



POPULATION PHARMACOKINETICS OF MYCOPHENOLIC ACID AND ITS METABOLITE IN PATIENTS WITH HIGH-GRADE LOCALLY ADVANCED OR METASTATIC OSTEOSARCOMA

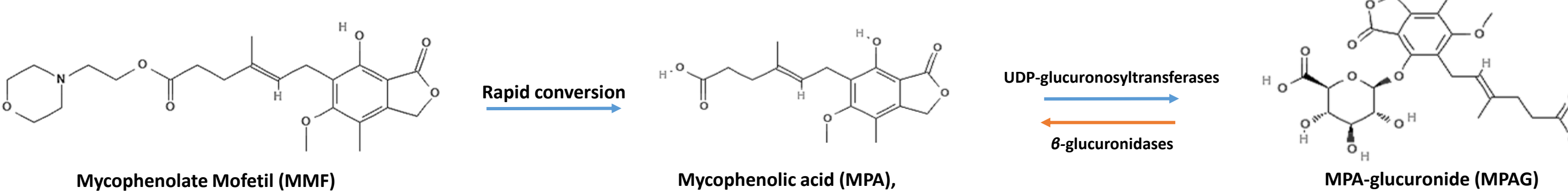


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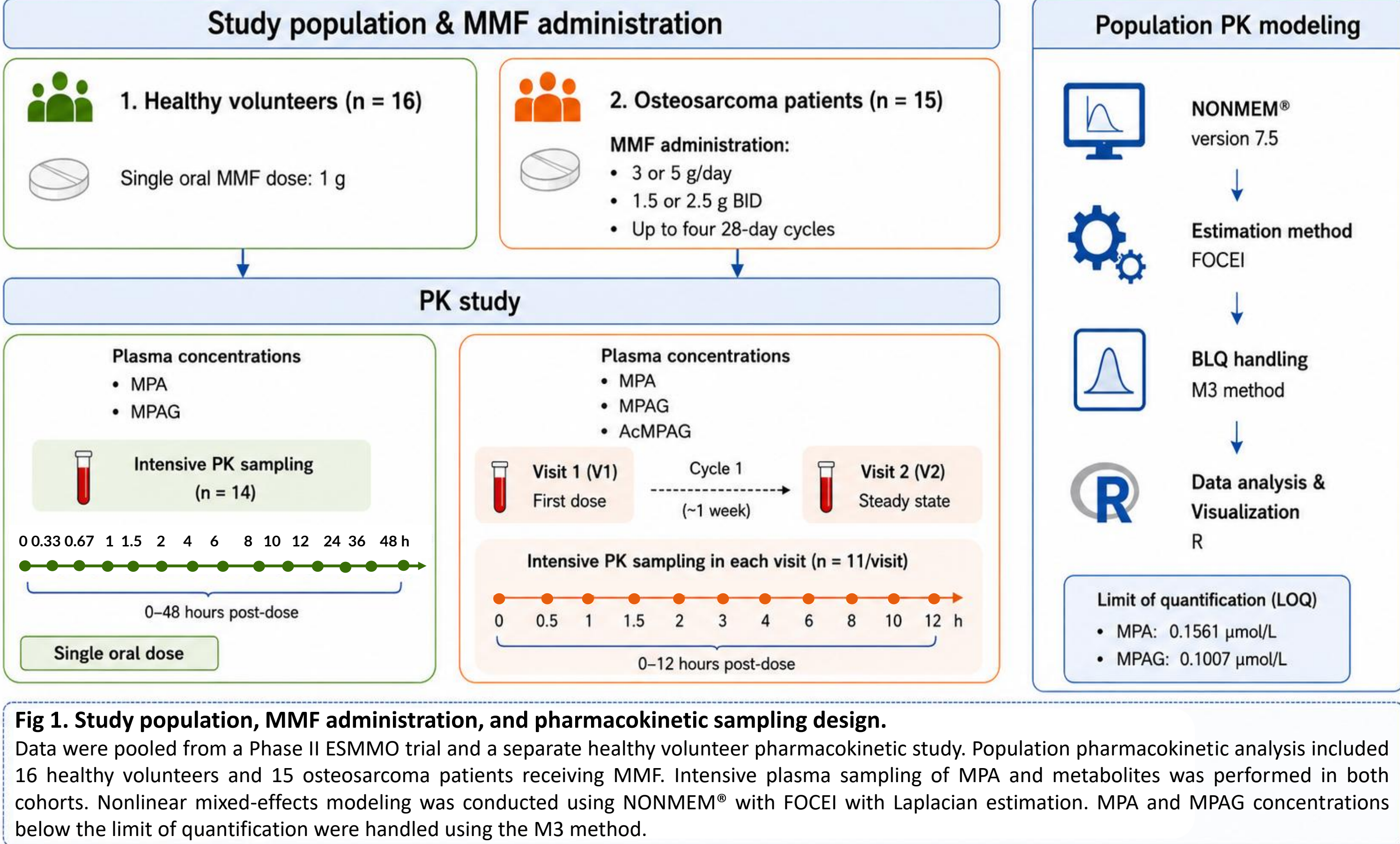
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INTRODUCTION

- Osteosarcoma:** Most common primary bone malignancy in youth, with poor outcomes in advanced or metastatic stages. [1–3].
- Anticancer Activity:** MPA inhibits tumor growth and metastasis in preclinical osteosarcoma models [4].
- MMF Metabolism:**


- The Recent Finding: A Phase II trial yielded negative results, likely due to insufficient drug exposure [5].
- Objective:** Develop a joint population pharmacokinetic (PopPK) analysis of MPA and MPAG in advanced osteosarcoma to support model-informed dose optimization.

