# Population Pharmacokinetic Modelling and Simulation of Anlotinib in Chinese Pediatric Patients with Advanced Soft Tissue Sarcomas

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## Abstract

Objective:Population pharmacokinetics analysis explored the pharmacokinetics of anlotinib in children with soft tissue sarcomas (STS) and identified the optimal dose for children across various age brackets. Method:From 2021 to 2023, a single dose of anlotinib (4.62 mg/m2) was orally administered in 16 children with advanced STS in 8 days. Anlotinib plasma concentration was evaluated by LC-MS/MS. Pharmacokinetic models were developed using nonlinear mixed-effects modelling. The effect of predefined covariates on pharmacokinetic parameters was assessed. Results:Totally 128 samples from 16 children (aged 5-14) were collected for pop-PK analysis. The two-compartment model was most consistent with the data of oral anlotinib in pediatrics with advanced STS, and the relevant parameters were: Ka (h-1) 0.419; Vc/F (L) 760; Q (L[?]h-1) 21.2; Vp/F (L) 547. Covariate screening showed that the clearance of anlotinib gradually increased with age in a sigmoidal relationship, the maximum CL/F was 15.7L[?]h-1, and age of median clearance (Age50) was 6.84 years; the Vc/F increased linearly with BSA. Dose of 8 mg anlotinib for children aged 5-7, and 10 mg or 12 mg for children aged 8-10 would be expected to lead to a similar exposure of anlotinib compared with an adult patient receiving 12 mg. Conclusion:The population pharmacokinetics of orally administrated anlotinib were evaluated in pediatric advanced STS patients. BSA and age were significant physiologic factors on PK. A simulation of 8 mg anlotinib in children aged 5-7, 10 mg or 12 mg in 8-10 and 12 mg for children over 11 would get similar exposure of adults receiving 12mg.

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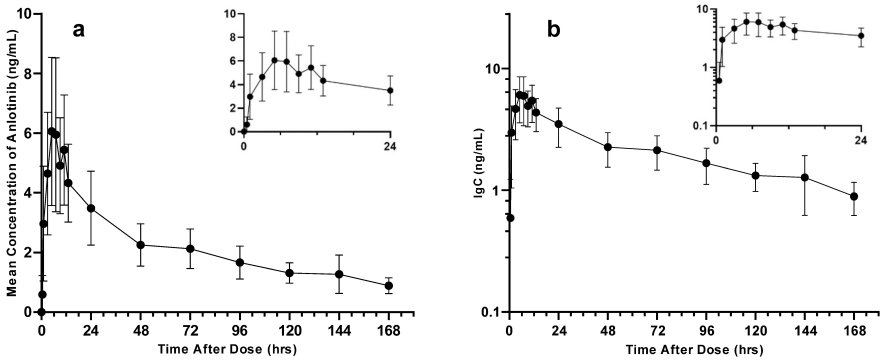

