13% vs. 3.2%, $p=0.048$), presence of lymphovascular space invasion (18.8% vs. 3.5%, $p=0.006$), and larger tumor size on MRI (59.71 ± 6.75 vs. 49.16 ± 16.40 mm, $p=0.009$). Moreover, a LNR >0.1 was associated with a higher recurrence rate (20% vs. 5.9%, $p=0.055$), particularly locoregional recurrence (23.1% vs. 5.8%, $p=0.027$), and with significantly worse overall survival (0% vs. 66.5%, $p<0.0001$) and 5-year progression-free survival (0% vs. 85.6%, $p<0.0001$).

Conclusion: A metastatic LNR >0.1 was associated with aggressive tumor features, higher locoregional recurrence, and poorer survival outcomes in LACC, supporting its value as a prognostic marker after chemoradiation and surgery.

Prognostic Factors and Impact of Multimodal Treatment on Progression-Free Survival in Node- Positive Gastric Cancer

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Background: This study aimed to identify clinical, therapeutic and histological factors associated with recurrence in node-positive gastric cancer (GC)

Methods: A retrospective study included patients undergoing curative gastrectomy for histologically node-positive GC at Salah Azaiez Institute (2005–2023). Clinicopathological, surgical, histological, recurrence, and survival data were analyzed. Factors associated with PFS were assessed using the Kaplan–Meier method.

Result: A total of 150 patients (median age: 61 years, range: 25–85) were included. Neoadjuvant chemotherapy (NADJ CT) was administered in 20% of cases. Total and partial gastrectomy were performed in 53.3% and 46.7% of patients, respectively, with D2/D2+ lymphadenectomy achieved in 62.7% of cases. Complete (R0) resection was achieved in 88.7% of patients. Adjuvant irradiation (ADJ RT/CTRT) was delivered in 40.7% of cases and adjuvant CT (ADJ CT) in 26%. After a mean follow-up of 28.80 months, recurrence occurred in 41.3%, with a 5-year PFS of 46.6%. Reduced PFS was significantly associated with stenosing tumors (33.6% vs 51.7%; $p=0.006$), elevated CA19-9 (31.7% vs 47.1%; $p=0.021$), tumor size >50 mm (50.5% vs 64.4%; $p=0.006$), advanced pT stage (20.4% in pT4, 49.4% in pT3, 62.5% in pT2, 64.9% in pT1; $p<0.0001$), NMLN >5 (36.7% vs 54%; $p=0.009$), LNR >25% (39.7% vs 54%; $p=0.011$), UICC stage III–IV (40.5% vs 62.9% in I–II; $p=0.004$), positive margins (24.8% vs 49.4%; $p=0.008$), LVI (5.5% vs 86.4%; $p<0.0001$), and PNI (8.2% vs 89.2%; $p<0.0001$) and poorly differentiated/undifferentiated tumors (54% vs 81.2%; $p<0.0001$). Regarding treatment, 5-year PFS was lower without ADJ RT/CTRT (38% vs 55.8%; $p=0.038$). In patients with NRLN 15 LN, ADJ RT/CTRT achieved higher PFS than ADJ CT or surgery alone (80% vs 29.6% vs 0%, respectively; $p=0.020$). Similarly, among patients treated with upfront surgery, ADJ RT/CTRT was associated with better PFS compared with ADJ CT or surgery alone (54.5% vs 39.7% vs 25%, respectively; $p=0.045$). In poorly differentiated/undifferentiated tumors, NADJ CT improved PFS versus upfront surgery (62.8% vs 15.5%; $p=0.017$).

Conclusion: Node-positive GC carries a high recurrence risk driven by advanced pathological features. ADJ RT/CTRT and NADJ CT may improve PFS in selected high-risk subgroups, particularly patients with limited NRLN, upfront surgery, or poorly differentiated tumors.

Association between hormone receptor profile and clinicopathological features of breast cancer: a 2018 population-based study in Northern Tunisia

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Introduction: Breast cancer is biologically heterogeneous, and receptor profiling shapes prognosis and treatment choices. The objective of this study was to describe hormonal receptors, and to assess the association of receptor status with stage at diagnosis and histological tumor size.

Methods: The Northern Tunisia Cancer Registry was the source of data of this study. Data collection, coding, and check followed the international recommendations of the International Agency for Research on Cancer (IRAC). We used the Khi square test and the exact of Fisher to compare between percentages.

Results: Regarding the distribution of hormonal receptors, 77.5% of cases had estrogen receptor positive (ER-positive),

and 70.1% were progesterone receptor positive (PR-positive). HER2 status was positive in 30% and 13.7% of cases showed Ki-67 proliferation index classified as low (10%) in 19.4%, intermediate (between 10 and 20%) in 18.5%, and high (>20%) in 62.1% of cases. The study of the association between the RE, RP and HER receptors and age groups did not show any significant difference. However, a significant difference was observed between all hormonal receptors according to the grade and the extension with $p < 0.001$. In fact, ER positive receptors were more frequently observed in local (45.8%) and regional stages (41.9%). Also, PR-positives were more expressed in local and regional stages with respectively 45.8% and 42.2%; $p < 0.001$. As for HER2, it was equally observed in localized and regional stages in 43.1% for each one. Concerning Ki67 proliferation there was no significant difference according to the extension. According to the grade, both ER and PR positive receptors were more frequent in grade 2 and 3 with respectively 61% and 24%. Also HER was more observed in moderately undifferentiated grade with 53.0% and 38.3%.

Conclusion: Results of the current study showed that hormonal receptor expression was most frequently observed in local stages and undifferentiated grade however there was no significant difference according to the age group.

Predictors of Patient and Healthcare System Delays in Colorectal Cancer Diagnosis: A Retrospective Cohort Study

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Background: In Tunisia, colorectal cancer (CRC) is the third most common malignancy, with over 4,000 estimated cases in 2024. Along with its high incidence, delayed diagnosis remains a major challenge; approximately 25% of cases are already metastatic at presentation according to the north Tunisia cancer registry. This diagnostic latency is driven by both patient-related barriers and healthcare system inefficiencies. This study aimed to determine diagnostic intervals for CRC and identify the factors associated with diagnostic delays among patients treated at the Salah Azaiez Institute (SAI) in 2025.

Methods: This was a retrospective cohort study conducted at the SAI in 2025. To accurately analyze timelines, specific clinical intervals were defined using standard consensus thresholds. Patient Delay (PD) was defined as the time elapsed from the onset of the first symptom to the first medical consultation, with a period exceeding three months classified as a Patient-Related Delay (PRD). Healthcare System Diagnostic Delay (HSDD) corresponded to the interval between the initial medical consultation and definitive histological confirmation of CRC, where a period exceeding one month was defined as a significant delay. We performed a multivariate analysis to determine factors independently associated with different delays.

Results: Overall, a substantial proportion of the study population experienced critical timeline bottlenecks: 43.9% of patients presented with a PRD (47.0% in males vs. 40.0% in females), 46.7% experienced an HSDD (43.0% in males vs. 51.2% in females), and 44.1% suffered from an overall TD (45.5% in males vs. 42.5% in females). Multivariate analysis revealed that a lack of baseline awareness regarding symptoms (OR = 11.5; 95% CI [5.1–25.9], $p < 10^{-3}$), symptom denial (OR = 8.9; 95% CI [3.5–22.5], $p < 10^{-3}$), and initial recourse to alternative medicine

(OR = 26.8; 95% CI [3.0–237.6], $p = 0.003$) were the independent predictors of Patient-Related Delay. Conversely, HSDD were independently driven by poor coordination between physicians (OR = 170.5; 95% CI [33.1–877.8], $p < 10^{-3}$), general barriers to healthcare access (OR = 4.64; 95% CI [1.58–13.62], $p = 0.005$), specialist appointment wait times exceeding 14 days (OR = 5.03; 95% CI [1.63–15.56], $p = 0.005$), and colonoscopy scheduling intervals exceeding 14 days (OR = 3.73; 95% CI [1.09–12.77], $p = 0.036$).

Conclusion: CRC diagnostic delays in Tunisia are driven by a combination of low public symptom awareness and structural system inefficiencies. While patient education is necessary to tackle symptom denial and reliance on alternative medicine, the primary operational priority must be resolving fragmented physician coordination and reducing specialist and colonoscopy wait times through streamlined clinical pathways.

Extensive Retroperitoneal Fibrosis Revealing Small Lymphocytic Lymphoma: A Case Report

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Introduction: Retroperitoneal fibrosis (RPF) is a rare fibro-inflammatory disorder, usually idiopathic. Secondary forms related to hematologic malignancies are exceptional and may represent a diagnostic challenge. Small lymphocytic lymphoma (SLL), an indolent mature B-cell lymphoma, rarely presents with compressive manifestations. We report a case of SLL revealed by extensive RPF.

Case presentation: A 60-year-old man with Parkinson's disease presented with inflammatory low back pain and acute urinary retention. Clinical examination revealed no peripheral tumor syndrome, but abdominal distension was noted. CT scan revealed a 14 × 9 cm retroperitoneal mass encasing the aorta, renal arteries, and iliac arteries, with bilateral ureteral contact, associated with pulmonary cystic lesions and osteolytic bone lesions (Lodwick IA). Laboratory tests showed microcytic anemia (Hb: 9.5 g/dL, MCV: 76 fL) and thrombocytopenia (78 G/L). CT-guided biopsy demonstrated a small B-cell lymphoid proliferation. Immunohistochemical analysis showed positivity for CD20, CD5, and CD23, and negativity for CD10 and Cyclin D1, consistent with small lymphocytic lymphoma, thereby excluding follicular lymphoma and mantle cell lymphoma. The patient was referred to the hematology department for further management. Pre-treatment evaluation demonstrated preserved cardiac function (LVEF: 60%). Viral serologies indicated past exposure to Epstein-Barr virus (EBV) and cytomegalovirus (CMV), as well as resolved hepatitis B infection. Given the risk of hepatitis B reactivation during immunochemotherapy, prophylactic entecavir was initiated prior to treatment with six cycles of rituximab bendamustine (RB). End-of-treatment evaluation demonstrated a complete response, with disappearance of the retroperitoneal mass and only residual fatty densification.

Conclusion: This case highlights that indolent lymphomas may rarely present as extensive retroperitoneal fibrosis, emphasizing the need to consider hematologic malignancies in the differential diagnosis of RPF.

Delayed Sperm Cryopreservation in Testicular vs. Hematological Cancer Patients: A Comparative Oncofertility Study (2018–2026)

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Background: Chemotherapy-induced gonadotoxicity poses a major risk to fertility in young male cancer patients. Sperm cryopreservation prior to cytotoxic treatment is the recommended gold standard fertility preservation strategy (ASCO 2018). Hematological cancers and testicular germ cell tumors (TGCTs) are the most frequent malignancies requiring chemotherapy in young men, yet they differ substantially in their pathophysiology, surgical management, and intrinsic impact on spermatogenesis. Direct comparative oncofertility data from North African series remain scarce.

Objective: To compare demographic characteristics, lifestyle habits, cancer staging, management timelines, and sperm parameters at cryopreservation between patients with hematological and testicular cancers.

Methods: A Retrospective single-center study was conducted at the Military Hospital of Tunis, from January 2018 – to March 2026. male patients referred for sperm cryopreservation before chemotherapy were included. A total of 76 patients: 55 in the hematological group including Hodgkin lymphoma, Diffuse large B-cell lymphoma (DLBCL), follicular lymphoma, non-Hodgkin lymphoma not otherwise specified (NOS), Burkitt lymphoma, T-cell lymphoma, and multiple myeloma. and 21 patients in the testicular group including germ cell tumors, Nonseminomatous germ cell tumors (NSGCT), Pure seminoma, Testicular carcinoma, germ cell tumor NOS, liposarcoma, and paratesticular rhabdomyosarcoma. Semen samples were collected after a recommended abstinence period of 2-6 days, in accordance with WHO 2021 criteria. Variables such as age, marital status, tobacco/alcohol use, cancer type and stage, diagnosis-to-cryopreservation delay, cycle number, ejaculate volume (mL), sperm concentration ($\times 10^6/\text{mL}$), progressive and total motility (%), and number of frozen straws were analysed. All participants Cryopreservation was performed using standardized slow-freezing protocols with glycerol based cryoprotectants.

Results: Among 76 patients included, the two groups were comparable in demographic characteristics : mean age (27.0 in hematological group vs 27.8, $p = 0.762$) and lifestyle habits (smoking ~50%, alcohol ~22–24%; $p > 0.05$ for both). Hodgkin lymphoma predominated in the hematological Cancer group (72.7%), Diffuse large B-cell lymphoma (DLBCL) represented the second most frequent entity at 16.4% ($n = 9$). The remaining cases were rare and evenly distributed, each accounting for 1.8% ($n = 1$): follicular lymphoma, non-Hodgkin lymphoma not otherwise specified (NOS), Burkitt lymphoma, T-cell lymphoma, and multiple myeloma. while non-seminomatous GCTs were most frequent in the testicular cancer group (42.9%). Pure seminoma accounted for 23.8% ($n = 5$), Testicular carcinoma was identified in 9.5% of cases ($n = 2$). The remaining cases (4.8% each) included one germ cell tumor NOS, one liposarcoma, and one paratesticular rhabdomyosarcoma. Cancer stage distribution was similar (stage II: 52.7% vs. 57.1%; $p = 0.817$). Two statistically significant differences were identified: (1) Testicular cancer patients had a significantly longer median delay from diagnosis to sperm banking (38 vs. 22 days; $p = 0.011$), likely attributable to prior orchidectomy extending the pre-chemotherapy pathway; (2)

Ejaculate volume was significantly higher in the hematological group (3.16 vs. 2.39 in the other group; $p = 0.021$). sperm concentration trended lower in testicular cancer patients (median 7 vs. $40 \times 10^6/\text{mL}$) though this difference did not reach statistical significance ($p = 0.106$), likely due to the wide variability and small testicular group size. Multiple published series corroborate impaired spermatogenesis in testicular cancer, with oligozoospermia or azoospermia rates ranging from 10 to 30% at baseline. Progressive and total motility showed no significant differences, contrary to some reports suggesting greater motility impairment in testicular cancer. The number of frozen straws was equivalent between groups (mean of 5 per patient), reflecting similar semen quality at banking.

Conclusion: This study demonstrates that despite sharing a similar demographic and oncological profile, hematological and testicular cancer patients differ significantly in their pre-banking delay and ejaculate volume. Testicular cancer patients, burdened by the surgical step of orchidectomy, face longer pathways to fertility preservation. These findings highlight the need for cancer-typespecific, multidisciplinary oncofertility referral protocols to minimize delays and optimize sperm banking outcomes before gonadotoxic chemotherapy.

Advanced-Stage Marginal Zone Lymphoma: Clinical Features, and Outcomes – Experience from the Clinical Hematology Department of Farhat Hached Hospital

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Introduction: Marginal zone lymphoma (MZL) is an indolent B-cell lymphoma with a heterogeneous presentation and usually slow progression. Advanced-stage disease may nevertheless lead to significant extranodal involvement and require systemic treatment. Rituximab-based immunochemotherapy remains the standard therapeutic approach in symptomatic or disseminated forms. The objective of the study is to analyze the clinico-biological characteristics, therapeutic modalities, and outcomes of patients with MZL managed in a Tunisian referral center.

Methods: A retrospective single-center study was conducted including 20 patients diagnosed with MZL and managed in the Clinical Hematology Department of Farhat Hached University Hospital, Sousse, between January 2018 and December 2024. Epidemiological, clinicobiological, therapeutic, and outcome data were retrospectively collected and descriptively analyzed.

Results: The median age at diagnosis was 61.8 years, with a slight male predominance (M/F ratio: 1.2). The mean diagnostic delay was 10.5 months, reflecting the indolent nature of the disease. According to the Ann Arbor classification, 70% of patients had stage IV disease at diagnosis. Bone marrow involvement was the most frequent extranodal site, observed in 71% of advanced cases, followed by pulmonary and hepatic involvement. Treatment was indicated in 14 patients (70%), mainly because of advanced-stage disease or systemic symptoms. Rituximab-based immunochemotherapy, predominantly R-CHOP and Rmini-CHOP, was the main therapeutic approach. Complete response was achieved in 92% of treated patients. One patient experienced disease progression during treatment and another had early relapse after remission. At the end of follow-up, 70% of patients were alive; three deaths were recorded, including two related to lymphoma progression.

Conclusion: Our series confirms that MZL is frequently diagnosed

at an advanced stage, often with bone marrow involvement. Nevertheless, rituximab-based immunochemotherapy provided high complete response rates and favorable outcomes. These findings underline the importance of earlier diagnosis and support the need for larger multicenter studies to better optimize therapeutic strategies in this rare lymphoma.

Bacterial Infections in Acute Myeloid Leukemia Patients with Febrile Neutropenia

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Introduction: Bacterial infections are among the most frequent and life-threatening complications in patients with acute myeloid leukemia (AML) undergoing chemotherapy-induced neutropenia. Their rapid progression toward septic shock requires prompt initiation of empirical antibiotic therapy. The objective of this study is to describe the epidemiological, clinical, and microbiological characteristics of bacterial infections complicating febrile neutropenia in AML patients and to analyze the antimicrobial resistance profile of isolated pathogens.

Methods: We conducted a retrospective descriptive single-center study including AML patients treated in the Clinical Hematology Department of Farhat Hached University Hospital, Sousse, who developed febrile neutropenia secondary to clinically documented bacterial infection between January 1, 2016, and December 31, 2023.

Results: The median age was 31 years. A total of 124 bacteriological samples were collected during febrile neutropenia episodes. Neutropenia duration exceeded 10 days in all patients, and infections occurred with an absolute neutrophil count between 0 and 99/mm³ in 77% of cases. Fever was isolated in 21.8% of episodes, whereas 78.2% were associated with a documented infectious focus, predominantly digestive (26.3%). Severe infections occurred in 27.4% of cases, mainly presenting as septic shock (25.2%) or respiratory distress (15.6%). Gram-negative bacilli predominated (76.4%), while Gram-positive cocci accounted for 23.6% of isolates. *Klebsiella pneumoniae* was the most frequent pathogen (30%), followed by *Escherichia coli* (17%) and *Staphylococcus aureus* (13%). Resistance rates of *K. pneumoniae* were 55.5% to piperacillin-tazobactam and 12.9% to imipenem. *E. coli* showed high resistance to amoxicillin (66.6%). *S. aureus* resistance rates were 26.6% to oxacillin and 21% to amoxicillin, with no resistance observed to third-generation cephalosporins, piperacillintazobactam, or imipenem.

Conclusion: The epidemiology of bacterial infections in febrile neutropenic AML patients has evolved considerably over recent decades. Knowledge of local bacterial ecology and antimicrobial resistance patterns is essential for optimizing empirical antibiotic therapy and improving patient outcomes.

Dorso-Lumbar Cutaneous Burkitt Lymphoma: A Rare Case in an Immunocompetent Adult

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Introduction: Burkitt lymphoma (BL) is a highly aggressive B-cell non-Hodgkin lymphoma characterized by MYC gene translocation and deregulation on chromosome 8. Three clinical variants are recognized: endemic, sporadic, and immunodeficiency-associated. In sporadic forms, abdominal involvement is the most common presentation, whereas cutaneous localization is exceptional and usually secondary to systemic dissemination or local extension.

Case presentation: We report the case of a 41-year-old immunocompetent man with no significant medical history, presenting with a 10 cm ulcerative and proliferative dorso-lumbar mass associated with local inflammatory signs, without other features of tumor syndrome. Skin biopsy with histological and immunohistochemical analysis revealed Burkitt lymphoma expressing c-MYC and BCL6, with a Ki-67 proliferation index of 100%. PET-CT showed a hypermetabolic cutaneous-subcutaneous lesion associated with bilateral hypermetabolic axillary lymphadenopathy. Bone marrow biopsy and steal aspiration showed no evidence of marrow infiltration. Viral serologies for HIV, HBV, HCV, and EBV were negative. The disease was classified as Murphy stage II. The patient was treated according to the LMB 02 protocol (group B), starting with a COP prephase on 25/07/2025 followed by RCOPADM1 chemotherapy, Resulting in a 70% reduction of the tumor mass. End-of-treatment PET-CT demonstrated complete metabolic remission.

Conclusion: This case highlights an exceptional cutaneous presentation of BL in an immunocompetent adult. Although BL is typically aggressive and systemic, isolated cutaneous involvement may rarely occur and should be considered in the differential diagnosis of rapidly progressive skin tumors.

Experience of the Salah Azaïez Institute in the Management of Brain Metastases with Hypofractionated Stereotactic RT: Results of a Tunisian Cohort

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Introduction: Hypofractionated stereotactic radiotherapy (HFSRT) is increasingly used in the management of brain metastases (BM), particularly for large lesions, postoperative cavities, or lesions in close proximity to organs at risk.

Objective: To evaluate the clinical, dosimetric, and oncological outcomes of patients treated with HFSRT for BM at the Salah Azaïez Institute (SAI).

Methods: A retrospective single-center study including 50 patients (65 lesions) treated between March 2020 and July 2025. Treatments were delivered on LINAC X2® and Halcyon® linear accelerators (Varian Medical Systems) using DCA and VMAT techniques with CBCT-guided repositioning. Primary endpoints included local control (LC), overall survival (OS), intracranial progression-free survival (ICPFS), local progression-free survival (LPFS), and radiation

Results: Median age was 57 years (range: 30–73). The predominant primary tumors were lung cancer and breast cancer (48% and 40%, respectively). Prior whole-brain radiation therapy had been performed in 10% of patients. Lesions were intact in 64.6% of cases and postoperative in 35.4%. The most frequently used regimens were 3 × 9 Gy (43.1%) and 5 × 5.7 Gy (21.5%). Dosimetrically, the median conformity index was 1.16, median PTV coverage (V100) was 99.7%, and median maximum

dose (D2) was 105.5% of the prescribed dose. After a median follow-up of 30.9 months, the 12-month LPFS was 83.7% overall, 77.2% for intact lesions, and 95.2% for surgical cavities. Final LC was 72.3%. Median ICPSF was 12.5 months. Median OS was 26.4 months, with 12- and 24-month OS rates of 73.4% and 50.8%, respectively. Distant intracranial progression was observed in 40% of patients. Among the 26 recorded deaths, 69.2% were attributable to extracranial disease progression. Asymptomatic radiological RN was observed in 16% of patients.

Conclusion: The SAI experience confirms the feasibility, efficacy, and good tolerability of HFSRT in the management of BM. Mode DCA/VMAT techniques on LINAC X2® and Halcyon® platforms achieve excellent local control with limited toxicity, including for postoperative or large-volume lesions.

Post-Stereotactic Hypofractionated Radiotherapy Radionecrosis in Brain Metastases: Incidence and Predictive Factors

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Introduction: Radionecrosis (RN) is one of the main late toxicities of hypofractionated stereotactic radiotherapy (HFSRT) for brain metastases (BM). Identifying clinical and dosimetric predictive factors remains essential to optimize the benefit-risk ratio of treatment. Objective: To evaluate the incidence, time to onset, and predictive factors of RN following HFSRT for BM at the Salah Azaiez Institute (SAI).

Methods: A retrospective single-center study including 50 patients (65 lesions) treated between March 2020 and July 2025. Treatments were delivered on LINAC X2® and Halcyon® linear accelerators using DCA and VMAT techniques with CBCT-guided repositioning. Analyzed parameters included the conformity index (CI), healthy brain irradiated volumes (V21, V24, and V28.8 for 5-fraction regimens), and target volumes. RN was defined radiologically on multimodal MRI.

Results: After a median follow-up of 30.9 months, RN was observed in 8 patients (16%), all exclusively asymptomatic. Median time to onset was 8.5 months [IQR: 6.7–11.5]. Corticosteroid therapy was required in 62.5% of patients, while no patient required bevacizumab or neurosurgical management. Median healthy brain irradiated volumes were 7.63 cc for V21, 3.63 cc for V24, and 0.08 cc for V28.8. Furthermore, 10% of patients had received prior whole-brain radiotherapy (WBRT). The RN incidence was 50% in these patients versus 13.6% in those without prior WBRT (OR = 6.33; $p = 0.124$), suggesting a cumulative dose-volume effect on healthy brain parenchyma.

Conclusion: In our experience, HFSRT for brain metastases demonstrates an excellent tolerability profile, with RN being predominantly asymptomatic. Although no statistically significant predictive factor was identified, a history of prior whole-brain irradiation appeared associated with a higher incidence of radionecrosis, suggesting a possible cumulative dose-volume effect on healthy brain parenchyma.

