

**Table 1** Milk concentrations and M/P ratios for citalopram and demethylcitalopram.

Volunteer	$t_{\max}$ (h)	Citalopram		M/P <sub>AUC</sub>	$t_{\max}$ (h)	Demethylcitalopram		M/P <sub>AUC</sub>
		Maximum <sup>1</sup> milk concentration ( $\mu\text{g l}^{-1}$ )	Average <sup>2</sup> milk concentration ( $\mu\text{g l}^{-1}$ )			Maximum milk concentration ( $\mu\text{g l}^{-1}$ )	Average milk concentration ( $\mu\text{g l}^{-1}$ )	
1	2.6	210	107	1.4	11.1	67	48	1.4
2	3.8	103	56	0.9	3.8	32	23	1.0
3	3.8	82	53	1.4	2.9	27	23	1.1
4	7.8	186	141	2.0	3.8	48	34	1.5
5	3.5	232	168	1.9	10.8	109	83	1.9
6	3.8	119	83	2.6	1.8	35	29	2.1
7	1.9	147	68	2.3	5.7	34	15	3.3
Mean	3.9	154	97	1.8	5.7	50	36	1.8
(95% CI)	(2.2, 5.6)	(102, 207)	(56, 138)	(1.2, 2.3)	(2.2, 9.2)	(23, 77)	(15, 58)	(1.1, 2.5)

<sup>1</sup> Maximum value recorded during the dose interval. <sup>2</sup> Calculated as  $\text{AUC}(0,24\text{h})/\text{dose interval}$ .

**Table 2** Estimated infant dose for citalopram and demethylcitalopram (as citalopram equivalents), and infant plasma concentrations of citalopram and demethylcitalopram.

Volunteer	Citalopram			Demethylcitalopram		
	Infant dose as % of maternal dose Method A <sup>1</sup>	Method B <sup>2</sup>	Infant plasma concentration ( $\mu\text{g l}^{-1}$ )	Method A <sup>1</sup>	Infant dose as % of maternal dose Method B <sup>2</sup>	Infant plasma concentration ( $\mu\text{g l}^{-1}$ )
1	3.9	3.6	2	1.8	1.7	ND <sup>3</sup>
2	1.6	3.0	ND	0.6	1.2	ND
3	1.3	2.0	ND	0.6	0.9	ND
4	5.6	5.9	2.3	1.6	1.5	2.2
5	3.9	4.4	2.3	1.9	2.3	2.2
6	2.7	4.0	ND	1.0	1.5	ND
7	3.6	3.0	ND	1.0	0.7	ND
Mean (95% CI)	3.2 (1.9, 4.6)	3.7 (2.6, 4.8)		1.2 (0.7, 1.7)	1.4 (0.9, 1.9)	

<sup>1</sup> Infant dose (cumulative dose over 24 h in  $\mu\text{g}/(\text{infant body wt in kg} \times 1000)/\text{mother's dose in mg kg}^{-1}$ ) as a percentage. <sup>2</sup> Infant dose (average milk concentration in  $\mu\text{g l}^{-1} \times 0.15 \text{ l kg}^{-1} \text{ day}^{-1} \times 1000)/\text{mother's dose in mg kg}^{-1}$ ) as a percentage. <sup>3</sup> ND = less than detection limit ( $1 \mu\text{g l}^{-1}$ ).

**Table 1** Milk concentrations and M/P ratios for V and ODV.

Patient	$t_{max}$ (h)	Venlafaxine			$t_{max}$ (h)	O-Desmethylvenlafaxine		
		$C_{max}^1$ ( $\mu\text{g l}^{-1}$ )	$C_{average}^2$ ( $\mu\text{g l}^{-1}$ )	$M/P_{AUC}$		$C_{max}^1$ ( $\mu\text{g l}^{-1}$ )	$C_{average}^2$ ( $\mu\text{g l}^{-1}$ )	$M/P_{AUC}$
1	1.75	2020	1187	2.40	1.75	335	277	2.61
2	1.67	1096	704	2.05	3.67	561	477	2.26
3	2.25	712	388	2.34	2.25	1120	925	2.75
4	2.25	1230	597	2.04	2.25	1010	651	2.5
5	2.28	1429	597	2.95	4.20	1336	815	3.08
6	5.67	477	354	3.22	7.67	413	502	3.24
Mean	2.25 <sup>3</sup>	1161	638	2.50	2.96 <sup>3</sup>	796	608	2.74
(95% CI)	(1.75, 2.28)	(588, 1734)	(322, 954)	(2.0, 3.0)	(2.25, 4.2)	(362, 1230)	(358, 858)	(2.36, 3.12)

