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GEMCITABINE (G) + CARBOPLATIN (C) AS 2nd LINE THERAPY IN GYNAECOLOGIC CANCER PATIENTS: A PHASE III STUDY OF THE ARBEITSGEMEINSCHAFT GYNAKOLOGISCHE ONKOLOGIE (AGO) STUDY GROUP
L. Quast, Dept. OB/GYN, University Hospital, Greifswald, Germany.

Objectives: Platinum (P)-sensitive malignant tumors of the ovary (relapsing >6 month after P and paclitaxel [T] are usually treated with P monotherapy. An advantage for monotherapy vs. a combination therapy is not yet established. Due to a persistent neuropathy at the time of relapsing (caused by the primary P/T therapy), non-neurotoxic substances for a P combination are wanted. G is an improved active substance in ovarian cancer (OC). To establish a study arm for a randomized phase II trial we performed a phase I/II trial with G/C.

Study Methods: 26 previously P and T treated patients (mostly OC) with a relapse >6 months were treated on day 1 with C (dose: AUC 5 according to the Calvert formula): G (doses escalating 800-1000-1200 mg/m²) was given on day 1 and 8. Maximum tolerable dose (MTD) was considered to be reached if 2/6 pts. experience dose-limiting toxicity (DLT) defined as Neutropenia grade 4 >7 days, febrile neutropenia, grade 4 thrombocytopenia or major organ toxicity grade 3 or higher.

Results: Neutropenia grade 3/4 in level I (12 pts/48 courses) and level II (6 pts/31 courses) was observed in 26% vs. 50%. Due to a grade 3/4 thrombocytopenia of 29% vs. 29% level 3 was canceled and a level II (C 1000 mg/m² day 1 and 8 & C AUC 4 day 1) was established. There were no grade 4 hematologic and non-hematologic toxicity’s to observe (7 pts).

Conclusions: The combination of G (1000 mg/m² day 1 and 8) with C (AUC 4 day 1) q21d is safe to be recommended for phase III trials. A prospective randomized trial comparing G/C with standard C in relapsed OC, has been initiated by the AGO OC Study Group in September 1999.