# 2016 ACR/EULAR Criteria for Minimal, Moderate and Major Clinical Response for Adult Dermatomyositis and Polmyositis and Juvenile Dermatomyositis

The ACR-EULAR Myositis Response Criteria Project Steering Committee

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# Definition of improvement for adult and juvenile DM/PM clinical trials

3 of any 6 core set measures improved ≥ 20%, with no more than 2 worse by ≥ 25% (which cannot include MMT)

| | IMACS core set measure | PRINTO core set measure |
|---|---|---|
| Physician global activity | Likert or VAS | Likert or VAS |
| Patient/parent global activity | Likert or VAS | Likert or VAS |
| Muscle strength | MMT | CMAS |
| Physical function | HAQ or CHAQ | CHAQ |
| Laboratory assessment | Enzymes | x |
| Extraskeletal muscle disease | Yes | x |
| Global disease activity tool | x | DAS |
| Health-related quality of life | x | CHQ-PhS |



*Rider L et al. Arthritis Rheum 2004; Ruperto N et al., Arthritis Care Res 2010*

# Definition of improvement for adult and juvenile DM/PM clinical trials

**PRELIMINARY**

and therefore

# ACR-EULAR PROJECT TO DEVELOP NEW RESPONSE CRITERIA FOR JDM AND ADULT DM/PM

# Specific aims of the project

- To develop definitions of improvement (DOIs) in adult DM, PM and in juvenile DM for therapeutic trials
  - Minimal, moderate and major improvement
- Response criteria in myositis
  - Consensus driven
  - Data driven
  - Prospectively validated in clinical trials

# Development of new response criteria

- The same Core Set Measures as for preliminary definition were used

- New definitions to formulate improvement were developed

# Steps to develop new response criteria

- Step 1: Expert survey on meaningful clinical improvement in the core set measures
- Step 2: Creation of patient profiles from natural history studies and open label trials
- Step 3: Rating of patient profiles and achieving consensus on improvement on profiles – consensus ratings as gold standard
- Step 4: Drafting the definitions to test
- Step 5: Definitions evaluated on profiles and externally validated on 2 randomized controlled trials
- Step 6: Examine performance of top candidate DOIs for myositis at consensus conference and reach consensus on DOI

# Definitions to Test

## Three types of traditional (categorical) definitions

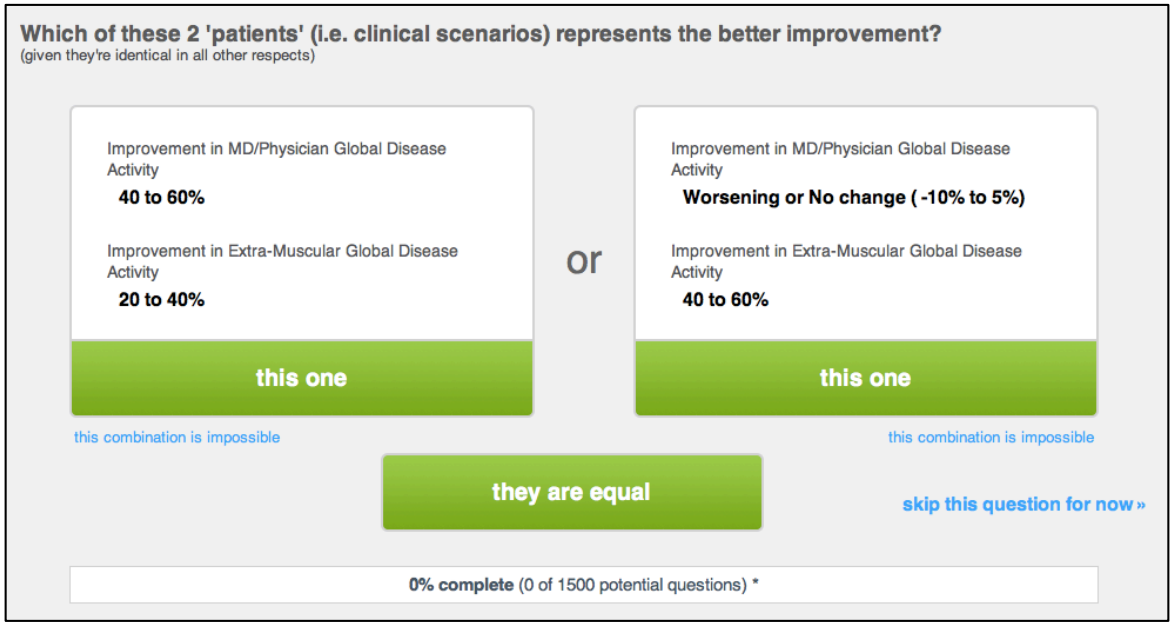
1. Previously published definitions
2. Newly drafted definitions based on expert survey
3. Weighted definitions