<sup>1</sup>Maximum concentration recorded during the dose interval.<sup>2</sup>Average concentration calculated as AUC/dose interval.<sup>3</sup>Median (25th and 75th percentiles).**Table 2** Estimated infant dose for V and ODV (as V equivalents), and infant plasma concentrations of V and ODV.

Patient	Venlafaxine		O-Desmethylvenlafaxine		Total dose V equivalents (%)
	Infant dose as percentage of maternal dose <sup>1</sup> (V equivalents)	Infant plasma concentration ( $\mu\text{g l}^{-1}$ )	Infant dose as percentage of maternal dose <sup>1</sup> (V equivalents)	Infant plasma concentration ( $\mu\text{g l}^{-1}$ )	
1	5.9	5	1.5	<2.5	7.4
2a <sup>2</sup>	3.8	<4	2.7	<3	6.5
2b <sup>2</sup>	3.8	<4	2.7	<3	6.5
3	2.1	<3	5.2	6.0	7.3
4	2.7	<2	3.1	38.0	5.8
5	2.5	ND <sup>3</sup>	3.5	20.0	6.0
6	2.1	ND <sup>3</sup>	3.1	3.0	5.2
Mean <sup>4</sup>	3.2		3.2		6.4
(95% CI)	(1.7, 4.7)		(1.9, 4.9)		(5.5, 7.3)

<sup>1</sup>Infant dose = (average milk concentration in  $\mu\text{g l}^{-1} \times 0.15 \text{ l kg}^{-1} \text{ day}^{-1} \times 1000$ )/mother's dose in  $\text{mg kg}^{-1}$ ) as a percentage.<sup>2</sup>Data obtained from twins.<sup>3</sup>ND = less than detection limit ( $1 \mu\text{g l}^{-1}$ ).<sup>4</sup>Twins counted as one observation,  $n=6$ .

Table 1

Drug Dose and Plasma Levels in Pregnancy and Postpartum

Subject	20 Weeks		30 Weeks		36 Weeks		Delivery		Postpartum 2 Weeks		Postpartum 4 to 6 Weeks <sup>a</sup>		Postpartum 12 Weeks	
	Dose, mg/d	Plasma Level, ng/mL	Dose, mg/d	Plasma Level, ng/mL	Dose, mg/d	Plasma Level, ng/mL	Dose, mg/d	Plasma Level, ng/mL	Dose, mg/d	Plasma Level, ng/mL	Dose, mg/d	Plasma Level, ng/mL	Dose, mg/d	Plasma Level, ng/mL
1														
S-citalopram	40	32	40	40	50	25	50	15	NA	NA	NA	NA	50	18
R-citalopram		62		64		41		24	NA	NA	NA	NA		36
2														
S-citalopram	20	14	20	14	40	18	NA	NA	40	54	NA	NA	40	27
R-citalopram		24		24		36		NA		101	NA	NA		75
3 <sup>b</sup>														
S-citalopram	30	19	30	9	20	5	—	—	—	—	—	—	—	—
R-citalopram		41		22		14		—		—		—		—
4														
S-citalopram	10	17	10	10	10	13	10	14	10	24	NA	NA	NA	NA
5														
S-citalopram	20	58	20	70	20	67	NA	NA	20	95	NA	NA	20	63
6														
S-sertraline	NA	NA	50	27	NA	NA	50	11	NA	NA	50	27	50	21
N-desmethylsertraline		NA		44		NA		26		NA		52		50
7														
S-sertraline	50	10	50	20	100	16	50	7	50	22	50	15	NA	NA
N-desmethylsertraline		18		40		66		32		41		29		NA
8														
S-sertraline	50	4	75	10	100	39	NA	NA	200	21	NA	NA	200	21
N-desmethylsertraline		16		17		74		NA		59		NA		29
9														
S-sertraline	NA	NA	150	17	200	43	200	32	200	39	NA	NA	NA	NA
N-desmethylsertraline		NA		141		147		120		149		NA		NA
10														
S-sertraline	100	93	100	45	NA	NA	100	28	NA	NA	100	62	NA	NA
N-desmethylsertraline		72		92		NA		59		NA		74		NA
11														
S-sertraline	50	32	75	18	75	23	100	32	NA	NA	100	83	125	99
N-desmethylsertraline		52		77		73		97		NA		128		183

