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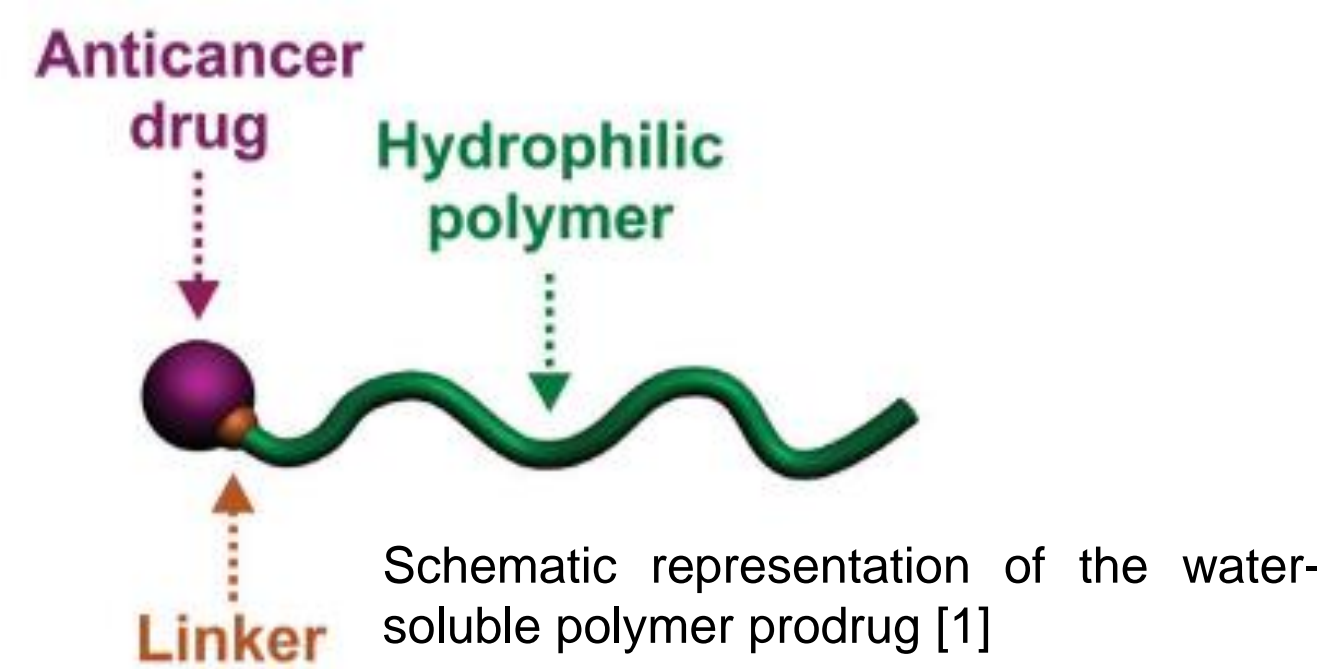
PK/PD MODELLING TO ADVANCE THE PRECLINICAL DEVELOPMENT OF A NOVEL POLYMER PRODRUG IN ONCOLOGY

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MOTIVATIONS & OBJECTIVES

- Taxanes such as **Paclitaxel** (PTX) are considered essential chemotherapeutics for the treatment of solid tumors. PTX formulations have been explored to **increase efficacy**, to **reduce toxicities** and have **improved pharmacokinetics** (PK).
- PTX linked to polyacrylamide (PTX-PAAm) is a new polymer prodrug which could result in an **effective** and **tolerable** anticancer treatment allowing for **subcutaneous** (SC) administration.



