Long-term quality-of-life and patient-reported improvements with garadacimab for hereditary angioedema: Phase 3 open-label extension study (NCT04739059)

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CONCLUSIONS

- Clinically meaningful and long-term improvements to quality of life (QoL) and patient-reported outcomes (PRO) were associated with garadacimab in the pivotal Phase 3 (VANGUARD)[1] and open-label extension (OLE) studies, consistent with the durable efficacy observed
- Among patients previously exposed to garadacimab, mean total angioedema quality of life (AE-QoL) and Work Productivity and Activity Impairment Questionnaire (WPAI) score improvements were sustained in the long-term OLE study from the pivotal Phase 3 study
- Among garadacimab-naïve patients, mean total AE-QoL and WPAI scores improved from baseline in the long-term OLE study
- Response to garadacimab per Subject's Global Assessment of Response to Therapy (SGART) was rated by most patients as "good" or better across the pivotal Phase 3 and long-term OLE studies

BACKGROUND

Hereditary angioedema (HAE)[1-3]

- Causes recurrent, unpredictable, debilitating, potentially life-threatening attacks of swelling which substantially impair QoL
- Results from increased levels of bradykinin, a key mediator of attacks in HAE

Garadacimab[1,4]

- First-in-class, fully human monoclonal antibody targeting activated factor XII (FXIIa), the key initiator of the contact system
- Fully human, high affinity/potency/specificity; decreases bradykinin production
- Garadacimab was evaluated vs placebo in the 6-month pivotal Phase 3 (VANGUARD) study for long-term prophylaxis of HAE attacks; evaluation is ongoing in the OLE (NCT04739059) study

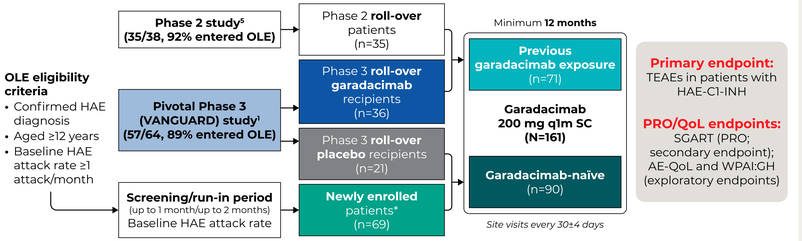
Mean monthly number of HAE attacks in pivotal Phase 3 and OLE studies

OLE, open-label extension.

OBJECTIVE

- To report long-term QoL and PRO measures (at Month 12) of garadacimab 200 mg subcutaneous (SC) once-monthly from the pivotal Phase 3 (VANGUARD) and ongoing long-term OLE (NCT04739059) studies

LONG-TERM PHASE 3 OLE STUDY DESIGN



*Newly enrolled patients received one SC 400 mg 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.
AE-QoL, Angioedema Quality of Life Questionnaire; HAE, hereditary angioedema; HAE-C1-INH, HAE with C1-esterase inhibitor deficiency; OLE, open-label extension; PRO, patient-reported outcome; q1m, once monthly; SC, subcutaneous; SGART, Subject's Global Assessment of Response to Therapy; TEAE, treatment-emergent adverse event; WPAI:GH, Work Productivity and Activity Impairment Questionnaire: General Health.

RESULTS

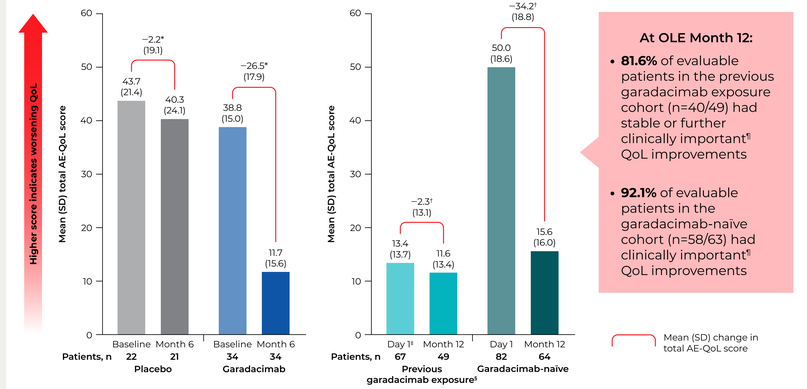
Baseline demographics and characteristics of patients in the OLE study

Characteristic	Garadacimab (N=161)
Mean (SD) age, years	42.3 (15.3)
Sex – Female, n (%)	101 (62.7)
Race, n (%)	
White	135 (83.9)
Asian	22 (13.7)
Black	2 (1.2)
Other*	2 (1.2)
Mean (SD) BMI, kg/m²	28.1 (6.2)
HAE-C1-INH type, n (%)	
Type I	145 (90.1)
Type II	14 (8.7)
HAE-nC1-INH†	2 (1.2)
Number of HAE attacks per month during run-in,‡ mean (SD)	3.6 (2.4)
Median (range) exposure in OLE, months	13.8 (3.0–21.1)

Median (IQR) total exposures§	
Previous garadacimab exposure cohort	21.9 months (17.7–37.4)
Garadacimab-naïve cohort	13.3 months (12.2–14.4)

*Includes Other and Multiple; †The two patients with HAE-nC1-INH were not included in the safety analysis and calculation of mean BMI; ‡All patients had their baseline attack rate measured during the run-in period; for roll-over patients, the run-in period was at the beginning of the first study the patient was enrolled in; §Integrated values across all studies.
BMI, body mass index; HAE, hereditary angioedema; HAE-C1-INH, HAE with C1-esterase inhibitor deficiency; HAE-nC1-INH, HAE with normal levels of C1-esterase inhibitor; IQR, interquartile range; OLE, open-label extension; SD, standard deviation.