## Three hybrid (continuous) definitions: New

4. Logistic regression definitions
5. Conjoint analysis definitions using 1000Minds
6. Weighted hybrid definitions: applying weights to CSMs
    - Hybrid definitions:
        - Calculate a total improvement score
        - Cut offs for minimal, moderate and major improvement

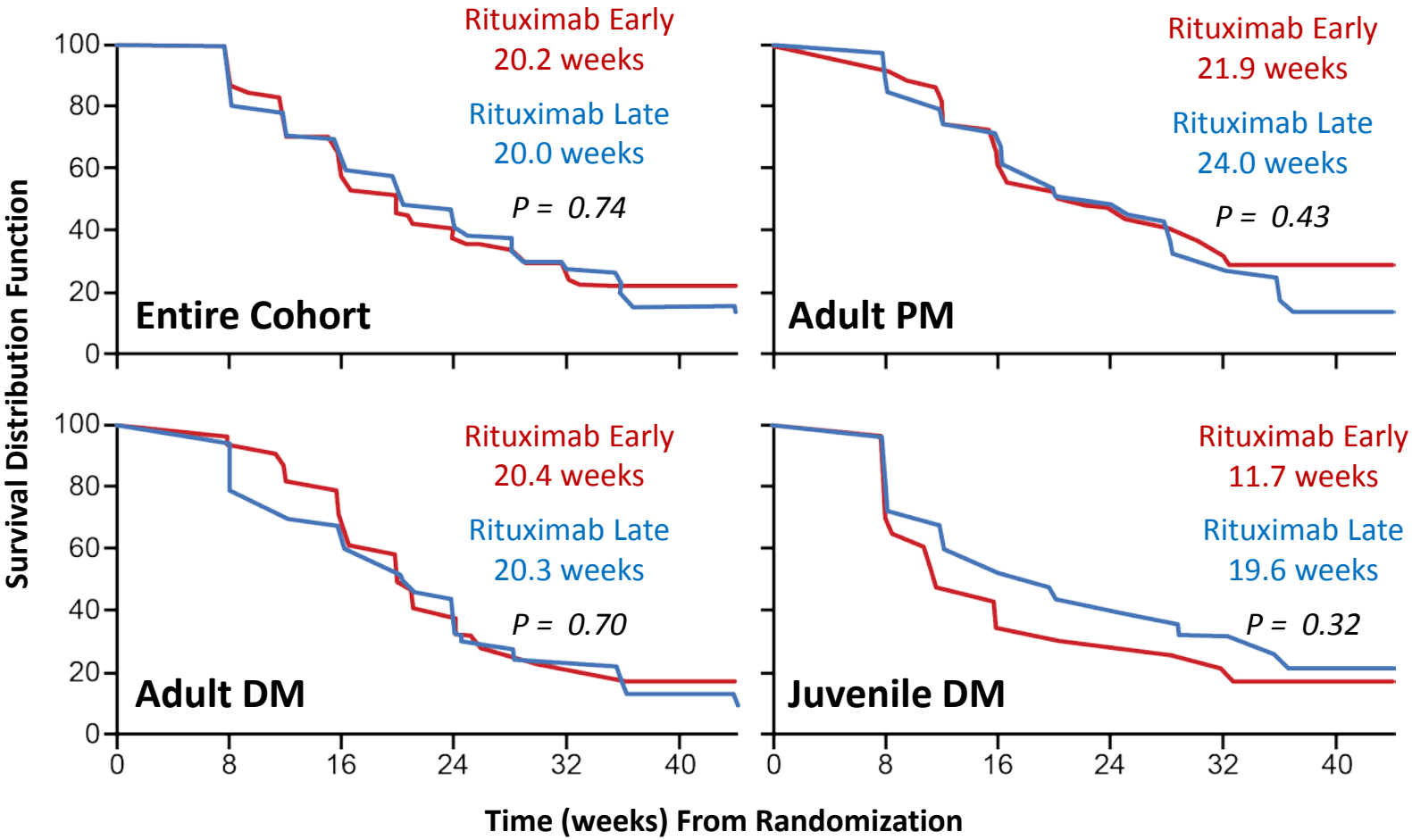
# 1000Minds survey to develop conjoint analysis DOIs

- Conjoint Analysis used to discover the relative importance of the various core set measures and different levels within each core set measure
- Pairwise-ranking of clinical scenarios each defined by degree of change in 2 core set measures only




- Repeat with different pairs of clinical scenarios until enough information about experts' preferences collected to estimate weights representing the relative importance of the core set measures
- Separate exercises completed for Adult IMACS, Peds IMACS and PRINTO CSMs

