



Sequential chemotherapy with carboplatin followed by weekly paclitaxel in advanced ovarian cancer: Results of a multicenter phase II study of the northeastern German society of gynecological oncology

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ABSTRACT

Background. For the adjuvant setting of advanced ovarian cancer (AOC) after primary radical surgery the combination of paclitaxel and platinum in a 3-week schedule has emerged as the current standard. In preclinical studies additional anti-angiogenic effects of low dose paclitaxel infusion were demonstrated. A sequential schedule of carboplatin and paclitaxel has the potential to improve the therapeutic index.

Methods. In this multicenter phase II trial four cycles of carboplatin at a dose of AUC 5 (d1/q21d) followed by 12 cycles of weekly paclitaxel at a dose of 80 mg/m² (d1/q7d) were applied after primary radical surgery. Eligible were all optimally or sub-optimally debulked patients with FIGO IA–IV ovarian cancer. All patients with hemoglobin levels <12 mg/dl received erythropoietin additionally.

Results. Between July 2003 and May 2005, 105 patients from 27 institutions were enrolled. The median age was 60 years (range: 23–80 years). A median number of 16 courses (range, 1–16) were applied. The incidence of non-hematological toxicities was very low. Only 41% of patients experienced alopecia (grade 1–2). Neurotoxicity (grade 3–4) was not observed. Grade 3–4 hematological toxicity (43% of all patients) included thrombocytopenia (17%), anemia (3%), leucopenia (23%), and neutropenic fever (0%).

Ninety-seven percent received erythropoietin. Thromboembolic events (4%) were not increased in patients who received erythropoietin. After a median time of 23 months (range: 1–42 months) 32 patients had died, and the median overall survival was not reached. The progression-free survival was 25.4 months (95% CI: 18.8–40+).

Conclusion. These results suggest that this sequential regimen using weekly paclitaxel represents an efficacious and well-tolerated regimen. A randomized study comparing this new schedule with the conventional 3-week protocol is warranted.

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Introduction

Radical surgery with the primary goal of maximum tumor reduction, followed by adjuvant chemotherapy with paclitaxel and platinum compound, has emerged as an international standard in the treatment of advanced ovarian cancer, but unfortunately with unsatisfying long-term results [1,2]. Preclinical data indicate that the duration of exposure is relevant for the induction of cell death

[3–5]. Additionally it seems to be advantageous to expose solid tumours with long doubling times to a continuous cytotoxic concentration to increase the chance of targeting cells that progress through the cell cycle during the chemotherapy interval [6]. Several phase II clinical trials using different schedules and doses of dose-dense weekly administration of paclitaxel and carboplatin (dd-TC) in ovarian cancer have demonstrated promising efficacy. In preclinical and early phase I studies additional anti-tumor effects caused by interaction of anti-angiogenic pathways were observed for paclitaxel but not for platinum compounds [7,8].

Nevertheless, the optimal schedule to combine weekly paclitaxel with carboplatin is still unclear. Therefore we have conducted the

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