Gynaecological Cancer

Oral presentations (Mon, 24 Sep, 10.45−12.15)
Gynaecological cancer (1)

5000 ORAL

Quality of life after radiotherapy for endometrial cancer: first results from the randomized PORTEC-2 trial

R.A. Nout[1], H. Putter[2], I.M. Schultz[3], J.J. Jobsen[4], L.C.H.M. Lutgens[5], E.M. van der Steen-Banasik[6], J.W. Mens[7], A. Slot[8], V.T. Smit[9], C.L. Creutzberg[1]. *[1]Leiden University Medical Center, Clinical Oncology, Leiden, The Netherlands; [2]Leiden University Medical Center, Biostatistics, Leiden, The Netherlands; [3]University Medical Center Utrecht, Dept of Radiation Oncology, Utrecht, The Netherlands; [4]Medisch Spectrum Twente, Dept of Radiotherapy, Enschede, The Netherlands; [5]MAASTtricht Radiation Oncology Clinic, MAASTtricht Radiation Oncology Clinic, Maastricht, The Netherlands; [6]Radiotherapy Institute Arnhem, Radiotherapy Institute Arnhem, Arnhem, The Netherlands; [7]Daniel den Hoed Cancer Center, Dept of Radiation Oncology, Rotterdam, The Netherlands; [8]Radiotherapy Institute Friesland, Radiotherapy Institute Friesland, Leeuwarden, The Netherlands; [9]Leiden University Medical Center, Pathology, Leiden, The Netherlands*

Background: Reported data on quality of life (QoL) after treatment for endometrial cancer have suggested that patients who undergo pelvic radiation (RT) have lower role functioning and higher diarrhoea and fatigue scores than the general population, but similar social functioning and global health/QoL scores. In the PORTEC-2 trial, patients with intermediate risk endometrial carcinoma were randomly assigned to external beam pelvic RT or vaginal brachytherapy, and QoL was evaluated using EORTC QLQ C-30 and subscales for bladder and bowel symptoms from PR25 and sexual symptoms from OV28.
Material and Methods: PORTEC-2 included 427 randomized patients, of whom 345 (81%) were evaluable for QoL. QoL questionnaires were filled in before RT (baseline), after RT, and 6−12 monthly until 5 years. Patient accrual closed October 2006. Two-year QoL outcomes were analysed.
Results: At baseline, after surgery, global QoL was at the lowest level and did not differ significantly between the treatment groups. From 6 to 12 months QoL gradually increased in both treatment arms, to reach a plateau between 12 and 24 months. From 6 months onwards global QoL scores were significantly higher in the vaginal brachytherapy group ($p < 0.01$). Symptom ratings showed significantly less acute bowel symptoms (e.g. diarrhoea) and less fatigue in the vaginal brachytherapy group (both $p < 0.001$), and this difference remained significant during further follow-up. Reported sexual symptoms, such as reduced sexual interest and vaginal dryness, did not differ between the treatment groups, $p = 0.36$.
Conclusions: Global QoL after radiotherapy for endometrial cancer was lowest at baseline, and increased thereafter to plateau after 12 months. From 6 months onwards patients in the vaginal brachytherapy group reported significantly better global QoL, and significantly less bowel symptoms and fatigue. This QoL benefit is an important factor to take into account when balancing risks and benefits of pelvic radiation and vaginal brachytherapy. Final outcome of the PORTEC-2 trial is awaited and will evaluate the efficacy of vaginal brachytherapy for intermediate risk endometrial carcinoma, and determine whether pelvic radiation can be replaced by brachytherapy to ensure local control with less morbidity and better quality of life. Updated results will be presented.

5001 ORAL

Intraperitoneal administration of the trifunctional antibody catumaxomab for treatment of malignant ascites due to ovarian carcinoma: Results of a phase II/III study

S. Parsons[1], E. Kutarska[2], P. Koralewski[3], M. Gore[4], P. Wimberger[5], A. Burges[6], M.A. Sroehlein[7], H. Friccius-Quecke[8], M. Jaeger[9], M.M. Heiss[7]. *[1]City Hospital Nottingham, Department of Surgery, Nottingham, United Kingdom; [2]Centre of Oncology of Lubelska Land, Department of Gynaecologic Oncology, Lublin, Poland; [3]L. Rydygier's Voievodship Specialistic Hospital, Department of Chemotherapy, Krakow, Poland; [4]The Royal Marsden Hospital, Gynaecology Unit Medical Oncology and Drug Development, London, United Kingdom; [5]University of Duisburg-Essen, Department for Obstetrics and Gynecology, Essen, Germany; [6]Ludwig-Maximilians University Munich Groβ hadern, Department for Obstetrics and Gynecology, Munich, Germany; [7]Klinikum Koeln-Merheim, Department of Surgery, Cologne, Germany; [8]Fresenius Biotech GmbH, Clinical Development, Munich, Germany; [9]TRION Research GmbH, Clinical Research, Martinsried, Germany*