Experience of the Salah Azaiez Institute (SAI): Strip Alopecia Following Hypofractionated Stereotactic Radiotherapy for Brain Metastasis – A Case Report

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Introduction: Radiation-induced alopecia is a common toxicity of brain irradiation, typically diffuse and transient. Strip alopecia represents a rare presentation, particularly following stereotactic radiotherapy. We report the case of a 47-year-old patient followed for metastatic pulmonary adenocarcinoma treated at the Salah Azaiez Institute (Tunis, Tunisia). The patient had undergone surgical resection of a solitary brain metastasis followed by postoperative hypofractionated stereotactic radiotherapy delivered on the Halcyon® platform (Varian Medical Systems) using VMAT technique with CBCT-guided repositioning. The initial course was marked by excellent radiological local control. A well-defined linear alopecia appeared early along the beam entry paths, without any associated cutaneous toxicity. In contrast to the diffuse alopecia typically observed after whole-brain irradiation, this presentation was strictly focal and concordant with the ballistic distribution of the VMAT arcs. Progressive hair regrowth was observed during follow-up, consistent with a transient radiation-induced follicular injury.

Discussion: Strip alopecia represents an unusual complication of intracranial stereotactic radiotherapy. Mode VMAT techniques may favor this focal distribution due to beam entry and exit zones. The reversibility observed in our case suggests a non-permanent follicular injury. Recognition of this rare toxicity appears important to improve patient information and optimize treatment planning.

Conclusion: Radiation-induced strip alopecia is a rare but characteristic toxicity of hypofractionated stereotactic radiotherapy. Its recognition promotes greater awareness among clinicians and patients regarding the potential focal toxicities of mode intracranial radiotherapy techniques.

Implementation of a Pilot Project for Germline Genetic Exploration of Myeloid Acute Leukemia in a North African Country

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Introduction : Over the past decades, major advances in the understanding of leukemia implementation of structured clinical pathways for detecting germline predisposition and diagnosing hereditary leukemia remains limited, particularly in low- and middle-income countries.

Objective : As part of a pilot study, the aim of our work was designed as a multidisciplinary collaborative initiative involving hematologists, pathologists, geneticists, and bioinformaticians, aiming to establish a structured national pathway for the identification and management of heredity.

Methods : We first conducted a review of international guidelines and published experiences to define a standardized diagnostic and ethical framework adapted to a low- to middle-income country context. A national expert consortium was established to define clinical and biological criteria for germline testing eligibility, including young age at diagnosis, personal or familial history of hematological malignancies and suggestive syndromic features. Germline DNA is obtained primarily from skin fibroblasts. A bioinformatics pipeline was designed for variant detection and classification according to guidelines. Patients fulfilling inclusion criteria are enrolled after informed consent, including consent for germline testing and family studies. A parent-patient trio strategy is implemented whenever possible.

Results : A national network of participating centers has been established, including tertiary hematology and pediatric departments in Tunisia. A structured patient pathway for germline investigation has been implemented, integrating clinical selection, genetic counseling, sample collection, sequencing and multidisciplinary interpretation. A predefined gene panel covering syndromic and non-syndromic germline predisposition genes has been valid. The bioinformatics pipeline is functional and allows standardized processing. The first eligible trio meeting inclusion criteria has been enrolled, and germline analysis is currently ongoing.

Conclusion : This project represents the first pilot study investigating genetic predisposition to leukemia development in Tunisia. Trio-based whole exome sequencing is a powerful method to identify germline predisposition in leukemia and addresses an important diagnostic gap. Its use in clinical practice might improve early detection, guide therapeutic decision making, aid in donor selection and promote genetic counseling. Ultimately, this approach contributes to the advancement of precision oncology and cancer interception strategies in this population. Athogenesis have largely relied on the characterization of somatic alterations. More recently, the contribution of germline mutations to the development of acute leukemia has gained increasing recognition. A growing number of germline variants associated with both familial and sporadic hematological malignancies have been reported, highlighting their clinical relevance. Revealing associated germline mutation in leukemia-patient, impacts treatment response, relapse risk, and therapeutic decision, particularly in the context of hematopoietic stem cell transplantation, where related donors are often considered. Despite this, the

Synchronous Multiple Primary Tumors with Breast and Gynecological Expression: Report of Three Cases

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Introduction : Multiple primary tumors (MPTs) are defined according to the Warren and Gates criteria by the histological malignancy of each tumor, their distinct histopathological nature, and the exclusion of metastatic spread between them. They are considered synchronous when the second tumor is diagnosed simultaneously or within six months of the first malignancy. In breast oncology, synchronous bilateral breast cancers (SBBC) are uncommon but not exceptional, with a reported incidence ranging from 1.5% to 3.5% depending on the diagnostic interval used. In gynecologic oncology, synchronous tumors of the female genital tract are rare, accounting for approximately 0.7–1.8% of gynecological malignancies, most commonly involving the endometrium and ovary. Their major

diagnostic challenge lies in distinguishing independent primary tumors from metastatic disease, a distinction with major prognostic and therapeutic implications. The aim of this study was to illustrate the diversity of presentation of synchronous tumors, highlight the role of immunohistochemistry in the diagnostic workup, and discuss their management.

Methods : We conducted a retrospective analysis of three cases managed in a tertiary gynecology and obstetrics department. The diagnosis was established through a multidisciplinary assessment integrating clinical, radiological, pathological, and immunohistochemical findings. The Warren and Gates criteria were applied to confirm multiple primary malignancies and exclude metastatic disease.

Results : Case 1: A 54-year-old woman with a family history of breast cancer presented with a left breast nodule. Imaging revealed a 4-cm mass in the upper outer quadrant of the left breast associated with axillary lymphadenopathy (BI-RADS 4C) and a contralateral lesion classified as BI-RADS 3. Core biopsy demonstrated a grade II invasive ductal carcinoma (IDC), luminal B/HER2-positive subtype, staged as T2N1M0. Following neoadjuvant chemotherapy, a right breast lesion was detected and confirmed intraoperatively. Bilateral mastectomy with bilateral axillary lymph node dissection revealed residual bilateral disease (RCB-II on the left and RCBIII on the right), leading to comprehensive adjuvant treatment. Case 2: A 60-year-old woman without a family history of cancer was diagnosed with a left-sided triple-negative IDC (T4bN1M0) and a right-sided luminal B/HER2-negative IDC identified through BI-RADS 5 microcalcifications (TONOM0). Following dose-dense neoadjuvant chemotherapy, a near-complete response was achieved, allowing bilateral breast-conserving surgery with bilateral axillary dissection. Pathological examination showed no residual invasive disease. Case 3: A 60-year-old woman previously treated in 2017 for left-sided invasive lobular breast carcinoma (luminal B, ER-positive, HER2-negative) presented with pelvic pain and postmenopausal bleeding. Workup revealed a 14-cm left ovarian mass (O-RADS 4) and an elevated CA-125 level of 107 U/mL. Total hysterectomy with bilateral salpingo-oophorectomy demonstrated three distinct pathological entities: (1) a sex cord-stromal ovarian tumor of uncertain subtype with negative inhibin staining; (2) a serous endometrial carcinoma characterized by mutant p53 expression and diffuse p16 positivity with superficial myometrial invasion; and (3) extensive para-aortic lymph node involvement by isolated tumor cells expressing cytokeratin and GATA3, with an ER-positive, PR-positive, HER2-negative immunophenotype. The morphological and immunohistochemical profile was consistent with metastatic breast carcinoma.

Discussion : These cases illustrate the heterogeneity of synchronous tumors. Risk factors associated with SBBC remain incompletely understood and include family history, younger age, lobular histology, and multifocal or multicentric disease. Management strategies vary among institutions. The third case highlights the principal diagnostic challenge in this field: differentiating multiple primary tumors from metastatic disease, a distinction associated with markedly different prognostic and therapeutic implications. Immunohistochemistry plays a pivotal role in this context. GATA3 is a highly sensitive marker of breast origin (>90%), outperforming mammaglobin and GCDFP-15, including in metastases of unknown primary origin [6]. In our patient, GATA3 positivity combined with hormone receptor expression supported a breast origin of the para-aortic nodal disease, identifying it as a metachronous metastatic recurrence of the 2017 breast cancer rather than dissemination from the gynecologic tumors. This finding substantially altered therapeutic decision-making.

Conclusion : Synchronous multiple primary tumors require a

rigorous diagnostic approach based on the Warren and Gates criteria and extensive use of immunohistochemistry. Accurate distinction between independent primary malignancies and metastatic disease is essential, as it directly influences prognosis and treatment strategies. Multidisciplinary management remains fundamental for optimal patient care.

Buschke–Löwenstein Tumor of the Vulva and Perianal Region: A Case Report and Review of the Literature

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Introduction : Buschke–Löwenstein tumor (BLT), also known as giant condyloma acuminatum, is a rare sexually transmitted disease caused by human papillomavirus (HPV), predominantly genotypes 6 and 11. It represents an uncommon but locally aggressive variant of condyloma acuminatum. The incidence of BLT is estimated at approximately 0.1% in the general population, with a higher prevalence among men. HPV infection is the principal etiological factor, transmitted mainly through sexual contact. Additional risk factors include multiple sexual partners, immunosuppression, poor hygiene, chronic inflammation, and smoking. Although histologically benign, BLT is characterized by progressive local invasion, a high recurrence rate, and a potential for malignant transformation into squamous cell carcinoma. Surgical excision remains the cornerstone of treatment and should aim for complete tumor removal. Methods We report a clinical case and review the relevant literature.

Case presentation : A 50-year-old woman with a history of type 2 diabetes mellitus and hypertension presented with a progressively enlarging vulvar and perianal mass that had evolved over several years. Physical examination revealed a large exophytic, cauliflower-like lesion involving the vulva and perianal region. The lesion was foul-smelling, friable, and measured approximately 10 cm in diameter. No palpable inguinal lymphadenopathy was detected. Cervical cytology was normal. Serological testing for HIV, hepatitis B virus, and hepatitis C virus was negative. Histopathological examination of a biopsy specimen demonstrated acanthotic and papillomatous hyperplasia consistent with Buschke–Löwenstein tumor without evidence of invasive carcinoma. The patient underwent complete surgical excision of the lesion under general anesthesia. Reconstruction was achieved without significant difficulty. Histopathological evaluation of the surgical specimen confirmed the diagnosis of Buschke–Löwenstein tumor with tumor-free resection margins. The postoperative course was uneventful. At one-year follow-up, no evidence of local recurrence was observed.

Discussion : Buschke–Löwenstein tumor is a locally aggressive proliferative lesion associated with HPV infection, particularly genotypes 6 and 11. Although histologically benign, BLT carries a substantial risk of local recurrence and malignant transformation. Therefore, histopathological confirmation is mandatory for diagnosis. Complete surgical excision with negative margins remains the treatment of choice and is essential to minimize recurrence risk. Long-term surveillance is required because recurrence may occur several years after treatment, with reported recurrence rates reaching approximately 30%.

Conclusion : Buschke–Löwenstein tumor is a rare but potentially aggressive HPV-related disease characterized by local invasiveness and a risk of malignant transformation. Management relies primarily on complete surgical excision with histologically negative margins. Careful long-term follow-

up is mandatory to detect recurrence early and improve patient outcomes.

Small Cell Carcinoma of the Ovary, Hypercalcemic Type (SCCOHT): A Case Report and Literature Review

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Introduction : Small Cell Carcinoma of the Ovary, Hypercalcemic Type (SCCOHT), is an extremely rare and highly aggressive ovarian malignancy. It typically affects young women and is most often diagnosed at an advanced stage, resulting in a poor prognosis. The disease is characterized by frequent recurrence despite multimodal treatment. We report a case of SCCOHT occurring in a young woman and review the relevant literature.

Methods : We present a clinical case managed in our department and conducted a review of the literature.

Case presentation : A 20-year-old nulligravid woman (G0P0), with no significant medical history, presented with chronic pelvic pain. Pelvic ultrasonography revealed a suspicious right ovarian mass. Magnetic resonance imaging (MRI) demonstrated a right ovarian lesion measuring 9 cm, classified as O-RADS MRI 5, associated with pelvic lymphadenopathy and a secondary peritoneal localization. Laboratory investigations revealed hypercalcemia with a serum calcium level of 2.65 mmol/L. The patient underwent primary surgical management consisting of a left adnexectomy, total hysterectomy, bilateral salpingo-oophorectomy, and pelvic and para-aortic lymphadenectomy. Histopathological examination confirmed the diagnosis of Small Cell Carcinoma of the Ovary, Hypercalcemic Type (SCCOHT). The patient subsequently received adjuvant chemotherapy with four cycles of BEP (Bleomycin, Etoposide, and Cisplatin), followed by four cycles of Paclitaxel–Carboplatin. Disease progression was documented despite treatment. A second surgical procedure was performed for tumor debulking, followed by a colostomy because of bowel involvement.

Discussion : Since its initial description by Dickersin and colleagues, SCCOHT has been recognized as a distinct clinicopathological entity. It is characterized by an aggressive clinical course, a high risk of recurrence, and poor overall survival. The diagnosis relies primarily on histopathological examination, supported by immunohistochemical and molecular analyses. In recent years, inactivating alterations of the SMARCA4 gene have emerged as a key molecular hallmark of SCCOHT, improving diagnostic accuracy and providing new insights into tumor biology. Due to the rarity of the disease, no standardized therapeutic strategy has been established. Current management generally involves aggressive multimodal treatment combining radical surgery, platinum-based chemotherapy, and, in selected cases, radiotherapy or high-dose chemotherapy with stem-cell rescue. Although several prognostic factors have been reported, including stage at diagnosis and tumor size, the overall prognosis remains poor. The rarity of SCCOHT limits the availability of prospective studies and large clinical series, making evidence-based recommendations challenging.

Conclusion : Small Cell Carcinoma of the Ovary, Hypercalcemic Type, is a rare and highly aggressive ovarian neoplasm that predominantly affects young women. Diagnosis is often delayed because of nonspecific clinical manifestations. Early recognition based on clinical, radiological, histopathological, and molecular findings is essential. Advances in molecular characterization, particularly the identification of SMARCA4 alterations, may contribute to improved diagnostic accuracy and the development of targeted therapeutic approaches in the future.

Cutaneous adverse events associated with treosulfan-based conditioning for peripheral blood stem cell transplantation

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Introduction: Treosulfan was introduced in Tunisia in 2023 as an alternative conditioning agent to busulfan for hematopoietic stem cell transplantation at the National Bone Marrow Transplant Center. Since its introduction, unusual cutaneous adverse events have been observed. This study aimed to identify the main adverse events related to treosulfan and assess their imputability in patients treated between June 2023 and September 2024 at the National Bone Marrow Transplant Center.

Methods: We conducted a retrospective descriptive study over a 15-month period, from June 2023 to September 2024, including all patients who received treosulfan as part of the conditioning regimen before a first allogeneic hematopoietic stem cell transplantation at the National Bone Marrow Transplant Center. Patients undergoing a second allogeneic transplantation, autologous transplantation, or presenting cutaneous graft-versus-host disease were excluded. All adverse drug reactions were assessed according to the French causality assessment method [1]. The seriousness of adverse events was evaluated according to World Health .

Results: During the study period, 25 patients received a treosulfan-based conditioning regimen before hematopoietic stem cell transplantation. Patients' age ranged from 8 to 53 years, with a mean age of 32.5 ± 13.4 years. Females represented 52% of the study population, with a sex ratio of F/M = 1.08. Acute myeloid leukemia was the main indication for transplantation (48%), followed by acute lymphoblastic leukemia (40%), Chronic myeloid leukemia (8%), and myelodysplastic syndrome (4%). Cutaneous adverse events were reported in 15 patients. Nine cases of cutaneous hyperpigmentation were reported. In all cases, hyperpigmentation was preceded by erythematous lesions, and in one case, skin biopsy confirmed a fixed drug eruption. Hyperpigmentation was diffuse in one case and localized in the remaining cases. The delay was ranging from 2 to 13 days after treosulfan administration. Six patients developed generalized pruritus which occurred from a few minutes to 2 days after drug administration, with rapid resolution following.

Discussion/Conclusion: In our study, nearly half of the patients developed cutaneous adverse events following treosulfan administration, indicating that skin toxicity is a relatively frequent but generally mild complication of treosulfan-based conditioning regimens. All reactions were non-severe in our series and resolved with The close temporal relationship between the cutaneous reactions and treosulfan administration and the favorable evolution support a plausible causal association. Our findings are consistent with previously published studies reporting predominantly cutaneous and mucosal toxicities with treosulfan-based conditioning regimens.

Borderline ovarian tumours: the input of ultrasound

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Objectives: The aim of this study is to evaluate the contribution of ultrasonography in the diagnosis and management of borderline ovarian tumours (BOT).

Methods: A retrospective descriptive cross-sectional study, conducted in the department of gynecology and obstetrics of Ben Arous hospital over a period of ten years. We included all women with a histologic diagnosis of BOT who had undergone preoperative ultrasound examination.

Results: 60 cases of borderline ovarian tumours were reported in our study. The mean age of patients was 43 years [21-61]. The ovarian mass was unilateral in 82% of cases with an average size of 98mm. The size of the tumour exceeded 10 cm in 48% of patients. A solid or mixed aspect of the tumour was noted in 75% of patients. A pure cystic aspect was seen in 25% of cases only. Papillary projections and septa were observed on ultrasound in 78% of the patients. Doppler flow was studied in all patients; the mass was vascularised in 63% of cases. More than four ultrasonographic criteria of malignancy were associated in 40% of patients. 20% of patients had four criteria. The cumulative percentage line on the Pareto chart shows that the combination of the following ultrasound signs: The existence of papillary projections as well as septa, the presence of a solid component and Doppler vascularity, allowed to predict the diagnosis in at least 60% of the tumours. The average tumour size was significantly larger for Mucinous- BOT (16.6 cm versus 9.7 cm). All solid tumours were Serous-BOT as well as 67% of purely cystic tumours. The mixed tumours were more or less equally divided between S-BOT (55%) and M-BOT (45%). Papillary projections and vascularisation were more common in S BOT (54% versus 47% and 55% versus 45%) while septa and ascites were more prominent in M-BOT (57% versus 43% and 52% versus 48%).

Conclusions: Borderline ovarian tumours are difficult to diagnose preoperatively. Ultrasound remains the first-line investigation for the exploration of ovarian tumours. Ultrasound pattern recognition by an expert examiner can be an excellent tool for the diagnosis as well as the management of borderline ovarian tumours.

PREGNANCY ASSOCIATED BREAST CANCER: ABOUT 10 CASES

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Introduction/Background : Pregnancy-associated breast cancer (PABC) is defined as breast cancer diagnosed during pregnancy or in the first postpartum year. While it is relatively uncommon (occurring in 1 per 3000 pregnancies), it represents a challenge to both the patient and the multidisciplinary team. We ought in this study to describe, the clinical, paraclinical and management of pregnancy associated breast cancer.

Methodology : we conducted a retrospective single-center cohort study of 10 patients diagnosed and treated for breast cancer during pregnancy between 2008 and 2024 in the obstetric and gynecology department of Ben Arous hospital.

Results : Five patients were diagnosed during the second trimester, 3 during the first trimester and 2 in the postpartum period. A suspicious area was detected by ultrasound in 10 of 15 women. A recurrent abscess was present in 2 cases and the biopsy revealed the cancer. Five patients had positive hormone receptors and 7 sub expressed. One patient was in stage 0, 2 in stage 1, 2 in stage 3 and 5 in stage 4. Three patients decided voluntarily to legally terminate their pregnancies. Seven patients were treated with chemotherapy during pregnancy

after the second trimester using anthracycline-based treatment. Three patients had gestation-related complications including preterm labor, intrauterine growth restriction dyspnea and chemotherapy related granulocytopenia .

Conclusion: pregnancy associated breast cancer is a rare entity. It is associated with a high number of complications. A multidisciplinary approach is needed and patients should be an integral part of therapeutic decisions.

Sexual dysfunction after breast cancer surgical treatment: comparative study among Tunisian women

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Introduction : When treating breast cancer, the choice between conservative and radical surgery can significantly impact a woman's physical and emotional well-being. While both approaches aim to achieve optimal cancer control, their effects on body image, self-esteem, and sexual health can vary considerably. Comparing the impact of these surgical approaches on sexuality is crucial to understanding how treatment decisions affect long-term emotional and psychological health in breast cancer survivors.

Objectives : we aimed in our study to compare sexuality after breast cancer surgery (radical versus conservative) and determine sexual dysfunction in women treated for breast neoplasm.

Methods : we included in our study women younger than 60 years old, operated for breast cancer and followed up in our outpatient clinic after adjuvant treatment. All the patients without a sexual partner were excluded from our study. Our patients were divided into two groups: Group A who underwent a mastectomy and group B having a conservative surgery. The sexuality was assessed using a questionnaire exploring the qualitative aspects of sexual life and Female Sexual Function Index (FSFI): a score including 6 domains of sexual life adapted and valid in Arabic. A sexual dysfunction is defined by a FSF<26.55. All our patients gave their consent before responding to our survey. Statistical analyses were performed using Excel.

Results : We enrolled in our study 60 patients. The mean age was 46.5 years old. Fifty six percent were menopausal. Twenty-three patients had a conservative surgery and 27 underwent mastectomy with oncoplastic surgery just in 3 cases. After surgery, seven patients reported sexual abstinence, they were all from the group A. The main complains of patients of Group A were about desire (70.3%), excitation (62.9%) and disturbance of body image leading to decreased self esteem (81,4%) while in Group B, patients complained about dyspareunia (43.47) vaginal dryness (65.2%) this was due to adjuvant treatments. According to FSFI, the mean score was 17.3+/-5.6 in Group A and 23,3+/-8.2 in Group B. All The domains were affected in group A while the most ones in Group B were lubrication, desire and pain. A sexual dysfunction was found in 92.59% of patients of group A and 56.5% of cases in group B. All the patients revealed that there wasn't a communication about sexuality neither in family or with partner nor with health care providers.

Conclusion : The physical changes Resulting from treatments for breast cancer negatively impact women's quality of life, notably their sexual life, by causing sexual dysfunctions affecting various aspects of sexuality. The health care providers should be aware of this aspect of life and discuss it with the patients during treatment.

GESTATIONAL TROPHOBLASTIC NEOPLASIA: MULTIMODAL APPROACH TO DIAGNOSIS AND TREATMENT

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Introduction/Background: Gestational trophoblastic neoplasia (GTN) is a rare entity. The diagnosis is difficult and based on histological and HCG assays. We report 15 cases of GTN diagnosed at our department.

Methodology : We included all patients that fulfill the FIGO criteria of GTN over a period of 18 years.

Results : We registered 15 cases of GTN over 18 years. Transvaginal sonography (TVS) revealed an enlarged uterus in 8/15 cases. In one of the 2 cases of Placental site trophoblastic tumor (PSTT), it revealed a well-circumscribed echogenic lesion, the patient was misdiagnosed with uterine fibroma. In the case of invasive mole (IM), the TVS showed intrauterine mass with cystic spaces and signs of myometrial invasion. The invasion has been suspected in the 2 cases of PSTT, the IM and 3 of 9 patients diagnosed with persistent trophoblastic disease (PTD). The biological features were mainly an increased level of HCG. The level exceeded 100000 in 7/9 PTD and in the case of IM. All patients diagnosed with PSTT and choriocarcinoma (CCG) had low values. Lung CT scans showed metastatic nodules in 4 cases but only one patient had visible nodules on the traditional chest X-ray. Five patients received multi-agent chemotherapy, six had single agent chemotherapy, hysterectomy was performed for the patients with PSTT. The overall survival rate was 100%.

Conclusion: The improvement of survival for patients with gestational trophoblastic neoplasia is based on early identification. Transvaginal sonography and HCG remain the tools of choice for initial diagnosis.

Scrotal sarcoma: from histological complexity to multidisciplinary therapeutic strategies

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Introduction: Scrotal sarcomas are rare mesenchymal tumors, characterized by great histological diversity and variable prognosis. Their therapeutic management is based on a multimodal strategy, dominated by surgery, associated with adjuvant treatments such as chemotherapy, depending on the histological subtype and risk of recurrence.

Observations: We report three cases of scrotal sarcomas managed in our institution: Case 1: Myxoid liposarcoma in a 65-year-old patient. After neoadjuvant chemotherapy with anthracyclines (adriamycin), complete surgical excision was performed. The course was marked by a 7-year survival, with the patient subsequently dying from a cardiac condition. Case 2: Scrotal leiomyosarcoma in a 59-year-old patient. The treatment consisted of surgery followed by chemotherapy with anthracyclines. Case 3: Dedifferentiated liposarcoma in a 52-year-old patient. Complete surgical excision was performed, followed by chemotherapy based on anthracyclines.

Discussion: These observations illustrate the histological heterogeneity of scrotal sarcomas, which requires individualized management. Surgery with curative intent is the reference treatment. Chemotherapy with anthracyclines, although nonspecific, can be proposed in an adjuvant or neoadjuvant setting, particularly for aggressive subtypes or those at high

risk of recurrence. A multidisciplinary approach, including oncologists, surgeons, pathologists, and radiologists, is essential to optimize the therapeutic strategy and prognosis of these rare tumors.

Conclusion: Scrotal sarcomas represent a clinical challenge due to their rarity and histological heterogeneity. Coordinated multidisciplinary management is essential to improve care for these patients and to define appropriate therapeutic strategies. **Keywords:** Scrotal sarcoma, mesenchymal tumor, histological heterogeneity, surgery, chemotherapy, multidisciplinary management, prognosis.

