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KRUKENBERG TUMORS: GASTRIC CANCER METASTASIS

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Introduction/Background* Krukenberg tumors (TK) are defined as bilateral ovarian metastases, they are rare and represent 1 to 2% of ovarian tumors. They are secondary to digestive tumors and mainly of gastric origin. Often detected at an advanced stage of the disease, the survival prognosis is poor despite chemotherapy, with or without surgical resection.

Methodology A retrospective study on the files of patients treated, in the Medical Oncology department -Tlemcen Hospital from 2010 to 2020, was realized.

The goal of our work is to determine the ovarian metastases frequency in the course of gastric cancers as well as the clinical and therapeutic characteristics of this secondary location.

Result(s)* Six cases have been reported. The mean age was 52 years [31, 66]. The gastric neoplasia was diagnosed by epigastralgia, deterioration of performance status, vomiting, anorexia and weight loss. The gastric endoscopy exploration revealed antral tumor in five patients and subcardial tumor in one case. The anatomic-pathologic study found a moderately differentiated gastric adenocarcinoma and the signet ring cell carcinoma (3/3).

A total gastrectomy with lymph node dissection was performed in three patients, one of whom was after perioperative chemotherapy.

Ovarian metastases were synchronous in four patients and metachronous in two patients after a free interval of 16 months and 30 months respectively. Ovarian metastases were bilateral and were revealed by abdomino-pelvic CT. Only one patient was operated, a total hysterectomy with bilateral oophorectomy was performed. Three patients received palliative chemotherapy. Only supportive care was offered in two patients.

Conclusion* Krukenberg tumors are rare. The diagnosis is facilitated by pelvic ultrasound performed as part of the assessment of the extension of a cancer of digestive or extra-digestive location. Advances in chemotherapy could improve the prognosis of these tumors, which remains bleak.

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CARBOPLATIN FOLLOWED BY OLAPARIB VERSUS BEVACIZUMAB IN MAINTENANCE THERAPY IN ELDERLY PATIENTS WITH ADVANCED OVARIAN CANCER

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Introduction/Background* *: The poly(ADP-ribose) polymerase inhibitor olaparib has shown antitumor activity in patients with platinum-sensitive, recurrent, high-grade serous ovarian cancer with or without BRCA1 or BRCA2 mutations. The aim of our study was to assess the efficacy and tolerability of Carboplatin in single agent therapy, followed by olaparib maintenance monotherapy, versus maintenance therapy bevacizumab in elderly patients with platinum-sensitive, recurrent, high-grade serous ovarian cancer according to BRCA status.

Methodology In our retrospective study, old patients (median age 80) with platinum-sensitive, recurrent, high-grade serous

ovarian cancer received carboplatin (area under the curve [AUC] 4 mg/mL per min, according to the Calvert formula, administered intravenously on day 1) followed by olaparib monotherapy (400 mg capsules twice daily, given continuously) or Bevacizumab 15 mg/kg on day 1 every 21 days until progression. The primary endpoint was progression-free survival.

Result(s)* Between Feb 17 and July 30, 2020, 17 patients were eligible and were assigned to the two treatment groups (5 to the olaparib group and 12 to the bevacizumab group). BRCA mutation status was known for all patients (either at baseline or determined retrospectively): 5 of 17 had a BRCA mutation. Progression-free survival was significantly longer in the olaparib group (median 24.2 months [95% CI 9.7-15.0]) than in the bevacizumab group (median 9.6 months [95% CI 9.1-9.7]) (HR 0.51 [95% CI 0.34-0.77]; p=0.0012), especially in patients with BRCA mutations (HR 0.21 [0.08-0.55]; p=0.0015). Adverse events more commonly reported in the olaparib group than in the placebo group (by more than 10% of patients) were nausea (68% vs. 35%), fatigue (49% vs. 38%), vomiting (32% vs. 14%), and anemia (17% vs. 5%); the majority of adverse events were grade 1 or 2.

Conclusion* *: Carboplatin in monotherapy followed by olaparib in maintenance therapy significantly improved progression-free survival versus bevacizumab plus carboplatin alone, with the greatest clinical benefit in BRCA-mutated patients, elderly patients and had an acceptable and manageable tolerability profile.

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INCIDENCE OF OVARIAN METASTASIS FROM NON-GENITAL TRACT PRIMARY TUMOR SITES

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Introduction/Background* Management of a pelvic mass is a common cause of surgery among women. In nearly 20% of cases, such masses represent primary ovarian malignancies, treated with complete surgical staging. However, in 6-7% of cases, the ovarian malignancy will present as a metastatic lesion from other sites, known as Krukenberg tumors. This term usually characterizes primary gastric cancer, but Krukenberg tumors can also arise from other primary sites. In the present study we assessed the characteristics of metastatic tumors to the ovaries from non-genital tract primary sites and attempted to determine the route of tumor spread.

Methodology We retrospectively reviewed medical records of patients whose indication for surgery was a pelvic mass from January 2000 to December 2018. The study was conducted after approval of the Institutional Review Board. Reports and medical files were reviewed for age at diagnosis, tumor size, laterality of metastasis and primary tumor site. Only patients with metastatic disease to the ovary were included in the study.

Result(s)* A total of 64 cases of metastasis to the ovary were identified. The median age the patients was 58 years old (range: 28 – 81). Primary gastric cancer was identified in 28 (43.9%) cases; breast cancer 14 (21.9%) and colon cancer 13 (20.3%). Pancreatic cancer and urinary bladder each contributed 3 (4.7%) cases, while B-cells lymphoma, primary

peritoneal cancer and lung cancer each recorded 1 (1.5%) case. In most cases bilateral disease was present (43 cases, 67.2%), while surface involvement was recorded in 55 patients (86%). Survival data existed only for a subset of 15 patients with median overall survival of 23.7 months (95% CI 12.7-34.8).