Background: Malignant ascites in ovarian carcinoma patients (pts.) is associated with a poor prognosis and reduced quality of life. Catumaxomab (anti-EpCAM x anti-CD3) is known to effectively eliminate tumor cells within ascites by simultaneously activating T cells and Fc gamma-receptor I/III cells and redirecting them against the tumor.
Materials and Methods: A total of 129 ovarian cancer pts. with recurrent symptomatic malignant ascites containing EpCAM+ tumor cells were enrolled in the study; 85 were randomized to treatment with catumaxomab (paracentesis plus 4 intraperitoneal infusions of 10, 20, 50 and 150 µg within 11 days), and 44 to the control arm (paracentesis alone). The primary endpoint was puncture free survival (time to first need for paracentesis after treatment or time to death, which ever occurred first).
Results: Pts. characteristics were well balanced in both arms. Median puncture free survival was 52 days for catumaxomab vs. 11 days for control ($p < 0.0001$) whereas the median time to first need for paracentesis was 71 days vs. 11 days ($p < 0.0001$). There was a pronounced decrease of tumor cell load accompanied by a distinct increase of leukocyte count during catumaxomab treatment within the ascites fluid. Overall and progression free survival data suggest longer survival for catumaxomab-treated pts. compared to control. 11 months after the last patient entered the trial, 9 patients of the catumaxomab group and one patient of the control group who also received catumaxomab as a cross-over option, are still alive. Detailed survival analysis will be presented. The most frequent AEs were symptoms related to cytokine release (pyrexia, nausea, vomiting). These were generally mild to moderate in intensity, and fully reversible. Transient increases in liver enzymes and bilirubin, and transient WBC abnormalities such as leukocytosis, neutrophilia and a decrease in peripheral lymphocytes were regularly observed as abnormal laboratory values but rarely considered clinically significant.
Conclusions: Intraperitoneal therapy with catumaxomab resulted in a significant and clinically relevant improvement of puncture-free survival time, decrease of tumor cell load, and prolonged time to first need for puncture compared to the control group of best available treatment. The safety profile reflects catumaxomab's mode of action and reveals a low and acceptable toxicity.

5002 ORAL

Results from a Phase II randomized, placebo-controlled, double-blind trial suggest improved PFS with the addition of pertuzumab to gemcitabine in patients with platinum-resistant ovarian, fallopian tube, or primary peritoneal cancer

S. Makhija[1], D. Glenn[2], F. Ueland[3], D. Dizon[4], V. Paton[5], C.Y. Lin[6], L. Amler[7], M. Sliwkowski[8], A. Strauss[9], U. Matulonis[10]. *[1]Univ of Alabama Birmingham, ObGyn, Birmingham, USA; [2]Sharp Rees-Stealy Medical Group, ObGyn, San Diego, USA; [3]UK HealthCare Markey Cancer Center, ObGyn, Lexington, USA; [4]Women and Infants Hospital, Program in Women's Oncology, Providence, USA; [5]Genentech Incorporated, Oncology Clinical Science, South San Francisco, USA; [6]Genentech Incorporated, Biostatistics – Oncology, South San Francisco, USA; [7]Genentech Incorporated, Oncology Diagnostic, South San Francisco, USA; [8]Genentech Incorporated, Translational Oncology, South San Francisco, USA; [9]Roche Diagnostics, GmbH, Penzberg, Germany; [10]Dana Farber Cancer Institute, Gynecology Oncology, Boston, USA*

Background: Pertuzumab is a humanized monoclonal antibody that blocks HER2's ability to heterodimerize with HER/ErbB receptors. As a single agent, pertuzumab has demonstrated clinical activity in relapsed/refractory epithelial ovarian cancer (EOC). Since platinum-resistant EOC remains a

