Acta Pharm. **24** (2024) 315–328 *Supplementary Data*

Population pharmacokinetics of ramipril in patients with chronic heart failure: A real-world longitudinal study

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Table S1. Parameters of the base pharmacokinetic model of ramipril.

	Estimate	**RSE**
Ka (h^{-1})	1.72	8%
CL (L/h)	176	10%
V_1 (L)	38.6	20%
V_2 (L)	426	18%
Q (L/h)	68.8	12%
CL_m (L/h)	10.1	8%
V_m (L)	86.3	14%
Between subject variability (BSV)		
BSV_{CL} (CV% [shrinkage])	26.3% [27%]	54%
BSV_{V1} (CV% [shrinkage])	137% [27%]	40%
BSV_{CLm} (CV% [shrinkage])	39.6 [3%]	35%
$BSVV_{Vm}$ (CV% [shrinkage])	64.9% [15%]	54%
Within subject variability (WSV)		
WSV_{CL} (CV% [shrinkage])	31.2% [25%]	22%
WSV_{CLm} (CV% [shrinkage])	13.1% [42%]	38%
WSV_{Vm} (CV% [shrinkage])	41.8% [42%]	126%
Residual variability [shrinkage]	[15%]	
Proportional (%)	38.6	12%
$Proportional_m$ (%)	15.1	16%

Ka - absorption rate constant of ramipril, CL - clearance of ramipril, V_1 - volume of central compartment for ramipril, V_2 - volume of peripheral compartment for ramipril, Q - distribution clearance of ramipril, V_m - volume of distribution of ramiprilat, CL_m - clearance of ramiprilat, CV - coefficient of variation, RSE - relative standard error

Table S2. Influence of covariates associated with body size on pharmacokinetics of ramipril and ramiprilat.

Model	**CL (□OFV)**	**CL_m (□OFV)**	**V_1 (□OFV)**	**V_m (□OFV)**
WT^1	-0.723	6.257	2.126	-0.362
$WT^{0.75}$	-3.064	2.825		
FFM^1	-3.872	1.139	**0.821**	**-1.896**
$FFM^{0.75}$	**-4.396**	**-0.680**		
NFM^1	-4.184	1.145	0.825	-1.893
$NFM^{0.75}$	-4.812	-0.675		

□OFV – difference of objective function value; WT – body weight, FFM - fat-free mass, NFM - normal fat mass

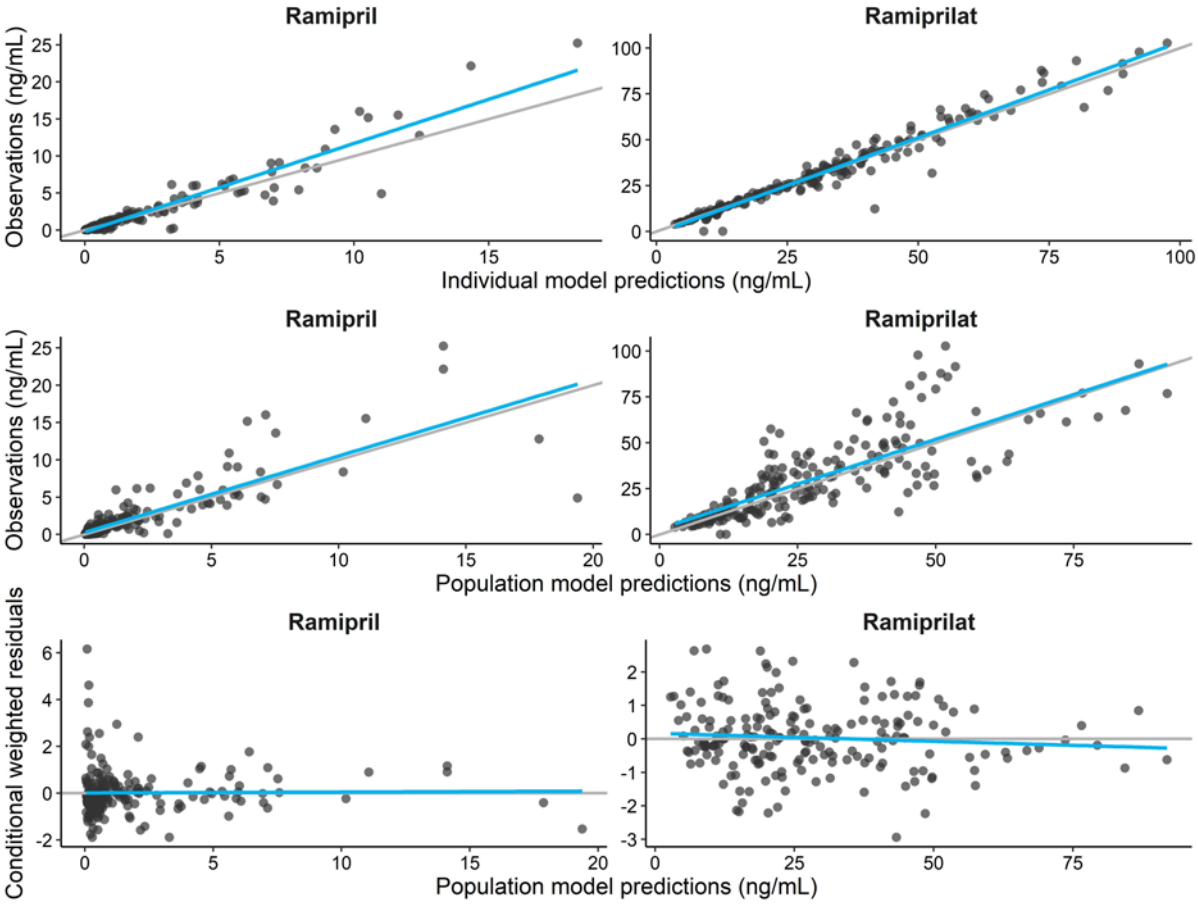

Figure S1: Standard diagnostic plots of the final population pharmacokinetic model of ramipril.

