

Real-world and recent clinical trials in NDM show consistent myotonia improvements with mexiletine

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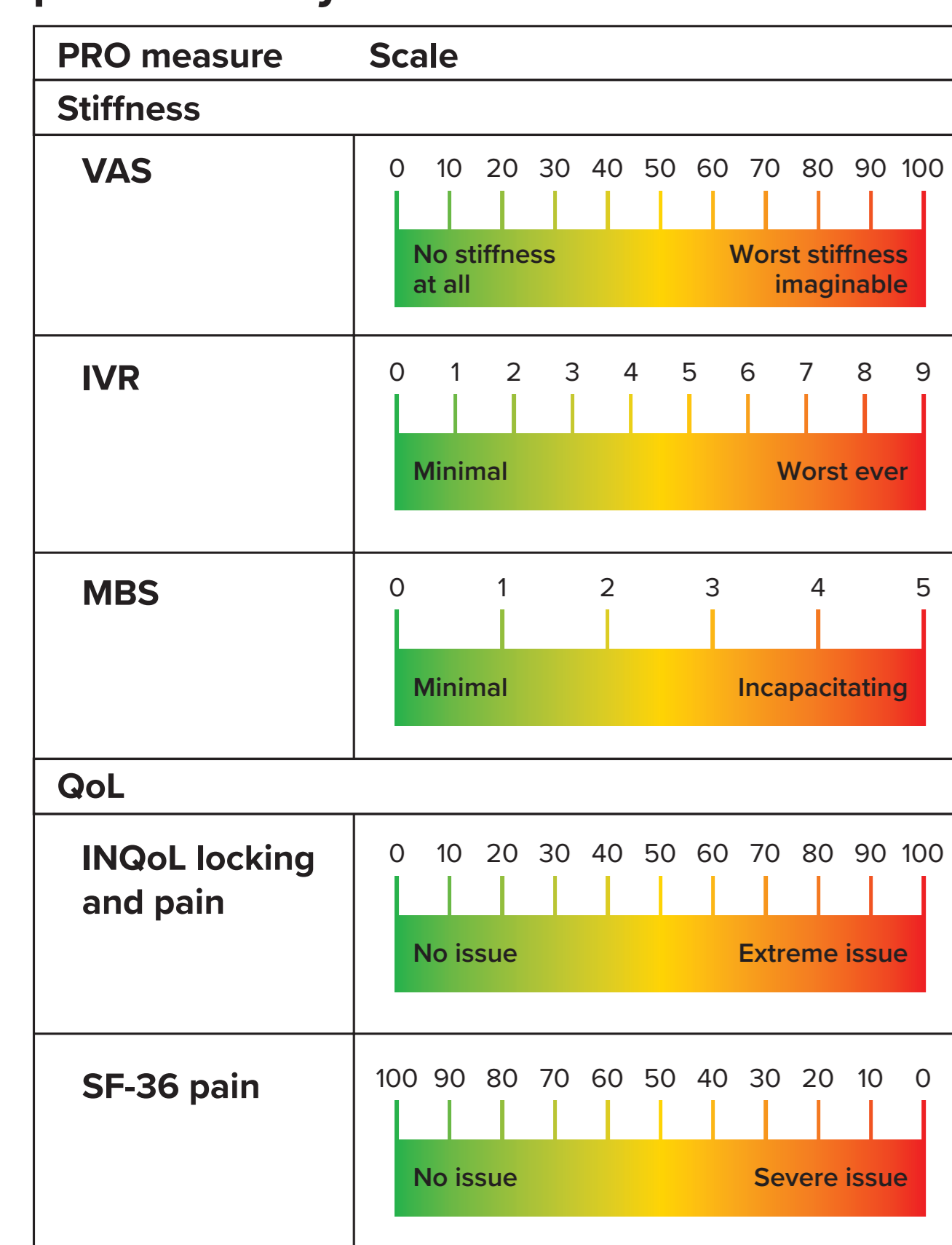
Introduction

