Appropriate Use of Rescue Medications

Permitted and Prohibited Medications

Consistency Across Disease Measures

Mar 2024

Rescue 1: Met Clinical Worsening Criteria

Background

- Participant with moderate skin and muscle disease at baseline
- After 12 weeks, skin had worsened, reflected in CDASI and EMGA
- **1st occurrence of meeting protocol worsening criteria**

> Global Extramuscular Activity-VAS worsened ≥ 2 cm and CDASI Activity Score worsening of 6 points and clinically meaningful worsening in the opinion of the investigator

  - ✓ Informed Medical Monitor
- Returned for an unscheduled visit 3 weeks later
  - ✓ **2nd occurrence of meeting *the same* protocol worsening criteria**
- Investigator initiated rescue therapy with increased corticosteroids and intends to return dose to baseline

	Baseline	Week 12	Week 15
CDASI-A	23	30	39
EMGA	4.0	6.2	7.1

Key Messages

- Patient met, per protocol, the same criteria on 2 occasions at least 3 weeks apart
- If needed, patient should return for an unscheduled visit to complete disease activity assessments
- Investigator informed Medical Monitor (as requested)
- Return to baseline dose as soon as clinically warranted

Rescue 2: Clinical Worsening Not Meeting Criteria

Background

- Participant with severe skin disease at baseline
- At Week 12 skin disease slightly worsened
- Clinical worsening criteria difficult to meet given severe baseline disease activity
- PI appropriately reached out to medical monitor to discuss the participant's situation and the next steps for clinical management
- PI and medical monitor agreed rescue therapy was appropriate

	Baseline	Week 12
PhGA VAS	7.5	8.9
PtGA VAS	6.9	7.4
CDASI-A	34	37
EGMA	8.5	9.5

Key Messages

- There are instances where a patients worsening does not meet criteria, but there is a clear picture of worsening of disease
- Medical monitor should be contacted so that there is a better understanding of the clinical picture and the course of action the investigator will take for the patient
- Return to baseline dose as soon as clinically warranted

Rescue 3: Insufficiently Documented Rescue Therapy

Background

- Mild muscle and moderate skin involvement
- At the visit when rescue was initiated, CSMs had improved, including CDASI
- Corticosteroid rescue was initiated based on vague description of the patient "not doing well" despite relative improvements across disease assessments
- Pt feels disease is not improving and wants rescue
- Medical monitor was not notified

	Baseline	Week 18
PhGA VAS	4.6	4.2
HAQ	1	0.75
PtGA VAS	6.8	7.0
MMT-8	138	140
CDASI-A	25	18

Key Messages

- To better understand the clinical picture and management decision of the investigator, the patient should be brought back for an unscheduled visit to complete disease activity assessments and ***medical monitor should be notified before the rescue is initiated*** (unless urgent)
- Appropriate per protocol use of rescue includes meeting clinical worsening criteria or reaching out to the medical monitor to discuss further management of the patient
- Justification of why a patient needs rescue therapy is to be documented in the EDC
- Return to baseline dose as soon as clinically warranted

Permitted and Prohibited Medications

Changes in medications can increase placebo responses and endpoint variability

Remind your patients:

- **Do not use a new medicine without contacting the site**
- **To let other providers know the patient is participating in a clinical trial and to inform you, the investigator, of potential medication changes**
- **Avoid "self-medicating" through use of a prior medications/steroids (oral or topical) they have at home – call the site**

Reminder for self:

- **Ask about new medications and check if any ongoing medications have been stopped**
- **Check for end-date of any short-term/prn medications (e.g., steroids, NSAIDs, opioids, topicals) used for non-DM indications**
- **Corticosteroids**
  - ✓ Permitted per protocol for short term "non-DM" use (systemic or topical)
  - ✓ Topical steroids for scalp are permitted if used at baseline, but should not be initiated during the study
  - ✗ Topical steroids for other body regions are prohibited during the study
- **NSAIDs and Opioids**
  - ✓ Stable NSAID and opioid use is permitted if used at baseline
  - ✓ PRN use is permitted; monitor and ask about regular use and end-dates
  - ✗ Initiation of chronic NSAIDs or opioids is not permitted
- **Permitted Immunosuppressants/Immunomodulators**
  - ✓ Dose should remain constant throughout the study, unless safety/tolerability issue
  - ✓ Be mindful if changing frequency (e.g., twice-a-day to once-a-day); total daily dose must remain constant
  - ✗ Reducing the dose based on observed clinical improvement during the study is not permitted

High Quality and Complete Assessments

Reminder:

- **Every assessment should be scored based on the day of visit. For MDAAT and PhGA-VAS review previous visit for anchoring. PhGIC is compared to start of study.**
- **Global assessments (MDAAT Global Activity-VAS and PhGA-VAS) are based off a holistic evaluation of the patient's disease activity during that visit, including as reflected in other day-of clinical assessments**

