## (A) WASO at days 1 and 2

	Dari	dorexa	int	PI	acebo		5	Std. Mean Difference	Std. Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV. Random. 95% Cl
1.9.1 Daridorexant 5	0mg								
dauvilliers 2020	-47.1	32.8	61	-21.4	32.5	60	12.6%	-0.78 [-1.15, -0.41]	<b>_</b>
zammit 2020	-61.4	33.4	56	-21.4	33.1	54	11.9%	-1.19 [-1.60, -0.79]	
Subtotal (95% CI)			117			114	24.6%	-0.98 [-1.38, -0.58]	◆
Heterogeneity: Tau <sup>2</sup> =	0.05; Cl	ni² = 2.1	16, df =	1 (P =	0.14);	l² = 54	%		
Test for overall effect:	Z = 4.75	i (P < 0	.00001	)					
1.9.2 Daridorexant 2	5mg								
auvilliers 2020	-37.7	32.5	60	-21.4	32.5	60	12.8%	-0.50 [-0.86, -0.13]	
zammit 2020	-45.1	33.5	55	-13.6	33.1	54	12.1%	-0.94 [-1.34, -0.54]	
Subtotal (95% CI)			115			114	24.9%	-0.71 [-1.14, -0.28]	◆
Heterogeneity: Tau <sup>2</sup> =	0.06; CI	ni² = 2.9	58, df =	1 (P =	0.11);	l² = 61º	%		
Test for overall effect:	Z = 3.23	6 (P = 0	.001)						
1.9.3 Daridorexant 1	0mg								
dauvilliers 2020	-32.3	32.7	58	-21.4	32.5	60	12.8%	-0.33 [-0.70, 0.03]	
zammit 2020	-32	33.1	54	-13.6	33.1	54	12.4%	-0.55 [-0.94, -0.17]	
Subtotal (95% CI)			112			114	25.1%	-0.44 [-0.70, -0.17]	$\bullet$
Heterogeneity: Tau <sup>2</sup> =	0.00; CI	ni² = 0.0	66, df =	1 (P =	0.42);	l² = 0%			
Test for overall effect:	Z = 3.23	6 (P = 0	.001)						
1.9.4 Daridorexant 5	mg								
auvilliers 2020	-28.4	32.5	60	-21.4	32.5	60	12.9%	-0.21 [-0.57, 0.14]	
zammit 2020	-18. <del>9</del>	33.4	56	-13.6	33.1	54	12.6%	-0.16 [-0.53, 0.22]	
Subtotal (95% CI)			116			114	25.4%	-0.19 [-0.45, 0.07]	◆
Heterogeneity: Tau <sup>2</sup> =	0.00; Cl	ni² = 0.0	04, df =	1 (P =	0.83);	l² = 0%			
Test for overall effect:	Z = 1.42	? (P = 0	.16)						
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									-2 -1 0 1 2
Test for subaroup diffe		0-12-	11.04	df - 2 /	D - 00	0021 12	- 74 09/		Favours [Daridorexant] Favours [Placebo]

(B) LPS at days 1 and 2

	Dari	dorexa	ant	PI	acebo			Std. Mean Difference	Std. Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV. Random. 95% CI	IV. Random. 95% CI
1.10.1 Daridorexant 5	0mg								
dauvilliers 2020	-37.2	29.7	61	-20.1	29.4	61	13.0%	-0.58 [-0.94, -0.21]	
zammit 2020	-45.4	26.9	56	-34.6	26.8	56	12.2%	-0.40 [-0.77, -0.03]	
Subtotal (95% CI)			117			117	25.1%	-0.49 [-0.75, -0.23]	◆
Heterogeneity: Tau <sup>2</sup> =	0.00; Cł	ni² = 0.4	44, df =	= 1 (P =	0.51);	l² = 0%			
Test for overall effect:	Z = 3.69	(P=0	).0002)						
1.10.2 Daridorexant 2	5mg								
dauvilliers 2020	-34.2	29.4	60	-20.1	29.4	60	12.9%	-0.48 [-0.84, -0.11]	
zammit 2020	-43.8	26.9	55	-34.6	26.8	55	12.0%	-0.34 [-0.72, 0.04]	
Subtotal (95% CI)			115			115	24.9%	-0.41 [-0.67, -0.15]	$\bullet$
Heterogeneity: Tau <sup>2</sup> =	0.00; Cł	ni² = 0.1	26, df =	= 1 (P =	0.61);	l² = 0%			
Test for overall effect:	Z = 3.08	(P=0	).002)						
1.10.3 Daridorexant 1	0mg								
dauvilliers 2020	-32	29.7	58	-20.1	29.4	58	12.6%	-0.40 [-0.77, -0.03]	
zammit 2020	-44.9	26.8	54	-34.6	26.8	54	11.7%	-0.38 [-0.76, -0.00]	
Subtotal (95% CI)			112			112	24.3%	-0.39 [-0.66, -0.13]	•
Heterogeneity: Tau <sup>2</sup> =	0.00; Cł	ni² = 0.	00, df =	= 1 (P =	0.95);	l² = 0%			
Test for overall effect:	Z = 2.90	(P = 0	).004)						
1.10.4 Daridorexant 5	mg								
dauvilliers 2020	-25.9	29.4	60	-20.1	29.4	60	13.2%	-0.20 [-0.55, 0.16]	
zammit 2020	-37.4	21.2	56	-34.6	26.8	56	12.4%	-0.12 [-0.49, 0.26]	
Subtotal (95% CI)			116			116	25.6%	-0.16 [-0.41, 0.10]	●
Heterogeneity: Tau <sup>2</sup> =	0.00; Cł	ni² = 0.	09, df =	= 1 (P =	0.76);	l² = 0%			
Test for overall effect:	Z = 1.19	(P = 0	).23)						
									-2 -1 0 1 2

-2 -1 0 1 2 Favours [Daridorexant] Favours [Placebo]

Test for subaroup differences: Chi<sup>2</sup> = 3.54. df = 3 (P = 0.32). l<sup>2</sup> = 15.3% sFig2. WASO and LPS at Days 1 and 2