Pegylated liposomal doxorubicin hydrochloride (PLD) and paclitaxel in recurrent or metastatic head and neck carcinoma: a phase I/II study conducted by the Hellenic Cooperative Oncology Group (HeCOG).

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Source

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Abstract

A phase I pharmacokinetics and dose-finding study and a phase II study of the combination of pegylated liposomal doxorubicin HCl (PLD) and paclitaxel were conducted in patients with recurrent or metastatic head and neck cancer (HNC). Sixty patients with recurrent or metastatic disease were enrolled in the study: 11 patients in the phase I study and 49 patients in the phase II study. In the phase I study, the initial dose level of PLD was 35 mg/m as a 1-h infusion with escalating increments of 5 mg/m until the maximum tolerated dose (MTD) was reached. A fixed dose of paclitaxel (175 mg/m) was administered as a 3-h infusion. The combination was administered every 28 days. Pharmacokinetic studies performed on 10 patients indicated that the sequence of drug administration did not cause clinically significant modifications in the pharmacokinetics of either drug. The MTD for PLD was 45 mg/m (dose level 3) and the dose-limiting toxicity was febrile neutropenia, occurring in three of five patients. The phase II dose of PLD was 40 mg/m (dose level 2) and a total of 214 cycles were delivered. Grade 3 or 4 neutropenia was observed in 26% patients and febrile neutropenia occurred in 16% of patients. Grade 3 palmar-plantar erythrodysesthesia (PPE) was recorded in only one patient. The overall response rate was 28% for patients with non-nasopharyngeal tumors [95% confidence interval (CI) 15-45%] and 28.6% for the study population (95% CI 17-43%). The median survival for the study population was 9.7 months; 1-year survival was 38%. We conclude that the recommended dose for the combination of PLD and paclitaxel is 40 and 175 mg/m every 28 days, without granulocyte colony stimulating factor support. The combination of paclitaxel with PLD demonstrated activity in recurrent or metastatic HNC, a favorable toxicity profile and relative ease of administration.