percentage for nausea (p= 0,0005) and vomiting (p= 0,0083). No significant differences were observed for specific sensory and motoric neurotoxic symptoms, except for a better skilfulness in the AM group (p=0,0404). In conclusion, AM improved sensory neuropathy according to NCI-CTC and results from objective neurological assessment, but there were almost no differences in self-estimated specific sensory or motoric symptoms. Disadvantages with regard to other toxicities and inconsistent results for QoL demand further evaluation of neuroprotection with AM in the treatment of OC. At this moment the presented results do not justify a standardized additional application of AM to platinum/taxane-based chemotherapy.

39 ORAL

Topotecan versus treosulfan in recurrent ovarian cancer after initial chemotherapy with platinum and paclitaxel. a prospective randomised phase III study of the AGO ovarian cancer study group.

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Background: After initial radical debulking surgery followed by combination chemotherapy most ovarian cancer patients will eventually relapse and will be in need of further treatment. Standard chemotherapy for recurrent disease after first line treatment with carboplatin and paclitaxel is not yet defined. Therefore, this multi-centre, prospective randomised trial, was conducted to compare the topoisomerase I inhibitor topotecan with the alkylating agent treosulfan in patients with relapsed ovarian cancer.

Material and Methods: The study was undertaken to define the progression-free survival time and the response rate. Patients were stratified according to treatment free interval: relapse between 0-6 or 6-12 months after end of primary treatment (2nd line) or relapse after re-induction chemotherapy with a platinum-containing regimen (3rd line). The therapy consisted of 1.5 or 1.25 (3rd line) mg/m* topotecan, d1-5 every three weeks or 7.0 or 5.0 (3rd line) g/m* treosulfan. In patients with SD or PR, treatment was continued until disease progression or intolerable toxicity occurred.

Results: 357 patients were recruited (topotecan 178, treosulfan 179), 8 patients were withdrawn after randomisation. Patient characteristics were equally distributed between the two groups. Significantly more patients progressed after treosulfan treatment compared to topotecan treatment (62.5% vs. 28.4%, respectively). Response data were validated by external radiological review. Haematologic toxicity grade 3/4 was more frequently observed during topotecan therapy: neutropenia in 46.8% vs. 5.4%, thrombocytopenia in 7.4% vs 1.5% and anaemia in 4.3% vs. 1.0% of the courses compared to treosulfan. Grade 3/4 infection was 2.9% and 1.1% for topotecan and treosulfan, respectively, demonstrating no significant clinical consequences caused by topotecan haematologic toxicity. Non-haematologic toxicities were mild and apart from alopecia, comparable in both treatment groups. The progression-free survival was 5.4 months in the topotecan group and 3.0 months in patients treated with treosulfan ($p < 0.0001$, all patients). The analysis of the subgroups is still ongoing.

Conclusion: This clearly stratified randomised study in exactly defined recurrent ovarian cancer patients after carboplatin/paclitaxel initial therapy demonstrates that, both regimens are well tolerated without clinically relevant side effects. It can therefore be concluded that, topotecan may be defined as the new standard in early recurrent ovarian cancer because of the improved progression free survival and remission rate.

40 ORAL

Prognostic significance of P53, EGFR and Her-2 expression in borderline and epithelial ovarian cancer.

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The study was approved by the Danish Ovarian Cancer Study Group (DACOVA), Odense University Hospital.

Background: Epithelial ovarian cancer (EOC) continues to represent a challenge in cancer treatment despite advances especially in the application of new cytostatic drugs. Several aspects are not yet elucidated and important prognostic factors still need to be defined.

Several molecular-biological factors have been investigated in order to reveal new prognostic factors. Prior studies have assessed the prognostic relevance of P53-protein, EGFR and Her-2 receptors using immunohistochemical methods. So far no previous study has evaluated the prognostic significance of all three factors including a large number of patients with a long follow-up period. The objective of the present study was to evaluate the prognostic significance of p53, EGFR and Her-2 in relation to currently known prognostic factors.

Material and methods: The study was based on two cohorts diagnosed from 1981-86 and 1991-94. 1073 patients were retrieved from the registry of DACOVA. Archival paraffin-embedded tissue blocks from the primary surgery were retrieved from the regional departments of pathology. One senior gynaecological pathologist who had no knowledge of clinical data and outcome performed histo-pathological revision. Only patients with confirmed borderline or frank epithelial ovarian cancer at revision were included. Representative samples of tissue were chosen from each patient and three tissue-slides were stained immuno-histochemically to assess p53, EGFR and Her-2.

The slides were evaluated semi-quantitatively in a light-microscope by one of the investigators who had no knowledge of clinical data and outcome. One hundred slides from each factor were selected by random in order to evaluate inter and intra-observer variation.

Results: From the initial 1073 patients 202 were excluded at time of revision. Another 3 patients were excluded just prior to statistical analysis due to missing data on revision, resulting in subset off 868 patients. Preliminary results including univariate analyses show a statistically significant association between overexpression of p53 ($p<0.001$) and Her-2 (p 0.027) and decreased survival. EGFR-overexpression was not significantly associated with a decrease in survival (p 0.15). The classical prognostic factors age, stage, histology and grade were all significantly associated with survival. Multivariate analyses are in preparation and will be presented at the conference.

Reproducibility for all receptors was acceptable with kappa-values between 0.57 0.88.

Conclusions: Preliminary results indicate that p53 and Her-2 may be defined as prognostic factors in epithelial ovarian cancer; EGFR, however, did not prove to be a prognostic factor.

41 ORAL

HER2- expression in advanced ovarian cancer: A prognostic and predictive marker? An Study of the AGO Ovarian Study Group

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In contrast to breast cancer the role of HER2 overexpression in ovarian cancer is under discussion. Up to now only small studies with contradictory results are published. The aim of this study was to analyse the role of HER2 overexpression in a uniform treated population of patients with advanced ovarian cancer, as a prognostic and/or predictive factor.

Materials and methods: The paraffin blocks of 361 patients from the AGO Ovar-3 trial were retrospectively analysed for HER2 expression (immunhistochemical DAKO antibody, and with FISH). The HER2 data were correlated for clinical factors.