OUTLINE

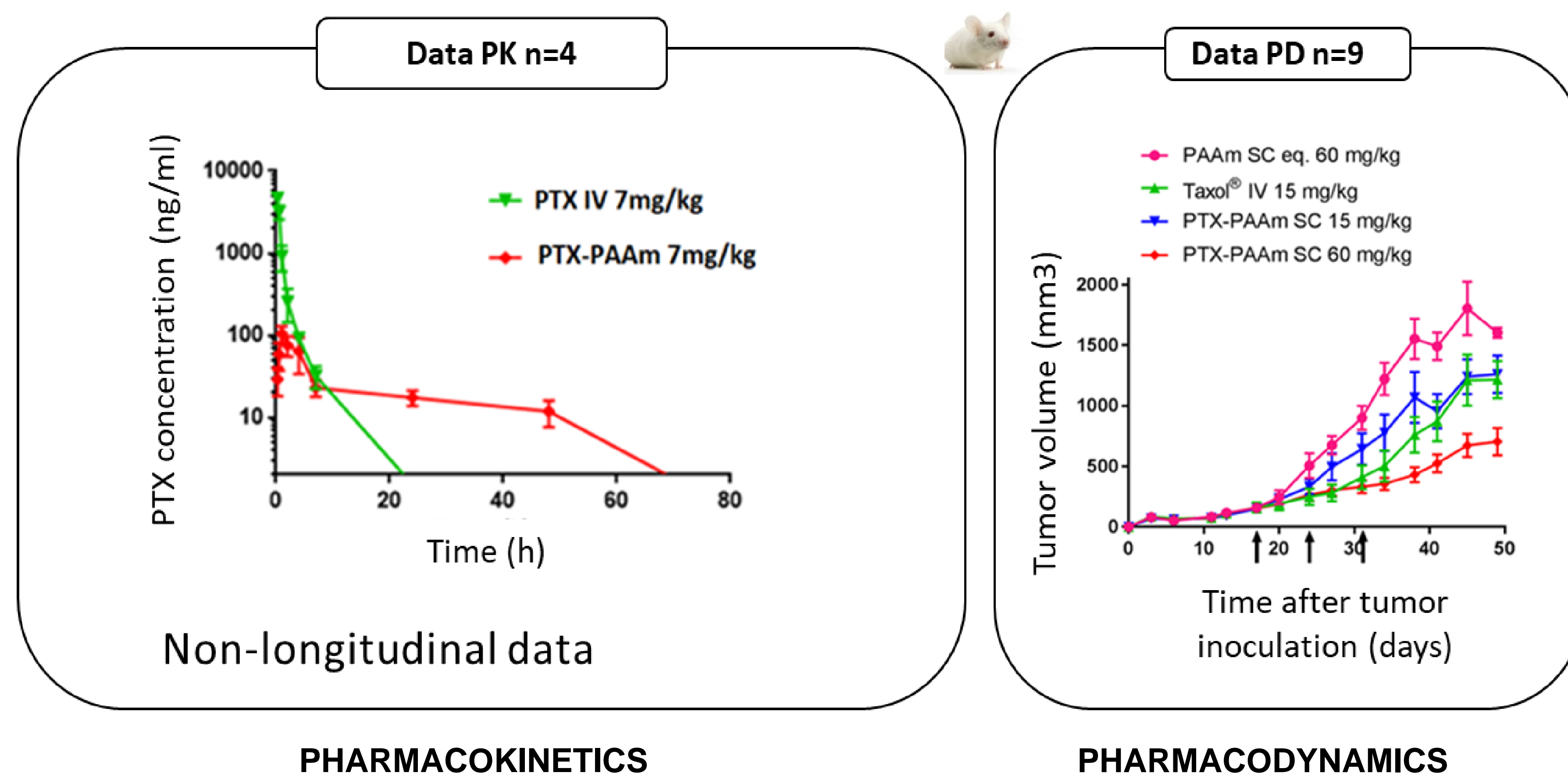
PK/PD modeling: **dose regimen optimization**

METHODS

SOFTWARES (version 2023R1)