# Primary Endpoint in RIM Trial: No Difference in Time to Response (DOI)

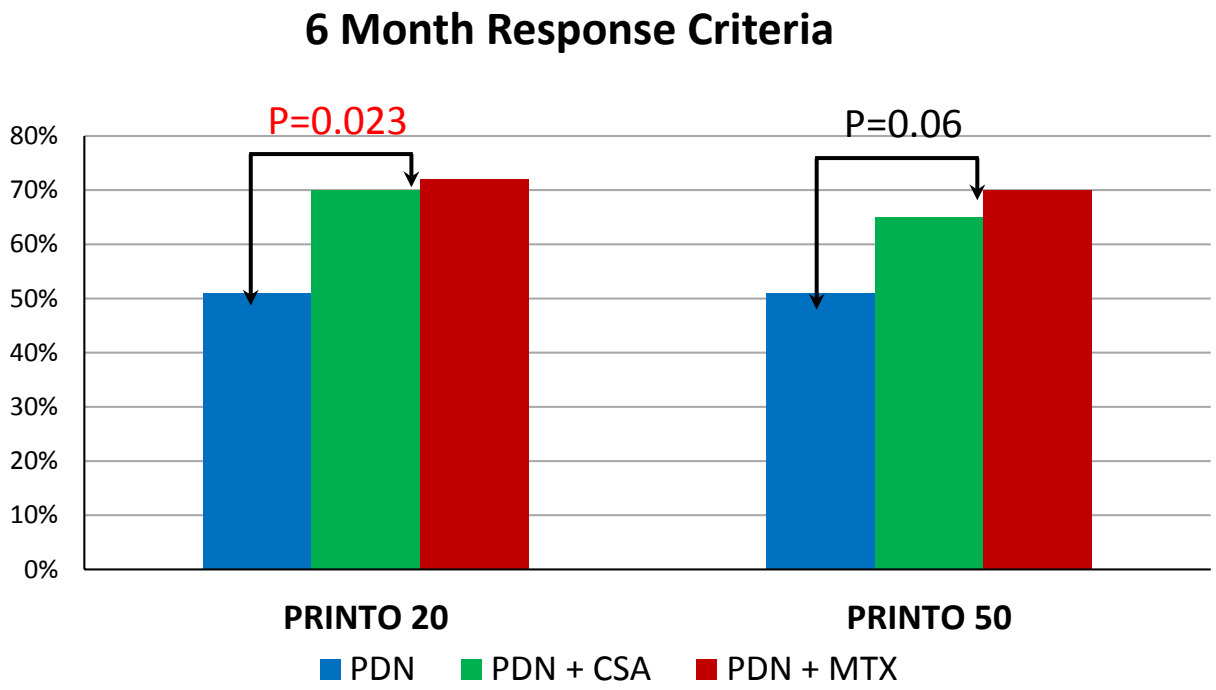



In response criteria project, examined MD assessment of improvement at week 24

*Oddis CV et al., Arthritis Rheum 2013;65(2):314-24.*

# PRINTO New Onset Juvenile DM Trial

- To determine the best treatment regimen associated with the lowest occurrence of flare/drug toxicity in ***new onset Juvenile DM*** randomised in an open fashion:
  - **Prednisone** (PDN) or
  - **Prednisone** plus **cyclosporine A** (CSA) or
  - **Prednisone** plus **methotrexate** (MTX)




In response criteria project, difference between treatment arms at month 6 was examined

*Ruperto N et al.* Lancet 2015;in press

# Consensus Conference – June 2014

- **DOIs:** 17 adult and 14 paediatric candidate definitions had high AUC, sensitivity and specificity
- **Experts for consensus conference**
  - US, Europe, Canada, S. America participants
  - Adult and paediatric myositis experts working groups: rheumatologists, neurologists, dermatologist
  - Separate for adult and paediatric experts and combined session
- **Goal:** To weigh the candidate definitions and their performance characteristics and develop CONSENSUS
  - Several rounds of nominal group techniques to select best DOIs
  - Ranking these candidate DOIs was mainly a clinical decision, as the performance characteristics were similar

