

SUPPLEMENTARY MATERIAL

Supplement Table 1. Descriptive characteristics of variables at baseline by sex.

	Female (n=9)		Male (n=29)		p-value
	N	Median [IQR] or Frequency (%)	N	Median [IQR] or Frequency (%)	
Age (years)	9	25.00 [21.00; 34.50]	29	26.50 [23.75; 33.75]	0.41
Smoking	9		29		0.01
No		6 (66.7)		6 (22.2)	
Yes		3 (33.3)		21 (77.8)	
DUP (weeks)	9	9.00 [5.00; 12.50]	29	12.00 [8.50; 16.00]	0.12
Drug before	9		29		0.74
Amisulpride		0 (0.0)		1 (2.6)	
Aripiprazole		1 (11.1)		2 (5.3)	
Haloperidole		0 (0.0)		1 (2.6)	
Olanzapine		4 (44.4)		21 (55.3)	
Risperidone		4 (44.4)		13 (34.2)	
Clozapine (mg/day)	9	350.00 [350.00; 450.00]	27	400.00 [350.00; 500.00]	0.45
CLO (ng/mL)	9	349.90 [191.75; 458.15]	29	334.85 [191.32; 427.02]	0.93
Nor-CLO (ng/mL)	8	153.20 [127.50; 178.15]	28	128.75 [61.87; 218.10]	0.36
CLO/Nor-CLO ratio	8	2.41 [1.70; 3.08]	28	2.46 [1.56; 4.78]	0.62
BMI (Pro clo)	9	23.50 [21.20; 23.90]	29	22.55 [22.00; 23.60]	0.85
PANSS-Positive	9	33.00 [32.00; 37.50]	29	35.00 [32.00; 37.00]	0.72
PANSS-Negative	9	24.00 [14.50; 30.50]	29	26.50 [15.75; 32.00]	0.20
PANSS-General	9	37.00 [32.00; 42.00]	29	40.50 [34.00; 44.25]	0.22
PANSS-Total	9	94.00 [82.00; 107.50]	29	100.00 [87.75; 110.00]	0.33

Abbreviations: BMI, body mass index; DUP: duration of untreated psychosis; IQR: interquartile range; PANSS: Positive and Negative Syndrome Scale.

Statistically significant differences are presented with **bold** font.

Supplement Table 2. Multivariable adjusted model for clozapine dose (mg/day) and other variables in a sensitivity analysis excluding one patient with only one visit (n=333, visits=37).

Covariate	β	95% Confidence Interval		p-value
Age (per year)	3.85	-5.20	12.90	0.405
Sex				
Female*				
Male	67.12	-42.06	176.29	0.228
Smoking				
No*				
Yes	-99.75	-203.01	3.51	0.058
Drug before clozapine				
Amisulpride*				
Aripiprazole	186.84	-212.01	585.69	0.359
Haloperidole	186.71	-224.86	598.29	0.374
Olanzapine	208.73	-125.37	542.84	0.221
Risperidone	208.80	-111.66	529.25	0.202
DUP (per week)	15.22	-2.20	32.65	0.087
BMI (before clozapine), per kg/m ²	-4.11	-43.37	35.15	0.837
PANSS-Total (before clozapine), per unit	-2.73	-6.50	1.04	0.155

* Reference category.

Abbreviations: BMI, body mass index; DUP: duration of untreated psychosis; PANSS: Positive and Negative Syndrome Scale.

Supplement Table 3. Multivariable adjusted model for blood clozapine levels (ng/mL) and other variables in a sensitivity analysis excluding one patient with only one visit (n=37, visits=331).

Covariate	β	95% Confidence Interval		p-value
Clozapine (per 50 mg/day)	28.79	18.09	39.49	<0.001
Age (per year)	-0.77	-13.56	12.01	0.905
Sex				
Female*	0			
Male	40.27	-113.49	194.03	0.608
Smoking				
No*	0			
Yes	-88.24	-235.05	58.57	0.239
Drug before clozapine				
Amisulpride*	0			
Aripiprazole	-177.42	-738.56	383.73	0.535
Haloperidole	36.18	-541.49	613.86	0.902
Olanzapine	-183.60	-653.72	286.52	0.444
Risperidone	-44.58	-495.55	406.40	0.846
DUP (per week)	-6.69	-31.43	18.05	0.596
BMI (before clozapine), per kg/m ²	-4.29	-59.30	50.71	0.878
PANSS-Total (before clozapine), per unit	-0.05	-5.37	5.27	0.984

* Reference category.

Abbreviations: BMI, body mass index; DUP: duration of untreated psychosis; PANSS: Positive and Negative Syndrome Scale.

