

Five-year disease specific survival (DSS) rates were as follows: All pts (N=110) 47%, mixed type pathology 78%, pure UPSC 39% (p<0.0064), stage 1&2 72%, stage 3&4 13% (p<10-6), pts receiving adjuvant CT 48%, no CT 46% (p=0.82), pts receiving RT 50%, no RT 43% (p=0.23).

5 yr disease free survival rates were as follows: all pts 42%, mixed type 66%, pure UPSC 36% (p=0.015), stage 1&2 60%, stage 3&4 15% (p<10-5), pts receiving CT 35%, no CT 47% (NS), pts receiving RT 53%, no RT 28% (p=0.016). In a Cox regression analysis for DSS including pathology, stage, adjuvant CT and RT: stage [HR 3.9 (CI 2.1-7.2) p=0.0001] and pathology subtype [HR 2.4 (CI 1.02-5.9) p=0.046] highly significant. Adjuvant CT not significant. RT was marginally significant [HR 0.6 (CI 0.3-1.02) p=0.059]. RT reduced pelvic recurrence rate (p=0.078).

Conclusions:

1. Stage of disease and pathology subtype are significant prognostic factors.
2. Results do not support any benefit from adjuvant chemotherapy.
3. For radiotherapy a trend of improvement in local control and disease free survival was observed.

920

POSTER

A randomized phase III trial of pelvic radiotherapy versus cisplatin-based combined chemotherapy in patients with intermediate risk endometrial carcinoma: a Japan Gynecologic Oncology Group study

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Background: Optimal adjuvant therapy for intermediate risk endometrial cancer patients is poorly defined.

Materials and Methods: A Japan Gynecologic Oncology Group conducted a multi-center randomized Phase III trial of pelvic radiotherapy (PRT) vs. cyclophosphamide-doxorubicin-CDDP (CAP) chemotherapy in women with intermediate risk endometrial carcinoma. As eligibility criteria, after initial surgical staging including TAH&BSO with pelvic and/or paraaortic lymphadenectomy, no residual tumor was required. Pathological examination showed >1/2 myometrial invasion, adenocarcinoma with any grade, but without central pathology review. PRT arm employed 50 Gray (Gy) in 20-25 fractions. CAP arm consisted of cyclophosphamide (333 mg/m²), doxorubicin (40 mg/m²) and cisplatin (50 mg/m²) every 4 weeks for 3 or more courses. Study endpoints were progression-free survival (PFS), overall survival (OS), and incidence and types of toxicity.

Results: 475 pts were entered from 1/1994 to 12/2000, but 41 were ineligible due to ≤ 1/2 myometrial invasion, histology of sarcoma, rapid progression after entry. Because of the different biological behavior of non-endometrioid histology, 49 patients were excluded. Of the 385 evaluable endometrioid adenocarcinoma, 193 were to receive PRT arm and 192, CAP arm. Patient characteristics were mostly well balanced including median age, co-morbidity, and type of hysterectomy. Postsurgical stages were roughly 60% of Ic, 25% of II and IIIa and 10% of IIIC. Tumor grades were G1 55%, G2 30%, and G3 15%. Pelvic lymphnode metastases were 10.9% in PRT arm and 11.5% in CAP arm. Both treatment arms were completed up to 95%. Median total dose was 50 Gy in PRT and 1,309 (c)/120(a)/180(p) mg/m² in CAP arm with median 3 courses. Adverse effects were not significantly increased in the CAP arm (4.7%), compared to PRT arm (1.6%) (p=0.077). Median follow-up was 60.8 months (range 2.2-60.8). Response and Survival: There were no statistically significant differences in PFS and OS between the 2 regimens for all 374 pts. The PFS of PRT and CAP arms was 84.0% and 82.1%, and the OS of PRT and CAP arms was 85.9% and 87.1%, respectively. In a subgroup analysis, among 184 pts with low intermediate risk as stage pT1c (except >70 yo., or G3), the PFS of PRT and CAP arms was 94.3% and 88.6%, and the OS of PRT and CAP arms was 95.0% and 91.7%, respectively. Among 119 pts with high intermediate risk as stage Ic (>70 yo., or G3), II and IIIa (positive cytology), CAP arm significantly improved PFS (p=0.03) and OS (p=0.01) when compared with PRT. Recurrence rate in each PRT and CAP arm was 15.1%, 16.5%, respectively, with 30% pelvic and 70% extrapelvic recurrent sites.