# 2016 ACR/EULAR Response Criteria for JDM and Adult DM/PM: Validated, Sensitive Endpoint for Future Therapeutic Trials

| Core set measures | Level of absolute % change in core set measures (improvements) | Improvement score for each level |
|---|---|---|
| Physician Global Disease Activity | Worsening or No change ( -ve change to ≤ 5%) | 0 |
| | > 5% up to ≤ 15% | 7.5 |
| | > 15% up to ≤ 25% | 15 |
| | > 25% up to ≤ 40% | 17.5 |
| | > 40% | 20 |
| Parent or Patient Global Disease Activity | Worsening or No change ( -ve change to ≤ 5%) | 0 |
| | > 5% up to ≤15% | 2.5 |
| | >15% up to ≤ 25% | 5 |
| | > 25% up to ≤ 40% | 7.5 |
| | > 40% | 10 |
| Muscle Strength (MMT) or Childhood Myositis Assessment Scale (CMAS) | Worsening or No change ( -ve change to ≤ 2%) | 0 |
| | > 2% up to ≤ 10% | 10 |
| | > 10% up to ≤ 20% | 20 |
| | > 20% up to ≤ 30% | 27.5 |
| | > 30% | 32.5 |
| Physical Function (CHAQ or HAQ) | Worsening or No change ( -ve change to ≤ 5%) | 0 |
| | > 5% up to ≤ 15% | 5 |
| | > 15% up to ≤ 25% | 7.5 |
| | > 25% up to ≤ 40% | 7.5 |
| | > 40% | 10 |
| Muscle enzyme or CHQ-PhS (HR-QoL) | Worsening or No change ( -ve change to ≤ 5%) | 0 |
| | > 5% up to ≤ 15% | 2.5 |
| | > 15% up to ≤ 25% | 5 |
| | > 25% up to ≤ 40% | 7.5 |
| | > 40% | 7.5 |
| Extramuscular Global or Disease Activity Score | Worsening or No change ( -ve change to ≤ 5%) | 0 |
| | > 5% up to ≤ 15% | 7.5 |
| | > 15% up to ≤ 25% | 12.5 |
| | > 25% up to ≤ 40% | 15 |
| | > 40% | 20 |
| **Total Improvement Score (Scale 0-100)** | | |

**Minimal Improvement ≥ 20 & 30, Moderate ≥ 40 & 45, Major ≥ 60 & 70 for JDM and Adult DM/PM**

*Rider…Ruperto A&R ARD 2017; Aggarwal…Rider A&R ARD 2017*

# Relative % change vs. absolute % change examined for each type of drafted definitions

$$\text{Relative \% change} = \frac{\text{Start value} - \text{End value}}{\text{Start value}} \times 100$$

$$\text{Absolute \% change} = \frac{\text{Start value} - \text{End value}}{\text{Range}} \times 100$$

| *Patient* | *Change in MD global (0-100) on Tx* | *Relative % change* | *Absolute % change* |
|---|---|---|---|
| A | MD global 20 to 10 | 50% | 10% |
| B | MD global from 90 to 80 | 11% | 10% |

# Performance Characteristics for Adult DM/PM of Top Consensus Definition – Conjoint Analysis Absolute % Change Model

High sensitivity, specificity and AUC in patients profiles and in the RIM trial, with the exception of major improvement category

| Adult IMACS Profiles | | | |
|---|---|---|---|
| **Improvement Category** | **Sensitivity** | **Specificity** | **AUC** |
| Minimal | 85% | 92% | 0.89 |
| Moderate | 90% | 96% | 0.93 |
| Major | 92% | 98% | 0.95 |
| **Adult DM/PM Patients in RIM Trial** | | | |
| **Improvement Category** | **Sensitivity** | **Specificity** | **AUC** |
| Minimal | 97% | 46% | 0.72 |
| Moderate | 93% | 58% | 0.76 |
| Major | 65% | 72% | 0.68 |
| **Improvement Category** | **DOI Improved (MD Change Median)** | **DOI Not Improved (MD Change Median)** | **P-value** |
| Minimal | 2.00 | 4.00 | <0.0001 |
| Moderate | 2.00 | 3.00 | <0.0001 |
| Major | 2.00 | 3.00 | <0.0001 |

# Performance Characteristics for Juvenile DM of Top Consensus Definition – Conjoint Analysis Absolute % Change Model

High sensitivity, specificity and AUC in patients profiles and trials.

| Pediatric IMACS and PRINTO Profiles | | | |
|---|---|---|---|
| **Improvement Category** | **Sensitivity** | **Specificity** | **AUC** |
| Minimal | 85-91% | 91-98% | 0.91-0.93 |
| Moderate | 94% | 97-98% | 0.95-0.96 |
| Major | 92-96% | 86-89% | 0.90-0.91 |
| **JDM Patients in PRINTO Trial** | | | |
| **Improvement Category** | **IMACS and PRINTO P value** | | |
| Minimal | 0.009 - 0.038 | | |
| Moderate | 0.023 – 0.057 | | |
| Major | 0.331 – 0.341 | | |
| **JDM Subjects in RIM Trial** | | | |
| **Improvement Category** | **Sensitivity** | **Specificity** | **AUC** |
| Minimal | 90% | 86% | 0.88 |
| Moderate | 89% | 80% | 0.82 |
| Major | 50% | 85% | 0.68 |
| **Improvement Category** | **DOI Improved (MD Change Median)** | **DOI Not Improved (MD Change Median)** | **P-value** |
| Minimal | 2.00 | 4.00 | <0.0001 |
| Moderate | 2.00 | 3.00 | <0.0001 |
| Major | 2.00 | 2.50 | 0.008 |

