# A Phase 2 Study of Safety and Efficacy of Lenabasum (JBT-101), a Cannabinoid Receptor Type 2 Agonist, in Refractory Skin-Predominant Dermatomyositis

**Poster # FRI0470**

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## ABSTRACT

**Background/Purpose:** Effective treatment options are limited for refractory skin disease in dermatomyositis (DM). Lenabasum is a non-immunosuppressive, synthetic, oral preferential CB2 agonist that triggers resolution of innate immune responses and reduces cytokine production by PBMC from DM patients. The purpose of this study was to test safety and efficacy of lenabasum (aka JBT-101, anabasum) in DM subjects with refractory, moderate-to-severely active skin disease.

**Methods:** A double-blind, randomized placebo-controlled 16-week Phase 2 trial (JBT101-DM-001; NCT02466243) enrolled adults with documented DM and a Cutaneous Dermatomyositis Disease Area and Severity Index (CDASI) activity score ≥ 14, minimal active muscle involvement and failure or intolerance to hydroxychloroquine and stable DM medications including immunosuppressants. Subjects received 2 escalating dose levels of lenabasum (20 mg QD X 4 weeks, then 20 mg BID X 8 weeks) or PBO X 12 weeks. Subjects were followed off study drug X 4 weeks. Safety and efficacy outcomes were assessed from Day 1 through end of study at Week 16. The primary efficacy objective was to assess efficacy of lenabasum using CDASI activity score.

**Results:** 11 adults each received lenabasum and PBO (N = 22). Demographic and disease characteristics were similar in both cohorts. Both cohorts had mean CDASI activity scores in the severe range (33-35) despite immunosuppressants (19/22 subjects). Lenabasum subjects had clinically meaningful improvement in CDASI activity scores with mean reduction ≥ 5 points at all visits after 4 weeks. Improvement had statistical significance at end of study (Fig. 1, P = 0.02, 2-sided MMRM) that first became apparent after 4 weeks. Lenabasum provided greater improvement than placebo in CDASI damage index, patient-reported global skin disease and overall disease assessments, skin symptoms including photosensitivity and itch, fatigue, sleep, pain interference with activities, pain, and physical function (examples in Fig. 1). Improvements in secondary efficacy outcomes reached statistical significance (P ≤ 0.1, 1-sided MMRM) at multiple visits after week 4. There were no serious, severe or unexpected adverse events (AEs) related to lenabasum. Tolerability of lenabasum was excellent with no study drop-outs. Subjects in the lenabasum cohort had numerically more mild AEs than placebo subjects (29 vs. 19) and fewer moderate AEs (4 vs. 7). AEs in ≥ 3 subjects in any cohort were diarrhea, dizziness (lightheadedness), fatigue and dry mouth.

**Conclusion:** Lenabasum demonstrated consistent evidence of clinical benefit across multiple efficacy outcomes and had acceptable safety and tolerability in this Phase 2 trial in refractory skin disease in DM. Further evaluation of lenabasum in the treatment of DM is warranted.

## BACKGROUND

- Dermatomyositis (DM) is a serious and rare systemic autoimmune disease characterized in part by chronic activation of innate immune responses
- 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 interferon α, TNFα , and IL-31 production by cultured peripheral blood mononuclear cells from DM patients
- A double-blinded placebo-controlled study of safety and efficacy of lenabasum in DM subjects with active skin manifestations was undertaken

## DESIGN, SUBJECT DEMOGRAPHICS AND BASELINE 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
- Stable doses of concomitant medicines for DM allowed, including immunosuppressive drugs

**Dosing**

- Weeks 1-4: lenabasum 20 mg QD or placebo QD
- Weeks 5-12: lenabasum 20 mg BID or placebo BID
- Weeks 13-16: Safety and efficacy assessments off-treatment

**Open-label Dosing**

- Subjects must complete Part A
- lenabasum 20 mg BID x 1 year

| Subject Demographics | Lenabasum N = 11 | Placebo N = 11 |
|---|---|---|
| Age, mean (SD) | 53.1 (9.3) | 52.5 (10.4) |
| Female, % | 91% | 100% |
| White, % | 100% | 91% |
| Hispanic or Latino, % | 27% | 0% |
| Body mass index, mean (SD) | 26.4 (5.8) | 27.3 (7.4) |

