Characterization Of Injection Site-Related Adverse Events With Garadacimab In Patients With Hereditary Angioedema

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CONCLUSIONS

- **In the garadacimab pivotal Phase 3 (VANGUARD) study and the Phase 3 open-label extension (OLE) for patients with hereditary angioedema (HAE), incidence of injection-site reactions (ISRs) such as erythema, bruising and pruritus was low**
- **The favorable injection-site tolerability profile of long-term prophylaxis (LTP) with garadacimab observed in patients with HAE may contribute to reduced treatment burden**

BACKGROUND

HAE[1-8]

- HAE is characterized by recurrent, unpredictable, debilitating, potentially life-threatening attacks of swelling
- The goals of HAE treatment are to achieve complete disease control and normalization of life, which can only be reached with LTP therapy
- Treatment-related ISRs are reported more frequently with approved injectable LTP options versus placebo (e.g., pain, erythema, bruising)
- Patients have indicated a preference for new LTP options that reduce treatment burden

Garadacimab[1,9,10]

- Garadacimab is a first-in-class, fully human monoclonal antibody targeting activated factor XII, the key initiator of the contact system
- Garadacimab demonstrated durable efficacy with a favorable long-term safety profile and substantial quality of life and patient-reported outcomes in the 6-month pivotal Phase 3 (VANGUARD) study and in the Phase 3 OLE

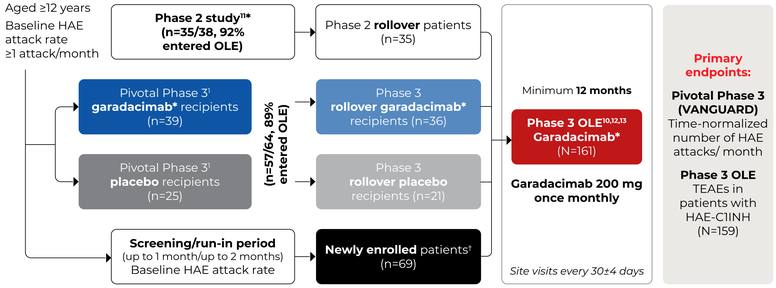
OBJECTIVE

- To report the results of a *post hoc* analysis of the Phase 3 clinical program to characterize the incidence, nature and outcomes of injection-site related adverse events

GARADACIMAB CLINICAL PROGRAM

Eligibility criteria

- Confirmed HAE diagnosis
- Aged ≥12 years
- Baseline HAE attack rate ≥1 attack/month

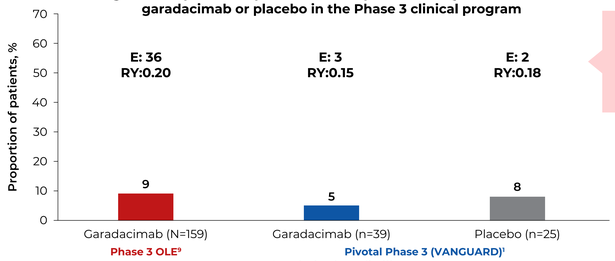


*Garadacimab was administered once monthly (Phase 2 = 28 ± 2 days; Phase 3 = 30 ± 4 days); †Newly enrolled patients received one garadacimab 400 mg SC loading dose as their first dose; ‡Patients may use acute on-demand therapy to treat emerging HAE attacks if the medication has previously been shown to be effective.
HAE, hereditary angioedema; HAE-C1INH, hereditary angioedema with C1-inhibitor deficiency or dysfunction; OLE, open-label extension; SC, subcutaneous; TEAE, treatment-emergent adverse event.

