Nutrition in cancer between myth and reality

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Introduction: The diagnosis of cancer is extremely hard to the patient and its family. Apart from the treatment prescribed by doctors, patients seek different means to heal resulting in many nutritious practices.
Methods: We conducted a survey with patients treated for cancer in Salah Azaiz Institute. The purpose of this study is to identify their nutritious beliefs and their dietary habits.
Results: This study included 100 patients, among them 80 women and 20 men with a median age of 50 years [28-80]. Only 10% of the patients were illiterate. The primary tumor site was breast cancer (n=54). The disease was metastatic in 18% of the cases. The treatment received was mainly chemotherapy (76%), along with hormonotherapy, surgery, and immunotherapy. The majority of the patients believe there is an immediate impact of their diet on the evolution of cancer (n=68). These beliefs were questioned in less than half of the patients (49%). The patients seek information to support their beliefs from doctors, surroundings, nutritionists, and inteet in respectively 56%, 60%, 13% and 53% of the cases. Patients stopped consuming basic food products (28% milk, 58% sugar, 60% red meat, and 6% fruits). Half of the study group still consume canned food. Patients require to different kind of herbs in 86% of the cases mainly represented with Turmeric (64%), Rosemary (60%), Amethyst Panicaut (50%), Ginger (40%), Propolis (33%), Royal Jelly and Carob Tree (28%). Some of the patients consumed camel products: milk (n=24), meat (n=11) and urines (n=9). Ten cases realized intermittent and water fasting. Almost half of the population (47%) feel an impact of their eating habits. The purpose behind these diets was mainly to boost the immune system (92%), to cure the disease (64%), for palliative purpose (44%), and to replace food (17%).
Conclusion: The majority of the patients diagnosed with cancer resort to nutritious practices based on their own beliefs. It is important to assist these patients from the beginning through their diets to prevent unhealthy habits.

Correlation Between Genetic Profile and Initial Ciclosporin Concentration in Bone Marrow Transplant Patients: A Study in the Tunisian Population

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Introduction: Ciclosporin is an immunosuppressant used to prevent transplant rejection, particularly in bone marrow transplants, and has important implications in oncology by reducing relapse rates in cancer patients. Administered intravenously during the first two weeks post- transplantation, ciclosporin's plasma concentrations vary between individuals, often requiring dose adjustments. Its metabolism and transport are influenced by genes such as ABCB1, CYP3A4, and CYP3A5. This study examines the impact of genetic variations on ciclosporin concentrations after initial dosing in Tunisian bone marrow transplant patients.
Methods: This study was conducted at the Pharmacogenetics Platform of the National Center of Pharmacovigilance of Tunisia (CNPV) and included 15 bone marrow transplant patients. DNA was isolated from whole blood using the Blood gDNA MiniPrep System Extraction Kit (PROMEGA, ReliaPREPTM; USA). The purity and concentration of the extracted DNA were quantified using the Thermo ScientificTM NanoDropTM One Spectrophotometer. Genotyping for polymorphisms in the ABCB1, CYP3A4, and CYP3A5 genes was performed using the Illumina Sequencing Kit and the iSeq 100 Sequencer. We studied the first ciclosporin concentration The concentrations were considered within the therapeutic range if they were between 100 and 300 ng/mL.
Results: The study included 15 bone marrow transplant patients. The patients' median age is 20 years [9-47 years]. The sex ratio was 2.75. The average ciclosporin dose was 147.33 mg/day, with a median of 150 mg. Weight-based dose varied from 1.86 to 4.375 mg/kg, with a median of 2.88 mg/kg. The average of the first ciclosporin concentration was 296.26 ng/mL [118.8 - 635.9 ng/mL]. Among them, 4 patients (26.66%) had supratherapeutic levels (> 300 ng/mL). Notably, there were no cases of subtherapeutic concentrations below the therapeutic range. Of these, 3 patients were homozygous (G/G) for the ABCB1 polymorphism (rs1045642). Additionally,

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2 patients had a combination of homozygous mutant polymorphism for ABCB1 (rs1045642) and heterozygous mutant genotype (C/T) for CYP3A4*1B.

Conclusion: Despite an average weight-based dose of 2.88 mg/kg, which is close to the recommended intravenous dosing range of 3 to 5 mg/kg for bone marrow transplant patients, ciclosporin blood concentrations showed considerable variability. This highlights the significant interindividual differences in metabolism. Pharmacogenetic analyses further support this observation, suggesting that genetic factors may influence ciclosporin metabolism and concentration. Specifically, the findings point to a possible association between the ABCB1 polymorphism (rs1045642) and elevated ciclosporin concentrations, likely due to reduced ciclosporin efflux. Additionally, the interaction between ABCB1 and CYP3A4 polymorphisms may impact ciclosporin pharmacokinetics. These results underscore the importance of incorporating pharmacogenetic approaches for dose adjustment. Collaboration between oncologists and pharmacologists will be essential for developing personalized treatment strategies.

Therapeutic Education: A Catalyst for relieving Vomiting, Nausea, Anxiety, and Depression in Cancer Patients

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Introduction: Cancer and related treatment often induce distressing symptoms such as vomiting, nausea, anxiety, and depression, profoundly impacting the quality of life of patients. Despite advances in medical interventions, managing these symptoms remains challenging. However, therapeutic patient education (TPE) emerges as a promising approach to address this multifaceted burden.

Methods: Patients were recruited based on inclusion criteria ; a confirmed diagnosis of cancer, undergoing chemotherapy or radiation therapy. Patients with severe cognitive impairment or communication barriers were excluded from the study. Participants received TPE interventions tailored to their individual needs. These interventions consisted of psychoeducation sessions, cognitive-behavioral techniques, and self- management skills training. The duration and frequency of sessions were determined based on patient preferences and treatment schedules.

Results: Data were collected using validated assessment tools such as the Common Terminology Criteria for Adverse Events (CTCAV) and Hospital Anxiety and Depression scale (HADS) Baseline measurements were obtained prior to the initiation of TPE, with follow-up assessments conducted at regular intervals post-intervention. Descriptive statistics were used to summarize patient demographics and baseline characteristics. Paired t-tests or non-parametric tests were employed to analyze changes in vomiting, nausea, anxiety, and depression scores pre- and post-intervention. Subgroup analyses may be performed to explore the impact of demographic or clinical variables on treatment outcomes.

Out of the initial 100 cancer patients enrolled in the study, eighty six (86) completed the therapeutic education intervention and were included in the analysis. The mean age of participants were 54 years, with a gender distribution of 37% males and 63% females. Following the TPE intervention, a statistically significant reduction in the frequency and severity of vomiting and nausea episodes was observed ($p < 0.05$).

Moreover, participants reported improvements in anxiety and depression symptoms post- intervention. The mean HADS score for anxiety decreased from 14 to 8, and the mean HADS score for depression decreased from 12 to 7. Both of which were statistically significant ($p <0.05$). Multivariate logistic regression models showed that undergoing a specific TPE [(OR) 0.489, 95% (CI) 0.329–0.948, P = 0.029] was correlated with a lower Hads score (fewer than 10) Subgroup analyses revealed that the efficacy of TPE was consistent across demographic and clinical variables, including age, gender, cancer type, and treatment modality.

Conclusion: TPE represents a valuable adjunctive strategy in the comprehensive care of cancer patients. Integrating TPE into routine clinical practice has the potential to alleviate vomiting, nausea, anxiety, and depression, thereby optimizing patient outcomes and promoting holistic well-being in this vulnerable population.

Factors influencing the response to induction chemotherapy in nasopharyngeal cancer

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Introduction: Induction chemotherapy (IC) for advanced nasopharyngeal carcinoma (NPC) has gained considerable attention. In fact, IC has a positive effect on primary tumor shrinkage and facilitates radiation therapy planning by down-staging locally advanced tumors. However, the response to induction chemotherapy can vary significantly among patients.The aim of our study was to assess the factors that influence the response to IC in NPC.

Methods: A monocentric retrospective study was conducted over a period of 8 years between 2017 and 2024 at the oncology department of Salah Azaïz Institute. Our study enrolled patients diagnosed with NPC aged 18 years and above. All data regarding patients were obtained from the medical record.

Results: 81 patients were included with a mean age of 45 years and a male predominance (69%). Most patients enrolled had a PS of 0 to 1 (97%). 26 patients underwent EBV serology and 25 were tested positive. According to the TNM classification, 34 patients were staged T1/T2, 17 were staged as T3 and 30 were classified as T4. A complete

response was observed in 13% of T3 patients and 44% of T4 patients (p=0.05). The most commonly used protocol was the TPF (docetaxel, cisplatin, 5-FU) regimen (n=43) followed by 5-FU cisplatin (n=26). The overall response rate was higher in the TPF group (79%) compared with the other protocols (p=0,012). 69.2% of the 57 patients who received the full dose of chemotherapy achieved a complete response, while 30.8% of the 17 patients who received a reduced dose experienced a complete response (p=0.09).
Conclusion: The patients staged as T4 had better clinical response. The TPF protocol showed superior response rates compared to the other protocols. Patients who received the full dose of chemotherapy tended to have better response rates. Our study underscores the multifactorial nature of treatment response in NPC and the need for personalized treatment approaches considering individual patient characteristics and treatment modalities.

Benefits of adjuvant chemotherapy among MSS stage II colon cancer patients

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Introduction: Colon cancer (CC) is a leading cause of cancer incidence and mortality worldwide. While adjuvant chemotherapy (ACT) has become a standard of care for stage III colon cancer patients since 2019, the advantages of ACT in stage II colon cancer in the setting of MSI/MSS status are less obvious. We tried through this study to describe the response to adjuvant chemotherapy in stage II (CC) in both MSI-H and MSS groups.
Methods: We retrospectively reviewed data of all patients with stage II colon cancer treated between 2016 and 2021 at the medical oncology department of Taher Maamouri Hospital in Nabeul.
Results: Sixty-two patients were included. The median age was 61 years-old, ranging between 38 and 78 years old. The sex ratio was 1.2. Ten patients had bowel obstruction, and 8 patients presented with tumor perforation. 34% of our patients were staged pT4N0, and 66% were staged pT3N0. 74% of our patients had an MSS phenotype, and 85% received adjuvant chemotherapy. Overall survival among MSS stage II colon cancer patients who received ACT was 54 months versus 58 months in stage II patients with MSI. Recurrence-free survival for patients with MSS was 46 months, compared with 49 months for stage II patients with MSI. The chemotherapy protocol used was Folfox in 78% of cases and Capox in 22%. The main toxicities observed were gastro-intestinal (vomiting and diarrhea) in 31% of cases and neurotoxicity (peripheral neuropathy) in 29%.
Conclusion: In conclusion, we found that ACT is beneficial for stage II I CC patients with either MSS or MSI-high tumors.

Bilateral breast cancer: A case series

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Introduction: Bilateral breast cancer (BBC) is an uncommon subset with an increasing incidence ranging between 2 and 11% of all breast cancers. This entity includes both metachronous and synchronous bilateral breast cancer. The diagnosis as well as the treatment of BBC can be challenging since the tumors can present at different stages and have various clinical presentations and histopathological characteristics. Here, we present our experience in the management of BBC. Our study aims to analyze BBC's epidemiological, therapeutic, and prognostic data.
Methods: We retrospectively reviewed data of 16 patients with BBC treated at the medical oncology department between 2016 and 2022. Clinico-pathological features, therapies, and follow-up data were retained from medical files.
Results: The median age of patients with bilateral breast cancer was 53 years, with extremes of 35 and 68 years. All patients were females. A family history of cancer was found in 6 patients. BRCA1 and BRCA2 gene mutation testing was negative in one patient. The average time between the first and second cancers in the case of metachronous cancer was 16 months. Multifocal characters were found in 30% of cases. Histologically, bilateral infiltrating ductal carcinoma was the most common type (93%); 75% of the cases had SBRII; hormone receptors were positive in 60%. HER2neu was amplified in 62% of patients. 4 patients were lost of view after, and 12 patients had surgical treatment: bilateral mastectomy in 10 cases, unilateral mastectomy, and contralateral lumpectomy in 2 patients. All of them received chemotherapy, radiotherapy, targeted therapy, and hormone therapy. The mean time of follow-up is 48 months. 2 patients had distant metastasis after 26 and 32 months of follow up.
Conclusion: BBC is relatively rare; however, given the increasing incidence of breast cancer, oncologists should be aware of this entity during diagnostics and post-treatment follow-up.

