Supplementary Material

Atogepant for the Prevention of Episodic Migraine in Adults: A Systematic Review and Meta-Analysis of Efficacy and Safety

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Table e-1. Certainty of the evidence

Certainty assessment							Summary of findings				
							Study event rates (%)			Anticipated absolute effects	
Participants (studies)	Risk of bias	Inconsistency	Indirectness	Imprecision	Publication bias	Overall certainty of evidence	With placebo	With Atogepant	Relative effect (95% CI)	Risk with placebo	Risk difference with Atogepant
Change in baseline monthly migraine days (atogepant 10 mg versus placebo)											
698 (2 RCTs)	not serious	not serious	not serious	not serious	none	⨁⨁⨁⨁ High	392	306	-	-	MD **-1.16** (1.6 lower to 0.73 lower)
Change in baseline monthly migraine days (atogepant 30 mg versus placebo)											
797 (2 RCTs)	not serious	not serious	not serious	not serious	none	⨁⨁⨁⨁ High	392	405	-	-	MD **-1.15** (1.54 lower to 0.76 lower)
Change in baseline monthly migraine days (atogepant 60 mg versus placebo)											
791 (2 RCTs)	not serious	not serious	not serious	not serious	none	⨁⨁⨁⨁ High	392	399	-	-	MD **-1.20** (2.18 lower to 0.22 lower)
Change in baseline monthly headache days (atogepant 10 mg versus placebo)											
698 (2 RCTs)	not serious	not serious	not serious	not serious	none	⨁⨁⨁⨁ High	392	306	-	-	MD **-1.40** (1.88 lower to 0.92 higher)
Change in baseline monthly headache days (atogepant 30 mg versus placebo)											
797 (2 RCTs)	not serious	not serious	not serious	not serious	none	⨁⨁⨁⨁ High	392	405	-	-	MD **-1.44** (1.9 lower to 0.98 lower)
Change in baseline monthly headache days (atogepant 60 mg versus placebo)											
791 (2 RCTs)	not serious	not serious	not serious	not serious	none	⨁⨁⨁⨁ High	392	399	-	-	MD **-1.48** (1.95 lower to 1.02 lower)
Change in baseline monthly days of use of medications for migraine (atogepant 10 mg versus placebo)											
698 (2 RCTs)	not serious	not serious	not serious	not serious	none	⨁⨁⨁⨁ High	306	392	-	-	MD **-1.30** (1.74 lower to 0.86 lower)

Certainty assessment							Summary of findings				
Change in baseline monthly days of use of medications for migraine (atogepant 30 mg versus placebo)											
797 (2 RCTs)	not serious	not serious	not serious	not serious	none	⨁⨁⨁⨁ High	405	392	-	-	MD **-1.40** (1.79 lower to 1.01 lower)
Change in baseline monthly days of use of medications for migraine (atogepant 60 mg versus placebo)											
791 (2 RCTs)	not serious	not serious	not serious	not serious	none	⨁⨁⨁⨁ High	399	392	-	-	MD **-1.30** (1.69 lower to 0.91 lower)
Reduction of at least 50% in baseline monthly migraine days (atogepant 10 mg versus placebo)											
698 (2 RCTs)	not serious	not serious	not serious	not serious	none	⨁⨁⨁⨁ High	134/392 (34.2%)	172/306 (56.2%)	**RR 1.70** (1.43 to 2.03)	342 per 1.000	**239 more per 1.000** (from 147 more to 352 more)
Reduction of at least 50% in baseline monthly migraine days (atogepant 30 mg versus placebo)											
797 (2 RCTs)	not serious	not serious	not serious	not serious	none	⨁⨁⨁⨁ High	134/392 (34.2%)	228/405 (56.3%)	**RR 1.63** (1.07 to 2.49)	342 per 1.000	**215 more per 1.000** (from 24 more to 509 more)
Reduction of at least 50% in baseline monthly migraine days (atogepant 60 mg versus placebo)											
791 (2 RCTs)	not serious	not serious	not serious	not serious	none	⨁⨁⨁⨁ High	134/392 (34.2%)	227/399 (56.9%)	**RR 1.64** (1.02 to 2.66)	342 per 1.000	**219 more per 1.000** (from 7 more to 567 more)
Any adverse event (atogepant 10 mg versus placebo)											
722 (2 RCTs)	not serious	not serious	not serious	serious[a]	none	⨁⨁⨁◯ Moderate	218/408 (53.4%)	178/314 (56.7%)	**RR 1.11** (0.78 to 1.56)	534 per 1.000	**59 more per 1.000** (from 118 fewer to 299 more)
Any adverse event (atogepant 30 mg versus placebo)											
819 (2 RCTs)	not serious	not serious	not serious	serious[a]	none	⨁⨁⨁◯ Moderate	218/408 (53.4%)	234/411 (56.9%)	**RR 1.08** (0.79 to 1.48)	534 per 1.000	**43 more per 1.000** (from 112 fewer to 256 more)
Any adverse event (atogepant 60 mg versus placebo)											