Conclusions: Adjuvant cisplatin-based combined chemotherapy might have potential as an alternative to radiotherapy for intermediate risk endometrial cancer, such as stage Ic, II, or IIIa (positive cytology).

921

POSTER

Cytoreductive surgery plus intraperitoneal hyperthermic perfusion in the treatment of recurrent epithelial ovarian cancer

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Background: The optimal salvage therapy for recurrent ovarian carcinoma has not been clearly established. We investigated the effect of an aggressive approach consisting of cytoreductive surgery plus hyperthermic intraperitoneal drug delivery followed by adjuvant systemic chemotherapy.

Patients and methods: 34 patients with recurrent ovarian carcinoma were treated by cytoreductive surgery plus intraperitoneal hyperthermic perfusion. Median patient age was 53 years (range, 30-67) and mean follow-up was 17.4 months (range, 0.3-36.0). All patients had been pretreated by surgery and cisplatin/Taxol-based regimens. The intraperitoneal hyperthermic perfusion was performed with the open Coliseum technique, using a preheated polysaline perfusate containing mitomycin (20 mg/m²) plus Mitoxantron (20 mg/m²) through a heart-lung pump (mean flow of 1500 mL/min) for 60 min in the hyperthermic phase (42°C). At the first 3 post-operative days 5-Fluorouracil 500 mg/m² was applied intraperitoneally with a dwell time of 23 hours. 3 cycles of adjuvant systemic chemotherapy were given using Topotecan 1.0 mg/m² d1-4 and Gemcitabine 1000 mg/m² d1, 8 with a treatment free interval of 14 days.

Results: 37 procedure have been performed in 34 pts. Two-year overall survival was 68% with 80% for pts. with complete cytoreduction (CC0 /1). Median time to progression was 14.5 months. Treatment-related morbidity, 30 days – mortality and acute toxicity (grade III+IV) rates were 10.8%, 0% and 6%, respectively.

Conclusion: Complete cytoreduction plus hyperthermic peritoneal perfusion plus adjuvant chemotherapy seems to be an effective treatment for recurrent ovarian carcinoma. Morbidity and mortality rates are in line with other major oncologic operations.

922

POSTER

Human leukocyte antigen (HLA) a2 as a negative prognostic factor in ovarian cancer patients

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Background: We have shown recently that HLA-A2 frequency and ovarian cancer mortality rates are higher in Scandinavia than in the rest of Europe. Furthermore we could define a selected group of ovarian cancer with high frequency of HLA-A2 phenotype, related to clinical parameters.

Material and methods: A total of 125 patients with epithelial ovarian cancer were recorded by age, histology, stage and treatment. Group 1 included 28 cases of advanced ovarian cancer, which were analyzed for HLA-A, -B, -C and -DRB1 expression by PCR/sequence-specific oligonucleotide hybridization procedure (PCR/SSOP). HLA frequencies from healthy Swedish and other European countries bone marrow donors (Bone Marrow Donors Worldwide, Leiden, The Netherlands) were used as comparison. Group 2 (n=97) represented patients consecutively admitted at our department during 1995. So far, HLA-A2 PCR/SSOP typing was performed on DNA extracted from paraffin-embedded tissue specimens in 35 patients.

Results: Group 1: The HLA-A2 genotype was found in 46% of the patients (healthy Swedish population-35%); among patients with serous adenocarcinomas the frequency was even higher. A3 allele was poorly represented (12% vs. 17%). Seven patients were homozygotes for A2 allele (25%), which is two times the healthy Swedish population (12%), and three times the median frequency in Europe (8%). We also observed an increase in several A2, B and DRB1 haplotypes. Median overall survival among HLA-A2 positive patients was 2.6 years (min 1.5 – max 6.2) versus 3.1 in non-A2 patients (min 1.3 – max 8.7).