Dihydropyrimidine Dehydrogenase Deficiency Genotypic-Phenotypic Correlation: Insights from The Clinical Pharmacology Department in Tunisia

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Introduction: Fluorouracil (FU) is a commonly used chemotherapeutic agent for treating a range of cancers. However, its efficacy is frequently accompanied by

severe, and occasionally fatal, toxicities, which are often linked to diminished dihydropyrimidine dehydrogenase (DPD) activity. This reduced enzyme activity can be attributed to genetic variations. Therefore, it is crucial to identify patients with partial or complete DPD deficiency prior to initiating FU therapy. The primary strategies for this identification include phenotypic testing to measure DPD enzyme activity and genotyping of the DPYD gene. This study aimed to assess the correlation between DPD genotypes and phenotypes in a group of Tunisian patients candidate for fluoropyrimidine therapy.

Methods: This study was carried out in the Clinical Pharmacology Department of the National Center of Pharmacovigilance of Tunisia during a period of four months from March 2024 to June 2024. DPD activity was indirectly measured by quantifying plasma uracil concentrations using High Performance Liquid Chromatography (HPLC).

Patients with partial or total deficiency (Uracil concentration>16 ng/ml) were screened by real- time PCR for the five DPYD polymorphisms (DPYD*2A, DPYD*13, c.2846A>T, c.1236G>A-HapB3 and DPYD*6). Genomic DNA was isolated by Blood gDNA MiniPrep®System Extraction Kit. DPYD genotyping was performed in a quantitative real time PCR (Applied Biosystems step one plus by thermo fisher scientific®) using the gene MAP TM DPYD Mutations Detection kit. The Step One software version 2.3 was used to identify samples with different genotypes.

Results: Out of 487 plasma samples, 53 (10.8%) had uracil concentrations above 16 ng/mL.Fourteen DPD-deficient patients were screened for DPYD SNPs, identifying three common polymorphisms: c.1236G>A HapB3, DPYD*2A or DPYD*6, in seven patients.

The c.1236G>A-HapB3 variant was identified in six patients, and its presence was correlated with associated phenotypes. The DPYD*2A variant was found in two patients, one of whom carried the heterozygous allele, which typically causes partial DPD deficiency; however, this patient exhibited total DPD deficiency with a uracil concentration of 489 ng/mL. The DPYD*6 allele variants were detected in only one patient. Notably, one case did not carry any of the targeted polymorphisms despite having a high uracil concentration (169 ng/mL).

Conclusion: This study highlights the critical value of integrating both phenotyping and genotyping methods to effectively identify patients with DPD deficiency who are at heightened risk for severe toxicity from fluoropyrimidine treatments.

Prevalence of ABCB1 Gene Polymorphisms and Imatinib Exposure in a Tunisian Population

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Introduction: Imatinib, a tyrosine kinase inhibitor, is widely used for treating gastrointestinal stromal tumors (GISTs). However, its pharmacokinetic variability requires close therapeutic drug monitoring (TDM). Recent pharmacogenetic research has identified a link between ABCB1 gene polymorphisms and imatinib exposure. Thus, this study aimed to evaluate the prevalence of ABCB1 gene polymorphisms in a Tunisian population.

Methods: This study was carried out in the pharmacogenetics unit of the Clinical Pharmacology Department of the Tunisian National Center of Pharmacovigilance. DNA was isolated from 54 unrelated Tunisian patients using the Blood gDNA MiniPrep System extraction kit (PROMEGA, ReliaPREP TM, USA). Genotyping was performed with the Illumina Sequencing Kit using the iSeq 100 sequencer. The pharmacogenetic analysis focused on the single nucleotide polymorphism (SNP) variation of ABCB1 (rs1045642).

Results: Fifty-four blood samples were sequenced, revealing a consistent rs1045642 allele frequency of 88.9%. Among these, 52% were found to be homozygous genotypes. This allele expression was associated with increased trough concentration of imatinib in people with GISTs.

Conclusion: The high prevalence of ABCB1 gene polymorphisms in the Tunisian population, with a significant proportion of homozygous genotypes, underscores the importance of considering genetic variability in imatinib therapy, notably that this SNP is associated with increased trough concentration of imatinib. These findings support the need for personalized medicine approaches, particularly in drugs.

Neoadjuvant chemotherapy in older women with early stage breast cancer

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Introduction: Neoadjuvant chemotherapy has evolved from its initial application in treating locally advanced breast cancer to becoming a standard approach for managing biologically aggressive diseases, particularly estrogen receptor-negative (ER-) and/or human epidermal growth factor receptor 2-positive (HER2+) cancers. This approach allows for the assessment of therapy response, with the potential for complete disease eradication or tumor volume reduction. Consequently, it offers the opportunity for breast-conserving surgery in patients who would have previously necessitated mastectomy before receiving neoadjuvant chemotherapy. The aim of our study is to elucidate the impact of neoadjuvant chemotherapy on older women with early-stage breast cancer, as demonstrated in a cohort of 19 patients treated at the Salah Azeiz institute in Tunis Tunisia.

Results: The average age of the patients was 55.61 years, with all tumors classified as stage II. Neoadjuvant chemotherapy was administered to all patients for invasive ductal carcinoma, predominantly exhibiting

luminal B immunohistochemical profile. Conservative treatment was pursued in 16 patients. Upon histopathological examination, a complete therapeutic effect on both the tumor and lymph nodes, classified as TA according to the Sataloff classification, was observed in nine patients. Seven patients exhibited a therapeutic response of more than 50% (TB), while three patients showed no therapeutic effect on the tumor. Additionally, a complete therapeutic effect on the lymph nodes was observed in nine cases.

Conclusion: Based on our findings, neoadjuvant chemotherapy demonstrates promising efficacy in the management of early-stage breast cancer.

Extemporaneous examination after neoadjuvant chemotherapy

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Introduction: Neoadjuvant chemotherapy (NAC) is currently the preferred treatment for advanced breast cancer, including inflammatory carcinoma and in triple negative and HER2 overexpressed breast cancer. It has the potential to stop tumor progression, lower the clinical stage, enhance surgical success rates, and even lead to pathological complete remission (pCR). This can significantly extend disease-free survival and overall survival. Despite the effectiveness of NAC, approximately 2% to 30% of patients do not experience significant benefits from this treatment. Extemporaneous examination is a macroscopic and microscopic assessment conducted during a surgical procedure to provide an immediate diagnosis. This rapid result informs surgical decisions, allowing for real-time adjustments to the intervention if necessary. However, this preliminary evaluation must be subsequently confirmed through a more comprehensive analysis of the surgical sample using standard methods of histopathology (paraffin embedding). Our study aims to compare the results of extemporaneous examination with the final histopathological outcomes in 30 breast cancer patients who received neoadjuvant chemotherapy at the Salah Azeiz Institute in Tunis, Tunisia.

Results: The average age of the patients was 49.12 years (range 37-70), with the most common tumor stage being T2N1M0. Histological type was invasive carcinoma in all patients, and the triple- negative immunohistochemical subtype was found in five patients. All patients underwent lumpectomy with axillary lymph node dissection, and sentinel lymph node biopsy was performed in only one patient. The mean size of the tumor bed in the frozen section examination was 22.44 mm, with residual tumor presence in 16 cases. The final histopathological result showed residual tumor presence in 16 cases, accompanied by ductal carcinoma in situ (DCIS) in seven cases. Frozen section examination indicated the absence of residual tumor in 14 cases, but the final histopathological result revealed the presence of DCIS in three cases and residual tumor in five cases.

Conclusion: Our results highlight the limitations of extemporaneous examination. Despite its utility in providing immediate feedback, it may not always detect microscopic disease, such as DCIS. Its role in the context of a NAC is limited.

Clinicopathological Characterization of Mucinous Breast Cancer

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Introduction: Mucinous carcinoma is a distinct subtype of breast cancer characterized by the presence of extracellular mucin. It comprises approximately 1 to 4% of all breast cancer cases. There are two recognized forms: pure mucinous carcinoma composed of 90% mucin) and mixed mucinous carcinoma (composed of >10% and <90% mucin). This study aimed to delineate the clinical and pathological features of 15 cases of mucinous carcinoma managed at the Salah Azaiez Institute in Tunisia.

Results: All patients presented with a palpable breast mass, with an average tumor size of 38.53 mm (range: 11–65 mm). The predominant tumor stage was T2, with clinical lymph node involvement (N1) observed in nine cases. Mastectomy and lymph node dissection were performed in seven patients, two of whom received neoadjuvant chemotherapy. Lymph node dissection was carried out in 13 patients, either concomitantly with mastectomy in seven cases or via sentinel lymph node biopsy in one case. Pathological examination revealed pure mucinous carcinoma in eight cases, mixed mucinous carcinoma in four cases, and mucinous carcinoma associated with intracanalicular carcinoma in three cases; lymph node involvement was identified in four cases. The majority of cases demonstrated low to intermediate histological grade (n = 11), with hormone receptor expression observed in 80% of cases, predominantly exhibiting a luminal B immunohistochemical subtype (60%).

Conclusion: Our study provides valuable insights into the clinicopathological characteristics of mucinous breast cancer.

The findings underscore the importance of accurately diagnosing and classifying mucinous carcinoma subtypes, as they exhibit distinct clinical behaviors. Importantly, our results reaffirm the generally favorable prognosis associated with pure mucinous carcinoma compared to invasive carcinoma. Further research is warranted to elucidate optimal management strategies tailored to the specific subtypes of mucinous breast cancer, ultimately improving outcomes for affected patients.

Impact of Hyperbilirubinemia on DPD Screening test : A Series of six Patients

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Introduction: Dihydropyrimidine dehydrogenase (DPD) deficiency screening is a pre-therapeutic standard to prevent severe fluoropyrimidine-related toxicity. Although several screening methods exist, the accuracy of their results remains debatable. Certain factors can interfere with testing and produce false results. In this study, we analyze a series of six patients with metastatic cancers who present with total hyperbilirubinemia. We highlight the possible false-positive results in DPD testing associated with hyperbilirubinemia.
Methods: Uracilemia was measured as part of DPD deficiency screening at our Clinical Pharmacology Laboratory at the CNPV of Tunis using High-Performance Liquid Chromatography (HPLC). Uracil plasma values between 16 and 150 ng/mL are associated with partial DPD deficiency, while values above 150 ng/mL indicate total DPD deficiency. Genotyping was performed for patients presenting total DPD deficiency, focusing on the five most common DPYD polymorphisms (DPYD*2A, c.1679T>G, c.2846A>T, c.1129-5923C>G, and c.1236G>A/HapB3).
Results: This study included six patients with total hyperbilirubinemia. The average age was 45 years, with a sex ratio (M/F) of 2. The average uracil concentration is 47.44 ng/mL. Among the six patients, three presented with uracil concentrations indicative of partial DPD deficiency (16.93, 55.01, and 33.33 ng/mL), while two patients had concentrations suggestive of normal DPD activity (3.98, 3.98 ng/mL). One patient presented a concentration of 169.40 ng/mL, exhibited a total DPD deficiency. Genotyping was performed for this patient, and no evident mutations were found in the DPYD gene, despite the high uracil levels. We concluded that regarding DPD phenotyping, the extremely high uracil concentration may have interfered with the elevated bilirubin levels. Given the absence of an explanation for the elevated uracil concentration, the patient received her first chemotherapy cycle at half the standard dose, and another DPD screening was planned after bilirubin levels decreased following the initiation of chemotherapy.
Conclusion: According to guidelines, uracil concentrations above 16 ng/mL necessitate dose reductions, while levels exceeding 150 ng/mL suggest that 5-FU should be contraindicated. In the literature, there are reports of hyperbilirubinemia leading to false-positive results in DPD testing, particularly in cases of liver cytolysis and cholestasis, where significant uracil elevations have been observed. In our cases, only two patients had normal uracil concentrations, while the average uracil levels suggest a tendency toward DPD deficiency in patients with hyperbilirubinemia, reinforcing the possibility of false-positive results in DPD testing due to liver dysfunction. Our study highlights the importance of considering these factors. This was further confirmed by the patient with total DPD deficiency, though genotyping did not reveal any mutations. Therefore, it's essential to reassess DPD deficiency after addressing liver function abnormalities, to avoid unnecessarily contraindicating treatments like 5-FU. Repeating the uracil test post-chemotherapy and after liver function improvement may be necessary to prevent unjustly contraindicating critical treatments.

