

Population PK-PD modeling Analysis of rhIL-7-hyFc, a hybrid Fc-Fused Long-Acting Interleukin-7, to support Optimal Dose Regimens in Patients with Solid Cancer

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INTRODUCTION

rhIL-7-hyFc (Efineptakin alfa) is a newly developed long-acting recombinant human interleukin-7, designed to amplify and enhance the number of T cells by increasing the lymphocyte count [1]. The aim of this study was to develop a population PK-PD model to investigate the optimal dosing regimen for multiple intramuscular administration of rhIL-7-hyFc in patients.

METHODS

- Thirty-five Korean patients with solid tumors received intramuscular doses of rhIL-7-hyFc every 3-week in phase 1b clinical trial (NCT03478995) [2].
- Plasma concentrations of rhIL-7-hyFc and absolute lymphocyte count (ALC) were measured.
- PK-PD model was built using NONMEM software. PD model [3] was constructed sequentially using individual PK parameter estimates.
- Monte Carlo simulations of serum concentration and ALC over time were conducted.
- E-R relationships at steady state were predicted after multiple intramuscular injections of rhIL-7-hyFc at various dosing regimens.

RESULTS

- ALC increased rapidly soon after the first intramuscular dose of rhIL-7-hyFc.
- Two-compartmental PK model with 1st order absorption kinetics with combined residual model best described the observed concentrations.
- Two-depot model, in which each dose was administered in two fractions with a time interval, effectively described the double peaks observed during the absorption phase.
- Including inter-occasional variability (IOV) in clearance improved the model for repeated dosing.
- EC₅₀ was estimated to be 0.066 ng/mL, which suggests that rhIL-7-hyFc will exert pharmacologic effects at relatively low doses.
- The steady-state average ALC was predicted to be 2,439 - 3,164 cells/mm³ with intramuscular administrations of 0.6 - 1.2 mg/kg every 6 weeks or 12 weeks, compared to 1,351 - 1,362 cells/mm³ with baseline ALC.

CONCLUSION

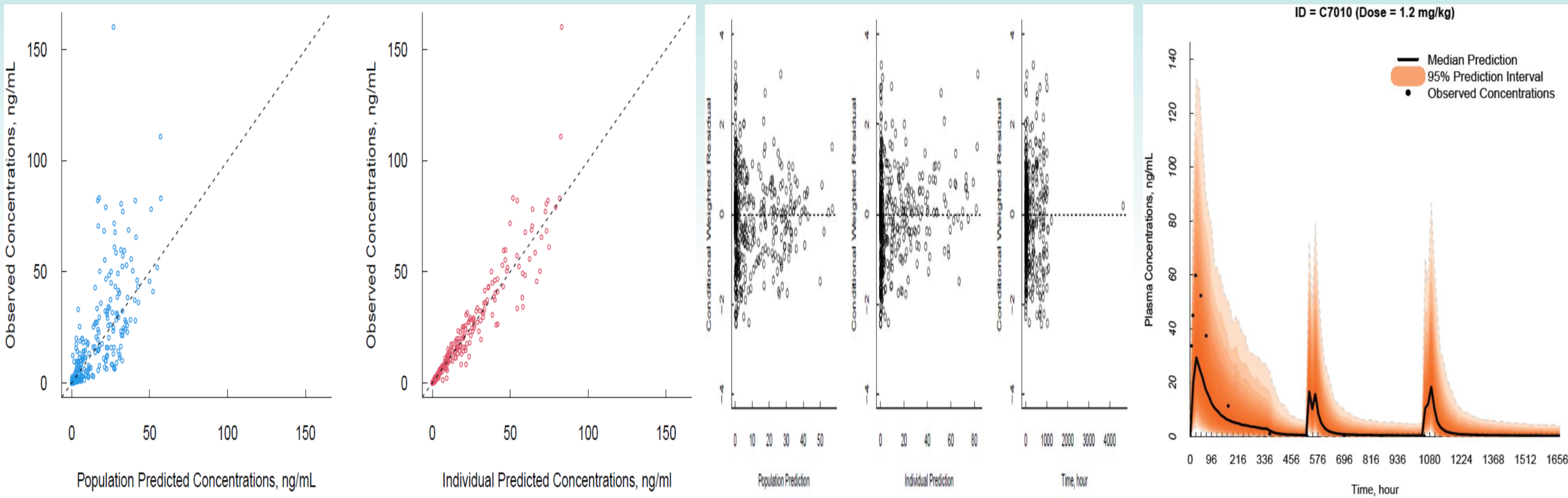
This analysis characterized the PK and PD of rhIL-7-hyFc which is under clinical development. The observed exposure-response relationship with respect to ALC supports the potential therapeutic efficacy of rhIL-7-hyFc.

