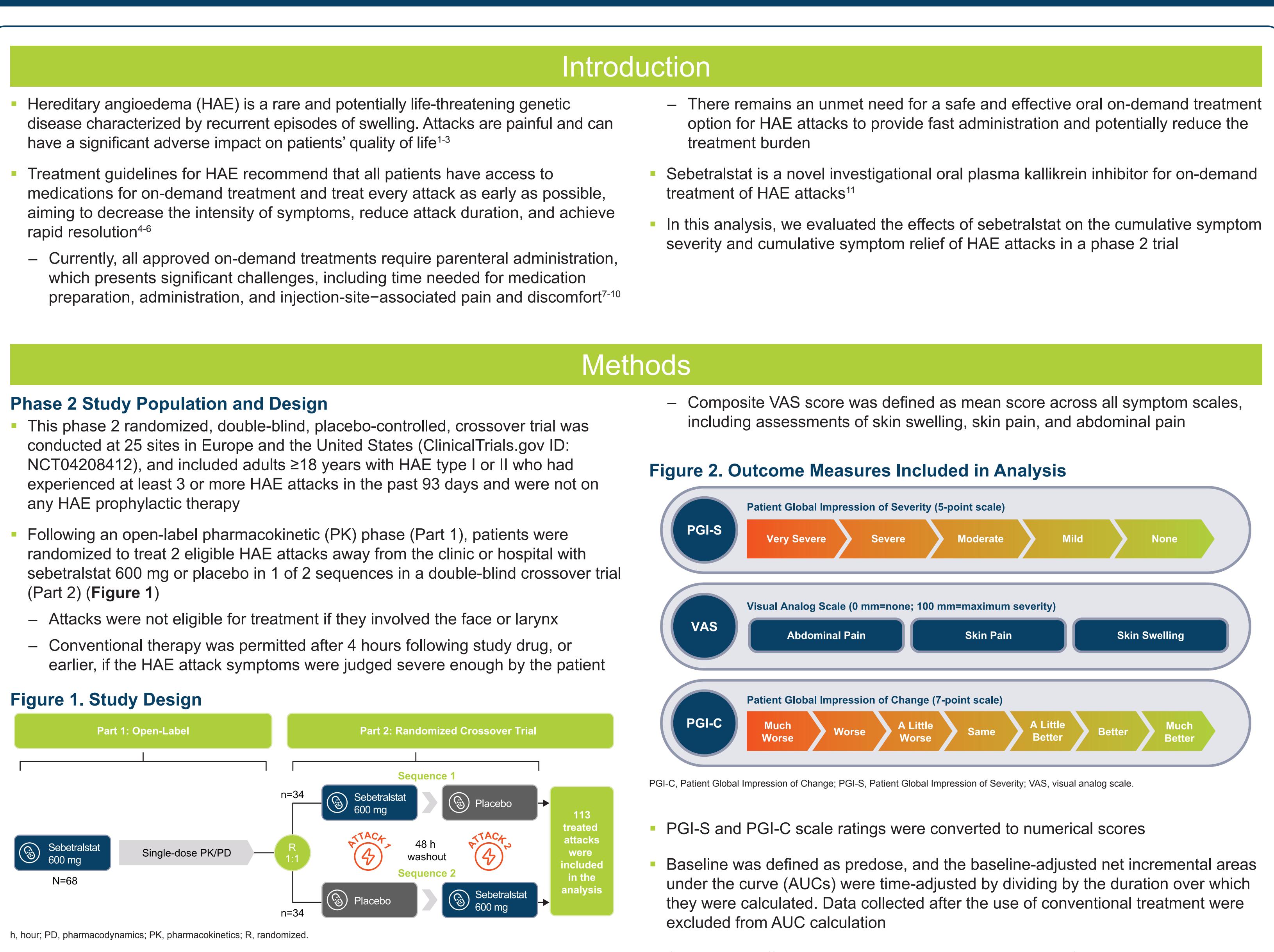
Treatment With Sebetralstat Reduces the Cumulative Symptom Severity of Hereditary Angioedema Attacks in a Phase 2 Trial

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- Overall HAE attack severity was assessed on the Patient Global Impression of Severity (PGI-S) scale ranging from none to very severe, HAE attack symptom severity was assessed on a 100-mm composite visual analog scale (VAS) ranging from 0 (none) to 100 (very severe), and symptom relief (change in attack symptoms) was assessed using the Patient Global Impression of Change (PGI-C) scale ranging from Much Worse to Much Better (Figure 2)
- Efficacy assessments after study drug administration in Part 2 were performed every 30 minutes between hours 0-4, every 1 hour between hours 4-12, and every 3 hours between hours 12-24