Pre Therapeutic screening for Dihydropyrimidine Dehydrogenase deficiency by measuring uracilemia in dialysis patients can lead to false results

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Introduction: Pretherapeutic screening for dihydropyrimidine dehydrogenase (DPD) deficiency is recommended prior to the administration of fluoropyrimidine-based chemotherapy. Concentrations above 16ng/mL are associated with partial DPD deficiency and call for reduction in dosing, whereas concentration values above 150 ng/mL are associated with complete DPD deficiency with contraindication of 5-FU.
However, the best strategy to identify DPD deficiency in End Stage Renal Disease (ESRD) patients is unknown. Here, we describe how determining the DPD status could be difficult in a cancer patient with severe kidney failure, and how it translated into adaptive dosing to secure the administration of 5-FU.
Case Report : A 43-year-old female patient with end-stage renal disease (ESRD) undergoing regular hemodialysis presented with fluctuating uracil levels, complicating the assessment of dihydropyrimidine dehydrogenase (DPD) activity. The initial uracil measurement, conducted between dialysis sessions, displayed an unidentifiable peak on the HPLC chromatogram, rendering the result uninterpretable. However, a subsequent uracil measurement taken immediately after the end of a dialysis session revealed a clear peak, with a uracil concentration of 27.4 ng/mL(partial DPD deficiency). This case highlights the significant impact of dialysis timing on uracil levels and emphasizes the need for careful consideration of sampling times in patients with renal impairment to avoid misleading results.
Commentaries: Despite being above the threshold associated with DPD deficiency (>16 ng/mL), the marked changes in uracil concentrations over time indicate that the timing of sampling relative to dialysis sessions has a significant impact on measured uracil levels in plasma, leading to erratic values. Our case suggests that the interpretable peak in the chromatogram first measured before dialysis was probably due to uracil accumulation resulting from renal impairment.
This case report confirms that sampling for functional DPD screening in a patient with severe kidney failure is more accurate when performed immediately after dialysis, once the excess uracil has been partly cleared from the body. Notably, our patient was consistently found to be DPD-deficient, although the uracil peak

that the interpretable peak in the chromatogram first measured before dialysis was probably due to uracil accumulation resulting from renal impairment.
This case report confirms that sampling for functional DPD screening in a patient with severe kidney failure is more accurate when performed immediately after dialysis, once the excess uracil has been partly cleared from the body. Notably, our patient was consistently found to be DPD-deficient, although the uracil peak became interpretable and closer to normal values when measured after dialysis. While DPD phenotyping remains the most sensitive method for detecting DPD deficiency, it is crucial to rapidly identify factors that may influence uracil concentrations to avoid false-positive or false-negative results.

TMC6 is associated with poor survival in patients with serous epithelial ovarian cancer

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Introduction: Epithelial Ovarian Cancer (EOC) is considered as the most lethal gynecological cancer. The identification of new diagnostic and prognostic biomarkers is crucial. An association between the Transmembrane-channel-like6 (TMC6) expression with human papillomavirus (HPV) was found implicated in cancer aggressiveness. This study aims to assess TMC6 protein expression in EOC, evaluate its prognostic value and its association with HPV expression.
Methods: We used 87 EOC samples to evaluate the TMC6 protein expression by immunohistochemistry (IHC) and to investigate its correlation with clinicopathological features, prognosis in terms of metastasis-free survival (MFS) and its association with HPV16-18.
Results: In 74 patients with serous EOC, those with a negative TMC6 tumor expression (60%) were associated with bigger tumor size at diagnosis (p=0,001), marked cytonuclear atypia (p=0,014), and higher serum CA-125 level (p=0,036). Univariate and multivariate analysis showed that negative-TMC6 was correlated with poor 5-year MFS (p=0.033 and p=0.067, respectively) as the only variable tested. Interestingly, our results showed a negative association between TMC6 and HPV16-18.
Conclusion: Prognostic features and poor clinical outcome were associated with TMC6-loss of expression in our cohort of serous EOC. A negative correlation between TMC6 and HPV infection was confirmed which led us to suggest that TMC6 might represent a new potential biomarker to be investigated.

Leukocytoclastic Vasculitis due to Thalidomide in Multiple Myeloma

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Introduction: The mechanism of thalidomide's effect in treating multiple myeloma is not fully understood, though it is known to affect plasma cells both directly and indirectly by preventing their adhesion and proliferation. Thalidomide's most common side effects are sedation, fatigue, constipation, neuropathy, pruritus, rash, tremor and edema . In the literature, only a single case of LCV occurrence under thalidomide therapy has been reported. We herein describe this rare complication of thalidomide therapy.
Case report: We report the case of a 58-year-old male diagnosed with multiple myeloma. After achieving a complete response to initial melphalan and prednisone treatment, the patient relapsed in 2005 and began thalidomide therapy. Initially prescribed 100 mg/day, the dosage was gradually increased to 400 mg/day, combined with monthly zoledronic acid infusions.
Nine months after the beginning of the treatment, the patient developed sudden purpuric exanthema on the lower extremities, accompanied by arthralgia . A skin biopsy confirmed the presence of leukocytoclastic vasculitis (LCV). Additionally, the patient experienced microscopic hematuria and proteinuria, although renal function tests and imaging were unremarkable.
Thalidomide therapy was promptly discontinued, and methylprednisolone was initiated. Within one week, the patient's skin lesions and joint pain improved, and hematuria and proteinuria resolved after a few months. The patient remained in complete remission for 12 months following the cessation of thalidomide, with no recurrence of LCV.
Conclusion: Thalidomide is an effective treatment option for relapsed or refractory multiple myeloma. However, it is associated with several side effects, including rare cases of LCV. Thiscase highlights the importance of monitoring for autoimmune complications during thalidomide therapy, as LCV, though rare, can occur and requires prompt intervention. The exact mechanism by which thalidomide might induce autoimmune responses

like LCV in the context of malignant diseases warrants further investigation.

Cutaneous vasculitis associated with gemcitabine therapy in advanced squamous non-small cell lung cancer

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Introduction: Leukocytoclastic vasculitis (LCV), can be induced by drugs such as nonsteroidal anti-inflammatory drugs, b-lactams, sulfonamides and diuretics. Gemcitabine, a nucleoside analogue used as chemotherapy, was exceptionally associated with LCV [1].
We report a case of gemcitabine-induced LCV.
Methods: This case was analyzed according to the updated French method of causality assessment [2].
Results: A 73-year-old man with a history of high blood pressure and coronary artery disease, has been followed for squamous cell carcinoma of the lung since 2012. He received two chemotherapy protocols (gemcitabine and cisplatin in 2013, carboplatin and paclitaxel in 2016) without incident.
During the third protocol, started in May 2019, he presented, five days after the first infusion of gemcitabine, with generalized pruritus and erythema of the upper chest. In the same month, the patient received a second gemcitabine infusion associated with premedication. Few hours later, the rash generalized. The diagnosis of vasculitis was suspected. The skin biopsy, performed on the arm, confirmed the diagnosis of LCV. Symptoms resolved in 20 days.
Conclusion: Gemcitabine vasculitis, although rare, is important to diagnose in order to discontinue the causative drug and thus avoid potentially serious systemic complications.

Sexual Function Evaluation in Breast Cancer Patients

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Introduction: Breast cancer is the most common cancer among women and can have a major negative impact on patients' sexuality, yet this aspect of care often remains overlooked.
In this study, we aimed to investigate the prevalence of sexual dysfunction (SD) in a population of breast cancer patients undergoing chemotherapy and determine the clinical and socio-demographic factors associated with it.
Methods: We conducted a cross-sectional, descriptive, and analytical study conducted in the oncology department of Salah Azaiez institut. It involved female patients over 18 years old, receiving chemotherapy for breast cancer. A questionnaire collecting socio-demographic and clinical data was used. Sexual function, depression, and anxiety were assessed using the Arizona Sexual Experience Scale (ASEX) and the Hospital Anxiety and Depression Scale (HADS), validated in Arabic.
Results: Our study evaluated 30 patients. The mean age was 48.5 years. The majority were employed (63.3%) and married (83.3%). Three patients (10%) were smokers. The mean age at diagnosis was 46.8 years. The prevalence of SD was 60%, consisting of sexual desire disorders (68%), arousal disorders (60%) and orgasmic disorders (23.8%). Depression was present in 33.3% of patients, while anxiety was observed in 46.7%. The presence of SD was significantly associated with concurrent depression (p=0.02). However, no other statistically significant associations were found with other clinical parameters.
Conclusion: Results show that SD is common in breast cancer patients. It may be associated with concurrent depression.

Evaluation of Depression and Anxiety in Breast Cancer Patients

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Introduction: Breast cancer has a significant impact on the quality of life of patients causing physical and psychological challenges. The aim of our study was to assess the prevalence of depression and anxiety in breast cancer patients undergoing chemotherapy and to identify the clinical and socio-demographic factors associated with these conditions.
Methods: We conducted a cross-sectional, descriptive study conducted at the oncology department of Salah Azaiez Institute including female patients over 18 years old, receiving chemotherapy for breast cancer. A questionnaire collecting socio-demographic and clinical data was used. Sexual function, depression, and anxiety were assessed using the Arizona Sexual Experience Scale (ASEX) and the Hospital Anxiety and Depression Scale (HADS), validated in Arabic.
Results: Thirty patients were included. The mean age was 48.5 years. The majority were professionally active (63.3%) and married (83.3%). Among these patients, 10% were smokers. The mean age at diagnosis was 46.8 years. The prevalence of sexual dysfunction (SD) was 60%, including sexual desire disorders (68%) and orgasmic disorders (23.8%).
Depression was present in 33% of patients, and anxiety in 47% of them. Depression was significantly associated with age (p=0.01)The incidence of depression was higher in the patients aged 50 years, the presence of sexual dysfunction (p=0.02), and anxiety (p<0.0001). Anxiety was significantly associated with leisure activities (p=0.04). However, no statistically significant associations were found between depression, anxiety, and other

clinical parameters.
Conclusion: A high rate of depression and anxiety among breast cancer patients was noted in our study. Prioritizing systematic screening and early detection of depression and anxiety is crucial, as promptly managing these conditions can greatly improve quality of life.

Study of morbidity and mortality of surgical management of ovarian cancer

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Introduction and aims: To evaluate the morbidity and mortality of the surgical management of epithelial ovarian cancer (OC).
Methods: We retrospectively conducted a mono-centric, longitudinal study including 182 patients surgically managed for advanced stage OC (FIGO IIB - IV) in the oncologic surgery department of the Salah Azaiez Institute, from January 2000 to December 2017. We reviewed early and late postoperative complications and analyzed factors associated with surgical morbidity.
Results: The mean age was 57 years ± [range 28-81]. We performed primary debulking surgery in 127 patients (69.8%) and 55 patients (30.2%) underwent and interval debulking surgery after neoadjuvant chemotherapy. We performed conventional cytoreductive surgery, consisting of hysterectomy, bilateral salpingo-oophorectomy, omentectomy, appendectomy, and limited peritonectomy in 55 patients (31%). This surgery was radical or supra-radical in 62 patients (34%), involving rectosegmoidectomy in 30 cases, right colectomy in 5 cases, transverse colectomy in 2 cases, small bowel resection 6 cases, splenectomy (5 cases), extended peritonectomy with resection of diaphragmatic domes in 13 cases. The procedure was limited to hysterectomy with bilateral salpingo-oophorectomy alone when another procedure was deemed impossible in 65 patients (65%). Maximal cytoreduction (R0) was achieved in 62 of patients (34%), 63 patients had a residual disease 1cm (35%) and 57 patients had a residual disease >1cm (31%). Lymphadenectomy was performed in 101 patients. Five patients experienced a perioperative complication: hemorrhagic complications (n=3), a diaphragmatic breach (n=1), and ureteral injury (n=1). Eighty patients received perioperative transfusion, with an average of 2.6±1 packed red blood cells (1-6). The average operative time was 221± 84 mn [range 90-400 mn] and was prolonged with peritonectomy (340mn vs 199mn, p=0.03), associated digestive resections (350mn vs 197mn, p=0.01) and splenectomy (400mn vs 206 mn, p=0.02). Performing lymphadenectomy did not significantly prolong operative duration, p=0.43. Medical complications occurred in 9.9% of cases with essentially thrombotic accident (5.4%). Early surgical post operative complications occurred in 8 patients (4.4%) with 1 case of hemoperitoneum, 1 case of peritonitis by anastomotic leak, 2 cases of deep abcess, 2 cases of parietal abcess and 2 cases of evisceration. The rate of post operative mortality was 2.2% (4 patients). Late postoperative complications occurred in 20.8% of cases (n=38) and were dominated by abdominal wall eventration 10.4 %, lymphoedema (6.5%) and pelvic lymphocyst (2.2%).
Conclusion: The study of morbidity of the surgical management of ovarian cancer is necessary in order to improve survival and reduce the median period of hospitalization.

