gynecological cancer

9702G CARBOPLATIN PLUS Paclitaxel versus CARBOPLATIN plus PEGYLATED LIPOSOMAL DOXORUBICIN AS FIRST-LINE TREATMENT FOR PATIENTS WITH OVARIAN CANCER: THE MITO-2 (MULTICENTRE ITALIAN TRIAL IN OVARIAN CANCER) RANDOMIZED PHASE III TRIAL

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Carboplatin + paclitaxel (CP) is standard 1st line chemotherapy (CT) for patients (pts) with ovarian cancer (OC). MITO-2 is an academic multicenter randomized phase III study testing the activity of carboplatin plus pegylated liposomal doxorubicin (P-GLD) vs CP. CP or P-GLD (6 cycles) was compared to CP (100 mg/m²/d1q3w) or to P-GLD (AUC5 80 mg/m²/d1q3w) or to C-PLD (C AUC5 70 mg/m²/d1q3w) for 6 cycles. Primary endpoint was progression-free survival (PFS). To date, 1430 pts have been enrolled, 197 dead or lost to follow-up. Median age was 52 years (range 27-77). Stage III (60%) and IV (30%) were prevalent. A plateau in PFS events was reached before obtaining the planned number. Thus, following an IDMC recommendation, final analysis was done with 596 events occurred by Dec 31, 2009. This size is consistent with HR to be detected 0.79, with 80% power. With a median follow-up of 40.2 months, median PFS was 19.0 months with C-PLD and CP respectively (HR 0.95, 95%CI 0.81-1.13; p=0.58). Cox model adjusted by stage, PS, residual disease, age and size of the center confirmed lack of significant difference between arms (HR 0.96, 95%CI 0.83-1.14). With 313 deaths, median OS was 61.6 and 53.2 months with C-PLD and CP, respectively (HR 0.89, 95%CI 0.72-1.12; p=0.30). CP-PLD produced a similar activity, with different toxicity profile, C-PLD could be considered an alternative to CP. Chemo-naive pts with OC stage IC-IV, aged 18-70, and with a PS≤1 were randomized by stratified blocks to C-PLD or CP. All other authors have declared no conflicts of interest.

Conclusions: Whilst olaparib 200 mg, 400 mg and PLD all demonstrated similar antitumour activity, numerically more confirmed responses were noted for olaparib 400 mg bid in BRCA1 and BRCA2 mutation carriers with ovarian cancer who had failed previous platinum-based chemotherapy. Disclosure: S. Kaye: I have served on an AstraZeneca Advisory Board for olaparib (AZD2281). U. Matulonis: Received research funding for this study from AstraZeneca. D. Taylor: Employee of AstraZeneca. M. Wickens: Employee of AstraZeneca. J. Carmichael: Employee of AstraZeneca. All other authors have declared no conflicts of interest.

Background: Src is overexpressed in ovarian tumours, Src activation is associated with poor prognosis for pts with EOC. Saracatinib (AZD0530) is a potent oral Src inhibitor with activity in EOC models including augmentation of taxane and platin activity. Src is overexpressed in ovarian tumours; Src activation is associated with poor prognosis for pts with EOC. Saracatinib (AZD0530) is a potent oral Src inhibitor with activity in EOC models including augmentation of taxane and platin activity. Saracatinib 175 mg/day once-daily monotherapy was well tolerated and inhibited Src in EOC preclinical models. Saracatinib has the potential to add to the efficacy of standard chemotherapy. Patients with ovarian cancer who have failed previous platinum-based chemotherapy were randomized to stratified blocks to saracatinib 175 mg/day or placebo plus carboplatin. Results: 298 pts were randomized (149 in each arm). There was a small excess of pts with poor prognostic factors (PS or mucinous/clear cell histology) in the saracatinib arm. 69% and 74% of pts in the saracatinib and placebo arms, respectively, received 26 chemotherapy cycles. Median PFS was 8.3 and 7.8 months in the saracatinib and placebo arms, respectively. Prolonged progression-free survival (PFS) and tolerability: 189 pts were enrolled (saracatinib arm, 96 placebo, 93). There was a small excess of pts with poor prognostic factors (PS or mucinous/clear cell histology) in the saracatinib arm. 69% and 74% of pts in the saracatinib and placebo arms, respectively, received 26 chemotherapy cycles. Median PFS was 8.3 and 7.8 months in the saracatinib and placebo arms, respectively. Prolonged progression-free survival (PFS) and tolerability: 189 pts were enrolled (saracatinib arm, 96 placebo, 93). There was a small excess of pts with poor prognostic factors (PS or mucinous/clear cell histology) in the saracatinib arm. 69% and 74% of pts in the saracatinib and placebo arms, respectively, received 26 chemotherapy cycles. Median PFS was 8.3 and 7.8 months in the saracatinib and placebo arms, respectively. Prolonged progression-free survival (PFS) and tolerability: 189 pts were enrolled (saracatinib arm, 96 placebo, 93). There was a small excess of pts with poor prognostic factors (PS or mucinous/clear cell histology) in the saracatinib arm. 69% and 74% of pts in the saracatinib and placebo arms, respectively, received 26 chemotherapy cycles. Median PFS was 8.3 and 7.8 months in the saracatinib and placebo arms, respectively. Prolonged progression-free survival (PFS) and tolerability: 189 pts were enrolled (saracatinib arm, 96 placebo, 93). There was a small excess of pts with poor prognostic factors (PS or mucinous/clear cell histology) in the saracatinib arm. 69% and 74% of pts in the saracatinib and placebo arms, respectively, received 26 chemotherapy cycles. Median PFS was 8.3 and 7.8 months in the saracatinib and placebo arms, respectively. Prolonged progression-free survival (PFS) and tolerability: 189 pts were enrolled (saracatinib arm, 96 placebo, 93). There was a small excess of pts with poor prognostic factors (PS or mucinous/clear cell histology) in the saracatinib arm. 69% and 74% of pts in the saracatinib and placebo arms, respectively, received 26 chemotherapy cycles. Median PFS was 8.3 and 7.8 months in the saracatinib and placebo arms, respectively. Prolonged progression-free survival (PFS) and tolerability: 189 pts were enrolled (saracatinib arm, 96 placebo, 93). There was a small excess of pts with poor prognostic factors (PS or mucinous/clear cell histology) in the saracatinib arm. 69% and 74% of pts in the saracatinib and placebo arms, respectively, received 26 chemotherapy cycles. Median PFS was 8.3 and 7.8 months in the saracatinib and placebo arms, respectively. Prolonged progression-free survival (PFS) and tolerability: 189 pts were enrolled (saracatinib arm, 96 placebo, 93). There was a small excess of pts with poor prognostic factors (PS or mucinous/clear cell histology) in the saracatinib arm. 69% and 74% of pts in the saracatinib and placebo arms, respectively, received 26 chemotherapy cycles. Median PFS was 8.3 and 7.8 months in the saracatinib and placebo arms, respectively. Prolonged progression-free survival (PFS) and tolerability: 189 pts were enrolled (saracatinib arm, 96 placebo, 93). There was a small excess of pts with poor prog...
the saracatinib arm vs placebo were nausea (63.5% vs 55.9%), alopecia (55.1% vs 62.4%) and diarrhea (43.7% vs 30.1%). There was no difference between arms in frequency of respiratory AEs. The most common CTCAE grade 2 or 3 events were neutropenia (31% saracatinib vs 24% placebo), febrile neutropenia (23% vs 5%), thrombocytopenia (13% vs 8%) and anemia (10% vs 6%). AEs were mainly reported during the chemotherapy combination period. AE reporting was balanced between arms in the monotherapy period after completing C-P.

