Safety and Efficacy of Lenabasum in an Open-Label Extension of a Phase 2 Study of Lenabasum in Refractory Skin-Predominant Dermatomyositis (DM) Subjects

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Abstract #OP0241

Disclosures of Victoria Werth of relevant relationships with industry

Grants

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Other

Developed and validated an outcome measure for cutaneous dermatomyositis (CDASI)

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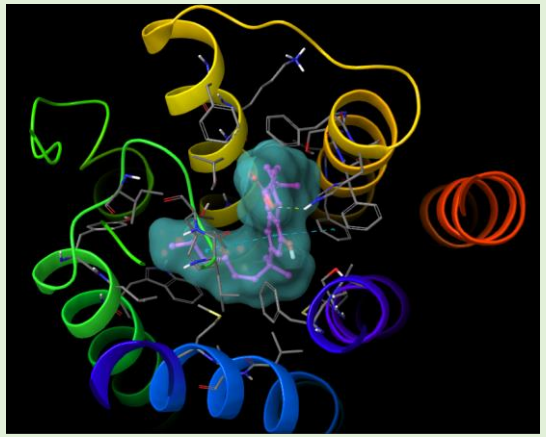
Background

Lenabasum

- Preferential CB2 agonist

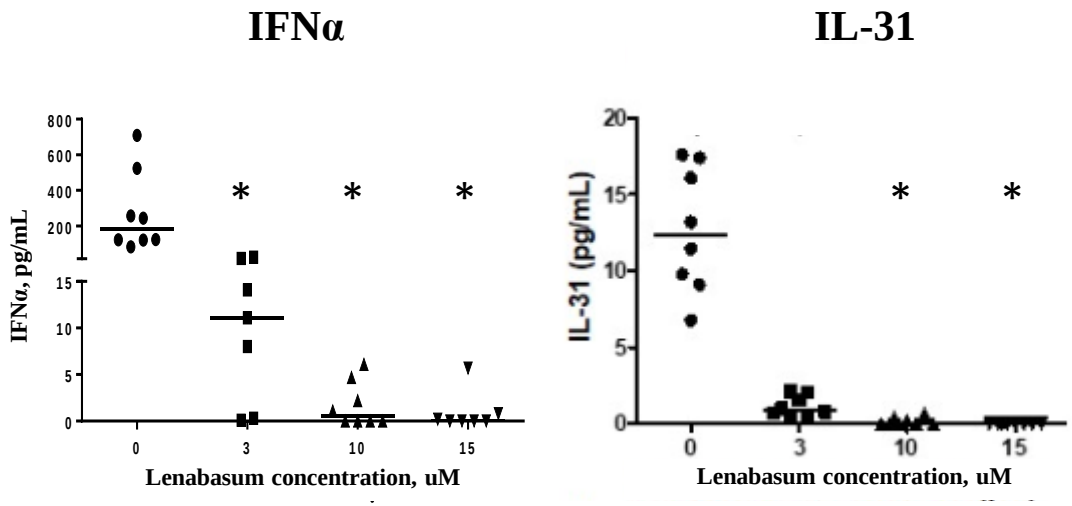


Lenabasum is purple structure shown docked in CB2 molecule

- Activates resolution in a human model of innate immune responses and reduces inflammation and fibrosis in multiple animal models Lucattelli et al. Respir Res. 2016;17:49; Motwani et al. Clin Pharmacol Ther. 2018t;104:675

DM PBMC

- Inhibits IFNα, IL-1β, TNFα, and IL-31 production by DM PBMC Robinson et al. J Invest Dermatol. 2017;137:2445; Kim et al. Br J Dermatol. 2018;179:669



Robinson et al. J Invest Dermatol. 2017;137:2445 Kim et al. Br J Dermatol. 2018;179:669