Prognostic factors of survival in advanced epithelial ovarian cancer

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Introduction and aims: This study aims to investigate the prognostic factors of overall survival (OS) in epithelial ovarian cancer (EOC).
Methods: We retrospectively conducted a mono-centric, longitudinal study including all patients surgically managed for advanced stage ovarian cancer (FIGO IIB - IV) in the oncologic surgery department of the Salah Azaiez Institute, from January 2000 to December 2017. Survival data were generated by Kaplan-Meier method and predictive factors of outcome were analyzed using Cox proportional hazards models.
Results: The mean age was 57 years ± [range 28-81]. We performed primary debulking surgery in 127 patients (69.8%) and 55 patients (30.2%) underwent an interval debulking surgery after neoadjuvant chemotherapy. We performed conventional cytoreductive surgery, consisting of hysterectomy, bilateral salpingo-oophorectomy, omentectomy, appendectomy, and limited peritonectomy in 55 patients (31%). This surgery was radical or supra-radical in 62 patients (34%). The procedure was limited to hysterectomy with bilateral salpingo- oophorectomy alone when another procedure was deemed impossible in 65 patients (65%).
Maximal cytoreduction (R0) was achieved in 62 of patients (34%), 63 patients had a residual disease 1cm (35%) and 57 patients had a residual disease >1cm (31%). Lymphadenectomy was performed in 101 patients. About 75.4% of patients were FIGO stage IIIC. Serous carcinoma was the most frequent subtype (84%) mostly high-grade (74.5%). Lymph nodes metastasis (LNM) was assessed in 55.4% of patients with isolated pelvic LNM in 40.8% of patients and associated to paraaortic LNM in 44% of cases. The mean node ratio (LNR) was 0.13 [0-1]. Adjuvant chemotherapy (ADJ CT) was administrated in 163 patients. After a median follow-up was 26 ± 31months, complete remission was found in 38% of cases and progression in 29.8% of cases. The median OS was 50.9 ± 5 months [range 0-193] and the 5 years OS was 21.2%. On univariate analysis, the median OS was associated to the extent of carcinomatosis (46 vs 63 months; p=0.021), to lymphadenectomy (66 vs 27 months; p<0.0001), the presence of LNM (p=0.006), to R0 resection (73 vs 30 months; p<0.0001) and to the

response after ADJ CT (65 vs 22 months; p<0.0001). On multivariate analysis, complete resection R0 (HR= 4.4; 95% CI= [2.05-9.4], p=0.001) and response after ADJ CT (HR= 2,272; 95% CI= [1.2-4]; p=0.005) were the only independent factors of OS.
Conclusion: The quality of debulking surgery and the response to chemotherapy represent the main prognostic factors survival in epithelial ovarian cancer.

Management of epithelial ovarian cancer: Comparative study of primary debulking and interval debulking surgery

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Introduction and aims: This study aims to compare the clinical, pathological and therapeutic characteristics of primary debulking surgery (PDS) and interval debulking surgery (IDS) in the management of epithelial ovarian cancer (EOC).
Methods: We retrospectively conducted a mono-centric, longitudinal study including all patients surgically managed for advanced stage EOC (FIGO IIB - IV) in the oncologic surgery department of the Salah Azaiez Institute, from January 2000 to December 2017.
Results: The mean age was 57 years ± [range 28-81]. We performed PDS in 127 patients
(69.8%) and 55 patients (30.2%) underwent an IDS after neoadjuvant chemotherapy (NADJ CT). NADJ CT was indicated in 32.1% of FIGO stage IIIC patients (n=44) and 47.05% of stage IV patients (n=8). Fifty-one patients received Taxol and Carboplatin (93%) and 4 patients received Endoxan and Cisplatin (7%). The average number of cycles was 5±1.7 (range 3 to 9):18% received 3 cycles, 18% had 4 cycles and 41% received 6 cycles. Evaluation after NADJ CT showed a clinical complete response in 35% of cases, radiological complete response in 17% of cases and a decrease in CA 125 levels in 89% of cases. We performed conventional cytoreductive surgery, consisting of hysterectomy, bilateral salpingo-oophorectomy, omentectomy, appendectomy, and limited peritonectomy in 55 patients (31%).
This surgery was radical or supra-radical in 62 patients (34%), involving rectosigmoidectomy in 30 cases, right colectomy in 5 cases, transverse colectomy in 2 cases, small bowel resection 6 cases, splenectomy (5 cases), extended peritonectomy with resection of diaphragmatic domes in 13 cases. The procedure was limited to hysterectomy with bilateral salpingo-oophorectomy alone when another procedure was deemed impossible in 65 patients (65%). Maximal cytoreduction (R0) was achieved in 62 of patients (34%). Lymphadenectomy was performed in 101 patients. Adjuvant CT was administrated in 163 patients. Comparing the two therapeutic strategies, there was no statistically significant difference between PDS and IDS regarding the presence of peritoneal carcinomatosis (87.4% vs 80%, p=0.6) and the Peritoneal Cancer Index (PCI) score (p=0.13), with a higher percentage of ascites in the PDS group (72.4% vs 52.7%, p=0.01). The performance of lymphadenectomy was more frequent in the IDS group (49.1% vs 34.6%, p=0.03). The rates of performing supra radical surgery (25.2% vs 30.9%, p=0.32) as well as achieving zero residual disease (31.5% vs 40%, p=0.26) were comparable. After a median follow-up of 26 ± 31 months, PDS was associated with improved overall survival compared to IDS (p=0.02).
Conclusion: The choice between PDS and IDS is based on clinical characteristics and disease staging, which define the extent of surgery and the possibility of achieving complete resection.

Osteosarcoma in the Tunisian center: epidemiological, clinical, anatomopathological, and therapeutic characteristics

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Introduction: Osteosarcoma (OS) is the most common bone sarcoma in adolescents and young adults. The objective of this work is to study the epidemiological, anatomopathological, therapeutic, and prognostic characteristics of adult OS.
Methods: This is a retrospective study of 59 cases of OS collected at the oncology department of Farhat Hached Hospital in Sousse between 2002 and 2022.
Results: The mean age was 26 years with a sex ratio of 1.8. The appearance of a spontaneously painful swelling or following a revealing trauma associated with pain (55.9%) was the first revealing sign. On clinical examination, the average tumor size was 20 cm. The lower limb was the most affected (69%) while the humerus was affected in 10.2% of cases. Eleven patients had metastases from the outset, 7 of them with pulmonary involvement. Osteoblastic osteosarcoma was the most observed type (42.4 %). Initial chemotherapy was indicated in 87.7 % of patients. A response was observed in 17 %. It was followed by surgical treatment in 67.9% of cases, with 84.6 % being poor responders histologically. Margins were clear in82.4 % of cases. A chemotherapy regimen for poor responders was then indicated in 66.7% of cases, with tumor relapse occurring in 23.7 % of cases. The overall 5-year survival rate was 5.9%.
The median survival was 21 months for non-metastatic cases and 7 months for metastatic cases, with a significant difference (P=0.031). The localized initial stage of the disease and histological response to chemotherapy were good prognostic factors with p<0.05.
Conclusion: Neoadjuvant chemotherapy has improved the prognosis of OS. However, the management of this entity faces considerable difficulties due to diagnostic delays. Multicenter studies are necessary for optimal management of refractory and metastatic forms.

Metastatic HER overexpressed breast cancer: Characteristics and prognostic factors in central Tunisia

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Introduction: In Tunisia, breast cancer is the first female cancer and represents the most common cause of cancer-related death (19.7%). The discovery of the role of HER2 gene amplification in defining a subtype of cancer likely to respond to therapies targeting the HER2 protein was a paradigm shift in oncology.
The main objective of our work is to determine prognostic factors for therapeutic response in patients with HER2-overexpressing breast cancer in the metastatic stage.
Results: The mean age of our patients was 49.1 years ,The general condition was preserved in the majority of our patients (98.4%),Thirteen patients were of normal weight (BMI<25),Thirty-six patients had clinical lymph node involvement ,Metastases were predominantly bone in 36 patients. Tumors were predominantly SBR III grade in 33 patients, and Ki 67 was above 20% in the majority of cases:46 patients.tumors were predominantly Luminal B subtypes in 44 patients. In 1st-line metastatic chemotherapy, 93.5% of our patients had received taxane- based chemotherapy in 50% of cases, combined with Trastuzumab in 30 patients.
The mean progression-free survival of our population was 9 months and the median was 8 months .There was no statistically significant relationship between SSP and both obesity and age . OS and PFS were better in women over 35 than in other age groups, with no statistically significant difference. The mean PFS for patients with grade SBR I was 11 months, and 8 months for those with grades SBR II and III. OS for patients with SBRI grade breast cancer was 27 months, and 23 months for patients with SBRII or SBR III grade. The mean survival for patients with a Ki67 greater than 20% was 21 months, while it was 30 months for those with a Ki67 less than 20%, (p= 0.11). Mean PFS was the same for both groups. The mean OS for HR-negative patients was 19 months and for HR-positive patients 26 months, but there was no significant association in the univariate study (p= 0.115). The 1-year OS for HR-negative patients was 65% and 78% for HR-positive patients, but there was no difference in terms of PFS. A decrease in mean OS in the case of lymph node invasion, but not significantly (p=0.77). While PFS was the same, the presence of multiple metastatic sites was not also a significant prognostic factor (p= 0.71). Treatment with Trastuzumab in the metastatic phase was associated with better overall survival (p<0.001) and without progression (p=0.015).
Conclusion: Trastuzumab has revolutionized the management of breast cancer, especially at the metastatic stage. The access to these treatments in Tunisia remains limited in the metastatic setting, as they are still considered to be ineffective. The recent emergence on the market of biosimilars is likely to facilitate access to these therapeutic innovations.

Porocarcinoma: A Rare but Aggressive Skin Tumor—Challenges in Diagnosis and Management

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Introduction: Porocarcinoma (PC) is a rare and aggressive sweat gland carcinoma, often posing diagnostic challenges due to its similarity to other skin malignancies, frequently leading to misdiagnosis.
Methods: This study includes three patients treated for eccrine PC at the Salah Azaiez Institute between 2008 and 2014.
Results: The patients were aged 62, 48, and 79, respectively, with lesions located on the back of the wrist, right leg, and scalp, with a median tumor size of 6 cm. Axillary lymphadenopathy was associated with the wrist lesion. All patients underwent wide tumor excision with skin defect reconstruction. Axillary lymph node dissection was performed on the first patient. Histopathological analysis confirmed porocarcinoma with clear margins in two cases, while the first patient had close margins and positive lymph nodes. Adjuvant radiotherapy to the tumor bed was administered. The first patient experienced an axillary recurrence seven months later, necessitating surgical resection and further axillary radiotherapy. A second, non-surgical loco- regional relapse occurred six months later and was managed with chemotherapy. The second patient experienced local and inguinal recurrence four years postoperatively, requiring excision and inguinal lymph node dissection. Adjuvant radiotherapy was delivered due to positive margins and lymph nodes, followed by multiple loco-regional recurrences managed with wide excision. Fourteen years post-relapse, the patient remains well. The third patient was lost to follow-up after surgery.
Conclusion: Given its rarity, porocarcinoma remains a challenging entity in terms of both presentation and management. Currently, no international guidelines exist for the treatment or follow-up of patients with PC.

Soft Tissue Sarcomas of the Trunk: A Rare and Complex Surgical Challenge

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Introduction: Soft tissue sarcomas (STS) are rare and diverse malignancies originating from mesenchymal tissues, accounting for less than 1% of adult cancers. When located in the trunk, these tumors pose significant challenges due to their potential for large size at diagnosis and the complexities in achieving adequate surgical margins.
Methods: This retrospective longitudinal study, conducted at the Salah Azaiz Institute, analyzes sarcomas

of the soft tissue of the trunk treated between 2013 and 2016. Data collected include demographic information, tumor characteristics, treatment methods, and follow-up outcomes.