Conclusions: Saracatinib 175 mg can be administered with C-P with additional manageable AEs. Addition of saracatinib to C-P did not provide additional benefit.

Data from a more mature analysis will be presented.

Disclosure: M. Cantarini: Employee of AstraZeneca. U. Emeribe: Employee of AstraZeneca. M. Stuart: Employee of AstraZeneca. All other authors have declared no conflicts of interest.

975PD A RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED PHASE 2 STUDY OF AMG 386 PLUS WEEKLY PaclITAXEL IN PATIENTS (PTS) WITH ADVANCED OVARIAN CANCER

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Background: This study evaluated the safety and efficacy of AMG 386, an investigational peptide-Fc fusion protein that neutralizes the interaction between the Tie2 receptor and angiopontin-1 and -2, plus paclitaxel in pts with advanced ovarian cancer.

Methods: Pts with recurrent epithelial ovarian, fallopian tube or primary peritoneal cancer were eligible. Pts were randomized 1:1:1 to receive paclitaxel (80 mg/m² IV onceweekly QW) 3 wks on/1 wk off) plus AMG 386 IV QW (Arm A; Arm B, 30 mg/kg) or placebo IV QW (Arm C) until disease progression, death, or unacceptable toxicity. The primary endpoint was progression-free survival (PFS). Secondary endpoints included objective response rate (ORR), CA-125 response (per GCIG), safety, and pharmacokinetics (PK).

Results: 161 pts were randomized. Efficacy results are reported below (table). Adverse events in Arms A/B/C included hypertension (8%/5%, no grade 3), thromboembolic events (arterial, 2/2/0%, all grade 3; venous, 8/8/11%, grade 3 = 6/6/6%), peripheral edema (71%/52%/29%, grade 3 = 4/6/4%), and hypokalemia (21%/15%/5%, grade 3 = 12/11/4%). No bowel perforations occurred in AMG 386–treated patients. None of the on-study deaths were considered treatment-related. AMG 386 exhibited linear PK properties at the tested doses. Mean Cmax and Cmin values were consistent with those from a phase 1 monotherapy study.

Conclusions: AMG 386 was tolerable when combined with weekly paclitaxel and had a manageable safety profile dissimilar from VEGF inhibitors. Promising evidence of antitumor activity and a dose-response effect were observed, warranting further studies. Updated efficacy data (incl overall survival) will be presented.

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TOLERABILITY OF TRABECTEDIN (TR) PLUS PEGLATATED LIPOSOMAL DOXORUBICIN (PLD) IN PLATINUM SENSITIVE (P-S) VS. PLATINUM RESISTANT (P-R) PATIENTS (PTS) WITH RELAPSED OVARIAN CANCER

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Background: OVA 301 was an open label, multicenter, randomized Phase III study comparing Tr+PLD to PLD alone in 672 pts with OVA, conducted in 21 countries. The combination improved PFS and RR with a trend toward longer OS and showed manageable non cumulative toxicity. The pts were stratified at randomization by platinum sensitivity, - (P-S vs. P-R). The safety and tolerability of PLD 50 mg/m2 and Tr 1.1 mg/m2, 3h-q3 wks vs. PLD 50 mg/m2 q4 wks were analyzed by these strata.

Results: Safety was evaluated in 663 treated patients, 425 P-S (64,1%) and 238 P-R pts (35,9%). Tolerability was evaluated by adverse events (AEs), laboratory data and physical findings (NCI CTC Version 3.0).

Conclusions: As expected more cycles of treatment were given to the P-S pts. Neutropenia managed by the growth factor and transaminase elevations, which were manageable non cumulative toxicity. The pts were stratified at randomization by platinum sensitivity, - (P-S vs. P-R). The safety and tolerability of PLD 50 mg/m2 and Tr 1.1 mg/m2, 3h-q3 wks vs. PLD 50 mg/m2 q4 wks were analyzed by these strata.

PROGNOSTIC VALUE OF EARLY COMPLETE METABOLIC RESPONSE BY FDG-PET DURING NEO-ADJUVANT CHEMOTHERAPY IN ADVANCED OVARIAN CANCER PATIENTS

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Background: Recently, we reported that complete metabolic response (CMR) by F-18-fluorodeoxyglucose positron emission tomography (FDG-PET) after 3 cycles of neoadjuvant chemotherapy (NACT) predicts the pathological response evidenced at the subsequent surgery in advanced epithelial ovarian cancer (AOC) patients (pts). The aim of the present study was to evaluate the prognostic role of FDG-PET as compared with serum CA125 in the same clinical setting.

Patients and methods: Women with newly diagnosed AOC unsuited to optimal upfront debulking surgery were treated with 6 cycles of carboplatin AUC 5 and paclitaxel 175 mg/m2, every 3 weeks before surgery. These pts were evaluated with FDG-PET and serum CA125 at baseline and early (after 3 cycles) during NACT. Changes in tumor FDG uptake, expressed as standardized uptake values (SUV), and in serum CA125 values were correlated with time to progression (TTP) and overall survival (OS). CMR and complete biochemical response (CBR) were defined as the normalization of SUV (SUV<2) and serum CA125 value (<35U/ml), respectively.

Results: Fifty pts were enrolled from November 2004 to June 2008. All the pts had a pathological baseline FDG-PET while serum CA125 was elevated in 98%. After 3 cycles pts with CMR and CBR were 34% and 38%, respectively. Surgery was performed after NACT in 33 (74%) pts and in 26 (52 %) pts residual tumour was achieved. After a median follow-up of 42 mos (range 22-67), 41 (82%) pts progressed (median TTP 10 mo.s) and 23 (46%) pts died (median OS 28 mo.s).

