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OC1-COMPLETION SURGERY AFTER CHEMO-RADIOTHERAPY IN LOCALLY ADVANCED CERVICAL CANCER

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Introduction: Cervical cancer is usually diagnosed at advanced stages in tunisia. The standard treatment is concomitant radiochemotherapy followed by brachytherapy. The place of surgery is widely debated in the literature. The purpose of this work was to define the effect of completion surgery after complete clinical response.

Methods: We Performed A Retrospective Study Of All Patients Treated At The Salah Azaiez Institute For Locally Advanced Cervical Cancer (IB2-IVA) Between January 1, 2000 And December 31, 2014.

Results: Two Hundred And Ninety-Two Patients Were Included. The Median Age Was 51 Years Old. The FIGO IIB Stage Was The Most Frequent (N = 172, 58.9%). All Our Patients Had External Radiotherapy. Concomitant Chemotherapy Was Delivered In 248 Patients (84.9%). Brachytherapy Was Administered To 234 Patients (80.1%). The Average Dose Delivered Was 58.17 Gy. One Hundred Eighty Two Patients (62.3%) Were Operated. A Case Of Urinary Fistula And A Case Of Digestive Fistula Have Been Reported. One Hundred And Sixty-Three Patients (55.8%) Were Classified In Complete Clinical Response, Of Whom 93 (57.1%) Had Completion Surgery. Completion Surgery Improved Recurrence-Free Survival (69.1% Vs. 47.5%, P=0.008) And Overall Survival At 5 Years (69.3% Vs. 49.4%, P = 0.008). In That Case Only 31.5% Of The Patients Had A Tumor Residue On A Hysterectomy Specimen. A Predictive Nomogram Of Complete Histological Response Was Developed And Validated Internally (Concordance Index At 0.776) And Externally (Concordance Index At 0.653).

Conclusion: Although completion surgery improved recurrence-free survival and overall survival with low morbidity, only one third of the operated patients had tumor residue on surgical specimen. The use of the predictive nomogram could improve the selection of the best candidates for surveillance after radiotherapy.

OC2-PACLITAXEL PLUS CISPLATIN VERSUS PACLITAXEL PLUS CARBOPLATIN IN THE TREATMENT OF RECURRENT AND METASTATIC CERVICAL CANCER; EXPERIENCE OF THE DEPARTMENT OF MEDICAL ONCOLOGY OF HASSAN II UNIVERSITY HOSPITAL OF FEZ.

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Introduction: The prognosis of patients with recurrent or metastatic cervical cancer is poor. Survival at one year usually varies between 15 and 20%. The standard treatment in the first line is based on platinum regime combinations. The aim of our work is to evaluate and compare the clinical benefits of platinum-based chemotherapy (cisplatin vs. carboplatin) as a first-line treatment for recurrent or metastatic cervical cancer.

Methods: During the period of January 2010 and December 2017, a series of 130 patients were admitted to our department of Medical oncology of Hassan II University Hospital of Fez; for the treatment of recurrent or metastatic cervical cancer. The clinical, therapeutic and prognostic data of these patients were collected. Overall survival was calculated according to Kaplan-Meier. The comparison of the survival curves was done according to the Log-Rank test.

Results: The average age was 53.8 years (+/- 11.351). 70% had received concurrent concomitant chemotherapy with cisplatin. The time to relapse of her last was 16.5 months on average. In the first line 38% received CDDP plus paclitaxel and 62% received carboplatin paclitaxel. A better tolerance was observed under the carboplatin-based doublet: less nephrotoxicity (1% vs 25%) and less grade 3-4 neutropenia (46% vs 75%). However, the objective response rate was better in the cisplatin group with 37% vs 25% partial response. The disease was stable in 65% for patients treated with cisplatin versus 60% for the carboplatin group. Overall survival was 12.87 months for the CDDP group and 9 months for the carboplatin group (p = 0.036). Subgroup analysis showed a particular survival benefit in patients who did not receive prior concomitant chemotherapy with radiotherapy; it was 14.57 months for patients treated with cisplatin versus 6.66 months for the carboplatin group (p = 0.069).

