PHARMACOKINETICS, TOXICITIES, AND TISSUE CONCENTRATIONS OF GEMCITABINE SPRAYED BY ROTATIONAL INTRAPERITONEAL PRESSURIZED AEROSOL CHEMOTHERAPY IN A PIG MODEL

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Abstracts

EP299/#684

PHARMACOKINETICS, TOXICITIES, AND TISSUE CONCENTRATIONS OF GEMCITABINE SPRAYED BY ROTATIONAL INTRAPERITONEAL PRESSURIZED AEROSOL CHEMOTHERAPY IN A PIG MODEL

We evaluated the pharmacokinetics, tissue concentrations, and toxicities of gemcitabine during rotational intraperitoneal pressurized aerosol chemotherapy (RIPAC) in pigs. Methods We sprayed gemcitabine of 10% and 30% of doses for intravenous chemotherapy in six pigs (cohort 1, n=3, 300 mg/m²; cohort 2, n=3, 1,000 mg/m²). We evaluated the time-dependent plasma concentrations of gemcitabine before RIPAC to 120 hr for the pharmacokinetics, tissue concentrations in twelve peritoneal regions, and hepatic and renal functions before RIPAC to 120 hr in the two cohorts. Results Mean values of the peak plasma concentration (C_max), the time to C_max (T_max), the time taken for C_max to drop in half (T_1/2), and the area under the curve from time zero to the time of last quantifiable concentration (AUC_last) were 1,320 and 7,476 ng/ml, 1.92 and 1.83 hr, 1.52 and 1.96 hr, and 4,718 and 26,347 ng·hr/ml in cohorts 1 and 2, respectively. Mean values of tissue concentrations were 1.3 to 11.2 times higher than in cohort 2 and in cohort 1 despite the similar ratio of tissue to plasma concentration, and tissue concentrations in the two cohorts were higher in the parietal peritoneum than in the visceral peritoneum. Cohort 2 showed the change of hepatic function after RIPAC, whereas there were no changes of hepatic and renal functions in cohort 1. Conclusion/Implications Considering the change of hepatic function in gemcitabine of 1,000 mg/m², gemcitabine of 300 mg/m² can be considered as the stazing dose for RIPAC in a phase 1 trial.

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A STUDY OF SURGICO-PATHOLOGICAL SPECTRUM AND LYMPH NODE EVALUATION IN EPITHELIAL OVARIAN CANCERS: AN AMBISPECTIVE STUDY

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Abstracts

EP301/#199

A STUDY OF SURGICO-PATHOLOGICAL SPECTRUM AND LYMPH NODE EVALUATION IN EPITHELIAL OVARIAN CANCERS: AN AMBISPECTIVE STUDY

Women with EOCs who underwent cytoreductive surgery (CRS) between Jan 2019 to April 2022 were included. Distribution of histology, stage and LN metastasis was studied. Predictive value of radiologic and surgically enlarged LNs with final histopathology was studied. Results A total of 101 women with EOCs underwent CRS, of which 5 (4.95%) with co-existent endometrial cancer were excluded. Fifty women (52%) underwent primary and 46 women (48%) interval CRS. HGSC was commonest (n=66, 68.75%), followed by mucinous (n=15, 15.63%), endometrioid (n=6, 6.25%), LGSC (n=4, 4.17%) and carcinosarcoma (n=2, 2.08%). Majority of women, 69 (71.88%) were stage III and IV at presentation. Complete cytoreduction was achieved in 75 (78.12%) cases. Seventy-five women (78.13%) of EOC underwent pelvic and/or para-aortic lymphadenectomy, out of which 23 (30.67%) were histologically positive. Both radiologically and surgically enlarged LNs significantly predicted LN metastasis on histopathology (p=0.02 and 0.006 respectively). The combined sensitivity, specificity, PPV, and NPV of both CECT and surgically enlarged LNs was 78.26%, 57.69%, 45%, and 85.71%, respectively. Conclusion/Implications Serous histology, high-grade tumors and suspicious LNs in CECT and during surgery are significantly associated with LN metastasis.