METHODS

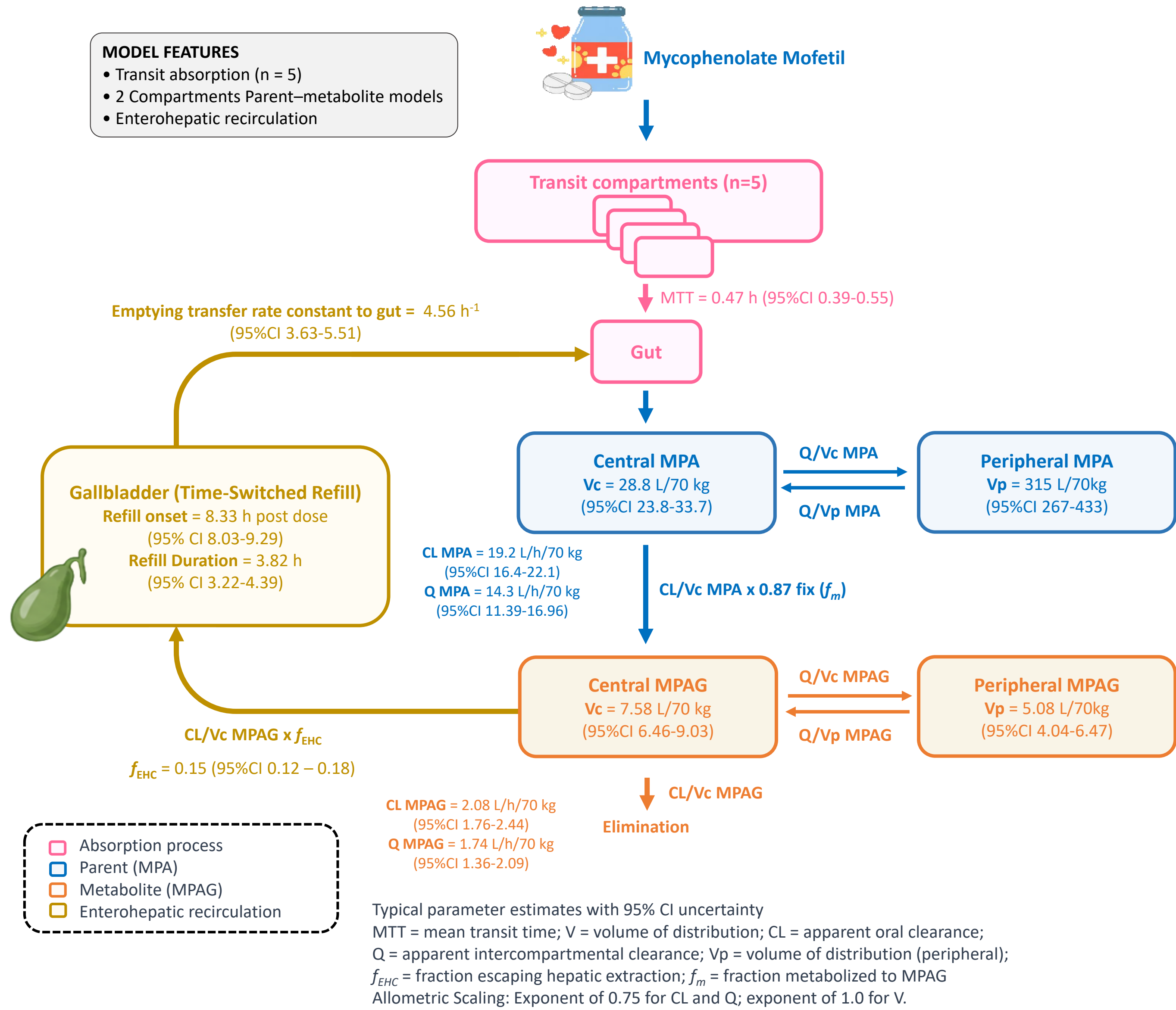


RESULTS

Table 1. Participants characteristics.