<sup>a</sup>Values were available at 4 to 6 weeks postpartum for breast-feeding mother-infant pairs only.<sup>b</sup>Subject discontinued medication at delivery.

Abbreviation: NA = not available.

TABLE 1

Chiral and Racemic Fluoxetine and Norfluoxetine Measures by Weeks Since Conception

Chirals	Week 20 N = 9	Week 30 N = 9	Week 36 N = 8	Delivery N = 0	12 Weeks PP N = 6	P
<i>R</i> -FLX	1.0 ± 0.5 (0.3–2.0)	0.8 ± 0.5 (0.0–1.4)	0.8 ± 1.3 (0.0–3.7)		1.3 ± 0.5 (0.9–2.0)	0.0354 <sup>*</sup>
	0.7, 1.3	0.4, 1.1	0.0, 1.0		1.0, 1.9	
<i>S</i> -FLX	3.0 ± 2.5 (0.7–7.1)	2.8 ± 2.4 (0.1–6.5)	2.7 ± 3.7 (0.0–10.7)		5.7 ± 2.7 (1.3–9.4)	0.0160 <sup>†</sup>
	0.9, 5.3	1.1, 4.1	0.2, 3.9		5.1, 7.6	
<i>R</i> -FLX + <i>S</i> -FLX	4.0 ± 2.8 (0.9–9.0)	3.6 ± 2.8 (0.1–7.6)	3.5 ± 4.9 (0.0–14.4)		7.0 ± 2.9 (2.3–10.4)	0.0255 <sup>†</sup>
	1.5, 6.1	1.9, 5.2	0.2, 4.6		6.2, 9.6	
<i>R</i> -NOR	1.5 ± 0.8 (0.4–2.4)	1.2 ± 0.8 (0.1–2.2)	1.9 ± 3.0 (0.0–9.2)		1.9 ± 0.8 (0.7–3.1)	0.4055
	0.8, 2.0	0.5, 2.0	0.4, 1.7		1.3, 2.4	
<i>S</i> -NOR	3.1 ± 1.6 (1.2–5.7)	3.0 ± 1.9 (0.3–5.8)	3.5 ± 3.9 (0.6–12.5)		3.5 ± 1.9 (1.9–6.8)	0.7539
	2.0, 4.2	1.1, 4.3	1.1, 4.1		2.2, 4.4	
<i>R</i> -NOR + <i>S</i> -NOR	4.5 ± 2.2 (1.6–7.6)	4.2 ± 2.6 (0.4–7.8)	5.4 ± 6.9 (0.7–21.8)		5.4 ± 2.6 (3.2–9.9)	0.6440
	2.6, 6.6	2.6, 6.5	1.8, 5.8		3.2, 6.8	
( <i>R</i> -FLX + <i>S</i> -FLX) / ( <i>R</i> -NOR + <i>S</i> -NOR)	1.0 ± 0.7 (0.2–2.5)	0.9 ± 0.8 (0.3–2.9)	0.6 ± 0.8 (0.0–2.4)		1.4 ± 0.7 (0.7–2.4)	0.0010 <sup>‡</sup>
	0.6, 1.2	0.5, 1.0	0.1, 0.6		0.7, 1.9	
<i>R</i> -FLX + <i>R</i> -NOR	2.5 ± 1.2 (0.6–3.9)	2.0 ± 1.3 (0.1–3.4)	2.7 ± 4.3 (0.0–13.0)		3.3 ± 1.2 (1.5–5.0)	0.1930
	1.7, 3.3	0.9, 3.1	0.5, 2.7		2.3, 4.0	
<i>S</i> -FLX + <i>S</i> -NOR	6.1 ± 3.4 (1.9–12.7)	5.7 ± 3.5 (0.4–12.0)	6.2 ± 7.3 (0.8–23.2)		9.2 ± 3.3 (3.2–11.9)	0.1920
	3.2, 8.3	4.1, 7.7	1.2, 6.8		7.9, 11.6	
<i>R</i> -FLX + <i>R</i> -NOR + <i>S</i> -FLX + <i>S</i> -NOR	8.5 ± 4.2 (2.5–16.6)	7.8 ± 4.7 (0.6–15.3)	8.9 ± 11.5 (1.1–36.2)		12.4 ± 4.2 (5.5–16.9)	0.1940
	6.1, 10.0	5.0, 10.2	1.9, 9.0		9.4, 14.8	
<b>Racemates</b>	<b>N = 7</b>	<b>N = 8</b>	<b>N = 7</b>	<b>N = 4</b>	<b>N = 2</b>	