- There is a growing body of patient-reported evidence encompassing subjective parameters of physical health and quality-of-life (QoL) that can help to inform real-world mexiletine use.
- However, individual studies contain low participant numbers and use different methodologies.
- To investigate signals of mexiletine efficacy, we reviewed key outcomes reported in three datasets evaluating treatment of adults with non-dystrophic myotonia (NDM): MYOMEX (N=25),¹ the Post Authorisation Safety Study (PASS; N=53),² and MEND (N=60).³

Methods

- Data for patient-reported outcomes (PRO) scoring including **stiffness** (Visual Analogue Scale [VAS],⁴ Interactive Voice Response [IVR],⁵ and Myotonia Behaviour Scale [MBS]⁶) and **quality-of-life** (QoL; Individualised QoL [INQoL] locking and pain,⁷ and pain questions from the 36-Item Short Form survey [SF-36]⁸) were examined across datasets from the three included trials¹⁻³ (**Figure 1**).
- Spearman correlations between baseline and post-mexiletine treatment data for myotonia-associated symptoms (stiffness, MBS) and QoL locking and pain were investigated.
- Changes were tested using the Wilcoxon signed rank test.

Figure 1. Scoring for patient-reported outcomes (PRO) used in the present analysis



- Improvement in VAS, IVR, MBS and INQoL indicated by **decreasing** score.
- Improvement in SF-36 indicated by **increasing** score.

D, day; EOS, end of study; RT, relaxation time; SD, standard deviation; V, visit.

Results

Study methodologies

- There were between-study methodological differences in study designs and comparators (**Table 1**).

Table 1. Characteristics of the three recent studies investigating mexiletine treatment in adult patients with NDM

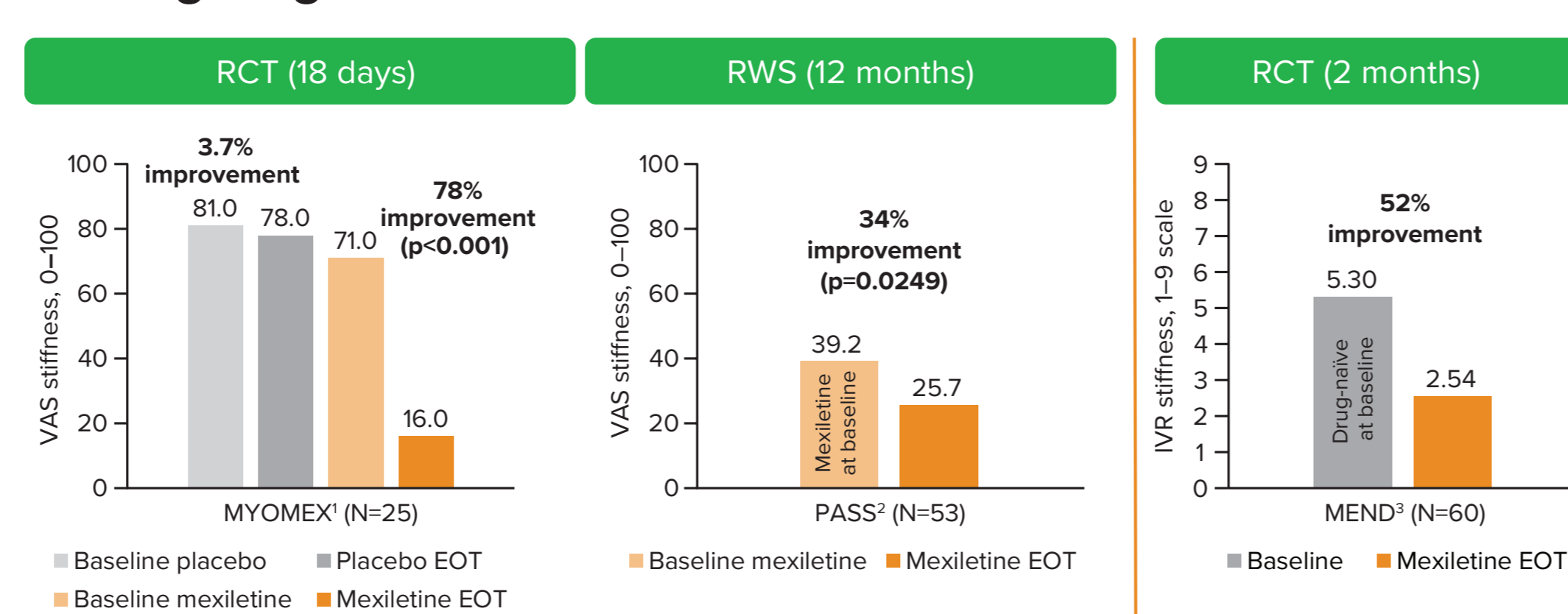
Study	MYOMEX (N=26) ¹	PASS (N=53) ²	MEND (N=60) ³
Design	Double-blind, crossover RCT	Prospective observational	Double-blind crossover RCT
Mexiletine dosage	600 mg/day max mexiletine hydrochloride	333 mg/day mean; 500 mg/day max mexiletine	600 mg/day max mexiletine hydrochloride
Comparator	Placebo	None	Lamotrigine
Treatment duration	18 days	12 months (interim analysis)	8 weeks