# Example of usage

| *Core set measures* | *Level of absolute % change in core set measures* | *Improvement score for each level* |
|---|---|---|
| Improvement in Physician Global Disease Activity **From 50 to 40 = 10%** | Worsening or No change ( -ve change to ≤5%) | 0 |
| | **>5% up to ≤15%** | **7.5** |
| | >15% up to ≤25% | 15 |
| | >25% up to ≤40% | 17.5 |
| | >40% | 20 |
| Improvement in Patient/Parent Global Disease Activity **From 60 to 48 = 12%** | Worsening or No change ( -ve change to ≤5%) | 0 |
| | **>5% up to ≤15%** | **2.5** |
| | >15% up to ≤25% | 5 |
| | >25% up to ≤40% | 7.5 |
| | >40% | 10 |
| Improvement in Muscle Strength (MMT or CMAS) **From 66 to 75 = 11%** | Worsening or No change ( -ve change to ≤2%) | 0 |
| | >2% up to ≤10% | 10 |
| | **>10% up to ≤20%** | **20** |
| | >20% up to ≤30% | 27.5 |
| | >30% | 32.5 |

# Example of usage

| *Core set measures* | *Level of absolute % change in core set measures* | *Improvement score for each level* |
|---|---|---|
| Improvement in Physical Function (HAQ/CHAQ) **From 2.0 to 1.2 = 27%** | Worsening or No change ( -ve change to ≤5%) | 0 |
| | >5% up to ≤15% | 5 |
| | >15% up to ≤25% | 7.5 |
| | **>25% up to ≤40%** | **7.5** |
| | >40% | 10 |
| Improvement in Muscle enzyme or CHQ-PhS **From 1500 to 800 = 18%** | Worsening or No change ( -ve change to ≤5%) | 0 |
| | >5% up to ≤15% | 2.5 |
| | **>15% up to ≤25%** | **5** |
| | >25% up to ≤40% | 7.5 |
| | >40% | 7.5 |
| Improvement in Extramuscular global or DAS **From 55 to 20 = 35%** | Worsening or No change ( -ve change to ≤5%) | 0 |
| | >5% up to ≤15% | 7.5 |
| | >15% up to ≤25% | 12.5 |
| | **>25% up to ≤40%** | **15** |
| | >40% | 20 |

# Example of usage

| *Core set measures* | *Level of absolute % change in core set measures* | *Improvement score for each level* |
|---|---|---|
| Improvement in Physician Global Disease Activity **From 50 to 40 = 10%** | Worsening or No change ( -ve change to ≤5%) | 0 |
| | **>5% up to ≤15%** | **7.5** |
| | >15% up to ≤25% | 15 |
| | >25% up to ≤40% | 17.5 |
| | >40% | 20 |
| Improvement in Patient/Parent Global Disease Activity **From 60 to 48 = 12%** | Worsening or No change ( -ve change to ≤5%) | 0 |
| | **>5% up to ≤15%** | **2.5** |
| | >15% up to ≤25% | 5 |
| | >25% up to ≤40% | 7.5 |
| | >40% | 10 |
| Improvement in Muscle Strength (MMT OR CMAS) **From 66 to 75 = 11%** | Worsening or No change ( -ve change to ≤2%) | 0 |
| | >2% up to ≤10% | 10 |
| | **>10% up to ≤20%** | **20** |
| | >20% up to ≤30% | 27.5 |
| | >30% | 32.5 |
| Improvement in Physical Function (HAQ/CHAQ) **From 2.0 to 1.2 = 27%** | Worsening or No change ( -ve change to ≤5%) | 0 |
| | >5% up to ≤15% | 5 |
| | >15% up to ≤25% | 7.5 |
| | **>25% up to ≤40%** | **7.5** |
| | >40% | 10 |
| Improvement in Muscle enzyme OR CHQ-PhS **From 1500 to 800 = 18%** | Worsening or No change ( -ve change to ≤5%) | 0 |
| | >5% up to ≤15% | 2.5 |
| | **>15% up to ≤25%** | **5** |
| | >25% up to ≤40% | 7.5 |
| | >40% | 7.5 |
| Improvement in Extramuscular global OR DAS **From 55 to 20 = 35%** | Worsening or No change ( -ve change to ≤5%) | 0 |
| | >5% up to ≤15% | 7.5 |
| | >15% up to ≤25% | 12.5 |
| | **>25% up to ≤40%** | **15** |
| | >40% | 20 |
| **Total Improvement Score in the patient (scale 0-100)** | | **57.5** |