Chirals	Week 20 N = 9	Week 30 N = 9	Week 36 N = 8	Delivery N = 0	12 Weeks PP N = 6	P
FLX	4.4 ± 3.0 (2.4–10.1)	4.8 ± 2.6 (2.5–8.8)	4.1 ± 2.2 (1.8–7.4)	2.3 ± 3.3 (0.5–7.3)	4.3 ± 5.4 (0.5–8.1)	0.1936
	2.5, 7.0	2.6, 7.1	1.9, 6.9	0.6, 4.0	0.5, 8.1	
NOR	4.2 ± 1.4 (1.8–5.7)	4.7 ± 2.0 (2.0–7.5)	4.5 ± 1.9 (1.8–7.4)	2.1 ± 0.9 (1.3–3.1)	3.7 ± 2.1 (2.2–5.2)	0.0491 <sup>§</sup>
	3.3, 5.5	2.8, 6.2	2.9, 6.3	1.4, 2.8	2.2, 5.2	
FLX + NOR	8.6 ± 2.4 (5.8–13.5)	9.6 ± 2.3 (5.5–12.0)	8.6 ± 2.7 (5.9–13.2)	4.4 ± 3.0 (2.0–8.8)	8.0 ± 7.5 (2.7–13.3)	0.1355
	7.2, 9.0	7.7, 11.4	6.3, 11.0	2.6, 6.2	2.7, 13.3	
FLX / NOR	1.4 ± 1.4 (0.4–3.9)	1.4 ± 1.5 (0.4–4.2)	1.3 ± 1.3 (0.4–4.2)	1.4 ± 2.2 (0.2–4.7)	0.9 ± 0.9 (0.2–1.6)	0.1884
	0.5, 3.0	0.5, 2.2	0.5, 1.2	0.2, 2.6	0.2, 1.6	

Data presented as mean ± SD, (min-max), and median, IQR.

Visits significantly different from one another (adjusted Tukey,  $P < 0.05$ ).<sup>\*</sup> Week 20/week 36.<sup>†</sup> Week 36/12 weeks pp.<sup>‡</sup> Week 20/week 36; week 30/week 36; week 36/12 weeks pp.<sup>§</sup> Week 30/Delivery.

pp indicates postpartum.

