

IGCS20_1437

405 IMPACT OF HYPERTHERMIC INTRAPERITONEAL CHEMOTHERAPY (HIPEC) ON TUMOR MICROENVIRONMENT (TME) IN OVARIAN CANCER – A SUBANALYSIS FROM A PHASE I CLINICAL TRIAL

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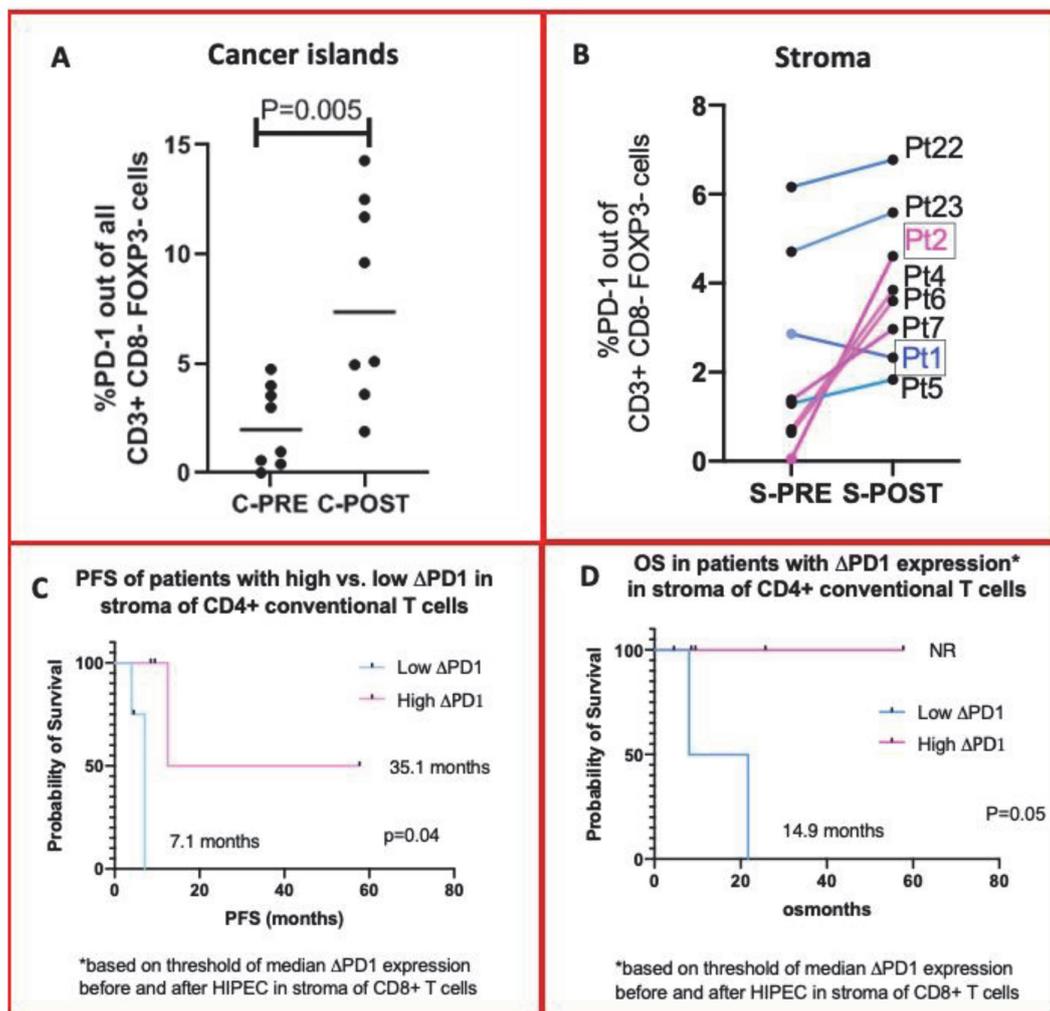
10.1136/ijgc-2020-IGCS.350

Background Immunogenic cell death has been suggested as a mechanism for HIPEC, through the release of heat shock proteins, and resulting in activation of tumor-specific T cells.

Methods This is a subgroup analysis of a Phase I trial using HIPEC with cisplatin 75 mg/m² at time of optimal cytoreduction. Metastatic tumors from nine ovarian cancer patients were collected intraoperatively before and after HIPEC. Differentially expressed genes and pathways of pre- and post-HIPEC

tumors were analyzed via whole-transcriptome sequencing (WTS). Immunofluorescent (IF) staining and multispectral imaging were used to determine composition and PD-1 expression of CD8+ and conventional CD4+ tumor-infiltrating lymphocytes (TILs), using antibodies against CD8, FOXP3, PD-1, and pancytokeratin (to distinguish cancer islands from stroma). Kaplan-Meier and log-rank tests compared the overall and progression free survivals (PFS) of patients with low versus high%PD-1 changes, based on dichotomization with respect to the median%PD-1 change.

Results Heatshock proteins comprised the top differentially upregulated genes in HIPEC-treated tumors. Gene set enrichment analysis revealed significant upregulation of immune pathways, including antigen processing/presentation. IF staining demonstrated increased%PD-1 in cancer islands of CD8+ and CD4+ TILs after HIPEC. In stroma, the largest%PD-1 change occurs in an exceptional responder (PFS, OS 5 years), while the lowest%PD-1 change occurred in a poor responder. Kaplan-Meier curves demonstrate superior PFS in patients with high stromal PD-1 changes in TILs after HIPEC.



