Long-term safety of garadacimab in patients with hereditary angioedema from the Phase 3 open-label extension study: an up to 3-year interim analysis

388

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BACKGROUND

- HAE attacks are recurrent, unpredictable, and potentially life-threatening[1,2]
- Garadacimab, a first-in-class, fully human mAb inhibiting FXIIa[3-5] was recently approved in adults and adolescents for routine prevention of recurrent attacks of HAE in Australia, Europe, Japan, Switzerland, and the UK[6-11]

STUDY DESIGN OF THE PHASE 3 OLE[5]

Eligibility

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

Screening/Run-in period
(up to 1 month/up to 2 months)
Baseline HAE attack rate established

- Phase 2 **rollover** patients (n=35)
- Phase 3 **rollover garadacimab** recipients (n=36)
- Phase 3 **rollover placebo** recipients (n=21)
- **Newly enrolled** patients (n=69)

Phase 3 OLE (NCT04739059):
Garadacimab SC 200 mg once-monthly
(N=161)

FOCUS OF THIS PRESENTATION

ANALYSIS OF LONG-TERM SAFETY DATA IN THE PHASE 3 OLE

Data cutoff: June 15 2024

Median (range) garadacimab exposure: 2.5 (0.3–3.1) years
Maximum garadacimab exposure: 3.1 years

SUMMARY OF TEAEs IN THE PHASE 3 OLE

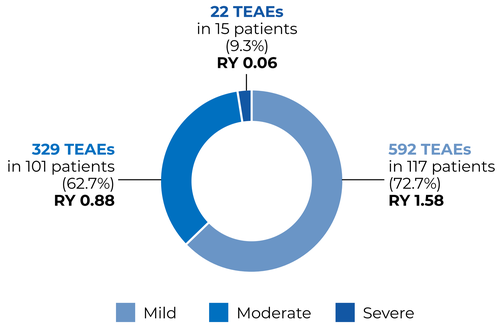
Patients with:

≥1 TEAE
90.1%
(145/161)
RY 2.52

≥1 garadacimab-related TEAE
14.9%
24/161)
RY 0.17

RY = rate per patient-year

TEAEs by severity:



No deaths occurred

No AESIs per protocol
(severe hypersensitivity, including anaphylaxis, thromboembolic events, and abnormal bleeding events)

Total discontinuations: four patients (2.5%); RY 0.01*
Garadacimab-related discontinuations: two patients (1.2%)
- Mild injection-site urticaria
- Moderate injection-site irritation

SAEs†
- Seven events in seven patients (4.3%); **RY 0.02**
- **None garadacimab-related**

SUMMARY OF THE MOST COMMON TEAEs IN THE PHASE 3 OLE

TEAEs in ≥5%of patients	Patients (N=161), n (%)	Related to garadacimab, n (%)
COVID-19	67 (41.6)	0
Nasopharyngitis	35 (21.7)	0
Influenza	13 (8.1)	0
URTI	13 (8.1)	0
Sinusitis	8 (5.0)	0
Abdominal pain	10 (6.2)	1 (0.6)
Diarrhea	8 (5.0)	0
Toothache	8 (5.0)	0
ISR	20 (12.4)	17 (10.6)
Headache	13 (8.1)	1 (0.6)
Arthralgia	10 (6.2)	1 (0.6)
Back pain	8 (5.0)	0
Cough	8 (5.0)	0

- Most common TEAEs: infections (including COVID-19, nasopharyngitis, influenza, URTI, and sinusitis)
- None related to garadacimab

- **Garadacimab-related ISRs: 45 (43 mild; 2 moderate). These included:**
  - Injection-site erythema: 17/45
  - Injection-site pruritus: 12/45
  - Injection-site urticaria: 9/45
  - Injection-site pain: 4/45
  - Injection site swelling: 2/45
  - Injection-site irritation: 1/45
- **Rate per injection:** 0.01

CONCLUSIONS

- **Garadacimab continued to demonstrate a favorable long-term safety profile over a maximum exposure of 3.1 years in the Phase 3 OLE**
- **These data are consistent with safety data from the Phase 2 and pivotal Phase 3 studies**

*Injection site urticaria, n=1; injection site irritation, n=1; moods swings, n=1, and breast cancer, n=1; †COVID-19, n=2, abdominal HAE attack, n=1, were observed at second interim analysis (data cutoff: February 13, 2023); breast cancer, n=1, food allergy, n=1, hand fracture, n=1, drug reaction to a non-study drug, n=1, were observed data cutoff June 15, 2024.
AESI, adverse event of special interest; FXIIa, activated Facattor XII; HAE, hereditary angioedema; HAE-C1INH, hereditary angioedema with C1 inhibitor deficiency/dysfunction; IQR, interquartile range; LTP, long term prophylaxis; mAb, monoclonal antibody; OLE, open-label extension; RY, rate per patient-year; SAE, serious adverse event; TEAE, treatment-emergent adverse event; URTI, upper respiratory tract infection.

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