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%

in the control arm and 34.9% in the study arm. The median progression-free survival were 1.9 months and 3.6 months (p = 0.04) respectively. The most common complications (CTCAE) in the study arm were grade 1 peripheral sensory neuropathy (2 patients), grade 1 fever (2 courses). The complications were not clinically significant.
Conclusion: Our study confirmed that the whole-body hyperthermia in combination with oxaliplatin is an active salvage treatment option in patients with platinum-resistant/refractory ovarian cancer. In view of the treatment results obtained, a randomized trial has started using combinations of oxaliplatin with other drugs in combination with whole-body hyperthermia.

8042 POSTER

Cisplatin plus topotecan in advanced/recurrent cervical cancer – experience from a single institution

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Cervical cancer (CC) is one of the most common gynaecological cancers and is the leading cause of cancer deaths among women in some developing countries. Advanced CC still remains an incurable disease with poor overall survival and available chemotherapy regimens have little impact. The combination of cisplatin plus topotecan (CT) was the first to demonstrate a survival advantage over cisplatin alone in this clinical setting. We propose a review of this regimen in our Institution.
The authors present the results of 33 patients (pts) with advanced, recurrent or persistent CC, who were unsuitable for curative treatment with surgery and/or concurrent chemoradiotherapy, treated with CT (cisplatin 50 mg/m^2 D1, topotecan 0.75 mg/m^2 D1−3, 3qw) between June/2006 and September/2008. Pts were evaluated for tumour response, time to tumour progression (TTP), overall survival (OS) and safety of treatment.
CT regimen was first-line treatment in 72.7% and second-line, or more, treatment in 27.2% of the pts.
Median age at diagnosis was 46 years. At diagnosis fifteen pts (45%) were in FIGO stage II and two pts were in stage IVB. Patterns of recurrence were: pelvic (24.2%), distant site (21.2%), lomboaortic lymph nodes (18.2%), a combination of these (36.4%). A total of 132 CT cycles were administrated with a median of 4 cycles per patient (range:1 to 6).
The clinical benefit was 39.4% (6% complete response, 6% partial response, 27.2% stable disease) and progression of disease occurred in 39.4%. Seven pts (21.2%) were not evaluated due to CT withdrawal. Median TTP, estimated since the beginning of CT, was 4.3 months. Median OS was 13.7 months. There was a trend to increased survival, but with no statistical significance, in the following subgroups: first-line treatment, adenocarcinoma histology, pelvic or lymph nodes recurrence. Most frequent toxicities were: anemia (66.7%), neutropenia (66.7%), nausea (51.5%), emesis (36.3%), asthenia (36.3%), infection (30%), sensitive neuropathy (27.2%). Main grade 3−4 adverse events occurred were: neutropenia (33.3%), febrile neutropenia (18.2%) and infection (18.2%). Two pts (6%) had grade 5 infection.
Our experience, being a retrospective analysis and with few pts, revealed a median TTP similar to the literature but a median OS slightly superior, which may confirm the effectiveness of this regimen outside clinical trial. We advise about serious haematological adverse events that were frequent, including two toxic-related deaths.

8043 POSTER

Small bowel volume in postoperative IMRT for endometiral cancer and acute lower GI toxicity: separate loops vs. bowel space

