Proof-of-Concept Phase-2a Clinical Trial of ANB020 (Anti-IL-33 Antibody) in the Treatment of Moderate-to-Severe Adult Atopic Dermatitis

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European Academy of Allergy and Clinical Immunology Congress
May 29th 2018
Disclosure

In relation to this presentation, I declare the following, real or perceived conflicts of interest:

<table>
<thead>
<tr>
<th>Type</th>
<th>Company</th>
</tr>
</thead>
<tbody>
<tr>
<td>Employment full time</td>
<td>University of Oxford and Oxford University Hospitals</td>
</tr>
<tr>
<td>Research Grant (P.I., collaborator or consultant; pending and received grants)</td>
<td>UCB, Celgene, Novartis, AnaptysBio</td>
</tr>
<tr>
<td>Other research support</td>
<td>None</td>
</tr>
<tr>
<td>Speakers Bureau</td>
<td>Sanofi/Genzyme, La Roche Posay</td>
</tr>
<tr>
<td>Ownership interest (stock, stock-options, patent or intellectual property)</td>
<td>Orbit Discovery</td>
</tr>
<tr>
<td>Consultant / advisory board</td>
<td>Novartis, UCB, Grunenthal, Evelo, Eli Lilly, Leo</td>
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A conflict of interest is any situation in which a speaker or immediate family members have interests, and those may cause a conflict with the current presentation. Conflicts of interest do not preclude the delivery of the talk, but should be explicitly declared. These may include financial interests (e.g. owning stocks of a related company, having received honoraria, consultancy fees), research interests (research support by grants or otherwise), organisational interests and gifts.
IL-33: Central Mediator of Type 2 Diseases
Key Role in Pathogenesis of Atopic Dermatitis

- IL-33 is a key cytokine in type 2 inflammatory responses to allergen
  - Responsible for activation of Th2 and ILC2
  - Functions upstream of IL-4, IL-5 and IL-13
  - Modulates mast cell degranulation

- IL-33 is rapidly released by epithelium upon allergen exposure

- Genetic association of IL-33 pathway mutations with type 2 diseases¹

- IL-33 is highly expressed in skin of atopic dermatitis patients with active disease²

¹ Ramirez-Carrozzi et al. 2014
² Savinko et al. 2012
ANB020: Anti-Human IL-33 Antibody

- ANB020 is humanized anti-human IL-33 monoclonal antibody
  - High affinity binding to human IL-33 with $K_d$ of approximately 1 pM
  - Potent neutralizing activity with an $IC_{50}$ of approximately 1.5 nM

- Healthy volunteer Phase 1 trial (n=96) reported safety, pharmacokinetics and pharmacodynamics
  - Subjects dosed with 10mg to 750mg of ANB020 in single dose cohorts (n=48), 40mg to 300mg of ANB020 weekly for 4 weeks in multiple dose cohorts (n=24) and placebo (n=24)
  - In vivo half-life of approximately 16 days for both intravenous and subcutaneous administration
  - Pharmacodynamic effect persisted for 85 days at certain single dose levels of ANB020
  - ANB020 was generally well tolerated and no dose-limiting toxicities were observed

![Single dose ANB020 healthy volunteer Phase 1 pharmacodynamic ex vivo assay measuring inhibition of IL-33 induced Interferon-gamma (IFN-g) relative to pre-dose levels](image-url)
ANB020 Phase 2a Atopic Dermatitis
Proof-of-Concept Trial

• Study design:
  - Enrolled 12 moderate-to-severe adult atopic dermatitis patients inadequately controlled with topical corticosteroids
  - Single intravenous dose of placebo (Day -7) followed by a single 300 mg intravenous dose of ANB020 (Day 1)
  - EASI, 5-D pruritus, SCORAD, DLQI and IGA clinical scores determined at specific time points

• Study objective:
  - Demonstrate EASI-50 response in at least 50% of patients at Day 29 (primary endpoint)
Baseline Characteristics

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Average (n=12)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>40.4 ± 13.5</td>
</tr>
<tr>
<td>Male, number (%)</td>
<td>11 (91.7%)</td>
</tr>
<tr>
<td>Caucasian race, number (%)</td>
<td>12 (100%)</td>
</tr>
<tr>
<td>Body-Mass Index</td>
<td>26.14 ± 4.145</td>
</tr>
<tr>
<td>EASI, score</td>
<td>32.25 ± 10.89</td>
</tr>
<tr>
<td>IGA, 0-5 scale</td>
<td>4 ± 0.74</td>
</tr>
<tr>
<td>SCORAD, score</td>
<td>64.79 ± 12.02</td>
</tr>
<tr>
<td>Pruritus, 5-D score</td>
<td>19.1 ± 4.85</td>
</tr>
<tr>
<td>DLQI, score</td>
<td>12.92 ± 6.54</td>
</tr>
<tr>
<td>Eosinophils, per microliter blood</td>
<td>588 ± 468</td>
</tr>
</tbody>
</table>

All 12 patients were inadequately controlled on corticosteroids pre-study.