Conclusion: The results of our study are in line with literature stressing that cisplatin remains the main treatment for naive treatment patients. The carboplatin paclitaxel combination is an alternative to treatment of metastatic or recurrent cervical cancer with a better tolerance profile.

OC3-MENDELIAN AND POLYGENIC INHERITANCE OF BREAST CANCER AMONG TUNISIAN CASES

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Introduction: Breast cancer genetic risk differs considerably due to different genetic and non genetic modifier factors. So far, the major part of breast cancer genetic component (80%) is unexplained in North African populations. Whole Exome Sequencing (WES) represents an appropriate technology that can be used to investigate the genetic make-up of underexploited populations and to identify the breast cancer missing heritability.

Methods: We perform WES using the Illumina technology. Variants were prioritized based on frequency, functional effects and gene VarElect score matched with breast cancer disorder. Selected high risk variants were confirmed and co-segregation analysis was performed using Sanger sequencing.

Results: In F1.1 case, we identified a pathogenic frame-shift loss of function variant in BRCA2: c.3847_3848delGT; p.Val1283Lysfs, in F1.1 case that co-segregate with ano ther rare variant, on the APC gene (c.3920T>A (p.Ile1307Lys) rs1801155, which clinical significance is conflicting and classified as a risk factor for familial cancer syndrome. In F2.2, no pathogenic variant has been found in BRCA genes in F2.2 case. However, a rare none sense variant in BRCA2, rs11571833, c.9976A>T:p.K3326X, described as a low penetrate variant associated with breast cancer but considered as benign in ClinVar, as well as 9 additional low penetrate alleles in different genes known to increase breast cancer risk. In addition, we identified a pathogenic rare variant in OGG1, c.137G>A:p.Arg46Gln. This later co-segregate with the variant Lys3326X in BRCA2 only in the breast cancer affected cases of F2 family.

Conclusion: We identified for the first time in the North African region, two rare low and high penetrance BRCA2 variants associated with two rare putat ive pathogenic variants in genes that encode for key proteins in DNA repair pathway. The Mendelian and polygenic inheritance are well illustrated in our two cases, however, other large studies should be considered to confirm the role and the interaction between these rare coding variants and breast cancer genetic etiology.

OC4-INDUCTION VS ADJUVANT CHEMOTHERAPY IN LOCALLY ADVANCED NASOPHARYNGEAL CARCINOMA (NPC): DO WE REALLY NEED TO INTEGRATE SYSTEMIC TREATMENT?

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Introduction: Concurrent chemo-radiotherapy (CCRTH) has proven to be the cornerstone in the treatment of locally advanced Nasopharyngeal carcinomas (NPC) and neither induction (I) nor adjuvant (A) chemotherapy has shown any impact on survival. This is a retrospective study comparing different chemotherapeutic schedules in treating patients with locally advanced NPC.

Methods: Between the period of Jan. 2010 & Dec. 2014, 136 patients of locally advanced NPC presented to Kasr El Einy Center of Clinical Oncology. Patients were clustered into 5 treatment arms; Arm 1: CCRTH, Arm 2: CCRTH+A, Arm 3: I+CCRTH, Arm 4: I+CCRTH+A, or Arm 5: RTH. Arm 1 was considered as the control arm. The number of patients in Arm 1, 2, 3, 4 & 5 were 28, 12, 68, 8 & 20 respectively. The dose prescribed was 70Gy/35F/7weeks (2Gy/fraction), 91 patients were treated by conformal radiotherapy (3D-CRT) while 45 patients received intensity modulated radiation therapy (IMRT). As for the concomitant chemotherapy, patients received Cisplatin 40 mg/m^2 intravenous on a weekly basis. For the adjuvant and induction chemotherapy, patients received Cisplatin & 5-Flourouracil based regimens.

