Garadacimab for hereditary angioedema prophylaxis in adolescents: efficacy and safety from the VANGUARD Phase 3 and 3b open-label extension trial (first interim analysis)

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CONCLUSIONS

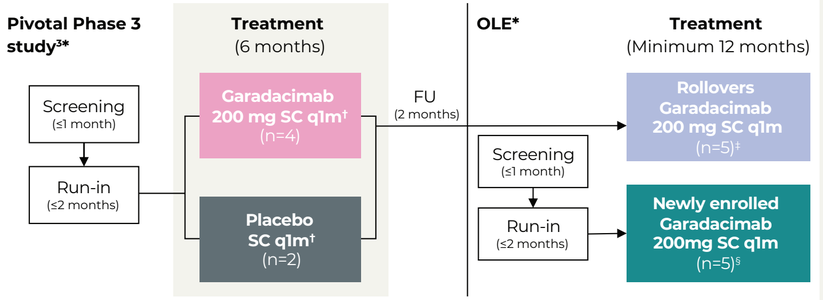
- **Once-monthly garadacimab was efficacious in preventing hereditary angioedema (HAE) attacks in adolescents (aged 12–≤17 years)**
- **Durability of effect is supported by results of the first interim analysis from the ongoing open-label extension (OLE) (NCT04739059)[1,2]**
- **Favorable safety and tolerability profile in adolescents**
- **Efficacy and safety in adolescents were consistent with the overall pivotal Phase 3 study[3] and OLE**
- **A planned Phase 3 trial will evaluate garadacimab in pediatric patients with HAE (aged 2–11 years) (NCT05819775, EudraCT: 2022-502386-13-00)**

BACKGROUND AND OBJECTIVE

- HAE is a rare, debilitating disease characterized by unpredictable submucosal or subcutaneous swellings (HAE attacks)[3]
- Symptoms of HAE typically begin in childhood with attack intensity worsening during puberty[4]
- Efficacy and safety of garadacimab (monoclonal antibody targeting activated factor XII) have been demonstrated in Phase 2 (adult only) and pivotal Phase 3 studies[3,5]
- Safety and efficacy data in adolescents from the pivotal Phase 3 study and ongoing OLE are reported

METHODS

Figure 1. Adolescent patients from Pivotal Phase 3 and OLE study design



Presented pivotal Phase 3 study endpoints
- Primary: time-normalized number of HAE attacks
- Secondary: reduction in HAE attack rate vs run-in
- Safety: TEAEs, AESIs, SAEs

Presented OLE endpoints
- Primary: TEAEs
- Secondary: time-normalized number of HAE attacks, reduction in HAE attack rate vs run-in

All patients were permitted to use on-demand therapy to treat HAE attacks throughout the pivotal Phase 3 and OLE studies.
*Eligibility criteria for entry into the pivotal Phase 3 study and OLE included: clinically confirmed HAE, aged ≥12 years and baseline attack rate ≥1 HAE attack/month;
†In the pivotal Phase 3 study, patients received a loading dose of garadacimab 400 mg SC as first dose (2 injections of 200 mg) or volume-matched placebo;
‡One patient aged 18 years at OLE enrolment was considered an adult; they were included in the pivotal Phase 3 analysis but were not included in the OLE analysis;
§Newly enrolled patients in OLE received a loading dose of garadacimab 400 mg SC as first dose.
AESI, adverse event of special interest; FU, follow-up; HAE, hereditary angioedema; OLE, open-label extension; q1m, once monthly; SAE, serious adverse event; SC, subcutaneous; TEAE, treatment-emergent adverse event.

RESULTS

Table 1. Baseline characteristics and attack reduction

			Monthly mean attack rate (% reduction vs run-in)		
Patient*	Sex	Garadacimab exposure (months)†	Run-in	Pivotal Phase 3	OLE
1	F	12.3	1.2	1.2 (–5.8)	0.6 (45.5)
2	M	13.1	2.2	0.2 (92.3)	0 **(100)**‡
3	F	6.0	2.9	0 **(100)**‡	§
4	M	11.8	1.2	0 **(100)**‡	0 **(100)**‡
5	M	8.3	1.0	Placebo: 1.2 (–12.2)	0.1 (88.3)
6	F	9.3	1.8	Placebo: 0.2 (90.8)	0 **(100)**‡
7	M	3.3	0.9	–	0.3 (65.7)
8	F	15.2	1.0	–	0.1 (93.8)
9	F	12.5	4.9	–	0 **(100)**‡
10	F	4.4	3.2	–	0 **(100)**‡
11	M	3.6	1.2	–	0 **(100)**‡