Conclusions: Pts with CMR after the third cycle of NACT showed a longer TTP and OS than pts who did not achieve an SUV normalization. According to previous reports, sequential FDG-PET can predict the patient outcome after 3 cycles of NACT and it could be more accurate than CA125.

Disclosure: All authors have declared no conflicts of interest.
Background: BEV, a humanized anti-VEGF monoclonal antibody, has demonstrated single-agent activity in patients with recurrent OC, but its therapeutic impact of concurrent maintenance BEV with standard chemotherapy (CT) was evaluated in an international, double-blind, placebo-controlled phase III trial. Methods: Eligible patients had newly diagnosed, untreated EOC, or FTC in first-line setting: Arm 1 (A1): 4 cycles of cisplatin and topotecan followed by 4 sequential cycles of GC (IV paclitaxel 175 mg/m$^2$ + carboplatin AUC 6 cycles 1-6) + placebo (C2-22 (R1) – current BEV (441 mg/m$^2$) + placebo C2-6 + concurrent BEV C2-6 + maintenance BEV C7-22 (R2)) Infusions were administered d1 of a 21-day cycle. The primary endpoint is progression-free survival (PFS) (radiographic, CA125, clinical criteria or death, secondary endpoints include overall survival, safety, and G0). Results: 1,873 patients, median age 60, were enrolled from 9/05 - 6/09. Stage II of optimally debulked (34%), stage III sub-optimally debulked (40%), and stage IV (26%) patients were similarly distributed in each treatment group. We intend to present detailed safety analyses, in addition to efficacy subset analyses. Conclusions: Detailed safety and efficacy subset analyses will be presented.

Disclosure: All authors have declared no conflicts of interest.

Expression of DNA repair genes as biomarkers of outcome in epithelial ovarian cancer: A GEOX study

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Background: Treatment of ovarian cancer (OC) is hindered by intrinsic or acquired resistance to platinum-based chemotherapy. Breast cancer 1 (BRCA1), ERCC1 and XPG genes play a crucial role in DNA repair and their expression levels have been associated to a worse Disease Free Survival (DFS) (p=0.009). High XPG expression was associated to a worse Disease Free Survival (DFS) (p=0.17). The use of CA 125 as a tumor progression criterion in relapsing ovarian cancer (ROC) trials remains controversial. CALYPSO is the first large randomized trial to incorporate CA 125 (OGC criteria) and clinical deterioration in addition to RECIST as criteria for progression evaluation. 976 patients (pts) with platinum-sensitive ROC were randomized to either: (arm A) PC (P 175mg/m2 + C 6 cycles every 21 days) x 4 cycles, or (arm B) C (AUC 4 d) + G (1000 mg/m2 d1-8 every 21 days) x 4 cycles followed by PC (as in arm A) x 4 cycles. Primary endpoint was response rate (RR) measured by RECIST and/or CA-125 Rustin criteria. Secondary endpoints included toxicity, PFS and overall survival (OS).

Results: From Feb/05 to May/07, 117 pts were included in the study. No significant differences were found in median age, PS, serous histology, grade, % of pts with measurable disease (78% vs 79.4%), number of previous lines (1 in 85.3% of pts) or PFI > 12 months (62.9% of pts). No significant differences in toxicity were found except for: G3-4 thrombocytopenia (B 15.8% vs A 3.4%, p 0.023), and Grade 3-4 neutropenia (B 61.4% vs A 22.8%; p < 0.001). Grade 2-4 neurotoxicity was higher in arm A (35.6% vs 22.8%; p=ns). In the intent to treat analysis, RR (CR+PR) was higher in arm B: 87.7% (95%CI: 87.6-88.6%) vs Arm A 72.9% (95%CI: 76.9-84.9%). The difference in RR of 14.8% was statistically significant (95%CI: 6.5-29%. Chi square 0.0145; Fisher-exact test p=0.067). Median PFS was 13.3 m in arm B vs 11.2 in arm A (HR 0.88; 95% CI 0.9-1.3). Median OS was 37.5 m in arm B vs 29.8 m in arm A (HR 0.81; 95% CI 0.8-1). Conclusion: In this randomized phase II study, a sequential doublet of GC followed by PC was associated with a trend in higher efficacy compared to PC. These data cannot exclude a significant benefit of the sequential arm.

Disclosure: All authors have declared no conflicts of interest.

Should CA 125 still be part of tumour evaluation criteria in ovarian cancer trials? Experience of the GGG CALYPSO trial

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The use of CA 125 as a tumor progression criterion in relapsing ovarian cancer (ROC) trials remains controversial. CALYPSO is the first large randomized trial to incorporate CA 125 (OGC criteria) and clinical deterioration in addition to RECIST as criteria for progression evaluation. 976 patients (pts) with platinum-sensitive ROC were randomized to carboplatin-paclitaxel (CP) or carboplatin-liposomal doxorubicin (CD). CT scan and CA 125 were performed every 3 months until progression. At the conclusion of study, the OGC criteria were found to be more sensitive and specific than RECIST for detecting progression. The use of CA 125 in addition to RECIST improved the detection of progression by 23% (p<0.001). The authors concluded that the use of CA 125 in addition to RECIST would be beneficial in the management of ROC patients. However, further studies are needed to determine the clinical utility of CA 125.
time of the analysis, 832 pts (83%) had progressed, of whom 502 (60%) experienced first a radiologic (RECIST) progression, 83 (10%) a cl 5 cycles and had 232 (28%) a CA 125 progression without any evidence of radiologic or clinical progression. RECIST first progression was observed in 67% and 40% of progressing pts with or without measurable disease at inclusion, respectively. In pts with mucinous carcinoma, clinical first progression was more frequent than in other cell types (29% vs. 10%). The benefit of CD arm compared to CP in term of progression-free survival was not influenced by the type of first progression: hazard ratios were 0.84 (95% CI: 0.66-1.00) and 0.85 (95% CI: 0.72-0.98) for CA 125 and RECIST first progression, respectively.

In pts with CA 125 first progression who subsequently progressed according to RECIST, a delay of 2.2 months was observed between the 2 types of progression. However, after CA 125 first progression, the median time to new treatment was 2.0 months, while it was only 0.9 months after RECIST first progression. 80% of patients with CA 125 or RECIST first progression received a subsequent treatment but this percentage dropped to only 57% following clinical progression.

Conclusion: CA 125 performed similar to CT scan in comparing efficacy between the two treatment arms in CALYPSO. Follow-up with CA 125 in addition to imagery and physical exam was not associated with pt overtreatment.

Disclosure: All authors have declared no conflicts of interest.