Results: The median follow up period was 47.8 months. The ORR was 60.7 % for Arm 1 compared to 66.67 % in Arm 2, 73.5 % in Arm 3, 50% in Arm 4 and 40% in Arm 5. All arms were not statistically significant except for arm 5, which was significantly inferior to control arm 1 at a P-value of 0.045. The Median PFS for Arm 1 was 62% compared to Arm 2 at 51%, Arm 3 at 63%, Arm 4 at 50% and in Arm 5 at 45%. All arms were not statistically significant except for arm 5, which was significantly inferior to control arm 1 at a P-value of 0.048. The Median OS for Arm 1 was 73% compared to 66% for Arm 2, 80.5% for Arm 3, 58% for Arm 4 and 52.4% for Arm 5. None of the numerical OS differences were statistically significant versus the control arm.

Conclusions: Although arm 3(I+CCRTH) showed the highest numerical survival values yet this was not translated to statistically significant benefit. Arm 5 (RTH only) showed the lowest survival results which is supported by a lot of historical data. These results are to be interpreted with caution given the known limitations of observational retrospective studies. Further prospective

randomized studies are warranted.

Key words: Nasopharyngeal cancer, Concomitant Chemo-radiotherapy, Adjuvant, Induction.

OC5-FIRST LINE CHEMOTHERAPY FOR LUMINAL ADVANCED BREAST CANCER: IS IT EFFECTIVE?

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Introduction: The aim of our study is to assess the efficacy of chemotherapy used as first line treatment for ABC, and to identify clinical, histological and IHC markers linked to objective response.

Methods: That was a retrospective study of 46 cases of luminal ABC, without over-expression of Her-2, treated with first line chemotherapy including anthracyclines and taxanes. Age, menopausal status, clinical, histological, IHC data were recorded. Objective clinico-radiologic response and pathologic response was assessed, and then analyzed according the cited parameters.

Results: Baseline characteristics are summarized in Table1. The median age was 49.4 (30-70) with 47.8% pre-menopausal women. The dominant histology was IDC (69.5%) of intermediate grade (78.2%). Both ER and PR were expressed in 93.4% of cases, with high proliferative index (Ki67>20%) in 39.5%. Stage IV disease represented 32.6%, mainly exclusive bone metastases in 73.3%. All patients received an anthracyclines-taxane containing regimen, sequential in most of cases (58.7%). Response evaluation found 68.8 objective response rate (ORR) with 4.4% complete response. Thirty-three patients underwent modified radical mastectomy, with 18.1% pathological complete response, and up to 75.7% intermediate and bad response.

Two patients experienced loco-regional recurrence in the LABC group, and 8 (53.3%) of the MBC group needed second line treatment, mainly chemotherapy (75%). One patient of the same group died during first line therapy, and 14 (93.3%) presented SD and received maintenance endocrine therapy, of which 4 (28.5%) progressed immediately at the first evaluation and required reintroduction of chemotherapy.

Analysis of Objective response sub-group found superior rate in young women less than 35 years (100 vs 62.5%), pre-menopausal (77.2 vs 62.5%), without PR expression (100 vs 72%), and if level of ER or PR are low <50% (90.9 vs 58.9% and 88.2 vs 61.5% respectively), and if Ki67 is high >20 (75 vs 56.5%). According to those later parameters, response differs between luminal A and luminal B sub-groups (53.3 vs 75%). TNM stage IV is less responsive than stage III (33.3 vs 83.8%), but IIIB is more responsive than IIIA (92.8 vs 76.4%).

Pathological complete response was more frequent in young women (25 vs 17.2%), pre-menopausal (25 vs 11.7%), without expression of PR (66.6 vs 13.3%), or if level of HR is low <50% (42.8 vs 8% and 21.4 vs 6.25%, for ER and PR respectively). pCR rate differs widely according to molecular sub-groups (9 vs 26.3% for luminal A and B respectively), and TNM stage.

