Safety and Efficacy of Lenabasum in Refractory Skin-Predominant Dermatomyositis Subjects Treated in an Open-Label Extension of Trial JBT101-DM-001

Poster # 2284

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ABSTRACT

Background: Lenabasum is a synthetic, non-immunosuppressive, selective cannabinoid receptor type 2 agonist that activates resolution of innate immune responses. Lenabasum had acceptable safety and tolerability and improved efficacy outcomes in the double-blinded, randomized, placebo-controlled (DBPC) part A of Phase 2 trial JBT101-DM-001 (NCT02466243) in dermatomyositis (DM) subjects with refractory, skin-predominant involvement.

Objective: To provide long-term safety and efficacy data in DM subjects in study JBT101-DM-001.

Methods: Subjects who completed Part A were eligible to receive oral lenabasum 20 mg BID in an open-label extension (OLE) that assessed safety and efficacy at 4 weeks, then every 8 weeks.

Results: 20/22 (90.9%) eligible subjects received open-label lenabasum, following a mean interval of 31 weeks from end of Part A to start of OLE when they received only standard-of care. 17/20 (85.0%) subjects were on stable baseline immunosuppressive drugs. At the time of data cut-off, no subjects had discontinued from the OLE, all completed Week 22 and 17 (85%) completed ≥ Week 28. Adverse events (AEs, n = 33) occurred in 13/20 (65.0%) subjects, with 5/20 (25.0%) subjects having ≥ 1 AE (all mild) related to lenabasum. No subject had a serious or severe AEs. All subjects had AEs with maximum severity of mild (12/20, 60.0%) or moderate (1/20, 5.0%). The only AE that occurred in more than 1 subject was DM flare (n = 2, 10%); the last recorded CDASI activity score prior to flare was 14 points lower than baseline in 1 subject and 5 points higher than baseline in 1 subject. Mild dizziness occurred in 1 (5.0%) subject. Improvement was seen in multiple physician- and patient-reported efficacy outcomes including: CDASI activity score; physician VAS assessments of skin activity and extra-muscular disease; physician Likert assessments of global disease, skin disease, and extra-muscular disease; and patient VAS assessments of overall disease, skin disease, itch, pain, and several SkinDEX-29 and PROMIS-29 domain scores. Examples in shown in Figure 1. Mean (SD) changes at Week 28 from study start were: CDASI activity score = –15.4 (9.24) points, with 14/17 (82.3%) subjects achieving ≥ 10-point improvement and 8/17 (47.1%) subjects achieving low disease activity with CDASI ≤ 14; 10-cm Physician Overall Disease VAS = -2.6 (1.90) points, with 14/17 (82.3%) subjects achieving ≥ 1 point and 20% improvement.

Conclusion: Lenabasum continues to have a favorable safety and tolerability profile in the OLE of the Phase 2 trial JBT101-DM-001 with no severe or serious AEs or study discontinuations related to lenabasum. The CDASI activity score and multiple other physician and patient-reported outcomes improved, although limitations of attributing efficacy to lenabasum in the setting of open-label dosing is acknowledged. These data support further testing of lenabasum for the treatment of DM.

BACKGROUND

- Dermatomyositis (DM) is a serious multi-system autoimmune disease characterized in part by chronic activation of the innate immune system
- Current therapies for DM are frequently ineffective and include immunosuppressive drugs
- Lenabasum (JBT-101) is an oral selective CB2 agonist that activates the resolution phase of innate immune responses
- Lenabasum has shown benefit in animal models of inflammation and fibrosis and reduces IFNα, TNFα , and IL-31 production by cultured PBMC from DM patients
- Lenabasum had acceptable safety and tolerability in DM subjects with active, refractory skin-predominant DM during the double-blinded placebo-controlled (DBPC) Part A of Phase 2 study JBT101-DM-001, Lenabasum improved CDASI activity score and multiple patient-and physician reported outcomes
- An open-label extension (OLE) of study JBT101-DM-001 was undertaken to evaluate long-term safety profile and effects on efficacy outcomes of lenabasum in DM
- **12-month OLE data are presented in this poster**

STUDY DESIGN AND SUBJECT CHARACTERISTICS

Eligibility Criteria

- DM by Bohan and Peter's or Sontheimer's criteria
- Moderate to severely active, refractory skin-predominant DM
  - CDASI activity score ≥ 14
  - Failed or intolerant of hydroxychloroquine
  - Minimal active muscle involvement
- Adults ≥ 18 and ≤ 70 years of age, N = 22
- Stable doses of concomitant medicines for DM allowed, including immunosuppressive medications
- For open-label extension (OLE), subjects must complete double-blind placebo-controlled (DBPC) Part A of study (N = 20)