DESP

NGR-HTNF IN COMBINATION WITH DOXORUBICIN IN PROGRESSIVE OR RECURRENT OVARIAN CANCER


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Background: NGR-HTNF consists of tumor necrosis factor fused with a peptide (NGR) that selectively binds to CD13 expressed on tumor blood vessels. Preclinical synergism that selectively binds to CD13 expressed on tumor blood vessels. Preclinical synergism and clinical trials indicated NGR-HTNF has potential in the treatment of progressive or recurrent ovarian cancer by targeting tumor blood vessels. In addition, the mechanism of action of NGR-HTNF is limited to the tumor, not to normal tissues, minimizing systemic toxicity. In this study, we investigated the combination of NGR-HTNF with doxorubicin in pts with progressive or recurrent ovarian cancer.

Methods: Ovarian cancer patients (pts) who had a treatment-free interval (TFI) either <6 or <12 months after prior chemotherapy were enrolled in this study. NGR-HTNF 0.8 µg/m2 plus doxorubicin 60 mg/m2 was given every 3 weeks. CA 125 levels were measured prior to administration and then every 4 weeks. CA 125 progression was determined by the RECIST criteria. PFS was defined as the time from the first day of protocol treatment until disease progression, death, or last known follow-up.

Results: 25 pts have been enrolled and 17 pts (11 with TFI <6 and 6 with TFI <12) were evaluable. Median TFI from last therapy was 3.9 months (2.5-7.8). Median age was 61 years (34-77). 9/17 (53%) pts had grade 3-4 NGR-HTNF related toxicity. Most common grade 1-2 toxicity was alopecia (41%). Median CA 125 progression was 2.0 months (1.0-4.6). Disease control rate (DCR) was 70% (4 pts with TFI <6 and 2 with TFI <12). There were no grade 3-4 NGR-HTNF related toxicities. Median time to new treatment was 3.8 months (1.0-7.8). Median PFS was 1.4 months (1.0-2.1). CA 125 first progression, the median time to new treatment was 2.0 months, while it was only 0.9 months after RECIST first progression. 80% of patients with CA 125 or RECIST first progression received a subsequent treatment but this percentage dropped to only 57% following clinical progression.

Conclusion: CA 125 performed similar to CT scan in comparing efficacy between the two treatment arms in CALYPSO. Follow-up with CA 125 in addition to imagery and physical exam was not associated with pt overtreatment.

Disclosure: All authors have declared no conflicts of interest.

DESP

TRABECTEDIN HAS A LOW CARDIAC RISK PROFILE: A COMPREHENSIVE SAFETY ANALYSIS

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Introduction: This analysis provides a cross-study evaluation of the cardiac safety of trabectedin (Yondelis®) in clinical trials as monotherapy or in combination with other agents, and during post-marketing experience.

Methods: Cardio events related to trabectedin were retrieved from phase I II and III trials, pharmacovigilance databases, and spontaneous cases since its approval in 2007. LVEF was monitored in combination phase I studies (with doxorubicin or pegylated liposomal doxorubicin, PLD) and in a phase III trial. Besides, the effects of trabectedin on the ECG QT interval were evaluated in a placebo-controlled sequential trial.

Results: Results from 6 single-agent phase I trials showed cardiac AEs in 4/283 pts (1.4%), consisting of Grade (G) 4 cardiac arrest with severe pancytopenia and sepsis in 1 pt, and tachycardia in 3 pts (G1 in 1 and G4 in 2 pts). In 1 phase I combination trials, cardiac AEs were observed in 2/10 pts (2%). In 2 phase II trials, cardiac AEs were observed in 2/15 pts (13%), consisting of G1 sinus tachycardia in a hypertensive pt and G1 ventricular dysfunction. Results from 19 single-agent phase II trials showed cardiac AEs in 17/1132 pts (1.5%), with arrhythmias (tachycardia and palpitations; n=13) as the most common event. In a phase III trial, trabectedin did not prolong the QTc interval in 75 pts; none had AEs suggestive of proarrhythmic potential. During single-agent trabectedin postmarketing experience in >2000 sarcoma pts, only 4 cardiac AEs (2 cardiac arrest, 2 cardiac failure; 0.2%) occurred in pts with pre-existing conditions.

Conclusions: Trabectedin has a low incidence of cardiac events (mainly arrhythmias). Other cardiac events were relatively infrequent and relevant predisposing factors were identified in patients’ baseline characteristics. This extensive data review indicates a low cardiac risk profile.

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PACLITAXEL / CARBOPLATIN VERSUS SINGLE AGENT CARBOPLATIN IN PATIENTS WITH EPITHELIAL OVARIAN CANCER AND CORRELATION TO SERUM MARKER VEGF

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Background and aim: Despite the fact that it is a highly curable disease if diagnosed early, cancer of the ovaries causes more mortality in women each year than all other gynecologic malignancies combined. The superiority of a platinum and Paclitaxel combination regimen over single agent platinum remains the subject of debate. Two randomized trials, ICON-3 and GOG-132, have suggested that single-agent platinum (Carboplatin and Cisplatin, respectively) is equivalent to combinations with Paclitaxel. Overexpression of VEGF by ovarian cancer cells is a major mediator of angiogenesis in this tumor type and serum values may therefore serve as a prognostic tool. The aim of this study is to compare the standard chemotherapy protocol for ovarian carcinoma (Paclitaxel / Carboplatin AUC 5) to single agent Carboplatin AUC 6 as regard the response rate, progression-free survival at 2 years, as well as prognostic value of different factors, namely: age, stage, grade, baseline CA-125 and serum VEGF at presentation.

Patients and methods: This study is a prospective non-randomized study including 90 patients with established diagnosis of epithelial ovarian carcinoma attending Kasr El Ainy Centre of Clinical Oncology, Cairo University, Egypt in the period from January 2006 to December 2007 inclusive. After complete diagnosis and staging work up, the patients received either Paclitaxel 175 mg/m2 followed by Carboplatin AUC 5 (Arm A) or single agent Carboplatin AUC 6 (Arm B) for 6 cycles provided adequate response occurred after 3 cycles as assessed by CA 125 and CT scan. Serum sample was collected at baseline and serum VEGF was measured using ELISA technique, the intensity of the colored product is directly proportional to the concentration of hVEGF present in the original specimen and the absolute value is read from the curve.

Results: At a median follow up of 16.3 months, the median progression free survival (PFS) was 10.8 months with a median value of 23.18 months. About 60 % of patients showed no disease progression at 2 years. Comparing the two arms, the overall response rate was 88 % in arm A versus 82.6 % in arm B (p = 0.771). Mean PFS in arm A was 20.31 ± 2.99 compared to 25.14 ± 2.77 in arm B (p = 0.311) with an odds ratio of 1.7 (95% confidence interval: 0.53 – 5.60). By analyzing the effect of different factors namely: age, performance status, parity, optimal surgery, stage, grade, baseline CA125, serum VEGF >100 pg/ml and treatment received using multivariate analysis; it was found that only stage was an independent prognostic factor. No correlation of either disease stage or outcome.