Results: Six patients were treated for trunk sarcomas during the study period, with a male predominance (83%). The mean age was 62 years, and the mean time from initial lesion notice to diagnosis was 43.5 months. Tumors were located in the thoracic wall, abdominal wall, back, and pelvis, with an average size of 10 cm. Dermatofibrosarcoma accounted for 67% of the cases. All patients underwent wide local excision, with 50% requiring reconstructive surgery.

One patient received additional radiation therapy due to inadequate surgical margins. The mean follow-up period was 19 months, during which only one recurrence was observed.

Conclusion: The study highlights the rarity and complexity of managing soft tissue sarcomas of the trunk. The findings emphasize the importance of a multidisciplinary approach, considering tumor size, grade, and surgical margins to optimize treatment outcomes.

Systematic detection of dihydropyrimidine dehydrogenase deficiency in digestive cancers: assessment of treatment response and relapse rate

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Introduction: The DPD enzyme is primarily responsible for metabolizing Fluoropyrimidines (FP), and its deficiency can result in varying degrees of toxicity.

Adjustments in FP dosage remain necessary for individuals with DPD deficiency to reduce the likelihood of severe adverse effects. Consequently, this condition may affect treatment response and patient relapse rates (RR).

Methods: A retrospective study involving patients treated for digestive cancers with an indication for FP-based chemotherapy who were systematically screened for DPD activity at the Department of Oncology at Farhat Hached Sousse from January 2019 to December 2021 by calculating UH2/U ratio (R). Among the 265 patients in the Study two groups were defined:

- Group1 : R>=1,5 : Normal DPD activity (n=228,86%)
- Group2: R<1,5: Reduced DPD activity (n=37,14%)

For the 2nd group doses were reduced by removing the 5-FU bolus and implementing a 50% reduction in continuous 5-FU throughout all treatment cycles.

Assessment of response to treatment was carried out using thoracoabdominal and pelvic CT scans and according to the RESPONSE EVALUATION CRITERIA IN SOLID TUMORS (RECIST) criteria.

Results: In group 1, the treatment response frequency at the initial assessment (comprising complete and partial responses) stood at 36.4%, while 29% experienced progressive disease. The RR was 22.9%, with an average delay of 11.8 months.

In the 2nd group, progression was more frequent after the initial evaluation (n=12, 57.1%), and the frequency of radiological response was reduced to 28.6% (p=0.078). The RR was higher in this group following dose reductions compared to the first group (57.1% vs. 22.9%). We found greater survival in group 1, who received full doses of FP, compared to the second group (41.66 vs.29.19 months),(p=0.191).Relapse-free survival was lower in the DPD-deficient group compared to the first group (23.28 vs. 35.04 months), p= 0.041.

Conclusion: Our study showed that systematic screening for DPD activity through UH2/U ratio calculation might help prevent severe toxicity but could lead to reduced treatment effectiveness and a higher RR.

Epidemiological profile of metastatic prostate cancer (Cap) in a population of northwestern Tunisia

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Introduction: Prostate cancer (Cap) is the most common cancer in men over the age of 50. It is the second leading cause of death after lung cancer. The objective of our work is to study the epidemiological and evolutionary profile of the metastatic Cap in the population of northwest Tunisia.

Methods: This is a retrospective study. We identified 35 cases of metastatic Cap treated at the Medical Oncology Department of the Jendouba oncology center over a period of 5 years from January 2018 to December 2022.

Results: The average age is 69 years (47 to 98 years). Forty percent of patients have a family history of Cap or other cancer. Urological clinical signs (dysuria, pollakiuria, hematuria, urinary retention) are revealing in 75% of cases. The diagnosis is often late, the average time is 30.5 months (3 to 53 months). Forty percent of our patients have a Gleason score of 8 to 10. The most observed T stages of the primary tumor are T3 and T4 in 37% and 33% respectively. The average PSA level in our series is 155.4 ng/ml (from 2 ng/ml to 1700 ng/ml). Seventy-five percent of patients have bone metastases. Ninety- three percent of our patients had chemical castration with Zoladex 10.8 or decapeptyl 11.25. Sixty-seven percent of cases had 1st line chemotherapy based on docetaxel combined with castration by 1st generation hormone therapy. Ten percent of our patients were able to benefit from abiraterone in the 2nd line. The side effects of hormone therapy are depressive syndrome found in 33% of cases, followed by digestive disorders (27%), metabolic syndrome (20%) and sexual impotence (13%). The median survival is 97% at 1 year, 80% at 3 years and 50% at 4 years.

Conclusion: Good multidisciplinary care allows for appropriate support for the patient, the relief of symptoms, the preservation of his autonomy and the improvement of the quality of life. Early diagnosis with PSA testing is currently the only screening method that could reduce mortality.

Epidemiological profile of primary malignant brain tumors (PBT) in a population of northwestern Tunisia

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Introduction: Brain tumors account for 1.4% of all new cancer cases and 2.4% of all cancer deaths. In Tunisia, brain tumors account for 2.2% of all new cancer cases. Each year, between 100 and 500 new cases are diagnosed with a mortality rate between 2.6% and 3%. The objective of our work is to describe the epidemiological profile and therapeutic management of patients with primary malignant brain tumors in northwest Tunisia.
Methods: This is a retrospective study of 66 cases of brain cancer treated at the medical oncology department of Jendouba Oncology Center between January 2018 and December 2022.
Results: There were 66 cases of PBT (3.5% of all cancers followed at the medical oncology department of Jendouba over the 5-year period). The average incidence is ten new cases per year. The average age is 55 years (15 to 65 years). The sex ratio is 2.3: (46 men/ 20 women). The location of PBTs is supratentorial in 80% and subtentorial for the rest. Motor deficit is the most frequent reason for consultation in 50% of cases. In our study, 45 patients (68%) had gliomas, 62% of whom were grade IV. In our series, 81% had surgical excision, 84% had radiation therapy, and 62% had chemotherapy. Forty-one patients (62%) received radiotherapy combined with concomitant temozolomide-based chemotherapy followed by adjuvant temozolomide-based chemotherapy with a total of 6 cycles. Survival is 47% at 12 months. The only factor of poor prognosis that stands out significant is age>45 years.
Conclusion: Scientific advances in the field of molecular biology have made it possible to develop new paradigms in diagnostic imaging, surgical techniques and technologies, and adjuvant treatments, resulting in improved quality of life and patient survival.

Epidemiological profile of gastric cancer (GC) in a population of northwestern Tunisia

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Introduction: Gastric adenocarcinoma is the fifth leading cause of cancer death worldwide, accounting for nearly 660,175 deaths per year. In Tunisia, it is the second most common digestive cancer. The objective of this work is to describe the epidemiological profile of GC and to identify prognostic factors.
Methods: This is a retrospective study of 77 patients treated at the medical oncology department of the Jendouba oncology center between January 2017 and December 2022.
Results: The sex ratio is 1.75 with 49 men and 28 women. The average age is 60 years (33 to 85 years). Epigastralgia is the most frequent reason for consultation (71% of patients). Forty-two percent of patients are metastatic from the outset. The peritoneum (16%) is the most common site of metastasis (10%) followed by the liver. The World Health Organisation score is 1 in 68% of patients. In our study, 30 patients had a partial or total gastrectomy surgery (i.e. 39%), chemotherapy was performed in 70 patients (i.e. 90%), radiotherapy was performed in five patients (i.e. 6%) concomitantly with chemotherapy and postoperatively. No patients benefited from immunotherapy. Thirty patients (39%) underwent Flot-type perioperative chemotherapy.
Forty-seven patients (61%) received 1st line chemotherapy for locally advanced or metastatic tumors.
Twenty patients (42%) had 2nd line chemotherapy. One patient had trastuzumab in the 1st line for HER+ tumor. Overall survival is 77% at 1 year and 40% at 2 years. Prognostic factors identified are: personal history of diabetes (p=0.03), partial gastrectomy (p=0.04), hypoalbuminemia (p=0.04), elevated CEA (p=0.01), presence of vascular emboli (p=0.05), perinenerve sheathing (p=0.01), secondary bone location (p=0.01), type of lymph node dissection (p=0.04), performance status (p=0.01).
Conclusion: A multidisciplinary approach is needed to improve the prognosis of gastric cancer. Continuous efforts at prevention and early detection are necessary. Clinical research is relied upon for the development of new targeted therapies and immunotherapies to improve survival.

Evaluating female sexual function in older women with breast cancer

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Introduction: The sexuality of elders is a subject that is rarely discussed, particularly in women. Female sexual function changes throughout life, and is influenced by a number of biological, social and psychological variables. The aim of this study is to assess sexual function in women aged 55 years.
Methods: The study concerned 23 patients treated for breast cancer at the Oncology Department of the Salah Azeiz Hospital in January 2023, who agreed to complete the FSFI (Female Sexual Function Index) questionnaire.
Résultat: The mean age was 61±4 years (55 to 72). Eleven patients felt that the purpose of sexuality was

procreation, 3 felt that sexuality was pleasure and well-being, and 39.1% (n=9) defined sexuality as a combination of the two.Sexuality was important for 7 patients and unimportant for 12 patients.
The total FSFI score ranged from 2.8 to 24.80 with a mean of 10.65± 8.10. Patients had at least one sexual disorder : decreased libido was observed in 17 patients, vaginal dryness in 18 patients, 20 patients were no longer reaching orgasm. Eighteen patients had dyspareunia and 15 were no longer seeking sexual satisfaction.
There was a linear correlation between age and the lubrication score (p=0.04) and the orgasm score (p=-0.023). There was no statistically significant correlation between age and the FSFI19 score.
Conclusion: Sexuality is redefined and modified with age. It has an important role in our health and well-being. Maintaining sexual activity with advancing age is a protective factor against the onset of a number of cardiovascular, neoplastic and psychiatric diseases.

Access to testing and to targeted therapy in metastatic NSCL: Many challenges

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Introduction: Molecular testing in Tunisia poses significant challenges, and data on the molecular profiles of metastatic adenocarcinoma are infrequently reported. Our study aimed to describe the characteristics of molecular testing for metastatic adenocarcinoma over the past five years.
Methods: We conducted a retrospective analysis of 416 patients diagnosed with metastatic adenocarcinoma and treated between 2018 and 2022. We assessed the number of molecular tests performed, the results obtained, and subsequent access to targeted therapies. During the study period, the most readily available test was the ALK rearrangement test.
Results: Among the cohort, 28% (n=116) of patients underwent molecular testing, with a notable increase in test availability: 32% of tests were performed in 2022 compared to only 5% in 2018. All patients who received testing (100%) underwent ALK rearrangement testing via immunohistochemistry and fluorescence in situ hybridization (FISH). Additionally, 80% of patients were tested for both ALK and EGFR mutations using Sanger sequencing, while only 23% underwent next-generation sequencing (NGS) for a broader range of oncogenes including ALK and EGFR. The mutation profile revealed that 46% of patients had wild-type tumors, 29% had ALK rearrangements, and 21% had EGFR mutations. Rare mutations were observed, including one case of BRAF mutation and two cases of KRAS G12C mutation Among patients with EGFR mutations, 56% had exon 19 deletions, 32% had exon 21 L858R
mutations, and 12% had exon 20 insertions. The median age of patients harboring actionable mutations was 53 years, with 52% being female and half of them being never-smokers. Of the 116 patients with targetable mutations, only 48% (n=56) received the appropriate targeted therapy: 57% in the first-line setting, 30% in the second-line, and the remainder in subsequent lines.
Conclusion: The proportion of patients undergoing molecular testing was relatively low. The high prevalence of ALK rearrangements in our cohort likely reflects the availability and accessibility of this test during the study period. Access to molecular testing should be accompanied by improved access to targeted therapies, which remains limited in our population.