REFERENCES

- Sojeong Kim, *et al.* A single administration of hIL-7-hyFc induces long-lasting T-cell expansion with maintained effector functions. *Blood Adv.* 2022. 6(23): 6093–6107.
- Kim GM, *et al.* GX-I7, a long-acting IL-7, safely and effectively increased peripheral CD8+/CD4+ T cells and TILs in patients with locally advanced or metastatic solid tumors. *Br J Cancer.* In press.
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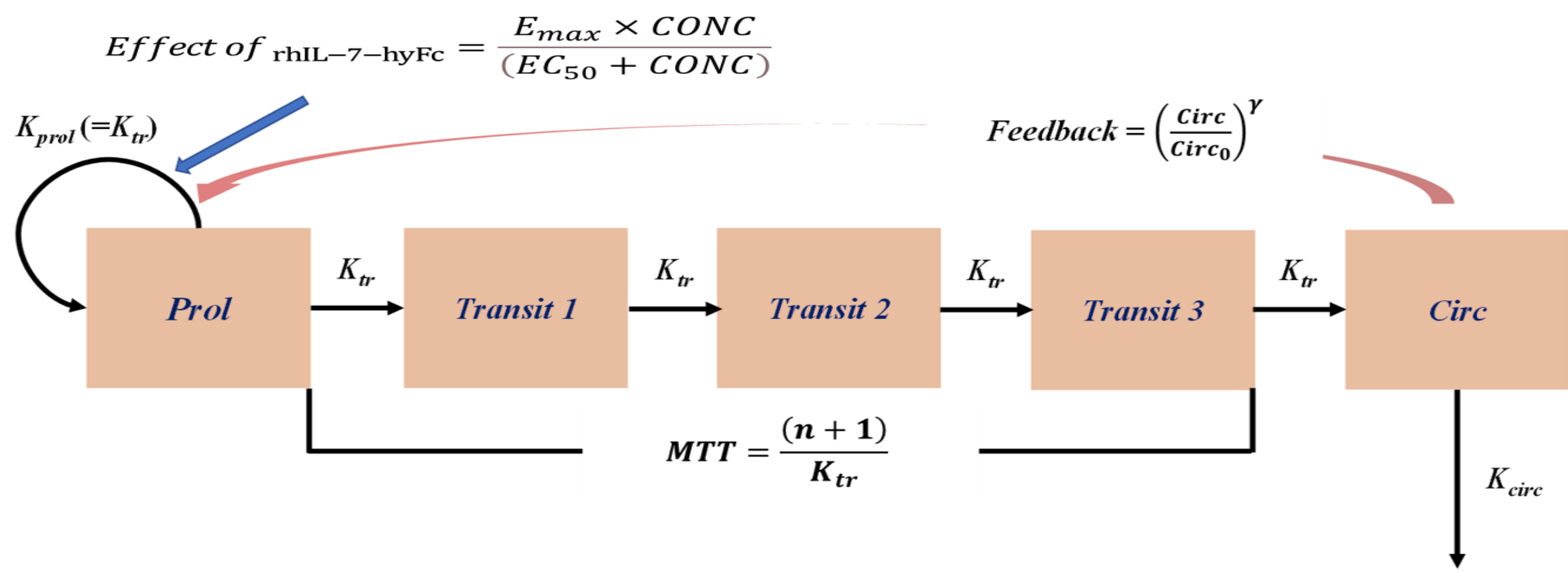
PK MODEL : rhIL-7-hyFc

