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

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Abstract #OP0006

Disclosure of Presenter

Robert Spiera, MD, has the following disclosures:

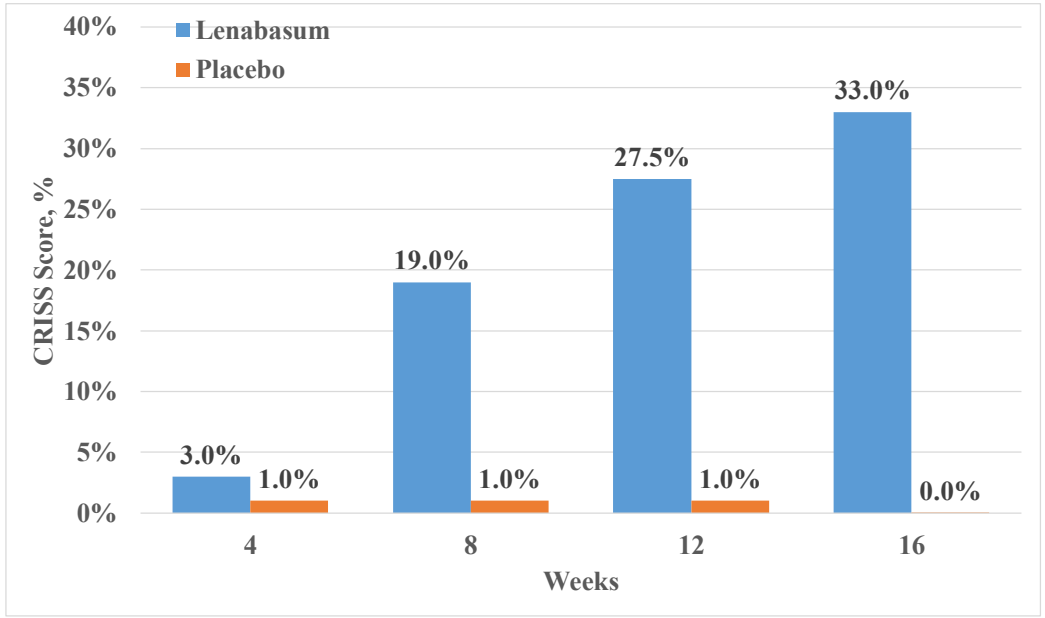
- Research Support
  - Roche-Genentech
  - GSK
  - BMS
  - Boehringer Ingelheim
  - Cytori
  - Chemocentryx
  - Corbus
  - Prism
- Consulting
  - Roche-Genetech
  - GSK
  - Boehringer Ingelheim