BORDERLINE OVARIEN TUMOR MANAGEMENT IN A TUNISIAN HOSPITAL

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Introduction/Background : The aim of this study was to determine the epidemiology and clinicopathological characteristics of the borderline ovarian tumors (BOTs). Additionally we sought to characterize the outcomes of the borderline ovarian management and identify variables affecting survival.

Methodology : A retrospective study of 49 patients with BOTs all stages taken together, treated or referred to our institutions was conducted over a period from June 2016 to July 2021. Data was analyzed by using SPSS Statistics for Windows, Version 23.0.

Results : The median age was 43.3 (range=21–61) years. The majority of BOTs was serous tumors (61.2%) followed by mucinous tumors (36.7%) and less common histotypes as Endometrioid borderline tumours (2.1%). In the case of 34 patients (66.7%) a frozen section was taken intraoperatively which matched the definitive histological Result in 80.5%. BOTs are mainly diagnosed at an earlier stage (34 cases at FIGO stage IA) 8 patients at stage IB and 3 patients at stage IC on the other hand 2 patients at stage IIIB and finally 2 patients at stage IIIC. All patients underwent surgery. We performed conservative treatment in Nineteen patients (38.7%). It consists of ovarian cystectomy and unilateral adnexectomy . Thirty patients (61.2%) underwent radical treatment which consist of bilateral adnexectomy and hysterectomy. Three patients with BOTs staged IIIB and IIIC received adjuvant chemotherapy. During an average follow-up of 5 years 4 patients developed tumor recurrence .

Conclusion : Borderline tumours usually affect young women aged between 20 and 40. They are usually diagnosed at an early stage (stage-I disease) . Prognosis is generally excellent, and long-term risk of recurrence is low.

Value of pelvic ultrasound in the suspicion of uterine sarcoma : A retrospective series of 5 cases in Tunisia

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Introduction: Uterine sarcomas are rare, making up less than 5% of all uterine cancers . The problem is that before surgery, they often look just like benign fibroids. This leads to mistakes – like morcellation – which can spread the tumour inside the abdomen . Pelvic ultrasound is usually the first exam we do when we find a uterine mass. Some signs on ultrasound, such as a heterogeneous look, necrotic areas, or chaotic blood

flow on Doppler, can point to a malignant tumour. But in our Tunisian setting, we don't really know how reliable these signs are . That's why we decided to look back at our own cases and see how helpful ultrasound really was in suspecting uterine sarcoma.

Objective: We wanted to see how often pelvic ultrasound helped raise suspicion of uterine sarcoma before surgery, based on a small series of 5 Tunisian cases.

Methods: We reviewed the records of 5 women treated in our gynaecology department between January 2020 and December 2025. All of them had a confirmed uterine sarcoma and had a pelvic ultrasound before surgery. We looked at: uterine size, whether the mass looked uniform or not, presence of necrotic areas, Doppler flow pattern (chaotic or not), resistance index, tumour borders (sharp or blurry), and whether the radiologist actually wrote "suspected sarcoma" in the report.

Results: The women were 52 years old on average (range 38–67). Histology showed: 3 leiomyosarcomas, 1 mixed Müllerian tumour, and 1 endometrial stromal sarcoma. The average uterine size was 13.4 cm (10–18 cm). All 5 tumours (100%) looked heterogeneous on ultrasound. Four (80%) had necrotic areas. Chaotic Doppler flow with a low resistance index (<0.40) was seen in 4 cases (80%). Blurred or infiltrative borders were noted in 3 cases (60%). Interestingly, the radiologist explicitly mentioned "suspected sarcoma" in only 2 cases (40%). In 2 other cases (40%), the report said "indeterminate tumour", and in 1 case (20%) it was called an "atypical fibroid". That last case turned out to be a low-grade endometrial stromal sarcoma.

Discussion: In our small series, ultrasound demonstrated signs suggestive of malignancy (heterogeneity, necrosis, and hypervascularity) in 80% to 100% of cases. However, the specific diagnosis of sarcoma was explicitly mentioned in only 40% of the radiology reports. This discrepancy may be explained by the rarity of uterine sarcomas and their sometimes misleading appearance on imaging, particularly low-grade endometrial stromal sarcomas, which can closely resemble benign fibroids. According to the literature, the most reliable predictors of sarcoma are the presence of necrotic areas combined with chaotic Doppler flow, with a reported sensitivity ranging from 70% to 90% . Nevertheless, one of our cases had no visible necrosis on ultrasound but was still confirmed as a sarcoma. Therefore, the absence of necrosis should not rule out malignancy. Pelvic magnetic resonance imaging (MRI), which was not performed in all of our patients, might have provided better lesion characterization and increased diagnostic accuracy. The main limitations of our study are the small sample size and its retrospective design, which warrant cautious interpretation of the findings.

Conclusion: Pelvic ultrasound is a good place to start. If you come across a large, mixed-looking mass with necrotic spots and crazy blood flow on Doppler, you should definitely think about sarcoma. But let's be honest – ultrasound alone isn't specific enough to make the call. So when you see those warning signs, we strongly suggest ordering a pelvic MRI to get a clearer picture. And most importantly, avoid morcellation during surgery. **Keywords :** Uterine sarcoma, pelvic ultrasound, diagnosis, Doppler, Tunisia

Prognostic factors of uterine sarcoma: a retrospective series of 6 Tunisian cases

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Introduction: Uterine sarcomas are rare, making up less than 5% of all uterine cancers. But they're aggressive. Patients

don't do well overall – high recurrence rates, limited survival. We know from the literature that things like age, FIGO stage, histology, grade, surgery quality, and adjuvant treatment can affect prognosis. But here in Tunisia, we don't have much data from small series. So we wanted to look at our own cases and see what really matters for survival in our setting.

Objective: We wanted to identify which factors – age, FIGO stage, histology, adjuvant treatment – actually influence survival in patients with uterine sarcoma. We based this on a small retrospective series of 6 Tunisian cases.

Methods : We went back through our records in our gynecology department between January 2021 and December 2025. We found 6 women with confirmed uterine sarcoma. We looked at: age (under 50 vs 50 or over), FIGO stage (I-II vs III-IV), histology (leiomyosarcoma vs other types), and whether they had adjuvant radiotherapy or chemotherapy. Our main measure was 2year .

Results : The average age was 51 years (range 34–69). Histology: 3 leiomyosarcomas, 2 mixed Müllerian tumours, and 1 endometrial stromal sarcoma. Four patients had stage III disease, and 2 had stage IV. Two years overall survival was 66.7% – that means 4 out of 6 were alive at 2 years. All 3 patients under 50 survived to 2 years (100%), but only 1 out of 3 older patients did (33%). Stage III gave 75% survival (3 out of 4), while stage IIIV gave 50% (1 out of 2). Leiomyosarcomas had 66% survival – the same as the other types (66%). Adjuvant radiotherapy didn't change survival: 66% with radiotherapy vs 66% without. Adjuvant chemotherapy actually seemed worse: 50% survival with chemo vs 75% without, but the numbers are tiny.

Discussion : In our small group, age really stood out. All the younger women (under 50) were alive at 2 years, but only a third of the older ones made it. That matches what the literature says – older age means worse prognosis . FIGO stage also mattered: localised tumours (stage III) did much better than advanced ones – no surprise there . But histology didn't seem to make a difference in our series, unlike some studies that say endometrial stromal sarcoma has a better outlook . As for adjuvant treatments – radiotherapy and chemotherapy – we didn't see any clear benefit. But honestly, with only 6 patients, it's hard to draw Conclusions. The treatment wasn't standardised either. So the main limitations are the small number of cases, the retrospective design, and the lack of uniform treatment protocols.

Conclusion : In this limited series, age and FIGO stage looked like the main prognostic factors. Younger women (<50) and those with localised tumours (stage III) had better survival. Histology and adjuvant treatments didn't show a significant impact – probably because our sample was too small. We really need larger, multicentre studies in Tunisia to confirm these findings.

Impact of Molecular Classification on Adjuvant Therapeutic Decisions in Early-Stage Endometrial Cancer

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Introduction: For a long time, the selection of adjuvant treatment in endometrial cancer was limited to classic clinico-pathological criteria (FIGO stage, histology, grade, lymphovascular space invasion). However, these parameters sometimes lack accuracy in predicting recurrence and avoiding over- or under-treatment. The routine integration of molecular classification now allows

for a more refined prognostic stratification. The objective of our study was to evaluate the impact of this molecular profile on adjuvant therapeutic decisions.

Methods: This is a retrospective study including 21 patients treated within the Department of GynecologyObstetrics and the Department of Radiation Oncology at the Farhat Hached Hospital in Sousse, from October 2024 to April 2026.

Results: The mean age of the patients was 59 years. The predominant histological type was endometrioid adenocarcinoma, found in 71.4% of patients, and 47.6% had grade 1 tumors. All patients underwent complete surgery. 81% of patients presented with FIGO 2023 stage I disease and other patients with stage II. Only four patients underwent POLE mutation testing, and all were wild-type (non-mutated). A p53 protein mutation was found in 11 patients (52.3%). Five patients had a mismatch repair-deficient (MMRd / MSI) profile, and a non-specific molecular profile (NSMP) was observed in five patients. The 17 patients who could not undergo POLE testing (due to current unavailability in most hospitals) could have avoided adjuvant treatment had they presented a mutated POLE profile. This highlights the primary objective of our study, which demonstrates the critical importance of POLE testing for optimized adjuvant therapeutic management in endometrial cancer.

Conclusion: The integration of molecular classification significantly modifies the adjuvant management of endometrial cancer. Identifying MMR and p53 profiles, complemented by hormone receptor status and particularly POLE status, overcomes the limitations of standard histological criteria alone. This biomarker-driven approach offers a major opportunity for therapeutic de-escalation in favorable profiles (POLE-mutated).

ADCs in HER2-positive metastatic breast cancer: access barriers and clinical outcomes in a limited resource setting

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Background: Antibody-drug conjugates (ADCs) have improved the therapeutic landscape of HER2-positive metastatic breast cancer (mBC). However, in a limited resource setting, drug availability remains a major challenge. We aimed to evaluate clinical outcomes and impact of treatments gaps in this context.

Methods: In this retrospective case series, we evaluated the efficacy and safety of ADCs in HER2positive mBC patients treated at the Medical Oncology Department of Taher Maamouri hospital (Nabeul, Tunisia).

Results: Ten patients were included with a median age of 50 years (range 36-60). At diagnosis, 50% had de novo metastatic disease. Common metastatic sites included lung (40%), bone (40%) and brain (20%). Following 1st line therapy (trastuzumab + pertuzumab 60%, trastuzumab 30%, lapatinib 10%), the median PFS was 12 months (range 5-25). Due to limited ADCs accessibility, 4 patients received capecitabine as bridging therapy (median 4.5 months) before starting 2nd line (2L) treatment. Overall, 6 patients received T-DM1 and 6 received T-DXd (including 2 sequential cases).T-DM1 was used in 2L (n=5) and 3L (n=1) with a median of 8 cycles (3-23). In the 2L setting, the disease control rate was 100% (partial response = 1; stable disease = 4). Median PFS was 11 months in 2L and 4 months in 3L. The most common adverse event was G1/2 thrombocytopenia.T-DXd was administered in 2L (n=4) and 3L (n=2) with a median of 7 cycles (4-19). In the 2L setting, the best objective response was partial response (n =2) and stable disease (n=2). Notably, three patients faced a 6-month treatment

discontinuation due to T-DXd unavailability: all three presented CNS progression during this period. Median PFS was 7 months in 2L and 12 months in 3L. No G3/4 toxicity was reported. Overall, seven patients are alive and still under treatment with ADCs. Median OS was 37 months (19-56 months).

Conclusion: ADCs demonstrate robust real-world efficacy in HER2+ mBC even after bridge therapy. However, the 100% CNS progression during treatment gaps indicates that continuous inhibition of HER2 is essential to prevent brain relapses and to maintain survival benefits.

Assessing the Burden and Safety of Cancer Patients Supplying Their Anticancer Treatments on their own

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Introduction: In Tunisia, the National Health Insurance Fund (CNAM) covers a range of anticancer treatments; however, patients are often required to personally collect and transport their medications from designated pharmacies rather than receiving them directly from the hospital pharmacy. This practice raises concerns about logistical burden, financial impact and medication safety.

Aims : Our study aims to characterize and quantify the burden and safety of supplying the anti cancer treatment among cancer patients.

Methods: We conducted a cross-sectional study at the Medical Oncology department in the university hospital center (UHC) Farhat Hached of Sousse .We included cancer patients receiving CNAM-covered anticancer treatments, predominantly collected from the polyclinic SousseKhezama.Data were collected on demographics, cancer type, treatment modality, logistical burden (transport,time,trip frequency), financial impact and safety perceptions regarding medication handling and storage.

Results: A total of 62 patients were included. Median age was 53 years [16-75] with a female predominance (58.1%). Most patients resided in Sousse (51.6%), followed by Kairouan (16.1%) and Kasserine (14.5%).Breast cancer patients were predominant (32.3%) followed by Colorectal cancer (21.2%) and prostate cancer (8.1%).Nearly all patients reported personally supplying their own treatments. The majority of them (77.4%) relied on a family member or friends to collect their medications. Most patients made 12 trips per month. The burden on daily life was considerable: 72.6% of patients reported a significant impact (sick leave, family disruption), while 27.4% reported moderate impact (fatigue, management issues). Notably 77.4% of patients reported having delayed or missed a treatment session due to difficulties obtaining medication.Additional monthly expenses were reported across all patients. Unreimbursed expenses were rated significant by 48.8% and financial concern was expressed by all patients. Additionally, 35.5% reported having been obliged to purchase treatment while waiting for CNAM approval.Compliance with storage requirements was self-reported as difficult by 41.9%. Exactly half of the patients (50%) reported having worried that a medication was improperly stored or expired. Only 14.5% had formally reported a medication-related issue. Regarding overall safety, 51.6% felt somewhat worried, 38.7% felt fairly safe, and 9.7% felt very worried. The primary perceived risks of self-supply were treatment delay (40.3%), medication damage (38.7%), and administration error (21.0%).All patients (100%) expressed a preference for a hospital-based medication supply model over the current patient-supply system.

Conclusion: Our Study has shown that Tunisia's current

system where cancer patients must get their anticancer drugs themselves through polyclinics, creates financial and management issues . Based on these Results, we recommend changing the policy, so hospitals provide all CNAMcovered anticancer drugs. This would reduce the burden on patients and make treatment safer and more available.

Predictive factors of pathologic complete response in triple-negative breast cancer: A regional experience from Cap-Bon, Tunisia

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Introduction : Triple-negative breast cancer (TNBC) is an aggressive and heterogeneous subtype characterized by a dismal prognosis. Achievement of pathologic complete response (pCR) after neoadjuvant treatment is strongly associated with improved survival. The aim of this study was to identify clinicopathological predictors of pCR in patients with TNBC in the Cap-Bon region.

Methods : This retrospective study, conducted at the Medical Oncology Department of Taher Maamouri Hospital, included all patients diagnosed with stage II-III triple-negative breast cancer who received neoadjuvant treatment followed by surgery. Clinical and pathological characteristics were analyzed. pCR was defined as the absence of invasive residual disease in the breast and lymph nodes (ypT0/is ypN0). The assessment of predictive factors for pCR was performed using Fisher's exact test for categorical variables and the Mann-Whitney test for continuous variables.

Results : A total of 51 patients were included (median age 50 years; range 27-74). Patients presented with T2, T3, and T4 tumors in 45%, 23% and 27% respectively. Clinical node involvement was found in 59% of cases. Tumors were mainly SBR grade 3 (88%) and Ki67 was > 50% in 67% of cases. Mitotic count was available for 36 patients with a median of 19 (range 2-74). All patients received neoadjuvant chemotherapy combining anthracyclines (100%) and taxanes (98%). Three patients received additional treatment with carboplatin and pembrolizumab. The overall pCR rate was 33.3% (n=17). No significant associations were found between pCR and age (p=0.9), T-stage (p=0.7), N-status (p=1), stage II/III (p=0.7), SBR grade (p=1) and ki67 (p=0.6). However, a trend toward significance was observed for mitotic count which was higher in the pCR group (mean rank 21 vs 15; p=0.1).

Conclusion : Our Results were aligned with previous studies regarding the pCR rate (33.3%). The lack of significance for classic clinicopathological features (age, T, N, grade) could be explained by the small sample size, the lack of TILs and germline BRCA testing, and the intrinsic biological heterogeneity of TNBC. However, a high mitotic count emerged as a potential predictor of chemosensitivity.

Impact of Tumor Size on Clinicopathological Characteristics and Survival Following Curative Resection for Gastric Adenocarcinoma

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Aim: To evaluate the prognostic impact of tumor size on clinicopathological features and overall survival (OS) in patients undergoing curative resection for gastric adenocarcinoma.

Methods: We retrospectively reviewed patients with gastric adenocarcinoma who underwent curative surgical resection at the Salah Azaiez Institute between January 2005 and December 2023. Receiver operating characteristic (ROC) curve analysis was used to determine the optimal tumor size cutoff based on maximum tumor diameter. Patients were subsequently classified into large-sized tumor (LST) and small-sized tumor (SST) groups. Clinicopathological characteristics and 5-year OS were compared between the two groups. Survival analysis was performed using the Kaplan–Meier method, and 5-year OS was further analyzed according to pT and pN stages.

Results: A total of 195 patients (mean age, 61.5 ± 13.9 years) were included. Neoadjuvant chemotherapy was administered in 22.6% of cases. Total and partial gastrectomy were performed in 49.7% and 50.3% of patients, respectively. Combined organ resection (COR) was required in 21% of cases, and D2/D2+ lymphadenectomy was performed in 64.6%. The mean tumor size was 62.1 ± 34.1 mm, with a median size of 55 mm. ROC curve analysis identified 45.5 mm as the optimal cutoff value for tumor size, yielding a sensitivity of 75.8% and a specificity of 46.2% (AUC = 0.597; 95% CI: 0.517–0.677; $p = 0.019$). Based on this threshold, 125 patients (64.1%) were classified as having large-sized tumors (LSTs; ≥ 45.5 mm) and 70 (35.9%) as having small-sized tumors (SSTs; < 45.5 mm). LSTs were significantly associated with elevated CA 19-9 levels (89.5% vs. 62.0%, $p = 0.020$), moderate or poor tumor differentiation (69.7% vs. 55.3% for well-differentiated tumors, $p = 0.040$), lymphovascular invasion (74.0% vs. 54.5%, $p = 0.005$), perineural invasion (74.0% vs. 54.5%, $p = 0.005$), deeper tumor invasion (68.1% in pT3/T4 vs. 53.7% in pT1/T2, $p < 0.0001$), lymph node metastasis (68.7% vs. 48.9%, $p = 0.015$), advanced nodal stage (48.9%, 56.8%, 67.4%, and 76.1% for pN0, pN1, pN2, and pN3, respectively; $p = 0.020$), a higher mean number of metastatic lymph nodes (8.42 ± 10.04 vs. 3.99 ± 5.60 , $p < 0.0001$), and a higher metastatic lymph node ratio ($p = 0.005$). In addition, patients with LSTs were more likely to undergo total gastrectomy (75.3% vs. 24.7%, $p = 0.001$) and COR (80.5% vs. 19.5%, $p = 0.014$), and more frequently required perioperative transfusion of 3 units of packed red blood cells (76.3% vs. 23.7%, $p = 0.008$). Patients with LSTs had significantly poorer oncological outcomes, with a lower 5-year OS rate (33.7% vs. 61.2%, $p = 0.011$) and a higher recurrence rate (77.8% vs. 56.1%, $p = 0.002$). Subgroup analysis demonstrated that the adverse prognostic impact of LSTs was confined to patients with advanced disease, with significantly lower 5-year OS rates observed in those with pT3/T4 tumors (31.6% vs. 70.1%, $p = 0.001$) and pN2/N3 nodal involvement (21.1% vs. 59.3%, $p = 0.012$). In contrast, no significant differences in 5-year OS were found between LST and SST groups among patients with pT1/T2 tumors or pN0/N1 disease ($p > 0.05$).

Conclusion: Tumor size ≥ 45.5 mm is associated with adverse clinicopathological features, more extensive surgical procedures, and poorer oncological outcomes in gastric adenocarcinoma. Large-sized tumors are associated with significantly reduced overall survival, particularly in patients with advanced pT and pN stages. Tumor size may therefore represent a simple and useful prognostic marker for risk stratification after curative resection.

First Epidemiological and Therapeutic Characterization of a Cancer Cohort in Gabes City: A Unicenter Retrospective Study of 426 Patients

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Introduction : Cancer remains a major public health challenge, with lung, breast, and colorectal cancers representing the most prevalent malignancies in clinical oncology practice. Comprehensive epidemiological and clinical profiling of cancer patients in real-world settings is essential to identify gaps in care and optimize therapeutic protocols. This study aims to describe the clinical, histological, and therapeutic characteristics of a unicenter cancer cohort, and to assess survival outcomes.

Methods : This is a retrospective observational study formed of 426 patients residents of Gabes city and followed up at the Oncology Department of Gabes Regional Hospital. The cohort included patients diagnosed with breast cancer ($n=111$), lung cancer ($n=75$), and colorectal cancer ($n=46$), among others. Data collected encompassed sociodemographic characteristics, tumor staging, histological subtype, molecular biomarker status, surgical outcomes, chemotherapy protocols, and final clinical status.

Results : Mean age was 60 years (range 17–92). Family history of cancer was reported in 57 patients (13.4%), predominantly breast cancer. Breast cancer ($n=111$) was the most frequent tumor type. Seventy percent of patients (78/111) underwent surgery, with an R0 resection rate of 93.5%. Hormone receptor positivity (HR+) was found in 74.8% and HER2 overexpression in 26%. The EC+Docetaxel protocol was the dominant chemotherapy regimen (72 cases). Lung cancer ($n=75$) presented the most aggressive profile. T4 stage accounted for 68% of cases and 69.3% of patients had distant metastases (M1). Adenocarcinoma was the dominant histological subtype (46/75 cases). Molecular testing (EGFR, ALK, etc.) was documented in only 10 patients, representing a critical under-utilization. Colorectal cancer ($n=46$) was advanced at diagnosis, with 97% of cases staged T3/T4. Seventy-six percent of patients underwent surgery, and Folfox was the predominant chemotherapy protocol. Across the entire cohort, the mean number of chemotherapy cycles was 5.7 (median 6, maximum 20). Regarding survival outcomes, 254 (60%) were alive, 147 (35%) had died, and 25 were lost to follow-up. Among the 257 patients alive, 134 (32%) were in remission.

Conclusion : This real-world cohort highlights a heterogeneous cancer population with an overall mortality rate of 35% and a remission rate of 32% among evaluable patients. Lung cancer presented the most aggressive profile, with advanced staging and near-absent molecular documentation, underscoring a critical gap in biomarker-driven care.

Use of Artificial Intelligence by Cancer Patients: A Prospective Study

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Introduction: Artificial intelligence (AI) is increasingly being used by cancer patients to search for medical information. This evolution raises questions regarding its impact and how it is perceived by patients. This study aims to evaluate the frequency and patterns of AI use among oncology patients, as well as their perception of this technology within the context of their care pathway.

Methods: We conducted a prospective monocentric study involving 80 cancer patients. Data were collected using a questionnaire covering AI use, level of trust granted, information verification practices, and perception of associated risks.

Results: Participants had a mean age of 50 years (range 30–76), 73.2% were female. Of all patients, 42.9% (n=34) used AI to seek information about their illness, with more frequent use among women (64%). The most represented cancers were breast cancer (57.1%), colon cancer (14.3%), and lung cancer (7.1%). Among AI users, trust in AI was high (30.8%), moderate (57.7%), or low (11.5%). The main reasons for using AI were speed of response (69.2%), immediate availability (19.2%), and simplicity of language (7.7%). However, the physician was unanimously considered the most reliable source of information (100%). The majority of patients (80.2%) discussed AI-obtained information with their physician. The main risks feared by patients were diagnostic errors (61.5%) and inappropriate advice (23.1%). Furthermore, 29.3% of AI-using patients reported increased anxiety linked to AI use. Finally, 84.6% believed that AI cannot replace the physician and 83.9% expressed a desire to receive better guidance on its use.

Conclusion : AI is already widely used by oncology patients but its use is accompanied by limited trust and may generate anxiety. The physician remains the central reference point underscoring the importance of medical guidance in the use of these tools in order to maximize their benefits while preserving the doctor-patient relationship.

Atezolizumab induced Hypereosinophilic Syndrome with cardiac and neurologic involvement in a Patient with Lung Cancer

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Introduction: Atezolizumab, an immune checkpoint inhibitor (ICI), is widely used in the management of nonsmall cell lung cancer (NSCLC). Despite its therapeutic efficacy, immune-related adverse events (irAEs) are increasingly reported. Hypereosinophilic syndrome is a rare but severe irAE associated with multiorgan involvement, including cutaneous, pulmonary, cardiac, and neurologic manifestations. [1] We report a rare case of atezolizumab-induced hypereosinophilic syndrome with cardiac and neurologic involvement.