Design

Double-Blind Placebo-controlled (DBPC) Part A of Study

- 12 weeks active treatment + 4 weeks additional safety and efficacy assessments

Off Study Drug

- End of double-blind dosing to start of open-label dosing
- Subjects remained on background immunosuppressive drugs
- Mean 31 weeks off study drug

Open-label Extension (OLE) Part B of Study

- Lenabasum 20 mg BID for subjects previously treated with lenabasum or placebo in Part A
- Allowed to adjust medications

DBPC → Off drug → OLE

Demographics and Baseline Characteristics

Subject Demographics and Baseline Disease Assessments at Study Entry	Mean (SD) or n (%)	
	Lenabasum N = 11	Placebo N = 11
Age, mean (SD)	**53** (9.3)	**53** (10.4)
Female, %	91%	100%
White, %	100%	91%
Immunosuppressive drugs, n, %	**9** (81.8%)	**10** (90.9%)
Physician CDASI activity score, 0 -100	**33** (9.7)	**36** (7.8)
Patient skin global assessment (PTGA), 1-10	**4.6** (2.2)	**6.4** (2.6)
Patient itch, VAS 1-10	**6.1** (2.7)	**5.1** (3.5)
Patient SKINdex-29 symptom score, 0-100	**61** (20.2)	**52** (24.3)
Patient SKINdex-29 functioning score, 0-100	**28** (15.7)	**27** (26.7)

- At entry, DM subjects had severely active and symptomatic skin disease despite current immunosuppressive therapy in most subjects

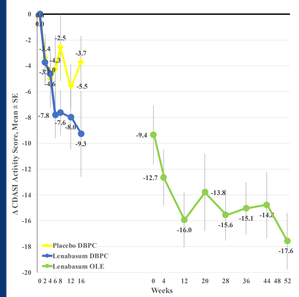
ADVERSE EVENTS DURING OPEN-LABEL DOSING

- There have been no serious AEs related to lenabasum and no deaths in the study to date
- The only adverse event (AE) related to lenabasum that occurred in more than 1 subject during the OLE was fatigue, which occurred in 2 (10%) subjects to date
- 18 (90%) subjects had at least 1 AE, with 52 total AEs in 20 subjects during the > 1 year OLE to date
- By maximum severity, 15 (75%) of subjects had mild AEs, 2 (10%) had moderate AEs, and 1 (5%) had severe AEs. That severe AEs was fatigue which was judged unrelated to lenabasum
- By maximum relatedness, 13 (65%) of subjects had AEs unrelated to lenabasum and 5 (25%) had AEs related to lenabasum. The rate of AEs related to lenabasum decreased with time
- AEs (n, % 20 subjects) occurring in ≥ 10% of OLE subjects were: dermatomyositis worsening, dizziness, fatigue, n = 3 (15%) each; and nasopharyngitis and upper respiratory tract infection, n = 2 (10%) each
- All subjects who entered the OLE completed 12 months of dosing

EFFECTS ON SKIN DISEASE

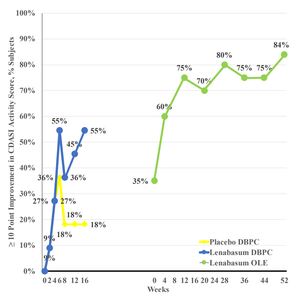
CDASI Activity Score

DBPC → Off → OLE



Improvement ≥ 10 Points in CDASI Activity Score

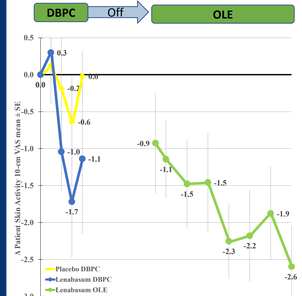
DBPC → Off → OLE



- CDASI activity scores improved (decreased) during the OLE, with mean (SD) change from Baseline in CDASI activity score = -17.6 (9.6) points at 12 months. An improvement of -4 to -5 points is considered a minimal important difference (MID) in CDASI activity score.
- 84% of subjects achieved an improvement in CDASI activity score of -10 points or more at 12 months, an improvement that exceeds the reported MID.
- Improvement was still continuing at Month 12

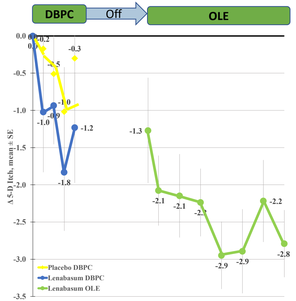
Patient Global Assessment Skin Disease, 10-cm VAS

DBPC → Off → OLE



5-D Itch Score

DBPC → Off → OLE

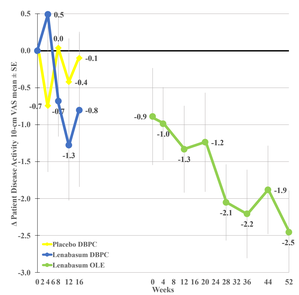


- Patient-reported skin disease, assessed as Patient Global Assessment of Skin Disease score and 5-D itch score, both improved (decreased) during the OLE