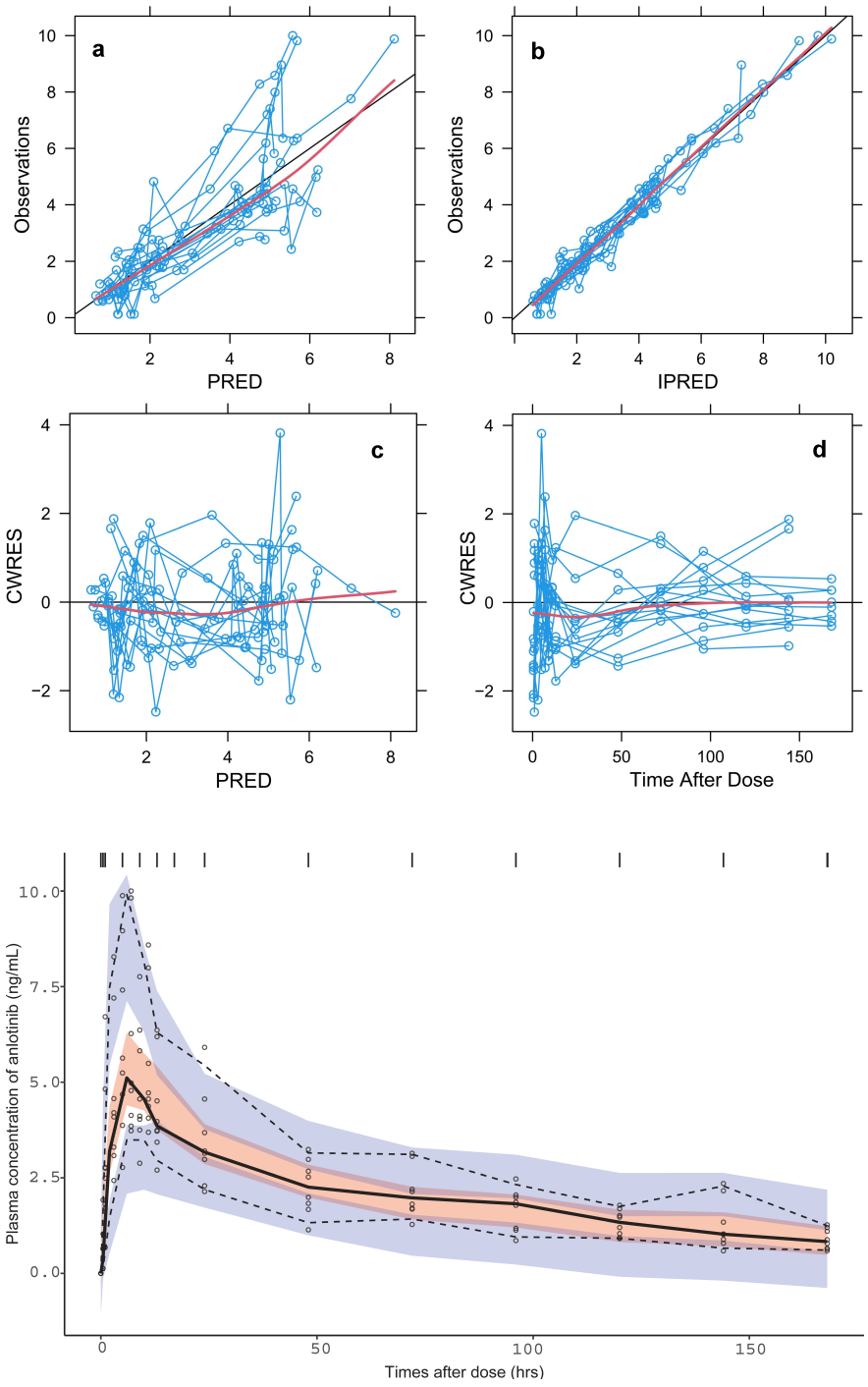

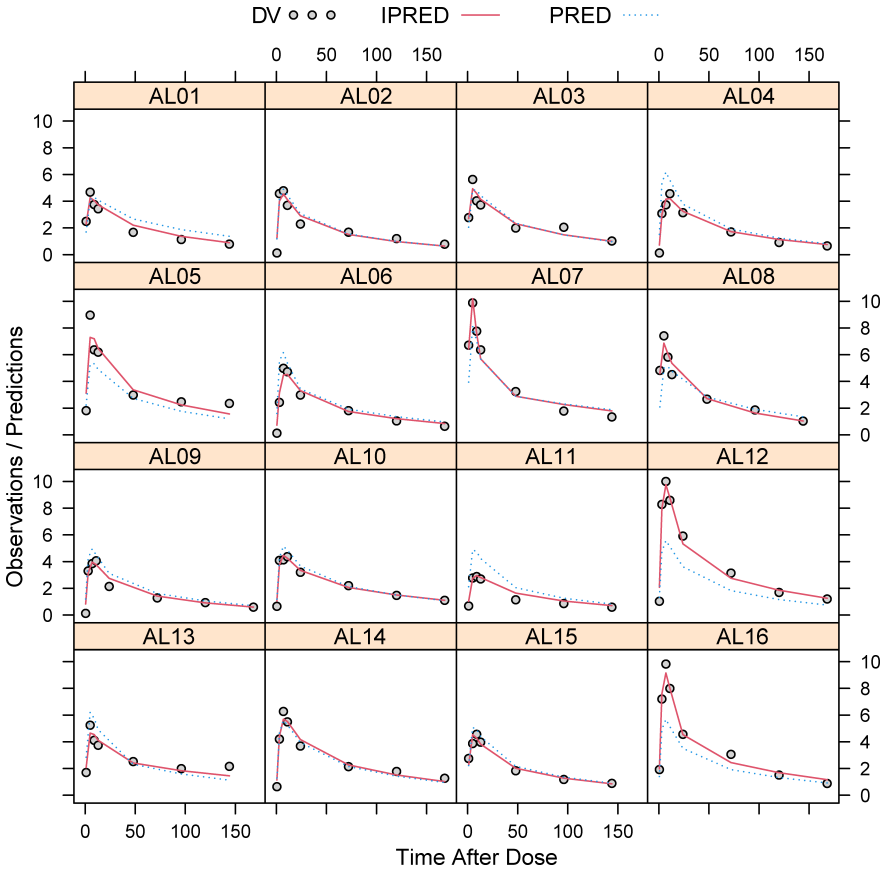


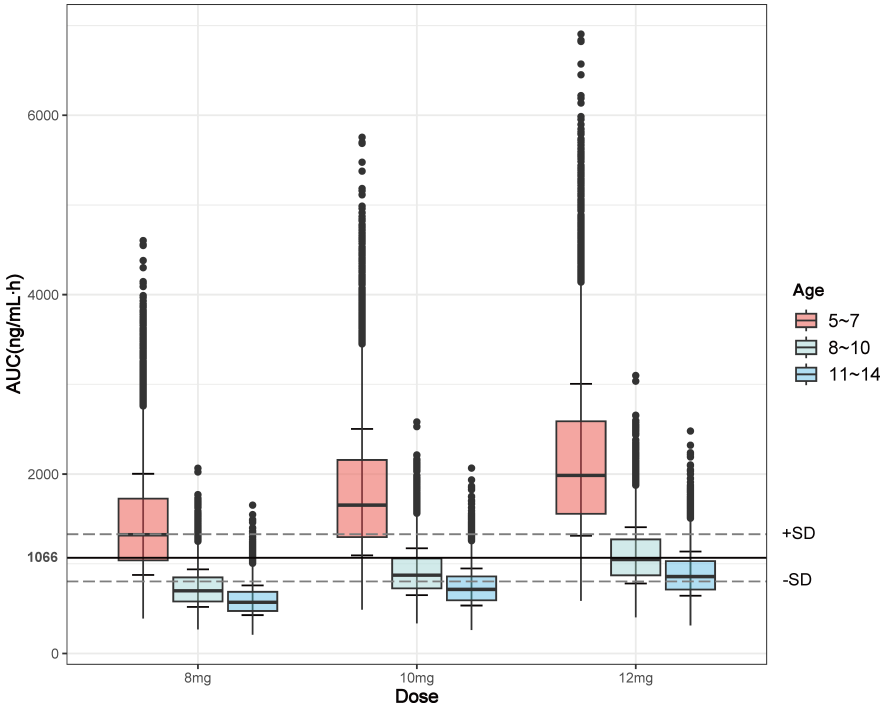

