Long-Term Efficacy of Garadacimab for Hereditary Angioedema in Patients With or Without Prior Exposure in a Phase 3 Open-Label Extension Study

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CONCLUSIONS

- **Garadacimab provided durable efficacy and sustained protection against hereditary angioedema (HAE) attacks throughout the Phase 3 open-label extension (OLE) study in patients with prior garadacimab exposure and garadacimab-naïve patients**
- **The efficacy of garadacimab for long-term prophylaxis against HAE attacks was consistent with previous findings**

BACKGROUND

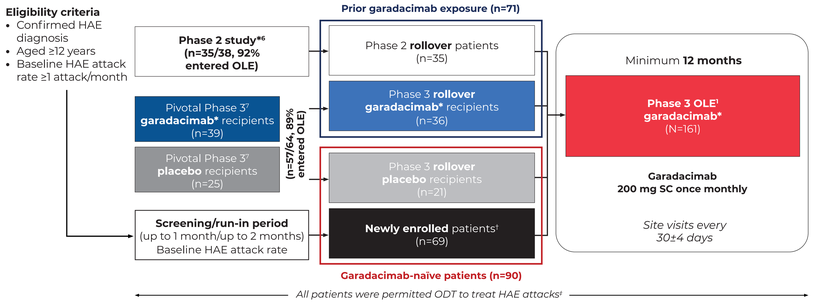
- HAE is characterized by recurrent, unpredictable, and potentially life-threatening attacks of angioedema[1–3]
- The key mediator of HAE attacks is bradykinin, which is overproduced in patients with HAE due to dysregulation of the kallikrein–kinin system[4,5]
- The principal initiator of the kallikrein–kinin system is activated factor XII (FXIIa)[4,5]
- Garadacimab is a first-in-class, fully human, monoclonal antibody inhibiting FXIIa under evaluation for the long-term prophylaxis of HAE attacks[6–8]
- The durable efficacy and favorable long-term safety profile of garadacimab 200 mg subcutaneous once monthly was previously reported for the Phase 3 OLE study in an analysis of rollover (received garadacimab or placebo in the Phase 2 or pivotal Phase 3 studies) and newly enrolled patient data, as per the primary analyses specified in the OLE study protocol[1]

OBJECTIVE

- To evaluate the long-term efficacy of garadacimab in patients with prior exposure (received garadacimab in a prior study) and garadacimab-naïve patients (received placebo in a prior study or were newly enrolled)

PHASE 3 OLE STUDY DESIGN

- Patients were stratified *post hoc* into prior garadacimab exposure and garadacimab-naïve cohorts (data cutoff: February 13, 2023)



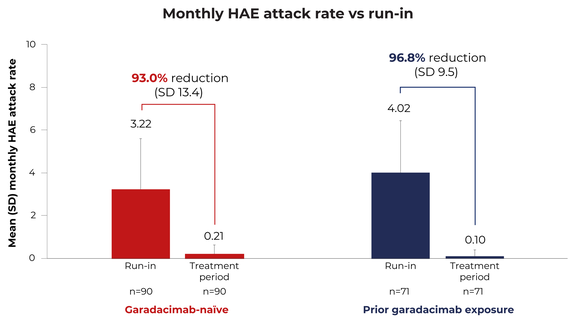
Primary endpoint
- TEAEs[§] in patients with HAE-C1INH (N=159)

Secondary efficacy endpoints
- HAE attack rate during run-in and treatment
- Attack rate reduction during treatment vs run-in
- ≥50%, ≥90%, or 100% attack rate reduction vs run-in
- Attacks treated with ODT
- Moderate and severe attacks

*Garadacimab was administered once monthly (Phase 2 = 28±2 days; Phase 3 = 30±4 days); †Newly enrolled patients received a garadacimab loading dose (two 200 mg SC injections) as first administration; ‡Patients were permitted to use acute ODT to treat emerging HAE attacks if the medication had previously been shown to be effective; §Including number/percentage of TEAEs, the number/proportion of patients with TEAEs, and TEAE rates per administration of study drug and per patient-year.
HAE, hereditary angioedema; HAE-C1INH, hereditary angioedema due to C1INH deficiency or dysfunction; ODT, on-demand treatment; OLE, open-label extension; SC, subcutaneous; TEAE, treatment-emergent adverse event.

RESULTS

Garadacimab substantially reduced the mean monthly HAE attack rate in patients with and without prior garadacimab exposure



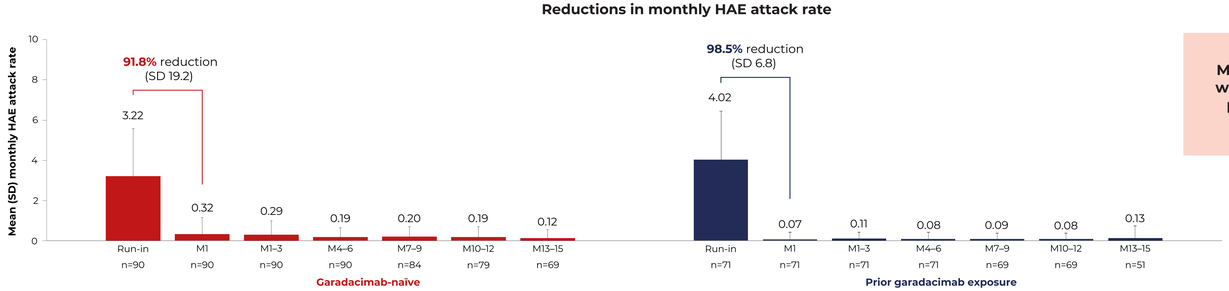
Median (IQR) total exposure

Garadacimab-naïve	**13.3 months** (12.2–14.4)
Prior garadacimab exposure	**21.9 months** (17.7–37.4)

Efficacy outcomes	Phase 3 OLE study: Garadacimab-naïve (n=90)	Phase 3 OLE study: Prior garadacimab exposure (n=71)
Monthly HAE attack rate, mean (SD)		
Run-in	3.22 (2.35)	4.02 (2.43)
Treatment period	0.21 (0.41)	0.10 (0.30)
Attack-free patients, n (%)	**49 (54.4)**	**47 (66.2)**
Attacks treated with ODT, mean (SD)		
Run-in	2.56 (2.60)	3.51 (2.66)
Treatment period	0.19 (0.40)	0.09 (0.30)
Moderate/severe attacks, mean (SD)		
Run-in	2.34 (2.05)	2.91 (2.17)
Treatment period	0.15 (0.34)	0.06 (0.16)

HAE, hereditary angioedema; IQR, interquartile range; ODT, on-demand treatment; OLE, open-label extension; SD, standard deviation.

Reductions in mean monthly HAE attack rates were evident at Month 1, and low attack rates were sustained throughout the treatment period for both cohorts



Mean monthly HAE attack rate reductions were consistent with previously published primary analyses evaluating rollover and newly enrolled cohorts[1]

HAE, hereditary angioedema; M, month; SD, standard deviation.

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