Table 1. Baseline characteristics:

	N (%)
Age : Med. 49.4 (30-70)	
≤35	5 (10.8)
36-45	15 (32.6)
46-55	14 (30.4)
56-65	11 (23.9)
>65	1 (2.1)
Menopausal status	
(+)	22 (47.8)
(-)	24 (22.2)
Stage	
IIIA	17 (36.9)
IIIB	14 (30.4)
IV	15 (32.6)
T2	4 (8.6)
3	23 (50)
4a-c	16 (34.7)
4d	3 (6.5)
N0	3 (6.5)
1	37 (80.4)
2	2 (4.2)
Histology	
IDC	32 (69.5)
ILC	9 (19.5)
Other	5 (10.8)
SBR I	1 (2.1)
SBR II	36 (78.2)
SBR III	3 (6.5)
SBR NA	6 (13.3)
IHC	
ER+PR+	43 (93.4)
ER+PR-	3 (6.5)
ER-PR+	13 (30.2)
Ki67	5 (11.6)
<14	17 (39.5)
14-20	11 (25.5)
>20	
NA	
Molecular group	
Lum A	15 (32.6)
Lum B	28 (60.8)
Lum	3

Conclusion: Response seems to be heterogeneous when using chemotherapy as first line treatment for luminal ABC. It's recommended to use endocrine therapy when rapid response is needed (as in case of organ crisis), or when hormone-dependence is considered not absolute (as in case of primary endocrine-resistance).

Many other parameters systematically evaluated in routine practice, seems interesting to refine our choice for a more rational and effective use of chemotherapy, when ET may be less attractive: in young woman, pre-menopausal, with luminal B disease (High Ki67,

negative/low PR), especially when ER expression is moderate.

OC6-ANDROGEN RECEPTOR EXPRESSION IN ESTROGEN RECEPTOR NEGATIVE BREAST CANCER

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Introduction: Growth of breast cancer is hormone-dependent. Estrogen and progesterone play a fundamental role in the pathogenesis and treatment of patients with estrogen receptor and Progesterone receptor positive breast cancer patients. Patients who lack the expression of these receptors get no benefit from hormonal treatment and are considered of poor prognosis. Androgen receptor is a member of nuclear steroid receptors with ambiguous role in breast cancer patients. There is growing evidence about its prognostic and predictive value in breast cancer patientsThe purpose of the present study was to analyze the expression of Androgen receptor in paraffin-fixed tissues in a subset of patients from Menoufia university hospital with predominantly Esttogen receptor negative tumors and to correlate Androgen receptor expression with other prognostic variables as well as clinical and pathologic data.
Methods: This study included 56 patients with pathologically proven invasive breast cancer and negatively expressing Estrogen receptor. Immunohistochemical study was done to evaluate the expression of androgen receptor on paraffin embedded formalin-fixed tissue, semi-quantitative H-score like method that details the percentage of cells showing no, weak, moderate or strong staining. The score is given as the sum of the percent staining multiplied by an ordinal value corresponding to the intensity level the resulting score ranges from zero (no staining in the tumor) to 300 (diffuse strong staining of the tumor). An Immunohistochemical score >10 was considered a positive. Data were collected regarding clinicopathological characteristics, treatment modalities, and survival analysis including progression-free survival and overall survival.
Results: Androgen receptor was expressed in 34% of patients and was correlated with advanced axillary nodal involvement and Human epidermal growth factor receptor over expression. It has poor impact on overall survival in patients with triple negative breast cancer and good impact on patients with estrogenreceptor negative Human epidermal growth factor receptor positive disease.
Conclusion: Androgen Receptor is a possible prognostic factor in breast cancer. Patients with triple negative breast cancer could be classified into androgen receptor negative and androgen receptor positive disease.

