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

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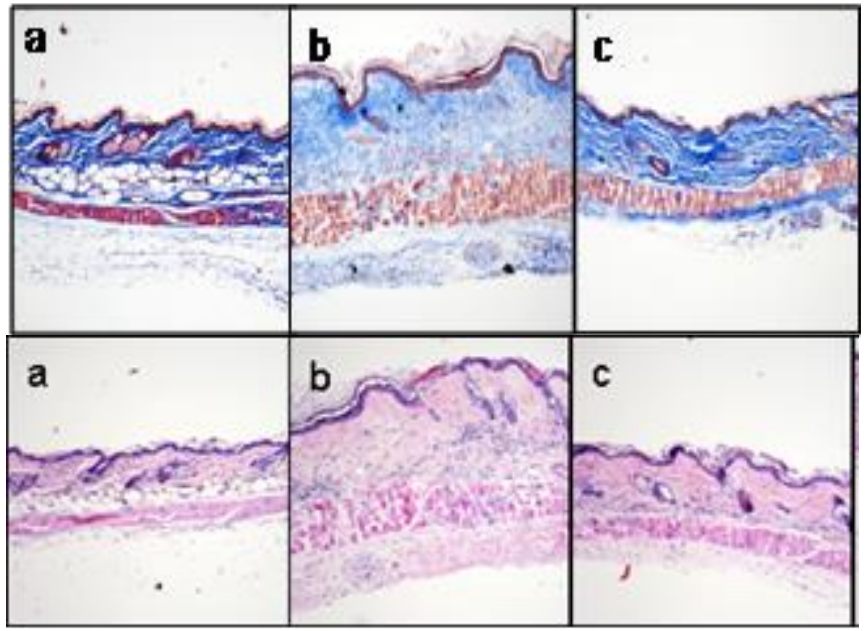
Abstract #865

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

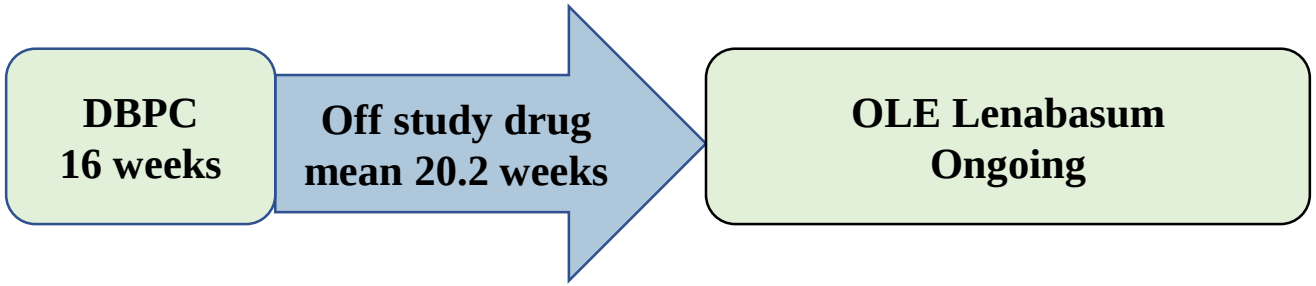


Bleomycin	–	+	+
Lenabasum	–	–	0.2 mg/kg

- Bleomycin intradermal injection in mice every other day from Day 1 to Day 21
- Lenabasum administered once daily by gavage from Day 1 to Day 21