	Healthy Volunteers	Osteosarcoma Patients		Total
		Visit 1 (Week 0)	Visit 2 (Week 2)	
Participants, n	16	15		31
Observations, n	208	166	165	539
Male, n (%)	10 (62.5)	8 (53.3)		18 (58.1)
Female, n (%)	6 (37.5)	7 (46.7)		13 (41.9)
Age, yrs., mean (range)	28.9 (25.0-32.0)	33.3 (15.0-73.0)		31.0 (15.0-73.0)
Body weight, kg, mean (range)	59.2 (43.0-83.0)	53.9 (33.2-84.4)		56.61 (33.2-84.4)

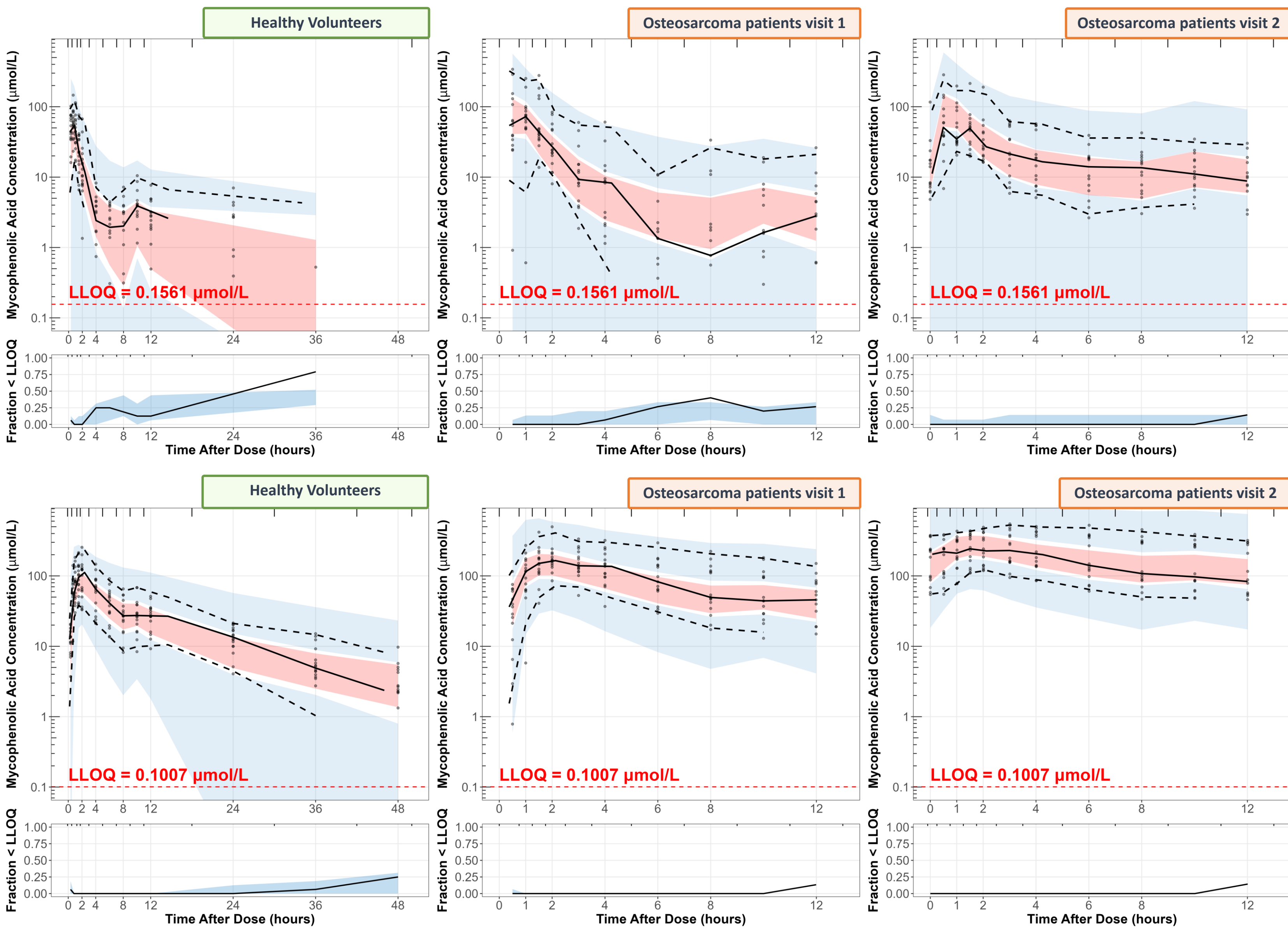
Schematic Representation of the Model



ACKNOWLEDGEMENTS

- We sincerely thank all patients, healthy volunteers, investigators, nurses, and clinical research staff who contributed to this study. Their participation and support made this pharmacometrics analysis possible.
- We also gratefully acknowledge the ESMO study team and collaborators for their valuable scientific and clinical contributions to this work.

Visual predictive checks (VPCs) for MPA and MPAG



CONCLUSION

- This study successfully developed a joint PopPK model for MPA and MPAG, characterizing complex enterohepatic recirculation (EHR) and high variability in an advanced osteosarcoma population.
- This model provides a robust framework for model-informed precision dosing to optimize MMF strategies, safely balancing efficacy within its narrow therapeutic window. Ultimately, these findings lay the groundwork for future evaluations of patient covariates, pharmacogenetic variability, and exposure-efficacy or exposure-safety relationships.

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