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EULAR-Highlights – Myositis

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A RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED PHASE III TRIAL OF IVIG 10% IN PATIENTS WITH DERMATOMYOSITIS. THE PRODERM STUDY: RESULTS ON EFFICACY AND SAFETY (OP0008)

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Background

Dermatomyositis (DM)

- Rare chronic systemic autoimmune disease with characteristic skin rash and progressive proximal muscle weakness
- Current therapies
  - Corticosteroids, other immunosuppressants, intravenous immunoglobulins (IVIg)
  - However, none of these therapies are proven by randomized controlled phase 3 studies
- Lack of large randomized clinical trials supporting the efficacy and safety of IVIg in DM

Aggarwal R, et al. Ann Rheum Dis, 2021; 80, S1:4

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Aims

To evaluate the efficacy and safety/tolerability of IVIg in DM patients in a double-blind, randomized, placebo-controlled, international multi-center, phase III clinical trial.

Aggarwal R, et al. Ann Rheum Dis, 2021; 80, S1:4

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Methods

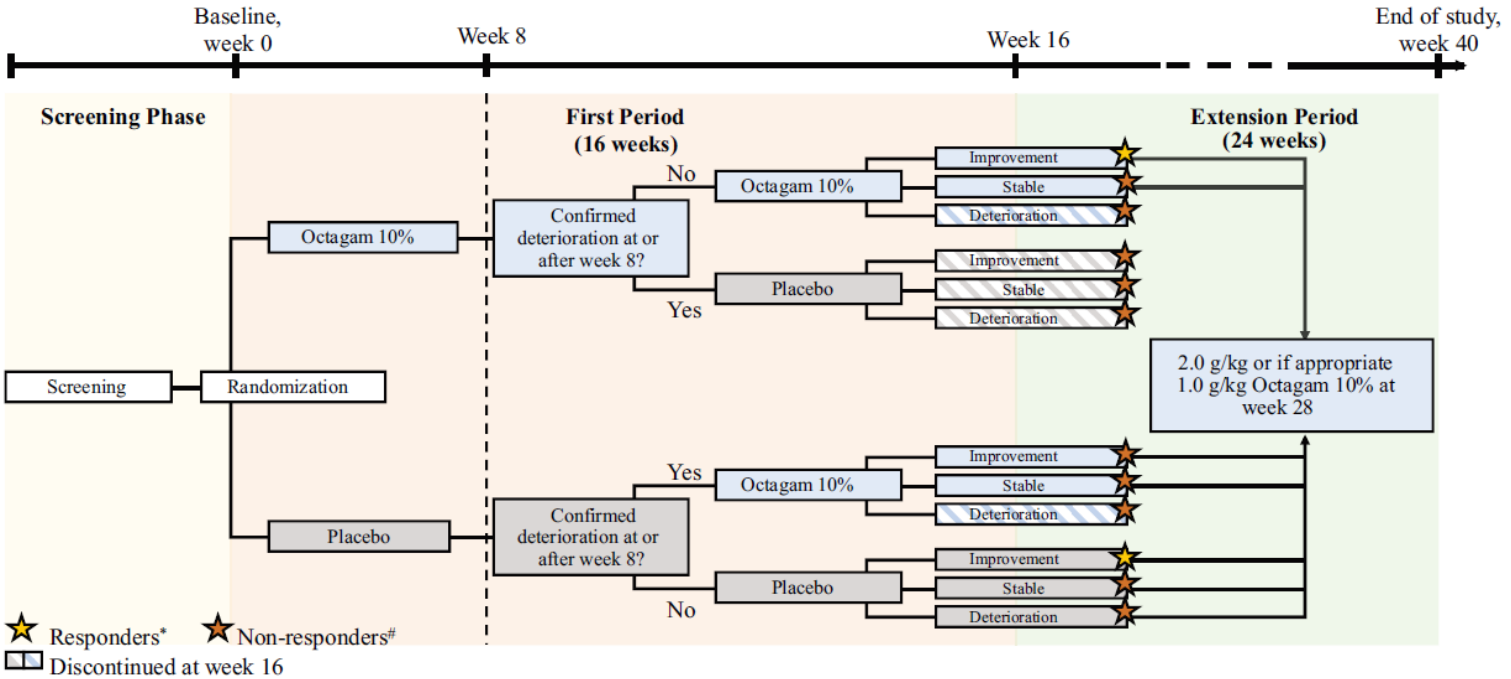

Figure 1. Overview of study design. *Patients with a total improvement score (TIS) ≥20 at week 16 and no prior confirmed deterioration up to and including week 16. #Patients discontinuing from the study due to confirmed deterioration and patients with no response.