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

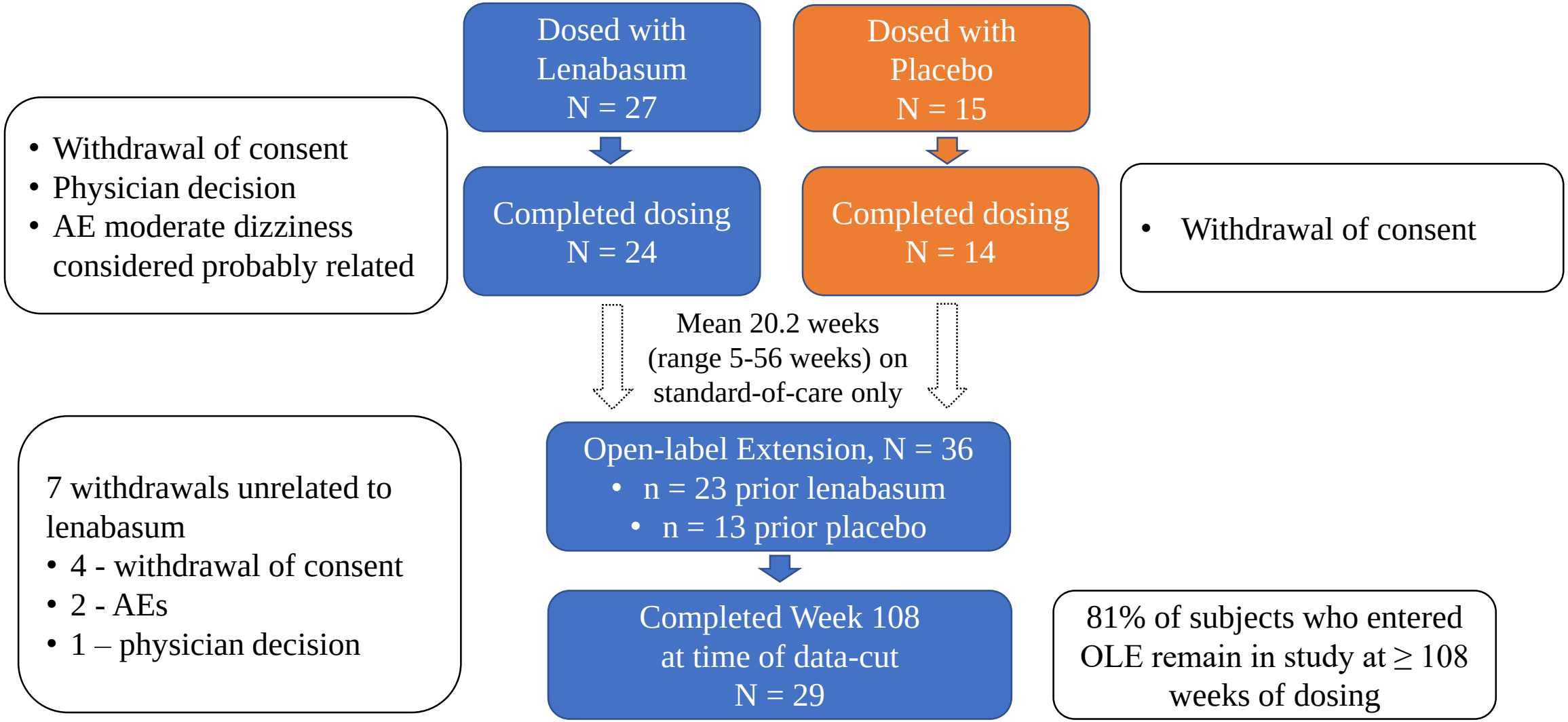
DOUBLE-BLIND PLACEBO-CONTROLLED (DBPC)

- 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



Subject baseline demographics and disease characteristics in OLE

Characteristic	Open-label N = 36
Female, %	75%
Age, mean (SD)	48 (11.1)
Caucasian, %	83%
Disease duration, months, mean (SD)	41 (17.4)
Concomitant immunomodulating drugs, %	92%
Modified Rodnan skin score (mRSS), mean (SD)	20 (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)	83 (14.4)