Supplement Table4. Multivariable adjusted model for nor-clozapine levels (ng/mL) and other variables in a sensitivity analysis excluding one patient with only one visit(n=37, visits=326).

Covariate	β	95% ConfidenceInterval		p-value
Clozapine (per 50 mg/day)	10.83	3.44	18.21	0.004
Age (per year)	-1.17	-8.21	5.88	0.746
Sex				
Female*	0			
Male	-13.91	-98.47	70.65	0.747
Smoking				
No*	0			
Yes	-25.49	-106.53	55.54	0.538
Drug before clozapine				
Amisulpride*	0			
Aripiprazole	-122.37	-430.41	185.67	0.436
Haloperidole	106.60	-209.88	423.08	0.509
Olanzapine	-90.32	-348.16	167.53	0.492
Risperidone	-65.02	-312.41	182.37	0.606
DUP (per week)	-4.77	-18.43	8.90	0.494
BMI (before clozapine), per kg/m ²	5.53	-24.61	35.66	0.719
PANSS-Total (before clozapine), per unit	0.67	-2.26	3.60	0.653

* Reference category.

Abbreviations: BMI, body mass index; DUP: duration of untreated psychosis; PANSS: Positive and Negative Syndrome Scale.

Supplement Table5. Multivariable adjusted model for clozapine/nor-clozapine ratio (ng/mL) and other variables in a sensitivity analysis excluding one patient with only one visit (n=37, visits=326).

Covariate	β	95% ConfidenceInterval		p-value
Clozapine (per 50 mg/day)	-0.19	-0.38	0.00	0.051
Age (per year)	0.04	-0.12	0.20	0.637
Sex				
Female*	0			
Male	0.62	-1.35	2.60	0.535
Smoking				
No*	0			
Yes	0.20	-1.69	2.10	0.836
Drug before clozapine				
Amisulpride*	0			
Aripiprazole	1.71	-5.47	8.89	0.640
Haloperidole	-0.29	-7.65	7.07	0.938
Olanzapine	1.25	-4.75	7.26	0.682
Risperidone	1.39	-4.37	7.15	0.636
DUP (per week)	0.04	-0.28	0.36	0.787
BMI (before clozapine), per kg/m ²	-0.58	-1.29	0.12	0.102
PANSS-Total (before clozapine), per unit	-0.01	-0.08	0.06	0.776

* Reference category.

Abbreviations: BMI, body mass index; DUP: duration of untreated psychosis; PANSS: Positive and Negative Syndrome Scale.

Supplement Table 6. Multivariable adjusted model for PANSS-Total after clozapine and risk factors (n=36).

Covariate	β	95% ConfidenceInterval		p-value
Clozapine (per 50 mg/day)	-0.26	-1.56	1.04	0.683
Age (per year)	-0.40	-1.15	0.35	0.278
Sex				
Female*	0			
Male	-3.32	-11.66	5.01	0.418
Smoking				
No*	0			
Yes	2.60	-6.08	11.28	0.542
Drug before clozapine				
Amisulpride*	0			
Aripiprazole	-7.39	-33.17	18.39	0.560
Olanzapine	-12.07	-34.22	10.07	0.272
Risperidone	-11.56	-34.60	11.47	0.311
DUP (per week)	1.00	-0.42	2.43	0.159
Number of visits (per unit)	-0.17	-0.91	0.58	0.648
BMI (before clozapine), per kg/m ²	-1.69	-4.78	1.40	0.271
PANSS-Total (before clozapine), per unit	0.26	-0.05	0.57	0.101

* Reference category.

Abbreviations: BMI, body mass index; DUP: duration of untreated psychosis; PANSS: Positive and Negative Syndrome Scale.

Supplement Table7. Multivariable adjusted model for change of PANSS-Total before and after clozapine and other variables (n=36).

Covariate	β	95% ConfidenceInterval		p-value
Clozapine (per 50 mg/day)	0.48	-1.26	2.23	0.573
Age (per year)	-0.16	-1.18	0.87	0.757
Sex				
Female*	0			
Male	-1.20	-12.66	10.26	0.831
Smoking				
No*	0			
Yes	8.48	-3.02	19.99	0.141
Drug before clozapine				
Amisulpride*	0			
Aripiprazole	0.70	-34.63	36.04	0.968
Olanzapine	-3.37	-33.56	26.83	0.820
Risperidone	0.51	-30.56	31.58	0.973
DUP (per week)	-0.93	-2.54	0.69	0.249
Number of visits (per unit)	-0.26	-1.29	0.77	0.610
BMI (before clozapine), per kg/m ²	-1.68	-5.95	2.59	0.426

* Reference category.

