Conclusions: Weekly administration of topotecan shows no substantial difference in endpoints of effectiveness compared to conventional dosing, but is associated with a significantly lower likelihood of severe hematological toxicity. Weekly topotecan should be considered as a possible treatment alternative in women with platinum-resistant ovarian cancer.

8003 ORAL

Bevacizumab in heavily pre-treated ovarian cancer patients and the predictive value of serum VEGF

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Background: Ovarian cancer remains the leading cause of death in gynecologic malignancy in the western world and therefore new treatment strategies are urgently needed. Bevacizumab, a recombinant humanized monoclonal antibody against VEGF (Vascular Endothelial Growth Factor), has shown antitumor activity in several cancer types including ovarian cancer with acceptable toxicity. The purpose of the present study was to evaluate treatment with single agent bevacizumab in heavily pre-treated advanced epithelial ovarian cancer patients, expressed by RR (response rate), PFS (progression free survival) and OS (overall survival).
Furthermore we aimed at defining the possible prognostic and predictive value of serum VEGF analyzed in blood samples by each cycle.
Material and Methods: Thirty-eight patients with advanced ovarian cancer were treated with bevacizumab every three weeks, 10 mg/kg. Serum VEGF concentration was analyzed before treatment and in every cycle by ELISA technique (Quantikine ELISA kit no: 1190951, R & D Systems, Minneapolis, USA).
Results: The median number of prior regimens was five and the median number of bevacizumab treatment cycles was four. Thirteen patients were still under treatment at the time of analysis. Nine out of 33 evaluable patients (27%) showed response by CA 125 according to the modified GCIG criteria's. Median PFS was 6.3 months (95% CI; 3.5−17.7) and median OS was 8.2 months (95% CI; 5.0−9.2).
Two patients suffered from gastrointestinal perforation during treatment, one from ileo-vaginal fistula and two were diagnosed with trombo-embolia and transient cerebral ischemia.
All patients decreased their serum VEGF concentration after the first cycle of treatment with a mean of 89%. There was a significant difference in VEGF level between responders and no responders ($p = 0.004$). The CA 125 response rate was 63% for VEGF <275 pg/ml whereas 14% for VEGF > 275 pg/ml ($p = 0.009$). This cut off was chosen as the 25% percentile for all serum VEGF analyses. No association with clinicopathological parameters was demonstrated and no significant difference in PFS or OS was shown according to low/high serum VEGF.
Conclusion: Single agent bevacizumab therapy demonstrated activity in heavily pre-treated ovarian cancer women with a CA 125 response rate of 27%. Gastrointestinal perforations were identified in 5% of patients. Baseline serum VEGF levels seem to have predictive importance for the effect of bevacizumab treatment.

8004 ORAL

Effectiveness of multiple lines of chemotherapy in platinum-resistant ovarian cancer: the Christie experience

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Background: Platinum-resistant ovarian cancer defined by a treatment-free interval of less than 6 months is characterised by chemoresistance with response rates in the range of 10−20% with non-platinum compounds. Higher response rates have been reported with combination chemotherapy from non-randomised studies although the effect on survival is uncertain. However the efficacy of multiple lines of chemotherapy in patients with platinum-resistant ovarian cancer remains to be determined. Crucially, is it appropriate to consider palliative chemotherapy in patients that have progressed through previous chemotherapy. Here we present data on over 150 patients treated sequentially with single-agent non-platinum compounds and combination chemotherapy.
Methods: Patients with platinum-resistant ovarian cancer treated with chemotherapy were extracted from the Christie ovarian cancer database. The regimens evaluated were Liposomal doxorubucin, Carboplatin/Liposomal doxorubicin, Cisplatin and oral Etoposide, weekly Paclitaxel, Gemcitabine/Platinum and Topotecan. Data were analysed for prognostic factors, response rates, toxicity, progression-free survival and overall survival.
Results: Majority of patients were stage III/IV at presentation and 80% had debulking surgery. Patients were evenly matched with respect to degree of tumour burden (> 2 sites of disease; tumour bulk> 5cms). Liposomal doxorubicin and the dose-dense weekly Cisplatin and oral Etoposide were used more commonly in 'early' platinum-resistant disease. The best response rates were seen with Carboplatin/Liposomal doxorubicin and the dose-dense cisplatin/oral etoposide regime. Progression-free survival and overall survival were significantly higher in the Carboplatin/Liposomal doxorubicin group perhaps indicative of its use early in platinum-resistant disease. On the other hand Topotecan was associated with negligible efficacy given its use in heavily pre-treated disease. The overall incidence of grade 3/4 toxicities was low. Mature data and full statistical analyses will be presented at the meeting.

