

**Table 1** Summary of patient characteristics and information related to the TDM analyses of vortioxetine and antidepressant switch frequencies according to CYP2D6 metabolizer phenotype

Patient characteristics (N = 516)	CYP2D6 Phenotype <sup>a</sup>			
	PM	IM	NM	UM
Males/Females (N)	14/21	65/108	90/152	4/4
Age (years) (median (IQR))	47.0 (38.0-59.0)	47.0 (33.0-57.0)	44.5 (33.0-55.75)	53.5 (46.0-63.0)
Time from last dose to blood sample (h) (median (IQR))	21.3 (15.2-25.1)	22.0 (13.2-24.5)	24.0 (14.0-25.5)	21.5 (20.9-24.1)
Vortioxetine dose (mg) (median (IQR))	10.0 (10.0-20.0)	10.0 (10.0-20.0)	13.5 (10.0-20.0)	15.0 (10.0-16.25)
<b>Vortioxetine exposure</b>				
Concentration (ng/mL) (median (95% CI))	31.6 (15.8-37.9)	15.5 (13.4-17.6)	11.2 (10.1-12.1)	8.1 (4.5-11.3)
Ratio of medians	2.8	1.4	Reference	0.7
<b>Vortioxetine exposure (dose-harmonized to 10 mg/day)</b>				
Concentration (ng/mL) (median (95% CI))	23.9 (16.9-31.6)	12.5 (11.3-13.5)	8.1 (7.6-9.0)	5.9 (4.0-8.1)
Ratio of medians	3.0	1.5	Reference	0.7
Ln-transformed concentration (mean (95%CI))	3.1 (2.9-3.3)	2.5 (2.4-2.6)	2.1 (2.1-2.2)	1.7 (1.5-2.0)
P value <sup>b</sup>	<0.001	<0.001	Reference	0.21
95% confidence interval	0.65-1.22	0.20-0.51	Reference	-0.14-0.99
<b>Patients switching to alternative antidepressant treatment within 3 months</b>				
Switch / No switch (N)	6/29	8/165	6/236	2/6
P value <sup>c</sup>	0.001	0.28	Reference	0.02
Odds-ratio (95% CI)	8.0 (2.0-32.3)	1.9 (0.6 – 6.8)	Reference	12.7 (1.1-94.9)
<sup>a</sup> CYP2D6 phenotype was assigned based on <i>CYP2D6</i> genotype according to recommendation from the Clinical Pharmacogenomics Implementation Consortium (CPIC)[4] <sup>b</sup> Tukey test (corrected for multiple testing) comparing the ln-transformed concentrations for each CYP2D6 phenotype group to the NMs. For the purpose of statistical comparison, vortioxetine exposure levels were dose normalized and ln-transformed to restore normal distribution in accordance with the formula $\Delta \ln(c) = K_e \times t$ ; where <i>c</i> is concentration, <i>K<sub>e</sub></i> is the elimination rate constant and <i>t</i> is time. <sup>c</sup> Fisher's exact test comparing the frequency of switching to an alternative antidepressant for each CYP2D6 phenotype group to the NMs				

