Immune mediated dermatosis: urticaria & hidradenitis
Dr. Antonio Martorell
Ligelizumab* achieves sustained symptom control up to 1 year in the majority of patients with chronic spontaneous urticaria

Results of the 1-year extension study of the Phase 2b trial

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*QGE031, fully humanized IgG1 monoclonal antibody directed against human IgE that binds with greater affinity than omalizumab (Xolair).
LIGELIZUMAB EXHIBITED A CLEAR DOSE-RESPONSE IN THE ACHIEVEMENT OF COMPLETE HIVES RESPONSE AT WEEK 12\textsuperscript{a} DURING THE CORE STUDY

The proportion of patients achieving HSS7=0 Week12 was the primary endpoint of the core study; \textsuperscript{b}The dose-response curve shows the median, 20 and 80 percentile, from 1000 bootstrap samples. Dots with error bars represent point estimates and asymptotic 60% confidence interval for each dose in observed data.
PATIENT DISPOSITION DURING THE CORE PHASE 2B TRIAL AND THE OPEN-LABEL, SINGLE-ARM EXTENSION STUDY

aPatients who discontinued treatment during the double-blind period were encouraged to remain in the study for the safety analysis and enter the post-treatment follow-up.
A HIGH RATE OF SUSTAINED AND COMPLETE SYMPTOM CONTROL WAS ACHIEVED WITH LIGELIZUMAB 240 MG Q4W UP TO 1 YEAR

- Complete responses were sustained and over 50% of patients achieved UAS7=0 at the end of Week 52
- Over 50% of patients were well-controlled (UAS7≤6) at Week 4 after one dose of ligelizumab 240 mg

CSU, chronic spontaneous urticaria; q4w, every 4 weeks; UAS7, 7-day urticaria activity score

High rates of complete (UAS7=0) and well-controlled (UAS7≤6) responses sustained up to 1 year
COMPARABLE RATES OF ADVERSE EVENTS RATES WERE REPORTED DURING THE PHASE 2B CORE AND 1-YEAR EXTENSION STUDIES

CURRENTLY ONGOING:
Two Phase 3 trials examining the efficacy and safety of ligelizumab 72 and 120 mg q4w treatment up to 1 year in patients with CSU inadequately controlled with H₁-antihistamines at approved doses

<table>
<thead>
<tr>
<th>Category</th>
<th>Ligelizumab q4w</th>
<th>Omalizumab 300 mg q4w (N=85)</th>
<th>Placebo 120 mg SD (N=42)</th>
<th>Total (N=382)</th>
<th>Ligelizumab 240 mg q4w (N=226)</th>
</tr>
</thead>
<tbody>
<tr>
<td>At least one AE</td>
<td>36 (83.7)</td>
<td>62 (72.9)</td>
<td>34 (79.1)</td>
<td>295 (77.2)</td>
<td>190 (84.1)</td>
</tr>
<tr>
<td>Mild</td>
<td>16 (37.2)</td>
<td>36 (42.4)</td>
<td>22 (52.4)</td>
<td>152 (39.8)</td>
<td>100 (44.2)</td>
</tr>
<tr>
<td>Moderate</td>
<td>16 (37.2)</td>
<td>21 (24.7)</td>
<td>13 (31.0)</td>
<td>117 (30.6)</td>
<td>77 (34.1)</td>
</tr>
<tr>
<td>Severe</td>
<td>4 (9.3)</td>
<td>5 (5.9)</td>
<td>2 (4.8)</td>
<td>26 (6.8)</td>
<td>13 (5.8)</td>
</tr>
<tr>
<td>At least one serious AE</td>
<td>3 (7.0)</td>
<td>3 (3.5)</td>
<td>4 (9.5)</td>
<td>18 (4.7)</td>
<td>13 (5.8)*</td>
</tr>
<tr>
<td>AEs leading to discontinuation</td>
<td>0 (0.0)</td>
<td>2 (2.4)</td>
<td>2 (4.7)</td>
<td>2 (4.8)</td>
<td>8 (2.1)</td>
</tr>
<tr>
<td>≥ 1 AE possibly related to treatment</td>
<td>5 (11.6)</td>
<td>24 (28.2)</td>
<td>6 (14.3)</td>
<td>54 (23.9)</td>
<td></td>
</tr>
</tbody>
</table>