* P < 0.001 compared to control without lenabasum

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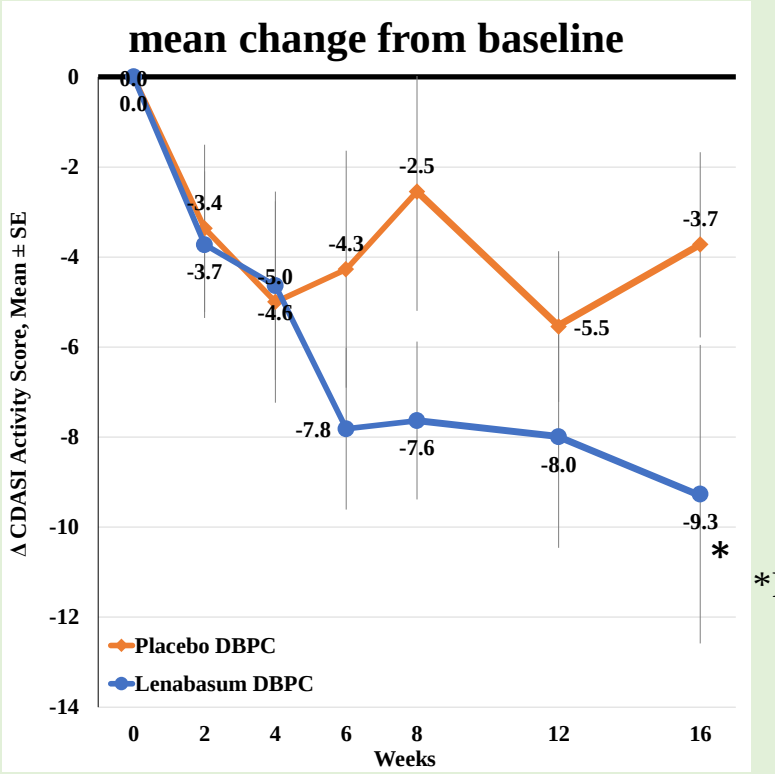
Phase 2 Study JBT101-DM-001 of lenabasum in DM subjects with active skin disease

Study Design

- Classic or amyopathic DM
- CDASI activity score ≥ 14
- No or minimally active concurrent muscle disease
- Background immunosuppressive medications allowed
- Initial 16-week randomized, double-blinded, placebo-controlled (DBPC) part of study (Part A)
- Lenabasum 20 mg BID in an open-label extension (OLE)
- **Safety and efficacy data through Week 68 of OLE will be presented**

CDASI activity score during Part A



*P = 0.04

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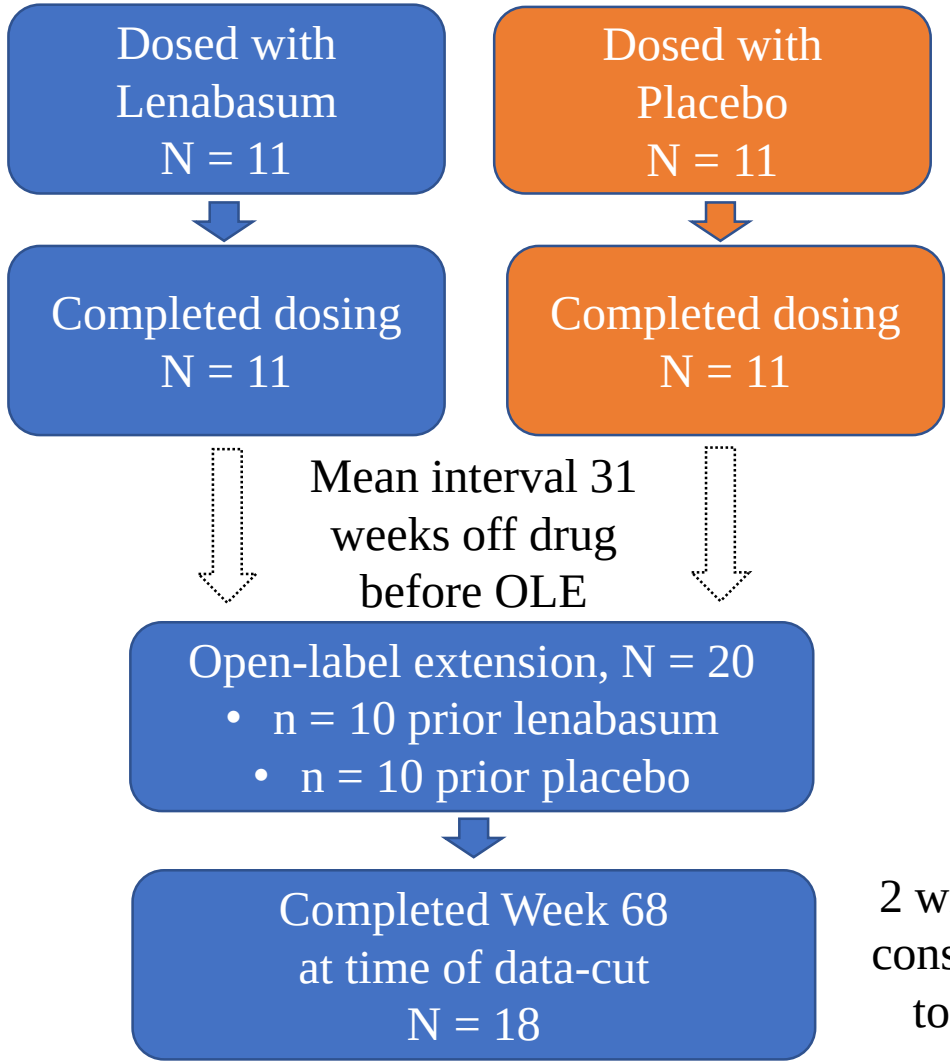
Subjects and disposition