Garadacimab-treated (Phase 3) Placebo Garadacimab-treated rollovers (OLE) Newly enrolled (OLE)

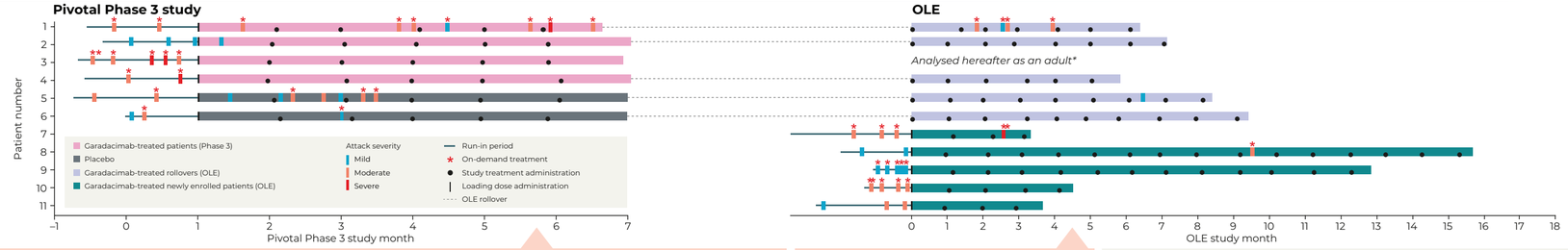
*All adolescents (aged 12–≤17 years) had HAE type 1, were White and had a BMI range of 17.9–42.3 kg/m²; †Garadacimab exposure inclusive of the pivotal Phase 3 study and OLE where applicable; ‡Attack-free patients; §Patient aged 18 years at OLE enrolment was considered an adult; therefore, they were included in the pivotal Phase 3 analysis but were not included in the OLE analysis.
BMI, body mass index; F, female; M, male; OLE, open-label extension.

Table 2. Favorable safety profile in adolescents

		Pivotal Phase 3 study Exposure: 6 months	OLE Exposure range: 3.3–15.3 months
AEs	Placebo (n=2)	Garadacimab (n=4)	Garadacimab (n=10)*
Patients with any TEAEs, n (%)	2 (100)	2 (50)	6 (60)
Total TEAEs, n	7	4	20
Mild, n (%)	7 (100)	3 (75)	16 (80)
Moderate,† n (%)	0	1 (25)	4 (20)
Severe, n	0	0	0
SAEs, n	0	0	0
TEAEs leading to discontinuation, n	0	0	0
TEAEs of special interest,‡ n	0	0	0
Treatment-related TEAEs, n	0	0	0
Injection-site reactions, n	0	0	0
Most common TEAEs in ≥2 patients			
COVID-19 infection, n (%)	2 (100)	0	3 (30)
Common cold, n (%)	0	1 (25)	2 (20)

*One patient aged 18 years at OLE enrolment was considered an adult; therefore, they were included in the pivotal Phase 3 analysis but were not included in the OLE analysis;
†Included one occurrence each of sore throat (pivotal Phase 3 study), upper respiratory tract infection, flu-like symptoms, COVID-19, and acid reflux (OLE);
‡Includes abnormal bleeding events, thromboembolic events and severe hypersensitivity, including anaphylaxis.
AE, adverse event; OLE, open-label extension; SAE, serious adverse event; TEAE, treatment-emergent adverse event.

Figure 2. HAE attacks during the Pivotal Phase 3 and OLE study



Pivotal Phase 3 entrants (range of exposure: 6.0–13.1 months)
Received garadacimab in the pivotal study (Patient numbers 1–4):
- **Pivotal:** 3/4 (75%) patients had ≥90% attack-rate reductions vs run-in; 2/4 (50%) were attack free
- **OLE:** 2/3 (67%) rollover patients still considered adolescents were attack free in ongoing OLE
- **Patient 1:** Non-responder in the pivotal study but attained a 45.5% attack-rate reduction in the OLE vs run-in and they have remained attack free for >2 months

Received placebo in the pivotal study (Patient numbers 5 and 6):
- **OLE:** Achieved 88% and 100% attack-rate reductions, respectively, vs run-in

3/5 (60%) rollover adolescents were attack free throughout OLE

Newly enrolled patients (Patient numbers 7–11)

Range of exposure: 3.3–15.2 months
- 1/5 subject had 65.7% attack-rate reduction vs run-in, and 4/5 had >93% reduction vs run-in
- 3/5 (60%) newly enrolled adolescents were attack free throughout OLE

*Patient aged 18 years at OLE enrolment was considered an adult; therefore, they were included in the pivotal Phase 3 analysis but were not included in the OLE analysis.
OLE, open-label extension.

References

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Disclosures

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