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Table 1

Antidepressant Drug, Dose, Cord and Maternal Concentrations, Maternal Depression and Smoking

ID#	PES	Drug	Dose		Taper at 36wks	Comment	Cord-Maternal Ratios		Cord Concentration		Maternal Concentration		MDD 3rd Trim	Sigh-ADS Scores			Smoking
			36wk	delivery			parent drug	metabolite	parent drug	metabolite	parent drug	metabolite		20wk	30wk	36wk	
1	3	sertraline	100	100	-		0.19	0.28	5.2	16.4	27.8	58.9	0	13	6	n/a	-
2	0	sertraline	50	50	-		0.24	0.31	2.7	7.9	11.2	25.9	0	n/a	5	9	-
3	1	sertraline	200	200	-	with bupropion SR	0.29	0.34	9.5	41.1	32.4	120	1	5	21	14	yes
4	0	sertraline	50	100	-	1st trim-citalopram	0.31	0.32	3.0	6.8	9.8	21.5	0	2	7	4	-
5	0	sertraline	**0	100	-		0.31	0.39	6.2	9.2	19.8	23.4	1	33	15	29	yes
6	0	sertraline	75	100	-		0.35	0.38	11.0	37.3	31.5	97.0	1	24	14	19	-
7	0	sertraline	75	75	-		0.60	0.55	3.5	15.8	5.8	28.5	1	21	19	12	-
8	1	sertraline	100	100			0.63	0.41	6.2	13.4	9.9	33.0	1	6	5	18	-
9	0	sertraline	100	50	yes		0.99	0.60	6.7	19.0	6.8	31.9	1	5	5	12	-
10	2	venlafaxine	75	*75	-	with bupropion SR	0.80	0.79	79.9	44.7	100	56.4	0	10			yes
11	1	venlafaxine	75	*75	-		1.64	0.56	46.4	105	28.3	188	0	13	15	10	yes
12	1	escitalopram	10	*10	-		0.00	0.67	0	3.6	5.6	5.4	1	18	16		-
13	0	escitalopram	10	*10	-		0.50	0.77	6.7	2.0	13.5	2.6	0	8	6	11	-
14	2	citalopram	50	*50	-		0.56	0.71	23.0	10.5	41.4	14.7	0	14	23	7	-
15	0	nortriptyline	75	0	yes	1st trim-escitalopram	0.47	0.65	10.6	20.1	22.6	30.8	0	15	18	10	-
16	0	fluvoxamine	400	200	yes		0.08		4.9		62.7		1	17	28	33	-
17	0	fluoxetine	40	40	-		0.50	0.48	66.5	122	132	255	1	6	6	12	-
18	0	fluoxetine	20	10	yes		0.54	0.70	10.1	38.0	18.7	54.3	0	7	3	4	-
19	0	fluoxetine	***20	***20	-		0.55	0.60	89.1	48.7	162	80.7	0	11	n/a	n/a	yes
20	0	fluoxetine	30	30	-		0.64	0.68	30.0	13.0	47.0	19.0	0	9	4	6	-
21	0	fluoxetine	40	0	yes		0.69	0.69	2.5	37.4	3.6	54.5	0	8	11	4	-

\* dose estimated from 36wk data

\*\* patient began treatment after 36wks

\*\*\* dose estimated from 20wk data

Subjects with PES=1 are highlighted

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Table 2

Concentrations of infliximab detected on day of birth

Pt #	IFX dose (mg/kg)	IFX interval (wks)	Time dose to birth (days)	IFX (µg/ml) at Birth			Ratio cord/Mother (%)	Month IFX undetectable	Newborn Complications
				Mom:	Cord:	Infant			
1 <sup>^</sup>	10	6	14	40 (6 wks)	--	39.5 <sup>*</sup> (6 wks)	--	7	None
2	5	6	30	15.1	--	25.3	--	5	Meconium
3 <sup>#^</sup>	5	6	2	1.4	2.0	2.9 <sup>*</sup> (2 wks)	143%	2	Hand-foot-mouth (9mos); respiratory distress (11 mos)
4 <sup>#^</sup>	5	6	14	19.2	26.5	23.6	138%	7	Oral candida (10 wks); GERD (4 mos)
5	5	8	91	3.8	3.3	4.2	87%	2	Jaundice
6	5	8	15	4.8	8.8	8.7	183%	3	None
7	5	8	55	14.5	20.5	28.2	141%	4	URI 2 weeks
8	5	6	46	16.5	26.5	27.5	160%	5	None
9	5	8	35	2.2	8.4	10.6	381%	4	None
10	5	6	77	4.1	13.6	4.7 <sup>*</sup> (4 wks)	332%	--	None
11	10	8	74	5.1	20.4	8.4 <sup>*</sup> (4 wks)	400%	4	None