Certainty assessment							Summary of findings				
825 (2 RCTs)	not serious	not serious	not serious	serious[a]	none	⨁⨁⨁◯ Moderate	218/408 (53.4%)	231/417 (55.4%)	**RR 1.04** (0.91 to 1.17)	534 per 1.000	**21 more per 1.000** (from 48 fewer to 91 more)
Any serious adverse event (atogepant 10 mg versus placebo)											
722 (2 RCTs)	not serious	not serious	not serious	very serious[b]	none	⨁⨁◯◯ Low	4/408 (1.0%)	3/314 (1.0%)	**RR 1.00** (0.22 to 4.54)	10 per 1.000	**0 fewer per 1.000** (from 8 fewer to 35 more)
Any serious adverse event (atogepant 30 mg versus placebo)											
819 (2 RCTs)	not serious	not serious	not serious	very serious[b]	none	⨁⨁◯◯ Low	4/408 (1.0%)	2/411 (0.5%)	**RR 0.56** (0.12 to 2.58)	10 per 1.000	**4 fewer per 1.000** (from 9 fewer to 15 more)
Any serious adverse event (atogepant 60 mg versus placebo)											
825 (2 RCTs)	not serious	not serious	not serious	very serious[b]	none	⨁⨁◯◯ Low	4/408 (1.0%)	2/417 (0.5%)	**RR 0.55** (0.12 to 2.54)	10 per 1.000	**4 fewer per 1.000** (from 9 fewer to 15 more)
Discontinuation due to adverse events (atogepant 10 mg versus placebo)											
722 (2 RCTs)	not serious	not serious	not serious	very serious[b]	none	⨁⨁◯◯ Low	11/408 (2.7%)	13/314 (4.1%)	**RR 1.54** (0.69 to 3.42)	27 per 1.000	**15 more per 1.000** (from 8 fewer to 65 more)
Discontinuation due to adverse events (atogepant 30 mg versus placebo)											
819 (2 RCTs)	not serious	not serious	not serious	very serious[b]	none	⨁⨁◯◯ Low	11/408 (2.7%)	15/411 (3.6%)	**RR 1.36** (0.63 to 2.92)	27 per 1.000	**10 more per 1.000** (from 10 fewer to 52 more)
Discontinuation due to adverse events (atogepant 60 mg versus placebo)											
825 (2 RCTs)	not serious	not serious	not serious	very serious[b]	none	⨁⨁◯◯ Low	11/408 (2.7%)	12/417 (2.9%)	**RR 1.07** (0.48 to 2.39)	27 per 1.000	**2 more per 1.000** (from 14 fewer to 37 more)

CI: confidence interval; MD: mean difference; RR: risk ratio

[a]Downgraded once for imprecision: the CI fails to exclude important benefit or important harm

[b]Downgraded twice for imprecision: the CI fails to exclude important benefit or important harm; there are very few events.

e-Appendix I

PubMed search strategy
The strategy was based on the Cochrane Highly Sensitive Search Strategy for identifying randomized trials.[e-1]

#1 random* OR placebo OR trial* OR group* [Title/Abstract]
#2 "Randomized Controlled Trial"[Publication Type]
#3 "Controlled Clinical Trial"[Publication Type]
#4 ((#1) OR #2) OR #3
#5 "Animals"[Mesh] NOT"Humans"[Mesh]
#6 #4 NOT #5
#7 atogepant [Title/Abstract]
#8 migraine [Title/Abstract]
#9 #7 AND #8
#10 #6 AND #9

CENTRAL search strategy
(atogepant) AND (migraine) in Title, Abstract, Keywords in Trials'

ClinicalTrials.gov search strategy
(atogepant) AND (migraine) | Interventional Studies

e-Reference

e-1 Lefebvre C,Manheimer E, Glanville J. Chapter 6: Searching for studies. In: Higgins JPT, Green S (editors). Cochrane Handbook for Systematic Reviews of Interventions Version 5.0.2 (updated September 2009). The Cochrane Collaboration, 2009. Available from www.cochranehandbook.org.