	Liposomal doxorubicin	Carboplatin/ Liposomal doxorubicin	Cisplatin/ Etoposide	Paclitaxel weekly	Gemcitabine/ Platinum	Topotecan
Median age	64	65	65	71	65	60
Lines of chemo-median	2	2	2	2	3	3
Ca125 response GCIG criteria	30%	48%	43%	63%	33%	11%
Radiological Response	22%	37%	35%	24%	17%	0
Median PFS weeks (range)	21.5*	26.6*	17 (1−110)	18.5 (2−80)	15.5 (1−48)	13.5 (1−34)
Median OS weeks (range)	58*	58*	36 (1−147)	35 (3−88)	46 (2−130)	36 (4−116)

*Data (range) not mature, available by presentation

Conclusion: Multiple courses of chemotherapy are effective in platinum-resistant ovarian cancer.

8005 ORAL

Correlation of RNA expression of DNA repair genes with clinical outcomes of advanced ovarian cancer (OC) pts treated with pegylated liposomal doxorubicin (PLD) vs Trabectedin (T) + PLD in the ET743-OVA-301 clinical trial

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Background: Enhanced sensitivity to T has been observed in cells that, in addition to a proficient NER pathway, are deficient in homologous recombination repair (HRR). In a retrospective series, pts with soft-tissue sarcoma expressing high levels of ERCC1 and XPD [NER] and low levels of BRCA1 [HRR] experienced more favourable outcomes with T. These markers were prospectively investigated in available OC samples from the randomised Phase III study OVA-301.
Materials and Methods: Tumor tissue blocks from 183 consenting pts of the 672 OC pts enrolled in OVA-301 were analysed by qRT-PCR. 139 (76%) samples had at least one detectable expression level. High and low mRNA expressions were defined for levels above *vs* below the median, respectively. For progression-free survival [PFS] and overall survival [OS] association analyses to investigate outcomes by expression levels, and the relative benefit due to T depending on expression were carried out.
Results: Both in the overall study population (SP) and in the analyzed cohort, PFS and OS were significantly longer in the platinum (P)-sensitive *vs* P-resistant pts. In the SP, T+PLD induced a significantly longer PFS and a trend for longer OS than PLD. Pts with low BRCA1 mRNA levels had significantly longer OS ($p = 0.0297$) and PFS ($p = 0.0427$) than those with high BRCA1 levels, indicating the prognostic value of BRCA1 expression in the OC population studied. A trend ($p = 0.0765$) for longer OS (but not PFS) was found for pts with high ERCC1 expression levels. No significant differences in PFS or OS emerged for low or high XPD expression levels. PLD-treated pts with high ERCC1 mRNA levels tended to have longer PFS than those with low ERCC1 levels. No significant differences in PFS or OS were observed with the combined expression of BRCA1+ERCC1. Caveats of these analyses include low numbers of pts in each of the subgroups, prior P-based therapy in all pts (+ 80% prior taxanes) which might have modified the tumor RNA expression levels, immature OS data, and the effect of PLD added to T in the assessment of outcomes *vs* mRNA expression levels.