difficult disease to treat, this phase II study was conducted to determine if the addition of pertuzumab to gemcitabine would improve clinical activity.
Methods: Patients with platinum-resistant EOC (including ovarian, fallopian tube, or primary peritoneal cancer) who had received up to one prior treatment for platinum-resistant disease were randomized to gemcitabine 800 mg/m^2 on Days 1 and 8 of a 21-day cycle plus pertuzumab or placebo. Pertuzumab was given as an 840 mg initial dose followed by 420 mg IV every 3 weeks. Tumor response was assessed by RECIST every 6 weeks. The primary endpoint was progression-free survival (PFS).
Results: One hundred thirty patients (65 patients per treatment cohort) were treated. Clinical characteristics were balanced between the treatment groups. The adjusted hazard ratio for PFS was 0.67 (95% CI: 0.43–1.02), p = 0.06 in favor of pertuzumab + gemcitabine. The median PFS was 3.0 months (range: 0−8.7 months) vs. 2.6 months (range: 0−9+), and the PFS rate at 4 months was 49% vs. 34% in the pertuzumab + gemcitabine and placebo + gemcitabine arms, respectively. The most common AEs increased in the pertuzumab-treated patients were fatigue, nausea, diarrhea, back pain, Grade 3−4 neutropenia, rash, headache, stomatitis, epistaxis, and rhinorrhea. CHF was reported in one patient in the pertuzumab + gemcitabine cohort. The left ventricular ejection fraction results were similar between treatment arms. One patient who received pertuzumab + gemcitabine experienced a fatal adverse event (hemolytic-uremic syndrome).
Conclusions: These data suggest that pertuzumab may add activity to gemcitabine as reflected by improvements in PFS in patients with platinum-resistant ovarian, primary peritoneal, or fallopian tube cancer. Clinical outcomes by biomarker analysis and overall survival data will be presented.

5003 ORAL

A randomised phase II study of carboplatin plus liposomal doxorubicin (CLD) vs carboplatin plus paclitaxel (CP) in potentially platinum sensitive ovarian cancer patients. A Hellenic Cooperative Oncology Group study

H. Linardou, D. Bafaloukos, A. Bamias, I. Xanthakis, H.P. Kalofonos, G. Aravantinos, P. Kosmidis, E. Briasoulis, G. Klouvas, A.M. Dimopoulos. *Hellenic Cooperative Oncology Group (HeCOG), Data Office, Athens, Greece*

Background: Platinum-based combinations are standard 2nd-line treatment for platinum-sensitive ovarian cancer. Liposomal doxorubicin is effective as monotherapy and combined with carboplatin in recent phase II studies. We evaluated CLD vs CP in platinum-sensitive ovarian cancer patients.
Materials and Methods: Patients with recurrent ovarian cancer, at least 6 months after platinum-based therapy, with measurable disease or elevated CA-125, entered this randomized phase II study. Patients received 6 cycles of CP (carboplatin AUC5 + paclitaxel 175 mg/m^2, d1q21) or CLD (carboplatin AUC5 + liposomal doxorubicin 45 mg/m^2, d1q28).
Results: From 11/1999 to 01/2006, 204 patients were randomized; 189 eligible patients are included in the analysis (CP 96, CLD 93). Median age was 63 years (37−89) and median PS 0. Platinum-free interval (PFI) was >12 months in 65% of patients (median 16.5 months). A median of 6 cycles per patient was delivered. The number of patients completing treatment did not differ between groups, however, the discontinuation rate due to toxicity was higher in CP (13.5% vs 3%, p = 0.016). Paclitaxel median RDI was 0.96, LD 0.92 and carboplatin cumulative dose was similar in both groups. Overall response rate was not statistically different between groups: CP 58% vs CLD 51% p = 0.309 (CR 34% for CP vs 23% for CLD, PR 24% for CP vs 28% for CLD). At median follow-up of 43.6 months there was no statistical difference in TTP or overall survival: median TTP was 10.8 months (95% CI 9.3−12.3) for CP vs 11.7 (95% CI 10.9−12.6) for CLD, while overall survival was 30.4 months (95% CI 23.4−37.4) for CP vs 24.4 (95% CI 21.1−27.6) for CLD. No toxic deaths were recorded in either arm. Neutropenia was the commonest grade 3−4 toxicity (CP 30% vs CLD 35%). Severe thrombocytopenia was more frequent in CLD (CP 2% vs CLD 12% p = 0.016); severe neurotoxicity and alopecia were significantly higher in CP (CP 7% vs CLD 0%, p = 0.029 and CP 83% vs CLD 11% p = 0.003, respectively). Supportive care parameters did not differ significantly between groups, except of RBC transfusion rate being higher in CLD (CP 3% vs CLD 14% p = 0.015). Cox regression analysis revealed PS and PFI as important individual prognostic factors for TTP and OS.
Conclusions: Carboplatin plus LD is highly effective with acceptable toxicity profile, similar to carboplatin plus paclitaxel in 2nd line treatment of platinum-sensitive ovarian cancer patients and should be considered as a treatment option for this patient population.