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

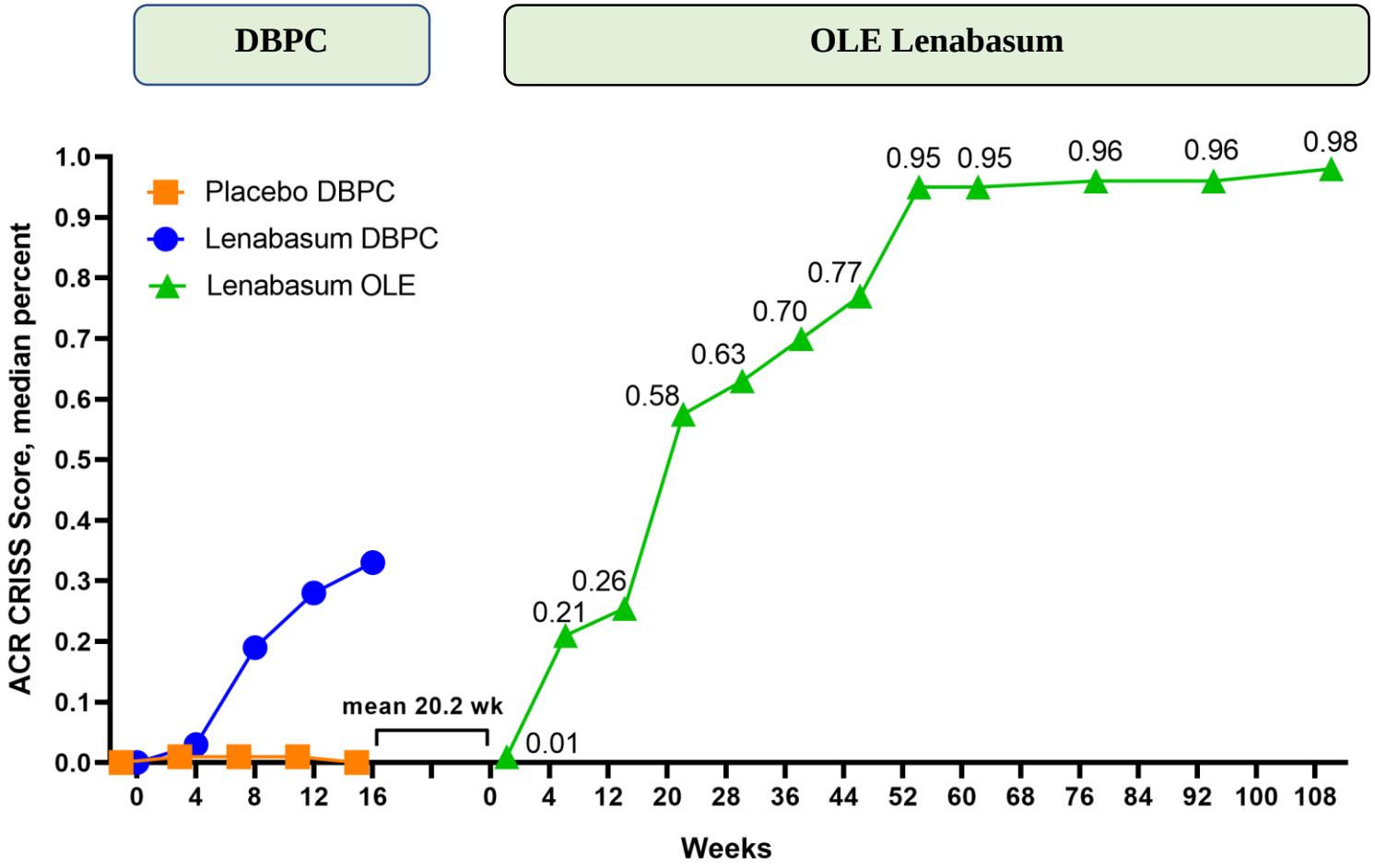
Adverse Event, Preferred Term	Subjects with AEs, n/36 (%)		
	All[1]	Unrelated[2]	Related[3]
Upper respiratory tract infection	13 (36.1)	13 (36.1)	-
Arthralgia	6 (16.7)	6 (16.7)	-
Urinary tract infection	6 (16.7)	6 (16.7)	-
Skin ulcer	5 (13.9)	5 (13.9)	-
Anemia	4 (11.1)	4 (11.1)	-
Cough	4 (11.1)	4 (11.1)	-
Depression	4 (11.1)	4 (11.1)	-
Diarrhea	4 (11.1)	4 (11.1)	-
Dizziness	4 (11.1)	2 (5.6)	2 (5.6)
Headache	4 (11.1)	3 (8.3)	1 (2.8)
Herpes zoster	4 (11.1)	4 (11.1)	-