Abbreviations: BMI, body mass index; DUP: duration of untreated psychosis; PANSS: Positive and Negative Syndrome Scale.

Supplement Table8. Multivariable adjusted model for PANSS-Positive after clozapine and other variables (n=36).

Covariate	β	95% ConfidenceInterval		p-value
Clozapine (per 50 mg/day)	-0.15	-0.69	0.40	0.580

Age (per year)	-0.29	-0.60	0.02	0.065
Sex				
Female*	0			
Male	-2.45	-5.90	1.00	0.155
Smoking				
No*	0			
Yes	3.45	-0.13	7.02	0.058
Drug before clozapine				
Amisulpride*	0			
Aripiprazole	-7.46	-18.03	3.11	0.158
Olanzapine	-10.29	-19.41	-1.17	0.029
Risperidone	-10.64	-20.02	-1.26	0.028
DUP (per week)	0.53	0.05	1.02	0.032
Number of visits (per unit)	-0.10	-0.41	0.21	0.526
BMI (before clozapine), per kg/m ²	-0.61	-1.88	0.67	0.338
PANSS-Total (before clozapine), per unit	-0.03	-0.54	0.48	0.892

* Reference category.

Abbreviations: BMI, body mass index; DUP: duration of untreated psychosis; PANSS: Positive and Negative Syndrome Scale.

Supplement Table9. Multivariable adjusted model for change of PANSS-Positive before and after clozapine and other variables (n=36).

Covariate	β	95% ConfidenceInterval		p-value
Clozapine (per 50 mg/day)	-0.47	-1.14	0.21	0.166
Age (per year)	-0.19	-0.58	0.21	0.337
Sex				
Female*	0			
Male	-1.66	-6.06	2.75	0.446
Smoking				
No*	0			
Yes	1.46	-2.96	5.88	0.503
Drug before clozapine				
Amisulpride*	0			
Aripiprazole	-6.50	-20.08	7.08	0.334
Olanzapine	-7.63	-19.23	3.98	0.188
Risperidone	-7.96	-19.91	3.98	0.182
DUP (per week)	0.48	-0.14	1.10	0.121
Number of visits (per unit)	-0.20	-0.59	0.20	0.314
BMI (before clozapine), per kg/m ²	-0.47	-2.11	1.17	0.563

* Reference category.

Abbreviations: BMI, body mass index; DUP: duration of untreated psychosis; PANSS: Positive and Negative Syndrome Scale.

Supplement Table10. Multivariable adjusted model for PANSS-Negative after clozapine and other variables (n=36).

Covariate	β	95% ConfidenceInterval		p-value
Clozapine (per 50 mg/day)	-0.11	-0.62	0.40	0.652
Age (per year)	0.03	-0.26	0.32	0.842
Sex				
Female*	-2.24	-5.46	0.99	0.165

Male				
Smoking				
No*	0			
Yes	0.30	-3.20	3.80	0.861
Drug before clozapine				
Amisulpride*	0			
Aripiprazole	1.64	-8.54	11.83	0.742
Olanzapine	0.14	-8.54	8.83	0.973
Risperidone	-0.16	-9.23	8.92	0.972
DUP (per week)	0.18	-0.35	0.71	0.488
Number of visits (per unit)	-0.03	-0.33	0.26	0.807
BMI (before clozapine), per kg/m ²	-0.63	-1.83	0.58	0.293
PANSS-Total (before clozapine), per unit	0.37	0.17	0.57	0.001

* Reference category.

Abbreviations: BMI, body mass index; DUP: duration of untreated psychosis; PANSS: Positive and Negative Syndrome Scale.

Supplement Table 11. Multivariable adjusted model for change of PANSS-Negative before and after clozapine and other variables(n=36).

Covariate	β	95% ConfidenceInterval		p-value
Clozapine (per 50 mg/day)	0.29	-0.51	1.09	0.466
Age (per year)	0.20	-0.27	0.67	0.400
Sex				
Female*	0			
Male	-2.04	-7.29	3.21	0.432
Smoking				
No*	0			
Yes	4.48	-0.79	9.75	0.092
Drug before clozapine				
Amisulpride*	0			
Aripiprazole	8.67	-7.52	24.85	0.281
Olanzapine	5.85	-7.98	19.68	0.392
Risperidone	7.58	-6.65	21.81	0.283
DUP (per week)	-0.68	-1.42	0.06	0.070
Number of visits (per unit)	0.07	-0.40	0.54	0.753
BMI (before clozapine), per kg/m ²	-0.69	-2.65	1.27	0.474

* Reference category.

