Results: The initial pilot-tested WOMAN-PRO instrument had a scale CVI of 0.98 based on six patients rating and a scale CVI of 0.92 based on six clinical experts' assessment. Clinical experts' assessments of 34 items showed excellent CVI ranging from 0.83 (15 items) to 1.0 (19 items). The remaining 3 items had a low CVI of 0.66. Patients assessment of 36 items showed excellent CVI of 0.83 (3 items) to 1.0 (33 items). The remaining item had a low CVI of 0.66. The content validity index and the comments from the initial piloting of the provisional instrument resulted in the decision to delete two items, revise three items, add one item and reduce the response options from five to four categories. The revised WOMAN-PRO showed an excellent item and scale CVI of 1.0.
Conclusions: The potential use of the WOMAN-PRO instrument in clinical practice offers patients guidance in early recognizing and self-assessing symptoms and related distress. The instrument provides clinicians with systematic information about key symptoms from a patient perspective and women's unmet informational needs related to assessing and managing symptoms in daily live. If the results of further ongoing psychometric testing are promising, the WOMAN-PRO will provide a useful outcome measure for clinical trials examining the post-surgery symptom experience in women with vulval neoplasia.

8029 POSTER

Health-Related Quality of Life (HRQoL)/Patient Reported Outcomes (PRO) of Patients (pts) With Partially Platinum Sensitive (PPS) Recurrent Ovarian Cancer (ROC) Treated in a Randomized Phase III Trial of Trabectedin and Pegylated Liposomal Doxorubicin (PLD) Vs PLD Alone (OVA-301) − an Exploratory Analysis

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Background: OVA-301 is a large randomized trial that demonstrated OS benefit (Monk B. 2011) of trabectedin plus PLD (T+P) *vs* PLD in PPS ROC pts.
Methods: This analysis provides an evaluation of PRO in PPS pts, analyzing single domains and the global health status (GHS). EORTC-QLQ C30 and OV28 questionnaires were completed at screening and on Day 1 of every other treatment cycle (C) starting with C1, and at end of treatment (EoT). Comparisons are exploratory so no adjustments for multiplicity to control the overall Type I error rate were done.
Results: 214 pts had PPS ROC (PLD: 91/ T+P: 123 pts). Questionnaire completion was ~90% at baseline and well maintained up to 21 cycles (~83%). A median of 4 and 6 cycles of PLD and T+P were administered. The table shows the cross-sectional analysis of the mean score changes from baseline (MCB) of the functional, symptoms and GHS scales, including relevant findings at the corresponding timepoint.

Item/Domain	C3			C5			C7			C9		
	PLD	T+P	p[a]	PLD	T+P	p[a]	PLD	T+P	p[a]	PLD	T+P	p[a]
Appetite loss[1]	2.5	16.7	0.054	−1.4	7.0	0.975	−1.6	4.3	0.837	0	1.4	0.796
Dyspnea[1]	−1.3	4.3	0.024	1.4	5.0	0.195	−1.6	−0.7	0.750	−4.8	−2.9	0.932
Nausea/ Vomiting[1]	1.6	13.8	0.003	0.7	7.2	0.022	1.6	5.8	0.149	−1.2	6.9	0.114
Pain[1]	−3.4	−2.7	0.862	−0.4	−5.3	0.054	−1.6	−6.5	0.053	0	−8.3	0.053
Peripheral Neuropathy[1]	7.9	4.4	0.666	10.8	3.1	0.229	9.1	3.3	0.074	9.4	4.6	0.159
GHS/QoL[2]	−2.4	−6.6	0.352	−0.6	−3.1	0.909	0.9	−1.4	0.371	0.6	4.0	0.023

[1]Lower is better; [2]Higher is better; [a]T-test p-values comparing real scores.