Priovant regularly reviews screening and blinded on-study data for completeness and quality. Some common issues we have noted to be mindful of:

MDAAT

- EMGA-VAS not reflecting the extent of skin disease noted on CDASI
  - E.g., a CDASI of 21 with an EMGA-VAS of < 1 cm
- MDAAT muscle VAS scored, but components not scored
  - E.g., MDAAT-muscle VAS = 5.0 cm, but MDAAT-muscle – myositis inflammation = 0/0/0

PhGA

- The PhGA should be scored last, after review of all systems (including MDAAT scoring)
  - E.g., inconsistent to score PhGA of 6.0 cm, with EMGA of 3.5 cm and MDAAT-muscle of 4.0 cm

MDI

- If screening value is > 5 cm, is there too much irreversible damage to show a response to a new treatment?


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Back Up

Clinical Worsening

Clinical worsening is defined as meeting at least 1 of the following criteria compared to **baseline**:

1) PhGA-VAS value worsened ≥ 2 cm and MMT-8 score worsened ≥ 10% and clinically meaningful worsening in the opinion of the investigator; **OR**

2) Global Extramuscular Activity-VAS worsened ≥ 2 cm and CDASI Activity Score worsening of 6 points and clinically meaningful worsening in the opinion of the investigator; **OR**

3) Global Extramuscular Activity-VAS worsened ≥ 2 cm and at least 1 extramuscular organ-specific MDAAT VAS worsened ≥ 2 cm and clinically meaningful worsening in the opinion of the

Before Visit 5 (Week 12):
If one criteria is met, a single burst of corticosteroid is allowed (≤ 60mg, ≤ 7 days, end by Visit 5), if needed

After Visit 5 (Week 12):
If same criteria is met 2 consecutive visits, at least 3 weeks apart, rescue therapy is allowed, if needed

Published Clinical Worsening (Flare) Criteria

1) PhGA-VAS worsening by ≥2 cm and worsening on MMT-8 by ≥ 20%; **or**
2) Extramuscular organ disease activity worsening by ≥ 2 cm; **or**
3) Any 3 of 6 IMACS CSMs worsening by ≥ 30%

Oddis CV et al. (2005)[1]

1. Oddis CV et al. International consensus guidelines for trials of therapies in the idiopathic inflammatory myopathies. Arthritis Rheum 52, 2607–2615 (2005).

EDC – CW CRF

Upcoming EDC update: CW CRF will only indicate whether the calculations of each criterion meet or does not meet the criteria. If the calculations meet criterion and if a participant requires a single burst of corticosteroids (before Week 12) or a rescue (after Week 12), indicate the change of medication in the Dermatomyositis Prior and Concomitant Medications CRF.

	Prior Visit	This Visit	Derived Message
V3 and V4	NA	Yes	The participant meets clinical worsening at this visit. If needed, a single course of corticosteroids is permitted, and if dosed, the Dermatomyositis Prior and Concomitant Medications eCRF should be completed.
V3 and V4	NA	No	The participant does not meet clinical worsening at this visit.
V5 and beyond	Yes or No	No	The participant does not meet clinical worsening at this visit.
V5 and beyond	Yes	Yes	The participant meets clinical worsening at this visit and the prior visit. If needed, rescue therapy is permitted, and if dosed, the Dermatomyositis Prior and Concomitant Medications eCRF should be completed.
V5 and beyond	No	Yes	The participant meets clinical worsening at this visit but not the prior visit. Rescue therapy is not permitted, please reach out to Medical Monitor.
V5 and beyond	Yes (diff criterion)	Yes (diff criterion)	The participant meets a different clinical worsening criterion at this visit from the prior visit. Rescue therapy is not permitted, please reach out to Medical Monitor.
UNS	N/A	Yes	The participant meets clinical worsening at this visit. Before Visit 5 (Week 12), a single course of corticosteroids is permitted, if needed. After Visit 5 (Week 12), rescue therapy **(if needed)** is permitted if same clinical worsening criteria is met at two consecutive visits 3 weeks apart. For all rescue medications, complete the Dermatomyositis Prior and Concomitant Medications eCRF.
UNS	N/A	No	The participant does not meet clinical worsening at this visit.

EDC – Rescue Therapy

Any change in medication, including rescue therapy, should be captured in the Dermatomyositis Prior and Concomitant Medications CRF

Is this a rescue medication during the Blinded Treatment Period? **Yes** or **No**

If Yes, you must choose reason for rescue therapy:

- **Met clinical worsening criteria**
- **Did not meet clinical worsening criteria but needed rescue** → Specify the reason for the rescue needed in free text. Enter symptoms, lab changes, or specific conditions that warranted a rescue therapy.