Conclusion: Single agent Carboplatin is not inferior to Combination chemotherapy with Paclitaxel and Carboplatin regarding response rate and PFS at 2 years. Serum Vascular Endothelial Growth Factor at baseline seems to have no prognostic value with any correlation to either disease stage or outcome.

Discussion: All authors have declared no conflicts of interest.

EVALUATION OF REBOUND ASCITES FOLLOWING DISCONTINUATION OF BEVACIZUMAB IN RECURRENT OVARIAN CANCER

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Background: Bevacizumab (BEV), an anti-VEGF monoclonal antibody, has activity in ovarian cancer, both as a single agent and in combination with chemotherapy. In murine models of ovarian cancer, BEV showed rapid tumor growth inhibition and is a potential anti-angiogenic tool. The aim of this study is to evaluate the frequency of paracentesis following discontinuation of BEV in patients with recurrent ovarian cancer.

Methods: We performed a retrospective electronic medical record review of pts with recurrent ovarian cancer who were treated off-protocol with BEV at MSKCC from Dec 2004 to Jan 2008.

Results: 106 consecutive pts received BEV for recurrent ovarian cancer. The median age was 58 years. Pts had advanced-stage (94% ≥ stage 3) and high-grade (82% grade 3) disease. The median number of chemotherapy regimens prior to BEV was 6 (range 1-15). 30 (28%) had prior intraperitoneal chemotherapy: 23 pts (22%) were platinum-sensitive, 92 pts (88%) received BEV in combination with chemotherapy. 48 pts (45%) had radiographic evidence of ascites prior to commencement of BEV. With BEV treatment 31 pts (65%) with ascites had resolution or improvement in ascites and a further 16 (33%) had stable ascites on follow-up imaging. 4 pts (10%) had increased ascites despite BEV. Of the 14 pts who had required paracentesis for symptomatic ascites (3% of 450 BEV episodes) 12 (88%) were able to discontinue or reduce the frequency of paracentesis. Following discontinuation of BEV (n=76) 18 (24%) had ‘rebound’ ascites on radiographic imaging [8 pts (11%) who had not required paracentesis prior to BEV treatment underwent paracentesis for palliation of symptomatic ascites]. The remaining 58 pts (76%) did not have any increase in the volume of ascites following withdrawal of BEV.

Conclusion: BEV treatment was associated with a reduction in malignant ascites. The majority of pts did not have evidence of “rebound” ascites following withdrawal of BEV treatment. As phase III clinical trials of BEV in ovarian cancer mature, it will be important to confirm this observation with regards to tumor growth following discontinuation of BEV.

Disclosure: C. Aghajanian: Dr Aghajanian receives research funding from Genentech. All other authors have declared no conflicts of interest.

BOWEL OBSTRUCTION IN OVARIAN AND PERITONEAL MALIGNANCY: THE CHRISTIE HOSPITAL EXPERIENCE

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Background: Patients with ovarian and peritoneal malignancy present with bowel obstruction at diagnosis or more commonly at advanced stages. Significant improvements in overall survival and quality of life can be gained in a minority of patient . We conducted a retrospective study of patients with malignant bowel obstruction in patients with malignant bowel obstruction and identify predictive factors that aid selection of patients most likely to derive benefit from palliative surgery and/or chemotherapy.

Method: 7000 inpatient episodes were screened identifying 75 patients admitted with bowel obstruction between 2003-2010. Retrospective case-note data was analysed for clinical outcomes and prognostic/predictive factors.

Results: The median time from diagnosis to inpatient admission with bowel obstruction was 533 days (range 0-3487). The median number of hospitalisations was 1 (range 1-5) with median inpatient stay 28 days (range 2-82). The commonest histology was serous adenocarcinoma (47%), mucinous histology was not observed. The majority of patients had high tumour burden at multiple sites, radiological evidence of serosal disease involving bowel and 41% developed bowel obstruction whilst on chemotherapy. Two-thirds of patients presented with obstructive symptoms (with full resolution in one-third) but one-third reported eradicating bowel habit including diarrhoea. Median survival following the first episode of bowel obstruction was 77 days (range 3-519) with no significant annual variation (p = 0.14). There was no difference in survival between patients who underwent palliative surgery or chemotherapy (p = 0.29).

Conclusion: Overall survival in patients with malignant bowel obstruction is poor and has not changed over the last decade. Judicious selection of patients for surgery and/or chemotherapy can double survival and is particularly relevant for chemo-naive patients at first presentation. Analyses of the economic implications of therapy and predictive factors of outcomes will be presented.

Discussion: All authors have declared no conflicts of interest.

CLINICAL FEATURES AND OUTCOMES IN EPITHELIAL OVARIAN CANCER (OC) ASSOCIATED WITH BRCA1 AND BRCA2 MUTATIONS IN POLISH POPULATION – AN OBSERVATIONAL STUDY

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Background: Epithelial ovarian cancer is the second most common gynaecologic malignancy. Highly penetrant cancer-predisposing genes such as BRCA1 and BRCA2 account for 10%-14% of all OC in the Polish population. Aim: The main aim of the study was to analyse the impact of BRCA1 and BRCA2 mutations on OC outcomes. Patients and methods: 438 OC pts were screened for BRCA mutations at one cancer institute in Poland. Forty five out of all 57 BRCA positive pts were eligible for survival analyses. The clinical course of 45 BRCA positive OC pts and 90 case-matched 1:2 BRCA negative OC pts was compared. Study endpoints were: Overall Survival (OS), Treatment Free Interval (TFI), Recurrence Free Survival (RFS), platinum sensitivity and response rate (RR). Additionally the type of recurrence, second primary cancers and Ca125 dynamics were analysed.

Results: A BRCA mutation was found in 57 of 438 (13%) OC pts. The most common were 5382insC (6.4%) and 3007delG (26.3%). A second malignancy was diagnosed in 33% of BRCA positive pts vs 5.5% of BRCA negative pts. BRCA positive pts had a statistically significant longer median OS than BRCA negative pts (p=0.0324). BRCA
positive pts were significantly more likely to present with liver or spleen metastases as first site of recurrence. Further data analysis is ongoing at the time of abstract submission.

Disclosure: All authors have declared no conflicts of interest.

**BRC1 GERMINE MUTATIONS ARE ASSOCIATED WITH GYNECOLOGIC SARCOMAS**
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**Introduction:** gynecologic sarcomas comprise less than 1% of all gynecologic malignancies and represent very heterogeneous group. Very little is known about etiology of these malignancies, the only documented etiologic factor in less then 25% of these tumors is previous pelvic irradiation. Some cases of uterine sarcoma have been linked to tamoxifen adjuvant treatment of breast cancer. Here we report that BRC1A germline mutations are associated with gynecologic sarcomas.

