Safety And Efficacy Of Lenabasum (JBT-101) In Diffuse Cutaneous Systemic Sclerosis Subjects Treated For One Year In An Open-Label Extension Of Trial JBT101-SSc-001


Abstract #OP0006
Disclosure of Presenter

Robert Spiera, MD, has the following disclosures:

• Research Support
  - Roche-Genentech
  - GSK
  - BMS
  - Boehringer Ingelheim
  - Cytori
  - Chemocentryx
  - Corbus
  - Prism

• Consulting
  - Roche-Genetech
  - GSK
  - Boehringer Ingelheim
  - CSL Behring
Lenabasum

• Selective CB2 agonist that activates resolution of innate immune responses

• Reduces inflammation and fibrosis in animal models of SSc and TGFβ and collagen production by SSc fibroblasts

• Associated with greater improvement than placebo in CRISS scores, mRSS, patient-reported outcomes, histological inflammation and fibrosis in skin biopsies, and gene transcript pathways associated with inflammation and fibrosis in skin biopsies in the 16-week double-blinded, randomized, placebo-controlled (DBPC) phase of study JBT101-SSc-001

• Provided in an open-label extension (OLE) to subjects who completed DBPC phase. Subjects returned for safety and efficacy evaluations after 4 weeks, then every 8 weeks.
Subject Disposition in Study JBT101-SSc-001

3 withdrawals unrelated to lenabasum
- Withdrawal of consent
- Physician decision
- AE moderate dizziness

5 withdrawals unrelated to lenabasum
- 3 withdrawal of consent
- AE disease flare with inflamed tendons
- AE steroid-induced scleroderma renal crisis

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 52 at time of data-cut
N = 27

Completers
- Week 12 N = 34
- Week 28 N = 32
- Week 52 N = 27

1 withdrawal
- Withdrawal of consent
## Subject Baseline Demographics and Disease Characteristics

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Open-label N = 36</th>
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<tbody>
<tr>
<td>Female, %</td>
<td>75.0%</td>
</tr>
<tr>
<td>Age, mean (SD)</td>
<td>48.2 (11.1)</td>
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<tr>
<td>Caucasian, %</td>
<td>83.3%</td>
</tr>
<tr>
<td>Disease duration, months, mean (SD)</td>
<td>40.8 (17.4)</td>
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<tr>
<td>Concomitant immunomodulating drugs, %</td>
<td>94.4%</td>
</tr>
<tr>
<td>Modified Rodnan skin score (mRSS), mean (SD)</td>
<td>20.4 (11.0)</td>
</tr>
<tr>
<td>Health Assessment Questionnaire Disability Index (HAQ-DI), mean (SD)</td>
<td>1.2 (0.8)</td>
</tr>
<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>82.6 (14.4)</td>
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</tbody>
</table>
Adverse Events

33/36 (91.7%) of subjects had ≥ 1 AE during the OLE

- **Serious AEs**, all unrelated to lenabasum, occurred in 3 (8.3%) subjects: high-dose steroid-induced scleroderma renal crisis, thumb fracture, and digital ulcer.

- **AEs leading to study discontinuation**, both unrelated to lenabasum, occurred in 2 (5.6%) subjects: scleroderma renal crisis and disease flare with moderate tendonitis.