Group 2: So far, 35 patients have been tested, and 21 were found positive for HLA-A2 phenotype (60%). Serous adenocarcinomas were found in an excess of A2 positive (67%) vs. 43% of A2 negative patients. After five years, 70% stage I-II and 20% stage III-IV patients were alive. None of the A2 positive patients was alive compared to 50% of the A2 negatives.

Conclusions: Presence of the HLA-A2 allele seems to be correlated with poor prognosis in ovarian cancer patients. HLA-A2 homozygotes and some HLA-A2-B and -DRB1 haplotypes are higher expressed than in healthy individuals. Ongoing investigations are launched to study HLA-A2 as a

prognostic factor and to analyze further possible genetic associations between HLA-A2 and ovarian cancer.

923

POSTER

Positron Emission Tomography (PET) with 2-[18F]-Deoxyglucose for detecting recurrence of epithelial ovarian cancer

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Background: EOC is a common gynaecological neoplasm. Recurrence is seen in up to 70% of cases. PET is a novel type of imaging study that works on the principle of detecting increased glucose uptake in neoplastic tissues.

Methods: PET scans were performed in patients pre-treated for EOC, whom during surveillance showed increasing CA-125 serum levels, or suspicious lesions detected by CT scan. Sensitivity, specificity and positive or negative predictive values were calculated for PET, CT scan and CA-125 antigen.

Results: From February 2002 to December 2004, 21 patients were included, mean age 56.2 years. Seventeen had increased CA-125 antigen (80.9%), suspicious lesions on CT scan (57.1%), both (42.8%) and positive PET in 18/21 patients (85.7%). Liver, lungs and lymph nodes were more commonly detected as positive anatomic sites. Average number anatomic sites 2.0±0.9. Mean size lesion 2.6±1.8 cm, mean SUV-max: 5.4±2.4. Quantitative analysis for PET, CT scan and CA-125 antigen demonstrated sensitivity 100%, 62%, 88%; specificity 60%, 60%, 50%; positive predictive value 88%, 83%, 88%; and negative predictive value 100%, 33%, 50%, respectively.

Conclusions: PET has elevated capability for detecting recurrence of EOC; the utility is limited for tumor size. Peritoneal carcinomatosis is detected in low frequency through PET, but this metabolic study identifies several anatomic sites with more frequency than other studies. It is necessary to create a consensus about clinical indications for PET scan in ovarian cancer.

924

POSTER

Radiotherapy vs. radiotherapy+chemotherapy of advanced cervical cancer: regression of tumour, early and late sequelae, relapses of disease and 3-years survival (the third phase)

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Background: A prospective randomised study of 184 patients with advanced cervical cancer (st. IIb – IVa) treated with either radio-therapy alone (RT group), or radiotherapy+chemotherapy (RT+CH group) was started at the beginning of May, 2002 and the last patient of this series was treated in March 2003. (Project N° 1683 of Ministry of Science, Technology and Development of Rep. Serbia-II Phase of study). The aim of this study is to show comparison of treatment results of advanced cervical cancer using either RT or RT+CT.

Material and methods: Clinical material of 184 cervical cancers was randomised in two groups: RT – 94 (51.1%) pts and RT+CT – 90 (48.9%) pts. Distribution of patients by stages (FIGO), histopathological type (and gradus) and age was very similar in both groups. Treatment regimes were: RT group: – EBT – 46 Gy/22 fractions, 2 parallel opposite fields without central Pb shields+HDR brachytherapy – 5×7 Gy/A (Ut. tube+2 vag. ovoids)

RT+CT group: RT as first group+CT using cisplatin (5 cycles during radiotherapy, once a week).

