IGCS19-0435

312 ARIES: A PHASE 2, OPEN-LABEL STUDY TO EVALUATE RUCAPARIB (PARP INHIBITOR) IN COMBINATION WITH NIVOLUMAB (ANTI-PD-1 ANTIBODY) IN PATIENTS WITH OVARIAN OR UROTHELIAL CANCER (UC)

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Objectives In the US and EU, rucaparib is approved for recurrent ovarian cancer (rOC) associated with or without homologous recombination deficiency (HRD; ie, *BRCA* mutation or high genomic loss of heterozygosity [LOH]); nivolumab is approved for recurrent, locally advanced/metastatic UC. Preclinical data suggest that PARP inhibition may work synergistically with PD-L1 blockade by stimulating the tumor microenvironment to enhance immune-mediated antitumor activity. ARIES (NCT03824704) is evaluating rucaparib plus nivolumab for rOC (Cohorts A1/A2) or locally advanced, unresectable/metastatic UC (Cohort B).
Methods Cohort A is enrolling 2 groups of patients (A1 and A2) with platinum-sensitive rOC who have received ≤2 prior treatments. The first group (Cohort A1) includes wild-type *BRCA* and high genomic LOH (≥16%) rOC; the second exploratory group (Cohort A2) includes *BRCA*-mutated rOC. Cohort B is enrolling UC patients regardless of HRD or PD-L1 status who are cisplatin-ineligible and declined carboplatin-based therapy or progressed following 1 line of platinum-based therapy. Patients in Cohorts A1 and B must have measurable disease (RECIST v1.1). Tumor sample is mandatory for tumor *BRCA*/LOH status assessment. Prior PARP or immune checkpoint inhibitor treatment is exclusionary. Patients are receiving rucaparib (600 mg PO BID) and nivolumab (480 mg IV Q4W). The primary endpoints are investigator-assessed objective response rate (RECIST v1.1; Cohorts A1 and B) and the effect of rucaparib on the immune microenvironment (Cohort A2).
Results Approximately 140 patients are being enrolled in the US.
Conclusions ARIES is assessing the efficacy of rucaparib plus nivolumab in patients with rOC or locally advanced, unresectable/metastatic UC.

IGCS19-0310

313 MODULATION OF CA125 EXPRESSION BY HTERT IN OVARIAN CANCER: POSSIBLE IMPLICATION OF PI3K/AKT/MTOR SIGNALING PATHWAY

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Objectives To investigate the possible inter-relationship between Ca125 secretion and telomerase activity, and the possible implication of the PI3K/Akt/mTOR pathway in this modulation.
Methods Ovarian cancer cell lines OVCAR-3, SK-OV-3 and IGROV-1 were treated with three different telomerase inhibitors, BIBR-1532, Costunolide and MST-312, one activator, LPS, and various inhibitors of the PI3K/Akt/mTOR pathway, PI828, wortmanin, GSK692690 and rapamycin. Ca125 expression was quantified by Q-PCR and its secretion by ELISA.
Results The three telomerase inhibitors decreased the Ca125 mRNA expression and protein secretion by the three cell lines. The same pattern was obtained when cells were treated with hTERT siRNA. The activation of hTERT lead to an increase in Ca125 expression and secretion, and to an increase in cell migration and motility. Interestingly, inhibition of PI3K/Akt/mTOR signaling pathway by PI828, wortmanin, GSK692690 and rapamycin lead to a decrease in Ca125 concentration suggesting the involvement of this pathway in Ca125 regulation. Moreover, an additive effect was shown when costunolide and BIBR 1532 were combined with the previous inhibitors. A decrease in telomerase expression and activity was obtained after gene silencing of Ca125 by the three cell lines, along with a decrease in PI3k, Akt and mTOR gene expression, which may explain the possible implication of this signaling pathway in the modulation of hTERT by Ca125.
Conclusions Both inhibition of telomerase and PI3K/Akt/mTOR signaling pathway decreased the Ca125 secretion, while inhibition of Ca125 decreased hTERT expression and activity suggesting a mutual modulation and a substantial role of Ca125 in cancer initiation and progression.

IGCS19-0302

314 PATIENTS WITH OVARIAN CLEAR CELL CARCINOMA ARE AT HIGH RISK OF SECONDARY MALIGNANCY

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Objectives Ovarian clear cell carcinoma (OCCC) has unique clinical and molecular features compared to other epithelial ovarian cancer histologies. Our objective was to describe the incidence of secondary malignancies (SM) in patients with OCCC.
Methods Retrospective cohort study of patients with pure OCCC at two tertiary academic centres in Toronto, Canada between 1995–2017. Demographic and histopathologic details were obtained from chart review and confirmed with a provincial cancer registry.
Results Of 209 patients with OCCC, 53 developed a SM (25.4%), of whom 7 developed 2 SM. SM included: breast (13), skin (10), gastrointestinal tract (9), other gynecologic malignancies (8), thyroid (6), lymphoma (5), head and neck (4), urologic (3) and lung malignancies.

Thirty-five SM occurred before index OCCC (median 9.4 years before), 21 after OCCC (median 5.8 years after), and 4 were diagnosed concurrently.

