8038 POSTER

Oxaliplatin-based hyperthermic intraperitoneal chemotherapy (HIPEC) in primary or recurrent epithelial ovarian cancer: a pilot study of 31 patients

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Aims: To evaluate feasibility, morbidity and toxicity of oxaliplatin-based hyperthermic intraperitoneal chemotherapy (HIPEC) associated to cytoreductive surgery in peritoneal carcinomatosis from primary or recurrent epithelial ovarian cancer.
Method: 31 patients (mean age, 57 years) underwent this procedure as consolidation of primary therapy (n = 19) or for relapsing disease (n = 12). Complete surgical cytoreduction defined as absence of macroscopic residu (CC0) was obtained to all patients and associated with oxaliplatin-based HIPEC 360 mg/m^2 (n = 28) or 460 mg/m^2 (n = 3) with an open procedure according to coliseum technic at a temperature of 42º. The data were analyzed retrospectively and complications grade III/IV according NCI classification from day 0 to day 60 were recorded.
Results: Median peritoneal carcinomatosis index was 2.7. Mean overall duration of surgery was 352 (105−614) minutes, mean intensive care unit (ICU) stay was 2 days (range 1−4) and median hospital stay was 11 days (range, 6−87). Nine patients (29%) had grade 3 toxicity requiring reintervention in 5 patients (16%), invasive procedure in 2 patients, new hospitalization for 4 patients and return to ICU for 3 patients. No grade IV toxicity occured. In the group of primary advanced ovarian cancer, median PFS is 13.2 months 1 year DFS is 59.3%. For relapsing patients, median PFS is 14.3 months and 1 year DFS is 54.4%.
Conclusion: Cytoreductive surgery with HIPEC using oxaliplatin is feasible and safe so much for recurrent or primary ovarian cancer. It's evaluation is ongoing with major drugs used in EOC as cisplatin, carboplatin.

8039 POSTER

Weekly cisplatin (wCDDP) with concurrent radiotherapy (cRT) in locally advanced cervical cancer (LACC) patients (pts): a monoinstitutional experience

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Background: Patients affected by LACC (stage Ib2-IV) could be equally treated with neoadjuvant CT followed by surgery or with radical cCTRT. The standard CT is based on wCDDP given concurrently to RT. The present report is aimed to describe the toxicities and the clinical outcomes of pts treated with wCDDP plus RT for LACC.
Patients and Methods: Between May 2001 and July 2008, we treated a consecutive series of 32 patients. The treatment consisted of whole pelvic external RT (plus RT boost in patients with parametrial invasion) and brachytherapy (B) in selected cases, with good clinical response to external RT. CDDP was given weekly at the dose of 40 mg/sqm for a total of 4−6 courses, starting on day 1 of RT. Acute and late toxicities were evaluated according to NCIC and LENT-SOMA criteria respectively.
Results: Major pts characteristics were: median age 52.5 yrs (range 30−74); median PS 0 (range 0−2); FIGO stage: Ib2 in 5 pts, IIb in 12, IIIa in 1, IIIb in 9, IVa in 2, IVb (without visceral metastasis) in 3. Histology: squamous in 27 pts and adenocarcinoma in 5. Pts treated with external RT alone received a median total dose of 63 Gy (range 45−67), which was 79.5 Gy (range 45−88.6) in pts receiving also B. The treatment was completed in 84% of the pts. The median number of delivered CT courses was 5 (range 1−8): one patient received only 1 course of wCDDP due to gastrointestinal toxicity. Out of the 166 administered courses of wCDDP, 3 were at reduced dose due to patient compliance, 6 due to non-hematological toxicities, 5 due to age and 3 courses were delayed due to haematological toxicity. Major acute toxicities consisted of grade 3 neutropenia (1 pt), grade 3 diarrhoea (1 pt), grade 3 constipation (1 pt). No grade late toxicity 3−4 was observed. The observed response rate was 94% (24 CR and 6 PR). After a median follow-up of 28.5 mos, the 2-year OS and DFS were 92.9% and 84% respectively, with median OS and DFS not reached.
Conclusions: Our experience of cCTRT in LACC appears superimposable to the literature data and confirms the good activity and tolerability of this combined CT-RT treatment.

