

Table 1. Patient characteristics. Presented data are obtained from study-interview, medical records and trial assays.

Patients Characteristics (n=46)	Numbers
<b>Demographics:</b>	
Male gender <sup>a</sup>	26 (56.5)
Age (years) <sup>b</sup>	42 (20 to 59)
Age ≥ 45 years <sup>a</sup>	21 (45.7)
<b>Clinical assessments:</b>	
<b>Clinical:</b>	
Smokers <sup>a</sup>	17 (37.0)
BMI (kg/cm <sup>2</sup> ) <sup>b</sup>	30.9 (20.1 to 48.8)
Daily caffeine <sup>c</sup> (mg) <sup>b</sup>	744.9 (0 to 2224.2)
Baseline CRP ≥ 5 mg/l <sup>a</sup>	16 (34.8)
<b>Observed chronic<sup>d</sup> blood dyscrasias (n= 42):<sup>a</sup></b>	
Leukocytosis (> 8,8 x 10 <sup>9</sup> /l)	16 (38.1)
Basophilia (> 0,1 x 10 <sup>9</sup> /l)	1 (2.4)
Eosinopenia (< 0,04 x 10 <sup>9</sup> /l)	19 (45.2)
Lymphocytosis (> 3,5 x 10 <sup>9</sup> /l)	3 (7.1)
Lymphopenia (< 1,0 x 10 <sup>9</sup> /l)	1 (2.4)
Monocytosis (> 7,6 x 10 <sup>9</sup> /l)	4 (9.6)
Neutrophilia (> 5,9 x 10 <sup>9</sup> /l)	13 (31.0)
Neutropenia (< 1,6 x 10 <sup>9</sup> /l)	1 (2.4)
<b>Clozapine dosing:</b>	
1 daily administration <sup>a</sup>	29 (63.0)
2 daily administrations <sup>a</sup>	12 (26.1)
3 daily administrations <sup>a</sup>	4 (8.7)
4 daily administrations <sup>a</sup>	1 (2.2)
Dose, evening (mg) <sup>b</sup>	237.5 (50 to 500)
Dose, daily (mg) <sup>b</sup>	300.0 (50 to 800)
<b>Co-medications of relevance<sup>a,c</sup></b>	
Antidepressants	21 (45.7)
Anticonvulsants	8 (17.4)
Proton pump inhibitors	9 (19.6)
Antibiotics	0 (0)
Hormonal contraceptives (n=20)	6 (30.0)
<b>Pharmacokinetic assessments:</b>	
<b>Clozapine (CLZ):<sup>b</sup></b>	
CLZ concentration, 10 hours post-dose (n=44) (nmol/l) / (ng/ml)	1418.2 (144.8 to 6300.8) / 463.4 (47.4 to 2059.2)
CLZ concentration, 12 hours post-dose (n=45) (nmol/l) / (ng/ml)	1258.6 (120.1 to 5870.4) / 411.4 (39.2 to 1918.3)
C/D <sup>f</sup> , 10 hours post-dose (n=44) (ng/ml/mg)	1.56 (0.39 to 4.74)
C/D <sup>f</sup> , 12 hours post-dose (n=45) (ng/ml/mg)	1.42 (0.42 to 5.07)
Maximum percentage change, across the 12-hour time-point (n=45)	16.2 (2.9 to 42.8)
Maximum percentage difference, related to 12-hour values (n=45)	17.2 (6.1 to 52.6)
<b>Norclozapine (NCLZ):<sup>b</sup></b>	
NCLZ concentration, 10 hours post-dose (n=44) (nmol/l) / (ng/ml)	879.9 (163.7 to 2634.4) / 287.6 (53.6 to 860.1)
NCLZ concentration, 12 hours post-dose (n=45) (nmol/l) / (ng/ml)	786.1 (80.3 to 2738.9) / 256.9 (26.1 to 895.1)
Maximum percentage change, across the 12-hour time-point (n=45)	14.2 (1.7 to 38.4)
Maximum percentage difference, related to 12-hour values (n=45)	18.0 (5.2 to 105.0)
<b>Metabolite and parent compound:<sup>b</sup></b>	
Combined (CLZ+NCLZ) C/D <sup>f</sup> , 10 hours post-dose (n=44) (ng/ml/mg)	2.55 (0.86 to 6.43)
Combined (CLZ+NCLZ) C/D <sup>f</sup> , 12 hours post-dose (n=45) (ng/ml/mg)	2.38 (1.01 to 7.13)
MR <sup>g</sup> (NCLZ/CLZ), 10 hours post-dose (n=44)	0.61 (0.33 to 1.17)
MR <sup>g</sup> (NCLZ/CLZ), 12 hours post-dose (n=45)	0.64 (0.36 to 1.39)

<sup>a</sup> Values are given as numbers and proportions (n (%))<sup>b</sup> Values are given as median and range (min-max)<sup>c</sup> Estimate based on daily cups (1.7 dl) of caffeinated beverages: coffee (73.6 mg/cup), the (42.5mg/cup), cola (25.9mg/cup), energy drinks (54.7mg/cup) [26]<sup>d</sup> Chronic blood dyscrasia was defined as a minimum of 50% of the observations, for a given cell line, located either under or above the normal reference range. Only subjects with three or more observations within the retrospective period were included for chronic blood dyscrasia evaluation. The mean deviation from inclusion day was -1.2 ± 11.3 days. The mean period of observation was 5.8 ± 1.1 months, and the mean number of observations within the retrospective follow-up period was 6.9 ± 3.2 observations<sup>e</sup> Medications of relevance defined as drug-groups with known affecters of s-clozapine<sup>f</sup> C/D = concentration to dose ratio<sup>g</sup> MR = metabolic ratio