EXPERIMENTAL BACKGROUND



PK/PD MODEL WAS BUILT GRADUALLY

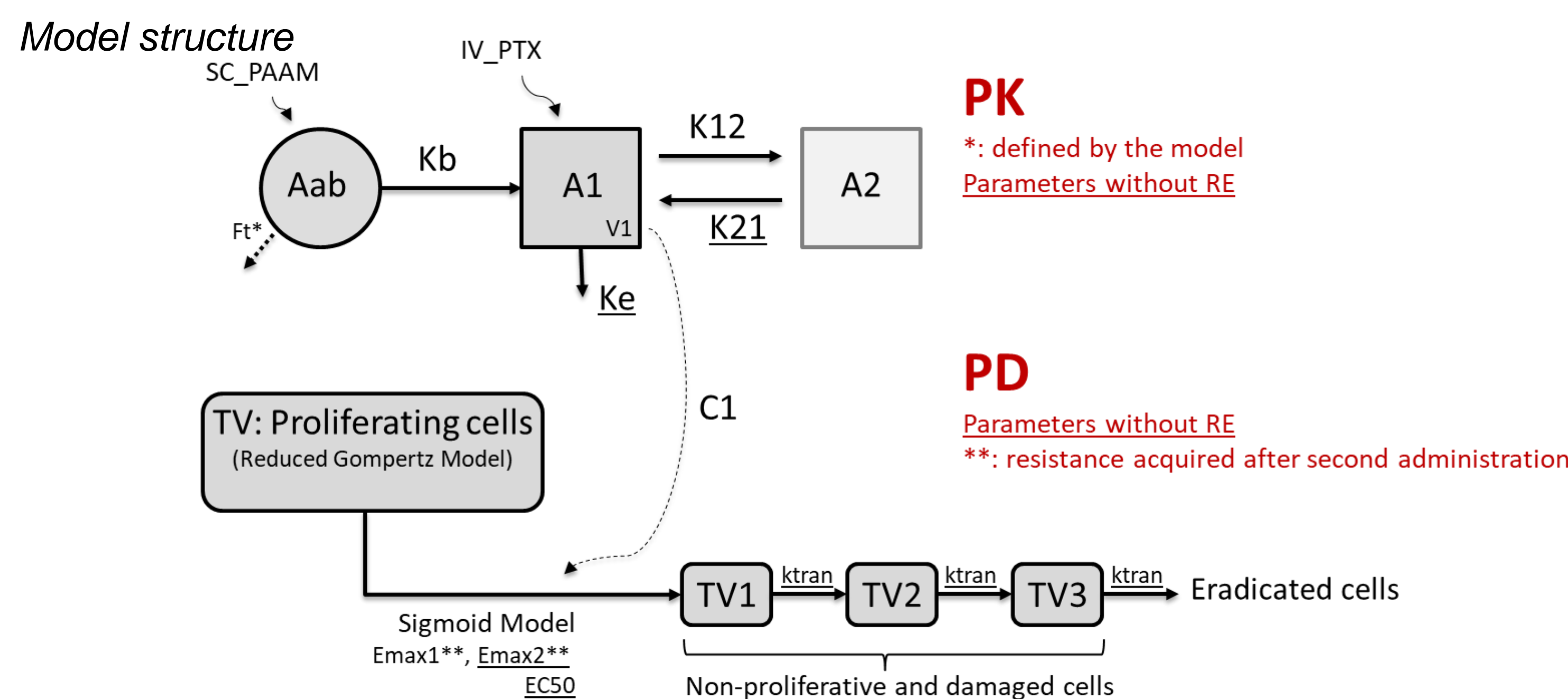
- (1) Pop-PK Model
- (2) Natural Tumor growth Model
Exponential, Power Law, Logistic & Gompertz's Models
- (3) PTX efficacy on cancer cells
Simeoni, Log Kill, Norton Simon & Treshold killing Models
- (4) Resistance model investigation

PK/PD MODEL WAS SELECTED ON

Numerical criteria
Objective function value (OFV) - Relative Standard Errors (RSE)
Graphical criteria
Visual Predictive Check (VPC) - Individual fits - Obs. vs Pred.