- No significant differences in baseline demographics between cohorts
- Mostly middle-aged white women

| Measurement | Mean (SD) Lenabasum N = 11 | Mean (SD) Placebo N = 11 | Comment |
|---|---|---|---|
| Physician CDASI activity score, 0 – 100 | **33.3** (9.7) | **35.8** (7.8) | >14 = moderate-severe |
| Immunosuppressive drugs, N | 9 (81.8%) | 10 (90.9%) | Refractory skin disease |
| Patient SKINdex-29 symptom score, 0 - 100 | **61.0** (20.2) | **52.3** (24.3) | ≥ 50 = extremely severe[1] |
| Patient SKINdex-29 functioning score, 0 - 100 | **27.8** (15.7) | **27.3** (26.7) | 11-32 = moderate[1] |
| Patient SKINdex-29 emotions score, 0-100 | **45.0** (24.2) | **56.6** (32.1) | 25-49 = moderate, ≥ 50 = severe[1] |
| Patient SKINdex-29 photosensitivity score, 0-100 | **55.7** (31.3) | **39.8** (35.7) | |
| Patient skin global assessment, VAS 1-10 | **4.6** (2.2) | **6.4** (2.6) | 0 = inactive, 10 = extremely severe[2] |
| Patient itch, VAS 1-10 | **6.1** (2.7) | **5.1** (3.5) | |
| Patient PROMIS-29 fatigue, 0-100 | **50.3** (9.9) | **51.3** (9.9) | 50 = population average |
| Patient PROMIS-29 sleep, 0 - 100 | **54.0** (7.8) | **55.6** (7.2) | 50 = chronic illness average |
| Patient PROMIS-29 physical function, 0 - 100 | **50.6** (7.4) | **54.0** (6.7) | 50 = population average |

[1] Nijsten et al, J Invest Dermatol 2006:126:1244-50. [2] Rider et al, Arthritis 2011

- No significant differences in baseline disease assessments
- Subjects have severely active and symptomatic skin disease despite immunosuppressive therapy

## ADVERSE EVENTS

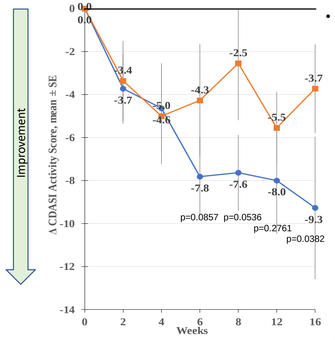
| Adverse Events | Subjects with AEs by Maximum Severity then Maximum Relatedness, n/N (%) Double-blinded Placebo-controlled Dosing, 12 weeks Lenabasum, N = 11 | Placebo, N = 11 |
|---|---|---|
| Total AEs | 11 (100%) | 9 (82%) |
| Unrelated to study drug | 3 (27%) | 5 (46%) |
| Related to study drug | 8 (73%) | 4 (36%) |
| Serious AE | 0 (0%) | 0 (0%) |
| AEs leading to study discontinuation | 0 (0%) | 0 (0%) |
| Mild | 7 (64%) | 5 (46%) |
| Moderate | 4 (36%) | 4 (36%) |
| Severe | 0 (0%) | 0 (0%) |

[1] Possible, probable, or definite relationship to anabasum as assessed by investigator

- No serious or severe AEs related to lenabasum to date
- AEs occurring in ≥ 2 subjects in the lenabasum cohort during active dosing were dry mouth (4 vs 1 subjects), dizziness (4 vs 1 subjects), dyspepsia (2 vs 0 subjects) headache (2 vs 0 subjects) and increased appetite (2 vs 1 subjects). Numbers are for lenabasum vs placebo cohorts.

## CDASI ACTIVITY SCORE

**Change from baseline**

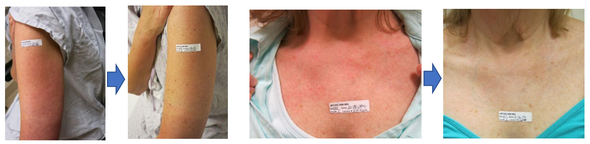



P-value = 2-sided, MMRM, LS Means difference from Week 0

- Medically meaningful improvement in CDASI activity score (≥ 5 point reduction) for lenabasum-treated subjects at all visits after Week 4 and reaching -9.3 vs -3.7 points vs placebo at end of study, p = 0.0382
  - 6/11 (56%) lenabasum subjects vs 2/11 (18%) placebo subjects had ≥ 10 point reduction in CDASI activity score at end of study, p = 0.09, Fisher's exact test, 1-sided
  - No lenabasum subject vs 4/11 (36%) placebo subjects developed skin erosions during active dosing, p = 0.05, Fisher's exact test, 1-sided

**Legend:** Blue = lenabasum; orange = placebo; Black horizontal line = no change from baseline (0)

**Example of improvement in skin erythema with lenabasum treatment**



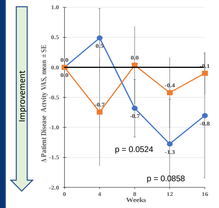
**Visit 1** **Visit 6** **Visit 1** **Visit 6**