RCT, randomised controlled trial.

Consistent improvements in myotonia across studies

- Despite differences in study design between MYOMEX, PASS and MEND, consistent benefits were observed in patients receiving mexiletine in terms of patient-reported stiffness and MBS (**Figures 2, 3**).

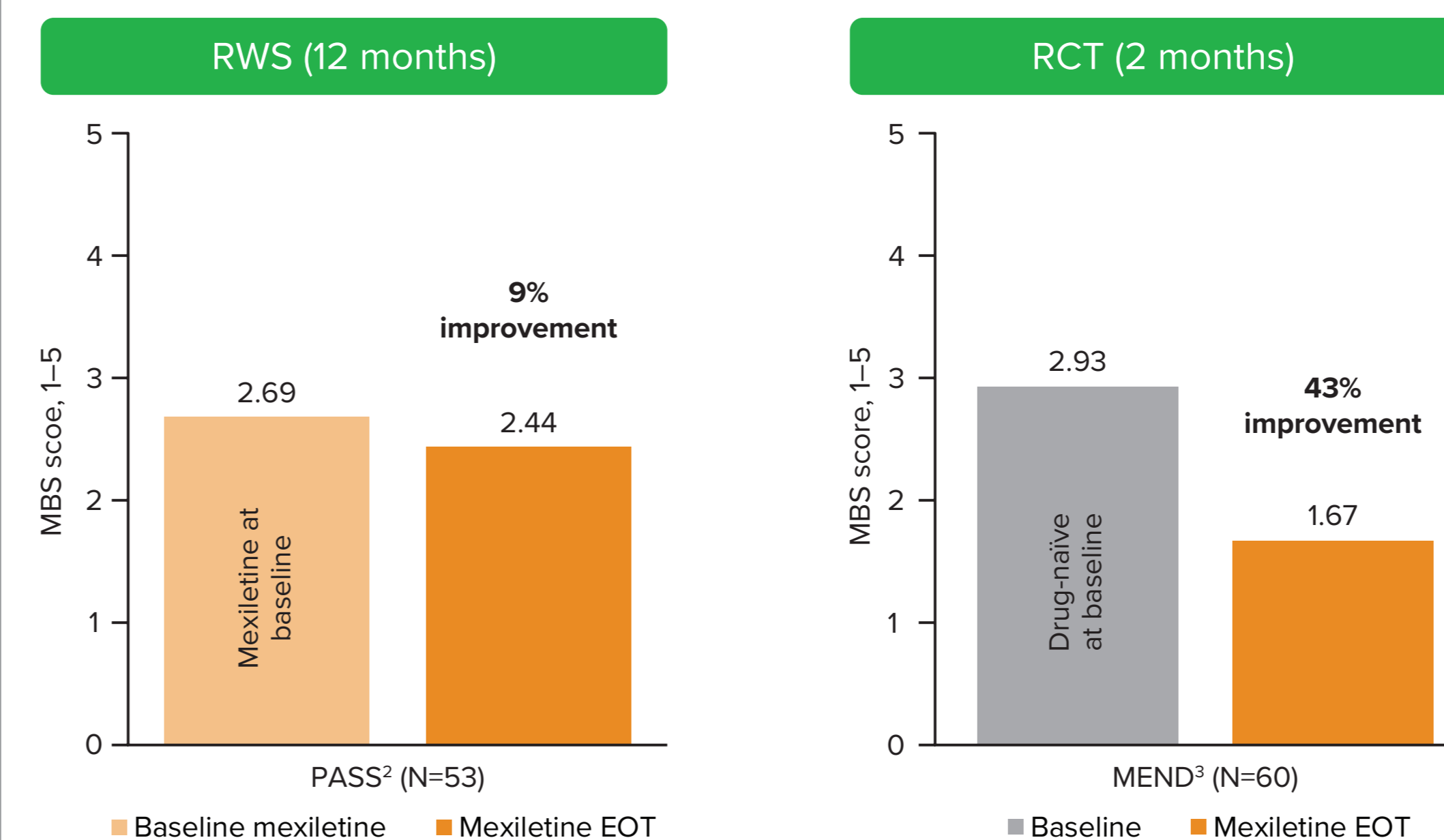
Figure 2. Stiffness scores as an outcome measure used to assess myotonia in patients with NDM: examples from three studies investigating mexiletine treatment