[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

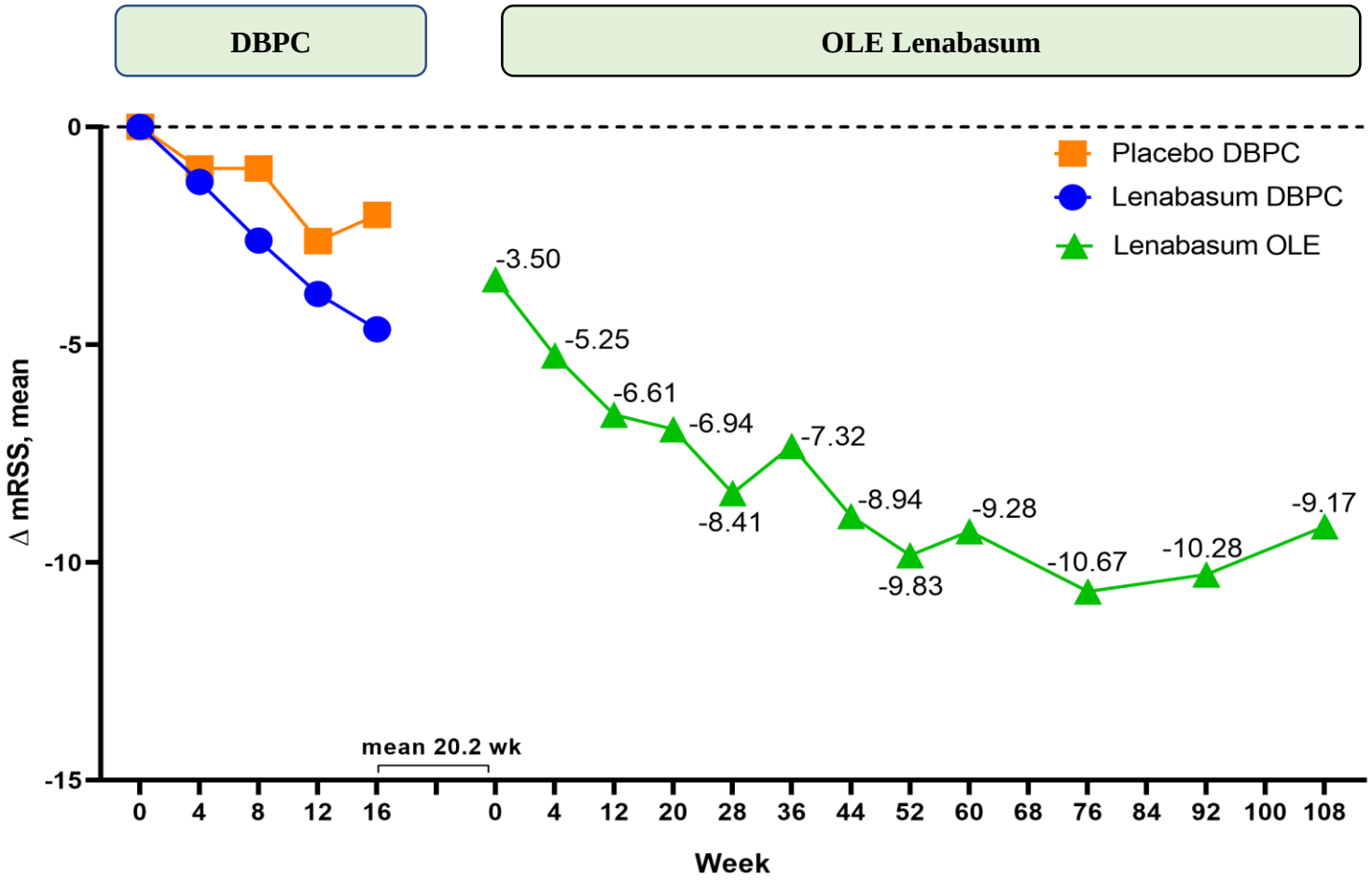
ACR CRISS score

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 1st year in OLE
- ACR CRISS score ≥ 0.95 maintained thereafter