7 of 12 enrolled patients were treated with systemic immuno-modulators pre-study and presented with a baseline EASI score of 36.

5 of 12 patients were not treated with systemic immuno-modulators pre-study and presented with a baseline EASI score of 27.
EASI Scores Following Single ANB020 Dose
Rapid response and all patients achieved EASI-50 on or before Day 57

<table>
<thead>
<tr>
<th>Timepoint</th>
<th>Average % EASI Score Reduction*</th>
<th>% Patients Achieving EASI-50*</th>
<th>% Patients Achieving EASI-75*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Day -21 (Baseline)</td>
<td>0%</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Day 1 (ANB020 Dosing)</td>
<td>4%</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Day 15</td>
<td>58%</td>
<td>9 of 12 (75%)</td>
<td>3 of 12 (25%)</td>
</tr>
<tr>
<td>Day 29</td>
<td>61%</td>
<td>10 of 12 (83%)</td>
<td>4 of 12 (33%)</td>
</tr>
<tr>
<td>Day 57</td>
<td>62%</td>
<td>9 of 12 (75%)</td>
<td>5 of 12 (42%)</td>
</tr>
<tr>
<td>Day 78</td>
<td>62%</td>
<td>9 of 12 (75%)</td>
<td>2 of 12 (17%)</td>
</tr>
<tr>
<td>Day 113</td>
<td>55%</td>
<td>8 of 12 (67%)</td>
<td>2 of 12 (17%)</td>
</tr>
<tr>
<td>Day 140</td>
<td>45%</td>
<td>5 of 12 (42%)</td>
<td>3 of 12 (25%)</td>
</tr>
</tbody>
</table>

* Relative to baseline upon enrollment at Day -21

**Average % EASI Score Reduction**
- **Day -21 (Baseline)**: 0%
- **Day 1 (ANB020 Dosing)**: 4%
- **Day 15**: 58%
- **Day 29**: 61%
- **Day 57**: 62%
- **Day 78**: 62%
- **Day 113**: 55%
- **Day 140**: 45%

**% Patients Achieving EASI-50**
- **Day -21 (Baseline)**: 0%
- **Day 1 (ANB020 Dosing)**: 0%
- **Day 15**: 9 of 12 (75%)
- **Day 29**: 10 of 12 (83%)
- **Day 57**: 9 of 12 (75%)
- **Day 78**: 9 of 12 (75%)
- **Day 113**: 8 of 12 (67%)
- **Day 140**: 5 of 12 (42%)

**% Patients Achieving EASI-75**
- **Day -21 (Baseline)**: 0%
- **Day 1 (ANB020 Dosing)**: 0%
- **Day 15**: 3 of 12 (25%)
- **Day 29**: 4 of 12 (33%)
- **Day 57**: 4 of 12 (33%)
- **Day 78**: 5 of 12 (42%)
- **Day 113**: 2 of 12 (17%)
- **Day 140**: 3 of 12 (25%)

- **Day 15**
  - **EASI Score Reduction**: 58%
  - **% Patients Achieving EASI-50**: 9 of 12 (75%)
  - **% Patients Achieving EASI-75**: 3 of 12 (25%)

- **Day 29**
  - **EASI Score Reduction**: 61%
  - **% Patients Achieving EASI-50**: 10 of 12 (83%)
  - **% Patients Achieving EASI-75**: 4 of 12 (33%)

- **Day 57**
  - **EASI Score Reduction**: 62%
  - **% Patients Achieving EASI-50**: 9 of 12 (75%)
  - **% Patients Achieving EASI-75**: 5 of 12 (42%)

- **Day 78**
  - **EASI Score Reduction**: 62%
  - **% Patients Achieving EASI-50**: 9 of 12 (75%)
  - **% Patients Achieving EASI-75**: 2 of 12 (17%)

- **Day 113**
  - **EASI Score Reduction**: 55%
  - **% Patients Achieving EASI-50**: 8 of 12 (67%)
  - **% Patients Achieving EASI-75**: 2 of 12 (17%)

- **Day 140**
  - **EASI Score Reduction**: 45%
  - **% Patients Achieving EASI-50**: 5 of 12 (42%)
  - **% Patients Achieving EASI-75**: 3 of 12 (25%)
### Additional Efficacy Data