OC7-EPIDEMIOLOGICAL AND CLINICOPATHOLOGICAL CHARACTERISTICS OF PATIENTS WITH T1 BREAST CANCER : A RETROSPECTIVE TUNISIAN STUDY

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Introduction: The aim of our study is to analyse epidemiological and clinico-pathological characteristics of patients with T1 breast cancer in the Tunisian population.
Methods: We retrospectively studied 334 women with T1 M0 breast cancer treated between 1994 -2010 in the department of medical oncology in Salah Azaiz Institute in Tunisia.
Results: The mean age was 49 years [23-84].Twelve percent of patients had a family history of breast cancer. Forty –six percent of patients were post menopausal and 13.1 % were nulliparous .Obesity was reported in 18% of patients. The most common cause of consultation was breast nodule (95%) with a mean tumor size of 16 mm [5 -20]. Primary tumors were mostly in T1c at diagnosis (80.8%). Palpable lymph nodes were reported in 120 cases (35.9 %). Invasive ductal carcinoma was the most common histological type (94%). The Scarff-Bloom-Richardson (SBR) grading was mostly II (51.3%). Lymph node involvement was reported in 32.2% of patients. The immunohistochemistry analysis showed that 68% of the tumors were classified as ER-positive and 64 % as PR-positive. HER2/neu gene amplification status was determined in 115 cases and was positive in 12 cases. Ki67 was determined in 10 cases. Seventy four percent of patients underwent conservative breast surgery and 26 % modified radical mastectomy. Chemotherapy, radiation therapy and endocrine therapy were received by 62%, 88% and 71 % of the patients ,respectively .Eight patients received Trastuzumab.
Conclusion: Epidemiological and clinicopathological characteristics of T1 breast cancer in Tunisia were consistent with literature.

OC8-RENAL AND NEUROLOGICAL TOXICITY PROFILE OF PLATINUM SALTS.

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Introduction: The toxicity of platinum salts is a factor that can hinder the proper use of treatment, and put at risk the vital prognosis of patients including renal toxicity, and neurological.
Given the limitations of the literature on the toxicity of platinum complexes, and the lack of this type of national clinical research, we have taken this initiative to describe the profile of the renal and neurological toxicity of platinum salts in the Algerian population.

The purpose of the study is to describe and evaluate the renal and neurological toxicity profile of platinum salts (cisplatin, carboplatin, and oxaliplatin), both biologically and clinically.

Methods: This is a prospective descriptive study, which was conducted at the medical oncology department Blida University, patients January 2, 2017, and continued inclusion until May 2, 2017. This study included chemotherapy patients receiving one of the 3 platinum salt molecules. The evaluation of different grades of toxicity was made based on the WHO toxicity rating table. The renal function is evaluated by two different formulas according to the characteristics of the patient: Cockcroft & Gault Formula and Formula MDRD (Modification of the Dite in Renal Disease).

Results: We included 72 patients of which 40 patients are evaluable. The average age is 53.26 (±14.12) years with a median of 53 years and extremes ranging from 14 to 75 years, with percentages respectively of 27.80% and 26.40% with predominant use of carboplatin. More than half of the patients received carboplatin, while cisplatin and oxaliplatin were used in (23.6%) and (20.8%) cases, respectively. According to platinum salts, the lungs and head and neck are the most common sites (25%) with predominant use of carboplatin for the lung, and cisplatin for head and neck. In third place is gastrointestinal and colorectal cancers with percentages respectively of (16.67%) and (12.5%).Patients diagnosed at the late stage (III and IV) represent 81.94% of cases with preferential use of carboplatin. The remainder is distributed between stages I and II, with respective percentages of 1.39% and 16.67%.In our study, all patients received the first course of treatment and more than half received 4 complete courses. 94.4% of patients received at least 2 treatments and 68.1% received at least 3 treatments. The evaluation of the toxicity of the patients concerned only in the 40 patients who received 4 complete courses with 4 biological balances and 3 clinical evaluations, and this in order to better evaluate the cumulated dose toxicity.

The average values of creatinine clearance are in the standards for the platinum salt class. The depth of the decrease in clearance is more marked with cisplatin with a drop of 16%, but this decrease remains within the tolerated range allowing its use. On the other hand, this decrease is less marked with carboplatin and oxaliplatin. The frequency of neuropathic pain encountered during treatment is more than 50% .all molecules combined and ototoxicity is 20%.