Adult cut offs: Min = 20, Mod = 40, Maj = 60

Peds cut offs: Min = 30, Mod = 45, Maj = 70

Moderate improvement

# How to Apply Conjoint Analysis Hybrid DOI in Trials

| *Treatment A* | *Improvement Score* | *Improved [ cut offs = 20 ]* | | *Placebo* | *Improvement Score* | *Improved [cut offs = 20]* |
|---|---|---|---|---|---|---|
| Tx_Pt 1 | 88 | Yes | | Placebo_Pt 1 | 14 | No |
| Tx_Pt 2 | 76 | Yes | | Placebo_Pt 2 | 54 | Yes |
| Tx_Pt 3 | 14 | No | | Placebo_Pt 3 | 13 | No |
| Tx_Pt 4 | 25 | Yes | | Placebo_Pt 4 | 64 | Yes |
| Tx_Pt 5 | 56 | Yes | | Placebo_Pt 5 | 10 | No |
| Tx_Pt 6 | 90 | Yes | | Placebo_Pt 6 | 9 | No |
| Tx_Pt 7 | 17 | No | | Placebo_Pt 7 | 12 | No |
| Tx_Pt 8 | 58 | Yes | | Placebo_Pt 8 | 34 | Yes |
| Tx_Pt 9 | 78 | Yes | | Placebo_Pt 9 | 19 | No |
| Tx_Pt 10 | 65 | Yes | | PlaceboPt 10 | 12 | No |
| Mean Total Improvement Score | 56.7 | 8/10 minimally improved | | Mean Total Improvement Score | 24.1 | 3/10 minimally improved |

Cut offs for adults: Minimal improvement ≥ 20;
Mean Total Improvement Score: Treatment A (56.7) vs. Placebo (24.1): < 0.001
Percentage of patients improved: Treatment A (80%) vs. Placebo (30%): = 0.02

# Final consensus definition of improvement

- Uses absolute % change in core set measures (CSMs)
- Conjoint analysis (1000minds) provides different weights to the various CSMs
  - MMT/CMAS > MD Global Activity > Extramuscular Global/DAS > Patient VAS > HAQ/CHAQ > Muscle enzymes/CHQ-PhS
- Uses same definition for adult DM/PM and juvenile DM
  - Different optimal cut points for each
- Defines criteria for minimal, moderate and major improvement
  - Major improvement is provisional for adult DM/PM
- Total improvement score is associated with magnitude of improvement
- Selected as a primary endpoint for future clinical trials
  - Pending approval from ACR/EULAR as final response criteria

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**Statistical Team**

- Rohit Aggarwal
- Brian Erman
- Nastaran Bayat
- Angela Pistorio
- Adam Huber
- Brian Feldman
- Howard Rockette
- Peter Lachenbruch
- Lisa Rider

**Conference Support**

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- Luca Villa
- Lara Poethig, MCI

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- Bob Goldberg, TMA
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- Patti Lawler, Cure JM
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- Ann M. Reed
- Kelly Rouster-Stevens
- Annet van Royen

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- Anthony A. Amato, Hector Chinoy, Lorinda Chung, Katalin Dankó, David Fiorentino, Ignacio Garcia de la Torre, Mark Gourley, Ingrid Lundberg, Frederick Miller, Chester Oddis, Paul Plotz, Ann Reed, Lisa Rider, Nicola Ruperto, Yeong Wook Song, Jiri Vencovsky

# Participants Who Contributed to the Core Set Measure Survey

- **Adult group:** (21 members)
  - Anthony Amato, Hector Chinoy, Lisa Christopher-Stine, Lorinda Chung, Robert Cooper, Lisa Criscione-Schreiber, Leslie Crofford, Mary E. Cronin, Katalin Dankó, Ignacio Garcia De la Torre, Patrick Gordon, James D. Katz, Andrew Mammen, Neil McHugh, Chet Oddis, Elena Schiopu, Albert Selva-O'Callaghan, Yeong Wook Song, Jiri Vencovsky, Gil Wolfe, Robert Wortmann

- **Pediatric group:** (26 members)
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# Summary of Participants in Patient Profile Ratings

- **Adult Group:** (60 members)

Rohit Aggarwal, Anthony A. Amato, Dana Ascherman, Richard Barohn, Olivier Benveniste, Jan De Bleecker, Jeffrey Callen, Christina Charles-Schoeman, Hector Chinoy, Lisa Christopher-Stine, Lorinda Chung, Robert Cooper, Leslie Crofford, Mary E. Cronin, Katalin Dankó, Sonye Danoff, Maryam Dastmalchi, Mazen Dimachkie, Steve DiMartino, Lyubomir Dourmishev, Floranne Ernste, David Fiorentino, Ignacio Garcia De la Torre, Takahisa Gono, Patrick Gordon, Mark Gourley, David Isenberg, Yasuhiro Katsumata, James D. Katz, John Kissel, Richard Leff, Todd Levine, Ingrid Lundberg, Andrew Mammen, Herman Mann, Galina Marder, Isabelle Marie, Neil McHugh, Joseph Merola, Frederick Miller, Chester Oddis, Marzena Olesinska, Nancy Olsen, Nicolo Pipitone, Sindhu Ramchandren, Seward Rutkove, Lesley Ann Saketkoo, Adam Schiffenbauer, Albert Selva-O'Callaghan, Samuel Katsuyuki Shinjo, Rachel Shupak, Yeong Wook Song, Katarzyna Swierkocka, Jiri Vencovsky, Marianne de Visser, Julia Wanschitz, Victoria Werth, Irene Whitt, Robert Wortmann, Steven Ytterberg