5-D Pruritus, SCORAD, DLQI and IGA Scores

<table>
<thead>
<tr>
<th>Timepoint</th>
<th>Average % 5-D Pruritus Score Reduction*</th>
<th>Average % SCORAD Reduction*</th>
<th>Average % DLQI Reduction*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Day -21 (Baseline)</td>
<td>0%</td>
<td>0%</td>
<td>0%</td>
</tr>
<tr>
<td>Day 1 (ANB020 Dosing)</td>
<td>10%</td>
<td>3%</td>
<td>21%</td>
</tr>
<tr>
<td>Day 15</td>
<td>28%</td>
<td>37%</td>
<td>43%</td>
</tr>
<tr>
<td>Day 29</td>
<td>32%</td>
<td>40%</td>
<td>45%</td>
</tr>
<tr>
<td>Day 57</td>
<td>21%</td>
<td>38%</td>
<td>48%</td>
</tr>
<tr>
<td>Day 78</td>
<td>25%</td>
<td>40%</td>
<td>55%</td>
</tr>
<tr>
<td>Day 113</td>
<td>17%</td>
<td>38%</td>
<td>35%</td>
</tr>
<tr>
<td>Day 140</td>
<td>21%</td>
<td>32%</td>
<td>43%</td>
</tr>
</tbody>
</table>

* Relative to baseline upon enrollment at Day -21

IGA scores of zero or 1 (clear/almost clear skin) observed in 25% (3/12) of patients
Biomarker Data
Clinical Efficacy Consistent With Reduction of Blood Eosinophil Levels and Ex Vivo Pharmacodynamic Assay

<table>
<thead>
<tr>
<th>Timepoint</th>
<th>% Blood Eosinophil Reduction*</th>
<th>% Ex Vivo IL-33-Mediated IFN-g Release Reduction*</th>
<th>% Patients Achieving EASI-50*</th>
<th>% Patients Achieving EASI-75*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Day -21 (Baseline)</td>
<td>0%</td>
<td>0%</td>
<td>0%</td>
<td>0%</td>
</tr>
<tr>
<td>Day 1-4**</td>
<td>25%</td>
<td>98%</td>
<td>0%</td>
<td>0%</td>
</tr>
<tr>
<td>Day 15</td>
<td>37%</td>
<td>Not measured</td>
<td>75%</td>
<td>25%</td>
</tr>
<tr>
<td>Day 29</td>
<td>40%</td>
<td>Not measured</td>
<td>83%</td>
<td>33%</td>
</tr>
<tr>
<td>Day 57</td>
<td>39%</td>
<td>86%</td>
<td>75%</td>
<td>42%</td>
</tr>
<tr>
<td>Day 78</td>
<td>18%</td>
<td>Not measured</td>
<td>75%</td>
<td>17%</td>
</tr>
<tr>
<td>Day 113</td>
<td>Not measured</td>
<td>27%</td>
<td>67%</td>
<td>17%</td>
</tr>
<tr>
<td>Day 140</td>
<td>16%</td>
<td>29%</td>
<td>42%</td>
<td>25%</td>
</tr>
</tbody>
</table>

*B Average relative to baseline upon enrollment
**6 to 72 hours post-ANB020 dose

ANB020-mediated eosinophil reduction is aligned with genotypic data from prior human IL-33 loss-of-function studies#

Inhibition of ex vivo IL-33-mediated interferon-gamma (IFN-g) release consistent with Phase 1 pharmacodynamic results

Key Conclusions & Next Steps

• Rapid and persistent efficacy following single dose of ANB020
  - Rapid efficacy observed as early as Day 15
  - Efficacy was maximized between Day 29 and Day 57
  - All patients achieved at least EASI-50 response on or before Day 57
  - EASI responses consistent with 5-D pruritus, SCORAD, IGA and DLQI scores

• Disease severity does not limit ANB020 efficacy
  - ANB020 was similarly efficacious in patients with higher baseline EASI scores (treated with systemic immuno-modulators pre-study) versus lower baseline EASI score patients that did not require systemic therapy pre-study

• Biomarker data consistent with ANB020 clinical efficacy
  - ANB020-mediated eosinophil reduction is aligned with genotypic data from prior human IL-33 loss-of-function studies
  - Ex vivo IL-33-mediated IFN-g release consistent with Phase 1 pharmacodynamic assay results

• ANB020 was well-tolerated and no drug-related safety signals observed
  - Most frequent adverse event was dizziness in 17% of patients post-placebo versus headache in 25% of patients post-ANB020
  - A single serious adverse event of depression reported on Day 140 post-ANB020, which was consistent with the patient’s pre-trial history of depression, and was deemed not drug-related

• Initiated multi-dose placebo-controlled, double-blind, randomized 300 adult moderate-to-severe atopic dermatitis Phase 2b trial
  - Assess different dose levels and dosing frequencies of subcutaneously-administered ANB020
Acknowledgements

Oxford
Yi-Ling Chen
Danuta Gutowska-Owsiak
Melanie Westmoreland
Teena MacKenzie
Liliana Cifuentes
Antonia Lloyd-Lavery

AnaptysBio
Allison Marquette
Brian Kenney
Marco Londei