

THE LANCET

Supplementary appendix

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Supplement to: Horne AW, Vincent K, Hewitt CA, et al. Gabapentin for chronic pelvic pain in women (GaPP2): a multicentre, randomised, double-blind, placebo-controlled trial. *Lancet* 2020; **396**: 909–17.

Supplementary Material

Table S 1 Sensitivity analyses of primary outcome

	Baseline		End of study ^x			
	Gabapentin Mean (SD, n)	Placebo Mean (SD, n)	Gabapentin Mean (SD, n)	Placebo Mean (SD, n)	Mean Difference ² (97.5% CI)	p- value ³
Worst NRS pain scores¹						
Per-protocol analysis*	8.5 (1.1, 101)	8.6 (1.2, 101)	7.3 (2.3, 98)	7.5 (2.2, 97)	-0.14 (-0.81, 0.53)	0.6 ³
Multiple imputation for missing data	-	-	-	-	-0.19 (-0.72, 0.33)	0.5 ³
Effect of time between screening and randomization	8.4 (1.3, 153)	8.6 (1.2, 153)	7.1 (2.6, 124)	7.4 (2.2, 122)	-0.20 (-0.82, 0.42)	0.5 ³
Average NRS pain scores¹						
Per-protocol analysis*	5.6 (1.6, 101)	5.4 (1.7, 101)	4.4 (2.0, 98)	4.5 (2.1, 97)	-0.23 (-0.81, 0.35)	0.4 ³
Multiple imputation for missing data	-	-	-	-	-0.21 (-0.66, 0.24)	0.4 ³
Effect of time between screening and randomization	5.5 (1.7, 153)	5.5 (1.7, 153)	4.3 (2.3, 123)	4.5 (2.2, 121)	-0.18 (-0.71, 0.35)	0.4 ³

^x Worst and average NRS pain scores measures weeks 13-16 post-randomization.

¹ Pain scores range from 0 to 10, where 0=no pain and 10=worst pain imaginable.

² Adjusted for baseline score and minimization variables (including time between screening and randomization for effect of time between screening and randomization sensitivity analysis only). Values <0 favour gabapentin.

³ Threshold for statistical significance $\alpha=0.025$ due to Bonferroni correction.

* The per-protocol cohort only includes those adherent with treatment allocation (gabapentin=101, placebo=101).

Table S 2 Repeated measures analysis

	Gabapentin Mean (SD, N)	Placebo Mean (SD, N)	Interaction p-value	Mean Difference² (97.5% CI)
Worst NRS pain scores ¹			0.8	-0.29 (-0.87, 0.29)
Week 13	6.0 (2.7, 123)	6.4 (2.5, 115)		
Week 14	5.9 (2.9, 119)	6.2 (2.6, 118)		
Week 15	5.8 (2.8, 118)	6.3 (2.4, 118)		
Week 16	5.8 (2.6, 116)	6.2 (2.7, 118)		
Average NRS pain scores ¹			0.8	-0.11 (-0.62, 0.41)
Week 13	4.5 (2.5, 122)	4.7 (2.4, 114)		
Week 14	4.3 (2.5, 118)	4.4 (2.5, 115)		
Week 15	4.4 (2.5, 118)	4.5 (2.3, 118)		
Week 16	4.4 (2.4, 115)	4.4 (2.4, 117)		

¹Pain scores range from 0 to 10, where 0=No pain and 10=Worst pain imaginable.

²Adjusted for baseline score and minimization variables. Values <0 favour Gabapentin.

Note: Average NRS was taken as the mean pain score across weeks 13-16, worst NRS was taken as the worst response (highest score) across weeks 13-16.

Table S 3 Subgroup analysis of primary outcome

	Gabapentin Mean (SD, n)	Placebo Mean (SD, n)	Interaction p-value
Worst NRS pain scores¹			
Dysmenorrhea			0.7
Yes	7.2 (2.3, 79)	7.4 (2.3, 78)	
No	6.8 (2.9, 45)	7.3 (2.2, 44)	
GHQ score			0.4
0-1	6.5 (2.4, 35)	6.6 (2.2, 33)	
2-12	7.3 (2.6, 89)	7.6 (2.2, 89)	
Use of sex hormones			0.1
Yes	7.2 (2.5, 81)	7.1 (2.3, 81)	
No	6.8 (2.7, 43)	8.0 (2.0, 41)	
Average NRS pain scores¹			
Dysmenorrhea			0.3
Yes	4.5 (2.1, 79)	4.4 (2.2, 77)	
No	3.9 (2.5, 44)	4.6 (2.2, 44)	
GHQ score			0.1
0-1	3.8 (2.2, 35)	3.6 (2.2, 33)	
2-12	4.5 (2.3, 88)	4.8 (2.1, 88)	
Use of sex hormones			0.3
Yes	4.5 (2.3, 81)	4.3 (2.1, 81)	
No	3.9 (2.1, 42)	4.8 (2.3, 40)	

¹Pain scores range from 0 to 10, where 0= No pain and 10=Worst pain imaginable.