Nausea/Vomiting favored PLD at C3 and C5, with a non significant trend across cycles. Meanwhile the pain scale favored T+P with improved results at C5 and beyond due to treatment.
Peripheral Neuropathy scale had a trend favoring T+P after 5 cycles, which was maintained.
In general the GHS scale had an important clinical difference in favor of T+P at C9, and was maintained for longer treated pts (EoT = MCB:PLD = −9.8, T+P = −3.4, p = 0.062).
Further findings will be discussed at the meeting.
Conclusions: Acknowledging the limitations of this analysis, differences were observed in different domains, characterizing the different profile of both treatments. The nausea/vomiting domain favored PLD, while T+P had better scores for pain and neuropathy, suggesting a non platinum/non-taxane treatment helps to recover from toxicities associated with prior therapies, which may offer new potential for following therapies. In general, addition of Trabectedin to PLD has no detriment in the global QoL and shows an improved outcome in the GHS for PPS ROC pts.

8030 POSTER

Phase II Study of NGR-hTNF Plus Doxorubicin in Relapsed Ovarian Cancer (OC)

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Background: NGR-hTNF consists of tumour necrosis factor fused with the peptide NGR, which selectively binds to a CD13 overexpressed on tumour blood vessels. NGR-hTNF is able to increase the intratumoral doxorubicin distribution by altering tumour vasculature.
Methods: OC patients failing at least one prior platinum-taxane line and with platinum-free interval either lower than 6 months (PFI <6) or between 6 to 12 months (PFI <12) received NGR-hTNF 0.8 $\mu g/m^2$ and doxorubicin 60 mg/m^2 on day 1 every 3 weeks. Doxorubicin was maintained up to 8 cycles and NGR-hTNF until disease progression. Primary endpoint was response rate. A 2-stage study design assumed that $\geqslant$2/17 and $\geqslant$6/37 patients with objective response would warrant further testing.
Results: Thirty-seven patients (25 with PFI <6; 12 with PFI <12) pretreated with 1 to 5 chemotherapy lines (median 1) were enrolled. Median age was 57 years (range 35−72) and 32 patients presented with a PS of 0. Median PFI was 4.6 months (95% CI 3.4−5.8).
Baseline CA125 ranged from 6 to 5,787 U/mL (median 549). Median baseline neutrophil-to-lymphocyte ratio (NLR), an index of systemic host immune response to tumour, was 2 (range 1−17). In total, 174 cycles were given (median 4; range 1−8). Neither increase of doxorubicin-related toxicities nor grade 3−4 NGR-hTNF related toxicity were registered.
Common grade 1−2 toxicity were transient chills (58%). After first study stage (n = 17), 6 patients showed partial response (2 with PFI <6; 4 with PFI <12) and the trial met its primary endpoint. After study completion (n = 37), a total of 17 patients had experienced stable disease (10 with PFI <6; 7 with PFI <12), yielding an overall disease control rate of 66% (92% in PFI <6; 48% in PFI <12). Median progression-free survival (PFS) was 4.9 months (95% CI 3.5−6.3) in overall population, 3.7 months in patients with PFI <6, and 8.2 months in patients with PFI <12. Moreover, median PFS was 7.8 vs 3.4 months (HR = 0.34; p = 0.01) in patients with baseline NLR lower or higher than the median value, respectively.
After a median follow-up of 10.8 months, 25 patients (68%) were still alive.
Conclusion: Tolerability and activity of NGR-hTNF plus doxorubicin deserve further randomized testing versus doxorubicin alone in platinum-resistant/refractory OC.

8031 POSTER

Prediction of Overall Survival (OS) Adjusted by Continuous Platinum-free Interval (PFI) at Fixed Timepoints in Patients With Recurrent Ovarian Cancer (ROC) − Results From OVA-301

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Background: OVA-301, a phase III study comparing trabectedin plus pegylated liposomal doxorubicin (PLD) *vs*. PLD alone in 672 patients progressing after one prior platinum-based regimen, showed significantly longer progression free survival and higher response rate for the combination, with acceptable tolerance (Monk et al; 2010). This study also showed longer OS in patients treated with the combination (Monk et al;