## IMPROVEMENT IN PATIENT-REPORTED OUTCOMES

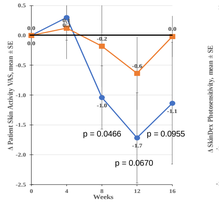
- All secondary efficacy outcomes were evaluated both from baseline at study start and end of Week 4 at p = 0.10 level, modified-intent-to-treat, 1-sided ANCOVA, least squares mean difference for continuous variables and Fisher's exact test for categorical variables
- Clinically meaningful change in VAS scores is ≥ 20% change from baseline (Rider et al, Arthritis Care Res, 2011;63:S1186)

**Change from baseline**

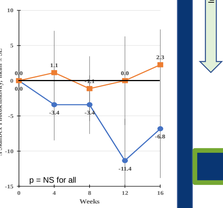
**Disease Activity VAS**



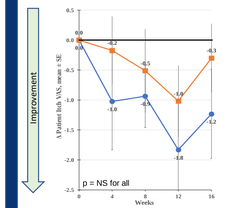

**Skin Activity VAS**



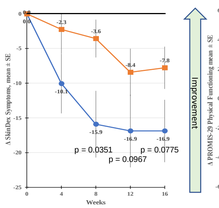

**SkinDex29 Photosensitivity**



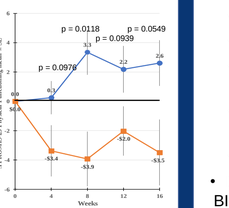

**Itch VAS**



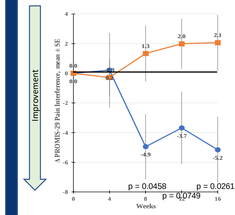

**SkinDex29 Symptoms**



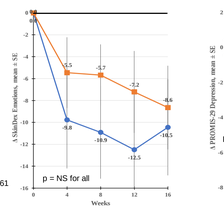

**PROMIS29 Physical Functioning**



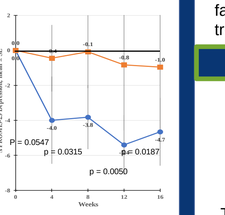

**PROMIS29 Pain Interference Domain**




**SkinDex29 Emotions**




**PROMIS29 Depression**

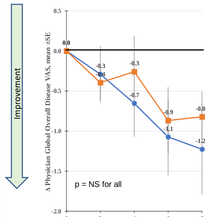



**Legend:** Blue = lenabasum; orange = placebo; Black horizontal line = no change from baseline (0)

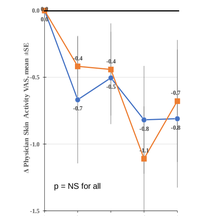
## IMPROVEMENT IN PHYSICIAN-REPORTED OUTCOMES

**Change from baseline**

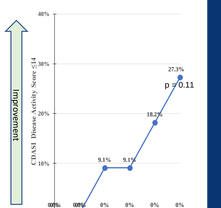
**Global Disease VAS**




**Skin Activity VAS**




**CDASI Low Activity (≤ 14)**




**Legend:** Blue = lenabasum; orange = placebo; Black horizontal line = no change from baseline (0)

## SUMMARY AND CONCLUSIONS

In this Phase 2 study, lenabasum:

- Had a favorable safety profile and was well-tolerated
- Provided greater improvement than placebo in multiple efficacy outcomes
  - ✓ CDASI activity score and CDASI low disease activity score (CDASI ≤ 14)
  - ✓ Patient-reported global disease activity and skin activity VAS
  - ✓ Symptoms including Skindex-29+3 Symptoms domain, Skindex-29+3 Photosensitivity question and Pain VAS
  - ✓ Quality of life measures including PROMIS-29 pain interference, depression, fatigue, sleep disturbance domains
  - ✓ Function including PROMIS-29 Physical Function and Social Role domains
- Differences from placebo generally were greater after start of lenabasum 20 mg BID dosing at end of Week 4 and greater for patient-reported outcomes than physician-reported VAS outcomes
- Changes from baseline reached or exceeded clinically important improvement for several efficacy outcomes
- The degree and consistency of improvement in efficacy outcomes combined with a favorable safety profile to date support further clinical testing of lenabasum for treatment of DM

## THANK YOU

❖ **To the individuals with DM who participated in this study**
❖ **To the study staff who executed this trial**
❖ **To Data Safety Committee Chairperson: Dr. Philip Cohen**
❖ **To NIH/NIAMS for funding for this study**

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