Table S 4 Summary of use of painkillers

	Week 4-5		Week 8-10		Week 16-17 ¹	
	Gabapentin	Placebo	Gabapentin	Placebo	Gabapentin	Placebo
	(N=118)	(N=121)	(N=111)	(N=108)	(N=103)	(N=101)
Use of painkillers since taking study medication <i>n</i> (%)						
Less	65 (55)	61 (50)	57 (51)	52 (48)	52 (50)	42 (42)
Same	42 (36)	46 (38)	38 (34)	42 (39)	40 (39)	45 (44)
More	11 (9)	14 (12)	16 (15)	14 (13)	11 (11)	14 (14)

¹Weeks 16-17 is the end of study assessment.

Table S 5 Rescue medication

	Baseline		Week 4-5		Week 8-10		Week 16-17 ¹	
	Gabapentin	Placebo	Gabapentin	Placebo	Gabapentin	Placebo	Gabapentin	Placebo
N ²	(N=153) n (%)	(N=153) n (%)	(N=136) n (%)	(N=138) n (%)	(N=119) n (%)	(N=119) n (%)	(N=112) n (%)	(N=109) n (%)
Rescue Medication ³	114 (75%)	112 (73%)	68 (50%)	70 (51%)	66 (55%)	58 (49%)	62 (55%)	64 (59%)
NSAIDS ⁴	62/114 (54%)	66/112 (59%)	31/68 (46%)	36/70 (51%)	26/66 (39%)	27/58 (47%)	25/62 (40%)	29/64 (45%)
Opiates ⁵	78/114 (68%)	68/112 (61%)	33/68 (49%)	34/70 (49%)	38/66 (58%)	31/58 (53%)	34/62 (55%)	27/64 (42%)
Other ⁶	61/114 (54%)	58/112 (52%)	39/68 (57%)	34/70 (49%)	38/66 (58%)	31/58 (53%)	34/62 (55%)	31/64 (48%)

¹Weeks 16-17 is the end of study assessment.

²Attended assessment.

³Rescue medications include NSAIDS, Opiates and Other.

⁴NSAIDS include Aspirin, Diclofenac, Ibuprofen, Mefenamic acid, Naproxen, Naproxen, Neobrufen, Feminax, Anadin and Meloxicam.

⁵Opiates include Zapain, Migraleve, Oramorph, Solpadeine, Pethidine, Tramadol, Morphine, Dihydrocodeine, Co-dydramol, Codeine Phosphate, Co-codamol, MST, Tramacet and Solpadol.

⁶Other includes Paracetamol.

Table S 6 Summary of number of visits to health care professionals

	Baseline ¹		End of study ¹	
	Gabapentin n (%)	Placebo n (%)	Gabapentin n (%)	Placebo n (%)
General Practitioner				
N	152	152	111	109
0	103 (68)	118 (78)	62 (56)	62 (57)
1	28 (18)	16 (10)	16 (14)	21 (19)
2	12 (8)	10 (7)	16 (14)	11 (10)
3+	9 (6)	8 (5)	17 (16)	15 (14)
Hospital Outpatients				
N	152	152	111	109
0	139 (91)	126 (83)	89 (80)	83 (76)
1	10 (7)	22 (14)	16 (14)	20 (18)
2	2 (1)	3 (2)	2 (2)	4 (4)
3+	1 (1)	1 (1)	4 (4)	2 (2)
Practice Nurse				
N	152	152	110	109
0	142 (93)	146 (96)	99 (90)	103 (94)
1	7 (5)	6 (4)	8 (7)	3 (3)
2	1 (1)	0 (-)	1 (1)	1 (1)
3+	2 (1)	0 (-)	2 (2)	2 (2)
Physiotherapist				
N	152	152	110	109
0	147 (97)	151 (99)	107 (97)	105 (96)
1	5 (3)	1 (1)	1 (1)	0 (-)
2	0 (-)	0 (-)	1 (1)	1 (1)
3+	0 (-)	0 (-)	1 (1)	3 (3)
Other²				
N	151	152	110	109
0	141 (93)	143 (94)	99 (90)	97 (89)
1	5 (4)	5 (4)	6 (5)	5 (4)
2	2 (1)	2 (1)	2 (2)	3 (3)
3+	3 (2)	2 (1)	3 (3)	4 (4)

¹Baseline-In month prior to randomization. End of study (week 16-17)-Since taking trial medication.

²Other includes alternative therapist, accident and emergency, occupational health, out of hour's doctor, health psychologist, pain specialist, massage therapist, research nurse, research midwife, hospital, dentist, paramedic, radiologist, eye hospital, and counsellor for cognitive behavioural therapy.

Table S 7 Adherence

	Gabapentin (N=112) n (%)	Placebo (N=109) n (%)
How frequently woman reported taking her study drug		
Never (0%)	0 (-)	2 (2)
Hardly any (1-24%)	7 (6)	1 (1)
Some (25-49%)	4 (4)	5 (5)
Most (50-74%)	10 (9)	10 (9)
Almost always (75-99%)	36 (32)	34 (31)
Every day (100%)	55 (49)	57 (52)

Figure S1 Overall median dose of study drug taken daily per week

