

Clinical Study

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Phase I/II trial of doxorubicin and fixed dose-rate infusion gemcitabine in advanced soft tissue sarcomas: a GEIS study

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[Top of page](#)

Abstract

The aim of the study was to determine the dose-limiting toxicity and maximum tolerated dose of a first-line combination of doxorubicin and gemcitabine in adult patients with advanced soft tissue sarcomas and to explore its activity and toxicity, and the presence of possible interactions between these agents. Patients with measurable disease were initially treated with doxorubicin 60 mg m⁻² by i.v. bolus on day 1 followed by gemcitabine at 800 mg m⁻² over 80 min on days 1 and 8, every 21 days. Concentrations of gemcitabine and 2',2'-difluorodeoxyuridine in plasma, and gemcitabine triphosphate levels in peripheral blood mononuclear cells were determined during 8 h after the start of gemcitabine infusion. Myelosuppression and stomatitis were limiting toxicities, and the initial dose level was applied for the Phase II trial, where grade 3–4 granulocytopenia occurred in 70% of patients, grade 3 stomatitis in 46% and febrile neutropenia in 20%. Objective activity in 36 patients was 22% (95% CI: 9–35%), and a 50% remission rate was noted in leiomyosarcomas. Administration of doxorubicin preceding gemcitabine significantly reduced the synthesis of gemcitabine triphosphate. Clinical activity, similar to that of single-agent doxorubicin, and the toxicity encountered do not justify further studies with this schedule of administration.