Comparison of Patients with Dermatomyositis in a Specialty Clinic versus Clinical Trial with Anabasum (JBT-101), a Cannabinoid Receptor Type 2 Agonist

Poster # 2156

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Abstract

Background/Purpose: There are limited treatment options and no published double-blind randomized placebo-controlled trials for the treatment of skin manifestations of dermatomyositis (DM). There is no information about patients enrolled in trials to study efficacy of treatments of skin involvement in DM. Anabasum is a non-immunosuppressive, synthetic, preferential CB2 agonist that resolves inflammation in animal and human models of innate immune responses and reduces cytokine production by isolated mononuclear cells from DM patients.

Methods: A double-blind randomized placebo-controlled Phase 2 trial (JBT101-DM-001), with NIH as a collaborator, was designed to test efficacy and safety of anabasum in adults with DM and refractory skin involvement. The trial is done at a clinic specializing in skin involvement in DM which allows comparison of trial subjects to the general DM population at the same clinic.

Results: Selection criteria included Cutaneous Dermatomyositis Disease Area and Severity Index (CDASI) activity score of ≥ 14, minimal active muscle involvement, failure or intolerance to hydroxychloroquine, and stable DM medications including immunosuppressive drugs. Trial subjects (N = 22) and the general clinic population (N = 221) were predominantly middle-aged white, non-Hispanic women (Table 1). Trial subjects had high skin disease activity compared to the clinic population and widespread use of immunosuppressive drugs (86%), including second-line immunosuppressive drugs (64%), with the mostly commonly used immunosuppressive drugs being antimalarial drugs (45%), mycophenolate (32%), methotrexate (23%), and systemic corticosteroids (23%).

Conclusion: This is the first report of subject demographics and disease characteristics in a clinical trial focused on safety and efficacy in skin-predominant dermatomyositis. Trial subjects had similar demographics to the overall DM clinic population. However, skin disease activity and patient-reported skin symptoms were greater in the trial subjects than in the overall DM clinic population, despite much higher use of second-line immunosuppressive medications. Disease activity in trial subjects was much higher than required by inclusion criteria. Combined, these data show that subjects enrolled in trials of treatment of skin involvement in DM may have disease that is more active and more difficult to control than the general population of patients, reminiscent of early efficacy trials in other systemic autoimmune diseases.

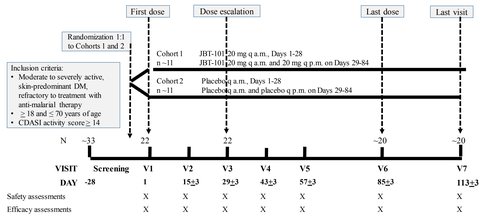
Background

- Dermatomyositis (DM) is a severe autoimmune disease with distinctive cutaneous manifestations that may be accompanied by inflammatory muscle disease
- Anti-malarial therapy is first-line treatment for cutaneous DM, is often ineffective and can cause drug reactions. Other immunosuppressive drugs are used to treat refractory skin manifestations of DM. More effective and safer therapies are needed for treatment of DM
- Anabasum is a selective cannabinoid receptor type 2 (CB2) agonist which triggers resolution of innate immune responses without immunosuppression
- A Phase 2 study (JBT101-DM-001) of safety and efficacy of anabasum in subjects with skin-predominant DM was undertaken with funding by the NIH
  - To our knowledge, this is the first double-blind randomized placebo-controlled trial for the treatment of skin manifestations of DM
  - This study is done at a clinic specializing in skin involvement in DM, which allows for comparison of study subjects (n = 22) to the general DM population (n = 221) at the same clinic
  - This is the first report of patient demographic information and disease characteristics in a trial in skin-predominant DM

Methodology: Trial Design

Inclusion Criteria

- Adults ≥ 18 and ≤ 70 years of age
- Moderate to severely active, skin-predominant DM with CDASI activity score ≥ 14
- Minimal active muscle involvement
- Refractory to or intolerant of hydroxychloroquine therapy
- Stable DM medications including immunosuppressive drugs allowed



Results

Subject Demographics and Baseline Characteristics

Characteristic	JBT101-DM-001 N = 22	DM Clinic Population N = 221
Age, median (range)	53 (36-69)	57 (23-88)
Sex, % female	95%	85%
Race, % white	95%	90%
Ethnicity, % not Hispanic or Latino	86%	97%
DM subset • Classic • Clinically amyopathic/ hypomyopathic	 41% 59%	 38% 62%