<sup>\*</sup> In some cases Infant levels were not obtained on the day of birth but a few weeks later

<sup>#</sup> Flare of disease in trimester 3

<sup>^</sup> Flare of disease in post-partum

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**Table 1 Subject characteristics**

Patient	Age (years)	Pre-pregnancy BMI (kg/m <sup>2</sup> )	Auto immune disease	Comorbidity	Pregnancy complications	Medication during pregnancy	Gestational age at delivery (weeks)	Birth weight neonate (percentile range)	Neonatal complications
1	37	21.5	Rheumatoid arthritis	Primary hypothyroidism Partial androgen insensitivity syndrome Uveitis Vitiligo	None	Infliximab Azathioprine Levothyroxine	40 <sup>*1</sup>	4050 g (p50–90)	None
2	27	22.3	Crohn's disease	Asthma	None	Infliximab	41 <sup>*6</sup>	3715 g (p10–50)	None
3	25	24.7	Crohn's disease	None	None	Infliximab, Hydroxocobalamin	38 <sup>*6</sup>	3100 g (p10–50)	None
4	30	21.5	Ankylosing spondylitis	Attention deficit disorder	Preeclampsia	Etanercept Nitrofurantoin Methyldopa	38 <sup>*5</sup>	3305 g (p50–90)	Suspicion for infection
5	31	24.4	Rheumatoid arthritis	None	None	Etanercept	40 <sup>*6</sup>	3780 g (p10–50)	None
6	37	23.1	Psoriasis vulgaris	None	None	Etanercept	39 <sup>*1</sup>	3780 g (p50–90)	None

p, percentile.

**Table 2 Placental transfer and placental exposure to infliximab and etanercept in patients with autoimmune diseases**

Patient	TNF inhibitor	Dosing regimen	Time from last dose to delivery (days)	TNF inhibitor			Cord-to-maternal ratio	Placenta-to-maternal ratio
				(µg/mL serum)		Mean ± SD (µg/g tissue)		
				Maternal	Cord	Placenta		
1	Infliximab	400 mg per 8 weeks (5 mg/kg)	23	25.3	29.8	5.8 ± 0.9	1.18	0.35
2	Infliximab	400 mg per 8 weeks (5 mg/kg)	57	12.0	24.0	1.8 ± 0.0	2.00	0.23
3	Infliximab	400 mg per 8 weeks (5 mg/kg)	31	17.0	29.0	4.8 ± 1.5	1.71	0.44
4	Etanercept	50 mg per 12 days	4	3.0	0.1	0.1 ± 0.1	0.04	0.03
5	Etanercept	50 mg per week	29	<0.1	<0.1	<0.1	NA	NA
6	Etanercept	50 mg per week	16	0.2	NA	<0.1	NA	NA

Placental transfer is represented as cord-to-maternal ratios based on serum levels, and placental exposure is calculated as placenta-to-maternal ratios based on placental tissue concentrations corrected for serum levels and maternal calculated whole blood concentrations. Cord blood of patient 6 was not available.  
NA, not assessed; TNF, tumor necrosis factor.

**Table 2.** Details of IFX/UST-Administered Births.

	Case 1	Case 2	Case 3	Case 4	Case 5
Discontinuation of bio	32w5d	31w5d	30w4d	26w2d	23w3d
Gestational age at birth	38w0d	38w3d	38w5d	38w3d	38w0d
Delivery method	CS	CS	CS	CS	CS
Apgar score	8	8	8	8	8
Birth weight (g)	3002	3260	3206	3076	2596
Congenital abnormalities	None	None	None	None	None
IFX/UST in mother’s blood	Not measured	Not measured	Not measured	Not measured	267.7 ng/ml
IFX/UST in cord blood	36.89 µg/ml	Not measured	Not measured	Not measured	756.5 ng/ml
IFX/UST at 6 months	0.94 pg/ml	Not detected	0.24 pg/ml	Not detected	Not detected

CS: caesarean section

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