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random effect

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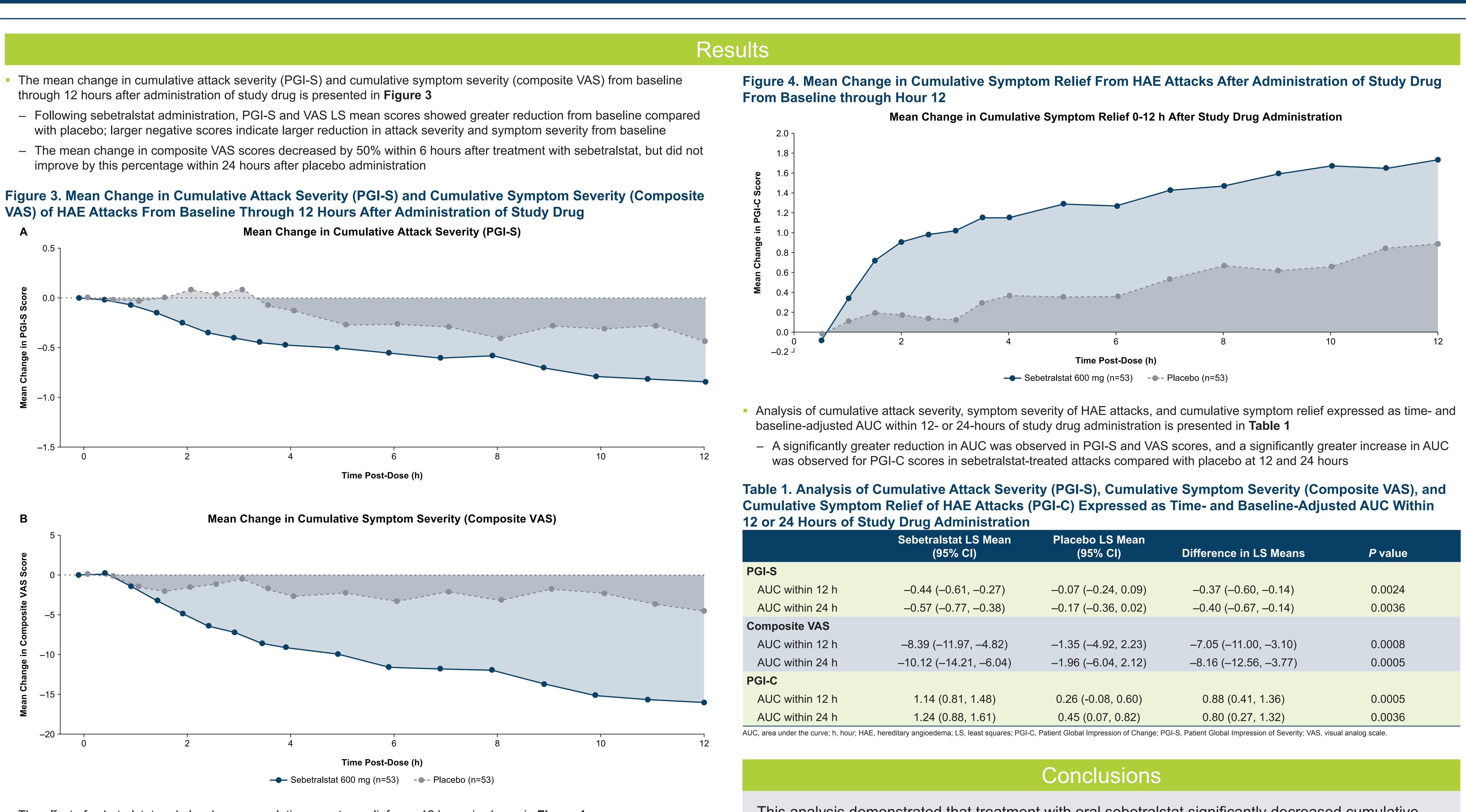
Sebetralstat effect on the cumulative symptom severity of HAE attacks was evaluated using the cumulative least squares (LS) means of PGI-S and composite VAS, and the AUC calculated within 12 and 24 hours of study drug administration

Cumulative symptom relief was evaluated using LS means of PGI-C and AUC within 12 and 24 hours

Analysis of variance was used with fixed effects of treatment, sequence, and HAE attack (first or second), and patient nested within sequence was a

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- larger positive scores indicate greater symptom relief
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The effect of sebetralstat and placebo on cumulative symptom relief over 12 hours is shown in Figure 4

- Following sebetralstat administration, PGI-C LS mean scores showed a greater increase from baseline compared with placebo, and sebetralstat was associated with a notable improvement in cumulative symptom relief by 2 hours postdose;

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Disclosures

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	Sebetralstat LS Mean (95% CI)	Placebo LS Mean (95% Cl)		
			Difference in LS Means	P value
	-0.44 (-0.61, -0.27)	-0.07 (-0.24, 0.09)	-0.37 (-0.60, -0.14)	0.0024
	-0.57 (-0.77, -0.38)	-0.17 (-0.36, 0.02)	-0.40 (-0.67, -0.14)	0.0036
	-8.39 (-11.97, -4.82)	-1.35 (-4.92, 2.23)	-7.05 (-11.00, -3.10)	0.0008
	–10.12 (–14.21, –6.04)	-1.96 (-6.04, 2.12)	-8.16 (-12.56, -3.77)	0.0005
	1.14 (0.81, 1.48)	0.26 (-0.08, 0.60)	0.88 (0.41, 1.36)	0.0005
	1.24 (0.88, 1.61)	0.45 (0.07, 0.82)	0.80 (0.27, 1.32)	0.0036

This analysis demonstrated that treatment with oral sebetralstat significantly decreased cumulative attack and symptom severity and increased cumulative symptom relief of HAE attacks relative to placebo over 12 and 24 hours following administration.