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EP303/#621

LOW DOSE LENVATINIB PLUS TORIPALIMAB IN PATIENTS WITH HEAVILY PRETREATED GYNECOLOGICAL SOLID TUMORS: A PILOT STUDY

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Conclusion/Implications The objective of the present study was to evaluate surgico-pathological findings, lymph node (LN) involvement, and prediction of LN metastasis by preoperative imaging and intraoperative assessment in women with epithelial ovarian cancer (EOC).

Conclusion/Implications The study, to our knowledge, is the first to explore the effects of low-dose lenvatinib plus Toripalimab in gynecological solid tumors. The encouraging efficacy of lenvatinib combined therapy has efficacy in treating advanced endometrial carcinoma (including non-endometrioid), but nearly half of patients were intolerable toxicity of the recommended doses. Accordingly, we performed this pilot study to evaluate the efficacy and safety of low dose lenvatinib plus toripalimab in patients with heavily pretreated gynecological solid tumors.

Conclusion/Implications Twenty-one patients (ovarian, n=14; endometrial, n=6; vulvar, n=1), who experienced disease progression after prior median 3 lines of systemic therapy, were enrolled and treated from September 2021 to April 2023. In the 21 patients, the median PFS was 5.0 months, the median duration of response (DOR) was 5.2 months, and disease control rate(DCR) was 38.1%. The most common grade 3 treatment-related adverse events(TRAEs) were hypertension (33.3%) and proteinuria (9.5%), respectively. No grade 4 TRAEs occurred.

Conclusion/Implications The primary endpoint was progression free survival (PFS). Results Twenty-one patients (ovarian, n=14; endometrial, n=6; vulvar, n=1), who experienced disease progression after prior median 3 lines of systemic therapy, were enrolled and treated from September 2021 to April 2023. In the 21 patients, the median PFS was 5.0 months; the median duration of response (DOR) was 5.2 months, and disease control rate (DCR) was 38.1%. The most common grade 3 treatment-related adverse events (TRAEs) were hypertension (33.3%) and proteinuria (9.5%), respectively. No grade 4 TRAEs occurred.
and safety of this pilot study strongly support the further investigation of low-dose Lenvatinib plus Toripalimab in patients with heavily pretreated gynecological solid tumors.

**EP304/#430**

**AUTOPHAGY DEFECT AND ITS CLINICAL SIGNIFICANCE IN SEROUS OVARIAN CARCINOMA**

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**Introduction**

Autophagy is a physiological cellular process for degradation and recycling of useless proteins, however it maintains survival of cancer cells with defects in apoptosis. This study aimed to evaluate autophagy status and the clinical significance in serous ovarian carcinoma (SOC).

**Methods**

Tissue microarray including 72 SOC, 10 serous adenoma, and 13 borderline serous tumors was used for immunohistochemical analysis. Immunoreactivity of LC3, Beclin-1, p62 and TFEB were semi-quantitatively scored. Clinicopathological parameters were obtained from medical records. Kaplan-Meier estimate and the Cox regression were used for survival analysis.

**Results**

LC3 and TFEB were present in 31.9% and 20.8% of SOC. Beclin-1 and p62 were significantly upregulated in SOC compared with controls (70.8% and 95.8%; p = 0.03 and p < 0.001, respectively). Significant correlation was observed among LC3, Beclin-1 and p62. A simultaneous accumulation of Beclin-1 and p62 represents coexistence of induction and last stage of autophagy, suggesting autophagy activation with impairment of autophagy flux. In univariate analysis, the presence of TFEB, suboptimality, advanced FIGO stage, and chemoresistance were significantly associated with worse disease-free survival and overall survival (OS). Multivariate analysis showed that surgical optimality and chemoresistance were independent predictor for OS. The expressions of p62 and TFEB were positively correlated with FIGO stage (p = 0.017 and p = 0.015, respectively) and Beclin-1 expression was lower in high-grade tumor than low-grade tumor (p = 0.001).

**Conclusion/Implications**

A dysregulation of autophagy was found in SOC. Beclin-1, p62 and TFEB were associated with aggressiveness and poor prognosis of SOC.

**EP305/#401**

**NEUTROPHIL LYMPHOCYTE RATIO AND PLATELET LYMPHOCYTE RATIO AS PROGNOSTIC MARKERS IN OVARIAN CANCER**

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**Introduction**

Inflammation plays an essential role in tumor development in cancer initiation, progression and metastasis. Immune cell components of blood count offer an attractive