Methods: This case was notified to the Tunisian National Center for Pharmacovigilance in June 2021, and analyzed using the updated French imputability method [2].

Results: An 80-year-old man with a history of hypertension, treated with losartan and hydrochlorothiazide for 5 years, was diagnosed with locally advanced non-small cell lung cancer (NSCLC) in November 2019. Immunotherapy with atezolizumab (1200 mg) was administered as a weekly infusion since October 2020. After 7 months of treatment, the patient developed erythema associated with bilateral lower limb edema. Laboratory investigations revealed peripheral hypereosinophilia at 600 cells/mm³. Given the therapeutic benefit of immunotherapy,

continuation of atezolizumab was considered, with dose reduction and premedication using corticosteroids and antihistamines. Few hours after the subsequent infusion, the patient developed acute onset of asthenia, mental confusion, and left-sided monoparesis. Brain computed tomography revealed a nonterritorial ischemic stroke. Laboratory tests showed marked peripheral hypereosinophilia (3600 cells/mm³). Cardiac evaluation using transesophageal echocardiography revealed restrictive cardiomyopathy consistent with Loeffler's endocarditis. Atezolizumab was discontinued, and the patient received systemic corticosteroids in combination with antihistamines, anticoagulation, and antiplatelet therapy. The clinical course was favorable, with progressive neurologic improvement and significant decrease in eosinophil count to 900 cells/mm³ within 7 days.

Discussion: In this case, the onset delay of symptoms after atezolizumab exposure and the marked improvement following corticosteroid therapy and treatment discontinuation strongly support a drug-induced immune-related adverse event. Immune checkpoint inhibitor-associated eosinophilic syndromes are rare but potentially severe, with reported cases ranging from isolated eosinophilia to life-threatening organ damage [1]. Cardiac involvement consistent with Loeffler's endocarditis is a recognized complication of hypereosinophilic syndromes and may lead to intracardiac thrombosis and systemic embolic events, including ischemic stroke. [3] This mechanism is consistent with the neurological manifestations observed in our patient. This case underlines the importance of early recognition of eosinophilia during immunotherapy, as timely intervention may prevent irreversible cardiac and neurologic complications.

Conclusion: This case highlights a rare but severe immune-related adverse event associated with atezolizumab. Clinicians should be aware of eosinophil-mediated toxicity as a potential cause of severe multiorgan complications during immune checkpoint inhibitor therapy.

Clinicopathological Features and Neoadjuvant Response in Triple-Negative Breast Cancer According to Menopausal Status

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Background: Triple-negative breast cancer (TNBC) is an aggressive breast cancer subtype with significant clinical and biological heterogeneity. Menopausal status has been suggested as a potential modifier of tumor biology and treatment response. This study aimed to evaluate the impact of menopausal status on clinicopathological features and response to neoadjuvant chemotherapy in patients with localized TNBC.

Methods: We conducted a retrospective descriptive study including 100 patients with localized TNBC treated at Abderrahmen Mami Hospital between 2022 and 2025. Patients were stratified according to menopausal status. Clinicopathological characteristics and response to neoadjuvant chemotherapy were compared between premenopausal and postmenopausal groups.

Results: A total of 100 patients were included, comprising 54 postmenopausal and 46 premenopausal women. The mean age was 54 years (range: 46–80) and 46 years (range: 28–51), respectively, with an overall median age of 52.03 years (range: 28–80). High-grade tumors (SBR III) were observed in 76% of postmenopausal and 64% of premenopausal patients (p=0.161). The mean Ki-67 index was higher in premenopausal

women (55.5% vs 51.5%), although not statistically significant ($p=0.329$). At diagnosis, stage II–III disease was frequent in both groups, with no significant association between menopausal status and stage distribution ($p=0.785$). Inflammatory breast cancer occurred in 15.2% of premenopausal and 16.7% of postmenopausal patients ($p=0.844$). Among 65 patients who received neoadjuvant chemotherapy (35 premenopausal, 30 postmenopausal), pathological complete response (pCR) was achieved in 33.3% and 40% of patients, respectively ($p=0.889$).

Conclusion: In this cohort, menopausal status was not significantly associated with clinicopathological characteristics or pathological complete response. However, consistent numerical trends toward higher proliferative activity, more advanced disease at presentation, and lower pCR rates were observed in premenopausal patients. These findings suggest potential biological heterogeneity within TNBC according to menopausal status and are in line with previously reported data in younger patients. Larger prospective studies incorporating molecular profiling are warranted to further define its prognostic and predictive relevance.

Prognostic Impact of Combined VISTA and EGFR Expression in High grade serous ovarian carcinoma

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Background : Epidermal Growth Factor Receptor (EGFR) is a major driver of tumor proliferation, while VISTA (V-domain Ig suppressor of T cell activation) is an emerging immune checkpoint involved in tumor immune regulation. The interaction between tumor proliferation pathways and immune checkpoints within the tumor microenvironment remains poorly understood. In this study, we evaluated the association between VISTA and EGFR expression and their prognostic impact in High grade serous ovarian carcinoma (HGSOC) samples.

Methods : A retrospective study was assessed in 44 HGSOC tissue microarrays by immunohistochemistry (IHC). EGFR expression was classified as High (H) or Low to Moderate (L-M), and VISTA expression was categorized as positive or negative. We subdivide the cohort into four groups: the VISTA+/EGFR (H), VISTA/EGFR (H), VISTA+/EGFR (L-M), and VISTA-/EGFR (L-M). The association between EGFR and VISTA was analyzed using Fisher's exact test. Overall survival (OS) was estimated using the Kaplan Meier method and compared using the log-rank test.

Results : VISTA was positive in 36% (16/44) of cases and EGFR was highly expressed (H) in 18% (8/44) of cases. A significant association between VISTA and EGFR expression was observed ($p < 0.001$). Survival analysis revealed significant differences among the four groups (log-rank $p < 0.001$). The VISTA+/EGFR High (2%, $N=1$) demonstrated the best overall survival, whereas the VISTA/EGFR High (15% $N=7$) had the poorest prognosis. Patients with low to moderate EGFR expression showed intermediate survival outcomes regardless of VISTA status VISTA+/EGFR (L-M) (31%, $N=14$), VISTA-/EGFR (L-M) (50%, $N=22$).

Conclusion : Our findings suggest that the combined expression of VISTA and EGFR has a significant prognostic impact. The effect of EGFR expression on survival appears to be modulated by the immune context, particularly VISTA expression. These Results highlight a potential interaction between tumor proliferation and immune regulation pathways, which may have implications for future therapeutic strategies in HGSOC. Key words: VISTA, EGFR, HGSOC, tumor microenvironment, prognosis.

Safety, Dose-Intensity, and Compliance of Neoadjuvant Carboplatin-Taxane Regimens in Triple- Negative Breast Cancer: Real-World Challenges

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Background: Adding carboplatin to neoadjuvant chemotherapy (NAC) increases pathological complete response (pCR) rates in triple-negative breast cancer (TNBC). However, increased hematological toxicity remains a major clinical challenge in routine practice. This study evaluates the real-world safety profile, treatment compliance, and the impact of dose adjustments on pathological outcomes in a TNBC cohort.

Methods: We retrospectively reviewed data from 47 TNBC patients treated with anthracycline- taxane NAC with or without carboplatin between 2023 and 2026 at Abderrahmen Mami Hospital. Treatment compliance was assessed using rates of therapeutic interruptions (TI), dose reductions, and the total number of cycles completed. Toxicity profiles were graded based on clinical records. The secondary endpoint was to evaluate whether compromised dose-intensity affected the pCR rate ($ypT0/is\ ypN0$).

Results: Carboplatin-containing regimens were administered to 38.3% of the cohort. Grade 3/4 hematological toxicity, predominantly pancytopenia, was significantly higher in the carboplatin group compared to the standard group ($p=0.02$). This led to a higher rate of dose reductions or therapeutic interruptions in patients receiving carboplatin (22.2% vs. 10.3%, $p=0.04$). Patients who maintained full dose-intensity without interruptions achieved a higher pCR rate compared to those requiring treatment modifications (44% vs. 31%). Nevertheless, the overall pCR rate remained favorable in the carboplatin group (44% vs 28% without carboplatin).

Conclusion: In a real-world setting, neoadjuvant carboplatin intensification for TNBC significantly increases hematological toxicity, leading to frequent dose modifications. While maintaining treatment schedule integrity is optimal for maximizing pCR, platinum-based regimens remain superior to standard chemotherapy despite these real-world tolerability challenges. Highly close monitoring is essential to balance efficacy and safety.

Predictors of Early Relapse in Non-Metastatic TripleNegative Breast Cancer: A Retrospective Study from a North African Cohort

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Background : Triple-negative breast cancer (TNBC) carries a high risk of early relapse, for which reliable predictors remain insufficiently defined in resource-limited settings. This study aimed to identify clinicopathological and logistical factors associated with early systemic recurrence in TNBC patients treated at a Tunisian referral center.

Methods : We conducted a retrospective study of 64 patients with non-metastatic TNBC treated at Abderrahmen Mami Hospital. Early relapse (ER) was defined as recurrence within 24 months of definitive surgery. Patients were classified into two groups: ER ($n=19$) and no progression (NP, $n=45$; disease-free survival >24 months). Variables analyzed included age, family history of malignancy, Ki-67 proliferation index, neoadjuvant

chemotherapy (NACT) receipt, pathological complete response (pCR), and time from diagnosis to NACT initiation.

Results : Patients in the ER group were younger (median age 42 vs. 53 years; $p=0.035$) and more frequently had a family history of cancer (61% vs. 37%; $p=0.042$). Ki-67 index was higher in the ER group (78% vs. 42%; $p<0.001$). Carboplatin was incorporated into NACT in 36% of patients, primarily those with high-risk features. Despite intensification, all patients in the ER group had residual disease, with 83% classified as RCB-III, compared to a pCR rate of 41% in the NP group ($p<0.0001$). The time to treatment initiation was longer in the ER group (112 vs. 48 days; $p=0.001$). The most frequent sites of initial relapse were the lungs and brain.

Conclusions : Primary chemoresistance, as reflected by the absence of pCR and high RCB scores, was the dominant driver of early relapse in this cohort. Prolonged treatment delays and elevated Ki-67 were additional independent contributors. Optimizing diagnostic pathways and escalating adjuvant therapy in non-responders represent the most actionable implications of these findings.

Oocyte vitrification : benefits and challenges in fertility preservation in women with breast cancer

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Introduction: Breast cancer, the most common cancer in women, increasingly affects those of reproductive age, with gonadotoxic treatments threatening fertility. Oocyte vitrification is a key fertility preservation technique. This systematic review assesses its value for women with breast cancer, evaluating efficacy, safety, and psychological and ethical implications.

Methods: A systematic review was conducted using PubMed, Scopus, and Embase, with keywords "oocyte vitrification," "fertility preservation," and "breast cancer." Articles in English or French, published between 2015 and 2026, available in full text, were included, excluding metaanalyses. After screening, 30 articles were qualitatively analyzed.

Results: Vitrification yields 8-12 oocytes per cycle, with clinical pregnancy rates of 35-45% and live birth rates of 25-35%. Letrozole-based protocols minimize hyperestrogenism risks, showing no tumor progression. In vitro maturation (IVM) produces 5-6 oocytes, with lower pregnancy rates (14-30%). About 70% of patients report reduced fertility-related anxiety, but 20-30% refuse stimulation due to hormonal concerns. Access is limited for 20-30% due to high costs.

Discussion: Vitrification is effective and safe, but tight timelines (25 days) and outcome uncertainties stress patients, necessitating psychological support. IVM, though promising, is underutilized. The 2021 bioethics law expands ART access, but financial disparities persist. Multidisciplinary care and inclusive policies are essential for integration.

Conclusions: Oocyte vitrification is a valuable fertility preservation strategy, but requires multidisciplinary coordination, psychological support, and equitable access. Long-term research is needed to optimize IVM and outcomes. Keywords : oocyte vitrification, oncofertility, chemotherapy; in vitro maturation (IVM), breast cancer

Is the cytoplasmic expression of BRCA1/BRCA2 significant for predicting outcomes in high-grade serous ovarian carcinomas?

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Background: BRCA1 and BRCA2 are critical tumor suppressor genes involved in homologous recombination DNA repair. Beyond genetic alterations, their protein expression and subcellular localization may impact ovarian cancer progression and patient outcomes. This study aimed to investigate BRCA1/BRCA2 expression patterns, their cellular localization, and their prognostic significance in high-grade serous ovarian carcinoma (HGSOC).

Methods: A retrospective cohort of 51 HGSOC patients was analyzed. BRCA1 and BRCA2 protein expression was assessed by immunohistochemistry (IHC) and categorized as low (L) or high (H). Subcellular localization (nuclear versus cytoplasmic) was systematically evaluated. Overall survival (OS) was estimated using the Kaplan–Meier method and compared using the log-rank test. Statistical significance was set at $p<0.05$.

Results: Strikingly, 100% of tumors demonstrated exclusive cytoplasmic expression of BRCA1 and BRCA2, with a complete absence of physiological nuclear staining. High BRCA1 expression was observed in 61% (N=29) of cases, and high BRCA2 in 45% (N=22). The co-expression of BRCA1/BRCA2 was significantly associated with advanced clinical features, including distant metastases, lymph node involvement, recurrence, and advanced stage ($p<0.001$), but also with higher chemotherapy sensitivity ($p<0.001$). Kaplan–Meier survival analysis revealed that these profiles translated into distinct prognostic outcomes ($p<0.001$). Paradoxically, the BRCA1 (H)/BRCA2 (H) subgroup (38%, N=17) showed the most favorable median survival (53 months), likely driven by chemotherapy hyper-sensitivity, whereas the BRCA1 (L)/BRCA2 (H) group (6%, N=3) had a dismal median survival of 17.1 months.

Conclusion: This study highlights a systematic, aberrant cytoplasmic sequestration of BRCA1/2 proteins in HGSOC, suggesting a wide spread functional loss of nuclear DNA repair. Rather than simple biomarkers, combined BRCA1/BRCA2 IHC profiles serve as a powerful dual indicator of tumor aggressiveness and treatment response, offering a cost-effective tool to stratify patient survival and optimize targeted therapeutic strategies.

Cowden Syndrome : A Case Report

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Introduction : Cowden syndrome (CS) is a genodermatosis characterized by multiple hamartomas developing in various tissues and by an increased risk of malignancies, primarily affecting the breast, thyroid, endometrium, kidney, and colorectum.

Case Report: We report the case of a 57-year-old patient who developed epithelial thyroid cancer at the age of 24, subsequently associated with a papillomatous papule, multiple lipomas, genitourinary tumors, and colorectal cancer. The family history was also highly suggestive, with the patient's mother having developed thyroid cancer at the age of 25 and a sister who, from the age of 40, developed three distinct cancers involving the breast, colon, and brain. Molecular analysis identified a constitutional pathogenic variant in the PTEN gene, consisting of a two-nucleotide deletion in exon 6 in the

heterozygous state.

Discussion and Conclusion: This case highlights the clinical and tumor heterogeneity of Cowden syndrome, as well as the importance of considering family history in the diagnostic workup. Genetic confirmation enables a definitive diagnosis and supports the implementation of appropriate surveillance strategies for both the patient and at-risk relatives. Management relies on multidisciplinary follow-up and personalized cancer screening to optimize the prevention and treatment of associated malignancies.

Clinical Profile and Management of BRCA-Mutated Ovarian Cancer: A 5-Year Descriptive Study

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Background: BRCA1 and BRCA2 mutations are important biomarkers in ovarian cancer (OC) that guide targeted treatments like PARP inhibitors (PARPi). In daily clinical practice, understanding the characteristics of these patients is essential to optimize screening, access to care and clinical outcomes. This study aims to describe the clinical and molecular features, as well as the management of BRCA-mutated OC patients in a real world setting.

Methods: We conducted a retrospective descriptive study at Abderrahmen Mami Hospital over a 5-year period (2020-2025). Among 374 screened patients diagnosed with OC, we included all cases with a confirmed BRCA1 or BRCA2 mutation. We analyzed clinico-demographic data, family history, surgical outcomes, systemic treatments, breast cancer screening, and survival outcomes.

Results: Among 374 patients with OC, 108 (28.8%) underwent BRCA testing, identifying 11 (10.2%) mutated cases. The median age was 56 years (47–62). High-grade serous carcinoma was predominant (91%, n=10), with all patients presenting at advanced stages (FIGO III : n=8 ; FIGO IV : n=3). A family history of BRCA-associated cancers was reported in 63.6% (n=7). BRCA1 and BRCA2 mutations were each found in 5 patients (45.5%), with one patient carrying both variants. Mutations were somatic in 7 cases and germline in 4. Management included neoadjuvant chemotherapy (n=7) or primary surgery (n=4), achieving complete cytoreduction in 72.7% (n=8). Only 4 patients received PARPi maintenance (alone: n=2; post Bevacizumab: n=2). No one received PARPi concurrent with Bevacizumab due to access to testing constraints and access to treatment constraints. Seven patients missed the PARPi prescription window due to delayed genetic testing, and concurrent PARPi Bevacizumab was precluded by logistical constraints. PARPi related grade 3 toxicities (hematologic/gastrointestinal) occurred in 3 patients, successfully managed with temporary interruption and dose reductions. Disease progression occurred in 6 patients (5 platinum-sensitive), though none progressed while on PARPi. Breast MRI screening (n=5) identified one second primary breast cancer. At last follow-up, 8 patients were alive (6 in complete remission), 2 had died from disease progression, and 1 was lost to follow-up.

Conclusion: BRCA-mutated OC is associated with a high familial cancer burden and significant risk of second malignancies. Despite high rates of optimal cytoreduction, PARPi maintenance remains underutilized, primarily due to delayed genetic testing and access barriers. These findings highlight the urgent need for timely systematic genetic counseling, improved access to targeted therapies, and structured long-term breast surveillance.

Real-World Outcomes of Neoadjuvant Chemotherapy With or Without Pembrolizumab in Triple-Negative Breast Cancer: A Single-Center Retrospective Study

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Introduction: Neoadjuvant chemo-immunotherapy has improved outcomes in early-stage triple-negative breast cancer (TNBC). However, real-world access and outcomes remain variable, particularly in resource-limited settings. We evaluated clinical and pathological outcomes of neoadjuvant treatment in TNBC patients treated at a tertiary cancer center. We conducted a retrospective study including 41 female patients with non-metastatic TNBC treated at Salah Azaiez Institute between July 2022 and October 2025. Patients received different neoadjuvant chemotherapy regimens with or without pembrolizumab depending on access through national health insurance. Clinical response, surgical outcomes, and Residual Cancer Burden (RCB) were assessed.

A descriptive comparison of pathological response according to treatment regimen was performed. Among 41 patients, 32 (78%) had access to pembrolizumab and 9 (22%) received chemotherapy alone. The mean age was 52.0 ± 12.8 years. Fifteen patients were premenopausal and 26 postmenopausal. At diagnosis, 73% had T1–T2 tumors, 17% T3, and 10% locally advanced disease. Node-positive disease was present in 22 patients (53.7%), and 78% had SBR grade III tumors. HER2 expression was score 0 in 37 patients and score 1+ in 4 patients. Regarding treatment delivery, 14 patients (34.1%) received dose-dense anthracycline-based chemotherapy, while 27 (65.9%) received anthracycline treatment every three weeks. Taxane-based therapy was administered weekly in 6 patients (14.6%), every three weeks in 26 patients (63.4%), and every two weeks in 9 patients (22.0%). Clinical response included complete response in one patient (2.4%), partial response in 33 (80.5%), stable disease in 4 (9.7%), and progressive disease in one patient (2.4%). Two patients were not operated. Among 39 operated patients, pathological response showed RCB-0 in 21 (53.8%), RCB-I in 3 (7.7%), RCB-II in 13 (33.3%), and RCB-III in 2 (5.1%). The combined favorable pathological response rate (RCB-0/RCB-I) was 61.5%. RCB-0 rates by regimen were 10% for AC or EC–taxane–carboplatin, 47% for EC–taxane–carboplatin–pembrolizumab, 43% for EC–docetaxel or EC–Paclitaxel. Overall, immunotherapy-containing regimens achieved a slightly better RCB-0 rate than chemotherapy alone regimens. During follow-up, 5 patients experienced disease recurrence. Among the 27 patients who received adjuvant chemotherapy, only 5 received adjuvant pembrolizumab. In this real-world retrospective cohort of TNBC patients, neoadjuvant treatment achieved a high rate of pathological complete response. Patients receiving pembrolizumab-based regimens demonstrated a higher rate of RCB-0. However, access to and continuation of immunotherapy in the adjuvant setting remained limited. These findings highlight the importance of improving perioperative immunotherapy access and warrant further evaluation in larger studies with survival outcomes.

EGFR-Mutant NSCLC in Tunisia: Characteristics and Real-World Outcomes

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Background : EGFR-mutant non-small cell lung cancer (NSCLC) represents a distinct molecular subtype with established sensitivity to tyrosine kinase inhibitors (TKIs). While EGFR-targeted therapies have reshaped NSCLC management, data from Tunisia and the North African region remain limited. We aimed to describe the prevalence, clinical characteristics, molecular profile, and treatment patterns of EGFR-mutant metastatic NSCLC in a Tunisian care center.

Methods : We conducted a retrospective study including 262 patients treated for non-small cell lung cancer (NSCLC) between 2020 and 2025 at the Medical Oncology Department of Abderrahmen Mami Hospital. EGFR mutation testing was performed in 98 patients (37.4%). Patients with EGFR-mutant NSCLC were analyzed for demographic and clinicopathological characteristics, smoking exposure, TNM stage, performance status, molecular subtype, treatment patterns, and response to EGFR-targeted therapy.

Results : Among the 98 tested patients, 18 had an EGFR mutation, corresponding to 18.4% of tested patients and 6.9% of the overall cohort. Median age at diagnosis was 61.5 years (IQR 50-67). Women represented 72% of cases, and all tumors were adenocarcinomas. All patients presented with metastatic disease, including 37% with oligometastatic involvement. Smoking exposure was documented in 70% of patients; among these, 30% were active smokers and 70% reported passive smoking. Performance status was generally preserved, with 83% of patients presenting WHO performance status 1. Exon 19 deletions were the most frequent mutation subtype (66.7%), followed by exon 21 (16.7%) and exon 20 (11.1%). Mutation subtype was unavailable in one patient. EGFR-TKIs were used across multiple treatment lines. Six patients received first-line erlotinib, achieving partial response in three and stable disease in two, with one non-evaluable patient. In the second line, five patients received TKI therapy, with two partial responses, two stable diseases, and one progression. One patient received third-line osimertinib with a partial response.

Conclusion : EGFR-mutant NSCLC accounted for a minority of tested cases in this Tunisian cohort and was characterized by a predominance of female patients with metastatic adenocarcinoma and exon 19 deletions. EGFR-TKIs demonstrated clinically meaningful activity in routine practice across treatment lines. These findings support the implementation of systematic molecular profiling in NSCLC to enable appropriate access to targeted therapies and improve real-world outcomes.

Clinical and Oncogenetic Landscape of Colorectal Cancer Associated with Familial Adenomatous Polyposis: A Real-World Descriptive Study

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Background: Familial Adenomatous Polyposis (FAP) is an inherited cancer predisposition syndrome characterized by diffuse colorectal polyposis and a near-complete lifetime risk of colorectal cancer (CRC) without prophylactic intervention. This study aims to describe the clinical, pathological, therapeutic, and oncogenetic characteristics of patients with FAP-associated CRC in a real-world setting.

Methods: We conducted a retrospective descriptive study of patients treated for FAP-associated CRC at Abderrahmen Mami Hospital between 2018 and 2026. Comprehensive data

regarding clinical presentation, endoscopy, pathology, genetics, treatments, and survival outcomes were analyzed.

Results: Seventeen patients were included, with a mean age of 54 years (range, 37–71). In 93.8% of cases (n=16), FAP was diagnosed concurrently with CRC presentation; only one patient was identified proactively through surveillance. A family history of CRC or FAP was reported in 47% of cases, and consanguinity in 29.4%. Four patients (23.5%) presented with synchronous dual colorectal tumors, and rectal involvement was observed in 41.2%. One patient also exhibited duodenal involvement. An attenuated FAP phenotype (<100 colorectal polyps), was observed in 68.8% of cases (n = 11). Advanced disease was highly prevalent: seven patients (41.2%) presented with upfront metastatic disease (primarily hepatic and peritoneal) while most non-metastatic cases had locally advanced (T3–T4) and/or node-positive tumors. Despite genetic counseling being initiated for five patients, molecular testing was completed in only three, all of whom harbored MUTYH mutations (consistent with MUTYH-associated polyposis). Surgery was performed in 70.6% of patients, predominantly by subtotal or total colectomy. Systemic therapies included FOLFOX, CAPOX, or FOLFIRINOX, with bevacizumab added in metastatic settings. Treatment-related toxicities remained generally manageable. At the last follow-up, nine patients were alive (either in complete remission or with controlled stable disease), six had died from disease progression, and one patient had developed a desmoid tumor.