  - CSL Behring

Lenabasum

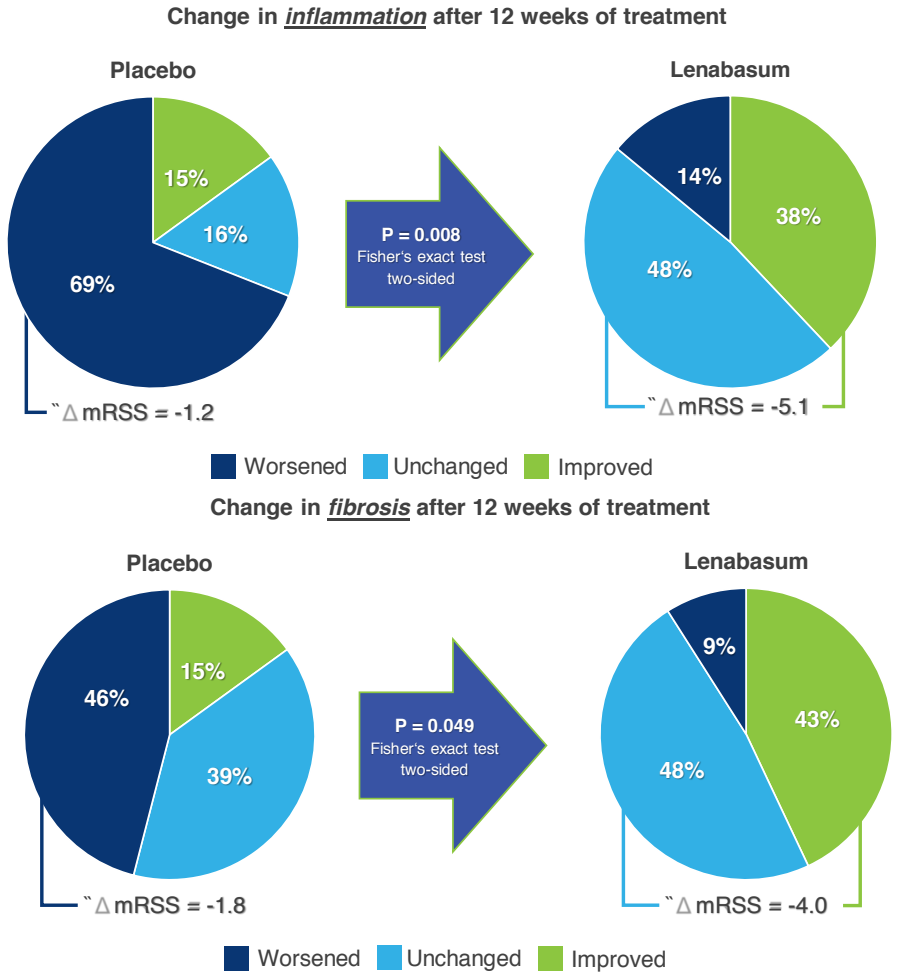
- Selective CB2 agonist that activates resolution of innate immune responses
- Reduces inflammation and fibrosis in animal models of SSc and TGFβ and collagen production by SSc fibroblasts
- Associated with greater improvement than placebo in CRISS scores, mRSS, patient-reported outcomes, histological 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.