Skin involvement – Change from Baseline in mRSS

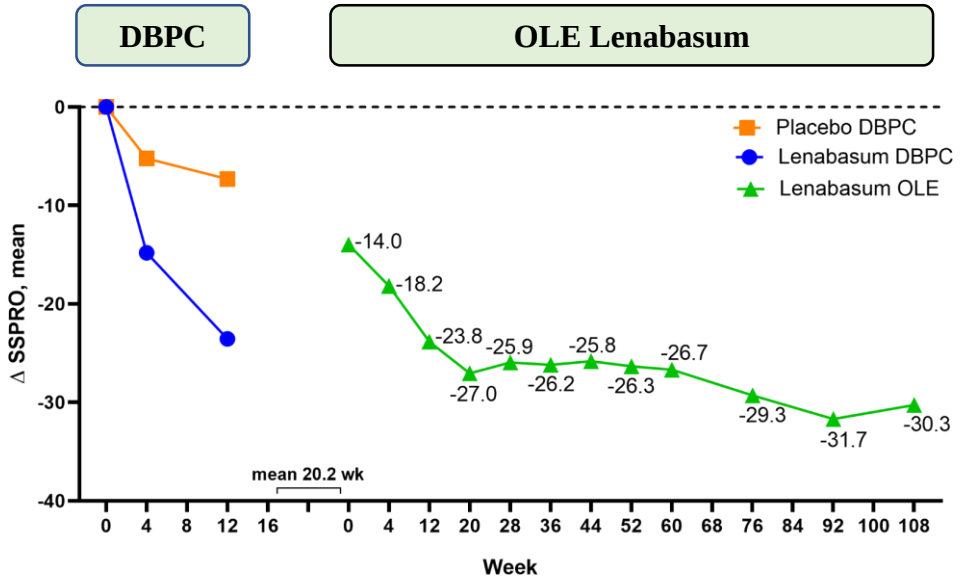


Baseline mRSS mean (SD) = 23.6 (10) for lenabasum arm and 26 (11) for placebo arm in DBPC and 20.4 (11) for all subjects at start of open-label dosing

- Improvement (reduction in mRSS) increases through 1st year in OLE
- Improvement of at least -9 points maintained thereafter

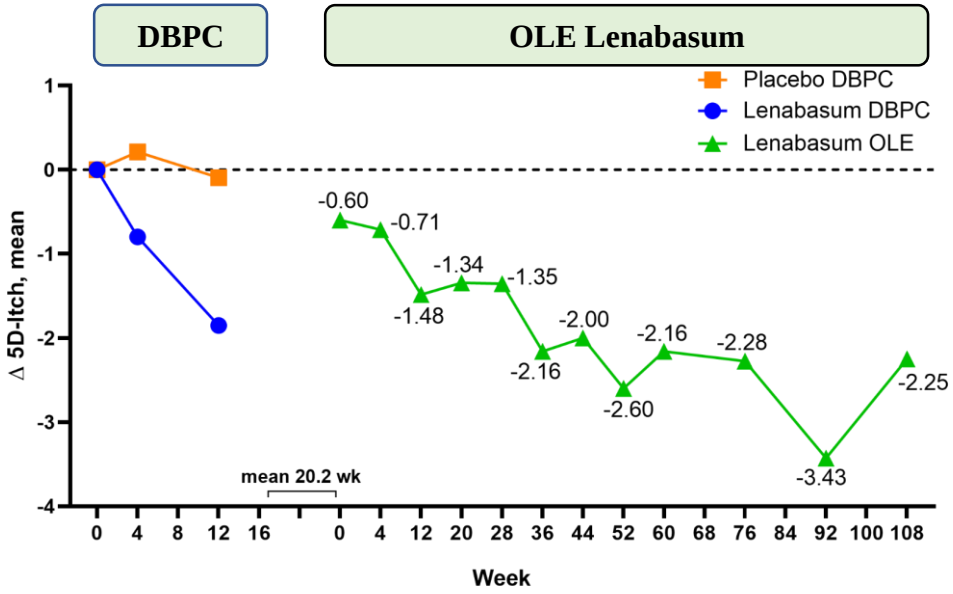
Skin involvement – Change from Baseline in SSPRO and 5D-Itch