Data presented as n (%)  
*One serious AE (hypersensitivity) reported related to ligelizumab (re-assessment ongoing with adjudication committee)

Ligelizumab was well tolerated with no unexpected safety signals
HIGHLIGHTS IN HIDRADENITIS SUPPURATIVA: ROLE OF IL-1\(\alpha\)

- Precursor IL-1\(\alpha\) protein made constitutively by keratinocytes, some epithelial cells and CNS cells
- Binds to IL-1 receptor present on all cells
- Upon stimulation, most inflammatory cells (e.g. Platelets, macrophages, neutrophils, dendritic cells and others) can produce IL-1\(\alpha\)
- Synergizes with TNF\(\alpha\) to produce cytokines, IL-8, PDGE, and others...

**Biologic effects include:**
- Induces pro-collagen I and III, fibroblast proliferation and collagen synthesis
- Induces TNF release
- Stimulates hepatocytes to make acute phase reactants
- Increases protease production
- Potentiates pain perception
- Drives neo-angiogénesis
Phase II Open Label Study of Bermekimab in patients with moderate to severe hidradenitis suppurativa

- IgG\textsubscript{1} subclass
- Derived from a natural human humoral response against IL-1\(\alpha\)
- Binds and neutralizes IL-1\(\alpha\)
- Does not bind IL-1\(\beta\)
- Binds all forms of IL-1\(\alpha\): full, processed, membrane-bound, soluble

**Patients who have previously failed anti-TNF\(\alpha\) therapy (Failures) 400 mg every week (n=24)**

**Patients with no prior treatment with anti-TNF\(\alpha\) therapy ("Naïve") 400 mg every week (n=24)**

**Week 0**

- Baseline Data 1\textsuperscript{st} injection

**Week 12**

- Endpoint Data after 12 injections
HIGHLIGHTS IN HIDRADENITIS SUPPURATIVA: ANTI IL-1- $\alpha$: BERMEKIMAB
HIGHLIGHTS IN HIDRADENITIS SUPPURATIVA: CURRENTLY ONGOING CLINICAL TRIALS

Phase II Open Label Study of Bermekimab in patients with moderate to severe hidradenitis suppurativa

There are now clinical trials in hidradenitis for:

- IL-17 inhibitor
- IL-23 inhibitor
- Anti-CD-40 monoclonal antibody
- C5a receptor inhibitor
- JAK inhibitor

Results are expected for the nex year!
HIGHLIGHTS IN HIDRADENITIS SUPPURATIVA: NEW INSIGHTS IN COMORBIDITIES

1. Evaluate the odds of stroke, coronary artery disease, peripheral artery disease, and heart failure in patients with HS compared to the general population (patients without a chronic inflammatory skin disease).

2. Evaluate the odds of stroke, coronary artery disease, peripheral artery disease, and heart failure in patients with HS compared to patients with psoriasis.

- Retrospective cohort study
- 4,914 HS patients, 4,641 psoriasis patients, and 23,266 controls.

Hidradenitis Suppurativa is Associated with Increased Odds of Stroke, Coronary Artery Disease, Heart Failure, and PAD

<table>
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<tr>
<th>Table 1: HS vs. Controls</th>
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<tr>
<td>Condition</td>
</tr>
<tr>
<td>Stroke</td>
</tr>
<tr>
<td>PAD</td>
</tr>
<tr>
<td>CAD</td>
</tr>
<tr>
<td>Heart Failure</td>
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Table 1: Multivariate analysis using logistic regression to study the odds of stroke, PAD, CAD, and heart failure after adjustment for gender, race, age, hypertension, hyperlipidemia, diabetes, smoking, and BMI in patients with HS vs. controls.

<table>
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<th>Table 2: HS vs. Psoriasis</th>
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<td>Condition</td>
</tr>
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Table 2: Multivariate analysis using logistic regression to study the odds of stroke, PAD, CAD, and heart failure after adjustment for gender, race, age, hypertension, hyperlipidemia, diabetes, smoking, and BMI in patients with HS vs. patients with psoriasis.