Abbreviations: BMI, body mass index; DUP: duration of untreated psychosis; PANSS: Positive and Negative Syndrome Scale.

Supplement Table 12. Multivariable adjusted model for PANSS-General after clozapine and other variables (n=36).

Covariate	β	95% ConfidenceInterval		p-value
Clozapine (per 50 mg/day)	-0.09	-0.61	0.42	0.707
Age (per year)	-0.04	-0.34	0.26	0.770
Sex				
Female*	0			
Male	0.12	-3.23	3.48	0.940

Smoking				
No*	0			
Yes	-2.17	-5.82	1.48	0.232
Drug before clozapine				
Amisulpride*	0			
Aripiprazole	0.73	-9.78	11.25	0.887
Olanzapine	-0.09	-9.01	8.83	0.984
Risperidone	-0.39	-9.71	8.93	0.932
DUP (per week)	0.59	0.06	1.12	0.032
Number of visits (per unit)	0.02	-0.29	0.32	0.906
BMI (before clozapine), per kg/m ²	-0.36	-1.62	0.90	0.556
PANSS-Total (before clozapine), per unit	0.02	-0.26	0.30	0.889

* Reference category.

Abbreviations: BMI, body mass index; DUP: duration of untreated psychosis; PANSS: Positive and Negative Syndrome Scale.

Supplement Table 13. Multivariable adjusted model for change of PANSS-General before and after clozapine and other variables (n=36).

Covariate	β	95% Confidence Interval		p-value
Clozapine (per 50 mg/day)	0.13	-0.76	1.01	0.770
Age (per year)	0.03	-0.49	0.55	0.906
Sex				
Female*	0			
Male	-0.23	-6.02	5.56	0.935
Smoking				
No*	0			
Yes	2.70	-3.11	8.52	0.347
Drug before clozapine				
Amisulpride*	0			
Aripiprazole	7.24	-10.61	25.09	0.411
Olanzapine	4.02	-11.24	19.27	0.593
Risperidone	6.67	-9.03	22.37	0.390
DUP (per week)	-0.25	-1.07	0.56	0.528
Number of visits (per unit)	0.12	-0.40	0.64	0.641
BMI (before clozapine), per kg/m ²	0.17	-1.99	2.33	0.873

* Reference category.

Abbreviations: BMI, body mass index; DUP: duration of untreated psychosis; PANSS: Positive and Negative Syndrome Scale.

Supplement Table 14. Multivariable adjusted model for BMI after clozapine and risk factors (n=36).

Covariate	β	95% Confidence Interval		p-value
Clozapine (per 50 mg/day)	-0.13	-0.31	0.06	0.174
Age (per year)	0.02	-0.09	0.13	0.691
Sex				
Female*	0			
Male	-0.30	-1.49	0.88	0.601
Smoking				
No*	0			
Yes	-0.10	-1.34	1.13	0.865

Drug before clozapine				
Amisulpride*	0			
Aripiprazole	1.61	-2.05	5.28	0.373
Olanzapine	0.90	-2.25	4.05	0.560
Risperidone	1.78	-1.50	5.05	0.274
DUP (per week)	-0.05	-0.25	0.15	0.633
Number of visits (per unit)	0.16	0.05	0.26	0.006
BMI (before clozapine), per kg/m²	0.74	0.30	1.18	0.002
PANSS-Total (before clozapine), per unit	0.03	-0.01	0.08	0.150

* Reference category.

Abbreviations: BMI, body mass index; DUP: duration of untreated psychosis; PANSS: Positive and Negative Syndrome Scale.

Supplement Table 15. Multivariable adjusted model for change of BMI before and after clozapine and other variables(n=36).

Covariate	β	95% ConfidenceInterval		p-value
Clozapine (per 50 mg/day)	-0.13	-0.31	0.06	0.173
Age (per year)	0.00	-0.10	0.11	0.932
Sex				
Female*	0			
Male	-0.30	-1.50	0.89	0.604
Smoking				
No*	0			
Yes	-0.08	-1.32	1.16	0.895
Drug before clozapine				
Amisulpride*	0			
Aripiprazole	1.60	-2.09	5.30	0.380
Olanzapine	0.94	-2.23	4.12	0.545
Risperidone	1.91	-1.39	5.20	0.244
DUP (per week)	-0.04	-0.24	0.16	0.684
Number of visits (per unit)	0.15	0.05	0.26	0.007
PANSS-Total (before clozapine), per unit	0.03	-0.01	0.08	0.153

* Reference category.

Abbreviations: BMI, body mass index; DUP: duration of untreated psychosis; PANSS: Positive and Negative Syndrome Scale.