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Pharmacokinetic and statistical analysis {#s0045} In the present study, population pharmacokinetic parameters were estimated in the patient group using NONMEM V 7.3 software (ICON Development Solutions, Ellicott City, MD, USA) with a first-order conditional estimation method using population pharmacokinetic parameters and inter-individual variability. Area under the plasma concentration time-curve from time zero to infinite (AUC<sub>∞</sub>) was calculated by the linear trapezoidal rule. The AUC from time zero to time, C<sub>max</sub>, T<sub>max</sub>, elimination rate constant (λ<sub>z</sub>), half-life (T<sub>1/2</sub>) and CL were estimated. To assess the goodness-of-fit of the population pharmacokinetic model, a visual analysis of the goodness-of-fit plots was performed. To assess inter-individual variability of pharmacokinetic parameters, scaled weighted residuals (SWRs) and the corresponding values of the conditional weighted residuals (CWRES) were evaluated. A value of \*p\* \. [ ^1]: the t1/2 is the distribution half-life and the α the distribution clearance; both indicate the duration of plasma concentration above \*C

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