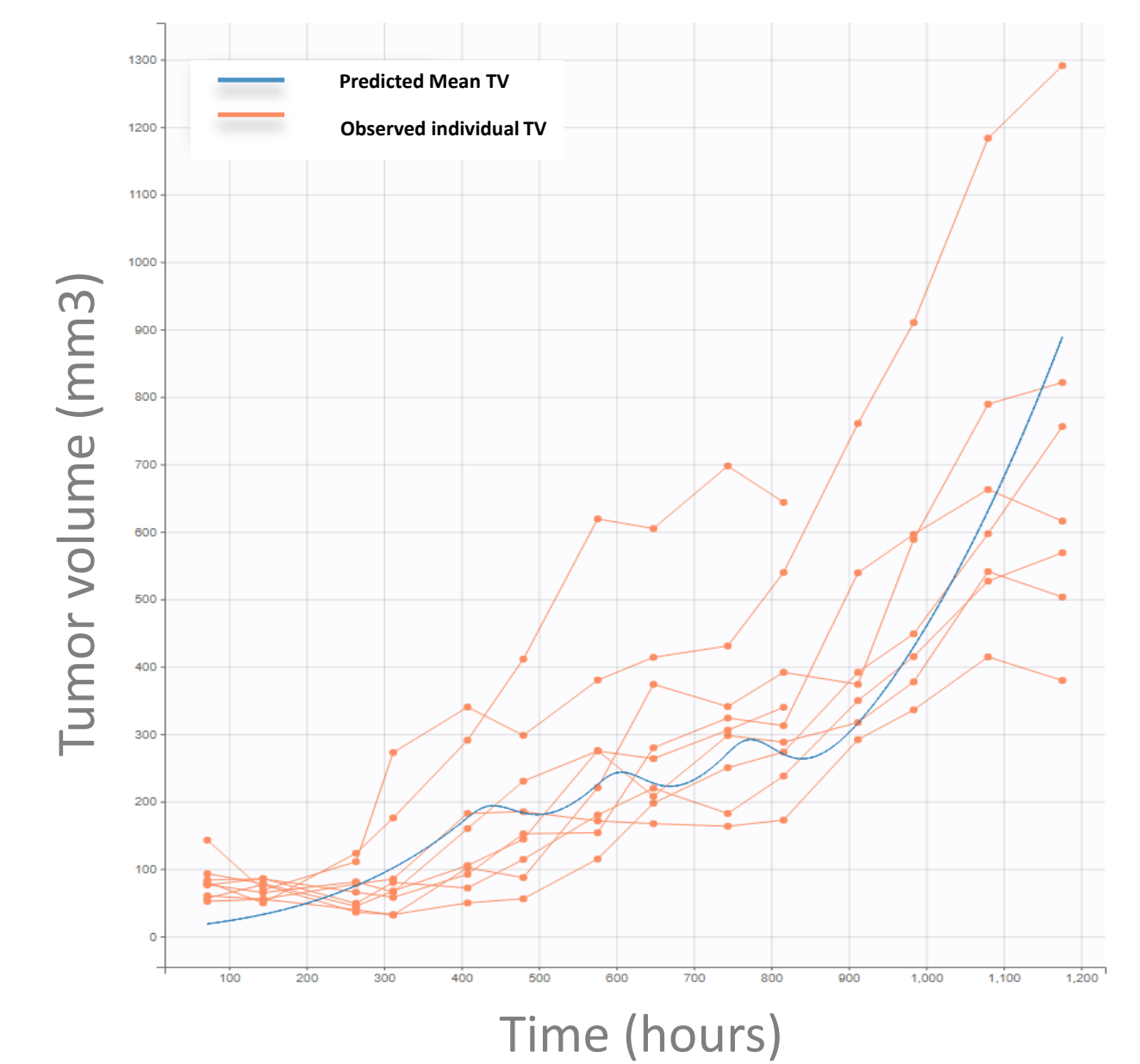
RESULTS

Final PK/PD MODEL

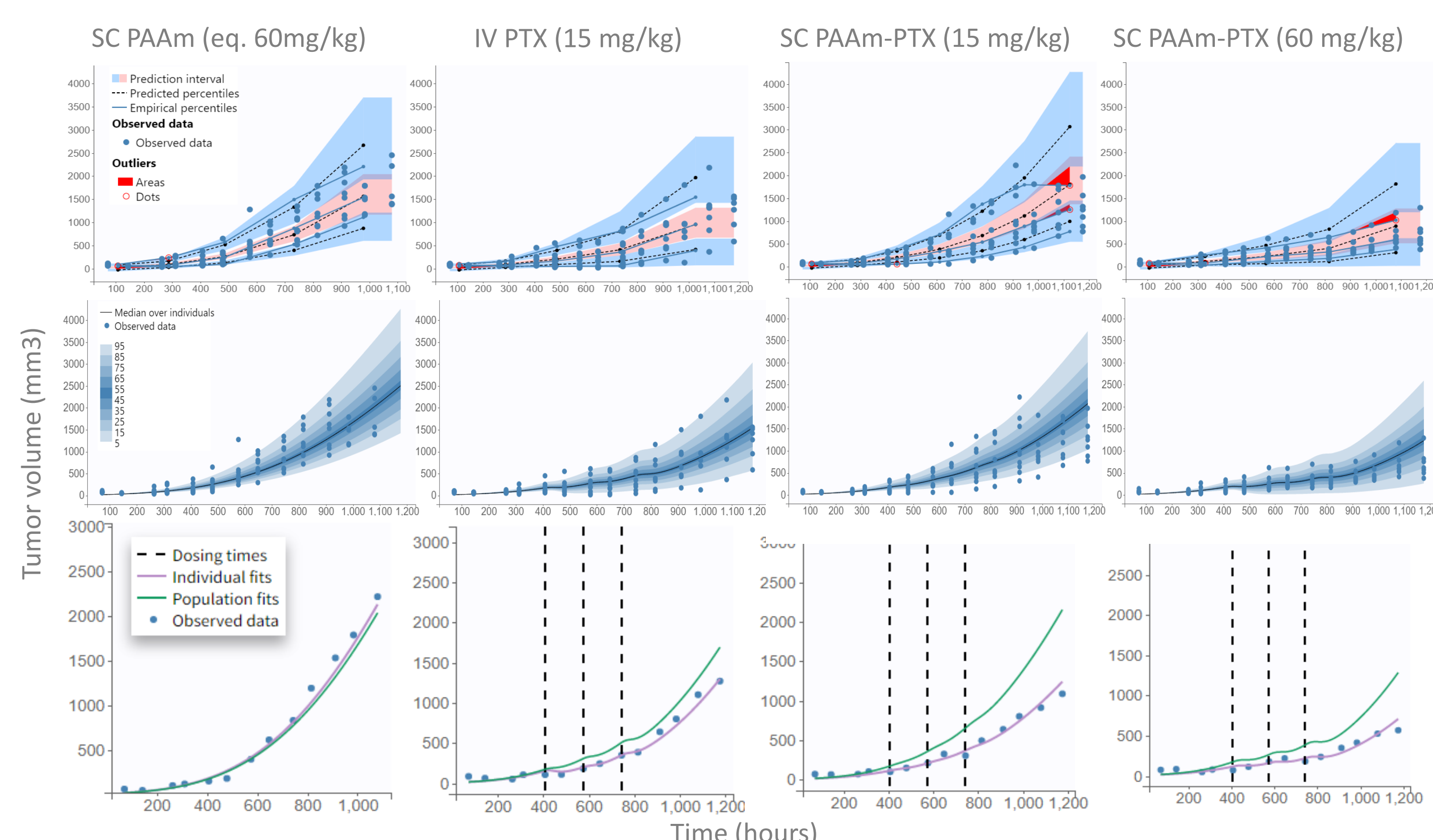


Model estimates and prediction power

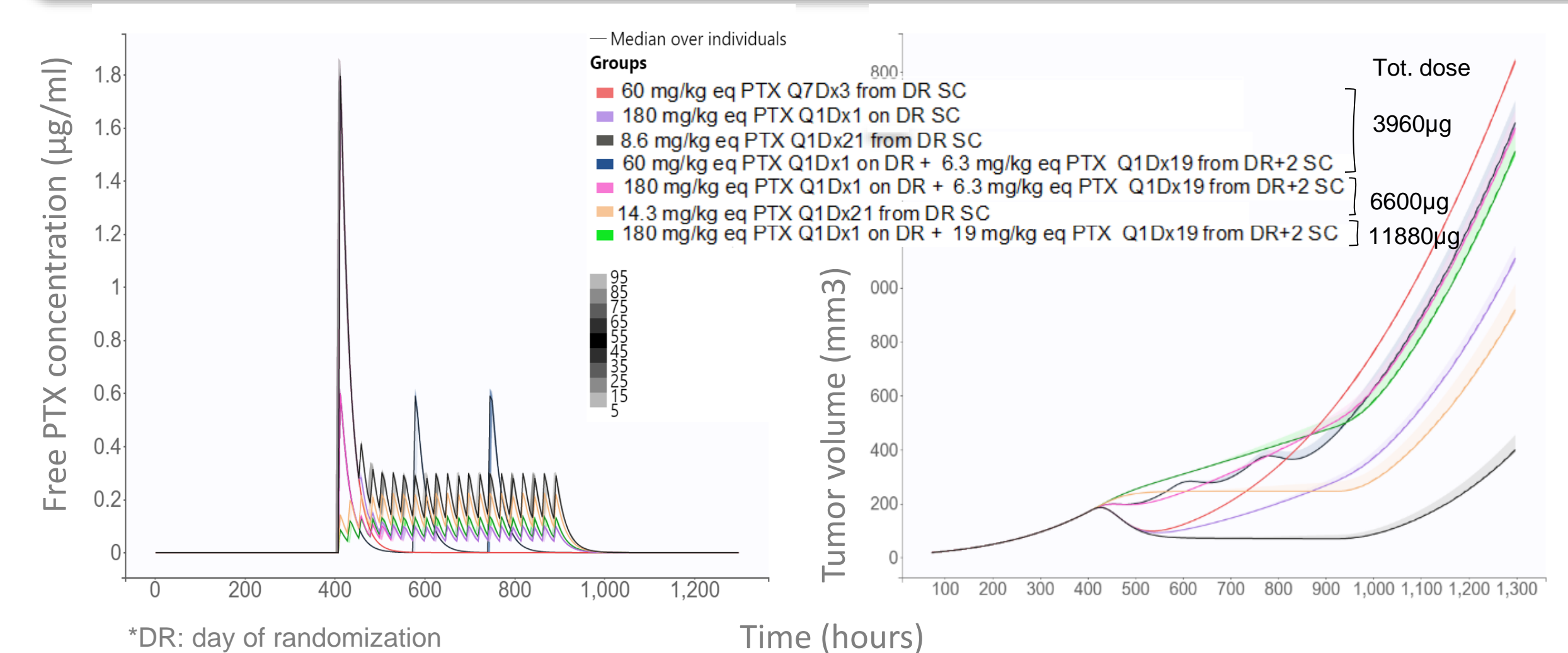
PARAMETER	ESTIMATE	RSE %
FIXED EFFECT		
V1 (ml)	10.73	5.82
k ₁₂	0.65	12.8
k ₂₁	0.51	0.852
k _e	2.76	0.134
k _b	0.047	13.5
γ	7.17	5.25
β	0.0013	10.3
k _{tran}	0.05	0.402
Emax1	15.48	40.1
Emax2	13.8	3.51
EC50	462.7	1.16
STANDARD DEVIATION OF THE RANDOM EFFECT		
ΩV1	0.26	19.4
ΩK ₁₂	0.21	37
ΩK _e	0.57	19.9
ΩK _β	1.15	24.5
ΩEmax1	1.23	25.4



Goodness of fit



TREATMENT SIMULATIONS



ACKNOWLEDGMENTS

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