EFFECTS ON OVERALL DISEASE

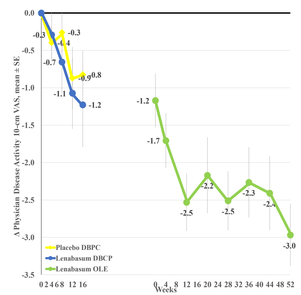
Patient Global Assessment Disease Activity, 10-cm VAS

DBPC → Off → OLE



Physician Global Assessment Disease Activity, 10-cm VAS

DBPC → Off → OLE

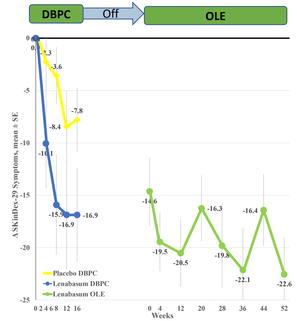


- Overall disease activity improved during the OLE, as assessed by both the patient and the physician
- Improvement was still continuing at Month 12

EFFECTS ON QUALITY OF LIFE AND FUNCTION

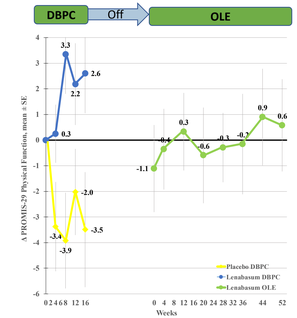
SkinDEX-29 Symptoms

DBPC → Off → OLE



Promis-29 Physical Function

DBPC → Off → OLE

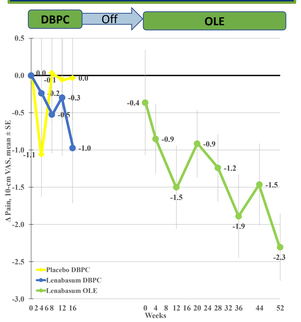


- Patient-reported quality of life improved during the OLE through 12 months, as assessed by a reduction in SkinDex Symptoms score and an increase in Promis-29 Physical Function score
- A change in SkinDex score of ≥ 10 points is considered meaningful.

EFFECTS ON PAIN AND OTHER SYMPTOMS

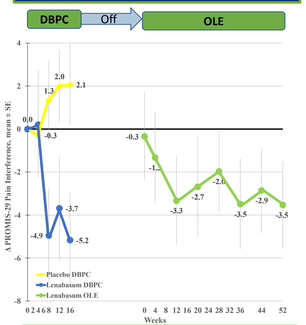
Pain, 10-cm VAS

DBPC → Off → OLE



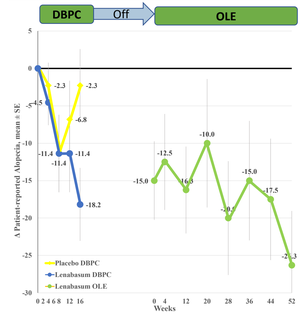
Promis-29 Pain Interference

DBPC → Off → OLE



Patient-reported Alopecia

DBPC → Off → OLE



- Improvements (decreases) in patient-reported pain10-cm VAS, pain interference, and alopecia were observed, and generally increased during 12 months dosing in the OLE
- Improvement in pain and alopecia were still continuing at Month 12 and improvement in pain interference had stabilized

Immunosuppressive Drugs

- 12 subjects had no changes during the OLE
- 3 reduced steroids (10 to 3 mg, 10 to 6 mg, 10 to 0 mg). One switched from methotrexate to mycophenolate in the middle of the steroid reduction. After steroid taper was nearly complete (10 mg to 2 mg), one started methotrexate and then switched to mycophenolate
- 2 reduced mycophenolate
- 1 switched from methotrexate to mycophenolate
- 1 started methotrexate early in the OLE
- 1 required a 1 month burst and taper of steroids (20 mg max dose) after 6 months in OLE

SUMMARY AND CONCLUSIONS

- Safety and tolerability profiles of lenabasum in DM were very favorable after 12 months dosing in the OLE, with no serious AEs related to lenabasum and no drop-outs from the OLE at 12 months
- Only 25% of subjects had AEs related to lenabasum. The most frequent AE related to lenabasum was fatigue which occurring in 2 (10%) subjects
- Improvement was observed in efficacy assessments of skin disease, overall disease, patient symptoms, and patient function. Generally, improvement increased over time in the first 12 months of the OLE.
- The limitations of assessing efficacy with open-label dosing are acknowledged, as is the potential impact of any change in concomitant medications

THANK YOU

- **To the people with DM who participated in this study and the study staff who took care of them**
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