# Summary of Participants in Patient Profile Ratings

- **Pediatric Group:** (69 members)

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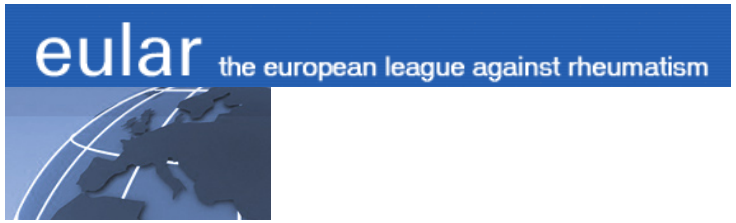




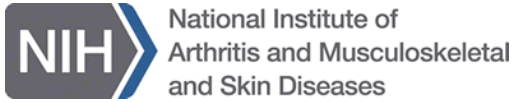







# Backup slides

# Performance Characteristics of Top 17 Candidate DOIs for Adult DM/PM brought to Consensus Conference

| RIM Trial (N=147) | | | | | | | |
|---|---|---|---|---|---|---|---|
| *Improvement Category* | *Improved N (%)* | *Sensitivity Mean (Range)* | *Specificity Mean (Range)* | *AUC Mean (Range)* | *DOI Improved Median MD Improvement Score (range[1])* | *DOI Not Improved Median MD Improvement Score (range[1])* | *P-value Mean (Range)* |
| Minimal | 119 (81%) | 85% (73%-97%) | 62% (46%-75%) | 0.73 (0.70-0.76) | 2 (2-2) | 3 (3-4) | <0.0001 (0.00-0.00) |
| Moderate | 73 (50%) | 80% (56%-93%) | 70% (58%-91%) | 0.75 (0.71-0.79) | 2 (2-2) | 3 (3-3) | <0.0001 (0.00-0.00) |
| Major | 20 (14%) | 64% (40%-80%) | 83% (72%-94%) | 0.73 (0.66-0.83) | 2 (1-2) | 3 (3-3) | <0.0001 (0.00-0.00) |

# Performance Characteristics of Top 14 Candidate DOIs for JDM brought to Consensus Conference

| | | PRINTO Trial (N=139) | | | RIM Trial (N=48) | | |
|---|---|---|---|---|---|---|---|
| *Improvement Category* | *Profile* | *Treatment (%) Mean (Range)* | *Control (%) Mean (Range)* | *P-Value Mean (Range)* | *DOI Improved, Median MD Improvement Score (range[1])* | *DOI Not Improved, Median MD Improvement Score (range[1])* | *P-value Mean (Range)* |
| Minimal | IMACS | 74% (70%-87%) | 56% (51%-77%) | 0.039 (0.009-0.120) | 2 (2-2) | 3 (3-4) | <0.0001 (0.000-0.000) |
| | PRINTO | 75% (71%-88%) | 56% (51%-77%) | 0.033 (0.011-0.080) | | | |
| Moderate | IMACS | 71% (66%-78%) | 53% (51%-68%) | 0.050 (0.011-0.191) | 2 (2-2) | 3 (3-3) | <.00001 (0.000-0.000) |
| | PRINTO | 71% (67%-80%) | 54% (51%-70%) | 0.052 (0.016-0.176) | | | |
| Major | IMACS | 62% (49%-66%) | 48% (40%-53%) | 0.177 (0.027-0.814) | 2 (1-2) | 3 (2-3) | 0.002 (0.000-0.011) |
| | PRINTO | 61% (53%-66%) | 50% (47%-55%) | 0.229 (0.106-0.472) | | | |

# Top 5 Adult DOIs from Consensus Conference

| Number | Category | % Change | Definition of Improvement |
|---|---|---|---|
| A1 | Conjoint Analysis | Absolute % Change | Conjoint Analysis Model 3 :<br>MINIMAL: Improvement Score ≥20<br>MODERATE: Improvement Score ≥40<br>MAJOR: Improvement Score ≥60 |
| A2 | Conjoint Analysis | Relative % Change | Conjoint Analysis Model 2:<br>MINIMAL: Improvement Score ≥30<br>MODERATE: Improvement Score ≥45<br>MAJOR: Improvement Score ≥65 |
| A3 | Conjoint Analysis | Relative % Change | Conjoint Analysis Model 1:<br>MINIMAL: Improvement Score ≥33<br>MODERATE: Improvement Score ≥55<br>MAJOR: Improvement Score ≥70 |
| A4 | Weighted definitions | Relative % Change | Improvement Score = 2X (MD Global % change) + (Patient Global % change) + 3X (MMT % change) + 1.5X (HAQ % change) + 1.5X (ExtraMusc % change) + Enzyme (% change)<br>MINIMAL: Improvement Score ≥100<br>MODERATE: Improvement Score ≥250<br>MAJOR: Improvement Score ≥400 |
| A5 | Logistic Regression | Relative % Change | Improvement Score = (MD Global % change) + (Patient Global % change) + (MMT % change) + (HAQ % change) + (ExtraMusc % change) + (Enzyme % change)<br>MINIMAL: Improvement Score ≥75<br>MODERATE: Improvement Score ≥150<br>MAJOR: Improvement Score ≥300 |