8040 POSTER

Feasibility and outcome of weekly carboplatin and paclitaxel in an unselected population of pre-treated patients with epithelial ovarian cancer

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Background: Combination 3 weekly carboplatin (C) and paclitaxel (P) is a well-established regimen in epithelial ovarian cancer (EOC). Alternative schedules of P administration have been studied. Dosing C and P at weekly intervals has resulted in response rates between 38−83% and median PFS of 11.5−14 months in pre-treated patients with EOC. We have conducted a retrospective review of our experience of dose-dense continuous weekly carboplatin AUC2 and paclitaxel 70 mg/m^2 (D1,8,15) to investigate its tolerability and efficacy in an unselected population of pre-treated patients with EOC.
Method: Pre-treated patients with EOC, fallopian tube and primary peritoneal cancer receiving dose-dense C and P between 01/01/2004−01/04/2009 in St James's Institute of Oncology were identified from electronic patient records.
Results: 36 pre-treated patients were identified with a median age of 65.5 (range 46−80). The median number of prior therapies was 2 (range 1−9). Of the 36 patients, 21 (58.3%) had received no platinum in the preceding 6 months; 38.9% were taxane naïve; 36.1% were platinum resistant; 2.8% were taxane resistant and 5.6% were resistant to both. Grade 3/4 anaemia, neutropenia and thrombocytopenia occurred in 13.9%, 27.7% and 2.8% of patients respectively. The only grade 3/4 non-haematological toxicity was fatigue (5.6%). Grade $\leqslant$2 fatigue, nausea and neuropathy occurred in 54.6%, 19.5% and 19.4% of patients respectively. Of the 36 patients, 8 (29.6%) failed to complete 2 cycles, 4 due to allergic reactions, 3 due to progressive disease and 1 died of non cancer-related death. 13 (36%) completed 3−4 cycles and 13 (36%) completed 5−6 cycles. The majority, 28 (70.4%), 20 (55.6%), 24 (66.7%) had no dose reductions, dose omissions (DO) or dose delays (DD) respectively. 12 (33.2%) had 1−2 DO, 4(11.1%) had $\geqslant$3 DO, 6 (16.6%) had 1−2 DD and 6 (16.6%) had $\geqslant$3 DD. The administered dose density was 83.7% for C and 82.7% for P. Radiological and CA125 response rate was 59.3% (16/27) and 87.5% (21/24) respectively. Median PFS was 7.4 (95% CI, 3.5−11.3) months and overall survival was 14 (95% CI, 9.6−18.3) months.
Conclusion: Continuous weekly dose-dense C and P was well tolerated and active in pre-treated patients with EOC.

8041 POSTER

Preliminary results of whole-body hyperthermia in combination with oxaliplatin in patients with platinum-resistant/refractory ovarian cancer

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Background: The combination of hyperthermic treatment with chemotherapy can produced a wide spectrum of molecular and cellular effects: improving permeability of cellular membranes and penetration of drugs into tumour cells, increasing DNA damage, inhibiting the mechanisms of tumour cell reparation, induction of primary protein damage. Hyperthermia was shown to improve the efficacy chemotherapy by changing the expression of apoptosis genes p53, Bcl-2 and Bax, and also to stimulate caspase activation. Oxaliplatin belongs to a new class of platinum derivatives of the 3rd generation and does not present with cross resistance. Therefore, the use of oxaliplatin in combination with whole-body hyperthermia may be one of promising trends in platinum-resistant/refractory ovarian cancer management.
Materials and Methods: From May 2006 through April 2009 our randomized study included 20 patients with platinum-resistant/refractory ovarian cancer. The follow-up period was 1 to 20 months (median 10.1 months). The patients were randomly assigned to two arms: the control arm (n = 10; i.v. oxaliplatin 135 mg/m^2 every 4 weeks) and the study arm (n = 10; i.v. oxaliplatin 135 mg/m^2 in the combination with whole-body hyperthermia and hyperglycemia (41.8−42.0°C, duration of the treatment 160 min), a course every 4 weeks). The control arm included patients aged 37.3 to 59.6 years (median 48.4), the study arm – 40.8 to 54.8 years (median 49.7). Second cancer was found in one patient of the study arm after two courses, and for that reason she was excluded from the study. Two patients are now in the induction phase.
Results: A total of 34 whole-body hyperthermia courses were administered (an average of 4 courses per patient). The overall response rate (the sum of partial response rate and stable disease rate) after 4 courses was 22.2%