- Demographics of subjects were similar between the study subjects and the general DM clinic population
- Study subjects and the general DM clinic population were predominantly middle-aged, white, non-Hispanic women
- DM subsets were similar between the two groups

Characteristic	JBT101-DM-001 N = 22	DM Clinic Population N = 221	Comment
CDASI Activity Score median (range)	**33** (22-57)	**13** (0-71)	≥ 14 is moderately to severely active skin disease
CDASI Damage Score median (range)	**2** (0-13)	**2** (0-14)	
≥ 1 immunosuppressive drug including anti-malarials ≥ 1 immunosuppressive drug excluding anti-malarials	**86%** **64%**	**40%** **19%**	Refractory skin disease on second-line immunosuppressive drugs

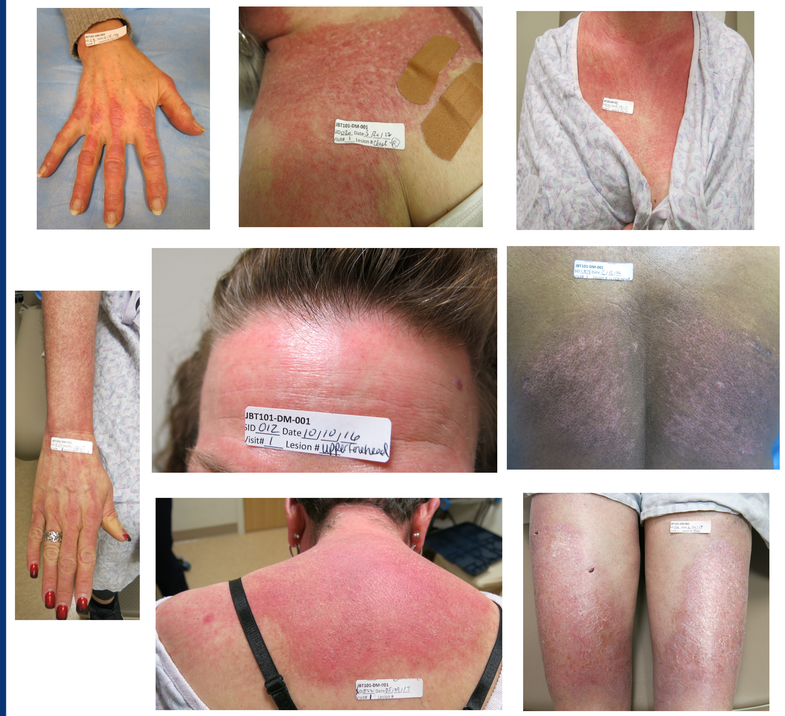
Compared to the general DM clinic population, study subjects:
- Had higher skin disease activity
- Were more likely to be on second-line immunosuppressive drugs

Characteristic	JBT101-DM-001 N = 22	DM Clinic Population N = 221	Comment
Patient Global Assessment median (range)	5.5 (0.4 – 9.7)	4 (0-10)	0 = inactive, 10 = extremely severe
Skindex-29 Symptoms median (range)	**60.7** (21-96)	**35.7** (0-96.4)	≥ 50 = extremely severe
Skindex-29 Emotions median (range)	**48.8** (8-97)	**30.0** (0-100)	25-49 = moderate ≥ 50 = severe
Skindex-29 Functioning median (range)	**30.2** (0-84)	**12.5** (0-100)	11-32 = moderate
Skindex-29 Photosensitivity median (range)	**50** (0-100)	**50** (0-100)	

Compared to the general DM clinic population, study subject reported:
- Worse overall health
- More skin symptoms and impact of skin disease on emotions and functioning

Results

Examples of Skin Manifestations of DM in Subjects in JBT101-DM-001



Conclusions

- ❖ Subjects who enrolled in this first double-blinded, randomized, placebo-controlled Phase 2 trial in skin-predominant DM have very active and refractory skin disease activity, despite concomitant use of immunosuppressive therapies
- ❖ Safer and more effective therapeutic approaches for cutaneous disease manifestations of DM are needed

Thank You

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For the results of this study, please see the late breaker abstract # 7L

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