

Supplementary Material

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Title:

Clinical Pharmacokinetics of a lipid based formulation of Risperidone, VAL401; analysis of a single, first dose in an open label trial of late stage cancer patients

Running header:

Clinical Pharmacokinetics of VAL401, a lipid based formulation of Risperidone, in late stage cancer patients

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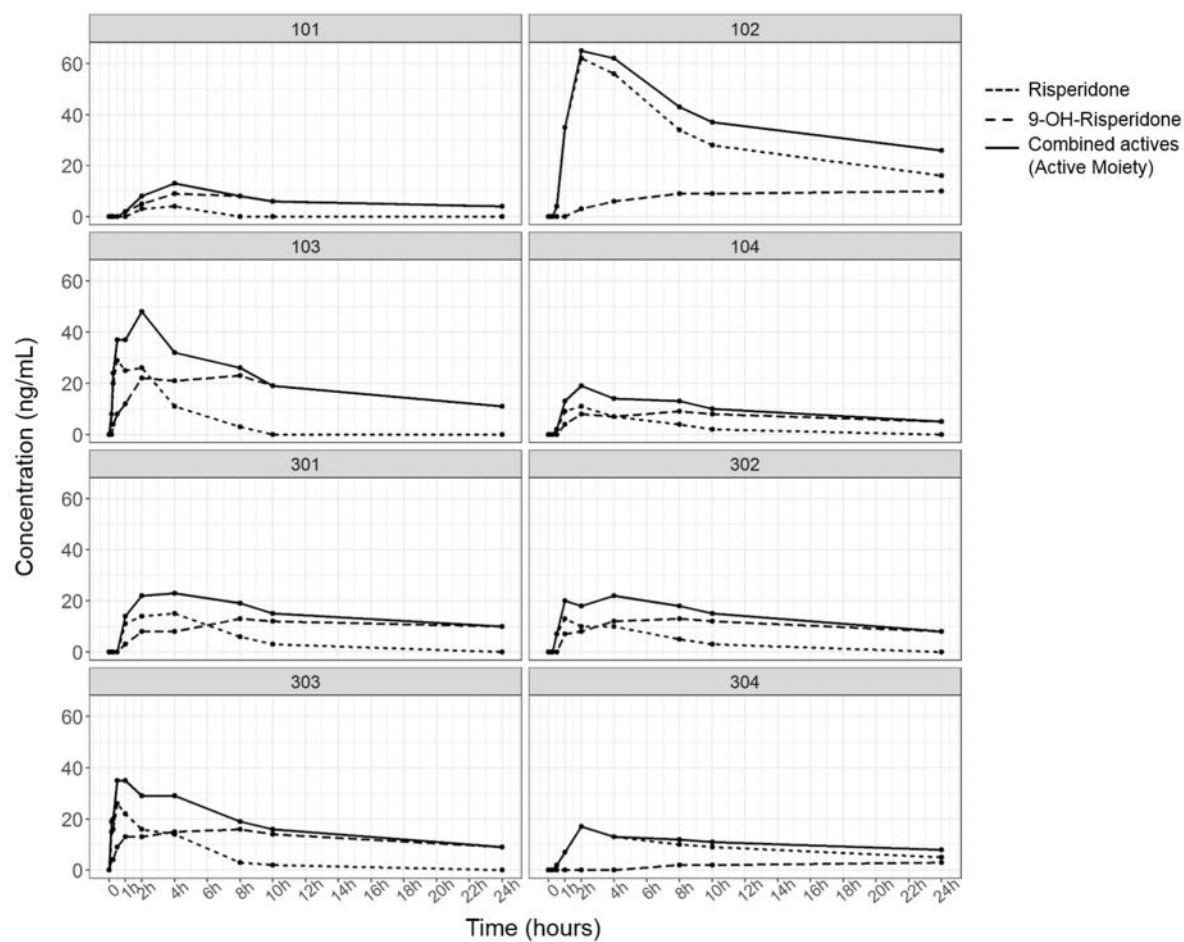
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Supplementary Figure S1: Concentration levels (ng/mL) of risperidone, active metabolite 9-hydroxy-risperidone and the combined actives, “active moiety” (a sum of risperidone and 9-hydroxy-risperidone) for each patient in the VAL-401 trial.

Time	Risperidone (ng/mL)		9-hydroxy-risperidone (ng/mL)		Total Active (ng/mL)	
	Mean	SEM	Mean	SEM	Mean	SEM
0	0.00	0.00	0.00	0.00	0.00	0.00
10 min	2.88	1.99	0.50	0.50	3.38	2.44
15 min	4.50	2.97	1.00	0.65	5.50	3.62
30 min	8.75	4.18	2.13	1.39	10.88	5.54
1 hour	15.25	3.99	5.13	1.80	20.38	4.85
2 hours	19.88	6.45	8.38	2.38	28.25	6.69
4 hours	16.25	5.82	9.75	2.23	26.00	5.74
8 hours	8.13	3.83	11.63	2.20	19.75	3.84
10 hours	5.88	3.31	10.25	1.84	16.13	3.31
24 hours	2.63	2.01	7.50	1.09	10.13	2.42

Supplementary Table S1: Mean and SEM (standard error of the mean) values stated across the time course for risperidone, active metabolite 9-hydroxy-risperidone and the combined actives (a sum of risperidone and 9-hydroxy-risperidone).

VAL-401 patients		
Active Moiety (risperidone + 9-OH-risperidone): "ParamSum"		
Parameter	unit	Lung cancer (median)
T _{max}	hour	3
C _{max}	ng/ml	11.3*
C _{last}	ng/ml	7.3*
t _{1/2}	hour	25.4
V _{dss}	mL	268.5
AUC (0-∞)	ng.h/mL	302.5*
AUC (0-last)	ng.h/mL	163*
AUMC (0-∞)	ng.h ² /mL	19021.4*
Cl oral	mL/min	352.8
MRT	hour	13

Supplementary Table S2: Summary of median values of pharmacokinetics parameter for the combination as the active moiety using the "ParamSum" approach in VAL-401 study. VAL-401 parameter values normalised by dose were reported for C_{max}, AUC_{0-∞}, AUC_{0-last} and AUMC_{0-∞}, characterised with an asterisk *, adjusting values to a dosage of 1mg of risperidone.

* normalised by dose