

Association of *OPRM1*, *MIR23B*, and *MIR107* genetic variability with acute pain, chronic pain and adverse effects after postoperative tramadol and paracetamol treatment in breast cancer

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SUPPLEMENTARY TABLE 1. The impact of investigated polymorphisms on the presence of acute pain (VAS) anytime during the first four weeks of tramadol treatment (N = 113)

SNP	Genotype	VAS 7 days Median (25–75 %)	P	VAS 14 days Median (25–75 %)	P	VAS 21 days Median (25–75 %)	P	VAS 28 days Median (25–75 %)	P
<i>OPRM1</i> rs1799971	AA	2 (1–3)	Pdom = 0.752	1.5 (0–2)	Pdom = 0.971	1 (1–2)	Pdom = 0.312	1 (0–2)	Pdom = 0.190
	AG+GG	2 (1–3)		2 (0–2)		1 (0–2)		1 (1–2)	
<i>OPRM1</i> rs677830	CC	2 (1–3)	Pdom = 0.549	1 (0–2)	Pdom = 0.989	1 (0–2)	Pdom = 0.391	1 (0–2)	Pdom = 0.608
	CT+TT	2 (1–2.5)		1.5 (0–2)		1 (1–2)		1 (0–2)	
<i>MIR23B</i> rs1011784	CC	2 (1–2.9)	Padd = 0.248	1.5 (0–2)	Padd = 0.326	1 (0–2)	Padd = 0.468	1 (0–2)	Padd = 0.537
	CG	2 (1–3)		2 (1–2.3)		1 (1–2.8)		1 (1–2)	
	GG	1 (0.8–2)		1 (0–1.8)		1 (0.5–1.5)		1 (0–1.5)	
	CG+GG	2 (1–3)		1.3 (0–2.1)		1 (1–2.1)		1 (0.5–2)	
<i>MIR107</i> rs2296616	GG	2 (1–3)	Padd = 0.378	1.5 (0.3–2)	Padd = 0.837	1.5 (0.3–3)	Padd = 0.646	1 (0–2)	Padd = 0.894
	GA	2 (1–2.5)		2 (0–2)		1 (0–2)		1 (0–2)	
	AA	1.8 (1–2)		1 (0–2.4)		1 (0.6–2)		1 (0.8–2)	
	GA+AA	2 (1–2)		1.5 (0–2)		1 (0.4–2)		1 (0–2)	

Add = additive model; Dom = dominant model; SNP = single nucleotide polymorphism; VAS = visual analog scale

SUPPLEMENTARY TABLE 2. The impact of investigated polymorphisms on constipation after 7, 14, 21, and 28 days of tramadol treatment (N = 99)