Conclusions: In our real-world cohort, FAP/MAP was rarely recognized prior to CRC development, resulting in frequent presentations at advanced stages. Furthermore, access to crucial genetic counseling and molecular testing remained markedly limited. Strengthening family screening programs and improving referral pathways to oncogenetic services are urgently needed to facilitate timely prophylactic interventions and reduce CRC-related mortality in affected families.

Clinically Relevant Drug–Drug Interactions with Tyrosine Kinase Inhibitors: Current Challenges and Emerging Perspectives

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Background : Tyrosine kinase inhibitors (TKIs) have substantially improved outcomes across multiple solid and hematologic malignancies and represent a cornerstone of modern precision oncology. However, their complex pharmacokinetic characteristics, including cytochrome P450 (CYP)-mediated metabolism and variable oral bioavailability, expose patients to clinically relevant drug–drug interactions (DDIs) that may compromise treatment efficacy and safety.

Objective : To review clinically significant DDIs associated with TKIs and discuss current challenges and emerging perspectives in interaction management within oncology practice.

Methods : A narrative literature review was conducted using PubMed, ASCO and ESMO guidance documents, and regulatory prescribing information. Publications addressing pharmacokinetic and pharmacodynamic interactions involving tyrosine kinase inhibitors (TKIs) were analysed, with emphasis on clinically relevant interactions encountered in routine

oncology practice and emerging data on newer-generation TKIs. **Results :** Many, although not all, TKIs are predominantly metabolized by CYP3A4 and are therefore susceptible to CYP3A4-mediated interactions. Strong CYP3A4 inhibitors such as azole antifungals and macrolide antibiotics may increase systemic exposure and toxicity risk, whereas CYP3A4 inducers including rifampicin, carbamazepine, and phenytoin may reduce plasma concentrations and compromise therapeutic efficacy. Acid-suppressive therapies, particularly proton pump inhibitors, may decrease the absorption of pH-dependent TKIs such as erlotinib and dasatinib. Pharmacodynamic interactions also remain clinically important, particularly when QT-prolonging TKIs such as nilotinib and vandetanib are administered concomitantly with other QT-active medications commonly used in supportive oncology care. Some TKIs such as afatinib and alectinib may exhibit reduced susceptibility to CYP-mediated interactions compared with earlier TKIs, although transporter-mediated interactions remain clinically relevant. Nevertheless, clinically relevant DDIs continue to represent an important challenge across TKI generations.

Conclusion : Clinically relevant DDIs remain a major challenge in patients receiving TKIs. Early identification of high-risk combinations, systematic medication review, and multidisciplinary collaboration involving oncologists and clinical pharmacologists are essential to optimize therapeutic efficacy while minimizing treatment-related toxicity in real-world oncology practice. **References :** van Leeuwen RWF, van Gelder T, Mathijssen RHJ, Jansman GFA. Drug–drug interactions with tyrosine-kinase inhibitors: a clinical perspective. *Lancet Oncol.* 2014;15(8):e315–e326. Teo YL, Ho HK, Chan A. Metabolism-related pharmacokinetic drug–drug interactions with tyrosine kinase inhibitors. *Br J Clin Pharmacol.* 2015;79(2):241–253. Hussaarts KGA, Veerman GDM, Jansman FGA, et al. Clinically relevant drug interactions with multikinase inhibitors: a review. *Ther Adv Med Oncol.* 2019;11:1758835918818347. Stromatt JC, Chowdhury AT, Huang KM, et al. Drug–drug interactions in targeted cancer therapies: a focus on tyrosine kinase inhibitors. *Expert Rev Clin Pharmacol.* 2025;18(12):1019–1035. Santamaria F, Roberto M, Maltese G, et al. Tyrosine-kinase inhibitors for lung or breast cancer and drug–drug interactions: a clinical guide. *Oncology Reviews.* 2025;19:1612249. Attwood MM, et al. Trends in kinase drug discovery: targets, indications and inhibitor design. *Nat Rev Drug Discov.* 2021;20:839–861.

Implementation and Evaluation of an Enhanced Recovery After Surgery (ERAS) Protocol in Endometrial Cancer Surgery

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Introduction: Endometrial cancer is the most common gynecologic malignancy in developed countries, with surgical management based primarily on total hysterectomy with bilateral salpingo-oophorectomy and appropriate surgical staging. Enhanced Recovery After Surgery (ERAS) programs have demonstrated significant benefits across various surgical specialties by reducing postoperative morbidity and length of hospital stay. However, data regarding their implementation in gynecologic oncology remain limited. This study aimed to evaluate the feasibility and clinical impact of an ERAS protocol in patients undergoing surgery for endometrial cancer.

Methods: We conducted a prospective observational study between January 2024 and June 2025 in a tertiary university gynecology department. Fifty-two consecutive patients

undergoing surgical treatment for histologically confirmed endometrial cancer were enrolled in a standardized ERAS pathway, including comprehensive preoperative counseling, reduced fasting periods, multimodal anesthesia, early mobilization, and early oral feeding. Outcomes were compared with those of a historical cohort managed according to conventional perioperative care protocols.

Results : Implementation of the ERAS protocol Resulted in a significant reduction in median length of hospital stay compared with conventional management (2.1 vs. 4.2 days, $p < 0.001$). No increase in readmission rates or postoperative complications was observed. The incidence of postoperative complications of Clavien-Dindo grade II or higher decreased from 18.0% to 9.6%. Operative time remained unchanged between the two groups. Patient satisfaction, assessed using a visual analog scale, was high, with a mean score of 8.7/10.

Conclusion: The implementation of an ERAS protocol in endometrial cancer surgery is both feasible and effective, leading to accelerated postoperative recovery and shorter hospital stays without compromising patient safety or quality of care. These findings support the broader adoption of ERAS pathways in gynecologic oncology centers and highlight their potential to optimize perioperative outcomes in women undergoing endometrial cancer surgery.

Keywords: Endometrial cancer; Enhanced Recovery After Surgery (ERAS); Gynecologic oncology; Perioperative care; Postoperative recovery; Length of hospital stay.

Colorectal Cancer Mimicking an Ovarian Mass: Diagnostic Challenge in Pelvic Tumors – A Case Series and Literature Review

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Background: Pelvic masses are frequently attributed to gynecologic pathology, particularly in women. However, non-gynecologic malignancies, such as colorectal cancer, may present as adnexal or pelvic masses, leading to diagnostic confusion. The aim of this study is to report a series of cases where colorectal cancer was initially misdiagnosed as an ovarian tumor and to highlight the importance of multidisciplinary assessment.

Methods: We conducted a retrospective review of five female patients referred to our gynecologic oncology unit between 2020 and 2024 for presumed ovarian masses based on clinical examination and pelvic imaging. All patients underwent preoperative imaging (ultrasound and CT scan) and tumor marker assessment (CA-125, CEA, CA 19-9).

Results: All five patients, aged 52 to 68, presented with lower abdominal pain, pelvic fullness, or postmenopausal bleeding. Imaging suggested complex adnexal masses with peritoneal involvement in 4 cases. CA-125 was mildly elevated in 3 patients; however, CEA was elevated in 4. Surgical exploration revealed invasive sigmoid or rectal tumors with secondary ovarian or peritoneal involvement. In 3 cases, cytoreductive surgery was initiated as for presumed ovarian cancer. Final histopathology confirmed primary colorectal adenocarcinoma with transcoelomic spread to the ovaries in 4 patients ("Krukenberg-like" tumors). All patients were referred postoperatively for colorectal cancer staging and treatment.

Conclusion: Colorectal cancer can closely mimic ovarian malignancy, particularly when presenting with pelvic masses and ascites. Misdiagnosis may delay appropriate treatment or Result in suboptimal surgical approaches. A high index of

suspicion, comprehensive preoperative evaluation—including colonoscopy and CEA assessment—should be considered in atypical or unclear cases. Multidisciplinary management involving both gynecologic and gastrointestinal teams is essential to optimize patient outcomes.

Pharmacogenetics of Imatinib: Toward Personalized Therapy

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Introduction : Imatinib, a first-generation tyrosine kinase inhibitor (TKI), remains a first-line treatment for chronic myeloid leukemia (CML) and gastrointestinal stromal tumors (GISTs) [1]. Despite its established efficacy, considerable interindividual variability in drug exposure, treatment response, and tolerability has been observed. In addition to therapeutic drug monitoring, pharmacogenetics (PGx) may help optimize imatinib therapy. Current evidence supports a potential role for CYP3A5 and ABCG2 in imatinib pharmacokinetic variability; however, available data remain insufficient to support routine genotype-guided dosing.

Objective : To summarize current evidence on the pharmacokinetic pharmacogenetic determinants of imatinib variability, evaluating their impact on imatinib exposure, treatment response, and adverse effects.

Methods : Literature search was performed using databases including PubMed, ScienceDirect and using the following keywords: 'Imatinib', 'Personalized medicine', 'Pharmacogenetics' and 'Genetic polymorphisms'.

Results : Genetic polymorphisms in imatinib-metabolizing enzymes and membrane transporters are wellrecognized contributors to interindividual variability in both therapeutic response and adverse effect susceptibility. Imatinib is primarily metabolized by CYP3A4 to its active metabolite, nor-imatinib, while CYP3A5, CYP2C8, and CYP2D6 contribute to a lesser extent. CYP3A4*22 has been investigated as a candi for genotype-guided dose reduction in GIST patients [2], though its clinical impact remains debated, with some studies reporting no significant effect [3]. In chronic phase CML, the CYP3A5*3 (c.6986A>G) GG genotype, associated with non-functional CYP3A5 expression, has been linked to higher imatinib plasma concentrations, better cytogenetic and molecular responses, and lower treatment failure rates [4]. CYP2C8*3 has been identified as a potential determinant of the nor-imatinib/imatinib conversion ratio, with carriers exhibiting a higher metabolic ratio consistent with its increased-function status demonstrated *in vitro* [4,5]. Additionally, a recent study suggested that decreased or non-functional CYP2D6 alleles, particularly CYP2D6*4, may be associated with reduced imatinib oral clearance, although the contribution of CYP2D6 to imatinib metabolism is considered limited [5]. Regarding membrane transporters, the ABCG2 c.421C>A variant has been associated with higher imatinib trough plasma concentrations [6], with homozygous A allele carriers displaying a more consistent pharmacokinetic effect than that reported for ABCB1 variants. Indeed, studies investigating the impact of ABCB1 polymorphisms, notably c.3435C>T, c.1236C>T, and c.2677G>T/A, on imatinib pharmacokinetics have yielded

inconsistent Results, likely attributable to small sample sizes, ethnic diversity, and methodological heterogeneity, although T allele carriers across these variants have been associated with higher drug exposure, better cytogenetic and molecular responses, and lower treatment failure rates in several studies [1]. Regarding tolerability, the CYP3A5*3 G allele has been associated with a higher incidence of anemia, while the ABCB1 c.2677G>T/A T allele has been linked to increased rates of diarrhea [4].

Conclusion : Further studies are needed to quantitatively assess the clinical relevance of genetic variants in key genes involved in imatinib metabolism and transport, particularly CYP3A5, CYP3A4, ABCG2, ABCB1, and CYP2D6 and their impact on treatment outcomes in patients treated with imatinib.

Prevalence of CYP2B6*6 Polymorphism in a Tunisian Population: Implications for Mitotane Pharmacokinetic Variability

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Introduction : Mitotane is the only approved drug for the treatment of adrenocortical carcinoma (ACC), a rare and aggressive malignancy. Despite its established clinical use, evidence on the genetic determinants of mitotane pharmacokinetic variability remains limited. Among the most relevant candis, CYP2B6*6 (c.516G>T, rs3745274) is a key polymorphism associated with reduced CYP2B6 enzymatic activity, though data in non-Asian populations remain scarce. **Objective :** To assess the prevalence of the CYP2B6*6 polymorphism in a Tunisian population not receiving mitotane, using Next-generation sequencing (NGS) data obtained from a study evaluating a pharmacogenetic gene panel, in patients not receiving mitotane.

Methods : NGS data were retrospectively analyzed from 42 patients using a predesigned AmpliSeq for Illumina gene panel targeting 42 genes encoding drug-metabolizing enzymes and transporters. Although none of the patients were receiving mitotane at the time of sampling, DNA was sequenced for clinically relevant pharmacogenetic variants, including CYP2B6*6 (c.516G>T, rs3745274).

Results : A high prevalence of the CYP2B6*6 variant was observed, with 59.5% of patients (n=25) carrying at least one T allele, including four homozygous carriers (TT genotype), suggesting that a significant proportion of this population may exhibit reduced CYP2B6 enzymatic activity. These findings are contextualized by two key studies. Liu et al. conducted a retrospective study in 76 ACC Chinese patients treated with mitotane for more than three months and demonstrated that carriers of the GT or TT genotype for CYP2B6*6 were associated with higher mitotane levels after three months of treatment, though this difference was no longer statistically significant at nine months. No significant associations were found between mitotane trough concentrations and CYP3A4 (c.653G>C, c.878A>G) or pregnane X receptor (PXR) polymorphisms in the same cohort [1]. Consistent with these findings, D'Avolio et al. confirmed in 27 Italian patients that T allele was associated with higher mitotane concentrations, with differences more evident after three and six months of treatment. The same group found

no significant influence of ABCB1 polymorphisms on mitotane pharmacokinetics [2].

Conclusion : The high prevalence of the CYP2B6*6 variant observed in this Tunisian patient sample may have potential implications for interindividual variability in mitotane exposure in this population. However, the clinical impact of this polymorphism on mitotane exposure could not be assessed, as none of the included patients were receiving mitotane at the time of sampling. Prospective genotype-phenotype studies in Tunisian ACC patients treated with mitotane are warranted to determine its clinical relevance.

CYP3A4 Induction by Mitotane: An Underrecognized Clinical Challenge in Adrenocortical Carcinoma

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Introduction : Mitotane is a potent inducer of cytochrome P450 3A4 (CYP3A4), the enzyme responsible for the metabolism of a broad spectrum of drugs. Despite its well-documented enzyme-inducing properties, CYP3A4-mediated drug-drug interactions (DDI) remain insufficiently recognized and managed in routine practice, potentially compromising the efficacy of co-administered drugs.

Objective : To summarize current evidence of the DDI profile of mitotane, with a focus on CYP3A4-mediated interactions and their clinical implications.

Methods : A literature search was conducted using PubMed, ScienceDirect databases, combining the following keywords: 'mitotane', 'drug-drug interaction', 'CYP3A4' and 'induction'.

Results : Cancer patients are frequently polymedicated, receiving treatment for comorbidities as well as supportive and adjuvant therapies alongside their antineoplastic treatment. Among analgesics, opioids are commonly prescribed for moderate-to-severe cancer pain. Fentanyl, a CYP3A4 substrate, is particularly susceptible to mitotane-induced CYP3A4 upregulation, which may reduce fentanyl exposure, resulting in inadequate analgesia [1]. Among supportive care medications, dihydropyridine calcium channel blockers, including amlodipine and nifedipine, and macrolide antibiotics are CYP3A4 substrates whose plasma concentrations may be reduced during mitotane treatment, warranting substitution with ACE inhibitors or beta-blockers for blood pressure management, and fluoroquinolones such as ciprofloxacin or moxifloxacin for the treatment of atypical pathogens [2]. Similarly, statins metabolized by CYP3A4, notably simvastatin and atorvastatin, which are frequently used to manage mitotane-induced hypercholesterolaemia, should be replaced by pravastatin and rosuvastatin, which are not CYP3A4 substrates. The consequences of mitotane-induced CYP3A4 induction are also relevant in oncology, where sunitinib was among the first tyrosine kinase inhibitors (TKIs) demonstrating a significant metabolism by CYP3A4 during mitotane treatment. Other TKIs including imatinib, dasatinib, erlotinib, and sorafenib, as well as cytotoxic agents such as etoposide, doxorubicin, docetaxel, and vincristine, are all CYP3A4 substrates whose plasma exposures may be substantially reduced during mitotane treatment [2]. Beyond CYP3A4, mitotane may induce other P450 monooxygenases, as suggested by the requirement of high doses of warfarin, a known substrate of CYP2C9, during

mitotane treatment to obtain therapeutic anticoagulation. This observation, while clinically relevant, warrants further investigation [3]. The clinical challenge is more significant when co-administered drugs act as both CYP3A4 substrates and inhibitors, resulting in bidirectional and unpredictable pharmacokinetic interactions. This may either counteract the inducing effect of mitotane and lead to less reduced plasma levels of this drug or outweigh the inducing effect of mitotane. Hence, therapeutic drug monitoring represents the most reliable approach to further explore the potential effect of mitotane on co-administered drugs [1].

Conclusion : DDI involving mitotane are frequent and clinically significant yet remain underrecognized in routine clinical practice. Therefore, not only the effect of mitotane on substrates of CYP3A4 but also the effect of mitotane on substrates of other members of the cytochrome P450 enzyme family should be investigated. The inducing effect of mitotane on CYP3A4 may persist for months following treatment discontinuation, extending the interaction risk well beyond the active treatment stage.

Clinical and Psychological Impact of a secondary MSH2 Variant Discovery in the Context of Martsolf Syndrome.

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Background: Whole-exome sequencing has significantly increased the detection of secondary oncogenic findings. We report the secondary discovery of an MSH2 variant (Lynch syndrome) in a child being evaluated for a rare neurodevelopmental disorder, highlighting the clinical and psychological impact on the family.

Case presentation: A 5-year-old female, presenting with severe psychomotor delay and multiple congenital anomalies, was diagnosed with Martsolf/Micro-Warburg syndrome via a homozygous RAB3GAP2 variant. Secondary analysis of genomic data incidentally revealed a likely pathogenic heterozygous MSH2 variant (PVS1, PM2), indicating a high risk for Lynch-related malignancies for the patient (surveillance recommended from age 20) and the carrier parent. Given the autosomal dominant inheritance pattern, systematic cascade testing among parents and relatives is imperative for effective prevention (Shao et al., 2020). The announcement of cancer predisposition, superimposed on a pre-existing neurodevelopmental burden, caused significant maternal distress. Assessment using the Multidimensional Impact of Cancer Risk Assessment (MICRA) scale yielded a score of 48, indicating a moderate-to-significant psychological impact. This score reflects anxiety regarding oncological uncertainty and the emotional weight of a "dual" genetic diagnosis (the rare syndrome and the hereditary cancer risk).

Conclusion: Incidental genomic findings present deep clinical and ethical complexities. A holistic approach is essential to help genetic counseling delicately navigate the balance between a child's immediate neurodevelopmental management and long-term familial oncological prevention and psychological support.

Gemcitabine-Induced Thrombocytopenic Purpura: Myelosuppression, Thrombotic Microangiopathy, or Immune Thrombocytopenia?

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Introduction: Gemcitabine is a widely used pyrimidine antimetabolite chemotherapy agent, primarily indicated in the treatment of various solid tumors, including pancreatic, lung, and ovarian cancers. While its haematological toxicity profile is well-documented, the emergence of purpura during treatment can present a complex diagnostic challenge for clinicians. Indeed, the underlying mechanisms can vary, including peripheral immune-mediated destruction of platelets, direct endothelial damage leading to thrombotic microangiopathy, and leukocytoclastic vasculitis.

Methods: We report a case of a gemcitabine-induced purpura. This case was notified to the Tunisian National Center of Pharmacovigilance in February 2024, analyzed, and valid according to the updated French imputability method².

Results: A 62-year-old man with a history of locally advanced pancreatic adenocarcinoma was receiving second-line chemotherapy consisting of weekly intravenous gemcitabine infusions. The first infusion was well tolerated, with no adverse drug reaction. Four days after the second gemcitabine infusion, the patient developed localized pruritus, followed by purpuric lesions on both lower limbs. Laboratory investigations revealed a leukocyte count of 3,730/ μ L, a platelet count of 93,000/ μ L, and a hemoglobin level of 10 g/dL. The cutaneous manifestations were completely resolved within seven days. Given the rapid clinical improvement, a skin biopsy was not performed, preventing histopathological confirmation of the diagnosis. The causality assessment was scored as C2S2 based on the suggestive delay and mainly the favorable outcome one week after drug discontinuation.

Conclusion: Purpura with thrombocytopenia following gemcitabine therapy may Result from bone marrow toxicity, thrombotic microangiopathy, or immune thrombocytopenia. Urgent evaluation, including peripheral blood smear, hemolysis workup, and renal function tests, is essential to identify the underlying mechanism. Bone marrow toxicity may allow dose-reduced reintroduction after recovery, whereas thrombotic microangiopathy and immune thrombocytopenia require permanent discontinuation of gemcitabine, underscoring the importance of early recognition to ensure appropriate management and prevent severe outcomes.

Pharmaco-economic Impact of Centralized Bortezomib Compounding

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Background: Bortezomib is widely used in the treatment of multiple myeloma. Centralized chemotherapy compounding strategies have been described in the literature as effective cost containment approaches for decreasing oncology drug waste. Objective: To evaluate the pharmaco-economic impact of centralized bortezomib preparation within the Centralized Chemotherapy Preparation Unit (UCPC) of CHU Aziza Othmana between 2023 and 2025.

Methods: A retrospective study was conducted using consumption data extracted and analyzed from Microsoft Excel

from January 2023 to December 2025. Theoretical consumption was calculated assuming one vial per patient without residual vial content sharing, while real consumption integrated centralized compounding and residual vial optimization. Economic savings were calculated using the hospital unit price of one 3.5 mg vial of Bortezomib (128.295 TND).

Results: Theoretical costs remained consistently higher than real costs throughout the study period. In 2023, the theoretical cost was approximately 250,000 TND versus 160,000 TND real cost, generating nearly 90,000 TND in savings. In 2024, the highest optimization level was observed, with approximately 150,000 TND saved. In 2025, savings remained substantial at nearly 130,000 TND. Overall, centralized preparation and residual vial optimization significantly decreased drug waste and optimized vial utilization.

Conclusion: Centralized bortezomib compounding combined with residual vial optimization represents an effective pharmaco-economic strategy for minimizing antineoplastic drug waste and improving hospital resource management. Key Findings: Maximum gain observed in 2024: ~150,000 TND Significant decrease in theoretical vial consumption centralized compounding and residual vial optimization minimized oncology drug waste.

Sexuality in Patients with Gynecological Cancers: A Descriptive Study and Impact According to Cancer Type

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Introduction: Gynecological cancers significantly affect patients' quality of life, particularly sexual function. However, this issue remains underrecognized in routine oncological practice, especially in middle-income countries where psycho-sexual care is insufficiently integrated into cancer management.

Objective: To evaluate sexual dysfunction in patients with gynecological cancers and analyze its variation according to cancer type.

Methods: A descriptive study was conducted among 60 patients followed for gynecological cancers between 2023 and 2025. Sexual function was assessed using the Female Sexual Function Index (FSFI), while sexual distress was evaluated using the Female Sexual Distress Scale-Revised (FSDS-R), adapted to the local sociocultural context. A descriptive subgroup analysis according to cancer type was performed.

Results: The mean age of patients was 51 $\pm$ 9 years. Cervical cancer accounted for 40% of cases, followed by endometrial cancer (30%), ovarian cancer (20%), and vulvar/vaginal cancers (10%). Sexual dysfunction (FSFI < 26.55) was identified in 73% of patients. According to cancer type, prevalence rates were: Cervical cancer: 82% Vulvar/vaginal cancers: 78% Ovarian cancer: 70% Endometrial cancer: 65% Dyspareunia was reported in 60% of patients, with higher frequencies in cervical (70%) and vulvar cancers (75%), particularly after pelvic radiotherapy or extensive surgery. Sexual distress (positive FSDS-R) was observed in 62% of sexually active patients, predominantly among cervical (66%) and vulvar cancer patients (63%). Only 20% of patients had received specific supportive care, including lubricants, psychosexual counseling, or psychological support, and fewer than 10% had spontaneously discussed sexual issues during oncology consultations.

Discussion: This study highlights the substantial impact of gynecological cancers on patients' sexual health, emphasizing

sexuality as an important yet often overlooked component of quality of life. Sexual dysfunction was common among patients, with variations observed according to cancer type. These differences may reflect the distinct anatomical, hormonal, and psychological consequences associated with each malignancy and its treatment. Our findings are consistent with previous studies reporting decreased sexual desire, dyspareunia, reduced arousal, and lower sexual satisfaction following treatment for gynecological cancers. Surgical procedures, chemotherapy, radiotherapy, and treatment-induced menopause may all contribute to these alterations, while body image concerns and emotional distress can further impair sexual well-being.

Conclusion : Sexual dysfunction is highly prevalent among patients with gynecological cancers, with a greater impact observed in cervical and vulvar cancers. These findings highlight the need for a multidisciplinary approach integrating sexual health into routine oncological care. keywords : Gynecological cancers; Sexuality; Sexual dysfunction; Quality of life; Female sexual function; Cancer type; Gynecologic oncology.