AE-QoL total scores: Month 6 vs baseline of pivotal Phase 3 (VANGUARD) study (left) and Month 12 vs Day 1 of OLE study (right)

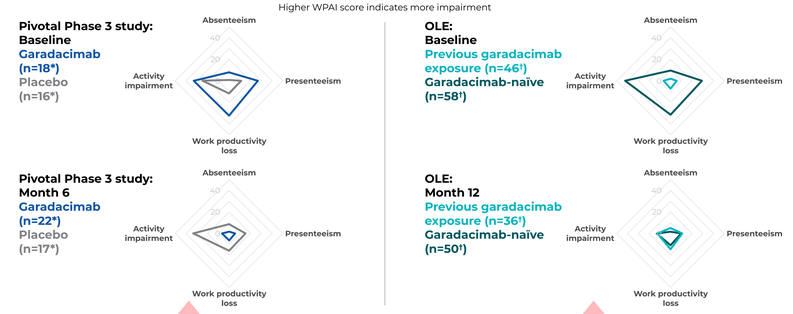


At OLE Month 12:

- **81.6%** of evaluable patients in the previous garadacimab exposure cohort (n=40/49) had stable or further clinically important¶ QoL improvements
- **92.1%** of evaluable patients in the garadacimab-naïve cohort (n=58/63) had clinically important¶ QoL improvements

*Evaluable patients included in change from baseline analysis are placebo (n=20), garadacimab (n=33); †Evaluable patients included in change from baseline are previous garadacimab exposure (n=49), and garadacimab-naïve (n=63 – one patient did not provide baseline data); ‡Day 1 scores for the previous garadacimab exposure cohort were obtained at the final visit from the previous study; §Previous garadacimab exposure cohort received garadacimab in completed Phase 2 or pivotal Phase 3 studies. Phase 2 data are not shown; ¶MCID ≥6-point decrease from Day 1.
AE-QoL; Angioedema Quality of Life Questionnaire; MCID, minimal clinically important difference; OLE, open-label extension; QoL, quality of life; SD, standard deviation.

WPAI scores: Pivotal Phase 3 (VANGUARD) study (left) and OLE study (right)



WPAI scores improved in garadacimab-treated patients in the pivotal Phase 3 (VANGUARD) study

WPAI score improved in garadacimab-naïve patients and was sustained in patients previously exposed to garadacimab

*Number of patients observed varied by WPAI domain as not all patients were in employment. Number of patients differs from n values presented above for baseline activity impairment score: Garadacimab, n=35; placebo, n=22; Month 6 activity impairment score: Garadacimab, n=36; placebo, n=21; Month 6 absenteeism score; Placebo, n=18; †Number of patients observed varied by WPAI domain as not all patients were in employment. Number of patients differs from n values presented above for baseline activity impairment score: Previous garadacimab exposure patients, n=69; garadacimab-naïve, n=83; Month 12 activity impairment score: Previous garadacimab exposure patients, n=49; garadacimab-naïve, n=64.
OLE, open-label extension; WPAI, Work Productivity and Activity Impairment Questionnaire.

SGART: Pivotal Phase 3 (VANGUARD) study and Month 12 of the OLE study

SGART ratings

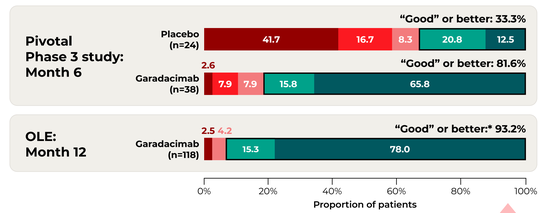
0 – "None"
No response, not acceptable

1 – "Poor"
Little response, not acceptable

2 – "Fair"
Acceptable response, could be better

3 – "Good"
Acceptable response

4 – "Excellent"
As good as can be imagined



Improvements in patient rating of response per SGART were observed with garadacimab vs placebo in the pivotal Phase 3 study and were sustained at Month 12 of the OLE study

*Response category values were rounded to one decimal place, including when summing "good" and "excellent" values to calculate "good" or better measure, which therefore may not reflect the exact sum of individual values.
OLE, open-label extension; SGART, Subject's Global Assessment of Response to Therapy.

References

1. Craig TJ et al. *Lancet* 2023;401:1079–1090; 2. Bork K et al. *Allergy Asthma Clin Immunol* 2021;17:40; 3. Maurer M et al. *Allergy* 2022;77:1961–1990; 4. Cao H et al. *J Allergy Clin Immunol* 2018;142:1355–1358; 5. Craig T et al. *Lancet* 2022;399:945–955.

Disclosures

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