RESULTS

In the Phase 3 clinical program, garadacimab-related ISRs were mostly mild in severity (95%) and all resolved by the end of the study

Figure 1: Proportion of patients who experienced any ISR event with garadacimab or placebo in the Phase 3 clinical program



Any TEAE	Garadacimab 200 mg (N=159)	Garadacimab 200 mg (n=39)	Placebo (n=25)
n	133	25	15
%	83.6	64.1	60
E	524	75	54
RY*	2.84	3.86	4.78

Rate of garadacimab-related ISRs was comparable in pivotal Phase 3 and Phase 3 OLE studies

Garadacimab was associated with lower rate of TEAEs than placebo (by RY)*

Figure 2: Proportion of patients who experienced ISR events per MedDRA classification with garadacimab or placebo in the Phase 3 clinical program

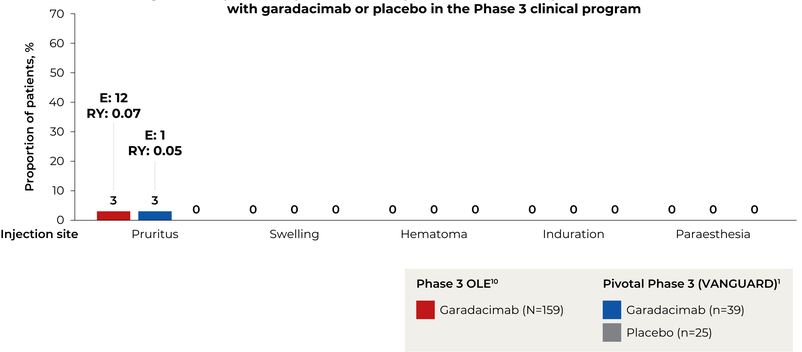


Figure 3: Proportion of patients who experienced ISR events per MedDRA classification with garadacimab or placebo in the Phase 3 clinical program

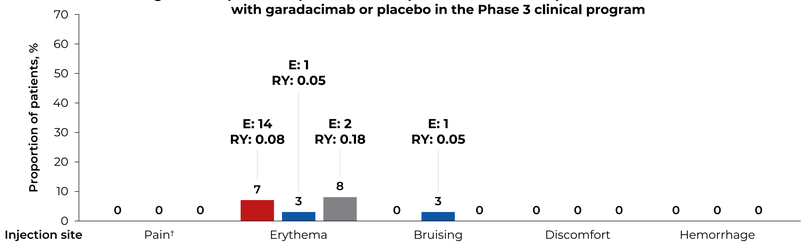
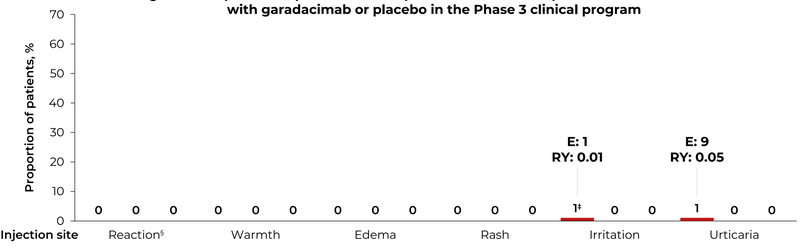


Figure 4: Proportion of patients who experienced ISR events per MedDRA classification with garadacimab or placebo in the Phase 3 clinical program



*Rate per year was calculated based on number of events per cumulative safety period duration in years. †Pain was not systematically recorded, per protocol; no unsolicited reports of injection-site pain were reported. ‡One patient discontinued garadacimab treatment in the Phase 3 OLE following a moderate ISR (abdomen irritation at injection site, discontinued at Month 6 of treatment) assessed as related to garadacimab by the investigator, which resolved. §Injection-site reaction defined according to MedDRA criteria.
E, event; ISR, injection-site reaction; OLE, open-label extension; RY, rate per year; TEAE, treatment-emergent adverse event.

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Disclosures

This study was sponsored by CSL Behring. Medical writing support provided by Hazel Shepherd, DPhil, of Helix, OPEN Health Scientific Communications and funded by CSL Behring, in accordance with Good Publication Practice (GPP) guidelines (www.ismpp.org/gpp-2022).

Originally presented at American College of Allergy Asthma & Immunology Annual Scientific Meeting | Boston, MA, USA | October 24–28, 2024