Modelling the effect of interleukin-6, an inflammatory cytokine, on time-dependent reduction of cyclosporine clearance: An application of the Simcyp Population-based Simulator to suppression of CYP345 by biologics

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Introduction

Biologics/therapeutic proteins (TPs) such as cytokines or modulators of cytokines, can differentially influence the expression and stability of specific CYP450 enzymes1,2,3,4. This has implications for drug development in humans.

Methods

A minimal PBPK model with a semi-mechanistic link model involving suppression of CYP34A4 was used in the present study. The effect of IL-6 was investigated on the cyclosporine PK following intravenous administration.

Results & Discussion

A zero order input rate and first order elimination adequately recovered the clinically reported endogenous IL-6 profiles in both patients (Fig. 3 & 4).

References


2. Minimal PBPK model (Simcyp Version 10.1)

The parameters obtained from eq.1 and eq.2 were used to define the IL-6 within Simcyp Simulator. The Minimal PBPK option (Fig. 2) was used to define the concentration time profiles for cyclosporine and IL-6.

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