Multi-disciplinary management of advanced uterine sarcoma: a retrospective clinical experience

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Background: Uterine sarcomas are rare and aggressive mesenchymal malignancies characterized by high recurrence rates and poor prognosis, particularly in advanced stages. Optimal management requires a coordinated multi-disciplinary approach integrating surgery, systemic therapy, and radiotherapy. This study evaluates the clinical outcomes of patients with advanced uterine sarcoma managed through a multi-disciplinary tumor board strategy.

Methods: We conducted a retrospective study of patients diagnosed with advanced-stage uterine sarcoma (FIGO stage III–IV) managed at a tertiary referral center between 2018 and 2025. Data collected included demographic characteristics, histological subtypes, treatment modalities, and outcomes. All cases were discussed in a dedicated multi-disciplinary tumor board including gynecologic oncology, medical oncology, radiation oncology, radiology, and pathology specialists. Outcomes assessed were progression-free survival (PFS), overall survival (OS), and treatment-related morbidity.

Results: A total of 18 patients were included, with a median age of 54 years (range 38–72). The most common histological subtype was leiomyosarcoma (61%), followed by high-grade endometrial stromal sarcoma (28%) and undifferentiated uterine sarcoma (11%). Primary management consisted of cytoreductive surgery in 72% of cases, achieving complete resection in 44%. Adjuvant chemotherapy (doxorubicin- or gemcitabine-based regimens) was administered in 83% of patients, while 39% received radiotherapy for local control. The median PFS was 11.4 months, and the median OS was 24.7 months. Patients managed with complete surgical resection followed by combined systemic therapy demonstrated improved survival outcomes compared to those with residual disease.

Conclusion: Multi-disciplinary management of advanced uterine sarcoma allows for individualized treatment strategies and may improve oncologic outcomes despite the aggressive nature of the disease. Complete surgical resection remains the most significant prognostic factor, while systemic and radiation therapies play a key role in disease control. Prospective studies are needed to optimize therapeutic sequences and evaluate

novel targeted therapies.

Hidden endometrial carcinoma in atypical endometrial hyperplasia: prevalence and risk factors in a Tunisian tertiary center

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Background: Atypical endometrial hyperplasia (AEH) is considered a premalignant lesion with a significant risk of concurrent or subsequent endometrial carcinoma. Data regarding its malignant potential in North African populations remain limited. This study aims to evaluate the prevalence of endometrial carcinoma in patients diagnosed with AEH in a Tunisian tertiary care center and to identify associated risk factors.

Methods: We conducted a retrospective study including patients diagnosed with atypical endometrial hyperplasia between 2015 and 2024 at a tertiary maternity and gynecology center in Tunisia. Clinical, ultrasound, histopathological, and surgical data were reviewed. All patients underwent endometrial sampling and/or hysterectomy. The primary outcome was the rate of concomitant or subsequent endometrial carcinoma. Secondary outcomes included clinical and metabolic risk factors associated with malignancy.

Results: A total of 118 patients with AEH were included, with a mean age of 52.6 ± 9.4 years. Endometrial carcinoma was identified in 29 cases (24.6%), either at initial diagnosis (occult carcinoma) or on final hysterectomy specimens. The majority were endometrioid adenocarcinomas, predominantly FIGO grade I–II. Significant associations were observed between carcinoma occurrence and postmenopausal status, obesity, and diabetes mellitus. Patients with complex atypical hyperplasia and increased endometrial thickness on ultrasound showed a higher risk of malignancy.

Conclusion: Atypical endometrial hyperplasia carries a substantial risk of concurrent endometrial carcinoma in the Tunisian population. Careful histological assessment and prompt definitive management are essential, particularly in high-risk patients. These findings support the need for standardized diagnostic and therapeutic strategies in this population. Keywords: Atypical endometrial hyperplasia; endometrial carcinoma; occult cancer; premalignant endometrial lesions; uterine cancer risk; Tunisia; hysterectomy; endometrial biopsy; gynecologic oncology.

Predictive value of HPV-positive ASC-US cytology for CIN2+ detection: a 2-year retrospective study in a level III maternity center

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Introduction: Atypical squamous cells of undetermined significance (ASC-US) represent the most frequent cytological abnormality detected during cervical cancer screening. The association with a high-risk human papillomavirus (hrHPV) positive test increases the risk of cervical premalignant lesions and warrants colposcopic evaluation. The aim of this study was to assess the predictive value of HPV-positive ASC-US for the detection of cervical intraepithelial neoplasia grade 2 or higher (CIN2+) in a level III maternity center.

Methods: We conducted a retrospective descriptive and analytical study including all patients who presented with ASC-US cervical cytology associated with a positive high-risk HPV test between January 2024 and December 2025. Demographic data, colposcopic findings, and histopathological Results were collected from medical records. All patients underwent colposcopy with directed biopsies when abnormalities were detected. The primary endpoint was the presence of CIN2+ on histological examination.

Results: A total of 138 patients were included. The mean age was 37.8 ± 8.6 years. Colposcopy was abnormal in 92 cases (66.7%). Cervical biopsy was performed in 104 patients (75.4%). Histopathological findings were as follows: No lesion or chronic cervicitis in 48 cases (46.2%); CIN1 in 29 cases (27.9%); CIN2 in 16 cases (15.4%); CIN3 in 9 cases (8.7%); Microinvasive carcinoma in 2 cases (1.9%). The overall prevalence of CIN2+ lesions was 20.3% (28/138). The detection rate of high-grade lesions was significantly higher in women older than 35 years (27.4% vs 12.5%, $p = 0.03$). High-grade colposcopic findings were strongly associated with CIN2+ lesions (OR = 6.8; 95% CI [2.5–18.4]; $p < 0.001$).

Discussion: Our study confirms that patients with ASC-US cytology associated with high-risk HPV positivity represent a population at significant risk for cervical precancerous lesions. The CIN2+ rate observed (20.3%) is consistent with the international literature, where it ranges between 15% and 25%. These findings support HPV-based triage strategies and systematic colposcopic evaluation in this subgroup. The strong association between major colposcopic abnormalities and high-grade histological lesions highlights the importance of accurate colposcopic assessment to optimize early diagnosis. The main limitations of this study are its retrospective and single-center design.

Conclusion: HPV-positive ASC-US cytology has a significant predictive value for CIN2+ detection. In our series, one in five patients had a high-grade lesion, supporting systematic colposcopic management in accordance with current guidelines. These Results reinforce the value of HPV testing in risk stratification and optimization of cervical cancer screening strategies.

HPV vaccine hesitancy in Arab and North African countries: cultural, social, and healthcare barriers – a narrative review

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Background: Cervical cancer remains the fourth most common cancer among women worldwide, with approximately 600,000 new cases and more than 340,000 deaths annually. Human papillomavirus (HPV) vaccination is highly effective, preventing over 70% of cervical cancer cases. However, vaccine uptake remains suboptimal in many Arab and North African countries, largely due to vaccine hesitancy rather than availability alone.

Methods: This narrative review was conducted using published literature from 2010 to 2025. A structured search was performed in PubMed, Scopus, and Google Scholar using the keywords: HPV vaccination, vaccine hesitancy, cervical cancer prevention, Arab countries, and North Africa. Studies reporting knowledge, attitudes, acceptance rates, and barriers to HPV vaccination were included. Data were synthesized qualitatively and, where available, summarized quantitatively.

Results: The literature demonstrates substantial variability in HPV awareness and vaccine acceptance across Arab and North African populations. HPV awareness among parents ranges

from 20% to 55%, while fewer than 40% of women correctly identify HPV as the main cause of cervical cancer. Awareness among adolescents is often below 30%. Vaccine acceptance rates vary between 30% and 75%, with an estimated regional average of 40–60%. Acceptance increases significantly when the vaccine is recommended by a healthcare provider, reaching 70–90%, whereas it drops below 40% in the absence of medical recommendation. Cultural and social barriers remain prominent. Between 40% and 80% of parents associate HPV infection with sexual activity, and up to 60% believe vaccination may encourage early sexual behavior. Social discomfort regarding adolescent vaccination is reported by 30–50% of respondents in several studies. Concerns regarding safety also contribute significantly to hesitancy. Fear of infertility is reported by 25–55% of parents, while 20–40% express concerns about serious adverse effects. Misinformation, particularly through social media, influences approximately 30% of negative vaccination decisions. From a healthcare system perspective, only 10–30% of countries in the region have implemented structured national HPV vaccination programs. Less than 50% of physicians systematically recommend the vaccine, and cost represents a barrier for 30–60% of families in non-subsidized settings. Conversely, facilitators of vaccine uptake include strong physician recommendation, school-based vaccination programs, and public awareness campaigns, which have been associated with coverage rates exceeding 70–90% in well-implemented systems.

Conclusion: HPV vaccine hesitancy in Arab and North African countries remains high and is driven by a combination of limited knowledge, cultural perceptions, misinformation, and healthcare system gaps. Overall vaccine acceptance ranges from 30% to 60% across studies. Strengthening education, improving physician engagement, and implementing school-based vaccination programs are essential strategies to improve coverage and reduce the future burden of cervical cancer in the region.

Palbociclib-induced interstitial lung disease with fibrosis in a patient with metastatic breast cancer

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Introduction: Palbociclib, a cyclin-dependent kinase (CDK) 4/6 inhibitor widely used in hormone receptor-positive metastatic breast cancer (BC), is generally well tolerated. However, rare but potentially severe pulmonary toxicities, including interstitial lung disease (ILD), have been documented. [1] We report a rare case of palbociclib-induced ILD presenting with bilateral interstitial parenchymal infiltrates and fibrotic changes.

Methods: This case was notified to the Tunisian National Center for Pharmacovigilance in November 2025, and analyzed using the upd French imputability method. [2]

Results: A 70-year-old female patient with a history of metastatic BC and lymph node involvement was receiving palbociclib (125 mg/day, 3 weeks on/1 week off) since June 2023. A complete remission was observed. Two years later, she developed a persistent dry cough associated with progressive dyspnea, leading to consultation in the pulmonology department. Chest X-ray showed bilateral interstitial parenchymal infiltrates suggestive of pulmonary fibrosis. Further evaluation with chest computed tomography confirmed diffuse bilateral interstitial infiltrates with fibrotic changes. An extensive etiological

investigation was performed (Viral panel and microbiological tests, including blood cultures and sputum cultures) and showed no evidence of infectious disease. Autoimmune serologies were also negative. The patient had no previous history of ILD or other pulmonary disorders. The patient was started on Long-Term Oxygen Therapy (LTOT). She received corticosteroid therapy, and palbociclib was discontinued. Six months after treatment discontinuation, the patient reported a slight improvement in her symptoms. However, she still complains of dyspnea at rest.

Discussion: CDK4/6 inhibitors, including palbociclib, have become a standard treatment in hormone receptor-positive metastatic breast cancer due to their efficacy and generally favorable safety profile. However, rare pulmonary toxicities such as interstitial lung disease have been increasingly reported. The clinical presentation is non-specific, often including cough and dyspnea. Several risk factors such as smoking, preexisting lung disease, and prior exposure to pneumotoxic drugs have been suggested. Although the exact mechanism remains unclear, an immune-mediated hypersensitivity reaction leading to inflammatory lung injury has been suggested. [3].

Conclusion: While CDK4/6 inhibitors have revolutionized the treatment of metastatic breast cancer by significantly improving progression-free survival and, in some cases, overall survival, their risk/benefit balance requires caution in elderly patients. Palbociclib is often preferred in older patients due to its lower toxicity compared to other CDK4/6 inhibitors. However, recent realworld data suggest that it may carry the highest risk of pneumonitis among the CDK4/6 inhibitors. In our case, the clinically stationary course is explained by progression of ILD toward irreversible fibrosis. Thus, early recognition, prompt drug discontinuation, and corticosteroid therapy are essential for managing palbociclib-induced ILD. Clinicians should be alert to unexplained respiratory symptoms, especially in elderly patients to prevent progression to irreversible fibrosis.

One-dose HPV vaccination: a paradigm shift in global cervical cancer prevention strategies – a narrative review

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Background: Cervical cancer remains a major global health challenge, accounting for approximately 600,000 new cases and over 340,000 deaths annually worldwide. Persistent infection with high-risk human papillomavirus (HPV) types is responsible for nearly all cervical cancer cases. Although HPV vaccination has demonstrated high efficacy, global vaccine coverage remains insufficient, particularly in low- and middle-income countries. Recently, a one-dose HPV vaccination strategy has emerged as a promising approach to improve vaccine accessibility and accelerate cervical cancer prevention worldwide.

Methods: A narrative review of the literature published between 2015 and 2025 was conducted using PubMed, Scopus, Google Scholar, and World Health Organization (WHO) reports. The search included the following keywords: HPV vaccine, one-dose vaccination, cervical cancer prevention, HPV immunogenicity, and global vaccination strategies. Clinical trials, observational studies, WHO recommendations, and systematic reviews evaluating the efficacy, immunogenicity, safety, and public health impact of one-dose HPV vaccination were included.

Results: Recent evidence suggests that a single dose of HPV vaccine provides substantial protection against high-risk HPV infection, particularly HPV-16 and HPV-18, which are responsible for approximately 70% of cervical cancer cases. Several large international studies demonstrated vaccine efficacy ranging

from 82% to 97% against persistent HPV infection following a single dose. Immunogenicity analyses revealed stable antibody responses lasting at least 10 years in vaccinated populations. The World Health Organization endorsed the one-dose strategy in 2022 for girls aged 9–20 years as an alternative to the traditional two-dose schedule. This approach is expected to significantly improve vaccine accessibility in low-resource settings. Globally, HPV vaccination coverage remains suboptimal, with complete vaccination rates below 20% in many low-income countries. Mathematical models suggest that adopting a one-dose strategy could increase vaccine coverage by up to 30–40%, while substantially reducing logistical and financial barriers. The economic impact is also considerable. One-dose schedules may reduce vaccination program costs by approximately 30–50%, facilitating broader implementation of national vaccination campaigns. Despite these promising findings, some uncertainties remain regarding long-term immunity, protection beyond 10–15 years, and efficacy in immunocompromised populations. Additional long-term surveillance studies are still required.

Conclusion: One-dose HPV vaccination represents a major advancement in global cervical cancer prevention strategies. Current evidence demonstrates high efficacy, durable immune response, and important public health and economic benefits. This simplified approach may substantially improve vaccine coverage, particularly in low- and middle-income countries, and contribute significantly to the global goal of cervical cancer elimination.

Imatinib-Induced Multi-System Toxicity: A Rare Combination of Acute Kidney Injury and Bilateral Retinal Hemorrhage

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Introduction: Imatinib, a first-generation tyrosine kinase inhibitor, is widely used in the treatment of gastrointestinal stromal tumors (GIST) and is generally associated with a favorable safety profile. Nevertheless, rare severe adverse events involving multiple organ systems have been observed [1]. We report a rare case of imatinib-associated multi-organ toxicity presenting as acute kidney injury and bilateral retinal hemorrhage.

Methods: This case was notified to the Tunisian National Center for Pharmacovigilance in March 2026, and analyzed using the upd French imputability method [2].

Results: A 77-year-old man with a history of type 2 diabetes, hypertension, and ischemic heart disease had been receiving metformin, perindopril, nebivolol, and acetylsalicylic acid for the past 4 years. In 2025, he was diagnosed with a gastrointestinal stromal tumor (GIST) and underwent multiple surgical procedures before the initiation of Imatinib in November 2025 at a dose of 400 mg per day. Two months after treatment onset, he developed asthenia, anorexia, vomiting, and bilateral visual blurring. Ophthalmologic evaluation confirmed bilateral retinal hemorrhages requiring urgent surgical management. Laboratory investigations revealed acute kidney injury with serum creatinine rising to 141 µmol/L. There was no history of pre-existing renal disease, with a normal renal function baseline before treatment initiation. Imatinib was discontinued, while his chronic medications were maintained. Clinical evolution was favorable with resolution of gastrointestinal symptoms, normalization of renal function within 15 days, and

improvement of visual symptoms following ophthalmic surgery. The causality assessment score was C1S2-I1, based on the compatible delay and mainly the favorable outcome two weeks after drug discontinuation.

Discussion: Very rare intraocular hemorrhagic events have been reported in patients treated with Imatinib. Advanced age, diabetes, hypertension, cardiovascular disease, and comorbidities may contribute to their occurrence, as observed in our patient [3]. Acute kidney injury has also been described during imatinib therapy. According to de Oliveira et al., Imatinib may induce renal tubular toxicity through inhibition of tyrosine kinases involved in tubular function, leading to electrolyte disturbances and acute kidney injury. The impairment appeared reversible after treatment discontinuation [4].

Conclusion: Rare but serious multi-organ toxicities may be associated with Imatinib treatment. Early recognition and timely drug discontinuation remain key to optimizing clinical outcomes and preventing potentially serious complications.

Hydroxycarbamide-Associated Longitudinal Melanonychia on Multiple Nails in Chronic Myeloid Leukemia

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Background: Hydroxycarbamide or hydroxyurea (HU) is a common antineoplastic agent prescribed for myeloproliferative disorders, generally well-tolerated (1). But, long-term treatment is associated with mucocutaneous adverse events and nail hyperpigmentation. Nail disorders are uncommon side effects; some reports indicated that melanonychia developed in about 4.3% of the patients receiving hydroxyurea therapy (2). **Objective:** We present a rare case of melanonychia likely induced by hydroxyurea.

Methods: The case was reported to the Tunisian National Centre of Pharmacovigilance in December 2025 and assessed according to the upd French method of imputability.

Case presentation: A 63-year-old female patient with a past medical history of hypertension and hypothyroidism was treated for chronic myeloid leukemia with Hydroxyurea 1000 mg once daily. Approximately five months after initiating hydroxyurea, she presented with discoloration of the fingernails. One month after continuing treatment, the discoloration had affected the toenails as well. Her family history was negative for melanonychia, melanoma and underlying systemic disease. On examination, she has longitudinal bluish black discoloration of all nails. There were no other cutaneous features of hyperpigmentation and her systemic examination was unremarkable. Hutchinson's sign was negative. Also, mycologic tests were negative. Diagnosis of melanonychia, likely hydroxyurea-induced, was made. The patient requested temporary discontinuation of the drug as she experienced cosmetic inconvenience due to the discoloured nails. Just six weeks after stopping treatment, a significant lightening of pigmentation was visible. The patient was unable to suspend the drug permanently.

Discussion: Melanonychia can be caused by infections, melanocytic origin, or an adverse effect of chemotherapy. The onset of melanonychia varies from 4 weeks to 5 years after initiation of hydroxyurea. Longitudinal bands seemed to be the most common pattern. Similarly in our case, melanonychia with longitudinal bands were developed five months after taking hydroxyurea. The nails returned to normal after the patient

discontinued taking this drug. There was no family history for melanonychia and melanoma, and mycologic tests were negative. In addition, subungual melanoma was also unlikely due to the absence of Hutchinson's sign. So we considered that the melanonychia was induced by hydroxyurea treatment.

Conclusion: Hydroxyurea-induced melanonychia is generally benign and antimycotic treatment is not useful. After discontinuation of the inducing drug, the melanonychia will disappear as the nail grows. But it can cause significant cosmetic concern and psychological distress for patients.

Reversible Cerebellar Syndrome Induced by High-Dose Cytarabine in Acute Myeloid Leukemia: A Case Report

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Introduction: Cytarabine is an antimetabolite chemotherapeutic agent primarily used as first-line therapy for acute myeloid leukemia, and as second or third-line treatment for lymphomas. Neurological toxicity, particularly cerebellar syndrome, is a rare but potentially serious dose-limiting adverse effect. It typically manifests with dysarthria, ataxia, and coordination disorders [1]. We report a case of reversible cerebellar toxicity following high-dose cytarabine in a patient with acute myeloid leukemia.

Methods: This case was notified to the Tunisian National Center for Pharmacovigilance in March 2025, and analyzed using the upd French imputability method [2].

Results: A 60-year-old woman was followed in the hematology department for acute myeloid leukemia diagnosed in October 2025. Induction therapy and the first consolidation cycle were well tolerated. Two days after the second consolidation cycle with high-dose cytarabine (4600 mg twice daily for 3 days), she developed an acute onset of headache, dysarthria, and gait disturbance consistent with cerebellar ataxia. Neurological examination revealed a combined static and kinetic cerebellar syndrome. Etiological investigations, including brain computed tomography, brain magnetic resonance imaging, and cerebrospinal fluid analysis, showed no abnormalities. A cytarabine-induced cerebellar syndrome was suspected, and cytarabine was immediately discontinued. The patient was treated with dexamethasone and vitamin B6 supplementation. Progressive clinical improvement was obtained within 5 days. The imputability assessment concluded a chronological score of C2 and a semiological score of S2 in favor of cytarabine involvement.

Discussion: Cerebellar toxicity is a dose-dependent adverse effect of cytarabine. Advanced age and renal or hepatic impairment may increase the risk of neurotoxicity. Genetic variability may also influence individual susceptibility. The mechanism of cytarabine neurotoxicity remains unclear, but neuropathological findings suggest cerebellar Purkinje cell loss with reactive gliosis and involvement of the molecular and granular layers [3]. Although usually transient, neurological impairment can occasionally be severe and irreversible [1].

Conclusion: Cerebellar toxicity remains a rare but clinically significant complication of high-dose cytarabine. Early recognition of neurological symptoms and prompt discontinuation of the drug are essential to prevent persistent deficits.

Rapid recurrence and malignant transformation of a borderline phyllodes tumor after incomplete surgical excision

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Introduction : Phyllodes tumors are rare fibroepithelial breast neoplasms with unpredictable clinical behavior. Borderline tumors are considered to have intermediate malignant potential, but incomplete excision can lead to early recurrence and malignant transformation. Surgical margins remain the main modifiable prognostic factor.

Methods : We report the case of a 46-year-old woman with no significant medical history who presented with a palpable mass in the upper outer quadrant of the right breast. Imaging revealed a 22 × 15 mm heterogeneous lesion classified as ACR 4a. Core needle biopsy suggested a fibro epithelial tumor suspicious for phyllodes tumor. The patient underwent breast-conserving surgery (lumpectomy).

Results : Histopathology confirmed a borderline phyllodes tumor with positive surgical margins. Five months later, the patient developed a rapidly enlarging local recurrence measuring 50 × 3 cm at the same site. A second lumpectomy was performed. Histology revealed a malignant phyllodes tumor (grade 3 sarcoma) with close margins. Staging workup showed no distant metastases. Given the aggressive features and inadequate margins, the patient subsequently underwent a completion right mastectomy.

Conclusion : This case illustrates that incomplete excision of borderline phyllodes tumors can lead to early recurrence and malignant transformation. It underscores the critical importance of achieving negative surgical margins at initial surgery and supports current recommendations advocating for systematic re-excision in cases of positive margins. This case serves as a clear reminder that margin status, rather than initial surgical approach (lumpectomy versus mastectomy), is the key determinant of early progression. keywords : Phyllodes tumor of the breast; Borderline phyllodes tumor; Positive margins; Breast fibroepithelial tumor; Surgical management.

Progressive Cauda Equina Syndrome: An Overlooked Danger of Combined Intrathecal Chemotherapy?

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Introduction: Intrathecal chemotherapy is a cornerstone in the management of hematologic malignancies, including acute lymphoblastic leukemia. Although effective, it may be associated with a broad spectrum of adverse effects, including rare but potentially severe neurological toxicities [1]. We report a case of progressive cauda equina syndrome following combined intrathecal chemotherapy.

Methods: This case was notified to the Tunisian National Center for Pharmacovigilance in March 2026, and analyzed using the updated French imputability method [2].

Results: A 19-year-old patient with no significant medical history was diagnosed with T-cell acute lymphoblastic leukemia harboring a PICALM::MLLT10 rearrangement, with initial central nervous system involvement in the absence of clinical neurological manifestations. Treatment was initiated according to the GRAALL-2014 protocol. Triple intrathecal chemotherapy

(methotrexate 15 mg, cytarabine 40 mg, and hydrocortisone 40 mg) was administered on Day 1 and Day 3. Six days after the second administration (Day 9), he developed acute urinary retention. Initial brain and spinal magnetic resonance imaging (MRI) showed no abnormalities. Within 2 weeks, the patient experienced progressive neurological deterioration characterized by saddle hypoesthesia, bilateral lower-limb heaviness, abolished deep tendon reflexes, and paraparesis. A second spinal MRI revealed peripheral enhancement of the cauda equina nerve roots. Electromyography showed severe acute sensorimotor polyradiculoneuropathy of both lower limbs with predominant motor involvement. A neurological consultation excluded alternative etiologies (infectious, leukemic infiltration, and compressive causes) and supported a diagnosis of cauda equina syndrome secondary to toxic polyradiculoneuropathy related to intrathecal methotrexate and cytarabine administration. According to the French upd pharmacovigilance method, the chronological score was C2 and the semiological score was S2. Management included intravenous methylprednisolone, vitamin E and C supplementation, and physical rehabilitation.