First-Line Pertuzumab and Trastuzumab for HER2-Positive Metastatic Breast Cancer

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Introduction: The phase III Clinical Evaluation Pertuzumab And Trastuzumab (CLEOPATRA) trial established the combination of Pertuzumab and Trastuzumab (TP) with docetaxel as the standard first-line (FL) therapy for HER2-positive locally recurrent or metastatic breast cancer (MBC).
This study aims to evaluate the safety and efficacy of TP in the first-line setting.
Methods: Patients with HER2-positive MBC treated at the oncology department of Hospital Abderrahmen Mami were administered chemotherapy with TP until disease progression or unacceptable toxicity in the first-line setting.
Results: Our study included 50 patients with HER2-positive MBC. The mean age of 46.6 years. Metastases were detected on the initial CT scan in 21 patients (42%) and during subsequent follow-up CT scans in 29 patients (58%). The majority of patients (31, or 62%) received dual blockade with TP as first-line treatment.
The three-month response rate was 93.5% in patients who received dual blockade compared to 82.4% in the Trastuzumab-only group. Progression-free survival (PFS) in the Trastuzumab- Pertuzumab group was 10 months. Subgroup analysis revealed variations in PFS based on the chemotherapy used with dual blockade: 15 months for patients receiving a taxane, 3 months for one patient receiving Vinorelbine, 24 months (range 4-43) for patients receiving capecitabine, and 9 months for one patient receiving hormone therapy.
The dual blockade was well tolerated, with only three cases (6%) of cardiac toxicity occurring
during first-line treatment. Detailed analysis of therapeutic response based on age, time of metastasis detection, metastasis site, hormone receptor expression, SBR grade, time to start Pertuzumab, and KI67 index did not show any impact on the therapeutic response.
Conclusion: This study demonstrates a safety and efficacy profile of TP consistent with the CLEOPATRA trial results, with Taxane as backbone chemotherapy.

Oral Health and Physical, Functional and Psychosocial Repercussions in Cancer Patients undergoing Zoledronic Acid Treatment

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Introduction: Zoledronic acid, a potent bisphosphonate, is commonly prescribed to manage bone metastases and osteoporosis in cancer patients. While effective for these indications, the oral health impacts of zoledronic acid therapy are less well documented. We aim to evaluate the prevalence of oral health issues among cancer patients receiving zoledronic acid.

Methods: A cross-sectional study was conducted at the medical oncology department of the Salah Azaiz Institute in July and August 2024, including patients receiving treatment with zoledronic acid. We collected demographic and medical data, dental examination data and conducted a survey using GOHAI score.

Results: A total of 28 patients (24 female, 85.7%) with a median age of 58 years were included in the study. The majority were treated for breast cancer (n=23), 2 patients treated for lung cancer, 2 for prostate and 1 patient was treated for endometrial cancer. Half of the patients had comorbidities, predominantly hypertension and diabetes (n=13, 46.4%). All were nonalcoholic and 5 had a history of smoking (17.9%). Only one patient had a history of cervicofacial radiation therapy. Zoledronic acid was administered for bone metastases in 82.1% of cases and for osteoporosis in 17.9%, with a median treatment duration of 17 months (range 3-124).

Baseline evaluation included a renal and phosphor-calcic profile for all patients, a DEXA scan for 15 patients (53.6%) but only 5 saw a stomatologist. Patients with bone metastases were less likely to be referred to a dentist before treatment (p=0.02). Dental examination revealed that 92.8% of patients had calculus, with 17.9% experiencing severe calculus. Mild stomatitis and gingivitis were observed in 64.3% and 53.6% of patients, respectively. The mean number of lost teeth was 7.82 ± 3.54. primarily molars and premolars (mean of 6.75 ± 2.82). Ten patients (35.71%) experienced dental loss after starting zoledronic acid, though this was not significantly correlated with treatment duration (p=0.837).

The mean GOHAI score, indicating perceived oral health problems, was 21.32 ± 7.72 out of 36, with high scores related to dental pain and discomfort (p=0.001). A correlation was found between GOHAI score and both age (p=0.006) and number of lost teeth (p=0.003), but not with smoking, diabetes, or treatment duration (p=0.813, p=0.962 and p=0.415, respectively). Six patients (21.4%) reported limitation in social interaction, smiling and self-consciousness due to dental loss, while 11 (39.3%) reported trouble chewing and swallowing comfortably. Despite the presence of oral health issues, only 11 patients (39.3%) had seen a dentist in the past 6 months, and only 10 (35.7%) had undergone dental cleaning in the past 2 years. Four patients have had dental implants (14.3%).

Conclusion: Oral health problems are prevalent among patients undergoing zoledronic acid therapy and are associated with reduced quality of life. Dental issues are often underreported and underdiagnosed in the context of underlying malignancies. Our survey highlights the need for proactive dental care in cancer patients receiving bisphosphonates. Integrating routine dental evaluations and preventative care into the cancer treatment regimen is essential to mitigate oral health complications and improve overall quality of life.

Safety of CDK4/6 inhibitors combined with tamoxifen in patients with HR-positive/HER2-negative metastatic breast cancer

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Introduction: After relapse or progression on an aromatase inhibitor in HR-positive/HER2-negative metastatic breast cancer without visceral crisis, fulvestrant is usually the endocrine therapy used in combination with CDK4/6 inhibitors. But, as fulvestrant is not always available in Tunisia, we have combined tamoxifen with anti CDK4/6 while awaiting approval of this treatment. The aim of our study was to assess the safety of CDK4/6 inhibitors combined with tamoxifen.

Methods: A monocentric retrospective study was conducted over a period of 2 years between December 2021 and December 2023 at the oncology department of Salah Azaïz Institute. Our study included 15 women with HR-positive/HER2-negative metastatic breast cancer without visceral crisis, eligible for CDK4/6 inhibitors combined with endocrine therapy. All these patients have relapsed on or within 12 months of adjuvant aromatase inhibitor therapy or have progressed on an aromatase inhibitor in the advanced setting. The CDK4/6 inhibitors used were ribociclib or palbociclib.. All data regarding patients were obtained from the medical record.

Results: Fifteen women were included. The median age was 58 years (34-75 years). Three patients had a history of hypertension without a heart failure. Seven patients had visceral metastasis, 5 had bone metastases and 3 had bone and visceral metastasis. Thirteen women had invasive ductal carcinoma, one had invasive lobular carcinoma and the other one had mixed invasive ductal and lobular carcinoma. Six patients relapsed on adjuvant aromatase inhibitor therapy, 6 relapsed within 12 months of adjuvant aromatase inhibitor and 3 progressed on an aromatase inhibitor in the advanced setting. Eight patients received ribociclib and seven received palbociclib combined with tamoxifen. Adverse events during treatment were: Grade 1 or 2 neutropenia in 8 patients, grade 3 neutropenia in 6 patients, grade 3 liver toxicity in one patient and vitiligo in one patient. No QT interval prolongation or thromboembolic events

were observed. Nine patients received tamoxifen combined with CDK4/6 inhibitor during 3 cycles while awaiting approval of fulvestrant. The six other patients did not receive fulvestrant and have continued tamoxifen combined with cdk4/6 inhibitor. Median follow-up time was 12 months. The median PFS was 8,5 months. Seven patients had partial response, one had complete response, 5 had stable disease and 2 patients had progressive disease.
Conclusion: The combination of tamoxifen with CDK4/6 inhibitors in case of non-availability of fulvestrant showed manageable adverse effects with no cardiac events. Nevertheless, cardiac monitoring is necessary, especially when tamoxifen is combined to ribociclib.

Assessing the nutritional status of patients with nasopharyngeal cancer undergoing chemotherapy

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Introduction: Patients with Undifferentiated carcinoma of the nasopharynx (UCNT) are at major risk of malnutrition, during cancer treatment and follow-up. The causes of malnutrition in these patients are multifactorial.
Methods: A descriptive study including 35 patients followed for an UCNT at the medical oncology department of the Salah Azaiez Institute between November 2023 and February 2024. We noted the dietary behaviors as well as the nutritional status of our population.
Results: The median age was 42 years, with sex ratio 2.8. The majority of patients (97.1%) had complications during and after treatment. The most frequent complications were nausea and vomiting (97.1%), asthenia (91.4%) and dysgeusia (91.4%). Loss of taste was observed in 71.4% of patients. A change in sense of smell was noted in 91.4% of the population. The dietary history survey showed a deficit in calorie intake in 82.9% of patients, with an average of 1459.8 kcal/day. The average protein intake was 0.84g/kg/day, which was below WHO recommendations (>1.2g/kg/day). 8.6% of patients were on a carbohydrate-restricted diet (ketogenic diet), 2.9% on a protein-restricted diet, 5.7% on a calorie-restricted diet and 82.9% had not been on any diet.
Micronutrient and fiber deficiencies were noted in 10%, with increased intakes of sodium, vitamin E and selenium. Only 5.9% of patients received oral nutritional supplements. 54.3% consumed ZRIGA-type medicinal plants. 88.6% of patients had a weight loss of 10%. The mean BMI was 23 kg/m2. Sarcopenia was estimated at 57.1%, and calf circumference was < 31 cm in 57.1% of cases. Only 25.7% of patients had received nutritional education. We found significant correlations between undernutrition number of chemotherapy sessions (p=0.047), socio-economic level (p=0.001), physical activity (p=0.030), nutritional advice (p=0.002), alteration of taste (p=0.002), evaluation of food intake (p=0.0001).
Conclusion: Nutritional education by experts is essential to avoid any weight loss that could affect treatment.

Is Fertility Preservation Being Discussed withYoung Cancer Patients?

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Introduction: As cancer treatments develop, increasing survival rates uncover long-term treatment toxicities. Discussing fertility before initiating treatment can improve the patient's and their family's anxiety and cancer .
Methods: We collected data relating to fertility discussion and FP of young patients aged 14 to 39 years with newly diagnosed cancer, excluding breast cancer, treated at the medical oncology department of Farhat Hached University Hospital from January 2019 to April 2024.
Results: We included 105 patients treated for newly diagnosed cancer at a median age of 32 years old. Young adults aged 18 or more represent 98.1%. There were 52.4% females: 47.5% were married with a mean number of living children of 1.9/parent and 19.6% of married patients had no children. Primary diagnosis was digestive cancer (32.4%) followed by head (1)and neck malignancies (17.1%). Treatment with curative intent was indicated in 61%. All patients presenting early-stage urogenital malignancies were offered fertility-sparing surgery. Gonadal toxicity and potential hypo-fertility was discussed with 24.8% of patients, and fertility preservation (FP) was accepted by 66.7% of them. Refusal of FP was mainly the patient's choice; 41.7% having had at least one child of either genders. Other patients didn't go through with the procedure out of lack of funding (16.7%; all female) and because of the COVID pandemic (8.3%).
The reasons for oncologists not offering FP in the first place were palliative intent (52.6%), patient's age (22.4%), low-risk of gonadal toxicity (10.5%), potential delay in treatment initiation (10.5%), prior hysterectomy (2.6%) and HIV positive status (1.3%). FP was more likely to be offered to patients aged <31 (p=0.023), treated with curative intent (p<0.0001).
Gender, marital status, presence of children and low-risk treatment didn't seem to influence the decision (p=0.236, p=0.273, p=0.47 and p=0.108, respectively). After discussion and referral for FP, the procedure was carried out more frequently in men than women (73.4% vs. 25%%; p=0.013).
Conclusion: While progress has been made in integrating FP into oncological care, barriers such as financial constraints persist and more effort should be provided to ensure equitable access to FP.

Genetic Profiling of Tunisian Ovarian Cancer Patients: Targeted NGS Analysis of BRCA, TP53, and CancerRelated Genes

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Introduction: Ovarian cancer is a leading cause of gynecological cancer-related mortality worldwide, with genetic mutations in genes such as BRCA1, BRCA2, and TP53 playing crucial roles in tumor development. The Tunisian population, with its unique genetic background, has not been extensively studied in this context.

Methods: We conducted a genetic profiling study of 50 Tunisian ovarian cancer patients using targeted next-generation sequencing (NGS). Both formalin-fixed, paraffin-embedded (FFPE) tissue samples and blood samples were sequenced for each patient. The analysis focused on identifying pathogenic mutations in BRCA1, BRCA2, TP53, and other related cancer susceptibility genes.

Results: Several pathogenic mutations were identified, with a significant number occurring in the BRCA1, BRCA2, and TP53 genes.

The study also uncovered novel mutations specific to the Tunisian population, which may contribute to the unique genetic landscape of ovarian cancer in this cohort

This study provides a comprehensive genetic profiling of Tunisian ovarian cancer patients, highlighting the prevalence of pathogenic mutations in key cancer-related genes.

Conclusion: These findings underscore the importance of genetic screening in the management and treatment of ovarian cancer, particularly in populations with unique genetic backgrounds.

