Safety and Efficacy of Lenabasum in an Open-label Extension of a Phase 2 Study in Diffuse Cutaneous Systemic Sclerosis

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Disclosures

• Grants/Research Support
  - Roche-Genetech
  - GSK
  - BMS
  - Boehringer Ingelheim
  - Cytori
  - Chemocentryx
  - Corbus
  - Formation Biologics
  - Sanofi
  - Inflarx

• Consulting
  - Roche-Genetech
  - GSK
  - CSL Behring
  - Sanofi
  - Janssen
  - Chemocentryx
  - Formation Biologics
Background

- Lenabasum is a preferential CB2 agonist that activates resolution of innate immune responses

- Lenabasum reduces inflammation and fibrosis in animal models of SSc, and TGFβ and collagen production by isolated SSc fibroblasts

Data from John Varga
Phase 2 Study JBT101-SSc-001 of lenabasum in diffuse cutaneous SSc

STUDY POPULATION
- dcSSc patients with disease duration ≤ 6 years on stable standard-of-care medications, including immunosuppressive medications

DOUBLE-BLIND PLACEBO-CONTROLLED (DBPC)
- Lenabasum treatment was associated with greater improvement than placebo in ACR CRISS scores, mRSS, patient-reported outcomes, histological inflammation and fibrosis, and gene transcripts in skin biopsies, and demonstrated acceptable safety and tolerability

OPEN-LABEL EXTENSION (OLE)
- Safety and efficacy evaluations were done after 4 weeks, then every 8 weeks, with efficacy assessment every 16 weeks after Week 60
- Data through Week 108 of OLE will be presented
Subject disposition

- Withdrawal of consent
- Physician decision
- AE moderate dizziness considered probably related

Dosed with Lenabasum
N = 27

Completed dosing
N = 24

Dosed with Placebo
N = 15

Completed dosing
N = 14

Mean 20.2 weeks (range 5-56 weeks) on standard-of-care only

Open-label Extension, N = 36
- n = 23 prior lenabasum
- n = 13 prior placebo

Completed Week 108 at time of data-cut
N = 29

7 withdrawals unrelated to lenabasum
- 4 - withdrawal of consent
- 2 - AEs
- 1 – physician decision

81% of subjects who entered OLE remain in study at ≥ 108 weeks of dosing

- Withdrawal of consent
Subject baseline demographics and disease characteristics in OLE

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Open-label N = 36</th>
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<tbody>
<tr>
<td>Female, %</td>
<td>75%</td>
</tr>
<tr>
<td>Age, mean (SD)</td>
<td>48 (11.1)</td>
</tr>
<tr>
<td>Caucasian, %</td>
<td>83%</td>
</tr>
<tr>
<td>Disease duration, months, mean (SD)</td>
<td>41 (17.4)</td>
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<tr>
<td>Concomitant immunomodulating drugs, %</td>
<td>92%</td>
</tr>
<tr>
<td>Modified Rodnan skin score (mRSS), mean (SD)</td>
<td>20 (11.0)</td>
</tr>
<tr>
<td>Health Assessment Questionnaire Disability Index (HAQ-DI), mean (SD)</td>
<td>1.2 (0.8)</td>
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<tr>
<td>Physician Global Assessment, mean (SD)</td>
<td>4.4 (2.2)</td>
</tr>
<tr>
<td>Patient Global Assessment, mean (SD)</td>
<td>4.8 (2.8)</td>
</tr>
<tr>
<td>FVC % predicted, mean (SD)</td>
<td>83 (14.4)</td>
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</tbody>
</table>
Adverse events during OLE

- 35/36 (97%) of subjects had ≥ 1 AE during ≥ 108 weeks dosing, with 294 total AEs through 25 Sept 2019
- No serious or severe AEs or study discontinuations related to lenabasum to date
- AEs leading to study discontinuation occurred in 2 (6%) subjects: tendonitis and scleroderma renal crisis
- 11 serious AEs, all unrelated to lenabasum, occurred in 7 (19%) subjects: anemia, Guillain-Barre syndrome, herpes zoster, hypoesthesia, inappropriate antidiuretic hormone secretion, thrombocytopenia, multiple fractures, scleroderma renal crisis, and thrombotic microangiopathy in 1 subject each; peripheral ischemia in 2 subjects
- 13 AEs possibly, probably, or definitely-related to lenabasum occurred in 7 (19%) subjects: apathy, conjunctivitis, constipation, disturbance in attention, fatigue, feeling abnormal, headache, infected skin ulcer, irritability, lethargy, and lymph node pain in 1 subject each; dizziness in 2 subjects
### Adverse events occurring in ≥ 10% of subjects in OLE