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

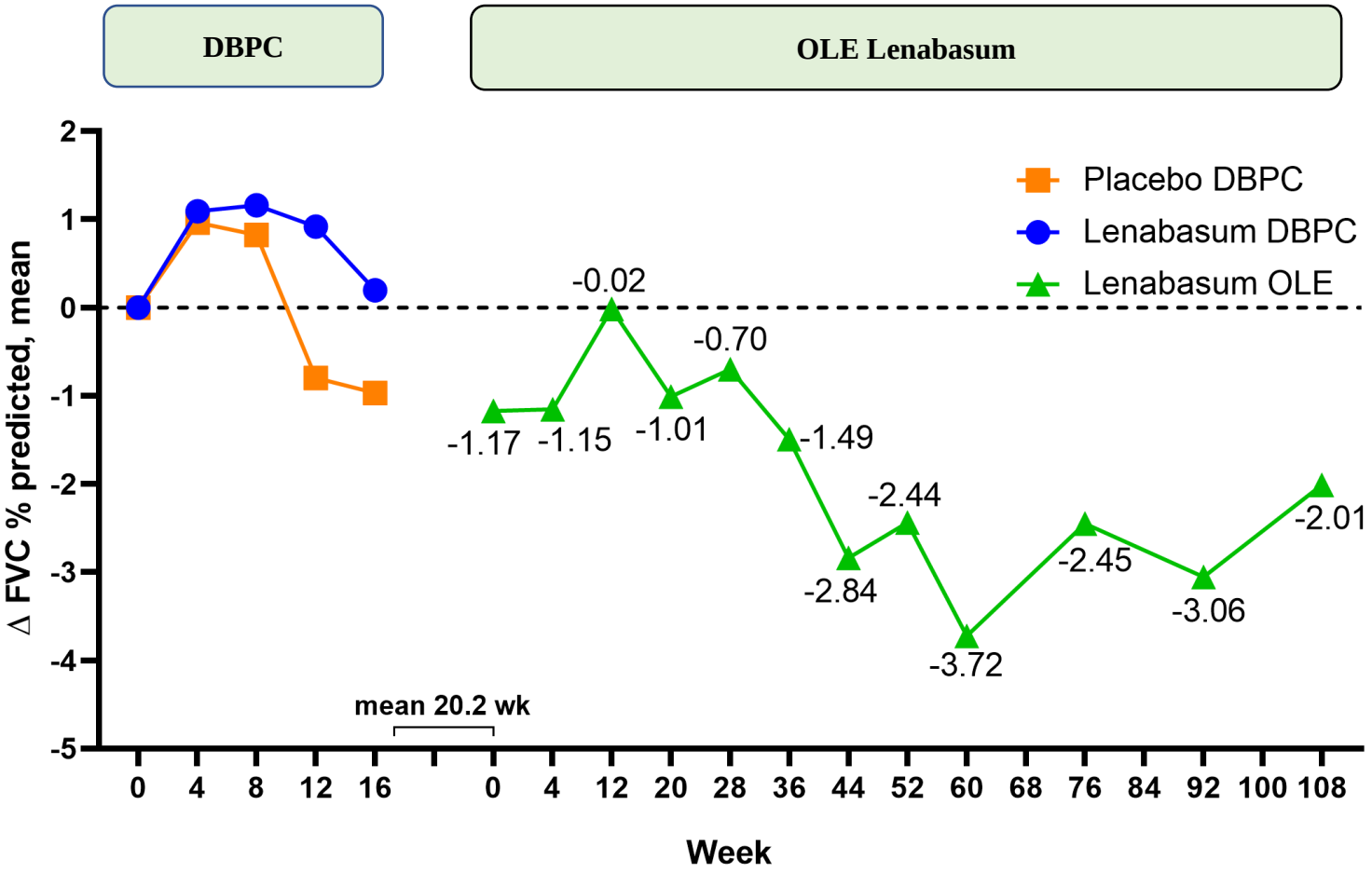
5D-Itch



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

- Improvement from baseline in both patient assessments of skin symptoms

