Phase I study and pharmacokinetic of CHS-828, a guanidino-containing compound, administered orally as a single dose every 3 weeks in solid tumours: an ECSG/EORTC study

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CHS 828 is a new guanidino-containing drug. The aim of this study was to determine the maximum tolerated dose (MTD), the recommended dose and the toxicity of CHS 828. CHS 828 was given orally once every 3 weeks. The starting dose was 50 mg, which was escalated to 500 mg. A total of 107 courses was administered to 37 patients. At the 500-mg dose level, two of three patients experienced dose-limiting toxicities (DLT) (grade 3 mucositis and grade 4 thrombocytopenia), establishing this as the MTD. One of seven patients treated at 420 mg dose experienced DLT (grade 4 leucopenia, grade 4 mucositis and grade 4 diarrhoea), and this was considered the recommended dose for phase II studies. Vomiting, haematuria, leucopenia and thrombocytopenia were other significant toxicities. The pharmacokinetics of CHS 828 showed large variations both between and within patients. No objective responses were seen. A dose of 420 mg of CHS 828 administered every 3 weeks is the recommended dose, while 500 mg is the MTD.

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