ACR CRISS Score and Skin Biopsy Histology Results from Part A

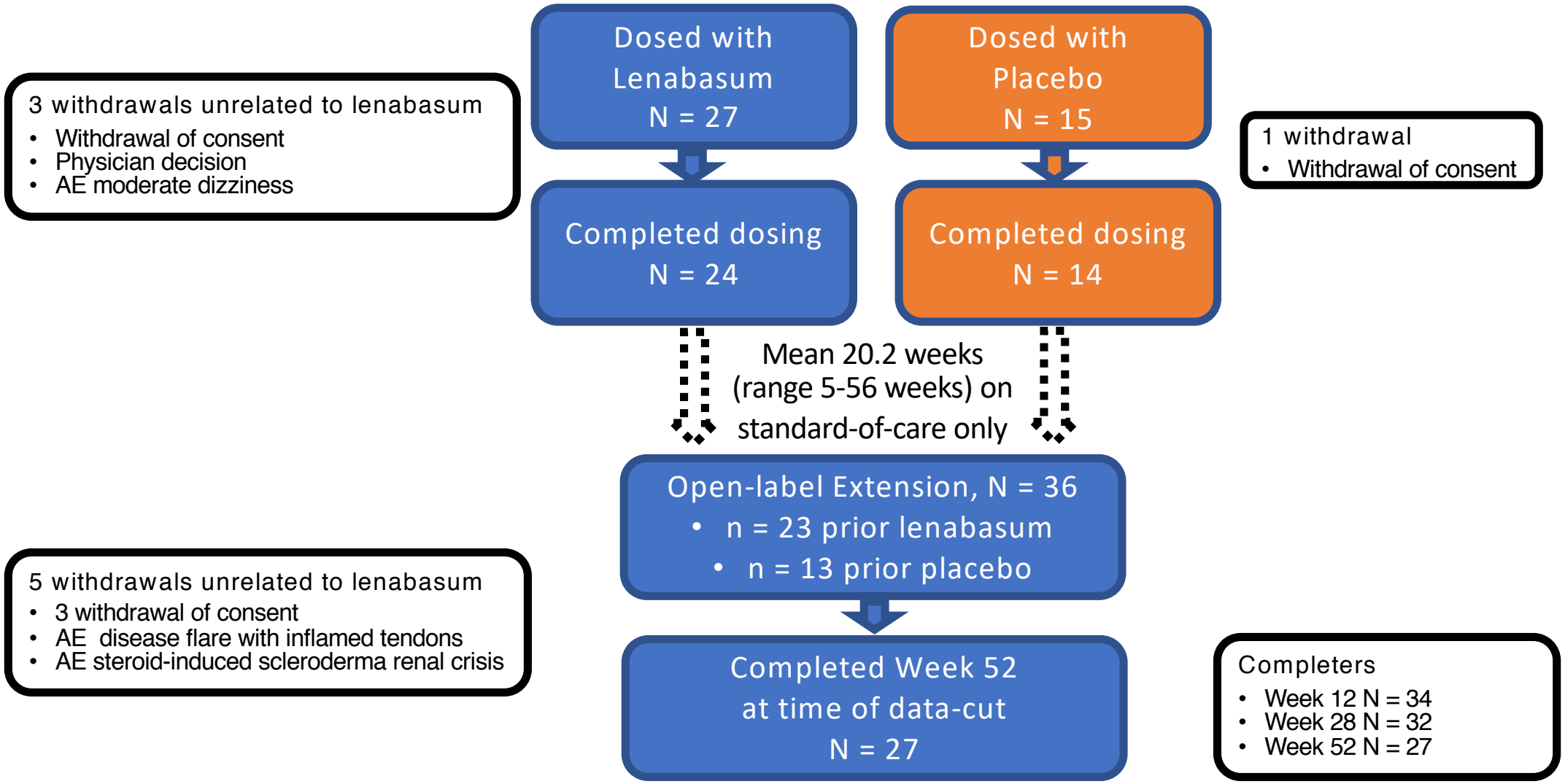
ACR CRISS Score



Skin Biopsy Histology



Subject Disposition in Study JBT101-SSc-001



Subject Baseline Demographics and Disease Characteristics

Characteristic	Open-label N = 36
Female, %	75.0%
Age, mean (SD)	48.2 (11.1)
Caucasian, %	83.3%
Disease duration, months, mean (SD)	40.8 (17.4)
Concomitant immunomodulating drugs, %	94.4%
Modified Rodnan skin score (mRSS), mean (SD)	20.4 (11.0)
