Interpreting statistical data

Q1. As stated in the study protocol, a p-value ≤0.0167 is required to claim statistical significance of the results. Use Figure 2 below to complete the following templated sentence that describes the results. To complete the sentence, insert the relevant numerical values wherever a variable (e.g., <X>) appears:

A1. Zavegepant 10 mg and zavegepant 20 mg were more effective than placebo for the coprimary endpoints of:

- Pain freedom at 2 h postdose; (placebo: 15.5%; 10 mg: 22.5% [p=0.0113]; 20 mg: 23.1% [p=0.0055])
- Freedom from the MBS at 2 h postdose; (placebo: 33.7%; 10 mg: 41.9% [p=0.0155]; 20 mg: 42.5% [p=0.0094]

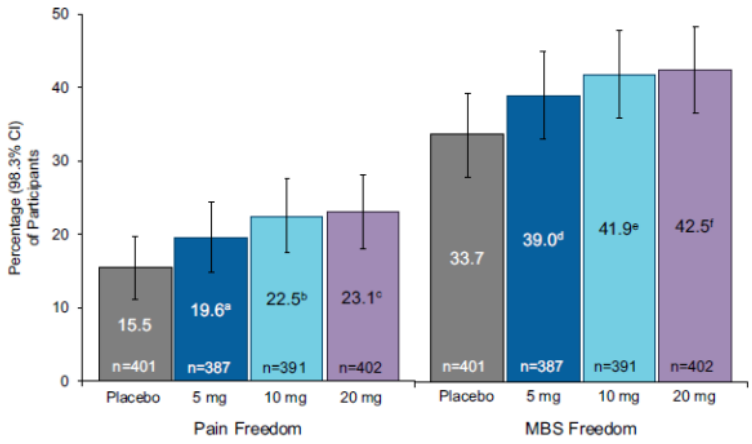

FIGURE 2 Efficacy of 5, 10, 20 mg zavegepant nasal spray versus placebo on the coprimary efficacy endpoints of pain freedom and MBS freedom at 2 h postdose. CI, confidence interval; MBS, most bothersome symptom. [a]$p = 0.1214$ versus placebo. [b]$p = 0.0113$ versus placebo. [c]$p = 0.0055$ versus placebo. [d]$p = 0.1162$ versus placebo. [e]$p = 0.0155$ versus placebo. [f]$p = 0.0094$ versus placebo

Q2. Secondary endpoints in the Phase 2/3 study of zavegepant were tested using a hierarchical gate-keeping procedure. This orders secondary endpoints using assumptions of their clinical relevance and likelihood of statistical significance. The secondary endpoints in the study were analyzed in order until an endpoint was reached that was not statistically significant (i.e., did not have a p-value ≤0.0167).

Once the first endpoint was reached that was not statistically significant, any subsequent endpoints with a p-value ≤0.0167 were designated "nominally significant" (i.e., significant in name only).

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Using the table below, list the secondary endpoints that were nominally statistically significant for each tested dose of zavegepant.

A2. Phonophobia freedom at 2 h was nominally significant for:

- 5 mg: 44.2% [p=0.0161]
- 10 mg: 44.8% [p=0.0115]

	Zavegepant			
	5 mg (*n* = 387)	10 mg (*n* = 391)	20 mg (*n* = 402)	Placebo (*n* = 401)
Pain relief at 2 h				
n/*N* (%)	224/387 (57.9)	237/391 (60.6)	246/402 (61.2)	215/401 (53.6)
Percentage difference[a]	4.2	7.1	7.5	
p-value	0.2296	0.0439	0.0302	
Return to normal function at 2 h[b]				
n/*N* (%)	115/363 (31.7)	122/354 (34.5)	129/372 (34.7)	101/369 (27.4)
Percentage difference[a]	4.3	7.1	7.3	
p-value	0.2039	0.0389	0.0305	
Rescue medication use within 24 h[c]				
n/*N* (%)	96/385 (24.9)	101/388 (26.0)	80/397 (20.2)	109/400 (27.3)
Percentage difference[a]	−2.4	−1.1	−7.1	
p-value	0.4502	0.7154	0.0172	
Photophobia freedom at 2 h[d]				
n/*N* (%)	118/337 (35.0)	121/340 (35.6)	134/354 (37.9)	109/358 (30.4)
Percentage difference[a]	4.6	5.1	7.4	
p-value	0.1986	0.1494	0.0352	
Phonophobia freedom at 2 h[d]				
n/*N* (%)	115/260 (44.2)	107/239 (44.8)	114/263 (43.3)	94/276 (34.1)
Percentage difference[a]	10.1	10.8	9.3	
p-value	0.0161	0.0115	0.0249	
Pain relief at 60 min				
n/*N* (%)	182/387 (47.0)	180/391 (46.0)	200/402 (49.8)	168/401 (41.9)
Percentage difference[a]	5.1	4.2	7.8	
p-value	0.1495	0.2274	0.0259	

[a]Stratified by preventive migraine medication use at randomization with Cochran–Mantel–Haenszel weighting.
[b]Among participants with functional disability at time of dosing.
[c]Participants with rescue medication start date on or before the study drug start date plus 1 day and missing rescue medication start time were excluded.
[d]Among participants with the symptom present at time of dosing.
[e]Among participants with pain freedom at 2 h postdose.