**Purpose:** to determine the role of BRC1A mutations in gynecologic sarcomas

**Methods:** During the last seven years 13 patients diagnosed with gynecologic sarcoma were seen at Genetic Counseling Unit at Cancer Center and Institute of Oncology in Warsaw. All the patients were offered genetic testing, after genetic counseling and after obtaining from all of them written informed consent. The consent protocol was accepted by the local ethical committee. BRC1A analysis was performed on DNA from the peripheral blood leukocytes. The mutations in BRC1A were detected using DHPLC and sequencing of exons 2, 5, 11 O, 11 P and 20, because in these exons the mutations are found most frequently in Polish population.

**Results:** Among 14 patients with gynecologic sarcomas, we found 5 (35%) patients carrying germline mutation in the BRC1A gene.

<table>
<thead>
<tr>
<th>patient ID number</th>
<th>diagnosis</th>
<th>age at diagnosis (years)</th>
<th>mutation in BRC1A</th>
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</thead>
<tbody>
<tr>
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<td>carcinosarcoma oviducti, adenocarcinoma</td>
<td>67</td>
<td>T300G</td>
</tr>
<tr>
<td>DN310</td>
<td>carcinosarcoma ovidii serosos G3 ovarii, carcinosarcoma stromale uteri</td>
<td>54</td>
<td>5382insG</td>
</tr>
<tr>
<td>DN1430</td>
<td>carcinosarcoma uteri, adenocarcinoma uteri, carcinosarcoma fusocellulare vulvae</td>
<td>52</td>
<td>5382insC</td>
</tr>
<tr>
<td>DN1659</td>
<td>carcinosarcoma vaginale, adenocarcinoma G3, carcinosarcoma stromale</td>
<td>75</td>
<td>5382insC</td>
</tr>
<tr>
<td>AN249</td>
<td></td>
<td>60</td>
<td>3875del11ins.7</td>
</tr>
</tbody>
</table>

**Conclusions:** In women diagnosed with gynecologic sarcoma screening for the germline mutations in the BRC1A gene is important.

Disclosure: All authors have declared no conflicts of interest.

**CYP3A4*1B (RS2740574) GENE POLYMORPHISM HAS PROGNOSTIC VALUE IN OVARIAN CANCER**
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**Introduction:** CYP3A4 encodes an enzyme critical for oxidation of oestrogens and its inhibition results in higher circulating oestrogen levels. In the CYP3A4*1B (rs2740574) variant, GG genotype has been associated with increased risk of developing invasive ovarian cancer. There is no available information about the prognostic value of this genotype in these patients (pts). The aim of this study is to evaluate the CYP3A4*1B gene polymorphism as prognostic factor in pts with epithelial ovarian cancer.

**Material and methods:** Retrospective cohort study. Exposure was defined as CYP3A4*1B G/G genotype. CYP3A4*1B gene polymorphism was analyzed by polymerase chain reaction of DNA samples from peripheral blood of pts with epithelial ovarian cancer treated in Instituto Portugues de Oncologia, Porto, Portugal, between June 1992 and November 2009. The following confounding factors were considered: FIGO stage, volume of residual disease after cytoreductive surgery, histologic subtype, histologic grade, age and malignant ascites. Survival analysis was performed with Kaplan-Meier method. A p value < 0.05 was considered significant.

**Results:** There were 185 DNA blood samples of pts with epithelial ovarian cancer available for analysis. Median age was 53 years (range: 22 – 80). No statistically significant differences were found regarding the association of CYP3A4*1B genetic polymorphism for any of the confounding factors analyzed between exposure groups (p > 0.05). The GG/AG genotype had no prognostic value when all histologic subtypes were analyzed. Pts with serous carcinoma histologic subtype carrying the GG/AG genotype had significantly decreased overall survival (median OS for GG/AG genotype of 50.0 months and median OS for AA genotype of 109 months; p = 0.005).

**Conclusion:** Our results suggest that CYP3A4*1B GG genotype may be a prognostic factor in pts with ovarian serous carcinoma. Further studies may help to define the role of this genetic variant in the pharmacogenomic profile of epithelial ovarian cancer.

Disclosure: All authors have declared no conflicts of interest.

**CARMA3: A NOVEL TARGET FOR CANCER THERAPY**
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CARMA3 (CARD domain and MAGUK domain-containing protein 3) is a novel scaffold protein. It is ubiquitously expressed and plays an indispensable role in several G protein-coupled receptor-induced Nuclear Factor kappa B (NF-kappaB) activation. NF-kappaB is an important transcription factor, which has been proven to induce tumorigenesis in many types of cancers, such as ovarian cancer. Ovarian cancer is the 4th most common type of cancer among women in the United States. The diagnostic marker of ovarian cancer is lysophosphatidic acid (LPA), which is a GPCR ligand and significantly elevated in 90% of ovarian cancer patients. Moreover, LPA receptors are aberrantly up-regulated in ovarian cancer patients. In our previous studies, we have demonstrated that CARMA3 is required in LPA-induced NF-kappaB activation in mouse embryonic fibroblast cells. In this study, we further investigated whether the CARMA3 plays an indispensable role in LPA-induced NF-kappaB activation in ovarian cancer cells, which promotes ovarian cancer cell migration and invasion. Using CARMA3 shRNA, we knockdowned the protein expression level of CARMA3 in ovarian cancer cell lines. Consistent with previous reports, we found that down-regulation of CARMA3 ablated LPA-induced IKK activity and NF-kappaB activation in ovarian cancer cells. In addition, in vitro transwell migration and matrigel invasion assays demonstrated that CARMA3 shRNA significantly impaired LPA-induced ovarian cancer cell motility and invasiveness. Together, our results provide the evidence that CARMA3 serve as a critical regulator in LPA-induced, NF-kappaB-mediated ovarian cancer migration and invasion. Therefore, CARMA3 may be a potential novel cancer therapy target for many types of malignancies, such as ovarian cancer.

Disclosure: All authors have declared no conflicts of interest.

**LONG-TERM FOLLOW-UP OF A PHASE II FEASIBILITY STUDY OF REGIONAL HYPERTERMHERIA ADDED TO CHEMORADIOTHERAPY IN ADVANCED CERVICAL CANCER**
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**Introduction:** In advanced cervical cancer, cisplatin-containing chemotherapy (CT) and regional hyperthermia (HT) added to radiotherapy (RT) have each been proven superior to RT alone in randomized controlled trials. We previously reported on the feasibility of combining all three modalities (triple therapy) in 68 patients in three simultaneous phase II trials in the Netherlands, Norway, and the USA. Here we present long-term follow-up of the Dutch patients in this prospective study.