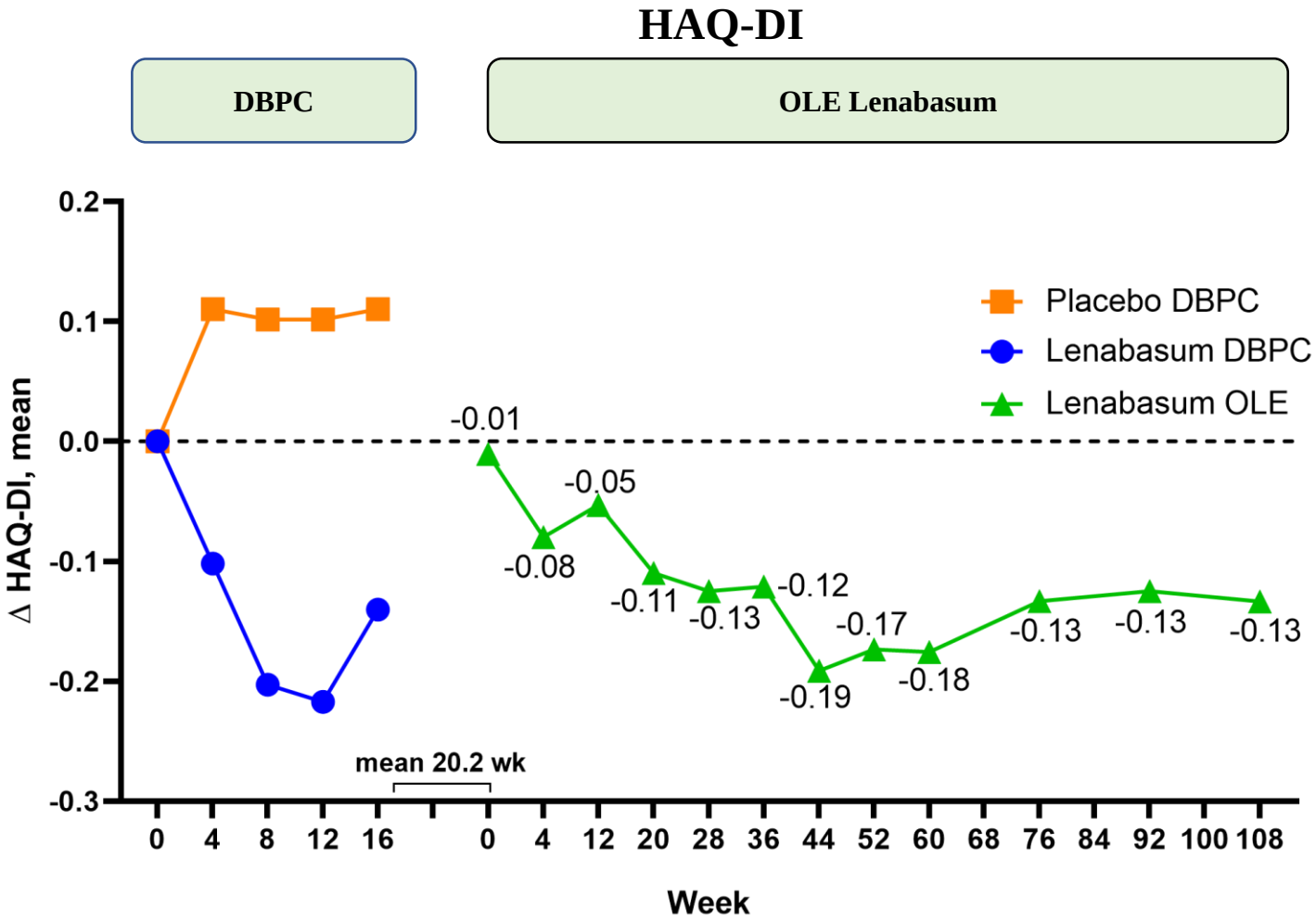
FVC percent predicted



- Stable through 9 months in OLE
- Slight decline thereafter

Baseline FVC % predicted mean (SD) = 86 (13) DBPC and 83 (14) for all subjects at start of open-label dosing