Health Assessment Questionnaire Disability Index (HAQ-DI), mean (SD)	1.2 (0.8)
Physician Global Assessment, mean (SD)	4.4 (2.2)
Patient Global Assessment, mean (SD)	4.8 (2.8)
FVC % predicted, mean (SD)	82.6 (14.4)

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.

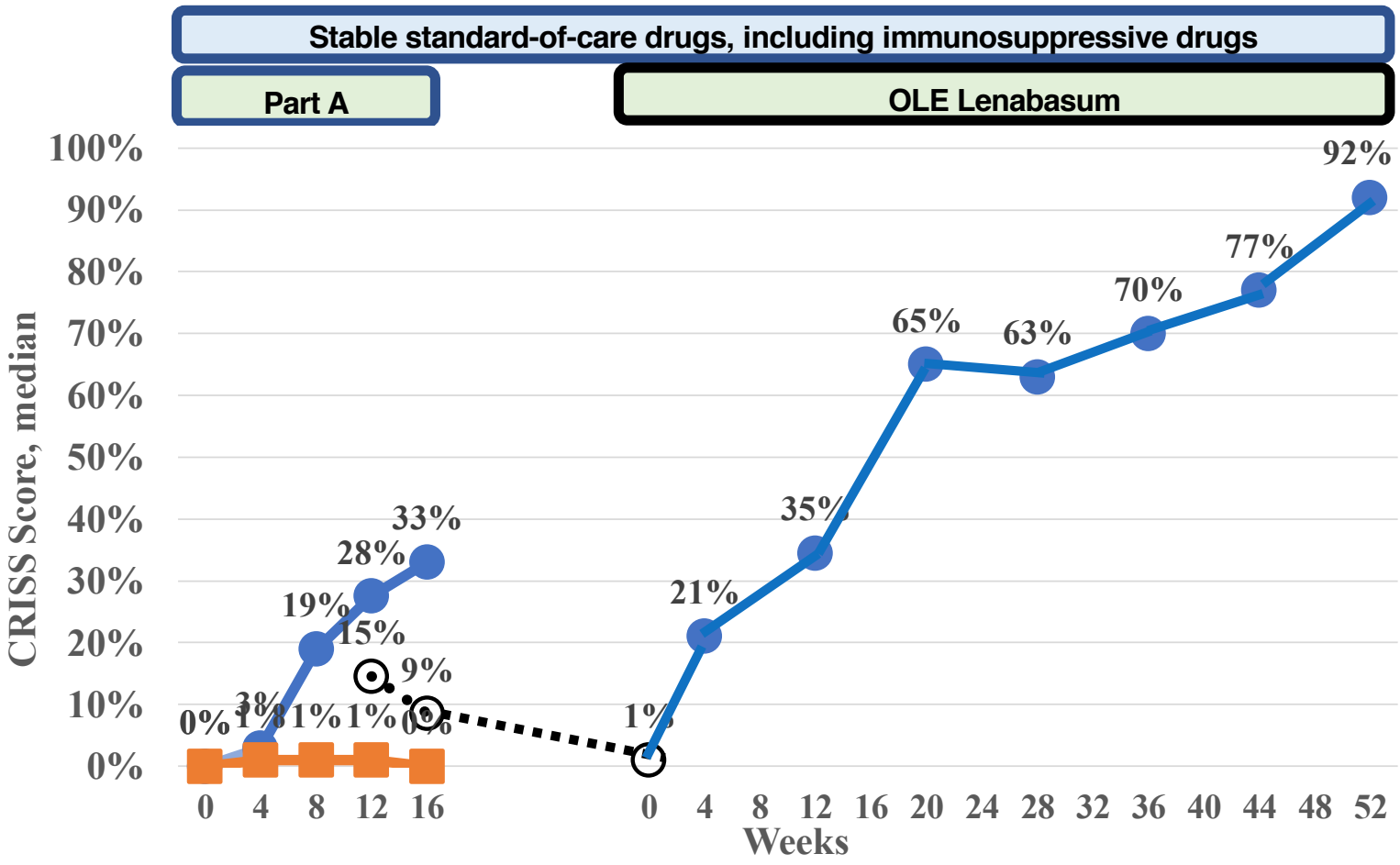
- **AEs leading to study discontinuation**, both unrelated to lenabasum, occurred in 2 (5.6%) subjects: scleroderma renal crisis and disease flare with moderate tendonitis