- In MYOMEX and MEND patients were drug-naïve at baseline, while in PASS they received mexiletine at baseline.
- Data shown summarise available patient-reported stiffness data across the trials, but should not be directly compared due to these differences.
- VAS stiffness was reported for MYOMEX and PASS; IVR stiffness was reported for MEND.
- Mexiletine treatment improved stiffness over the study periods even in patients who were already on treatment at baseline.

RCT, randomised controlled trial; RWS, real-world study; EOT, end of trial

Figure 3. The MBS has been developed to assess impact of myotonia on patient burden with NDM: examples from two studies with mexiletine



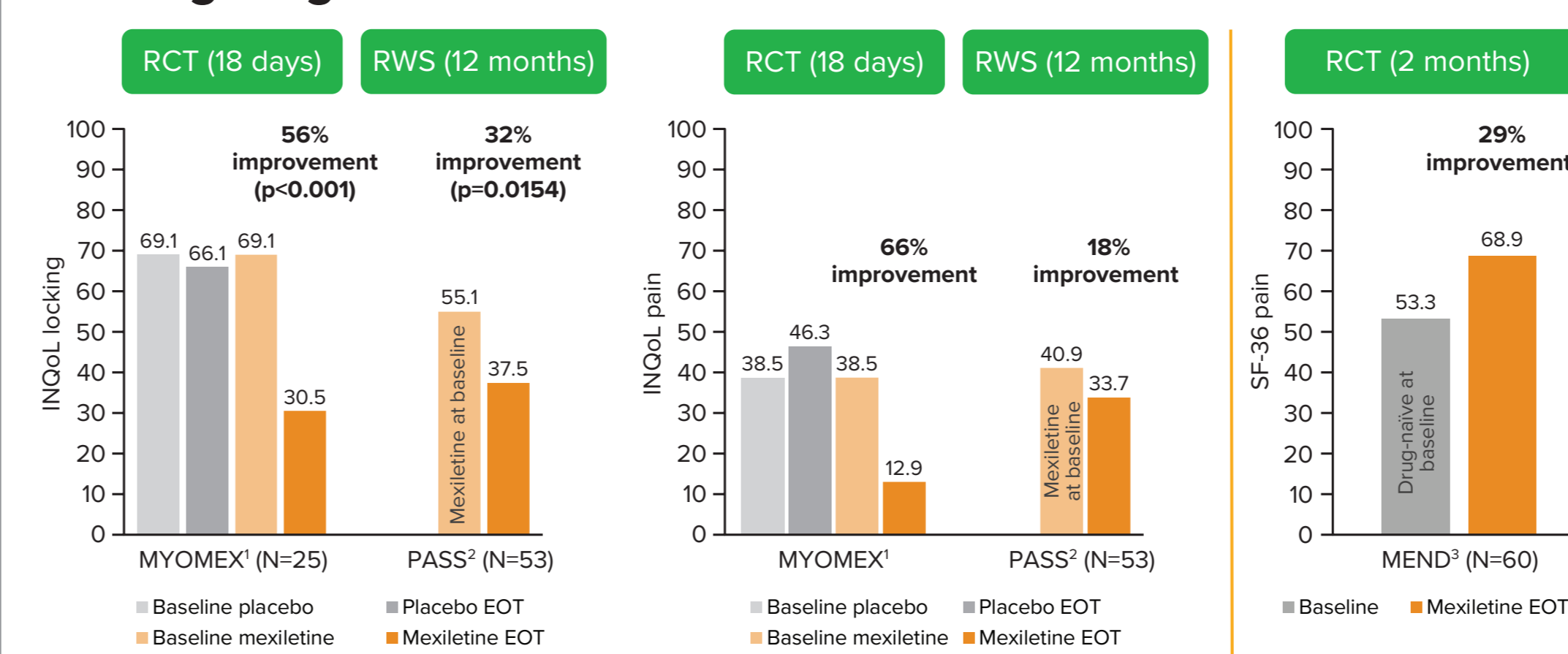
- These data summarise MBS scores across two studies, but should not be directly compared due to differences in the patient populations.
- Mexiletine treatment improved MBS scores across both studies.
- The improvement was particularly marked in patients who were drug-naïve at baseline.

