Clinical Activity of Antolimab (AK002), an Anti-Siglec-8 Monoclonal Antibody, in Treatment-Refractory Chronic Urticaria

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Disclosures

• Sabine Altrichter is an investigator for this study
• Antolimab (AK002) is an investigational drug candidate and is not FDA/EMA approved
Prevalence of Antihistamine-Refractory CSU in US

**Chronic Spontaneous Urticaria (CSU)**
~1.6 M to ~3.5 M patients

~80% inadequate response to labeled dose of antihistamines

**Antihistamine Refractory (1x)**
~1.3 M to ~2.8 M patients

~60% inadequate response to increased dose of antihistamines

**Antihistamine Refractory (up to 4x)**
~800 K to ~1.7 M patients

Antolimab (AK002) Targets Siglec-8 on Mast Cells and Eosinophils

Activating Receptors

Siglec-8

Cell Membrane

Activation

Mast cell

Eosinophil

Inflammatory response

Antolimab

Inhibition

Mast cell

Eosinophil

Inhibition

ADCC/Apoptosis
## Study Design

<table>
<thead>
<tr>
<th>Design</th>
<th>Key Endpoints</th>
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</table>
| • Open-label  
• 45 patients – 4 cohorts  
  - Omalizumab-naïve CSU  
  - Omalizumab-refractory\(^1\) CSU  
  - Cholinergic urticaria  
  - Symptomatic Dermographism  
• One month screening period  
• Dosed once monthly for 6 months  
• 8 weeks safety follow up  
• 0.3 mg/kg starting AK002 dose; increased to 1.0 mg/kg (dose 2 and 3); if UCT <12, increased to 3.0 mg/kg (dose 4, 5, and 6) | • Change in Urticaria Control Test (UCT) Week 22 from BL  
  - Complete Response: UCT score ≥12 and ΔUCT ≥ 3  
  - Partial Response: ΔUCT ≥ 3  
  - No Response: ΔUCT < 3 |
| **Primary** |  |
| **Secondary** | • Change in disease activity by UAS7 (CSU only)  
• Safety and tolerability |

\(^1\) Patients refractory to omalizumab (n=11): AH treatment up to 4x labeled dose, OMA doses up to 600 mg, average OMA treatment duration ~10 months; UCT on OMA: 4.1
Urticaria Disease Assessment Tools

**URTICARIA CONTROL TEST (UCT)**

- Measures disease control (symptoms and quality of life)
- Used in clinical practice
- Can be used in both chronic spontaneous urticaria and chronic inducible urticarias (e.g. cholinergic and symptomatic dermographism)

**URTICARIA ACTIVITY SCORE (UAS)**

- Comprised of measures of itch & hives:
  - Itch Severity Score (ISS)
  - Hives Severity Score (HSS)
- UAS7 used as primary endpoint for regulatory approval in CSU (can only be used in CSU)

UCT and UAS7 recommended by EAACI CU Guidelines to assess CSU disease
Baseline Patient Characteristics

<table>
<thead>
<tr>
<th></th>
<th>Chronic Spontaneous Urticaria</th>
<th>Chronic Inducible Urticaria</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>Omalizumab Naïve (n=13)</td>
<td>Omalizumab Refractory (n=11)</td>
</tr>
<tr>
<td>Age</td>
<td>65 (30-75)</td>
<td>29 (22-60)</td>
</tr>
<tr>
<td>Female</td>
<td>100%</td>
<td>82%</td>
</tr>
<tr>
<td>BMI</td>
<td>32 (20-44)</td>
<td>26 (20-42)</td>
</tr>
<tr>
<td>UCT</td>
<td>3.2</td>
<td>3.7</td>
</tr>
<tr>
<td>UAS7</td>
<td>18.5 (8.6-41.0)</td>
<td>28.7 (18.1-35.8)</td>
</tr>
</tbody>
</table>
# High Response Rate by UCT with Antolimab in CSU

## Chronic Spontaneous Urticaria

<table>
<thead>
<tr>
<th>Urticaria Control Test Response(^1)</th>
<th>Omalizumab Naïve (n=13)</th>
<th>Omalizumab Refractory (n=7)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Complete Response</td>
<td>92%</td>
<td>57%</td>
</tr>
<tr>
<td>Partial Response</td>
<td>0%</td>
<td>29%</td>
</tr>
<tr>
<td>No Response</td>
<td>8%</td>
<td>14%</td>
</tr>
</tbody>
</table>

1 Patients who received all 6 doses
2 UCT complete response: ≥3-point improvement from baseline and score ≥12; partial response ≥3-point improvement from baseline; no response <3-point improvement from baseline
Omalizumab Naïve CSU: Substantial Improvement in UAS7