2011). In ROC the efficacy of chemotherapy is broadly accepted to be highly correlated with the PFI. Patients with PFI $\geqslant$ 6 months (mo) are considered as platinum sensitive (PS). Within this subset, a PFI of 6−12 mo implies partially platinum-sensitive (PPS) disease. Thus, the PFI represents an important factor to interpret the results in this setting. Kaplan–Meier survival estimates according to stratification categories are widely used for plotting time-to-event curves (e.g. <6 *vs.*$\geqslant$6 mo) but it may not account for imbalance within strata. (i.e. a patient with PFI=12 mo may have higher risk of death than one with PFI=36 mo). Allmer and Sargent (SUGI-2003) proposed a method to plotting survival estimates at a specified point in time, adjusted by a continuous explanatory variable.
Methods: Adjusted estimates of OS by continuous PFI at fixed timepoints (12, 18, 24 and 36 mo) according to Allmer and Sargent method have been considered.
Results: A Cox regression model using treatment group and continuous PFI as covariates was performed in the overall population, resulting both variables statistically significant ($p = 0.0029$ and $p < 0.0001$, respectively). After adjustment by PFI, the plots representing the OS rate prediction at 12, 18, 24 and 36 mo showed a significant difference along PFI axis favoring the combination of trabectedin and PLD. The PS and PPS subgroups showed consistency in the main effect model, enhanced for the combination (adjusted HR = 0.72 and 0.62, respectively; $p = 0.0036$, $p = 0.0018$).
Conclusions. The outcome of chemotherapy in ROC is strongly influenced by the PFI. Therefore, it is important to adjust for it in the analysis of OS. In accordance with previously published estimates for OS, the new approach for presenting predicted survival data based on the continuous PFI showed an improved OS in patients treated with the combination of trabectedin and PLD.

8032 POSTER

Catumaxomab Administered as a 3-hour Infusion − Results From a Newly Integrated Safety Analysis Comprising 7 Clinical Studies

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Background: Catumaxomab (anti-EpCAM x anti-CD3) is approved in the EU for the intraperitoneal treatment of malignant ascites with an infusion time of 6 hours (h), as used in the pivotal phase II/III clinical study. Experience with a 3-h infusion has grown substantially as all studies conducted thereafter used a reduced 3-h infusion time. The exiting database was enlarged by data from 2 clinical studies (additional 42 patients).
Methods: A newly integrated safety analysis (ISA) comprising 7 completed studies of patients with ovarian or gastric cancer primarily without malignant ascites treated with a 3-h catumaxomab infusion was conducted. In 4 of 7 studies, catumaxomab was administered in a perioperative setting. This 3-h database (ISA-3 h, N = 224) was compared with the reference database of the 6-h catumaxomab infusion (ISA-6 h, N = 293), which mainly includes patients with malignant ascites. Symptomatic adverse drug reactions (ADRs) of intensity grade $\geqslant$3 occurring in $\geqslant$1% of patients were used to describe the safety profiles derived from two databases.
Results: The nature of these ADRs and their intensity on System Organ Class level was comparable between both databases. The frequency of ADRs of intensity grade 3 or 4 was comparable for reactions such as abdominal pain, pyrexia and vomiting. Increased occurrence rates were observed for specific ADRs of intensity 3 or 4 with the 3-h vs the 6-h infusion, e.g. diarrhea (4.0% vs 1.4% of patients) and nausea (5.4% vs 2.4% of patients). In contrast, Ileus of severity grade 3 or 4 was reported more frequently in patients receiving catumaxomab as 6h infusion (0.4% vs 2.4%). For ADRs of lower intensity grade 1 or 2, a higher occurrence rate was observed in the ISA-3 h data set for a few ADRs, e.g. chills, hypotension, fatigue and diarrhea. The observed ADRs are well-known and partly expected due to catumaxomab's mechanism of action. All ADRs reported with a higher occurrence rate can be well controlled with pre- and/or concomitant medication.
Conclusions: The available safety data support the reduction of the catumaxomab infusion time from 6 h to 3 h. The reduction of the infusion time represents a significant advance in terms of the time spent at a healthcare facility. A variation of the EU product information in this regard was submitted.