OLE

- 52 (9.9) mean (SD) years of age
- 95% Caucasian
- 95% female
- CDASI activity score 25 (12.9) mean (SD), was 35 (8.7) at study start
- 17 (85%) on immunosuppressive drugs
  - 9 (45%) antimalarials
  - 8 (40%) mycophenolate
  - 7 (35%) methotrexate
  - 5 (25%) prednisone
  - 1 (5%) azathioprine
  - 11 (55%) on ≥ 2 immunosuppressive drugs



2 withdrawals of consent unrelated to lenabasum

Adverse events

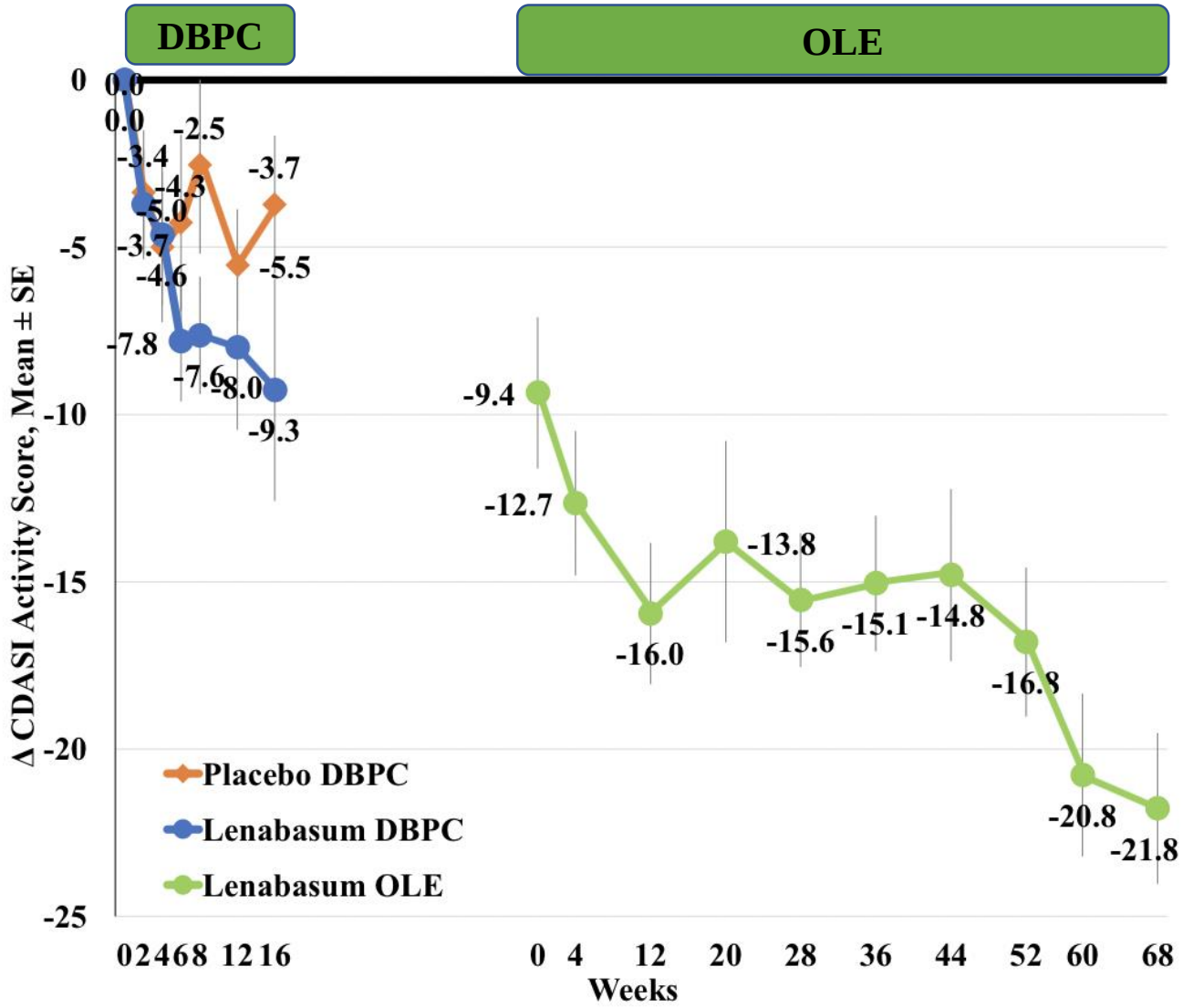
- All subjects had ≥ 1 AE during ≥ 68-weeks dosing the OLE, for a total of 75 AEs in the OLE through March 5, 2019
- **No serious AEs** occurred
- **No study discontinuations** related to lenabasum
- By maximum severity
  - 16 (80%) had mild AEs
  - 3 (15%) had moderate AEs (DM flare, actinic keratosis, and sinusitis)
  - 1 (5%) subject had severe (fatigue, unrelated)
- By maximum relatedness
  - 12 (60%) had unrelated AEs
  - 7 (35%) had possibly related AEs
  - 1 (5%) had probably related AEs (mild fatigue)