Discussion: Neurological complications following intrathecal chemotherapy are rare but potentially severe. Cases of progressive motor and sensory neurotoxicity have been reported after administration of methotrexate and cytarabine [3] suggesting either direct neurotoxic effect or drug-induced immune dysregulation [1]. The clinical course can be progressively ascending or partially reversible, while complete recovery remains uncommon. Our case is consistent with these reports, presenting a rapidly progressive cauda equina syndrome with electrophysiological and imaging findings supporting an acute toxic polyradiculoneuropathy after combined intrathecal chemotherapy.

Conclusion: This case underscores a rare but severe neurotoxic complication following intrathecal methotrexate and cytarabine administration, presenting as cauda equina syndrome due to toxic polyradiculoneuropathy. Early recognition of neurological symptoms is essential for prompt diagnosis, exclusion of alternative etiologies, and appropriate management.

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Immediate Breast Reconstruction: Beyond Aesthetic Restoration, an Integral Part of Breast Cancer Treatment

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Background: Immediate breast reconstruction (IBR) has become an essential component of mode breast cancer management. Performed at the time of mastectomy, it improves quality of life, body image, and psychological well-being while maintaining oncological safety. Advances in reconstructive techniques now allow individualized treatment tailored to each patient's characteristics and expectations.

Objective: To evaluate current practices and early outcomes

of immediate breast reconstruction in breast cancer patients treated at our institution.

Methods: A retrospective single-center study was conducted at the René-Dubos Hospital in Pontoise between January 1 and December 31, 2025. During the study period, 293 patients were diagnosed with breast cancer, of whom 52 underwent mastectomy. Demographic characteristics, reconstructive techniques, and postoperative complications were analyzed in patients who underwent immediate breast.

Results: Among the 52 patients who underwent mastectomy, 26 received immediate breast reconstruction, corresponding to a reconstruction rate of 50%. The mean age was 62 years. Nipple-areola complex preservation was achieved in 9 patients (34.6%). Reconstructive techniques included implant-based reconstruction in 7 patients (26.9%), minilatissimus dorsi flap combined with lipofilling in 7 patients (26.9%), exclusive lipofilling in 7 patients (26.9%), DIEP flap reconstruction in 3 patients (11.5%), and latissimus dorsi flap reconstruction in 2 patients (7.7%). Three major complications were observed: two cases of skin necrosis following implant-based reconstruction and one case of DIEP flap necrosis requiring salvage surgery with a latissimus dorsi flap and implant reconstruction. The overall major complication rate was 11.5%.

Conclusion: In our experience, one out of every two patients undergoing mastectomy had access to immediate breast reconstruction. The availability of multiple reconstructive options allowed a personalized approach with an acceptable complication rate. Immediate breast reconstruction should be considered an integral part of breast cancer treatment, combining oncological safety, quality of life improvement, and aesthetic benefits.

Moving beyond pathological nodal staging: superior prognostic stratification using lymph node ratio and log odds of positive lymph nodes in gastric

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Introduction : Background and Aims: Accurate lymph node (LN) assessment is essential for prognostic stratification in gastric adenocarcinoma. Although the pathological nodal stage (pN) remains the standard classification system, alternative nodal metrics such as the lymph node ratio (LNR) and the log odds of positive lymph nodes (LODDS) have been proposed to improve prognostic accuracy. This study aimed to compare the prognostic performance of pN stage, LNR, and LODDS in predicting progression-free survival (PFS) following curative resection for gastric adenocarcinoma.

Methods: We conducted a retrospective single-center study including 195 patients who underwent curative-intent gastrectomy for gastric adenocarcinoma at the Institut Salah Azaiez, Tunisia, between January 2005 and December 2023. LNR was defined as the ratio of metastatic to examined LN and categorized as LNR0 = 0, LNR1 = 0.01–0.10, LNR2 = 0.11–0.25, and LNR3 > 0.25. LODDS was calculated as $\log \left[\frac{\text{positive lymph nodes} + 0.5}{\text{negative lymph nodes} + 0.5} \right]$ and classified according to the system proposed by Chen Jian-hui et al.: LODDS1 1.5, LODDS2 > 1.5 to 1.0, LODDS3 > 1.0 to 0, and LODDS4 > 0. Prognostic performance was assessed using receiver operating characteristic (ROC) curve analysis, Kaplan–Meier survival analysis with log-rank testing, Cox proportional hazards regression models, and Akaike Information Criterion

(AIC) comparisons.

Results: The 5-year PFS rates decreased significantly with increasing nodal burden across all classification systems. According to LNR categories, 5-year PFS was 61.3%, 58.8%, 52.3%, and 39.7% for LNR0, LNR1, LNR2, and LNR3, respectively ($p = 0.003$). According to LODDS categories, corresponding 5-year PFS rates were 57.5%, 56.3%, 56.3%, and 26.1% for LODDS1, LODDS2, LODDS3, and LODDS4, respectively ($p < 0.001$). For pN stage, 5-year PFS was 61.3%, 61.6%, 48.0%, and 37.0% for pN0, pN1, pN2, and pN3, respectively ($p = 0.002$). ROC analysis demonstrated significant prognostic discrimination for all three nodal classifications. LNR achieved the highest discriminatory performance (AUC = 0.637, 95% CI: 0.556–0.717, $p = 0.001$), followed by LODDS (AUC = 0.627, 95% CI: 0.544–0.710, $p = 0.003$) and pN stage (AUC = 0.614, 95% CI: 0.534–0.695, $p = 0.008$). In survival analysis, LODDS showed the strongest prognostic stratification (log-rank $\chi^2 = 22.166$), compared with pN stage ($\chi^2 = 14.481$) and LNR ($\chi^2 = 13.734$). Cox regression analysis confirmed the prognostic significance of LODDS (HR = 1.465, $p < 0.001$), LNR (HR = 1.467, $p = 0.001$), and pN stage (HR = 1.488, $p < 0.001$). Model comparison using the Akaike Information Criterion identified LODDS as the best-fitting model (AIC = 646.8), followed by pN stage (AIC = 649.8) and LNR (AIC = 650.2).

Conclusion: All three nodal classification systems were significant predictors of progression-free survival after curative gastrectomy for gastric adenocarcinoma. While LNR provided the highest discriminatory accuracy on ROC analysis, LODDS demonstrated superior prognostic stratification and the best overall model fit, as reflected by the lowest AIC value. These findings suggest that LODDS may represent the most informative nodal staging system for postoperative risk assessment in gastric cancer.

Impact of Local Treatment of Metastases on Overall Survival in non small cell lung cancer (NSCLC)

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Introduction: Non-small cell lung cancer (NSCLC) remains the leading cause of cancer-related mortality worldwide. Most patients are diagnosed at a locally advanced or metastatic stage, placing them in a palliative setting since diagnosis. This raises the question of the potential benefit of metastasis-directed local treatment (radiotherapy and/or surgery) on overall survival in patients with stage IV NSCLC.

Method: This was a retrospective, monocentric study including 169 patients with stage IV NSCLC treated between 2022 and 2023 in the medical oncology department of Abderrahmen Mami Hospital. Demographic, clinical, paraclinical, and outcome data were collected in a standardized manner and analysed using SPSS version 26.0.

Results: An independent and significant gain of overall survival (endpoint) was shown with patients who got a local treatment of their metastasis (HR = 0.57 ; IC 95 % : 0.35–0.93 ; $p = 0.023$).

Conclusion: Our findings suggest that an adaptive treatment strategy in patients with stage IV NSCLC may be beneficial. These Results emphasize the potential role of metastasis-directed local treatments on improving survival and quality of life.

TCHP Versus Sequential Anthracycline based Chemotherapy With Dual HER2 Blockade in Localized HER2-Positive Breast Cancer: A Real-World Comparison

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Background: Neoadjuvant chemotherapy combined with dual HER2 blockade yields high pathological complete response (pCR) rates in localized HER2-positive breast cancer. However, the optimal chemotherapy backbone, specifically regarding anthracyclines, remains debated. This study aimed to compare baseline characteristics and pCR rates between patients treated with an anthracycline-free regimen (TCHP) and those receiving a sequential anthracycline-taxane regimen.

Methods: We conducted a retrospective single-center study including 24 patients with localized HER2-positive breast cancer treated at Abderrahmen Mami Hospital between 2025 and 2026. Patients received either TCHP (docetaxel, carboplatin, trastuzumab, and pertuzumab) or a sequential anthracycline-taxane regimen with dual HER2 blockade. Baseline clinicopathological characteristics and pCR rates were compared between the two cohorts.

Results: A total of 24 patients were included (TCHP: n=11; sequential regimen: n=13). The mean age was 49.3 years (24–75). Patients in the TCHP cohort were significantly older than those in the sequential group (mean age 55 vs. 43 years, $p = 0.014$). No significant differences were observed regarding Other baseline characteristics, including menopausal status, health coverage, hormone receptor status (positive vs. negative), [MSI] Ki-67, stage, and nodal involvement, were well-balanced between the groups. The overall pCR rate was 70%. Precisely, pCR was achieved in 63.6% of patients treated with TCHP and 69.2% of those receiving the sequential regimen, showing no statistically significant difference between the two treatment strategies ($p = 0.556$).

Conclusion: Both neoadjuvant strategies achieved similarly high pCR rates, supporting the efficacy of the anthracycline-free TCHP regimen as a robust alternative to sequential regimen. Given the significant age difference between the cohorts, our findings highlight that treatment selection can be safely individualized, sparing older or at-risk patients from anthracyclines-associated toxicities, without compromising surgical and pathological outcomes.

IMPACT OF INCOMPLETE ACCESS TO DUAL ANTIHER2 BLOCKADE ON PATHOLOGICAL COMPLETE RESPONSE: A REAL-WORLD NORTH AFRICAN EXPERIENCE

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Background: Dual HER2 blockade combining trastuzumab and pertuzumab (T+P) with neoadjuvant chemotherapy is the standard of care for HER2-positive localized breast cancer. However, access to pertuzumab and sometimes trastuzumab remains limited in low- and middle-income countries due to drug availability constraints and healthcare resource limitations. Furthermore, the impact of incomplete anti-HER2 therapy on pathological complete response (pCR) in realworld North African settings is an important problem that we need to

shed the light on.

Methods: We conducted a retrospective cohort study of 81 patients with HER2-positive non-metastatic breast cancer treated with sequential anthracycline-taxane neoadjuvant chemotherapy at Institut Salah Azaiez, Tunis, Tunisia (2023–2025). All patients had a guideline-based indication for dual HER2 blockade (T+P). Patients were classified into three ordered groups: (1) complete dual blockade, (2) pertuzumab insufficiency alone, and (3) insufficiency of both agents. Pathological complete response (pCR) was defined as ypT0/is ypN0 on surgical specimen.

Results: Median age was 52 years (range 27–73). Most patients presented with stage III disease (62.5%) and grade III tumors (SBR III: 77.5%); 56.2% were hormone receptor-positive. Despite a universal guideline-based indication for T+P, complete dual blockade was achieved in only 10 patients (12.3%), while 34 (42.0%) had pertuzumab insufficiency alone and 37 (45.7%) had insufficiency of both agents. The overall pCR rate was 59.3% (48/81). A statistically significant dose-response gradient was demonstrated: 80.0% pCR in the complete dual blockade group, 67.6% in the pertuzumab insufficiency group, and 45.9% in the dual insufficiency group (Cochran-Armitage trend test: $p = 0.021$).

Conclusion: In this North African real-world cohort, incomplete access to dual HER2 blockade was observed in 87.7% of eligible patients, reflecting the significant drug availability barriers. These findings underline the urgent need for equitable access to anti-HER2 therapies and highlight the inequality of chances of survival for patients coming from less developed countries such as Tunisia.

Clinical Impact of Pre-Therapeutic DPD Screening and Secondary Dose Adaptations During Fluoropyrimidine-Based Chemotherapy: A Real-World cohort study

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Introduction: Pre-treatment DPD screening by plasma uracil measurement is increasingly recommended to prevent severe fluoropyrimidine-related toxicities. However, data on longterm toxicity pates and dose adaptations in routine practice remain limited. This study evaluated the impact of systematic DPD phenotyping on treatment safety and fluoropyrimidine dose individualization.

Methods: This retrospective real-world study included oncology patients treated with at least one cycle of 5-fluorouracil (5-FU) at Institut Salah Azaiez between January and May 2026. Pretreatment DPD phenotyping was performed by plasma uracil measurement established thresholds (normal <16 ng/mL; partial deficiency 16–150 ng/mL). Toxicity was graded per CTCAE v5.0. Clinical, biological, and treatment data were extracted from the Asclepius healthcare software and analyzed descriptively.

Results: The cohort comprised 315 patients (mean age: 60 ± 12 years; 41.3% female). [WB1] Colorectal and rectal cancers were predominant (72.4%), followed by nasopharyngeal (8.3%) 37.5% of patients were metastatic, 30.5% locally advanced. The most frequent regimens were FOLFOX (42.5%), FOLFIRI (14.3%), FOLFIRINOX (11.1%), and TPF (10.5%). DPD status was assessed by plasma uracil measurement in 312 patients (99.0%); three patients (1.0%) had no pre-treatment assessment available. Partial DPD deficiency was identified in 34 patients (10.8%), with plasma uracil levels ranging from 14.6 to 82.6 ng/mL. No

complete DPD deficiency was detected. This prevalence exceeds the 3–9% reported in European populations, consistent with ethnic-specific variation in DPYD polymorphism frequency across non-European cohorts. DPD deficiency rates were highest in cavum/ORL tumors (30.8%) and lowest in colorectal/rectal cancers (7.5%). A significant association with disease stage was observed ($p = 0.041$), with the highest deficiency rate among locally advanced disease (17.7%) compared to localized (8.2%) and metastatic (7.6%) stages. Nearly all deficient patients underwent empirical dose reduction: 55.9% received a 25% reduction and 38.2% a 50% reduction. Grade 2 toxicity occurred in 25.4% of patients and Grade 3 in 3.8%, exclusively among DPD-proficient patients (4.3% vs. 0%; $p = 0.375$), supporting the protective effect of upfront dose reduction. All diarrhea (6.3%), mucositis (4.8%), and neutropenia (3.2%) events were confined exclusively to the proficient group, confirming its non-DPD-related cumulative mechanism. Toxicity was predominantly cumulative, with a median onset at cycle 4 (mean 4.7); 27.3% of patients experienced their first toxicity by cycle 3 and 30.3% at cycle 6 or beyond, indicating a wide cumulative kinetic window extending well past the initiation phase.

Conclusion: Systematic DPD phenotyping enabled personalized fluoropyrimidine dosing at initiation and effectively prevented severe early toxicities in deficient patients — a population representing 10.8% of this cohort, with notably higher prevalence in cavum/ORL tumors. However, cumulative non-DPD-mediated toxicities drove secondary dose adaptations in over 40% of proficient patients beyond cycle 4, demonstrating that baseline phenotyping alone is insufficient. These findings advocate for a two-phase precision strategy: upfront DPD screening combined with structured longitudinal toxicity-guided dose individualization throughout treatment.

Quantifying Toxicity and Dose-Reduction of Fluoropyrimidine-Based Multidrug Regimens in Oncology: A 315-Patient Real-World study

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Introduction: Fluoropyrimidine-based multidrug regimens combined with oxaliplatin, irinotecan, cisplatin, or taxanes remain key standards of care in oncology. While effective, their clinical use is frequently complicated by overlapping cumulative toxicities that compromise dose intensity and treatment continuity, with regimen-specific signatures remaining incompletely characterized in real-world settings.

Objective: To quantify toxicity signatures and dose-reduction dynamics across fluoropyrimidine-based multidrug regimens and to identify clinical factors associated with treatment adaptation in a real-world oncology population

Methods: This retrospective real-world study included patients treated with fluoropyrimidine-based combination regimens at the Institut Salah Azaïez between January and May 2026. Clinical, biological, treatment, and toxicity data were extracted from the Asclepios e and compiled using Microsoft Excel. Adverse events were graded according to CTCAE v5.0, and analyses focused on toxicity profiles and treatment-related dose modifications.

Results: The cohort comprised 315 patients (mean age 60.0 ± 12 years; %58.6 male). %72.4 of cases involved colorectal or rectal cancers ($n = 228$), followed by cavum (%8.3, $n = 26$),

gastric (%6.7, $n = 21$), and head-and-neck cancers (%4.8, $n = 15$). Secondary dose adaptations were required in %36.8 of patients ($n = 116$), comprising 111 dose reductions and 4 protocol changes. Adaptation rates varied markedly across regimens: %47.0 for FOLFOX, %37.8 for FOLFIRI, %31.4 for FOLFIRINOX, %21.4 for FLOT, and %6.1 for TPF. The leading trigger for adaptation was Grade 2 toxicity, accounting for %60.3 of cases, followed by general condition deterioration or poor treatment tolerance (%18.1, $n = 21$), and Grade 3 toxicity (%8.6, $n = 10$). %23.2 of patients ($n = 73$) required secondary 5-FU dose reductions. The predominant drivers were cumulative Grade 2 mucositis (%4.1, $n = 13$), Grade 2 neutropenia (%3.2, $n = 10$), and Grade 3 neutropenia (%1.6, $n = 5$). Hand-foot syndrome remained infrequent (Grade 2: %0.6), and no cardiotoxicity was recorded across the entire cohort. Among the 183 oxaliplatin-exposed patients, cumulative peripheral neuropathy was the dominant toxicity, affecting %28.4 of patients at Grade 1, %24.6 at Grade 2, and %2.2 at Grade 3. %42.6 of oxaliplatin-exposed patients ($n = 78$) underwent dose reduction, with individual reductions ranging from %10 to %50. Among the 80 irinotecan-exposed patients, clinically significant diarrhea was the hallmark toxicity, occurring in %20.0 of patients overall (Grade 2: %17.5; Grade 3: %1.2). %25.0 of patients ($n = 20$) required dose reduction. As for docetaxel-exposed patients Grade 2 cutaneous toxicity and peripheral neuropathy each occurred in %2.1 of patients ($n = 1$ each). %6.4 of patients ($n = 3$) underwent docetaxel dose reduction, between %20–%25. The number of completed treatment cycles was the only significant predictor of dose adaptation (6.3 ± 3.0 vs. 4.9 ± 2.7 cycles; $p < 0.001$). Age, sex, and creatinine clearance were not associated with dose modification.

Conclusion: Distinct toxicity signatures drive dose adaptation in fluoropyrimidine-based multidrug regimens. Cumulative neurotoxicity and gastrointestinal toxicity were the main determinants of treatment modification, supporting proactive toxicity monitoring and personalized dose management in routine oncology practice.

PAIN SCREENING AND MANAGEMENT IN CANCER PATIENTS: A CROSS-SECTIONAL STUDY FROM TWO TUNISIAN ONCOLOGY REFERENCE CENTERS

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Background: Cancer pain affects 54–77% of patients worldwide and represents the most feared symptom in oncology. Despite available analgesic strategies, it remains frequently underassessed and inadequately controlled, with a major impact on patient quality of life. This study aimed to characterize the prevalence, intensity, and neuropathic features of cancer pain, to evaluate current pharmacological and non-pharmacological management practices, and to assess the relationship between pain assessment frequency and patient satisfaction in two Tunisian oncology reference centers.

Methods: A descriptive cross-sectional study was conducted between March and April 2026 at the Military Hospital of Tunis and the Salah Azaïez Institute. Adult patients (20 years) with confirmed cancer diagnoses and capacity to consent were enrolled by convenience sampling ($n = 59$; response rate 84.3%). Pain intensity was assessed using the Numeric Rating Scale (NRS; 0–10) and neuropathic pain was screened with the valid DN4 questionnaire (threshold 4/10). Associations between

pain severity, quality-of-life (QoL) domains, analgesic use, and pain assessment frequency were examined using Spearman's rank correlation and chi-square tests (significance threshold: $p < 0.05$).

Results: Fifty-nine patients were included, 59% female, with 31% aged 66 years or older. Tumor types included colorectal (22%), lung (19%), and breast cancer (14%). Disease was metastatic in 33%. Chemotherapy was administered in 92%, surgery in 73%, and radiotherapy in 49%. Pain severity was high, with a median NRS score of 6–7/10; 83.6% of patients scored 7. Pain occurred during nursing procedures in 36% of cases, during physical activity in 33%, and at night in 21%. DN4 screening identified burning sensations in 67% of patients, electric shock sensations and tingling in 49% each, and cold allodynia in 33%. Pain impaired quality of life in 91%. Mood was the most affected domain (58%), followed by nutritional status (52%) and sleep (48%). Pain severity (NRS 7) correlated significantly with QoL impairment across all domains ($p < 0.05$). WHO step III opioids were prescribed in 63% of patients, step II in 53%, and step I in 42%. Coanalgesics were used in a minority: antidepressants in 31% and anticonvulsants in 28%. Nonpharmacological strategies were reported alongside medical treatment, including spiritual practices (74%), social support (65%), and therapeutic massage (40%). Pain assessment was reported as frequent or systematic in 48%, occasional in 39%, and rare or absent in 14%. Assessment frequency correlated significantly with patient satisfaction ($p < 0.05$): patients assessed regularly more frequently reported feeling listened to (64% vs. 37%; $p = 0.03$). Overall, 63% of patients expressed low or no satisfaction with pain management, reflecting a gap between analgesic prescription and perceived care quality.

Conclusions: Cancer pain remains severe and undertreated in Tunisian oncology settings, with a frequently underrecognized neuropathic component. Systematic pain assessment significantly impacts patient satisfaction, highlighting the need for structured multidisciplinary pathways integrating valid tools and non-pharmacological approaches.

First-line therapy in HER2-positive metastatic breast cancer: A real-world retrospective study

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Background: The management of HER2-positive metastatic breast cancer (mBC) has been revolutionized by the emergence of targeted anti-HER2 therapies. This study aims to evaluate real-world clinical outcomes and the safety profile of first-line systemic treatment in this population.

Methods: We conducted a retrospective, observational study including patients treated for HER2-positive mBC at the Department of Medical Oncology of Taher Maamouri University Hospital, (Nabeul, Tunisia), between 2021 and 2025. Data were analyzed regarding therapeutic regimens, treatment response and toxicity profiles.

Results: A total of 30 patients were included. The median age at diagnosis of metastatic disease was 50 years (range: 32–70). Sixteen patients (54%) presented with de novo mBC. The most common metastatic sites were bone (50%), liver (36%) and lung (50%). Poly-metastatic disease (3 sites) was observed in 8 patients (27%) and brain metastases were found in 3 cases. Hormone receptor expression was identified in 54% of cases. First-line therapy consisted of chemotherapy plus dual HER2 blockade (trastuzumab and pertuzumab) in 83% of cases. Chemotherapy agents included docetaxel (77%), paclitaxel (13%), and vinorelbine (3%). During induction therapy, the

disease control rate was 79%, with an objective response rate of 55% (complete response: 7%; partial response: 48%). Maintenance therapy (trastuzumab plus pertuzumab) was administered to 16 patients with the addition of hormone therapy in 7 patients. Median progression free survival (PFS) was 23 months (95%CI :14 - 32). Regarding safety, main toxicities included G3/4 neutropenia (13%), G1/2 diarrhea (24%) and peripheral neuropathy (21%). One patient experienced reversible cardiac toxicity.

Conclusion: Despite the limitations of this single-center retrospective study, including the modest sample size and treatment heterogeneity, our findings confirm the effectiveness and safety of antiHER2 based therapy in HER2-positive mBC, with survival outcomes consistent with those reported in pivotal studies. Given the variability in treatment response, future research is needed to identify predictive factors of response for more personalized care.

Impact of Tumor Biology on Survival in Young Women with Breast Cancer

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Introduction: Breast cancer in young women is often associated with aggressive tumor biology and poorer outcomes. Hormone receptor status, HER2 expression, proliferation index, and molecular subtype are key factors influencing prognosis. The aim of this study was to evaluate the impact of tumor biology on the risk of metastasis in young women with breast cancer.

Methods: We conducted a retrospective study of young women with breast cancer at the regional hospital of Jendouba from 2012 to 2021. We analyzed immunohistochemical (IHC) markers including estrogen receptor (ER), progesterone receptor (PR), HER2, and Ki-67. Tumors were classified into molecular subtypes (Luminal A, Luminal B, HER2-enriched, triple-negative). Clinical outcomes, including distant metastasis occurrence and timing, were recorded.

Results: We included 134 patients. Hormone receptors were positive in 106 patients (79%), with ER positivity in 105 cases (78%) and PR positivity in 97 cases (72%). HER2 overexpression was observed in 37 patients (28%), and FISH/CISH confirmed amplification in 9 of 12 equivocal cases. The proliferation marker Ki-67 was >20% in 109 patients (81%). Luminal B was the predominant molecular subtype, while triple-negative tumors represented 8% of cases, half of which occurred in patients younger than 30 years. During follow-up, distant metastases developed in 34 patients, with a median interval of 28 months. Among these, 76% occurred within three years. Metastatic progression was more frequent in patients under 30 years, with 60% developing metastases, compared to a lower proportion in older patients. Analysis by molecular subtype showed the highest metastasis rates in triple-negative tumors, with 50% progressing to metastatic disease.