Management of Osteosarcoma in the Event of Methotrexate Shortage

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Introduction: The standard treatment of osteosarcoma consists in chemotherapy and surgery. High-dose methotrexate with ifosfamide and etoposide (MTX-IE) is commonly used in the treatment of osteosarcomas but has the inconvenience of high toxicity. An alternative protocol using Doxorubicine/Cisplatine/Ifosfamide (API-AI) is also available . The aim of our study is to compare both protocols in terms of toxicity, histological response and overall survival in our population.

Methods: 56 patients treated between 1986 and 2023 for osteosarcoma in the medical department of Salah Azaiz institut were analyzed. Patients received either MTX-IE or API-AI preoperative chemotherapy regimens. Baseline characteristics were compared between the two treatment groups.

Toxicity and Histological response after surgery was assessed and compared between the two groups using the Pearson Chi-Square test. Survival analysis was performed using the Kaplan-Meier estimator and compared using a log-rank test.

Results: Mean age at diagnosis was 15.37 (9 -24) years with a majority of males (55.8%). Thirty eight patients received MTX-IE protocol and 18 patients received API-AI based chemotherapy. The two groups had similar characteristics.

The majority of patients (96%) had primary tumors located in the limbs. Femur was the most observed location (64.3%). Osteoblastic osteosarcoma was the most frequent histologic subtype (46.4%). Three patients had metastatic disease at baseline. All patients had surgery which was conservative in 75% of the cases. Twelve MTX-IE patients (31.6%) and 10 API-AI patients (55.6%) had a good histological response to preoperative chemotherapy (p=0.08). Median follow up was 18 months (11 – 29.25). Mean overall survival was 38.7 (28 – 49) months for patients treated with MTX-IE and 14.2 (12 – 16) months for patients treated with API-AI (p=0.31).

Conclusion: Histological response and survival outcomes with MTX-IE and API-AI weren't significantly different. However, our study was affected by a poor quality follow-up.

Pronostic role of serum cytokines and plasma Epstein Barr virus DNA loads in patients with nasopharyngeal carcinoma

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Introduction: Nasopharyngeal carcinoma (NPC) is a distinctive head and neck cancer primarily prevalent in east and southeast Asia, with an increasing global incidence. Factors such as Epstein-Barr virus (EBV) infection, environmental influences, genetics, and chronic inflammation contribute to its complex etiology. Chronic inflammation plays a pivotal role in promoting NPC progression, invasion, and metastasis, with key inflammatory cytokines like IL-1, IL-6, IL-8, and TNF implicated in these processes. This study aims to globally assess serum concentrations of these cytokines and investigate their correlations with NPC prognosis. Furthermore, the investigation will delve into the relationship between the presence of EBV DNA and the prognosis of NPC patients. Unraveling these molecular intricacies, including the role of EBV DNA, holds promise for advancing therapeutic strategies and identifying prognostic markers in managing this challenging cancer.

Methods: Serum samples were systematically gathered from a prospective cohort comprising 60 patients with nasopharyngeal carcinoma (NPC) undergoing treatment at the Department of Medical Oncology. The collection intervals included pre-treatment, 7 weeks, 3 months,

and 6 months post-treatment. Quantification of TNF-, IL1beta, IL6, and IL8 levels was conducted through a solid-phase chemiluminescent immunometric assay utilizing the IMMULITE 1000 automated system. Additionally, the detection of Epstein-Barr virus (EBV) DNA was performed using real- time PCR.

Results: In our comprehensive investigation, a discernible correlation was established between peak cytokine levels and the age group ranging from 31 to 40 years. Noteworthy cytokine variations were also identified across distinct stages of the disease, with patients in stages T1-T2 exhibiting heightened levels of IL6 and IL1 beta, while those in advanced stages manifested elevated IL8 levels. Significantly, an affirmative treatment response was observed, marked by an augmentation in cytokine levels by the seventh week post-treatment, indicative of a favorable prognosis. Intriguingly, metastatic patients exhibited a notable escalation in cytokines, including IL8 (P=0.01), IL6 (P=0.001), and TNF alpha (P=0.038), commonly associated with metastatic progression. Furthermore, our scrutiny of Epstein-Barr virus (EBV) DNA unveiled a heightened incidence within the 41-50 age group. Encouragingly, a favorable treatment response was evidenced by a reduction in viral DNA burden seven weeks post-treatment, underlining a positive prognosis. Additionally, the examination of serum levels at three and six months post-treatment disclosed a substantial elevation in EBV load in metastatic patients. Remarkably, we are the first to document a statistically significant correlation between the initial EBV load and the initial levels of TNF alpha (p=0.011), IL1beta (0.011), IL6 (0.011), and IL8 (0.012), providing novel insights into the intricate interplay between EBV infection and cytokine expression in nasopharyngeal carcinoma.

Conclusions: Our study on nasopharyngeal carcinoma unveils age-related cytokine variations, distinct profiles linked to disease stages, and positive treatment responses. Groundbreaking findings establish a significant correlation between initial EBV load and key cytokines. These insights offer promising prognostic indicators and potential for personalized therapeutic approaches in NPC management.

The prognostic role of VISTA/CTLA4/PD1 and TILs in the high grade serous ovarian carcinoma

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Introduction: Studying the interactions of the host immune system with immune checkpoints in the tumor microenvironment (TME) is essential for understanding tumor immunity and developing an effective immunotherapy strategy. Here, we evaluated the expression profile of a panel of immune-regulatory checkpoints (VISTA, CTLA4, PDL1, and PD1), its correlation with TILs (CD3, CD4, CD8, and FOXP3), and its prognostic value in high-grade serous ovarian carcinoma (HGSOC) cohort. Methods: The expression of checkpoints VISTA, CTLA4, PDL1, PD1, and TILs was assessed in 135 HGSOC tissue microarrays by immunohistochemistry (IHC). We analyzed the associations between the checkpoints, TILs, and overall survival (OS). VISTA, CTLA4, PDL1, PD1, CD8, CD4, and FOXP3 mRNA extracted from patients with ovarian cancer in the Cancer Genome Atlas (TCGA) database was included as a validation cohort.

Results: VISTA+/CTLA4+/PD1+ (37.98%) group has the best prognosis when VISTA is expressed on tumor cells. Univariate analysis showed that CD3+ (p=0.01), CD4+ (p<0.001), CD8+ (p<0.001), and FOXP3+ (p=0.001) TILs were correlated with the synergistic expression of these checkpoints. Multivariate analysis proved that CD4+ (58.7%) and CD8+ (56.5%) TILs (p=0.008) remain independent factors for the co-expression of VISTA+/ CTLA4+/PD1+.Furthermore, the gene encoding VISTA was positively associated with the CD4+ encoding gene (p<0.01, R=0.49).

The TME rich with TILs: CD4+, CD8+, FOXP3+, and coexpressed checkpoints VISTA+/ CTLA4+ / PD1+ was correlated with a favorable prognosis in terms of 2 years OS (p=0.04; R=0.4). Conclusion: These data showed that positive VISTA, CTLA4, and PD1 expressions were associated with high density of TILs in HGSOC.

Conclusions: Our data suggest that an increased immune cell infiltration may be insufficient to generate antitumor response and that combined blockade of the immune checkpoints VISTA, CTLA4, and PD1 may be necessary to provide longer OS for patients with HGSOC.

CT-scan based follow up of early breast cancer (BC):good practice or overdiagnosis?

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Introduction: There is no consensus regarding the role of CT-scan during follow up of early- stage BC, in one hand it may lead to early detection of relapse, on the other hand it may cause unnecessary excessive stress to the patient. The aim of this study was to report "non malignant" events discovered on CT-scans during follow-up of BC and to describe their impact on patient's management.

Methods: We conducted a retrospective study of 202 patients treated for early-stage breast cancer between 2011-2017 who had intensive follow up, with at least 3 monthly visits, yearly mammography and yearly CT scan CA15-3. Authors assessed the incidence and described the profile of non-malignant lesions discovered on CT scan. Results: Mean age was 47 years [27-79]. Median follow up was of 7 years with 66% of the patients having a follow up of more than 5 years, non-compliance with missed or delayed surveillance appointments was observed in 12% of cases. Among the 88% remaining patients, the median number of performed CT-scans was 4 [0-11], with an additional initial brain CT scan conducted in 28 % of cases. We observed that 28 % of patients experienced incidental asymptomatic events leading to further investigations: 51% were benign lesions, 44% were primary cancer recurrence and 5% were new cancer diagnoses. Brain CT scans allowed an

early detection of brain metastases in 5%, the diagnosis of cerebral hemangioma in 1 case and meningioma in 1 case. Other benign lesions were nonspecific pulmonary nodules (14%), hepatic lesions (3%), uterine fibroma (3%), non specific enlarged lymph nodes (5%). These lesions lead to additional imaging modalities such as ultrasound, MRI or biopsies for definitive diagnosis which confirmed the benign nature with a final diagnosis of sarcoidosis for one patient and hepatic hemangioma for two patients; other lesions remained under surveillance.

Conclusion: Patient's adherence to intensive follow up containing CT scan was high and allowed a high percentage of relapse diagnosis. However, it also showed a high level of overdiagnosis detecting benign lesions and causing unnecessary investigations and probably increased patients' psychological distress. A tailored follow-up schedule is needed.

Adverse Drug Reactions in Oncology: Insights from theTunisian Pharmacovigilance database

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Introduction: There is an increasing number of cancer patients receiving chemotherapy as a first-line treatment each year. Cancer itself often induces physiological changes, affecting the body's pharmacokinetic processes and altering its sensitivity to various drugs. Furthermore, the introduction of chemotherapeutic agents into a compromised system places patients at an increased risk of additive toxicity, drug-drug interactions, and adverse drug reactions (ADR). The aim of this work was to investigate the profile of side effects associated with chemotherapy.

Methods: We conducted a 12 month research on the database of the pharmacovigilance center of Tunisia from January to December 2023. The inclusion criteria were: -patients aged >=18 -adverse drug reactions related to systemic anti-cancer drugs -drug imputation was retained according to the French method.

Results: 155 patients were included.Females comprised 67.1% of the population (n=104). The median age was 58years (range : 28-79) with 25.7% (n=42) aged 65 years. The majority of notifications (69%) were received from oncologists, followed by pneumologists accounting for 9%, dermatologists for 7.7%, gastrologists for 7.1%, hematologists for 6.5%, and a single case from a neurologist. Most patients were diagnosed with gynecological cancers (43.8%) predominantly breast cancer (34.8%) followed by gastro-intestinal cancers (22.5%), lung cancer (17.9%), hematological malignancies (9.6%), urologic cancers (4.4%) and cavum cancer represented in only one case. The toxicity of chemotherapeutic agents occurred predominantly in the skin in over half of the cases (50.3%), followed by hepatic toxicity (14.2%), neurological toxicity (10.3%), and respiratory toxicity (6.5%). Other affected systems included the cardiovascular system (1.9%) and the digestive system (1.3%). Additionally, there was one case each of hematological, renal, and visual involvement. Causative medications included mainly docetaxel (17.4%), oxaliplatin(12.3%), carboplatin (9.6%), ribociclib (6.5%), imatinib (5.8%), paclitaxel (5.2%) and cisplatin (5.2%).

The most frequently reported ADR were mucocutaneous manifestations associated with taxanes (22.6%), notably docetaxel. Skin eruptions generally manifested within a median of 8 days, with variations ranging from 24 hours to 10 months. The second common ADR were acute infusion reactions to platinum salts (21.7%), with oxaliplatin being the most prevalent. The majority of these reactions were classified as mild or moderate in severity. Four infusions (12%) were associated with severe reactions, characterized by anaphylactic shock with hypotension. Among these cases, carboplatin and oxaliplatin were the administered molecules in two patients each. Infusion reactions occurred with an average onset delay of 18 minutes, ranging from 2 minutes to one hour. Other frequent reactions comprised acute hepatitis (9.6%) or transient elevation of liver enzymes (4.2%), with ribociclib being implicated in half of the cases, followed by trastuzumab(2.5%), gemcitabine, etoposide, and 5-Fluorouracil, each occurring in two cases. Liver injury typically manifested over one month after initiating drug treatment, with occurrences ranging from 3 days to 8 months. Less common ADR included side effects related to tyrosine kinase inhibitors (13.5%), manifested in particular as cutaneous reactions to erlotinib and pleural effusion to imatinib. Moreover, side effects of hormone receptor inhibitors primarily headache and pruritus presented 7.7% of cases and neurotoxicities attributed to platinum salts accounted for 5.4% of cases. More severe reactions were observed in three cases including acute coronary syndrome associated with arsenic, cytarabine-induced paralysis, and optic neuropathy attributed to vincristine. All cases showed a favorable evolution, with no reported fatalities. Within the infusion reactions group, five patients underwent a positive rechallenge upon drug reintroduction, despite having received premedication with corticosteroids and antihistamines. The majority of these patients experienced one to three additional infusion reactions, all of which were mild.

