Comparison of Study Designs for Primary Phase III Trials for Omalizumab Versus Dupilumab for Patients With Chronic Spontaneous Urticaria

Andrew Alexis,1 Kyle Anders,2 Arpamas Seetasith,2 Michael Holden2
1Weill Cornell Medicine, New York, NY, USA; 2Genentech, Inc., South San Francisco, CA, USA

Introduction

- Omalizumab is currently the only biologic approved and recommended as second-line treatment for patients with chronic spontaneous urticaria (CSU).
- However, clinical trial programs are underway for other biologic treatments such as dupilumab.
- Given head-to-head trials will not be conducted, consideration of study design may be important.
- We compared the participants, interventions, outcomes, and results for Phase III primary efficacy clinical trials for omalizumab versus dupilumab for patients with CSU (using published information only):
  - Omalizumab trials - ASTERIA I and II (NCT01287117 and NCT01292473)
  - Dupilumab trial - LIBERTY-CSU-CUPID (NCT04180488).

Participants

ASTERIA I/II (omalizumab)
- 12–75 years
- Diagnosis of CSU refractory to H1 antihistamines for ≥6 months
- Presence of itch and hives for >6 consecutive weeks despite H1 antihistamines plus H2 antihistamines, LTRAs, or both, or >8 weeks despite use of H1 antihistamines
- UAS7 score ≥16
- ISS7 score ≥8
- UAS >4 on at least 1 screening day

LIBERTY-CSU-CUPID (dupilumab)
- 6–80 years
- Diagnosis of CSU refractory to H1 antihistamines for ≥6 months
- Presence of itch and hives for >6 consecutive weeks despite H1 antihistamines (standard or ≤4-fold dose)
- UAS7 score ≥16
- ISS7 score ≥8
- Known immunodeficiency
- Use of any H2 antihistamine or LTRA within 7 days

Key Exclusion Criteria

ASTERIA I/II (omalizumab)
- Weight <20 kg
- Other skin disease associated with itch
- Routine daily doses of the following within 30 days prior: systemic steroids, hydroxychloroquine, methotrexate, cyclosporine, cyclophosphamide, IV Ig
- History of malignancy
- History of atopic dermatitis
- History of nasopharyngitis
- History of malignancy
- Use of any H2 antihistamine or LTRA

LIBERTY-CSU-CUPID (dupilumab)
- All patients with CSU refractory to H1 antihistamines
- Known immunodeficiency
- Active TB or active infection
- Presence of itch and hives for >6 consecutive weeks despite H1 antihistamines
- History of malignancy
- Presence of other skin morbidity including atopic dermatitis
- History of malignancy
- Active TB or active infection
- Known immunodeficiency
- Use of any H2 antihistamine or LTRA

Interventions

ASTERIA I/II (omalizumab)
- 24-week (ASTERIA I) or 12-week (ASTERIA II) treatment (every 4 weeks)
  - Placebo
  - Omalizumab 75 mg
  - Omalizumab 150 mg
  - Omalizumab 300 mg

LIBERTY-CSU-CUPID (dupilumab)
- 24-week treatment (every 2 weeks)
  - Placebo
  - Dupilumab 200 mg for adolescents <60 kg or children ≥30 kg
  - Dupilumab 300 mg for adolescents ≥60 kg

Outcomes

ASTERIA I/II (omalizumab)
- Primary Outcome - Week 12
  - Change from baseline in ISS7 at Week 24
  - Percentage of participants UAS7 ≤6
  - Percentage of participants ISS7 MID responders

LIBERTY-CSU-CUPID (dupilumab)
- Primary Outcome - Week 24
  - Change from baseline in ISS7 at Week 24
  - Percentage of participants UAS7 ≤6
  - Percentage of participants ISS7 MID responders

Secondary Efficacy Outcomes

ASTERIA I/II (omalizumab)
- Change from baseline in ISS7 at Week 24
- Percentage of participants UAS7 ≤6
- Percentage of participants ISS7 MID responders
- Percentage of participants UAS7 ≤6 (complete responders)
- Percentage of angioedema-free days from Week 4

LIBERTY-CSU-CUPID (dupilumab)
- Change from baseline in ISS7 at Week 24
- Percentage of participants UAS7 ≤6
- Percentage of participants ISS7 MID responders
- Percentage of participants UAS7 ≤6 (complete responders)
- Percentage of participants receiving OCS
- Time to receiving OCS
- (Safety) Incidence of treatment-emergent ADAS

Results

ASTERIA I/II (omalizumab)
- All patients with CSU refractory to H1 antihistamines

LIBERTY-CSU-CUPID (dupilumab)
- All patients with CSU refractory to H1 antihistamines

Conclusions

- Comparing study designs for primary clinical trials for omalizumab and dupilumab for patients with CSU will aid in the comparative analysis and clinical evaluation of final trial results.
- Based on published information, key differences between ASTERIA I/II (omalizumab) and LIBERTY-CSU-CUPID (dupilumab):
  - No restrictions on participants for omalizumab
  - Treatment every 4 weeks for omalizumab and every 2 weeks for dupilumab
  - Primary endpoint of 12 weeks for omalizumab versus 24 weeks for dupilumab
  - Data are complete and validated in real-world studies for omalizumab and incomplete/ongoing for dupilumab.

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