**Methods:** Eligible patients had FIGO stage IB-IVA cervical cancer not previously treated, good performance status and were able to tolerate cisplatin treatment. The study was IRB approved and all patients gave written informed consent. Triple therapy consisted of 5 weeks of external radiotherapy (45-50 Gy) and brachytherapy (minimum of 70 Gy bio-equivalent dose, depending on technique used, to point A), with weekly cisplatin 40 mg/m2 and weekly HT during external RT.

**Results:** Thirty-six patients were included in the Dutch study, with stages IIB (n=26), IIIb (n=9) and IVA (n=1). Complete remission was achieved in 32 patients (88%). After a median follow-up of 62 months (range, 6-97 m), twelve patients have died of disease and one is alive with disease. Five year disease-free survival is 66% (95% CI: 52 – 84) and overall survival is 74% (95% CI: 60 – 90).

Disclosure: All authors have declared no conflicts of interest.

**PHASE II STUDY OF NEOADJUVANT CHEMOTHERAPY WITH CPT-11 AND NEDAPLATIN (CPT-11/NDP) FOR STAGE IB2/II CERVIX (JAPANESE GYNECOLOGIC ONCOLOGY GROUP 1065 STUDY)**

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**Patients and methods:** Twenty five patients (pts) with recurrent or metastatic cervical cancer were enrolled between March 2005 to April 2007. All pts had measurable disease, ECOG PS 0-2, adequate renal, liver and bone marrow functions. No prior chemotherapy. 6-8 cycles of weekly paclitaxel 90mg/m2 (1h IV infusion) D1,18,5 and paclitaxel AUC 4 (30 min IV infusion) D1 every four weeks with premedication administered 30-60 min (IV Dexamethasone 20 mg, IV Diphenhydramine 50 mg and IV cimetidine 300 mg). Radiotherapy (external or brachytherapy) or surgery were allowed if indicated. Response was assessed every 2 cycles and toxicity every cycle, patients showed an objective response (CR, PR or SD) will continue to 8 cycles.

**Results:** All patients were evaluable for response, toxicity and survival. The median age was 54 years (range 45-65), Median PS 1. The main location of disease was local recurrence in 20 pts (80%), lung metastasis in 6 pts (24%) and PALN metastasis in 2 pts (8%). A total of 193 cycles were administered with a median of 7 cycles/patient with no dose reduction. The ORR was 68% (CR 20%, PR 48%), 6 pts (24%) had SD and 2 pts (8%) had PD. Median time to progression 17 months and median overall survival 22 months. No WHO G3 or G4 toxicities were noted. Three pts (12%) developed G2 neuropathy and G2 neuropathy was reported in 4 pts (16%).

**Conclusion:** Weekly Paclitaxel and paclitaxel showed significant efficacy and mild toxicity as first line treatment for patients with recurrent or metastatic cervical cancer.

Disclosure: All authors have declared no conflicts of interest.

**CHEMOTHERAPY USING GEMCITABINE (G) and CISPLATIN (C) in recurrent and metastatic squamous cell carcinoma of the cervix**

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**Background:** Genticibine shown activity in locally advanced, recurrent or metastatic squamous cell carcinoma of the cervix (ASCO 1996, 2000, 2001).

**Aim of the study:** to access efficacy, safety, time to progression, and overall survival in patients with recurrent or metastatic squamous cell carcinoma of the cervix.

**Methods:** Patients (pts) with recurrent or metastatic squamous cell carcinoma of the cervix, ECOG performance status [less than or equal to] 1, no prior chemotherapy, measurable disease, adequate renal and liver function, good bone marrow reserve, and informed consent, All pts received G 1250 mg/m2 in 30 min on d1, 8 and C70 mg/m2 in 60 min on d 1, every 21 day, for six cycles.

**Results:** 64 patients, median age 58 (33-70) years, were enrolled in the study, 42 with recurrent disease and 22 with metastatic disease. The objective response were 46.0%, four pts achieved complete response, (with one pathologic complete response), 22 pts partial response, 26 stable diseases and 12 progressive diseases. Grade 3-4 toxicity was: anemia (12%), neutropenia (5%), thrombocytopenia (5%), asthenia (12%), and nausea (12%). The time to progression was 7, 2 months; the median survival was 12 months.

**Conclusion:** GC show efficacy and good toxicity profile in locally advanced and recurrent squamous cell carcinoma of the cervix.

Disclosure: All authors have declared no conflicts of interest.
EGFR MUTATION STATUS AND THE EFFICACY OF GEFTINIB IN COMBINATION WITH PACLITAXEL AND CARBOPLATIN AS NEOADJUVANT TREATMENT IN LOCALLY ADVANCED CANCER OF CERVIX: A STUDY FROM EASTERN INDIA

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Purpose: To study the incidence of EGFR mutation (exon 19-21) in locally advanced cervical cancer and assess whether geftinib, in combination with paclitaxel + carboplatin, leads to better outcomes in patients with EGFR mutation. Also to study the response rates of paclitaxel / carboplatin as neoadjuvant treatment in locally advanced cervical cancer.

Materials and methods: From Jan 2008 to April 2010, 108 patients of inoperable cancer cervix (Stage Ib - II only) were prospectively evaluated for EGFR mutations (exon 19-21) and were randomised to receive paclitaxel / carboplatin with geftinib (for mutation +ve patients) and without geftinib (for mutation -ve patients). EGFR mutation, response to treatment and conversion to operability after receiving neoadjuvant chemotherapy were assessed. The patients who were still inoperable after this treatment were offered chemoradiation.

Results: 80/108 patients (30.5%) were positive for EGFR mutation. 58/78 who received paclitaxel/carboplatin/geftinib had a more than partial response to treatment giving response rate of 64.1%. 20/78 (25.6%) patients had a stable disease while 8/70 (11.4%) patients had a progressive disease. 29/50 patients who were EGFR mutation +ve had a response to paclitaxel+carboplatin/geftinib giving a response rate of 83.3%. This was significantly higher (P<0.001) compared with mutation -ve patients. Only 1.30 (0.03%) patients in this subgroup had a progressive disease. 20/25 (80%) patients in mutation +ve group and 10/20 (50%) patients in mutation -ve group (P=0.02).

Inference: Approximately 1/3rd of cervical cancer patients were +ve for EGFR mutations. When given geftinib in combination with chemotherapy they had a significantly higher response rate and conversion to operability. Also that paclitaxel and carboplatin is an effective neoadjuvant regimen with a response rate of 60% high conversion to operability.

Disclosure: All authors have declared no conflicts of interest.