Conclusion : The rate of decline in renal clearance was greater in patients treated with cisplatin (16%) than with carboplatin (7%) and oxaliplatin (7%). This is probably related to the selection of patients treated with cisplatin who must have a clearance (> 100 ml / min), but a lower clearance is tolerated when treated with carboplatin and oxalipaltine (> 60 ml / min). The ototoxicity analysis did not show a difference in toxicity between platinum salts, compared to theoretical data, or the ototoxicity was more marked with cisplatin. In our study the incidence is lower than that described in the literature with only 9% of which 3% of grade III or IV toxicity for cisplatin.

OC9-APOPTOTIC AND ANTI-APOPTOTIC ACTIVITY IN LIBYAN COLON CANCER

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Introduction: We studied the association of the immunohistochemical bcl-2 expression in Libyan colon cancer with clinicopathological variables and patient outcome.

Methods: Histological samples from 77 patients of colon cancer were retrospectively studied by quantifying the Bcl-2 IHC staining and were expressed as Bcl-2 index. Then they compared with different clinicopathological features, and patient's survival.

Results: Positive expression of bcl-2 was found in 57 %. The bcl-2 expression was significantly associated with lowering of apoptotic index (p=0.04), small tumor size ((p<0.04), and early stages (p=0.04), and low risk of metastasis (p<0.06).Positive expression was also associated with low risk of metastasis particularly in older patients. Histological subtypes, axillary lymph nodes involvement and tumor location of colon cancer did not have significant relationship with bcl-2. Patients with positive expression of bcl-2 had lower recurrence and metastatic rate than bcl-2-negative patients.

High bcl-2 expression was invers correlated with apoptotic index and it was also correlated with a better survival rate after median follow-up of 36 months.

Conclusions: Patients with positive expression of bcl-2 were associated with low progressive of malignancy, with lower recurrence rate, and with longer survival time. Thus, it could be used with classical clinicopathological factors to separate the patients into good and poor prognosis groups.

Key words: bcl-2 expression, Libyan colon cancer, Prognosis, survival, clinicopathological features.

OC10-CLINICAL IMPLICATION OF PDL1 EXPRESSION AND TILS IN MALE BREAST CANCER: MORE HYPE OR NEW HOPE? RESULTS FROM THE UMBREAC TRIAL (NCT03240510)

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Introduction: Whether PDL1 or TILs have any indication for prognosis in male breast cancer (MBC) patients remains unknown. In this study, we investigated the relationship between the expression and degree of PDL1 and TILs and evaluated the prognostic value of these factors in MBC.
Methods: We retrospectively identified 130 MBC patients diagnosed between 2003 and 2013 at Salah Azaïz Cancer Institute. PDL1, Stromal (str) CD8+ and CD4+ TILs were evaluated immunohistochemically. TILs levels were evaluated following 2014 International TILs Working Group guidelines.
Results: Fifty three percent of MBC patients had low str-TILs and 47% had moderate str-TILs. No lymphocyte predominant breast cancer was identified. Only 12% of MBC patients had high str-CD8+TILs and 11% had high str-CD4+TILs. TNBC and HER2 subtypes had higher median levels of str-TILs. On univariate analysis, higher levels of str-CD8+TILs, str-CD4+ TILs and str-TILs were associated with better OS (p=0.035, p=0.043 and p=0.040 respectively). Multivariate analysis identified str-CD8+ TILs and str-TILs as independent prognostic factors for OS ([HR= 0.851 (0.706-0.997), p=0.000] and [HR= 0.69 (0.43-0.96), p=0.045] respectively). High expression of PD-L1 was observed in 64.5% of MBC samples. Patients with high PD-L1 expression had significantly shorter OS than patients with low expression (p=0.002, hazard ratio HR = 5 [2.624 –10.642]). Multivariate analysis identified PD-L1 as independent prognostic factor for OS (p<0.001, HR = 0.775 [0.680–0.870]).
Conclusion: PD-L1 expression, Str-CD8+ T cells and str-TILs represent promising novel biomarkers with prognostic significance in MBC. Thus, successful inclusion of these markers in prognostic clinical models is becoming a realistic hope in MBC.