SNP	Genotype	Constipation 7 days N (%)	OR (95% CI)	P	Constipation 14 days N (%)	OR (95% CI)	P	OR (95% CI) _{adj}	P _{adj}
OPRM1 rs1799971	AA	26 (35.6)	Ref.		16 (21.9)	Ref.		Ref.	
	AG+GG	13 (59.1)	2.61 (0.98–6.93)	0.054	9 (39.1)	2.29 (0.84–6.25)	0.106	2.08 (0.74–5.83)	0.165
OPRM1 rs677830	CC	21 (45.7)	Ref.		11 (22.9)	Ref.		Ref.	
	CT+TT	18 (36.7)	0.69 (0.3–1.57)	0.378	14 (29.2)	1.39 (0.55–3.46)	0.486	1.23 (0.48–3.17)	0.662
MIR23B rs1011784	CC	23 (41.8)	Ref.		16 (28.1)	Ref.		Ref.	
	CG	13 (40.6)	0.95 (0.39–2.31)	0.913	8 (25.8)	0.89 (0.33–2.4)	0.820	0.83 (0.3–2.31)	0.721
	GG	3 (37.5)	0.83 (0.18–3.85)	0.817	1 (12.5)	0.37 (0.04–3.22)	0.365	0.23 (0.02–2.15)	0.197
	CG+GG	16 (40)	0.93 (0.4–2.12)	0.859	9 (23.1)	0.77 (0.3–1.97)	0.585	0.66 (0.25–1.77)	0.410
MIR107 rs2296616	GG	9 (47.4)	Ref.		5 (26.3)	Ref.		Ref.	
	GA	19 (42.2)	0.81 (0.28–2.38)	0.705	12 (26.7)	1.02 (0.3–3.44)	0.977	1.16 (0.33–4.07)	0.816
	AA	11 (35.5)	0.61 (0.19–1.96)	0.407	8 (25)	0.93 (0.26–3.42)	0.917	0.93 (0.25–3.54)	0.921
	GA+AA	30 (39.5)	0.72 (0.26–1.99)	0.532	20 (26)	0.98 (0.31–3.08)	0.976	1.06 (0.33–3.42)	0.924
SNP	Genotype	Constipation 21 days N (%)	OR (95% CI)	P	Constipation 28 days N (%)	OR (95% CI)	P		
OPRM1 rs1799971	AA	15 (20.3)	Ref.		13 (18.1)	Ref.			
	AG+GG	6 (28.6)	1.57 (0.52–4.74)	0.421	3 (15)	0.8 (0.2–3.14)	0.750		
OPRM1 rs677830	CC	6 (12.8)	Ref.		6 (13.3)	Ref.			
	CT+TT	15 (31.3)	3.11 (1.08–8.89)	0.035	10 (21.3)	1.76 (0.58–5.32)	0.319		
MIR23B rs1011784	CC	11 (19.6)	Ref.		9 (17)	Ref.			
	CG	8 (25.8)	1.42 (0.5–4.03)	0.506	6 (19.4)	1.17 (0.37–3.68)	0.784		
	GG	2 (25)	1.36 (0.24–7.7)	0.725	1 (14.3)	0.81 (0.09–7.62)	0.857		
	CG+GG	10 (25.6)	1.41 (0.53–3.74)	0.489	7 (18.4)	1.1 (0.37–3.28)	0.859		
MIR107 rs2296616	GG	2 (10.5)	Ref.		3 (15.8)	Ref.			
	GA	13 (28.9)	3.45 (0.7–17.12)	0.129	9 (20)	1.33 (0.32–5.59)	0.694		
	AA	6 (19.4)	2.04 (0.37–11.33)	0.415	4 (14.3)	0.89 (0.18–4.51)	0.887		
	GA+AA	19 (25)	2.83 (0.6–13.41)	0.189	13 (17.8)	1.16 (0.29–4.55)	0.836		

adj = adjustment for tramadol dose; N = sample size; OR = odds ratio; SNP = single nucleotide polymorphism; 95% CI = 95% confidence interval

SUPPLEMENTARY TABLE 3. The impact of investigated polymorphisms on nausea after 7 and 14 days of tramadol treatment (N = 99)

SNP	Genotype	Nausea 7 days N (%)	OR (95% CI)	P	Nausea 14 days N (%)	OR (95% CI)	P
OPRM1 rs1799971	AA	19 (26.4)	Ref.		11 (15.1)	Ref.	
	AG+GG	5 (21.7)	0.77 (0.25–2.38)	0.656	1 (4.3)	0.26 (0.03–2.1)	0.205
OPRM1 rs677830	CC	12 (25.5)	Ref.		8 (16.7)	Ref.	
	CT+TT	12 (25)	0.97 (0.39–2.45)	0.952	4 (8.3)	0.45 (0.13–1.63)	0.225
MIR23B rs1011784	CC	13 (23.6)	Ref.		7 (12.3)	Ref.	
	CG	8 (25)	1.08 (0.39–2.97)	0.886	4 (12.9)	1.06 (0.28–3.94)	0.933
	GG	3 (37.5)	1.94 (0.41–9.23)	0.406	1 (12.5)	1.02 (0.11–9.58)	0.986
	CG+GG	11 (27.5)	1.23 (0.48–3.11)	0.669	5 (12.8)	1.05 (0.31–3.58)	0.937
MIR107 rs2296616	GG	6 (31.6)	Ref.		3 (15.8)	Ref.	
	GA	10 (22.2)	0.62 (0.19–2.05)	0.432	4 (8.9)	0.52 (0.1–2.59)	0.425
	AA	8 (25.8)	0.75 (0.21–2.65)	0.659	5 (15.6)	0.99 (0.21–4.7)	0.988
	GA+AA	18 (23.7)	0.67 (0.22–2.02)	0.480	9 (11.7)	0.71 (0.17–2.91)	0.630

N = sample size; OR = odds ratio; SNP = single nucleotide polymorphism; 95% CI = 95% confidence interval