A PHASE II TRIAL OF PACLITAXEL PLUS DOXORUBICIN PLUS CARBOPLATIN IN PATIENTS WITH INTERMEDIATE RISK, HIGH RISK, OR RECURRENT ENDOMETRIAL CANCER: A JAPAN ENDOMETRIAL CANCER STUDY GROUP TRIAL

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Objective: Although 40% of women with endometrial cancer still have a disease recurrence and/or progression after surgical treatment, the optimal neoadjuvant chemotherapy remains to be elucidated. This study evaluated the efficacy of paclitaxel plus doxorubicin plus carboplatin in women with intermediate to high risk of recurrence.

Materials and methods: 76 patients were treated with paclitaxel (150 mg/m2 day 1), doxorubicin (60 mg/m2 day 1) plus carboplatin (AUC 5 day 2) every 21 days for six cycles. The other eligibility criteria included preserved organ function, aged 20 – 75, and no prior chemotherapy. Response to treatment were assessed. The primary endpoint was treatment effectiveness and the secondary endpoints included efficacy and safety. EGFR mutation and EGFR expression were assessed before and after chemotherapy.

Results: The overall response rate was 76.9% (40/52 pts). Grade 3/4 adverse effect included leukopenia (84.6%), neutropenia (98.0%), anemia (65.4%), and thrombocytopenia (34.6%). Neuronal death and nausea (11.5%). No grade included leukopenia (84.6%), neutropenia (98.0%), anemia (65.4%) and thrombocytopenia (34.6%).

Inference: Combination TAC chemotherapy is well tolerated with minimum term adverse effects and conversion to operability was assessed. The patients who were still inoperable after this treatment were offered chemoradiation.

Disclosure: All authors have declared no conflicts of interest.

INCIDENCE OF SECOND MALIGNANCIES (SM) IN THE TREATMENT FIELD FOLLOWING PELVIC RADIOTHERAPY (RT): A CASE-CONTROL STUDY: FROM SOUTH EAST WALES (SEW)

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Objective: To examine the incidence and characteristics of SM occurring within 10 years of RT in SEW.

Materials and methods: SM in the first 10 years following RT in SEW were compared with a group of controls. Controls were from the general population of SEW. Follow-up was achieved by linkage to hospital records. Significant levels were determined using the Mantel Haenszel chi squared tests. 95% CIs were calculated.

Results: There were 1375 cases and 6140 controls with a mean follow up of 9.4 and 10.6 years, respectively. The rate of SM was not different between the two groups (7.0% and 6.1%, respectively; p=0.218). However, there was a trend towards significance for pelvic SM with less events in cases (1.6% and 2.4%, respectively; p=0.073). Whereas rate of extra-pelvic SM was significantly higher in cases (5.7% and 2.9%, respectively; p=0.002). Finally, the rate of haematological SM was the same between the two groups (0.5% and 0.6%).

Conclusion: Further studies are required to further confirm this findings and identify risk factors for the development of SM after RT. These studies could help in identifying patients at risk and in the development of novel treatments to prevent SM.
INTRA-ARTERIAL CHEMOTHERAPY IN COMPLEX TREATMENT OF CERVIX CANCER STAGE II B

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Background: We conducted a study of combined intra-arterial methotrexate, 5-fluorouracil, Cisplatin for cervical cancer stage IIb.

Patients and methods: Patients with cervical cancer stage IIb were included in this study. Methotrexate, 5-fluorouracil and cisplatin were given as a 48-72 hour infusion with hydration as neoadjuvant chemotherapy. Patients received 2 courses of intra-arterial chemotherapy. After that if in our patients we got resorption of parametral infiltration we performed radical hysterectomy type II.

Results: 87 patients were entered through the two courses of intra-arterial chemotherapy. The dose-limiting toxicities were leukocytopenia, neutrocytopenia and alopecia. Grade 3/4 leukocytopenia and alopecia were observed in 46 (53%) and 15 (17%) of 87 patients. Tumor responses included 17 complete responses, 65 partial responses and 4 stabilization. The overall response rate was 95.4% (83 of 87) (95% confidence interval 60.3% to 100%). After intra-arterial chemotherapy in 72 cases we performed radical hysterectomy.

Conclusion: Neoadjuvant intra-arterial chemotherapy in complex treatment of cervix cancer makes radical hysterectomy in patients with stage IIb possible.

Disclosure: All authors have declared no conflicts of interest.

PHASE II STUDY OF DOCETAXEL AND CARBOPLATIN AS FIRST LINE CHEMOTHERAPY IN OVARIAN CANCER

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Objectives: It was open level, prospective, multicentre study designed to evaluate the efficacy and safety profile of docetaxel (Taxotere®) and carboplatin in patients with ovarian cancer.

Materials and methods: Patients with ovarian cancer were enrolled by the Ovarian Cancer Study Group (OCSTUD), Bangladesh. Docetaxel (60 mg/m2) and carboplatin (AUC 5) were given at 3 weeks intervals for up to 4-6 cycles to all patients. Clinical response was assessed by symptoms, detection of residual tumor on abdominal and vaginal examination, and by CA-125 levels, ultrasonography, CT scan and/or MRI prior to receiving therapy (baseline). All patients were assessed regularly for potential adverse events by NCI-CTC criteria (v2).

Results: The study was conducted during 2000-2008 on 41 patients. The overall response rate for the study was 90%. The result is given in a chart below:

<table>
<thead>
<tr>
<th>Staging</th>
<th>CR</th>
<th>PR</th>
<th>NR</th>
<th>Total</th>
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<td>1</td>
</tr>
<tr>
<td>Stage II</td>
<td>15</td>
<td>6</td>
<td>0</td>
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</tr>
<tr>
<td>Stage III</td>
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<td>4</td>
<td>1</td>
<td>12</td>
</tr>
<tr>
<td>Stage IV</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>6</td>
</tr>
</tbody>
</table>

Among the patients, complete response was seen in 24 patients; partial response was seen in 12 patients and no-response was observed in 4 patients. All 24 responders are clinically free of disease and the CA-125 level decreased to normal value (<35 U/ml) after the end of 4-6 cycles of chemotherapy. One patient (2.4%) discontinued treatment due to neurotoxicity. Grade 1 and 2 neutropenia was seen in 3 (7.5%) and 4 (9.7%) patients respectively. Grade 3 neutropenia was observed in 3 (7.5%) patients and grade 3 thrombocytopenia in 2 (3.3%). Non-hematologic toxicity was not observed in this study.

Conclusions: Our study indicates that docetaxel and carboplatin combination therapy is feasible and efficacious in the treatment of ovarian cancer as first-line chemotherapy, with a detectable and manageable toxicity profile.

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