5004 ORAL

Survival risks and benefits with adjuvant therapy for endometrial cancer: systematic review and meta-analysis

P.G.S. Cornes[1], N. Johnson[2]. *[1]Bristol Haematology & Oncology Centre, Oncology, Bristol, United Kingdom; [2]Bath – Royal United Hospital, Gynaecology Oncology, Bath, United Kingdom*

Background: The contribution of adjuvant post-operative pelvic external beam radiotherapy (EBRT) to disease free survival (DFS) in early endometrial cancer is well established but no convincing overall survival (OS) benefit has been shown.
Materials and Methods: meta-analysis of randomised controlled trials (RCT).
Results: 2431 patients' data were accessed from RCTs. Patients were stratified into three risk groups for recurrence: low (1524 patients), intermediate (557 patients), and high (350 patients). Pelvic EBRT affected survival odds ratios (OR) differently in the three groups: low OR 0.71 (95% CI 0.52−0.96); intermediate OR 0.97 (95% CI 0.69−1.35); high OR 1.76 (95% CI 1.07−2.89). Not all patients died from cancer progression. For high risk cancers EBRT reduces the chance of death by cancer OR 0.59 (95% CI 0.30−1.17). Pelvic EBRT reduced pelvic recurrence in all groups; OR 0.27 (95% CI 0.08−2.51).
Conclusions: Pelvic EBRT is very effective in reducing pelvic relapse of early endometrial cancer but is either harmful or ineffective in improving overall survival in women with low or intermediate risk cancers. In contrast, for high risk cancers EBRT reduces the absolute chance of death by cancer by approximately 10%.

5005 ORAL

Randomized, multicenter, 2-dose-level, open-label, phase IIa study with the intraperitoneally infused trifunctional bispecific antibody catumaxomab (anti-EpCAM x anti-CD3) to select the better dose level in platinum refractory epithelial ovarian cancer patients

S. Loibl[1], J. Pfisterer[2], P. Wimberger[3], C. Kurzeder[4], A. Du Bois[5], J. Sehouli[6], A. Belau[7], N. Burchardi[8], I. Vergote[9], U. Wagner[3]. *[1]Klinik der J.W. Goethe Universität, Obstetrics and Gynaecology, Frankfurt/Main, Germany; [2]University Mannheim, Obstetrics and Gynaecology, Mannheim, Germany; [3]University Marburg, Obstetrics and Gynaecology, Marburg, Germany; [4]University Ulm, Obstetrics and Gynaecology, Ulm, Germany; [5]HSK Wiesbaden, Obstetrics and Gynaecology, Wiesbaden, Germany; [6]Charite Berlin, Obstetrics and Gynaecology, Berlin, Germany; [7]University Greifswald, Obstetrics and Gynaecology, Greifswald, Germany; [8]KKS Marburg, Obstetrics and Gynaecology, Marburg, Germany; [9]University Leuven, Obstetrics and Gynaecology, Leuven, Belgium*

Background: The trifunctional antibody catumaxomab specifically binds EpCAM+ tumor cells, CD3+ T lymphocytes and accessory cells via the Fcγ RI/III thereby inducing a tumor specific cell mediated cytotoxicity in vitro and in vivo. This study was conducted to evaluate efficacy and safety of two different regimens of catumaxomab.
Methods: Women with platinum-refractory (progressing during or <6 mos. after the last platinum containing regimen) epithelial ovarian cancer and measurable recurrent disease were randomized to receive either 10–10–10–10 μg or 10–20–50–100 μg of catumaxomab over 6 h i.p on days 0, 3, 7 and 10.
Results: 45 pts. were entered (22 high dose [HD]-arm, 23 low dose [LD]-arm). Both groups were well balanced concerning ECOG-performance score, with a median age of 65.6 y. in the HD- and 57.6 y. in the LD-arm and with a median diameter of measurable lesions of 90 mm in the HD- and 104 mm in the LD-arm. Based on the AEs, changes in laboratory parameters and other safety variables observed in the safety population in the course of this study, the accumulated safety experience is consistent with the key features of the mode of action of catumaxomab. Their intensity on median level was mostly mild to moderate. A clinical benefit was detectable in 27.3% of pts. for the HD- (1PR/5SD) and 8.7% of pts. for the LD-arm (2SD). After a median follow-up of 4.96 months, the median overall survival time was 182 d for the HD- and 114 d for the LD-arm.
Conclusion: The results demonstrate that catumaxomab is safe with acceptable toxicity when administered as a sequence of 4 IP infusions at 10, 20, 50 and 100 μg. A modest dose effect is observed for the higher doses of catumaxomab.