Adverse events occurring in ≥ 10% of subjects in OLE

Adverse Event, Preferred Term	Subjects with AEs, n/20 (%)		
	All	Unrelated	Related
Fatigue (4 mild, 1 severe)	5 (20%)	3 (15%)	2 (10%)
Dizziness (3 mild)	3 (15%)	2 (10%)	1 (5%)
DM flare (2 mild, 1 moderate)	3 (15%)	3 (15%)	
Upper respiratory tract infection (3 mild)	3 (15%)	3 (15%)	
Common cold (2 mild)	2 (10%)	2 (10%)	
Herpes zoster (2 mild)	2 (10%)		2 (10%)
Nausea (2 mild)	2 (10%)	1 (5%)	1 (5%)
Numbness (2 mild)	2 (10%)	2 (10%)	
Sinusitis (1 mild, 1 moderate)	2 (10%)	1 (5%)	1 (5%)
Urinary tract infection (2 mild)	2 (10%)	2 (10%)	

- No laboratory test abnormalities or vital sign abnormalities related to lenabasum

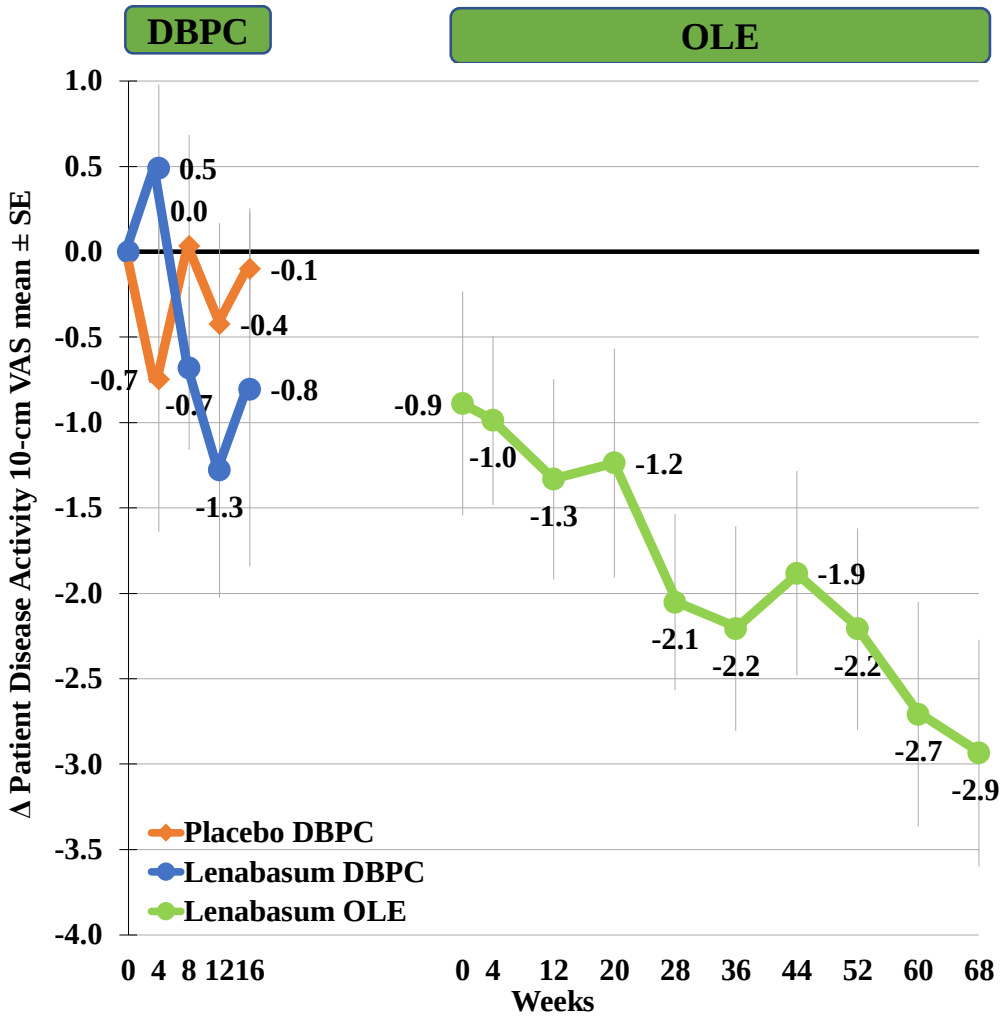
Change in CDASI activity score



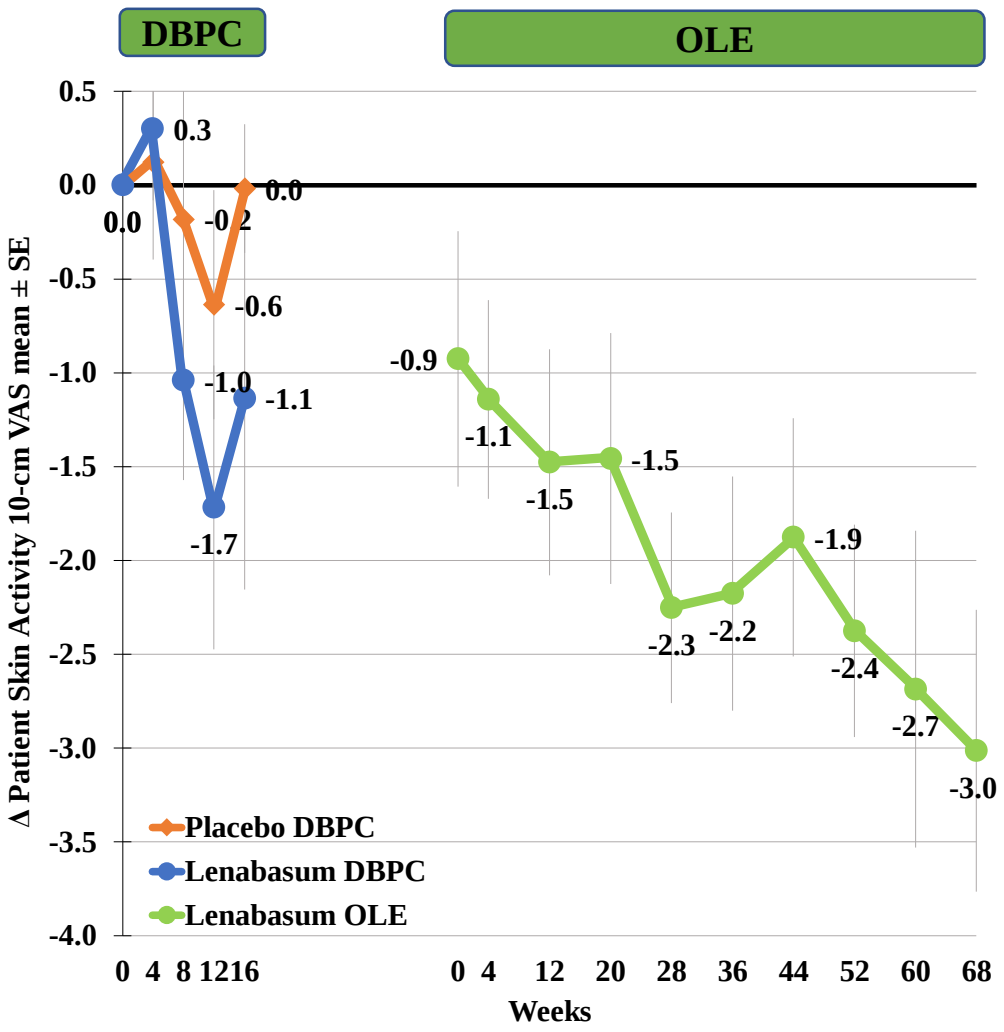
- Continued improvement in OLE
- 67% achieved low skin disease activity (CDASI ≤ 14) by Week 68
  Anyanwu et al Br J Dermatol. 2015;173:969
- Improvement -4 to -5 points is considered medically meaningful
  Anyanwu et al Br J Dermatol. 2015;173:969
- Improvement of -4 points or more is associated with improvement in skin-related quality of life outcomes, itch, and pain Robinson et al. Br J Dermatol. 2015;172:169