Conclusion* Metastatic ovarian cancer is more usually seen from primary gastric, breast and colon cancer. Hematogenous spread appears a more common route in these cases, rather than transserosal pathway. Despite survival data were limited in a subset of patients, data indicate the presence of long-term survivors. Analysis of larger datasets is warranted to optimize surgical and medical treatment in patients with metastatic disease to the ovary.

918 CORRELATIVE ANALYSES OF PHASE 1B STUDY OF NAVICIXIZUMAB PLUS PACLITAXEL IN PATIENTS WITH PLATINUM RESISTANT OVARIAN CANCER USING XERNA™ TME PANEL

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Introduction/Background* No biomarkers have been established yet to predict response to anti-angiogenic treatment. To test whether the Xerna™ TME Panel, a novel biomarker, is predictive of anti-angiogenic treatment outcome, an exploratory, retrospective analysis of the Phase 1b study of navicixizumab in combination with paclitaxel in platinum resistant ovarian cancer was performed. Navicixizumab is a bispecific anti-angiogenic antibody to vascular endothelial growth factor (VEGF) and delta-like ligand 4. The Xerna™ TME Panel evaluates RNA gene expression data of ~100 genes defining the immune and angiogenic biologies that dominate the tumor microenvironment (TME). This novel diagnostic employs a machine learning model to classify a patient's TME along immune and angiogenic axes, resulting in classification into one of four TME subtypes—Angiogenic (A), Immune Suppressed (IS), Immune Active (IA) and Immune Desert (ID). We hypothesized that patient TME subtypes classified with angiogenic dominant biology (A/IS) are more likely to benefit from treatment with navicixizumab relative to those in the biomarker negative subgroup (IA/ID).

Methodology The Phase 1b study of navicixizumab (3 mg/kg or 4 mg/kg, IV, q2w) in combination with paclitaxel (80 mg/m² IV on D0, D7, and D14 of 28-day cycle) was an open-label, non-randomized study that included 44 patients with platinum-resistant, grade 2/3 ovarian cancer. Patients received a median of 4 prior treatments (63% prior bevacizumab, 45% prior PARP). Pre-treatment tumor tissue was analyzed retrospectively using the Xerna™ TME Panel.

Result(s)* The objective response rate per RECIST 1.1 was 43.2% in the overall patient population (n=44). Responses were durable (median 6 months [95% CI, 5.4 months, not estimable]). Pre-treatment tumor tissue was available for 33 patients. In the B-positive subgroup (A/IS, n=13), 62% of patients had an objective response, compared to 25%, in the B-negative subgroup (IA/ID, n=20). PFS was 9.2 months in the B-positive subgroup vs. 3.9 months in the B-negative subgroup, HR = 0.43 [95% CI 0.188 to 0.999]).

Conclusion* Navicixizumab plus paclitaxel demonstrated promising clinical activity in this heavily pretreated patient population. The Xerna™ TME Panel may identify patients more likely to benefit from treatment with navicixizumab and should be prospectively evaluated in a future study.

946 LONG TERM FOLLOW-UP OF A LARGE SERIES OF STAGE II/III SEROUS OVARIAN BORDERLINE TUMORS

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Introduction/Background* The aim of this study was to assess prognostic factors and implications on further management in a large series of stage-II or III Serous Borderline Ovarian Tumors (SBOTs) with a long-term follow-up.

Methodology Patients with SBOTs and peritoneal implants treated in, or referred to, our institution were retrospectively reviewed. Prognostic factors on invasive recurrence, disease-free (DFS) and overall survival (OS) were analyzed.

Result(s)* Between 1971 and 2017, 212 patients were identified and followed (33 having invasive implants). After a median follow-up of 115 months, 70 recurrences were observed, 28 of them under the form of invasive disease. DFS at 5 years and 10 years was 73% and 62% respectively. The use of a conservative treatment (HR=5.5[3.33-9.08], p<.0001), the presence of ≥ 3 peritoneal sites with implants (HR=1.65[1.01-2.72], p=.045) were unfavorable prognostic factors for DFS. The presence of ≥ 3 peritoneal sites with implants (HR=3.02[0.96-9.53], p=.049) and the presence of stromal microinvasion (HR=3.19[1.12-9.1], p=.022) were unfavorable prognostic factors for OS. Non-conservative surgery (HR=7[2.35-20.87], p=0.0002), invasive implants (HR=5.37[1.29-22.26], p=0.013), and ≥ 3 peritoneal sites with implants (HR=3.56 [1.11-11.39], p=0.024) were identified as predictors of recurrence in the form of an invasive disease. Invasive implants were not associated with DFS (HR=1.39[0.77-2.51], p=0.27), nor OS (HR=1.76[0.57-5.47], p=0.32).

Conclusion* After a long-term follow-up, type of peritoneal implants is no longer a prognostic factor for OS. Implants ≥ 3 peritoneal sites seem to impact significantly OS and then require a specific follow-up in this subgroup of patients.

953 SURVIVAL IN ADVANCED STAGE EPITHELIAL OVARIAN CANCER PATIENTS WITH CARDIOPHRENIC LYMPHADENOPATHY WHO UNDERWENT CYTOREDUCTIVE SURGERY: A META-ANALYSIS

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Introduction/Background* Favourable survival outcomes for patients with advanced stage ovarian cancer are associated