8033 POSTER

Metastatic Endometrial Cancer at Diagnosis − Survival Patterns

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Introduction: Endometrial carcinoma is the most common gynecologic malignancy in industrialized countries. The majority of cases with endometrial carcinoma are found at an early stage, with disease apparently confined to the uterus. Distant metastasis at diagnosis are uncommon and usually involves lung and/or liver. Systemic treatment represents the cornerstone of endometrial cancer management in advanced, relapsed and metastatic disease, which is still characterized by poor prognosis. Caboplatin and paclitaxel is an increasingly used regimen for advanced/metastatic or recurrent endometrial cancer, the response rate is about 40%, and median overall survival is about 13 months. The aim of this study was to characterize patients with metastatic endometrial cancer at diagnosis, describe treatment options and evaluate overall survival (OS) patterns.
Material and Methods: A retrospective review of medical records of 34 women with metastatic endometrial cancer treated with palliative chemotherapy with carboplatin and paclitaxel, and some of them with radiotherapy in Cancer Centre in Porto, between January 2005 and December 2010 was performed.
Results: A total of 34 patients were in stage IV disease at the diagnosis and underwent chemotherapy with carboplatin and paclitaxel. The median age was 65 years old (min: 46 max: 77). Endometrioide carcinoma of endometrium was the predominant (70%). Most of patients presented with peritoneal carcinomatosis and lung metastasis. There were 21 (61%) patients undergoing only palliative chemotherapy and 13 patients (38%) did palliative chemotherapy and radiotherapy. The median number of cycles of chemotherapy was 6. The median of progreesion-free interval was 6 months (min:5 months, max: 42 months). The median of OS was 21 months (min: 1month, max: 64 months).
Conclusion: Aggressive treatment including systemic chemotherapy prolongs survival of patients with metastatic endometrial carcinoma at diagnosis. In our study 61% of patients had overall survival beyond 2 years, of which 14% had higher overall survival at 4 years.

8034 POSTER

Capecitabine as Second- and Third-line Chemotherapy in the Treatment of Platinum-refractory Epithelial Ovarian Cancer

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Background: The aim of the study is to evaluate the value of Capecitabine (Xeloda) in the treatment of epithelial ovarian cancer, after failure of initial chemotherapy. Response rates to first-line chemotherapy in women with ovarian cancer are high but most patients relapse and need further treatment. Recurrent disease is incurable, however, many patients can obtain good palliation from further treatment.
Material and Methods: The study included 20 patients with epithelial ovarian cancer treated initially with cytoreductive surgery and followed by chemotherapy treatment: 14 patients received platinum/paclitaxel therapy and 6 patients received platinum/cyclophosphamide therapy. Progression of disease was manifested with hepatic metastases in 11 patients (55%), lung metastases in 2 (10%), carcinosis peritonei in 2 (10%) and an increase in serum CA125 in 5 patients (25%). Comparison of the value of serum CA125 before and after treatment was taken as an indicator of response to chemotherapy. The treatment schedule consisted of oral capecitabine 1250 mg/m^2 administered twice daily for 14 days, followed by a 7-day rest period. Treatment was administered orally within 30 min of breakfast and dinner, and swallowed with approximately 200 ml of water. The cycle was repeated every 21 days.
Results: 16 patients (80%) received 6 courses chemotherapy with Capecitabine, 4 (20%) did not achieve the planned 6 courses of chemotherapy due to the deterioration of their general condition. In 10 patients (50%) decreased value of serum CA125 was observed, in 8 (40%) value was unchanged, and in 2 (10%) an increase in serum CA125 was noted. All 20 patients were evaluable for safety. Capecitabine was very well tolerated, with the most common clinical adverse events being nausea and diarrhoea, neither of which occurred with grade 3 or 4 intensity.
Conclusions: Capecitabine has demonstrated promising activity and a favourable safety profile in the treatment of platinum-refractory epithelial ovarian cancer. The safety and convenience advantages afforded to patients over current i.v. options make capecitabine an ideal agent for administration in the outpatient setting, potentially freeing them from the burden of i.v. therapy.