Changes in patient activity VAS scores

Disease Activity

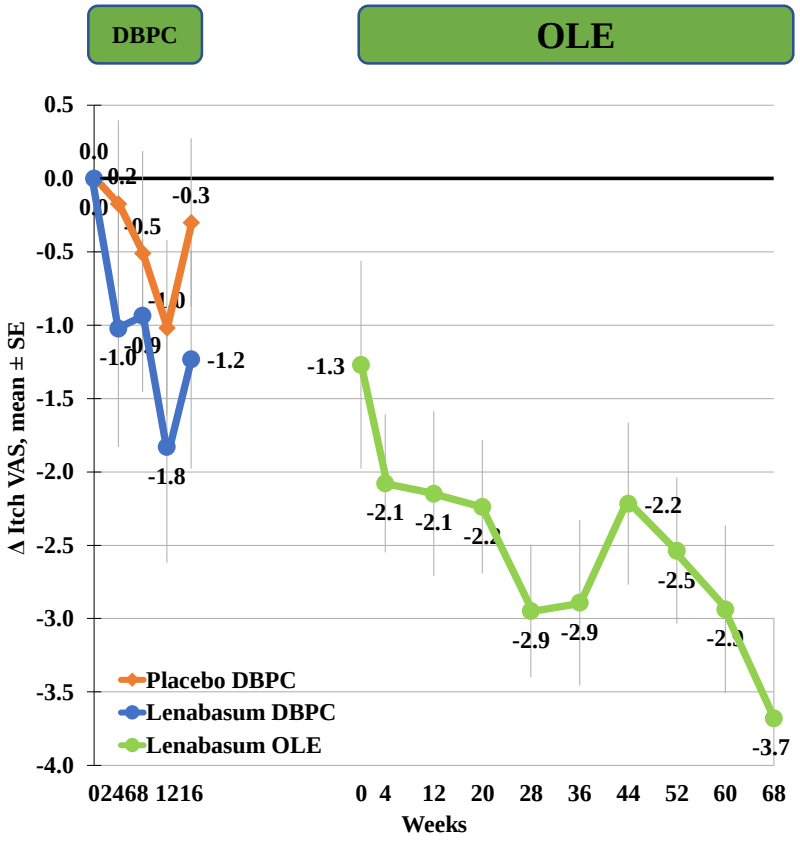


Skin Activity

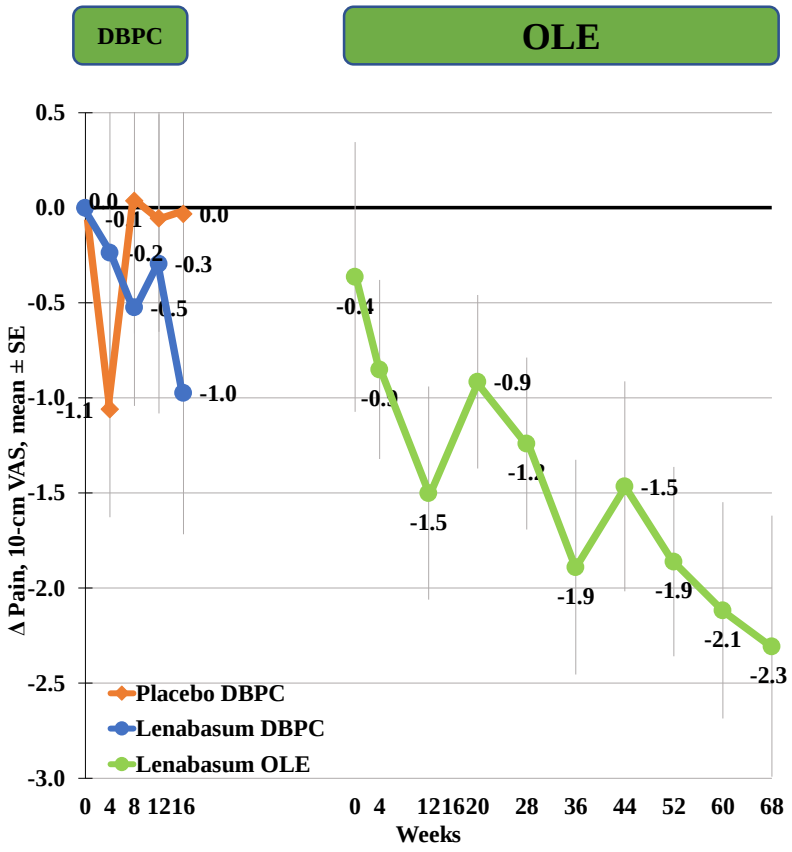


Changes in other patient-reported outcomes

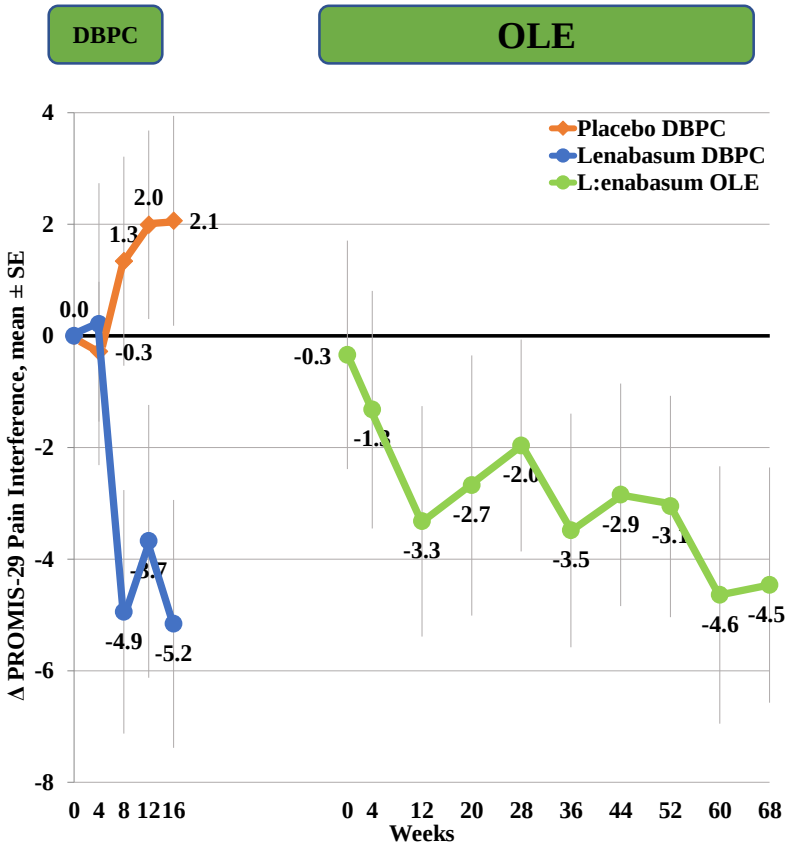
Itch VAS



Pain VAS

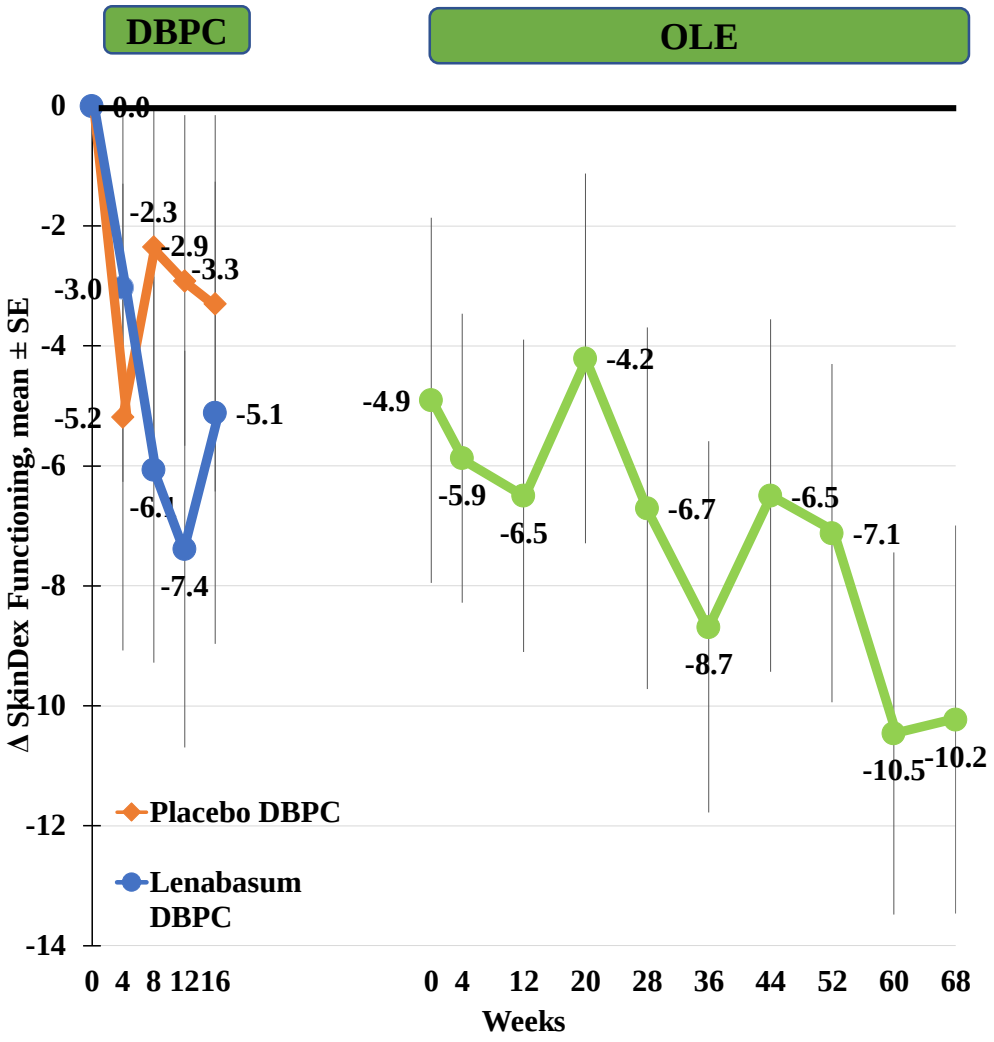


PROMIS-29 Pain Interference

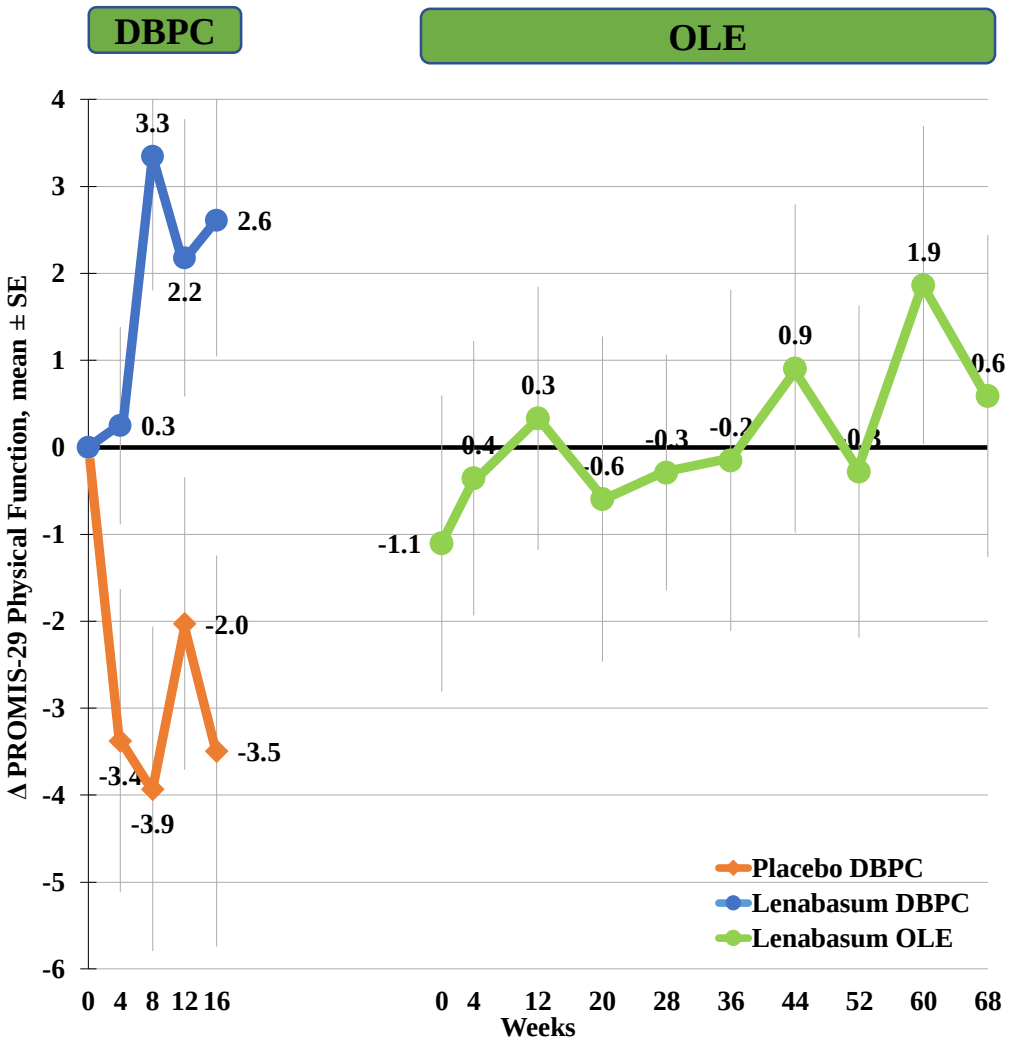


Changes in patient reported functioning

SkinDex-29 Functioning



Promis-29 Physical Function



Summary and Conclusions

- Lenabasum has been safe and well-tolerated in study JBT101-DM-001 through Week 68 of the OLE. There have been no severe AEs and no study discontinuations related to lenabasum to date in this study
- Improvement in multiple efficacy outcomes was observed through year 1 in the OLE, with stability or continued improvement thereafter
- Limitations of ascribing efficacy to lenabasum during the OLE are acknowledged
- A Phase 3 study testing safety and efficacy of lenabasum in DM is ongoing

Acknowledgements

- NIH/NIAMS for funding for the DBPC portion of this study

Change in patient-reported function