Conclusion: In this study, we provide a brief overview of the various side effects associated with chemotherapy reported to the Tunisian pharmacovigilance center over a one-year period. Patients with cancer have high levels of multimorbidity and polymedication, which require vigilance for related adverse effects.

Dihydropyrimidine dehydrogenase pharmacogenetics: A brief review

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Introduction: Tunisia annually records 20,000 new cancer patients who receive various chemotherapy protocols. 5-fluorouracil (5-FU) remains one of the most prescribed chemotherapeutic drugs for the treatment of numerous malignancies. Dihydropyrimidine dehydrogenase (DPYD)

is a key enzyme in the metabolism of pyrimidine bases, mainly 5-FU. Genetic variation in DPYD is involved in both drug response to 5-FU and related toxicity.

Methods: This work provides a brief overview of the pharmacogenetic findings of DPYD in Tunisia. Databases were identified using PubMed, ScienceDirect and Google Scholar databases. The search strategy was applied, using the following keywords : pharmacogenetics, dihydropyrimidine dehydrogenase, tunisia, 5-fluorouracil, gene.
Results: To the best of our knowledge, only two studies have investigated DPYD pharmacogenetics in the Tunisian population. The first study focused on the distribution of DPYD gene polymorphisms in Tunisia. Ben Fredj et al. identified twelve different variant alleles in their research. Among these, the DPYD*5 allele, not linked to DPD deficiency, exhibited a frequency of 12.7%. The second most prevalent polymorphism in Tunisia was DPYD*9A, occurring at a frequency of 13.7%. Regarding DPYD*6, an allele not associated with deficiency, it was observed with a frequency of 7.1% in our population. The variant A496G (Met166Val) allele was detected at a frequency of 5.7% in our population, with its impact on DPD function being controversial. Allelic frequencies in Tunisia were largely similar to those found in other populations, except for the deficient variant allele DPYD*2A, which was absent in the Tunisian population. Furthermore, the study identified a new intronic polymorphism, IVS 6–29 g>t (intron 6), with allelic frequencies of 4.8% in Tunisia. The authors suggested that this variant might be unique to the Tunisian population and neighboring populations, as it was not observed in Caucasian individuals. The DPYD*9A allele (85T>C, C29R) was found in both heterozygous and homozygous states, indicating its prevalence as a common polymorphism in the Tunisian population. The second study concerns the association of DPYD polymorphisms with 5-FU treatment toxicities in the Tunisian population. In this prospective study by Khalij et al., it was revealed that the polymorphisms 496A>G were significantly associated with hepatotoxicity. Additionally, DPYD*9A showed a significant association with mucositis and neurotoxicity.
Conclusion: Very limited number of studies on 5-fluorouracil have been identified in Tunisia. Screening for DPYD deficiency holds promise in averting severe and potentially fatal toxicities in cancer patients undergoing 5-FU treatment. Further investigation is warranted to clarify the impact of genetic variations on drug response and to broaden our understanding in this field.

Gastric cancer in young patients under the age of 45 years old: A comparative study with older patients

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Introduction: Over the last decade the incidence rate of gastric cancer in young patients has a trend towards a gradual increase. This retrospective comparative study aims to identify clinico-pathological characteristics of young patients with gastric cancer.
Methods: Patients diagnosed with gastric cancer at our department between 2016 and 2020 were identified and divided into two groups: the group of the young patients who are under the age of 45 years old (A group) and the group of old patients who are over this age limit (B group).
Results: A total of 37 patients were studied.11 patients (29.7%) were younger than 45 years. Preserved general status was more common in A group (72.7% had a 0-1PS vs 61.5%, p= 0.5). Proximal tumors were respectively seen in 72.7% and 80.7% p=0.6. Linitis was more frequent in B group (3.84% VS 0%, p=0.6). Signet ring cell adenocarcinoma was more common in A group (90.9% versus 30.7%, p=0.001). Adenosquamous carcinomas and well differentiated tumors were more commun in older patients (69.2%% VS 9%; p=0.001). Synchronous metastases were more frequent in young patients (54.4% vs 46.15%, p=0.6). Young patients had less curative surgery than old ones (respectively 45.4% vs 57.5%, p=0.3). Advanced stages after surgery were more common in A group: pT 3-4 stages (36.3% vs 23.07%; p=0.6) They also had a higher positive lymph nodes ratio (36.3% vs 26.1%; p=0.05). 73% of the patients received chemotherapy: DCF was the preferred neo adjuvant chemotherapy regimen in B group (34.6%) whereas only 9% had neoadjuvant chemotherapy in A group (p=0.1). More Complete radiological responses were seen in older patients than younger (42.3%,18.1%; p=0.4). Similar proportion of young and old patients received first line palliative chemotherapy (respectively: 45.4% vs 45.2%p=0.3) ,A higher proportion of young ones received a second line treatment (40% vs 30%; p=0.5). EOX was the most commonly used protocol in the first line in the two groups (60%, p=0.3). Higher proportion of radiologic progression was noted in young patients after first and second line palliative chemotherapy (100% vs 66.6%; p=0.5)Toxicity related to chemotherapy was less in young patients (27.2% VS 34.61% , p=0.1).
Conclusion: Young patients with gastric cancer seemed to have more aggressive tumors: more signet cell adenocarcinoma subtype, metastases at diagnosis, and advanced pTN stages. More aggressive treatments should be recommended for this group of patients.

Innovative Therapies in Metastatic HER2-Positive Breast Cancer

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Introduction: HER2-positive breast cancer, affecting 15-20% of patients, is associated with a poor prognosis due to a high risk of metastasis. Although targeted therapies such as Trastuzumab-Pertuzumab (T-P), TDM1, and TDXd have improved the prognosis, access to these therapies remains limited in Tunisia.
This study evaluates the efficacy and tolerability of Trastuzumab-Pertuzumab,TDM1, TDXd, and Tucatinib

in treating metastatic HER2-positive breast cancer in a Tunisian cohort.

Method: We performed a retrospective analysis of 50 patients with metastatic HER2-positive breast cancer, treated between 2011 and 2023 at the medical oncology department of Abderrahmane Mami Hospital. We assessed therapeutic response, progression-free survival (PFS), overall survival (OS), and response rates at three months, alongside treatment tolerability.

Results: First line TP (31 patients) achieved a 93.5% response rate with a median PFS of 10 months. PFS varied with associated chemotherapy: 15 months with taxanes (23 patients), 3 months with vinorelbine (4 patients), 24 months with capecitabine (3 patients), and 9 months with hormone therapy (1 patient). Second line TDM1 (12 patients) demonstrated a 100% response rate at three months and was well-tolerated. On the third line setting, TDXd (4 patients) showed promising efficacy with minimal adverse effects. Tucatinib (2 patients) was used for brain metastases, showing good tolerance but limited data on efficacy. Toxicities were predominantly grade 1 or 2, with rare occurrences of neutropenia and cardiac issues with T-P.

Conclusion: TP, TDM1, Tucatinib and TDXd, and are effective and well-tolerated options for metastatic HER2-positive breast cancer. The study highlights their significant impact on patient outcomes with tolerable toxicity and underscores the need for improved access to these therapies.

Accuracy of Breast Imaging in Inflammatory Breast Cancer

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Introduction: Inflammatory breast cancer (IBC) is a rare but highly aggressive form of breast cancer, accounting for 1-10% of all cases. IBC is known for its rapid progression, with frequent distant metastases at diagnosis. While the diagnosis is primarily clinical, accurate locoregional radiological staging plays a critical role in guiding effective treatment planning.

Methods: This retrospective study analyzed the records of patients with metastatic and non-metastatic IBC treated at the Salah Azaiz Institute between 2010 and 2016. Imaging data from mammography and ultrasound were compared with clinical examination.

Results: A total of 79 patients were included in the study. Among these, 72% were classified as stage IIIB, 11% as stage IIIC, and 17% as stage IV. Histologically, 95% of cases were invasive ductal carcinoma, 4% invasive lobular carcinoma, and 1% carcinosarcoma. Of the patients, 70 underwent mammography and 63 had ultrasound. For skin thickening, the sensitivity of
mammography and ultrasound was 69% and 58%, respectively. For increased tissue density or echogenicity, mammography demonstrated 71% sensitivity, while ultrasound showed 75%.
A palpable mass was identified on clinical examination in 90% of cases, while it was detected by ultrasound in 70%, and by mammography as an opacity in only 58% of cases. In terms of ACR classification, 94% of the mammography were rated ACR 4/5, 5% ACR 3, and 1% ACR 0.

Conclusion: Conventional imaging with mammography and ultrasound is standard for all patients with IBC, but our findings suggest that adding breast MRI could enhance locoregional staging and improve diagnostic accuracy.

Non-metastatic colon adenocarcinoma: Clinico-pathological prognostic factors

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Introduction: Colon cancer is a major cause of morbidity and mortality worldwide. Its prognosis depends on several epidemiological, clinical, and especially histological factors that influence its progression and treatment plan. The aim of our study was to evaluate the impact of various histo prognostic factors on survival and recurrence in a population of patients with non-metastatic colon adenocarcinoma.

Methods: This was a retrospective study of patients with colon adenocarcinoma, operated at the Salah Azaiez Institute over a period of 10-year (2010-2020). We analyzed clinical, pathological, and outcome data of our patients, as well as the different factors related to overall survival and event-free survival.

Results: The study included 30 patients with an average age of 60 years. Cancer was discovered in an emergency context in three cases. Histopathological examination of surgical specimens identified synchronous colonic tumors in two patients, colorectal NOS adenocarcinoma in 24 cases, mucinous adenocarcinoma in nine cases, perineural invasion in three cases, vascular emboli in six cases, and tumor budding in two cases. The majority histological grade was low grade in 29 cases. MSS status was present in seven cases and MSI status in three cases. Thirteen patients were at stage II and sixteen patients at stage III. Twenty-three patients received adjuvant chemotherapy. The 5-year overall survival rate was 59%. Factors influencing overall survival included surgical circumstances, postoperative outcomes, lymph node involvement, histological grade, and tumor recurrences. Multivariate analysis retained two factors: surgical circumstances and tumor recurrences. The 5-year event-free survival rate was 72.4%. Factors influencing recurrence included the presence of an abdominal mass and deep tumor invasion.

Conclusion: The management of colon cancer relies on a therapeutic strategy based on prognostic factors, primarily pathological ones. New molecular approaches, such as MSI/MSS status, have allowed for better management codification.

Closing remarks

Selma Gadria

Chirurgien Oncologue
Secrétaire générale de l'association Nourane

We want to extend our deepest gratitude to all of you for your presence, engagement, and the invaluable contributions each of you has made. Over these past two days, we have shared groundbreaking research, inspiring stories, and new innovations that will shape the future of oncology. Together, we have strengthened our resolve in the fight against cancer.

Next year, we have another very special event: ICCO25, which will bring together senior and junior, Tunisian and African oncologists, in collaboration with the Institut Gustave Roussy, to create the first African congress dedicated to the latest innovations in oncology. It will be a unique opportunity to share even more groundbreaking advancements and strengthen scientific collaboration between Africa and the rest of the world.

I would like to take a moment to thank our sponsors, who believe in us, who believe in NOURANE, and whose generous support has made this event possible.

Additionally, I want to express my sincere appreciation to the organizing committee, professor Chouaib, professor Jerbi, Mouna from Addvalue and all the Nourane Team, whose tireless efforts and meticulous planning have ensured the success of this conference. Without your dedication, none of this would have been possible.

As we return to our respective fields, I hope that the connections and insights gained here will continue to drive us forward, propelling us toward the shared goal of a world where cancer is no longer a devastating diagnosis.

Once again, thank you all for your dedication and passion. I look forward to seeing how each of us will continue to contribute to this critical mission. Dear Tunisian, let's meet the 3rd of November for NOURANE marathon, dear internationals, Safe travels, and until we meet again next year."