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Background: Previous studies have demonstrated a correlation between the volume of small bowel(VSB) irradiated and acute lower GI toxicity. Specifically, pelvic IMRT was shown to decrease the VSB irradiated. The small bowel may be delineated as a bowel space, or separate bowel loops. In this study, we investigated whether the VSB irradiated correlates with acute lower GI toxicity when the small bowel is delineated with the 2 different approaches. In addition, our clinical outcome is reported.
Methods and Materials: 32 endometrial cancer patients were treated with postoperative pelvic IMRT between 7/27/2004 and 11/28/2007. They were staged as FIGO IB-IVA. The prescription dose delivered was 48.2±3.1 Gy. Dose volume histograms were used to assess doses to the VSB irradiated as separate loops(SB), or as a space including the outer boundaries of the small bowel loops(BS). The VSB at various dose levels(prescription dose, 40, 30, 20, 10, and 5 Gy) in cc, or a fraction of the total VSB were recorded. Acute lower GI toxcitiy score per RTOG criteria was obtained during treatment. The relationship between VSB and this score was assessed for each dose level.
Results: After a median follow up of 19.6 months, the median survival was 40.9 months. The local–regional control was 81.2%, PFS was 62.5%, DMFS was 68.8%. 31.5% of the patients experienced grade 2 lower GI toxicity, while there was no $\geqslant$ grade 3 acute toxicity. This compared favorably to patients treated with 3D CRT, 45% of whom developed grade 2 acute lower GI toxicity. The % VSB receiving 100% or 90% of the prescription dose when it was delineated as SB or BS were not statistically different. However, BS > SB in actual volume for all dose levels ($p < 0.05$). The irradiated VSB did not correlate with acute lower GI toxicity when the small bowel was delineated as either SB or BS (toxicity grade 0 vs. 1 vs. 2, 0 vs. 1+2, or 0+1 vs. 2, p ns). On average, an increase up to 10 cc of the VSB delineated as SB or BS receiving 90% or 100% of the total dose was observed in patients who had grade 1 or 2 acute toxicity vs. those who did not develop any.
Conclusion: Our postoperative pelvic IMRT experience demonstrated an excellent acute lower GI toxicity profile. However, the VSB, delineated as separate loops or a bowel space, did not correlate with acute lower GI toxicity due to the large degree of variation in VSB observed. The SB and BS's actual volume is significantly different, and one common definition needs to be established in future investigations.

8044 POSTER

Comparison of conventional and CT-based planning for intracavitary brachytherapy for cervical cancer for target volume coverage and organs at risk doses

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Background: To compare intracavitary brachytherapy (ICBT) planning methods for cervical cancer, based on either orthogonal radiographs (conventional plan) or CT sections (CT plan); the comparison focused on target volume coverage and dose volume analysis of organs at risk (OARs), by representing point doses defined by the International Commission on Radiation Units and Measurement (ICRU) and dose volume histograms (DVHs) from 3D planning.
Materials and Methods: We analyzed the clinical and dosimetric data for 62 conventional and CT-based ICBT plans. The gross tumor volume (GTV), clinical target volume (CTV) and OARs were contoured on the CT-plan. Point A, and 38 ICRU rectal and bladder points were defined on reconstructed CT images. The DVHs of tumor volumes and OARs were created for each application. The volumes were calculated for the dose matrices receiving 50% (3.5 Gy), 100% (7 Gy), 150% (10.5 Gy), and 200% (14 Gy) of the point-A doses obtained from the conventional plan and the 3D CT plan. The extent of tumor coverage within the prescribed 7 Gy isodose volume obtained from orthogonal films and CT were compared. To compare the respective ICRU rectal and bladder point doses with the 3D volume dose, the minimum dose value in the 2.0 cc and 5.0 cc volumes receiving the highest dose (D2 and D5) the was determined from DVHs for bladder, rectum. A comparison of the conventional plan and CT-plan was performed using the Wilcoxon signed-ranks test for all doses and volumes. P values less than 0.05 were considered statistically significant.
Results: Patients were categorized on the basis of whether the >95% isodose line of the point-A prescription dose encompassed the CTV (group 1, n = 24) or not (group 2, n = 38). The mean GTV and CTV (8.1 cc and 20.6 cc) were smaller in group 1 than in group 2 (24.7 cc and 48.4 cc) ($P < 0.001$). The mean percentage of GTV and CTV coverage with the 7 Gy isodose was 93.1% and 88.2% for all patients, and decreased with increasing tumor size and stage. The mean D2 and D5 rectum doses were 1.66 and 1.42 times higher than the corresponding ICRU point doses, and the mean D2 and D5 bladder doses were 1.51 and 1.28 times higher. The differences between the ICRU dose and the D2 and D5 doses were significantly higher in group 2 than in group 1 for the bladder, but not for the rectum.
Conclusions: The CT-plan is superior to the conventional plan in target volume coverage and appropriate evaluation of OAR doses, as the conventional plan overestimates tumor doses and underestimates OAR doses.