Goodness-of-fit plot & Representative VPC

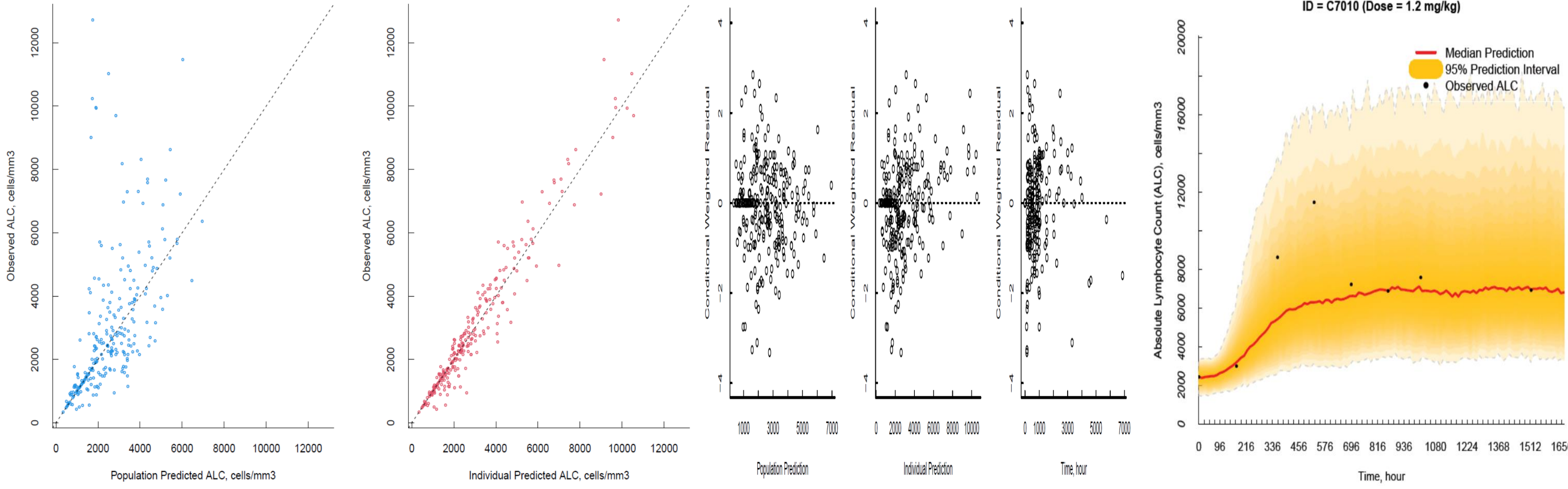


PD MODEL : ALC

Pharmacodynamic model scheme

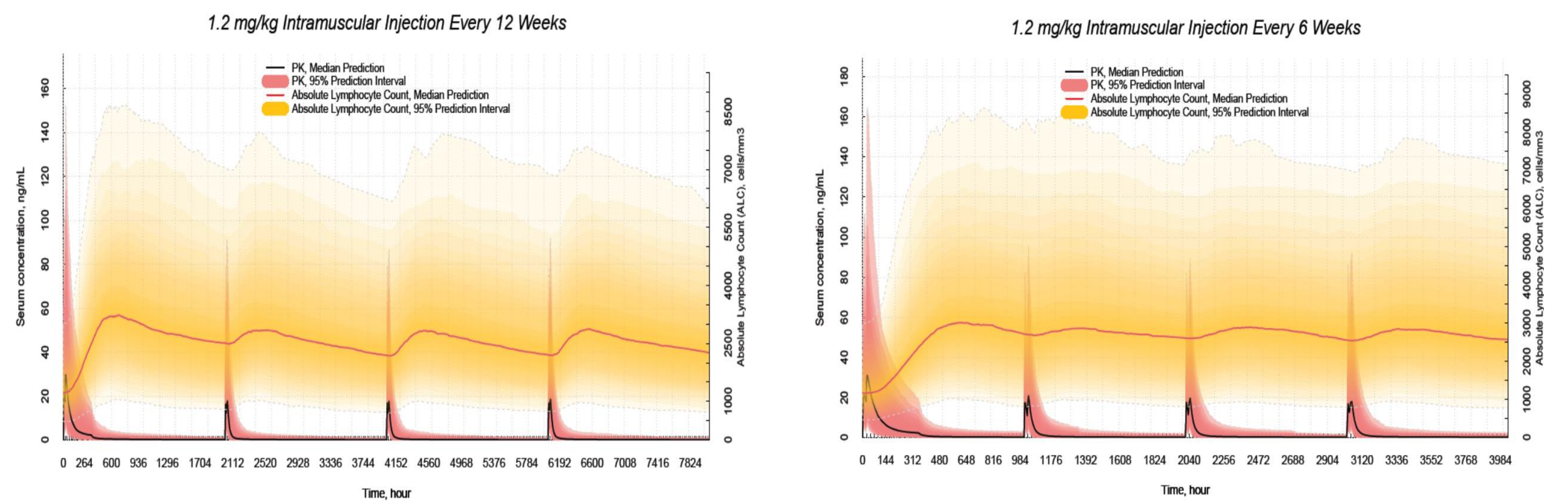


Goodness-of-fit plot & Representative VPC



SIMULATIONS

Monte-Carlo simulation



Exposure-Response Relationship