Patient-reported function – Change from Baseline in HAQ-DI

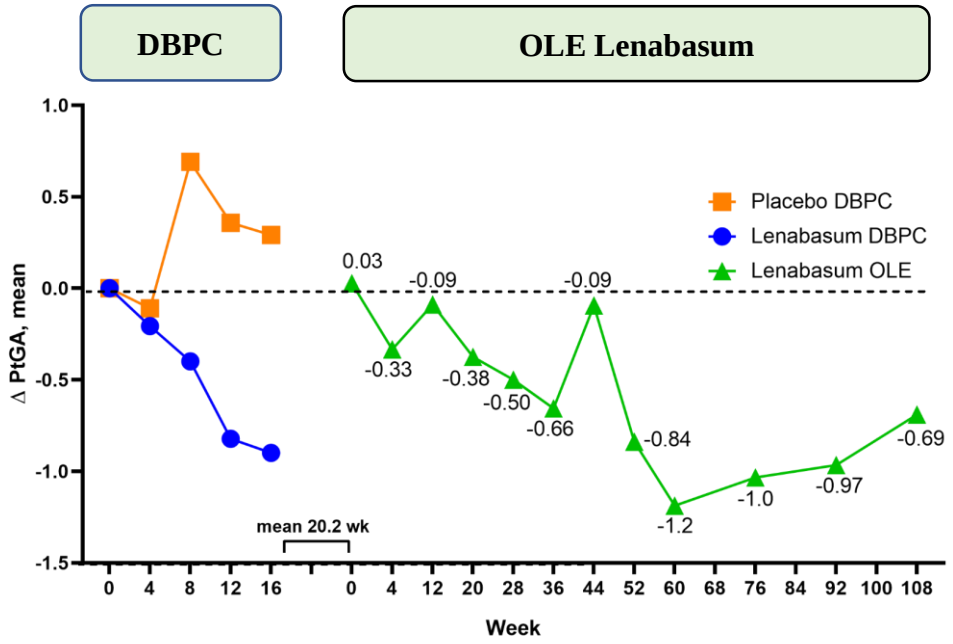


- Improvement (reduction) increased during first year in OLE and persists thereafter

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

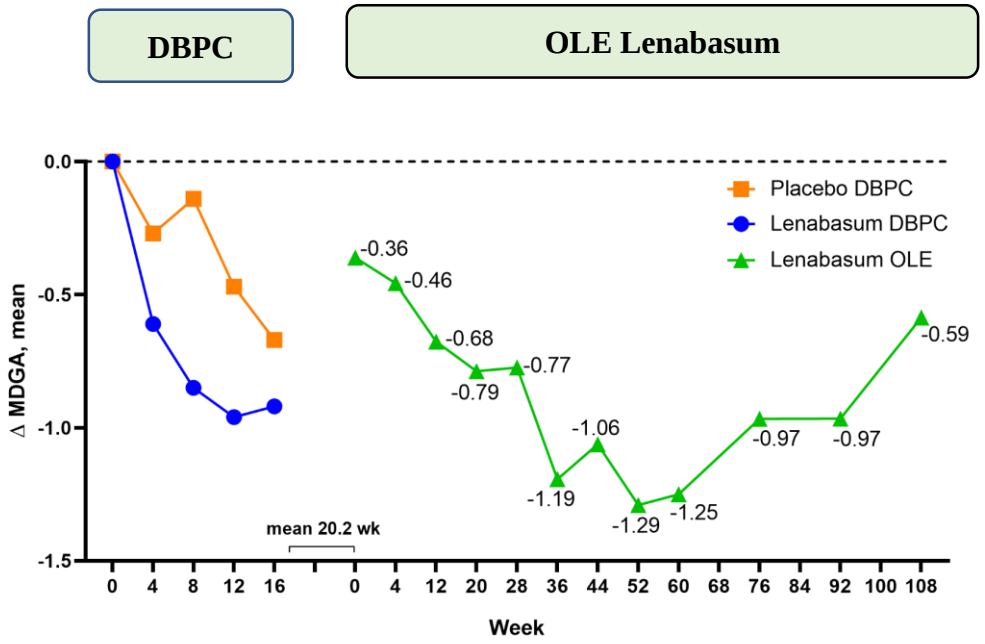
Patient and Physician Global Assessments of health related to SSc

PtGA



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

MDGA



Baseline MDGA mean (SD) = 4.9 (2.3) for lenabasum arm and 4.8 (2.8) for placebo arm in DBPC 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 ≥ 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

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