# Performance of Top Adult DOIs and other Consensus Decisions of the Adult Working Group

- Patient profiles: Sensitivity and specificity ≥ 85% minimal, AUC ≥ 0.89
- RIM trial: Physician assessment of improvement at week 24 differed ($P < 0.001$) when DOI improved vs not improved
- Adult Working Group experts uniformly agreed that the Major Definition of Improvement will be a Provisional or Draft Definition, due to limited data on major improvement in adult DM/PM
- Adult Working Group experts agreed to re-test the top 5 Definitions of Improvement in future studies and clinical trials
- Experts agreed to add the SF-36 as a quality of life measure, to have congruence with PRINTO measures for future clinical trials

# Top 6 Pediatric DOIs from Consensus Conference

| Number | Category | % Change | Definition of Improvement |
|---|---|---|---|
| P1 | Conjoint Analysis | Absolute % Change | Conjoint Analysis Model 3:<br>MINIMAL: Improvement Score ≥ 30<br>MODERATE: Improvement Score ≥ 45<br>MAJOR: Improvement Score ≥ 70 |
| P2 | Conjoint Analysis | Relative % Change | Conjoint Analysis Model 1:<br>MINIMAL: Improvement Score ≥ 33<br>MODERATE: Improvement Score ≥ 60<br>MAJOR: Improvement Score ≥ 80 |
| P3 | Conjoint Analysis | Relative % Change | Conjoint Analysis Model 2:<br>MINIMAL: Improvement Score ≥ 33<br>MODERATE: Improvement Score ≥ 55<br>MAJOR: Improvement Score ≥ 77 |

# Top 6 Pediatric DOIs from Consensus Conference

| Number | Category | % Change | Definition of Improvement |
|---|---|---|---|
| P4 | Weighted definition | Relative % Change | Improvement = at least 3.5 Improvement Points out of 10 Total Improvement Points, and no more than 1.5 Worsening Points, where MD Global=2 points; Parent Global = 1 point ; MMT or CMAS = 3 points; CHAQ = 1.5 points, ExtraMusc or DAS = 1.5 points, Enzyme or CHQ-PF50 = 1 point |
| | | | MINIMAL: Improvement Points given when CSM≥ 20%; Worsening Points given when CSM worse by >30% |
| | | | MODERATE: Improvement Points given when CSM≥ 50%; Worsening Points given when CSM worse by >30% |
| | | | MAJOR: Improvement Points given when CSM≥ 75%; Worsening Points given when CSM worse by >30% |
| P5 | Previously published | Relative % Change | MINIMAL: 3 of any 6 improved by ≥ 20%; no more than 1 worse by > 30%; which cannot be MMT/CMAS (Published PRINTO) |
| | | | MODERATE: 3 of any 6 improved by ≥ 50%; no more than 1 worse by > 30%; which cannot be MMT/CMAS (Published PRINTO) |
| | | | MAJOR: 3 of any 6 improved by ≥ 70%; no more than 1 worse by > 30%; which cannot be MMT/CMAS (Published PRINTO) |
| P6 | Logistic Regression | Absolute % Change | Improvement Score = (MD Global % change) + 0.5X (Parent Global % change) + 0.5X (ExtraMuscular or DAS % change) |
| | | | MINIMAL: Improvement Score ≥ 15 |
| | | | MODERATE: Improvement Score ≥ 30 |
| | | | MAJOR: Improvement Score ≥ 60 |

# Performance of Top Pediatric DOIs and Other Consensus Decisions of the Pediatric Working Group

- Patient profiles: Sensitivity and specificity ≥ 88% minimal, AUC ≥ 0.90, slight decrease for major improvement
- PRINTO Trial: Difference in treatment arms (Prednisone alone vs. Prednisone + MTX or Cyclosporin) generally significant ($P < 0.05$) for minimal and moderate improvement
- RIM trial: Physician assessment of improvement at week 24 differed ($P < 0.001$) when DOI improved vs not improved
- Pediatric Working Group experts agreed to re-test the top 6 Definitions of Improvement in future studies and clinical trials
- Participants agreed to have a joint IMACS-PRINTO DOI for JDM and to measure both IMACS and PRINTO core set measures in future myositis trials
  - Childhood Myositis Assessment Scale (CMAS) and MMT
  - Global tool - the Disease Activity Score (DAS) and Extramuscular Global Activity
  - Health-related quality of life - CHQ-PF50 and Muscle enzymes.