RCT, randomised controlled trial; RWS, real-world study; EOT, end of trial

Improvements in QoL across studies

- Improved QoL (INQoL locking/pain or SF-36 pain) were seen across all three studies (**Figure 4**).
- Notably, MYOMEX data showed that although patients still reported locking at study end, the overall impact of locking on patients' QoL significantly reduced.

Figure 4. QoL as an outcome measure to assess myotonia in patients with NDM: examples from three recent clinical trials investigating mexiletine treatment



- These data should not be compared directly across studies due to differences in patient populations and QoL scores (INQoL and SF-36).
- Mexiletine treatment improved QoL scores across all studies.

RCT, randomised controlled trial; RWS, real-world study; EOT, end of trial¹⁻³

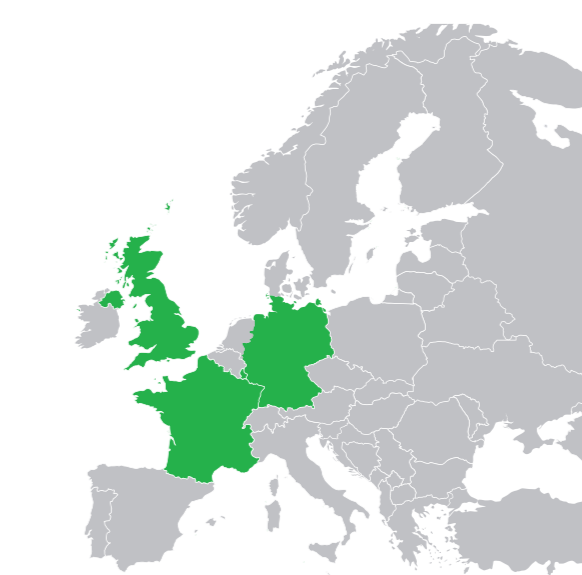
Correlations between clinical myotonia scores and INQoL stiffness

- Spearman correlation indicated that VAS stiffness and MBS provide consistent measures of stiffness (**Figure 5**).
- Improvement in MBS score was associated with positive impact on patient QoL (**Figure 5**).