<table>
<thead>
<tr>
<th>Adverse Event, Preferred Term</th>
<th>Subjects with AEs, n/36 (%)</th>
<th>All¹</th>
<th>Unrelated²</th>
<th>Related³</th>
</tr>
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<tbody>
<tr>
<td>Upper respiratory tract infection</td>
<td>13 (36.1)</td>
<td>13</td>
<td></td>
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<tr>
<td>Arthralgia</td>
<td>6 (16.7)</td>
<td>6</td>
<td></td>
<td></td>
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<tr>
<td>Urinary tract infection</td>
<td>6 (16.7)</td>
<td>6</td>
<td></td>
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<tr>
<td>Skin ulcer</td>
<td>5 (13.9)</td>
<td>5</td>
<td></td>
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<tr>
<td>Anemia</td>
<td>4 (11.1)</td>
<td>4</td>
<td></td>
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<tr>
<td>Cough</td>
<td>4 (11.1)</td>
<td>4</td>
<td></td>
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<tr>
<td>Depression</td>
<td>4 (11.1)</td>
<td>4</td>
<td></td>
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<tr>
<td>Diarrhea</td>
<td>4 (11.1)</td>
<td>4</td>
<td></td>
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<tr>
<td>Dizziness</td>
<td>4 (11.1)</td>
<td>2</td>
<td>2 (5.6)</td>
<td></td>
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<tr>
<td>Headache</td>
<td>4 (11.1)</td>
<td>3</td>
<td>1 (2.8)</td>
<td></td>
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<tr>
<td>Herpes zoster</td>
<td>4 (11.1)</td>
<td>4</td>
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</table>

¹ All AEs were mild to moderate in severity except for severe anemia in 1 subject
² Includes AEs with an unrelated or unlikely related relationship
³ Includes AEs with a possible, probable or definite relationship

- No laboratory or vital sign AEs related to lenabasum to date
ACR CRISS score

Composite measure of probability of improvement from baseline, combines change in mRSS, MDGA, PtGA, HAQ-DI, and FVC % predicted, range 0.00 – 1.00

- Increases through 1\textsuperscript{st} year in OLE
- ACR CRISS score $\geq 0.95$ maintained thereafter
Skin involvement – Change from Baseline in mRSS

Baseline mRSS mean (SD) = 23.6 (10) for lenabasum arm and 26 (11) for placebo arm in DBPC and 20.4 (11) for all subjects at start of open-label dosing

- Improvement (reduction in mRSS) increases through 1st year in OLE
- Improvement of at least -9 points maintained thereafter
Skin involvement – Change from Baseline in SSPRO and 5D-Itch

Skin Symptoms (SSPRO)

Baseline SSPRO mean (SD) = 73 (27) for lenabasum arm and 83 (33) for placebo arm in DBPC and 59 (37) for all subjects at start of open-label dosing.

- Improvement from baseline in both patient assessments of skin symptoms.

5D-Itch

Baseline 5D-itch mean (SD) = 11 (4.4) for lenabasum arm and 13 (5.1) for placebo arm in DBPC and 11 (4.9) for all subjects at start of open-label dosing.
Baseline FVC % predicted mean (SD) = 86 (13) DBPC and 83 (14) for all subjects at start of open-label dosing

- Stable through 9 months in OLE
- Slight decline thereafter
Patient-reported function – Change from Baseline in HAQ-DI

Baseline HAQ-DI mean (SD) = 1.1 (0.8) for lenabasum arm and 1.5 (0.8) for placebo arm in DBPC and 1.2 (0.8) for all subjects at start of open-label dosing

- Improvement (reduction) increased during first year in OLE and persists thereafter
Patient and Physician Global Assessments of health related to SSc

Baseline PtGA mean (SD) = 4.9 (2.3) for lenabasum arm and 4.8 (2.8) for placebo arm in DBPC and 4.8 (2.8) for all subjects at start of open-label dosing

Baseline MDGA mean (SD) = 4.9 (2.3) for lenabasum arm and 4.4 (2.2) for all subjects at start of open-label dosing

- Improvement from baseline in both assessments of global health related to SSc
Summary and Conclusions

- Lenabasum has been safe and well-tolerated in study JBT101-SSc-001 through Week 108 of the OLE. No serious or severe AEs or study discontinuations related to lenabasum to date in the OLE
- ACR CRISS scores remain $\geq 0.95$ from year 1 in the OLE onward
- Improvement from baseline in multiple efficacy outcomes occurred in the OLE
- Limitations of ascribing efficacy to lenabasum during the OLE are acknowledged
- A Phase 3 study testing safety and efficacy of lenabasum in SSc is ongoing
## Investigators and study coordinators

<table>
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<tr>
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