Omalizumab-Naïve

Baseline: 18.5
Week 22: 4.6

Baseline Week 22 (n=13)
Omalizumab Naïve CSU: Response by UAS7 Measures

Response Rate by UAS7 Measures

<table>
<thead>
<tr>
<th>Measure</th>
<th>% of Responders at Week 22</th>
</tr>
</thead>
<tbody>
<tr>
<td>HSS=0</td>
<td>77% (10/13)</td>
</tr>
<tr>
<td>ISS=0</td>
<td>54% (7/13)</td>
</tr>
<tr>
<td>UAS7=0</td>
<td>54% (7/13)</td>
</tr>
<tr>
<td>UAS7≤6</td>
<td>62% (8/13)</td>
</tr>
</tbody>
</table>

Omalizumab Naïve Patients
Omalizumab Refractory CSU Cohort – Medical History

Inadequate disease control despite extensive use of omalizumab (OMA)

<table>
<thead>
<tr>
<th>Prior OMA Treatment Experience</th>
<th>Antolimab (AK002) Experience</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Average treatment duration: ~10 months</td>
<td>• Time since last OMA dose: &gt;2 months</td>
</tr>
<tr>
<td>• Treatment regimen:</td>
<td>• Treatment regimen:</td>
</tr>
<tr>
<td>• Omalizumab: up to 600 mg</td>
<td>• Antihistamine: up to 4x labeled dose</td>
</tr>
<tr>
<td>• Antihistamine: up to 4x labeled dose</td>
<td></td>
</tr>
</tbody>
</table>
Omalizumab Refractory CSU: Substantial Improvement in UAS7

All Omalizumab-Refractory

Baseline: 28.7
Week 22: 14.7
Baseline Week 22 (n=11)

Received All 6 Doses

Baseline: 28.4
Week 22: 11.2
Baseline Week 22 (n=7)
Omalizumab Refractory CSU: Response by UAS7 Measures

Response Rate by UAS7 Measures

% of Responders at Week 22

HSS=0: 14% (1/7)
ISS=0: 14% (1/7)
UAS7=0: 14% (1/7)
UAS7≤6: 29% (2/7)
△UAS7 ≥10 (MID): 86% (6/7)

Omalizumab Refractory Patients

2 Patients who received all 6 doses; in entire OMA-refractory CSU cohort, 8 of 11 patients met MID change in UAS7 ≥10
High Response Rate by UCT with Antolimab in CIndU

<table>
<thead>
<tr>
<th>Urticaria Control Test Response(^1)</th>
<th>Cholinergic (n=11)</th>
<th>Symptomatic Dermographism (n=10)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Complete Response</td>
<td>82%</td>
<td>40%</td>
</tr>
<tr>
<td>Partial Response</td>
<td>0%</td>
<td>30%</td>
</tr>
<tr>
<td>No Response</td>
<td>18%</td>
<td>30%</td>
</tr>
</tbody>
</table>

\(^1\) UCT complete response: ≥3-point improvement from baseline and score ≥12; partial response: ≥3-point improvement from baseline; no response: <3-point improvement from baseline.
Cholinergic Urticaria: 100% Response Rate by PCE\(^1\) Test

<table>
<thead>
<tr>
<th></th>
<th>Baseline</th>
<th>END OF STUDY</th>
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<tbody>
<tr>
<td></td>
<td>Provocation(^2)</td>
<td>Number of Wheals after 30 mins</td>
</tr>
<tr>
<td></td>
<td>Response &lt; 10 mins</td>
<td></td>
</tr>
<tr>
<td>CholU-1</td>
<td>+</td>
<td>21 - 50</td>
</tr>
<tr>
<td>CholU-2</td>
<td>+</td>
<td>1 - 20</td>
</tr>
<tr>
<td>CholU-3</td>
<td>+</td>
<td>1 - 20</td>
</tr>
<tr>
<td>CholU-4</td>
<td>+</td>
<td>&gt;50</td>
</tr>
<tr>
<td>CholU-5</td>
<td>+</td>
<td>Positive</td>
</tr>
<tr>
<td>CholU-6</td>
<td>+</td>
<td>&gt;50</td>
</tr>
<tr>
<td>CholU-7</td>
<td>+</td>
<td>&gt;50</td>
</tr>
</tbody>
</table>

1 Pulse Control Ergometry
2 Provocation - exercise on stationary bike elevates body temperature to trigger symptoms, positive response if hives occur ≤10 minutes from start of sweating. Test terminated at 30 mins
Safety Summary

- Generally well-tolerated
- No drug-related Serious Adverse Events
- Most common adverse event was mild to moderate infusion-related reactions (IRRs; flushing, feeling of warmth, headache, nausea, or dizziness)
Antolimab in Chronic Urticaria

- Demonstrated activity in all forms of antihistamine-refractory Chronic Urticaria tested
- Substantial activity in patients refractory to omalizumab
- Continued activity observed in 12-month open-label extension
- Antolimab is potentially a front-line biologic treatment for Chronic Urticaria
Thank you