Results: Partial regression of cervical tumour immediately after the end of the treatment was 86% of pts. for RT group vs. 83% of the pts in RT+CT group. Early complications (diarrhoea, dysuria, abdominal pains, nausea, vomiting, leucopenia, thrombocytopenia, anemia, febricity) were noted in 37.5% pts of RT group vs. in 58.3% of the pts of RT+CT group (I Phase of study). Corrected actuarial 3-years survival (RT vs. RT+CT): st. IIb – 78% vs. 84%; st. IIIB – 55% vs. 60%; total – 68% vs. 76%. Late sequelae were noted as follows (French – Italian glossary): RT group vs. RT+CT group: G1 – 23% vs. 20%; G2 – 29% vs. 30%; G3+4 – 14% vs. 22%, all of late seq. – 66% vs. 72%. Relapses were: (RT vs. RT+CT): local

(regional) 5% vs. 3%, metastatic 12% vs. 13%, local and metastatic 4% vs. 6%, total 21% vs. 22%.

Conclusion: There was no benefit of RT+CT vs. RT alone in treatment of locally advanced cervical cancer. We shall follow-up treatment outcome and compare results of these two groups of treated patients next 5 years.

925

POSTER

Impact of epidermal growth factor receptor (EGFR) expression in disease free survival and rate of pelvic recurrences in advanced cervix cancer patients treated with chemoradiotherapy

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Background: Concurrent chemoradiotherapy has improved the prognosis in advanced cervix cancer patients. Nevertheless at least the half of the patients die from the progression of the disease.

Objective: To analyze the prognosis significance of the EGFR expression by means of disease free survival (DFS) in patients with advanced cervix carcinoma treated with concomitant chemoradiotherapy.

Methods: 112 biopsies of patients with advanced cervical cancer (11 IB2-IIA, 25 IIB, 63 IIIB, 13 IVA) were analyzed prospectively to detect EGFR expression using an immunohistochemical method. EGFR expression was graded as 0 if <10% of tumor cells were stained; +, 10–30%; ++, 30–70%; and +++, >70%. Tumors with grades ++ and +++ were considered as EGFR positive.

Patients received pelvic radiotherapy, brachytherapy and concurrent chemotherapy based in two protocols: (i) 47 women: Tegafur (800 mg/day per os) until three months after the end of radiotherapy; (ii) 63 women: 6 cycles of weekly cisplatin 40 mg/m² (46 of them also received Tegafur, same schedule). Only 2 patients not received chemotherapy.

Results: 32 (28.6%) biopsies were EGFR negative and 80 (71.4%) EGFR positive. The mean time follow-up to the relapse was 12 months (median: 9.5 months, r 2–40), and for patients without failure was 48 months (median: 40 months, r 5–121). EGFR expression did not correlate with clinicopathological characteristics as age, EOG, histology, tumor size, FIGO stage and lymph node involvement by CT. EGFR positive tumors were associated significantly with a higher rate of pelvic recurrences (Chi-Square p = 0.006). On multivariate analysis, EGFR positive tumors had a significant decrease in DFS (p = 0.03, HR 2.25, CI: 1.05–4.81). Cisplatin therapy increased DFS of all our patients (p = 0.03, HR 0.49 CI: 0.25–0.95), but only was significantly in patients with EGFR negative tumors (p = 0.05).

Conclusion: EGFR expression was correlated significantly with a decrease in DFS and an higher rate of pelvic recurrences. The poor prognosis of these tumors EGFR positive could result in an increase of the radioresistance and a reduced sensitivity to cisplatin.

926

POSTER

Phase II Austrian AGO study of pegylated liposomal doxorubicin and gemcitabine in platinum-refractory and resistant ovarian cancer following previous platinum-taxane therapy

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Platinum-resistance is a significant problem in ovarian cancer. The Austrian AGO conducted a phase II trial combining PEG-liposomal doxorubicin (PEG-L-DXR) and gemcitabine (GEM).

Material and methods: Between 2002 and 2004, 31 patients (median age 59 years) have been included in a AGO phase II study: PEG-L-DXR 30 mg/m² on day 1 and GEM 650 mg/m² on days 1+8 every 4 weeks×6 cycles. 30 patients are evaluable for analysis. All patients had previously received platinum and a taxane and had platinum-resistant or refractory disease.

Results: Six patients achieved a complete (20%) and 4 a partial remission (33% overall response rate). 13% additional patients had stable disease. The mean and median progression-free survival was 9.6 and 3.8 months, respectively. The median overall survival was 15.8 months. Toxicity was