Aggarwal R, et al. Medicine (2021) 100:1

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Primary Endpoint

Proportion of responders in the IVIg vs. placebo arm at week 16

- Response defined per 2016 ACR/EULAR Myositis response criteria of at least minimal improvement [Total Improvement Score (TIS) ≥ 20 points)] and without clinical worsening at 2 consecutive visits up to week 16

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Results

- A total of 95 adult DM patients (mean age: 53 years; 75% females; 92% Caucasian) were enrolled, with 47 and 48 randomized to IVIg and placebo
- Baseline clinical characteristics (including medical history and prior DM medication) were balanced between the 2 arms

Table 1.

Total Improvement Score – Analysis of Proportion of Responders at Week 16 (Full Analysis Set, N=95)

TIS Response	*octagam 10%* N=47	Placebo N=48	Difference *octagam 10%* – placebo
Number (%) of responders	37 (78.72%)	21 (43.75%)	
Difference in response rates			34.97
[95% CI] p-value [a]			[16.70, 53.24] 0.0008

[a] Cochran-Mantel-Haenszel TestCI=confidence interval; N=number of patients; TIS=total improvement score

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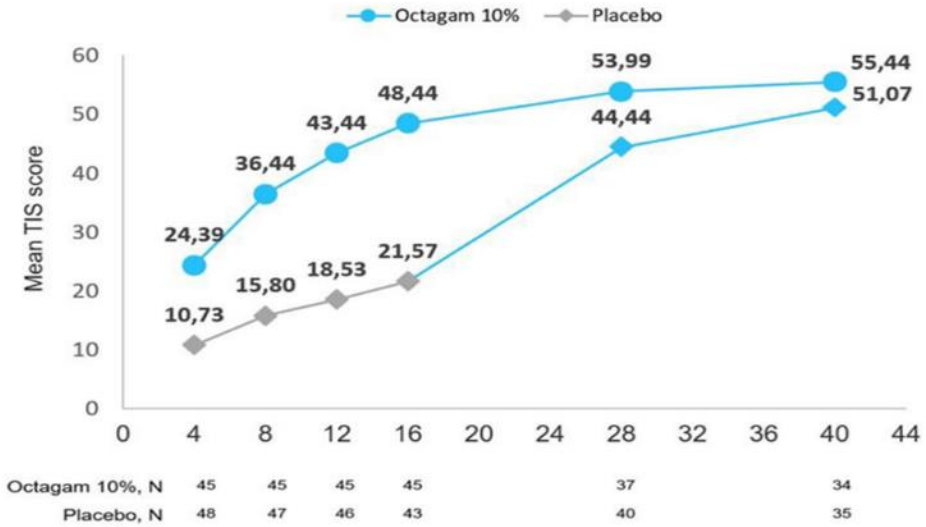
Results

In the analysis of responders per improvement category at week 16, a 45.2% higher response rate for **at least moderate** improvement (TIS ≥n40 points; p < 0.0001) and a 23.6% higher response rate for **at least major** improvement (TIS ≥060 points; p < 0.0062) was observed in the IVIG group as compared to the placebo group.



The mean (SD) TIS was significantly higher in IVIg group [48.4 (24.4)] than in placebo arm [21.6 (20.2)] at week 16.

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Results

- After switching to IVIG in the extension period the placebo group attained a similar response rate at Week 40 as did the IVIg treated patients at Week 16, i.e. approx. 70% for minimal improvement.
- Secondary end points including all of the sub-components of TIS except muscle enzyme (MMT-8, MD global, Extramuscular global, patient global, HAQ,) as well as CDASI (Cutaneous Dermatomyositis Disease Area and Severity Index), also showed statistically significant improvement under IVIg treatment compared to placebo treatment.
- The safety and tolerability profile of IVIg was consistent with previously reported safety outcomes for IVIg administration.

Aggarwal R, et al. Ann Rheum Dis, 2021; 80, S1:4

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Conclusion

First large international phase III randomized, placebo-controlled trial demonstrating the efficacy and safety of IVIg as a treatment for patients with DM.