Table S3: Ramipril pharmacokinetics at the initial and follow-up study visit (N=19).

	Initial visit	**Follow-up visit**	**Wilcoxon signed-rank test**
	Median (range)	Median (range)	P-value
CL (L/h)	182.1 (79.8-322.8)	199.2 (86.0-456.7)	0.126
V_1 (L)	40.1 (13.4-304.7)	44.6 (14.2-304.7)	0.084
V_2 (L)	441.4 (288.7-601.1)	459.2 (290.7-599.2)	**0.036**
Q (L/h)	72.9 (53.0-91.9)	75.1 (53.3-91.7)	**0.036**
CL_m (L/h)	10.1 (5.3-24.2)	10.0 (5.0-26.6)	0.841
V_m (L)	86.4 (29.7-704.3)	68.5 (26.0-323.6)	0.117

CL - clearance of ramipril, V_1 - volume of central compartment for ramipril, V_2 - volume of peripheral compartment for ramipril, Q - distribution clearance of ramipril, V_m - volume of distribution of ramiprilat, CL_m - clearance of ramiprilat

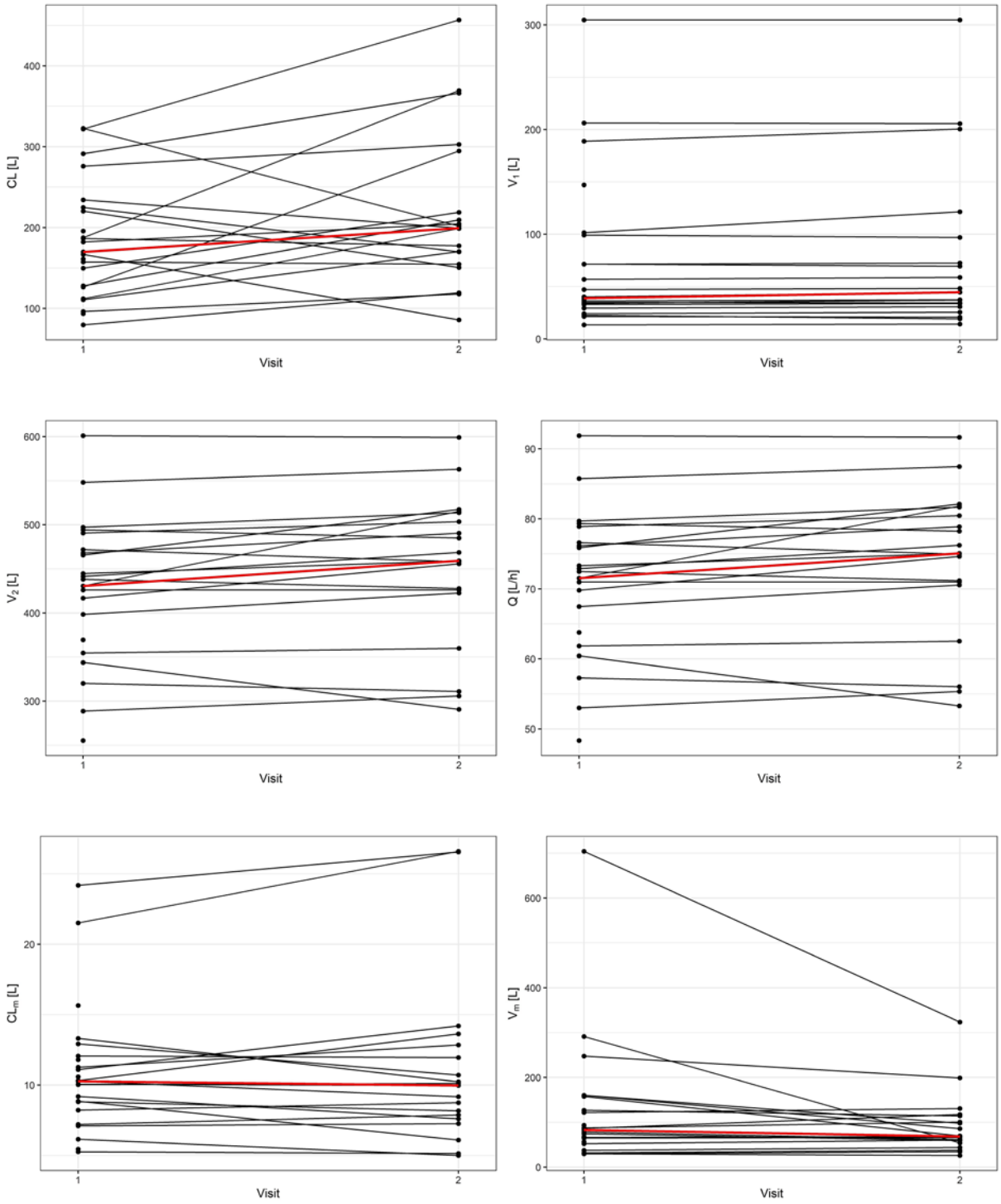

Figure S2: Changes in individual pharmacokinetic parameters (circles and black lines) of ramipril between the two study visits and median (red line).