- 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.

Adverse Events Occurring in ≥ 3 Subjects by Relatedness

Adverse Event, Preferred Term	Subjects with AEs, n/36 (%)		
	All	Unrelated	Related
Dizziness	3 (8.3%)	1 (2.8%)	2 (5.6%)
Fatigue	3 (8.3%)	2 (5.6%)	1 (2.8%)
Skin ulcer	5 (13.9%)	4 (11.1%)	1 (2.8%)
Upper respiratory tract infection	8 (22.2%)	8 (22.2%)	
Arthralgia	5 (13.9%)	5 (13.9%)	
Urinary tract infection	5 (13.9%)	5 (13.9%)	
Diarrhoea	4 (11.1%)	4 (11.1%)	
Musculoskeletal pain	3 (8.3%)	3 (8.3%)	
Dysphagia	3 (8.3%)	3 (8.3%)	
Nausea	3 (8.3%)	3 (8.3%)	
Pyrexia	3 (8.3%)	3 (8.3%)	
Nasopharyngitis	3 (8.3%)	3 (8.3%)	

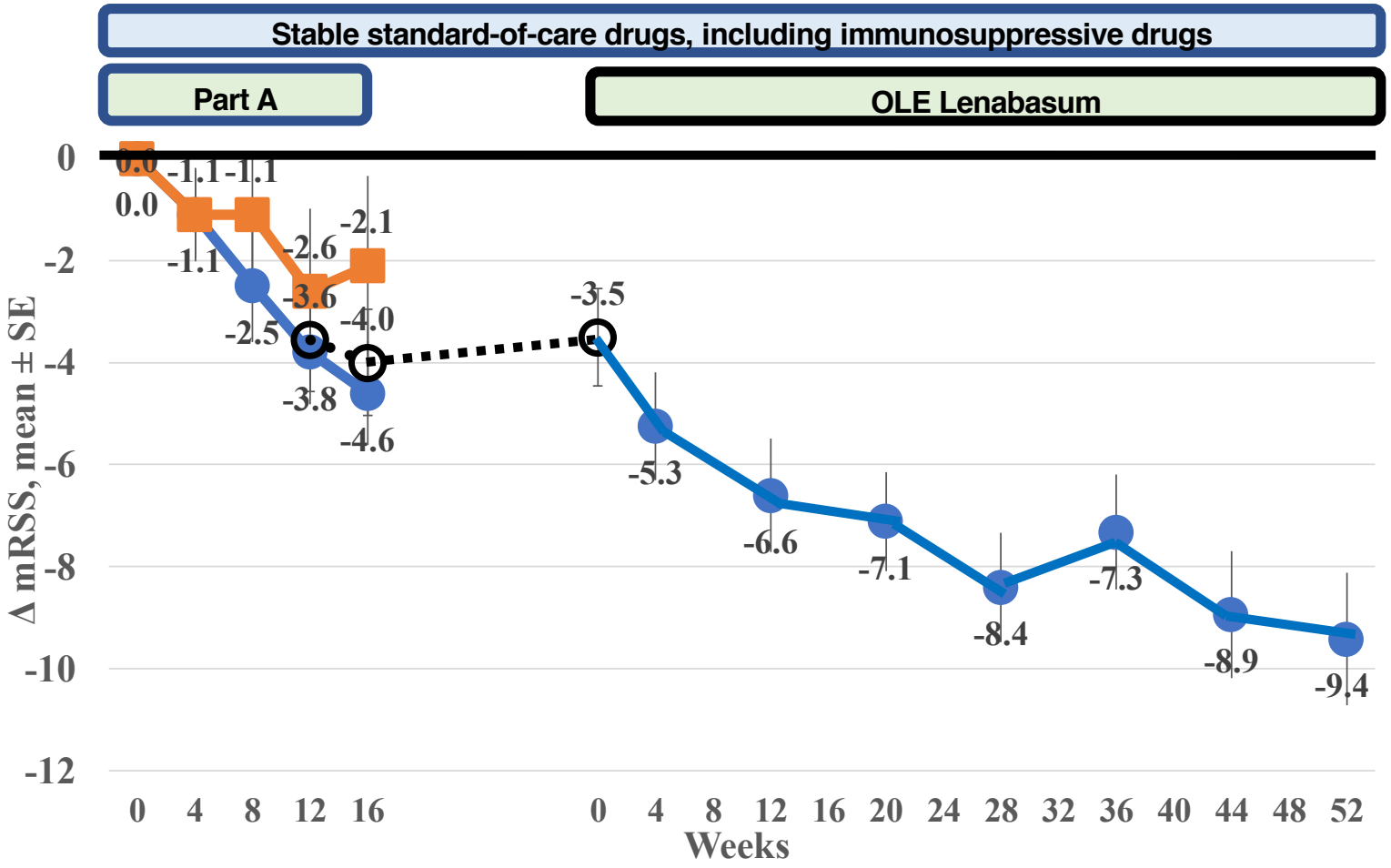
CRISS Score



- 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

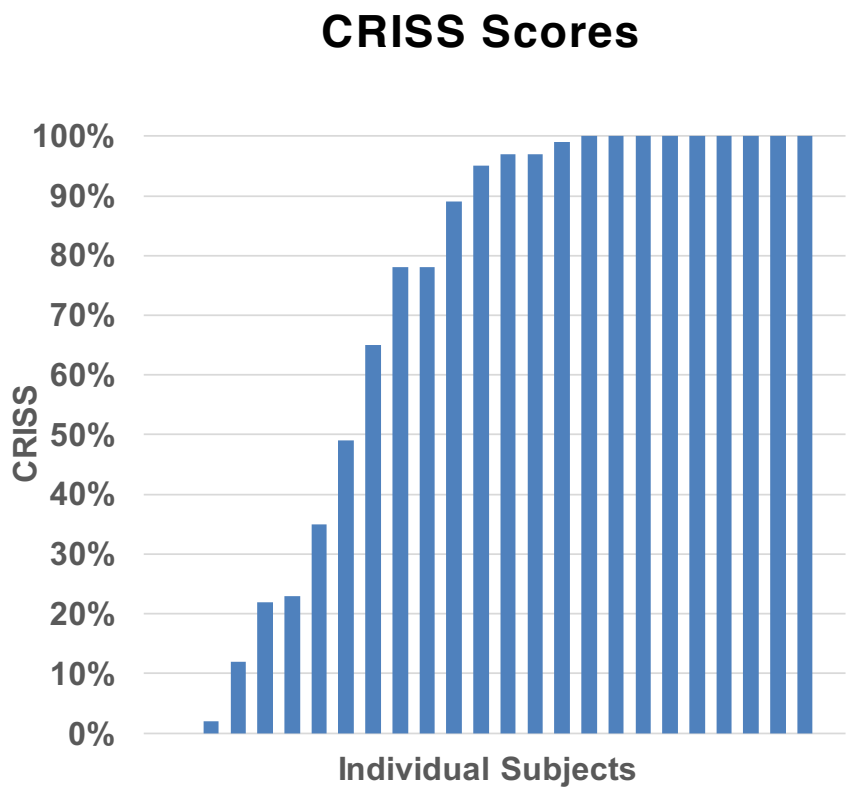
Modified Rodnan Skin Score



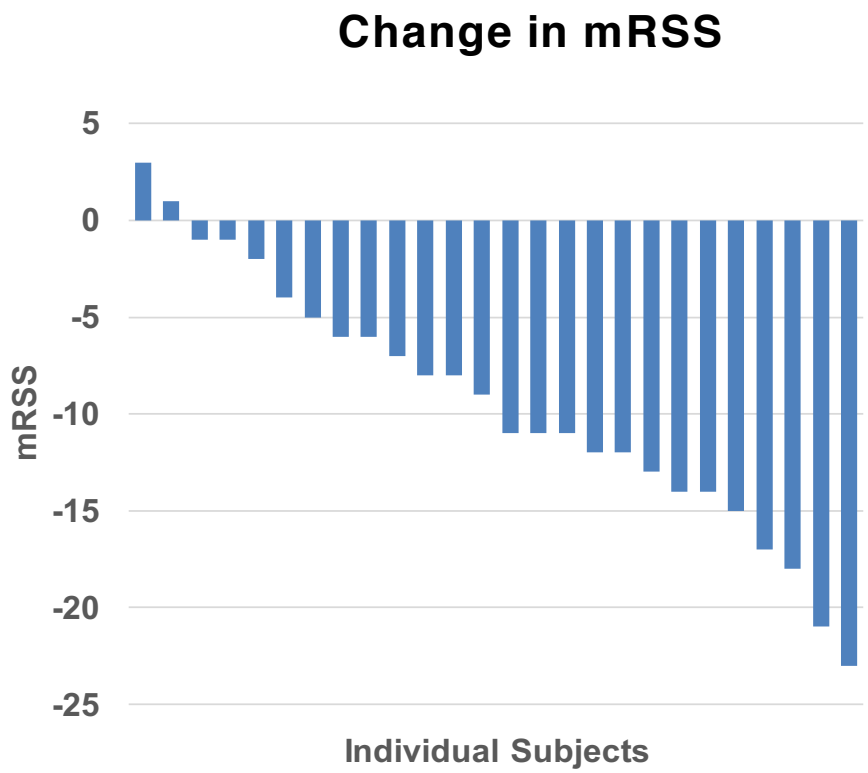
- DBPC: Improvement with lenabasum
- Standard-of-care only: Stability
- OLE: Additional improvement

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.