- 7/36 (13.9%) subjects had AEs **related to lenabasum** during the 52-weeks dosing in the OLE, whereas 7/27 (25.9%) subjects had AEs related to lenabasum during 12-weeks dosing in Part A.
<table>
<thead>
<tr>
<th>Adverse Event, Preferred Term</th>
<th>Subjects with AEs, n/36 (%)</th>
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<tbody>
<tr>
<td></td>
<td>All</td>
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<tr>
<td>Dizziness</td>
<td>3 (8.3%)</td>
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<tr>
<td>Fatigue</td>
<td>3 (8.3%)</td>
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<tr>
<td>Skin ulcer</td>
<td>5 (13.9%)</td>
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<tr>
<td>Upper respiratory tract infection</td>
<td>8 (22.2%)</td>
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<tr>
<td>Arthralgia</td>
<td>5 (13.9%)</td>
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<tr>
<td>Urinary tract infection</td>
<td>5 (13.9%)</td>
</tr>
<tr>
<td>Diarrhoea</td>
<td>4 (11.1%)</td>
</tr>
<tr>
<td>Musculoskeletal pain</td>
<td>3 (8.3%)</td>
</tr>
<tr>
<td>Dysphagia</td>
<td>3 (8.3%)</td>
</tr>
<tr>
<td>Nausea</td>
<td>3 (8.3%)</td>
</tr>
<tr>
<td>Pyrexia</td>
<td>3 (8.3%)</td>
</tr>
<tr>
<td>Nasopharyngitis</td>
<td>3 (8.3%)</td>
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</tbody>
</table>
CRISS Score

- **Part A**: Stable standard-of-care drugs, including immunosuppressive drugs
- **OLE Lenabasum**

- **DBPC**: Improvement with lenabasum
- **Standard-of-care only**: Worsening
- **OLE**: Additional improvement

Blue circles = lenabasum. Orange squares = placebo. Black open circles = standard-of-care only
Blue circles = lenabasum. Orange squares = placebo. Black open circles = standard-of-care only
Baseline mRSS mean mRSS (SD) = 23.6 (10.4) for lenabasum arm and 26.2 (11.1) for placebo arm in Part A and 20.4 (11.0) for all subjects at start of open-label dosing.

DBPC: Improvement with lenabasum
Standard-of-care only: Stability
OLE: Additional improvement
50% of subjects achieved CRISS score \( \geq 95\% \) after 1 year in OLE

77% of subjects had \( \geq 5 \) point reduction in mRSS
Health Assessment Questionnaire-Disability Index and Forced Vital Capacity, % Predicted

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

- **DBPC:** Improvement with lenabasum
- **Standard-of-care only:** Worsening
- **OLE:** Recovery of improvement

Baseline FVC % predicted mean (SD) = 86.1 (13.4) for lenabasum arm and 81.1 (8.9) for placebo arm in Part A and 82.6 (14.4) for all subjects at start of open-label dosing.

- **DBPC:** Stability with lenabasum
- **Standard-of-care only:** Worsening
- **OLE:** Stability, then slight worsening

Blue circles = lenabasum. Orange squares = placebo. Black open circles = standard-of-care only
### Patient-Reported Skin Symptoms

**SSc PRO Skin Symptoms**

Baseline SScPRO mean (SD) = 73.0 (23.7) for lenabasum arm and 82.7 (32.6) for placebo arm in Part A and 59.1 (50.5) for all subjects at start of open-label dosing.

- **DBPC:** Improvement with lenabasum
- **Standard-of-care only:** Stability
- **OLE:** Additional improvement with lenabasum

**5-D Itch Score**

Baseline 5-D itch score mean (SD) = 10.7 (4.4) for lenabasum arm and 12.9 (5.3) for placebo arm in Part A and 10.7 (4.9) for all subjects at start of open-label dosing.

- **DBPC:** Improvement with lenabasum
- **Standard-of-care only:** Worsening
- **OLE:** Additional improvement with lenabasum
Summary and Conclusions

• In the open-label extension of Phase 2 study JBT101-SSc-001,
  ✓ Lenabasum continues to have a favorable safety profile and was well-tolerated. AEs related to lenabasum occur with lower frequency during chronic OLE treatment than during initial DBPC phase of the study
  ✓ Improvement in ACR CRISS scores, mRSS, and HAQ-DI were observed
  ✓ Improvement in patient-reported skin symptoms and functioning were observed

• Limitations of ascribing efficacy to lenabasum during open-label dosing are acknowledged

• Data support further testing of lenabasum in Phase 3 study
Thank You

• The participants who took part in our Phase 2 study
• The investigators and site study teams for their commitment during the study
## Investigators and Study Coordinators

<table>
<thead>
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