Abstract 405 Figure 1 PD-1 expression increases after HIPEC in cancer islands of CD4+ conventional T cells, and stromal PD-1 expression changes correlate with survival. **A.** %PD-1 expression in CD4+ T cell cancer islands, before and after HIPEC. %PD-1 expression is significantly increased after HIPEC. **B.** %PD-1 expression changes in individual patients after HIPEC (in stroma). Pt 2 is an exceptional responder with PFS and OS of 5 years, while Pt 1 is a poor responder. **C and D.** Kaplan-Meier curves of Progression-free survival (PFS) and Overall Survival (OS) in patients with high (pink) vs low (blue) HIPEC-induced%PD-1 expression changes in CD4+ T cell stroma (based on median%PD-1 expression threshold).

Conclusions Increased PD-1 expression after HIPEC suggests early HIPEC-induced T cell activation, and is associated with improved survival, implicating a potential future role for PD-1 inhibitors following HIPEC in ovarian cancer.

IGCS20_1438

406

SENTINEL LYMPH NODE IN CERVICAL AND ENDOMETRIAL CANCER: REVIEW OF THE FIRST 58 CASES IN A UNIVERSITY SETTING

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10.1136/ijgc-2020-IGCS.351

Introduction Lymphadenectomy is a common procedure in gynecologic oncology. Nonetheless, it is associated to important number of side effects. During the last decade there have been enormous efforts to develop different SLN techniques to reduce complications without affecting survival.

Objective Evaluate the experience of SLN technique in a university setting.

Methods Retrospective review of 58 cervical and endometrial cancers evaluated with SLN.

Results Forty-one of the patients presented with uterine cervical cancer and 17 endometrial cancer. The method used for detection of the SLN was patent blue dye only in 42 patients (72%), technetium 99 in 2 (3.5%), both techniques was used in 10 (17%) and ICG in 4 (%) cases. 40 (69%) patients had laparoscopy. At least one pelvic SLN was detected in 53 (91.4%) 7 patients. Bilateral detection was achieved in 39 (67.2%). Most of the SLN were identified next to external iliac vessels and the obturator fossa. In 97% of the 92 samples identified as SLN had at least one lymph node detected. The mean of lymph-node count was 1.8 (1–7). Patients with uterine cervical cancer had neither SLN nor non-SLN positive. Four patients with endometrial cancer (23.52%) had metastasis on SLN. There were no false negative SLN on those patients who underwent lymphadenectomy. There were no surgical complications derived from de SLN technique.

Conclusion SLN technique in cervical and endometrial cancer is technically feasible. Our results show that a good detection rate can be achieved for a proper diagnostic of lymph node status.

IGCS20_1441

407

LEIOMYOMA WITH BIZARRE NUCLEI: CLINICAL AND PATHOLOGIC FEATURES OF 10 PATIENTS

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10.1136/ijgc-2020-IGCS.352

Introduction Leiomyoma with bizarre nuclei (LBN) is defined histologically by significant cytologic atypia, but high mitotic rate and tumor cell necrosis are absent. Despite its benign clinical behavior, differential diagnosis from leiomyosarcoma can sometimes be difficult.

There have been a few sizable studies that have described the clinical and pathologic features of LBN with follow-up data.

Objective we investigated the clinical and pathologic features of LBN and compared them with related studies.

Methods A total of 10 patients diagnosed with LBN in our department were included.

In all cases, clinical data, macroscopic with microscopic features, and follow-up data were evaluated.

Results The median age of the patients was 46 years. Six patients had undergone hysterectomy and 4 myomectomies. The mean tumor diameter was 6 cm.

The tumor was intramural in all cases. Margins were regular in 7 cases, but expansive in 3 cases.

Microscopically, the bizarre cell distribution was multifocal. Their density was low in 8 cases and high in 2 cases. Mitosis was observed in 3 cases, not exceeding 8/10 high power fields. The prognosis was favorable in all cases, with no signs of recurrence or metastasis after a median follow up of 10 years.

Conclusion LBN is a histologic variant of benign uterine smooth muscle tumors. Expansive margins, a multifocal distribution with a high density of the bizarre cells, are possibly noted. Other morphologic criteria for malignancy, such as high mitotic rate and coagulative tumor cell necrosis, should be excluded. Additional sampling may be needed for an accurate diagnosis.

IGCS20_1442

408

DOSE-DENSE PACLITAXEL AND CARBOPLATIN PLUS BEVACIZUMAB IS AN EFFECTIVE AND A TOLERABLE FIRST-LINE REGIMEN FOR ADVANCED OVARIAN CANCER

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10.1136/ijgc-2020-IGCS.353

The JGOG 3016 showed that dose-dense paclitaxel and carboplatin (ddTC) improved progression-free survival (PFS) and overall survival (OS) in advanced ovarian cancer (AOC). ICON7 and GOG-0218 showed that bevacizumab (Bev) improved PFS. GOG-0262 suggested that ddTC+Bev showed no superiority in PFS. The aim of this study is to evaluate the efficacy and safety of ddTC+Bev compared with ddTC in AOC.

We retrospectively investigated patients with FIGO stage III-IV OC who received ddTC or ddTC+Bev as first-line chemotherapy. PFS was investigated about ddTC+Bev compared with ddTC using log-rank test. Age (<60 vs 60≤), FIGO stage (III vs IV), histological type (serous/endometrioid vs others), initial treatment (primary debulking surgery (PDS) vs neoadjuvant chemotherapy±interval debulking surgery (NAC±IDS)), debulking (complete vs others) and regimen (ddTC+Bev vs ddTC) were investigated by multivariate analysis using cox proportional hazards model to predict prognostic factors.

A total of 134 patients were enrolled. Median follow up periods was 30.5 months. 80.1% of patients had stage III disease. 76.7% had serous/endometrioid histologic findings. 59.7% received PDS. 61.9% received complete surgery.