More patients with SM had a smoking history that those without SM (28.3% vs 11.5%, p=0.004). Other demographic characteristics were similar between groups (age (56 vs 54, p=0.23), body mass index (25.7 vs 25.5, p=0.70), diabetes (5.7% vs 5.8%, p=0.76), proportion of patients of Asian ethnicity (18.9% vs 23.1%, p=0.66)). The proportion presenting with stage I OCCC was comparable (66% vs 59%, p=0.46).

Only one patient had documented Lynch syndrome. Survival analysis is pending.

Conclusions Patients with OCCC are at increased risk of SM, most frequently non-Lynch syndrome related. This could suggest that a subset of patients with OCCC harbor mutations rendering them susceptible to SM. SM that could be associated with Lynch syndrome warrants genetic testing.

IGCS19-0306

315 IS IT SAFE TO IMMEDIATELY INITIATE ADJUVANT INTRAPERITONEAL CHEMOTHERAPY FOLLOWING BOWEL RESECTION IN PATIENTS WITH NEWLY DIAGNOSED ADVANCED OVARIAN CANCER?

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Objectives To determine if early administration of intraperitoneal chemotherapy (IPC) and intra-operative insertion of an intraperitoneal (IP) port are associated with increased complications in patients who undergo a bowel resection procedure as part of primary cytoreductive surgery.

Methods Retrospective cohort of patients with ovarian cancer at 2 institutions between 2008–2018. Patients included in this study had primary cytoreductive surgery which included one or more small or large bowel resections and either received or were scheduled to receive adjuvant intraperitoneal chemotherapy.

Results The majority of patients had stage III or IV disease (86.2%) and high grade serous histology (91.6%). 120 out of 138 patients (87%) received at least 4 cycles of IPC. A small proportion of patients (5.4%) received all chemotherapy intravenously, despite having had an IP port inserted. Compared to patients who received their first cycle of chemotherapy intravenously (IV), patients who started with IPC were not at increased risk of delayed infection (1.8% vs 1.3% (p=0.8)), IP port related complications which included port obstruction, leakage, infection, pain and erosion (19.6% vs 20% (p=0.96)), or anastomotic leak (3.6% vs 2.7% (p=0.8)). The rates of anastomotic leak (5.6% vs 3.3% (p=0.62)), intra-abdominal infection (16.7% vs 6.7% (p=0.17)) and IP port related complications (24.1% vs 13.3% (p=0.21)) were not statistically different in patients who had intra-operative IP port insertion compared to delayed post-operative insertion.

Conclusions IPC during the first cycle of adjuvant treatment and intra-operative IP port insertion are not associated with increased complications after primary cytoreductive surgery for ovarian cancer which includes a bowel resection.

IGCS19-0502

316 OVARIAN TUMOR IN PATIENTS WITH PREVIOUS GASTROINTESTINAL CARCINOMA

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Objectives To evaluate demographic and clinical-pathological characteristics of ovarian tumors diagnosed in women with previous gastrointestinal cancers.

Methods A tranversal study of 59 patients with diagnosis of ovarian tumors who had previously been treated for gastrointestinal adenocarcinoma at a hospital in Sao Paulo, Brazil, from 2009 to 2018. Demographic data were collected: age, follow-up of primary gastrointestinal tumor, tumor markers CA-125, CA- 19.9 and CEA, radiological characteristics, type and extent of surgery performed, amount of residual disease, primary tumor site, anatomopathological diagnosis and survival.

Results The primary gastrointestinal carcinoma sites were: stomach (15.3%), colorectal (64.4%), appendix (3.4%), pancreas (3.4%), gallbladder (3.4%) and undetermined gastrointestinal cancer (10.2%). The median follow-up was 16 (1–87) months. The overall survival from the diagnosis of gastrointestinal carcinoma was 33 (2–187) months and the overall survival from ovarian tumor diagnosis was 16 (1–87) months. The mortality rate varied according to the site of origin of gastrointestinal carcinoma: stomach (77.8%), colorectal (53.1%), appendix (50%), gallbladder (50%), pancreas (50%) and undetermined gastrointestinal carcinoma (16.7%).

Conclusions Metastatic gastrointestinal tumors to the ovaries present variable overall survival according to the primary site of origin. Tumors of the stomach, gallbladder and pancreas present worse prognosis. Colorectal metastatic tumors are the most frequent and the ones with the highest overall survival. These differences should be considered when deciding whether to perform surgical treatment in these patients with metastatic tumors.

IGCS19-0379

317 FEASIBILITY OF AN OUTPATIENT 12-STEP DESENSITIZATION FOR PATIENTS WITH HISTORY OF CARBOPLATIN HYPERSENSITIVITY REACTIONS (HSR) UNDERGOING RETREATMENT WITH CARBOPLATIN FOR RECURRENT OVARIAN OR ENDOMETRIAL CANCER

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Objectives To retrospectively evaluate the safety and efficacy of an outpatient 12-step carboplatin desensitization regimen in patients with prior carboplatin HSR.

Methods Patients with a history of carboplatin HSR undergoing carboplatin desensitization for mullerian cancer were