Conclusion: Tumor biology significantly influences the risk of metastasis in young women with breast cancer. Patients under 30 years and those with triple-negative tumors demonstrate particularly aggressive disease and shorter metastasis-free survival. Early identification of high-risk biological profiles is essential for tailoring treatment and improving outcomes in this population.

The Burden of Treatment-Related Complications Among Young Patients with Breast Cancer

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Introduction: Breast cancer in young women is commonly associated with aggressive pathological features and poorer oncologic outcomes. However, the relationship between young age and treatment-related complications remains unclear. While tumor biology may be more aggressive, younger patients may better tolerate multimodal therapies. This study aimed to evaluate whether young age influences the risk of postoperative complications and systemic adverse events in breast cancer patients.

Methods: We conducted a retrospective study including patients under 40 years old treated for breast cancer at the regional hospital of Jendouba from January 1, 2012 to June 30, 2021. Clinicopathological characteristics, surgical procedures, adjuvant treatments, postoperative complications, and systemic adverse events related to therapy were collected. Complications were classified as local (surgical and post radiotherapy) or systemic (treatment-related toxicities and general adverse events).

Results: The study included 134 patients, with a mean age of 34 years (range 23–40). Clinically, 51% of tumors were classified as T2, 8% were multifocal, and 46% were associated with clinically positive lymph nodes. All patients underwent surgical treatment, predominantly mastectomy (66%). Postoperative complications were reported in 10 women (7.5%) who underwent mastectomy: delayed wound healing in three cases, lymphocele in seven cases, and limited skin necrosis in one case. Chemotherapy was administered to 130 patients (98%). Overall tolerance was favorable, with good tolerance observed in 115 cases (86%). Most adverse events were mild, with grade 1 toxicities reported in 108 patients. Radiotherapy was delivered in 122 patients (92%). This treatment was well tolerated in 106 cases (79%). The most frequently reported complication was low-grade radiodermatitis, observed in 42% of patients. Trastuzumab was generally well tolerated: 12 patients (9%) experienced minor adverse events, including flu-like syndrome, skin rash, and asthenia.

Conclusion: Although young women with breast cancer often present with biologically aggressive tumors, they appear to experience fewer postoperative and systemic treatment-related complications. These findings suggest better treatment tolerance in younger patients and support individualized management strategies that balance oncologic aggressiveness with therapeutic safety.

Duct Excision in the Evaluation of Bloody Nipple Discharge with Unremarkable Imaging: A Clinicopathological Review

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Introduction: Sanguinolent nipple discharge is closely associated with intraductal neoplasia and frequently prompts surgical referral. When mammography and ultrasound are normal, MRI may improve detection of occult lesions but remains largely inaccessible, leading most patients directly to

surgery. Duct excision thus stands as the definitive diagnostic and therapeutic procedure in this setting. This study aimed to evaluate the clinicopathological findings in patients undergoing duct excision for persistent sanguinolent nipple discharge with normal conventional imaging.

Methods: A retrospective cohort study was conducted over a five-year period (2020–2025) at the Department of Surgical Oncology, Regional Hospital of Jendouba. Patients presenting with spontaneous, unilateral, single-duct sanguinolent nipple discharge and normal or probably benign imaging (BI-RADS 1–3 on both mammography and ultrasound) were included.

Results: A total of 42 patients were included. The mean age was 48 years and 45% were premenopausal. The mean time from symptom onset to surgical referral was under one month in 71% of cases. Discharge was spontaneous and unilateral in all cases. Imaging was classified as BI-RADS 2 in 10 patients (24%) and BI-RADS 3 in 32 patients (76%). MRI was performed in 12 patients (28%), of whom 10 (83%) returned normal or non-contributive Results, leading to surgical decision in all cases. Selective microdochectomy was performed in 19 patients (45%) and total duct excision in 23 patients (55%). The predominant histological finding was ectatic galactophoritis. Intraductal papilloma was diagnosed in 4 patients (11%). Occult malignancy (DCIS or invasive carcinoma) was identified in 2 patients, both aged over 60 years and presenting with persistent sanguinolent discharge exceeding 6 months, underscoring the association between postmenopausal status and malignancy risk (8% vs. 0% in premenopausal women). Surgical morbidity was low, limited to wound infection in 3 cases.

Conclusions: Duct excision remains the definitive diagnostic and therapeutic procedure for persistent sanguinolent nipple discharge with normal or non-contributive imaging, yielding a clinically significant rate of occult malignancy, particularly in postmenopausal women. These findings support its systematic use in this setting, even in the absence of a targetable lesion on conventional imaging or MRI.

Beyond Clinical Factors: Impact of the General Practitioner–Surgeon Relationship on Referral Delays in Breast Surgery

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Background: Referral delay is a major barrier to timely surgical care. In many healthcare systems, access to surgical consultation is mediated through general practitioners (GP), whose personal or professional acquaintance with the surgeon may play a decisive role in the speed and directness of referral. This interpersonal dimension of the referral pathway remains poorly studied despite its potential impact on time to specialist consultation. This study aimed to assess whether prior acquaintance between the referring GP and the operating surgeon is associated with reduced referral delay in a breast surgery unit.

Methods: A cross-sectional study was conducted at the Department of Surgical Oncology, Regional Hospital of Jendouba over a four-month period from December to March 2026. All new referral patients consulting for a breast complaint were enrolled. A structured face-to-face questionnaire collected sociodemographic data, clinical presentation, referral pathway, nature of the GP and surgeon relationship (personal, professional, or none), and referral delay, defined as time from

first symptom to first surgical consultation.

Results : A total of 71 new referral patients were included. Prior acquaintance between the referring GP and the surgeon was identified in 19 patients (26.8%), while 52 patients (73.2%) were referred through non-acquainted pathways. In the acquaintance group, referral delay was under 7 days in all 19 cases (100%), including under 3 days in 9 cases (47.4%). In contrast, among nonacquainted referrals, a delay under 7 days was achieved in only 17 of 52 patients (32.7%), with the remainder experiencing delays extending to several weeks or months ($p < 0.001$). GP–surgeon acquaintance emerged as a strong independent predictor of referral delay under 7 days, followed by urban residence and higher educational level.

Conclusions: A prior personal or professional relationship between the referring GP and the surgeon significantly shortens referral delay, demonstrating that strong interpersonal networks between healthcare providers can be a powerful driver of timely access to specialist surgical care. These findings provide a valuable model for designing formalised referral protocols and structured inter-specialty communication channels that could replicate this efficiency benefit for all patients, regardless of personal connections.

The CALR mutation in myeloproliferative neoplasms patients: a single institution experience

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Background: Myeloproliferative neoplasms (MPNs) are hematological disorders characterized by abnormal production of myeloid cells due to genetic mutations. Somatic mutations in the Calreticulin (CALR) gene are one of the most driver mutations, with relevant heterogeneity in frequency worldwide. Aims: To assess the prevalence of CALR mutations in South Tunisian patients with JAK2negative myeloproliferative neoplasms (MPNs).

Methods: A seven-year retrospective study was carried out at the Hospital University of Sfax, south of Tunisia, including all JAK2-negative MPN patients. The genomic DNA of patients was isolated from peripheral blood samples. Sanger sequencing was performed using a highfidelity DNA polymerase to identify the somatic mutations of CALR.

Results: Sixty-eight patients with JAK2-negative MPN were enrolled. The median age was 50 years, and the sex ratio M/F was 0.3. Mutational frequencies were 19.2% (13 / 68). CALRmutated patients harbor one of only two mutation variants: type 1, a 52-bp deletion (p.L367fs*46), and type 2, a 5-bp TTGTC insertion (p.K385fs*47), in 62% and 38%, respectively.Summary/.

Conclusion: Our finding highlights that this driver mutation is less common in southern Tunisia unless it is an important marker for the diagnosis of JAK2-negative MPN. A larger study with genetic screening of other mutations is mandatory to elicit the genetic landscape of this subset of MPN and specific individual disease outcomes.

Trends in consumption and expenditure of targeted anticancer therapies in a specialized clinical hematology hospital

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Introduction: Targeted anticancer therapies have improved survival and overall quality of cancer yet these increasingly expensive medicines imposed financial burdens on hospital budgets. This study aimed to evaluate trends in the utilization and expenditure of targeted anticancer therapies.

Methods: A retrospective observational study was conducted from 2023 to 2025 to assess expenditure and consumption volume of targeted therapies in a specialized hospital in clinical hematology. Monthly data were collected from the STKMED medication management software of the hospital's internal pharmacy. Using a time series design with Autoregressive Integrated Moving Average (ARIMA) models, we estimated trends in use and costs of targeted therapies.

Results: During the study period, a total of 8 targeted anticancer therapies were identified. Overall consumption increased from 421 units in 2023 to 839 units in 2025.Total expenditure on targeted anticancer therapies rose from 1255750 TND (2023) to 1830228 TND (2025), corresponding to an increase of 45%.Among all targeted therapies in 2025, Bortezomib and Daratumumab generated the highest expenditure, representing 31% and 23% of total targeted therapy costs, respectively. In contrast, Rituximab was the most frequently utilized agent, accounting for 35% of total consumption. Time-series analysis demonstrated an upward trend in the consumption and expenditure of targeted anticancer therapies throughout the study period. The fitted ARIMA model adequately described the observed data and projected a continued increase in future utilization and associated costs.

Conclusion: In Tunisia, targeted therapies are increasingly used for hematologic malignancies, representing a substantial economic burden. It is important to establish mechanisms to monitor their use and outcomes.

Clinical Presentation and Diagnostic Delays in Cervical Cancer: A Five-Year Experience from a Tunisian Tertiary Center

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Introduction: Cervical cancer remains a leading cause of cancer-related morbidity and mortality among women worldwide. Although early symptoms may prompt timely medical evaluation, delayed consultation remains a major concern in many low-resource settings. This study aimed to describe the clinical presentation of cervical cancer patients and assess its relationship with stage at diagnosis in a Tunisian tertiary maternity center.

Methods: We conducted a retrospective descriptive study including all patients diagnosed with cervical cancer between January 2021 and December 2025 in a tertiary maternity center in Tunis, Department B. Data were collected from medical records and included demographic characteristics, presenting symptoms, delay before consultation, histological subtype, and FIGO stage at diagnosis.

Results: Thirty-five patients were included. The mean age at diagnosis was 57.5 years, and 62.9% of patients were postmenopausal. More than half of the women (51.4%) originated from rural areas.Postmenopausal bleeding was the predominant presenting symptom, reported in 77.2% of cases. Other symptoms included pelvic pain (14.2%), leucorrhea (5.8%), and lower back pain (2.8%). Despite the presence of alarm symptoms, most women sought medical attention only after several months of recurrent or persistent bleeding. The delay before consultations ranged between 3 months and 2

years. Despite the presence of alarm symptoms, particularly postmenopausal bleeding, most patients delayed seeking medical attention for several months. This delay is explained by multiple factors, including limited health literacy and poor recognition of the significance of gynecological symptoms (49%) , denial or underestimation of disease severity, (11%) , socioeconomic constraints, and difficulties accessing healthcare services (40%) especially for women living in rural areas. These barriers may contribute substantially to the high proportion of advanced-stage disease observed at diagnosis. Squamous cell carcinoma was the most frequent histological subtype (88.6%). The majority of patients presented with advanced disease, with 60.0% diagnosed at FIGO stage III or IV.

Conclusion: The frequent diagnosis of cervical cancer at advanced stages suggests that opportunities for earlier detection are often missed. Delayed consultation, likely influenced by poor symptom awareness, socioeconomic barriers, and limited access to preventive healthcare, remains a major challenge. Public education campaigns focusing on the recognition of warning symptoms, together with improved access to screening and gynecological care, are essential to facilitate earlier diagnosis and improve patient outcomes.

Clinical, Biological, and Treatment-Related Predictors of Major Histological Response in Locally Advanced Rectal Cancer

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Introduction: Neoadjuvant therapy, particularly Total Neoadjuvant Therapy (TNT), has transformed the management of locally advanced rectal cancer (LARC). Achieving a Major Histological Response (MHR) is a reliable surrogate for improved survival. This study aimed to identify baseline and treatment-related factors predictive of MHR in a Tunisian cohort.

Methods: We retrospectively analyzed 72 patients with LARC treated with neoadjuvant therapy followed by surgery at the oncology department of Tahar Maamouri Hospital in Nabeul from 2018 to 2025. MHR was defined as Mandard Tumor Regression Grade (TRG) 1-2 or Dworak grade 3-4 on final pathology. Clinical, biological and radiological characteristics were evaluated. Categorical variables were analyzed using the Chi-square test to identify factors associated with MHR.

Results: The median age was 62.5 years, with 52.8% males. Baseline staging revealed cT3-T4 in 87.1% and cN+ in 76.4% of patients. Long course CRT was given in 33.3% of the cohort and TNT was administered in 62.5% of the cohort, 27.7% of them had SCRT followed by consolidation chemotherapy, 19.4% had induction chemotherapy followed by SCRT and 15.2% received induction chemotherapy followed by long course CRT. After surgical resection, MHR was achieved in 33.3% (n=24). On univariate analysis, a Neutrophil-to-Lymphocyte Ratio (NLR) 1.8 (p=0.005), mid-rectal location (p=0.045), absence of internal sphincter involvement (p=0.030), and an interval to surgery of 12 weeks (p=0.029) were associated with higher MHR rates. However, on multivariate logistic regression, a baseline NLR 1.8 remained the sole independent predictor of achieving MHR (p=0.013).

Conclusion: In our real-world cohort, baseline systemic inflammation, reflected by a low NLR (1.8), is a strong and independent predictor of Major Histological Response following neoadjuvant therapy for LARC. While surgical timing and tumor location showed univariate associations, NLR remained the most robust predictive biomarker. Integrating this cost-effective, accessible marker into initial workups can significantly

assist multidisciplinary teams in optimizing LARC management and predicting treatment efficacy.

Nutritional Challenges in Digestive Cancer Patients: Assessment and Clinical Implications

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Introduction : Malnutrition and sarcopenia are frequent complications in patients with digestive cancers and are associated with reduced treatment tolerance, increased toxicity, and poorer clinical outcomes. Early identification of nutritional disorders is therefore essential to optimize patient management. This study aimed to assess the nutritional status of patients with digestive cancers and evaluate the prevalence of malnutrition and sarcopenia and their impact on treatment outcomes.

Methods : We conducted a cross-sectional study involving patients with digestive cancers followed at the Sectoral Cancer Center of Jendouba over a period of four months period from February to May 2022. Clinical, nutritional, and treatment-related data were collected and analyzed to evaluate nutritional status, dietary habits, treatment tolerance, and nutritional support.

Results: A total of 65 patients were included, with a predominance of rectal cancer cases. The mean age was 64 years. Thirty-three patients (50.8%) experienced significant loss of appetite and weight loss, frequently attributed to chemotherapy-related side effects, while 51 patients (78.5%) demonstrated reduced dietary intake, reflecting a high prevalence of malnutrition. Hematological toxicity occurred in 31 patients (47.7%), and treatment discontinuation due to nutritional complications was reported in 9 patients (13.8%). Regarding dietary habits, 37 patients (56.9%) rarely consumed fresh fruits and 35 patients (53.8%) avoided red meat, suggesting substantial dietary restrictions associated with anorexia, food aversions, and gastrointestinal symptoms. Sarcopenia was identified in 20 patients (30.8%), representing a major comorbidity with potential consequences for treatment tolerance and functional status. Despite the high burden of nutritional impairment, only 23 patients (35.4%) received oral nutritional supplementation, which was generally initiated at an advanced stage of the disease.

Conclusions: Malnutrition and sarcopenia are highly prevalent among patients with digestive cancers and are associated with impaired treatment tolerance and adverse clinical outcomes. Systematic nutritional screening and early nutritional intervention should be integrated into routine oncological care to improve treatment adherence, reduce complications, and enhance patient outcomes.

Real-World Neoadjuvant Therapy Outcomes for Locally Advanced Rectal Cancer in Tunisia

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Introduction: Neoadjuvant therapy is the cornerstone of management for locally advanced rectal cancer (LARC). While total neoadjuvant therapy (TNT) has rapidly shifted treatment paradigms, evaluating real-world feasibility and final pathological responses within specific national health systems

is essential. This study aimed to report the epidemiology, treatment patters, safety profiles, and oncological outcomes of a cohort of LARC patients undergoing neoadjuvant treatment in Tunisia.

Methods: We retrospectively reviewed 85 consecutive patients with LARC managed between 2018 and 2025 at the Oncology Department of Tahar Maamouri Hospital in Tunisia. Epidemiological data, baseline staging (clinical and radiological), treatment modalities, toxicity profiles, and post-neoadjuvant surgical and pathological outcomes were analyzed descriptively.

Results: The median age was 63 years (range: 33–84), with 32.9% of patients older than 70 years and a slight male predominance (54.1%). Tumors were located in the low rectum in 49.4% and mid-rectum in 50.6%. Baseline staging showed that 87.1% had cT3-T4 disease and 76.4% were node-positive (cN+), with 38.8% presenting as cN2. The median time from diagnosis to treatment initiation was 69 days (range: 18–203). Overall, 62.4% of the cohort received TNT, utilizing three main sequencing strategies: short-course radiotherapy (SCRT) followed by consolidation chemotherapy (43.3%), induction chemotherapy followed by SCRT (33.9%), and induction chemotherapy followed by long-course CRT (22.6%). Treatment was well tolerated, with low rates of severe adverse events: grade 3/4 digestive toxicity occurred in 5.9% and grade 3/4 hematological toxicity in 7.1%. Following pelvic MRI restaging, 11 patients achieved a clinical complete response (cCR). Surgical resection was indicated for 91.8% of patients, and 73 patients ultimately underwent surgery (5 patients refused). The median interval from neoadjuvant completion to surgery was 12.7 weeks (89 days). Sphincterpreserving surgery (anterior resection with TME) was achieved in 64.4% of cases, while 32.9% required an abdominoperineal resection. On final pathology, pathological complete response (pCR) was achieved in 22.2% of evaluated specimens, and a major histological response (Mandard 1-2 / Dworak 3-4) was observed in 33.3%. Nodal downstaging was highly effective, with 66.7% reaching ypN0 status.

Conclusion: Neoadjuvant management of LARC in Tunisian real-world practice is safe and highly effective. Delivering advanced mode sequencing like TNT is feasible and yields a favorable, manageable toxicity profile. However, the median systemic delay from diagnosis to treatment start (69 days) identifies an area for public health optimization.

Endometrial Cancer in Young Women: Epidemiological, Clinicopathological and Therapeutic Characteristics in a Tunisian Population

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Background : Endometrial cancer is traditionally considered a disease of postmenopausal women; however, its incidence among younger women has been steadily increasing, largely due to the rising prevalence of obesity and metabolic disorders. Managing endometrial cancer in reproductive-aged women poses unique challenges, particularly regarding fertility preservation. This study aimed to describe the epidemiological, clinicopathological, therapeutic, and oncological characteristics of young women diagnosed with endometrial cancer in a Tunisian tertiary referral center.

Methods : We conducted a retrospective descriptive study including all patients aged 45 years or younger who were treated for histologically confirmed endometrial cancer at the Department C of the Tunis Maternity and Neonatology Center between January 2015 and December 2024.

Demographic characteristics, risk factors, clinical presentation, histopathological findings, treatment modalities, and outcomes were collected from medical records and analyzed.

Results: Thirty-seven patients met the inclusion criteria, representing 12.5% of all endometrial cancer cases managed during the study period. The median age at diagnosis was 41 years (range: 28–45 years). Obesity (BMI 30 kg/m²) was identified in 73% of patients, while polycystic ovary syndrome was present in 24%. Nulliparity was observed in 43%, and 19% had a history of infertility. Abnormal uterine bleeding was the most common presenting symptom, occurring in 89% of cases. Histological examination revealed endometrioid adenocarcinoma in 92% of patients, with grade 1 tumors accounting for 68% of cases. According to FIGO classification, stage IA disease was diagnosed in 78% of patients, stage IB in 14%, and stage II or higher in 8%. Twenty-eight patients underwent standard surgical management consisting of total hysterectomy with bilateral salpingo-oophorectomy, with lymph node assessment performed when indicated. Fertility-sparing treatment using high-dose progestins was proposed to nine carefully selected patients presenting with grade 1 endometrioid carcinoma confined to the endometrium. Complete response was achieved in seven patients (77.8%) after a median treatment duration of nine months. Two patients experienced persistent disease and subsequently underwent definitive surgery. After a median follow-up of 48 months, disease recurrence occurred in four patients (10.8%), including two patients initially managed conservatively. No cancer-related deaths were recorded during the study period.

Conclusion : Young women with endometrial cancer predominantly present with early-stage, low-grade endometrioid tumors and frequently exhibit obesity-related risk factors. Fertility-sparing treatment appears to be a feasible and effective option in carefully selected patients, with acceptable oncological outcomes. These findings highlight the importance of individualized management strategies and multidisciplinary counseling in reproductive-aged women diagnosed with endometrial cancer. **Keywords:** Endometrial cancer; Young women; Fertility preservation; Obesity; Endometrioid adenocarcinoma; Tunisia.

Sacrificing the Future to Save the Present: Intergenerational Financial Toxicity and Treatment Abandonment in Tunisia

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Introduction: Cancer care in low-and-middle income countries often leads to enormous health expenditure, forcing families into a cycle of psychological and financial stress, thus increasing the risk of treatment drop-out. In Tunisia, the socio-economic burden of care extends beyond the patient to impact the intergenerational future of the household. This study aimed to evaluate the financial toxicity among patients receiving intravenous treatment and to identify its associated factors.

Methods: A cross-sectional study was conducted including 70 patients receiving systemic therapy at Tahar Maamouri Hospital, Nabeul, Tunisia. Data were collected via a comprehensive survey covering socio-demographics, logistic costs and economic coping mechanisms. Statistical analysis was performed using Jamovi, with p-values < 0.05 considered significant.

Results: Median age was 54 years and median treatment duration was 12 months. rural housing accounted for 38.6% of patients. permanent job loss due to cancer was detected in 30% of patients. household monthly income was below the minimum

wage in 22.9% of the cohort. The coping mechanisms identified were exhausting life savings in 55.7% of patients, loans from relatives in 64% of the cohort and 7 patients were forced to sell a property. Most notably, 21.4% of the patients reported that at least one of their children had to interrupt their education to provide financial support. High risk for treatment drop-out was identified in 35.7% of the cohort, with 22.9% having already considered treatment abandonment. Significant associations to treatment drop-out risk were low monthly income ($p=0.041$), necessity of borrowing money ($p=0.01$), treatment duration over 12 months ($p=0.024$) and most critically the interruption of children's education ($p<0.001$) and patient work stoppage ($p<0.001$).

Conclusion: The significant association between children's education withdrawal and the risk of treatment drop-out reveals a profound social crisis, triggering an intergenerational cycle of psycho-social distress. These Results highlight the need for an early financial toxicity screening to protect both the patient's clinical outcome and the family's socioeconomic future.

Breast Cancer in Young Women: Clinicopathological Features and Outcomes in a Tunisian Cohort

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Background : Breast cancer is the most common malignancy among women worldwide. Although predominantly diagnosed after the age of 50 years, a substantial proportion of cases in North Africa occur in younger women. Breast cancer in this population is often associated with aggressive pathological characteristics, unique psychosocial challenges, and fertility concerns. This study aimed to evaluate the clinicopathological features, treatment patterns, and outcomes of young women diagnosed with breast cancer in a Tunisian tertiary care center.

Methods : We conducted a retrospective study including all women aged 40 years diagnosed with invasive breast cancer between January 2015 and December 2024. Demographic, clinical, histopathological, therapeutic, and follow-up data were collected from medical records. Molecular subtypes were classified according to immunohistochemical profiles.

Results : A total of 124 patients were included, representing 17% of all breast cancer cases managed during the study period. The median age at diagnosis was 36 years (range: 24–40). A family history of breast or ovarian cancer was reported in 18.5% of patients. The median tumor size was 3.4 cm. Axillary lymph node involvement was present in 56% of cases at diagnosis. Histologically, invasive ductal carcinoma accounted for 89% of tumors. According to molecular classification, 58% were luminal, 21% HER2-positive, and 21% triple-negative. High histological grade (grade III) was observed in 44% of patients. Breast-conserving surgery was performed in 39% of cases, while 61% underwent mastectomy. Neoadjuvant chemotherapy was administered to 52% of patients. Pathological complete response was achieved in 24% of patients receiving neoadjuvant treatment. After a median follow-up of 56 months, disease recurrence occurred in 21% of patients. Five-year disease-free survival and overall survival rates were 78% and 88%, respectively.

Conclusion : Breast cancer in young Tunisian women is characterized by advanced-stage presentation, high-grade tumors, and a substantial proportion of aggressive molecular subtypes. Early detection and personalized therapeutic strategies remain essential to improve long-term outcomes in this vulnerable population.