Distribution of CRISS Scores and Change in mRSS at Week 52

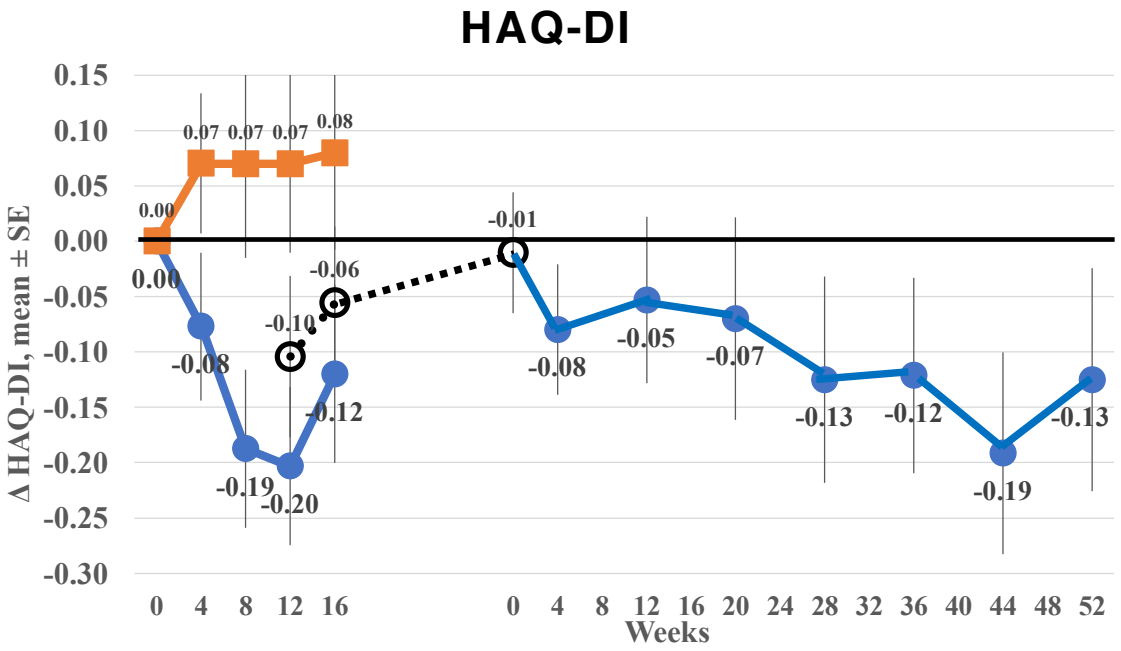


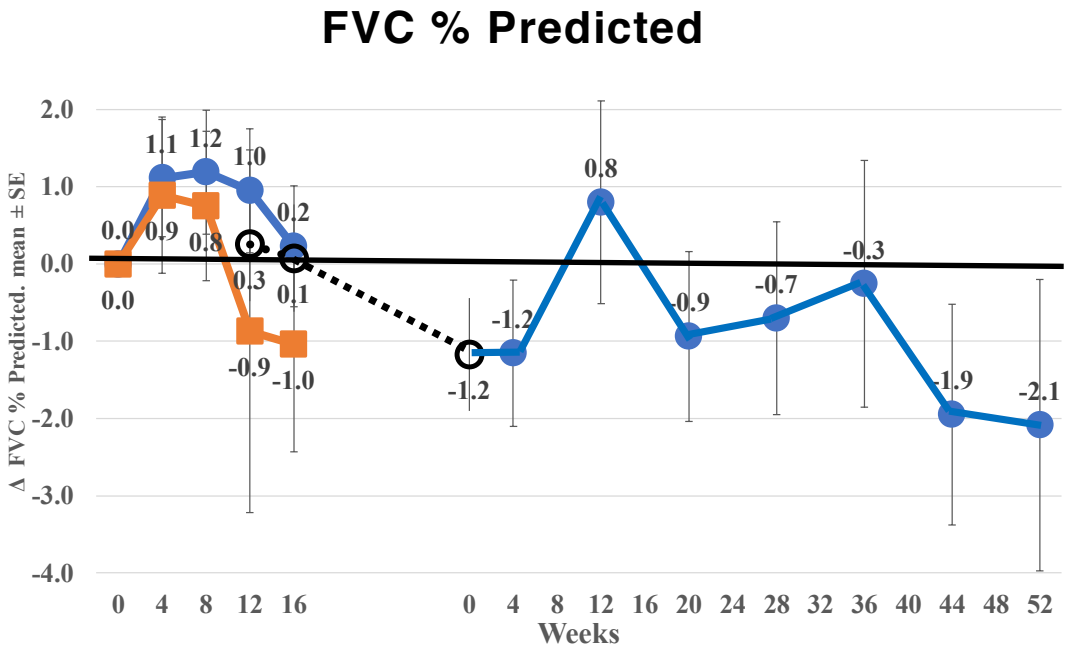
50% of subjects achieved CRISS score ≥ 95% after 1 year in OLE



77% of subjects had ≥ 5 point reduction in mRSS

Health Assessment Questionnaire-Disability Index and Forced Vital Capacity, % Predicted





Blue circles = lenabasum. Orange squares = placebo. Black open circles = standard-of-care only

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.