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LONG-TERM SAFETY AND EFFICACY OF LENABASUM DURING 3 YEARS IN AN OPEN-LABEL EXTENSION (OLE) OF A PHASE 2 STUDY OF LENABASUM IN REFRACTORY SKIN DISEASE IN DERMATOMYOSITIS (DM) (POS0315)

Background

Lenabasum

- Synthetic, non-immunosuppressive, selective cannabinoid receptor type 2 agonist that activates resolution of inflammation
- Acceptable safety and tolerability and improved efficacy outcomes in the initial 16-week double-blinded, randomized, placebo-controlled Part A of Phase 2 trial JBT101-DM-001 (NCT02466243) in DM subjects with refractory skin involvement.
- In that study, lenabasum or placebo was added to stable background treatment, with immunosuppressive therapies allowed.

Werth V, et al. Ann Rheum Dis, 2021; 80: 383

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Aims

To assess long-term safety and efficacy in DM subjects in this study.

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Methods

Subjects who completed Part A of the Phase 2 study (n = 22) 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.

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Results

- 20/22 (91%) subjects enrolled in the OLE, following a mean interval of 31 weeks from the end of Part A, during which they continued to receive standard-of care treatments, to the start of the OLE during which lenabasum 20 mg BID was added.
- 17/20 (85%) subjects were on stable baseline immunosuppressive drugs.
- At the time of this data cut-off, 17 subjects were still enrolled, 17 had completed 140 months (2.7 years), and 15 had completed 156 months (3 years) of OLE dosing.

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Results

- All OLE subjects experienced at least 1 adverse event (AE), with 118 AEs during the OLE through Dec 2020.
- Most AEs were mild (n = 111, 94%): fatigue, nausea, common cold, DM flare
- No serious AEs related to lenabasum have been reported in this OLE to date.
- No subject discontinued the OLE because of an AE related to lenabasum.

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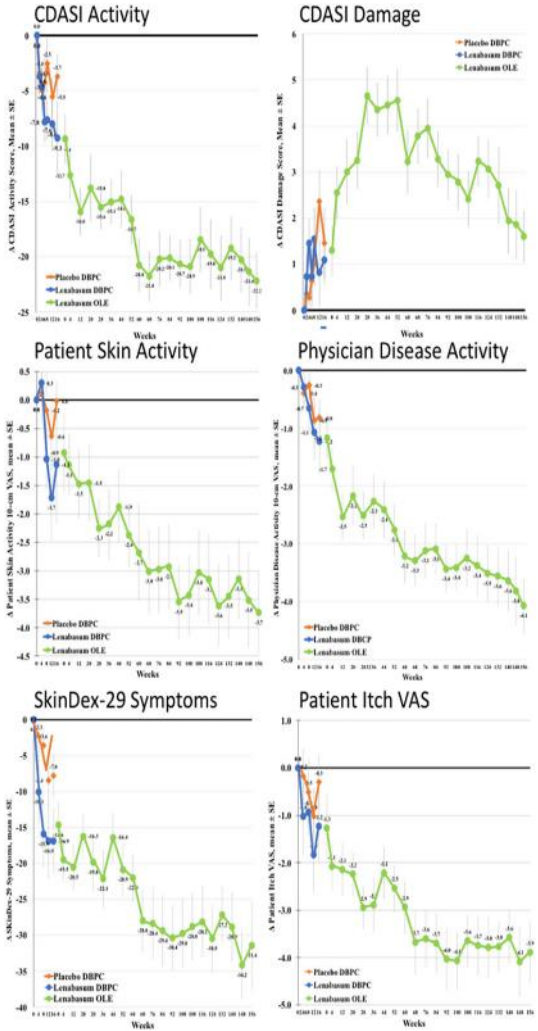
Results



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Conclusion

- Lenabasum continues to have a favorable safety and tolerability profile in the OLE of the Phase 2 trial JBT101-DM-001 with no serious AEs or study discontinuations related to lenabasum.
- The CDASI activity score and multiple other physician and patient-reported outcomes improved and have remained stable, showing durability of improvement in these patients with refractory skin disease.
- Skin damage was reversible and began to improve once skin activity stabilized.
- The limitations of attributing this improvement to lenabasum in the setting of open-label dosing is acknowledged.
- These data support further testing of lenabasum for the treatment of DM, and a Phase 3 study of lenabasum in DM is ongoing.

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Vielen Dank für die Aufmerksamkeit

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