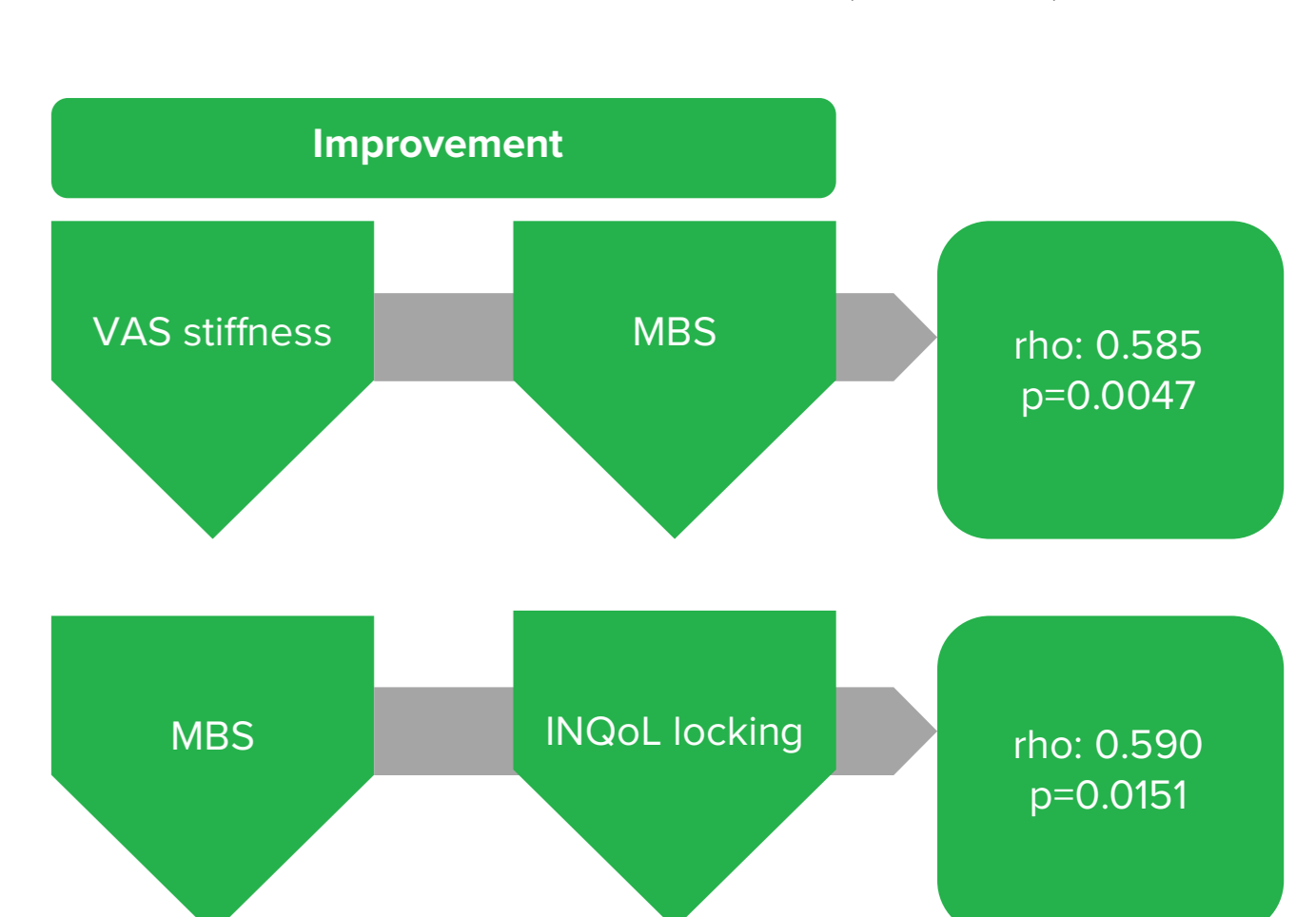
Figure 5. How meaningful are patient-perceived changes in VAS stiffness and MBS with respect to patient QoL, in NDM?

Post-authorisation safety study (PASS)

- Non-interventional, prospective, observational
- 53 mexiletine-treated patients with NDM
- Outcomes: safety, tolerability, VAS stiffness, INQoL, MBS
- Six study centres: Germany, UK, France



Correlations between clinical outcomes (12 months) and QoL



- VAS stiffness and MBS are correlated.
- Improvement in a clinical PRO score (MBS) correlated with improvement in QoL.

Conclusions

- Together, evidence from three studies (N=138 adults with NDM) illustrate the consistent and positive impact of mexiletine on myotonia-associated PROs, especially stiffness and locking.
- These data strengthen the evidence base for mexiletine treatment, further validating the meaningful QoL benefits that symptom improvements bring to people living with myotonia.

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