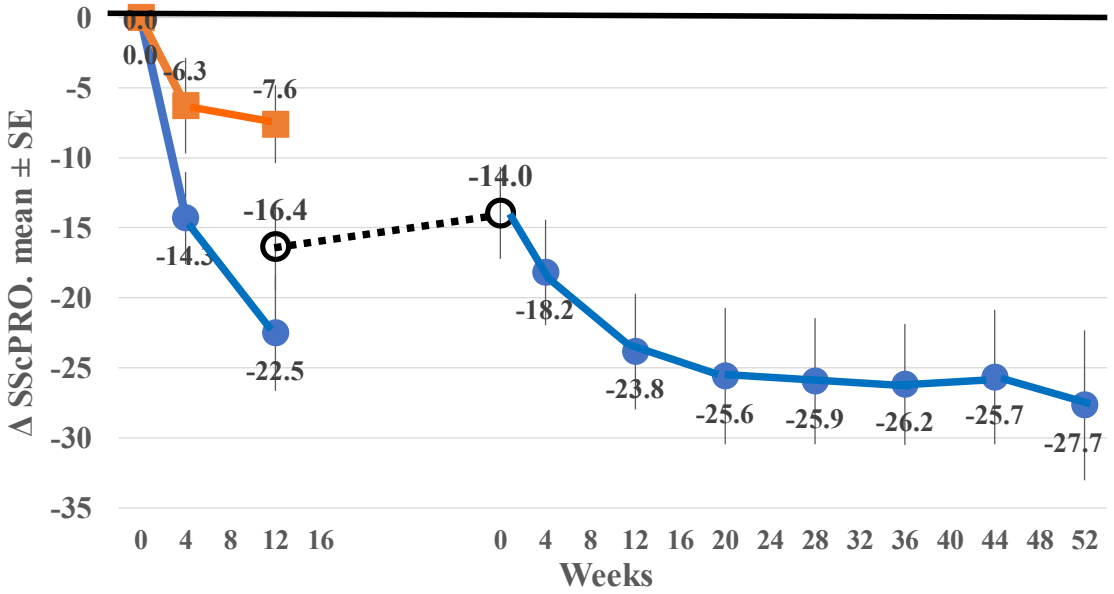
- DBPC: Improvement with lenabasum
- Standard-of-care only: Worsening
- OLE: Recovery of improvement

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.

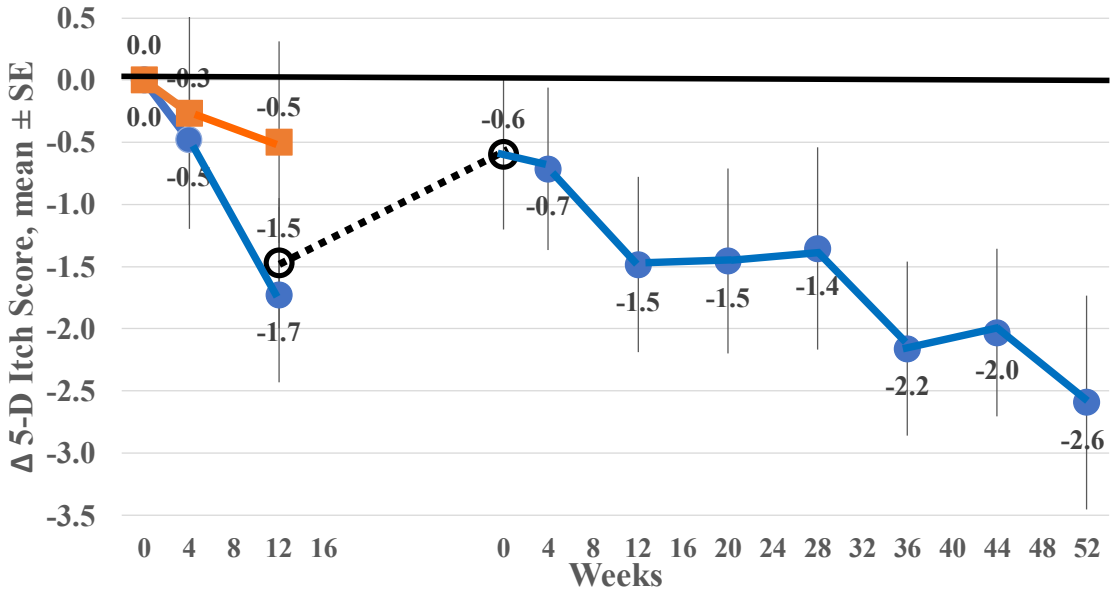
- DBPC: Stability with lenabasum
- Standard-of-care only: Worsening
- OLE: Stability, then slight worsening

Patient-Reported Skin Symptoms

SSc PRO Skin Symptoms



5-D Itch Score



Blue circles = lenabasum. Orange squares = placebo. Black open circles = standard-of-care only

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

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

Principal Investigator	Study Coordinators	Institution
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Vivien Hsu	Deborah McCloskey	Robert Wood Johnson Medical School
Laura Hummers	Gwen Leatherman	Johns Hopkins School of Medicine
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Robert Simms	Jessica Ziemek Christopher Zammitti	Boston University