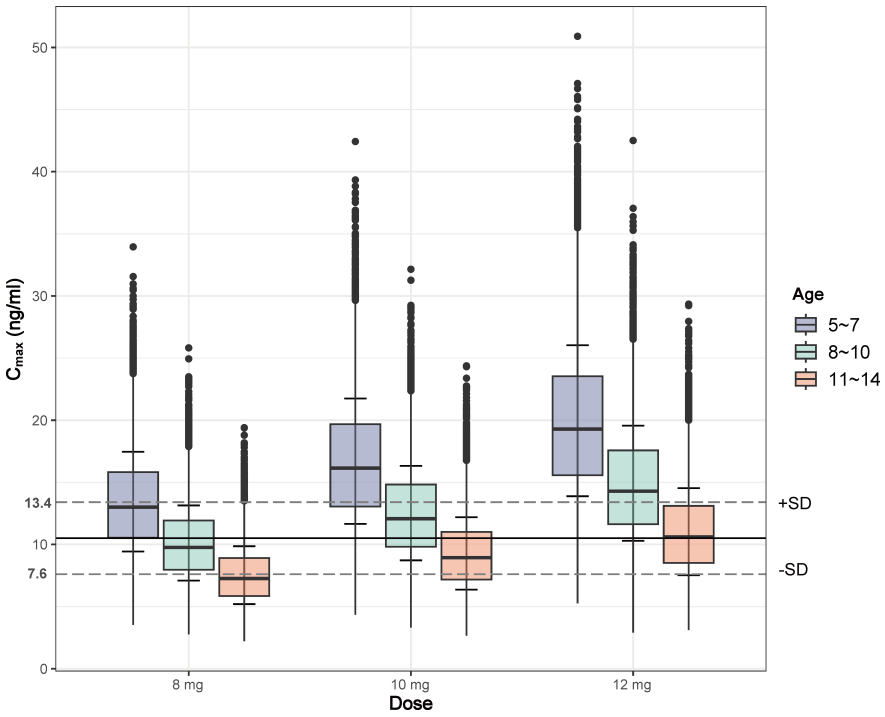


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