Greater clinical benefit with tiomolibdate choline versus standard-of-care in neurologic WD patients in the Phase 3 FoCus trial

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Disclosures

- Travel expenses to attend and present at AAN 2026 were paid for by Monopar Therapeutics
- Dr. Peter Hedera serves as a member of the DMC for Ultragenyx UX-701 for Wilson disease

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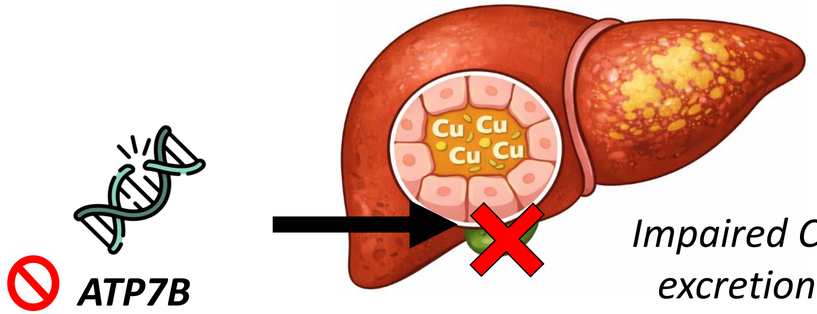
Wilson Disease and Tiomolibdate Choline

Wilson disease (WD) is a genetic disorder of copper (Cu) overload due to *ATP7b* dysfunction

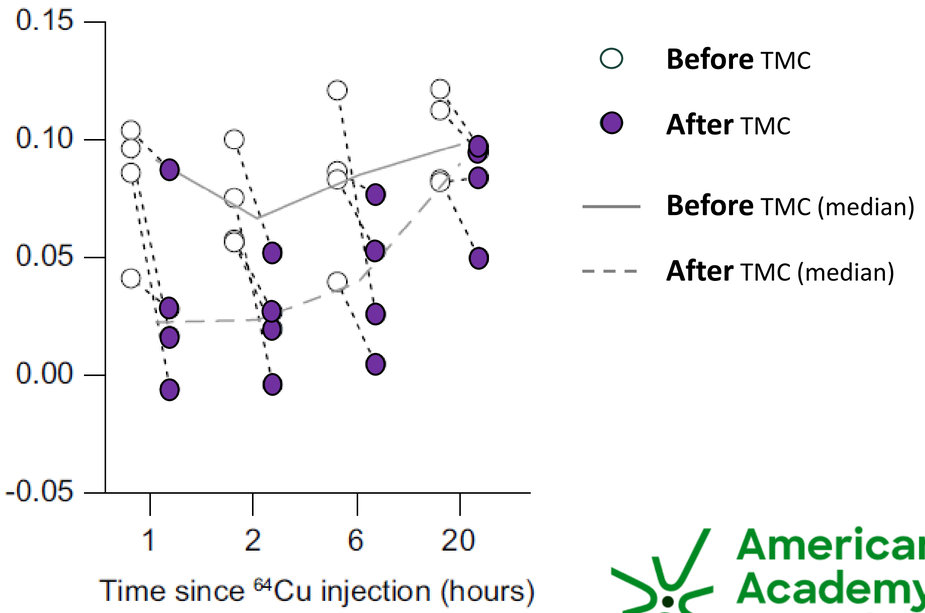
Tiomolibdate choline (TMC) is an investigational, first-in-class albumin tripartite complex (ATC) activator that binds Cu with high selectivity and affinity[1]

The stable albumin tripartite complex (TMC-albumin-Cu) **mobilizes and sequesters** toxic Cu and prevents it from crossing the blood-brain barrier[2,3]

TMC is an **oral, once daily** small molecule



Brain Cu Uptake[4]



1. Smirnova J *et al*. *Sci Rep*. 2018;8(1):1463; 2. Zhang L *et al. Biochemistry*. 2009;48(5):891-897; 3. Kim P *et al*. *Biomedicines*. 2021;9(12):1861; 4. Kirk FT et al. *J Hepatol*. 2024;80(4):586-595.

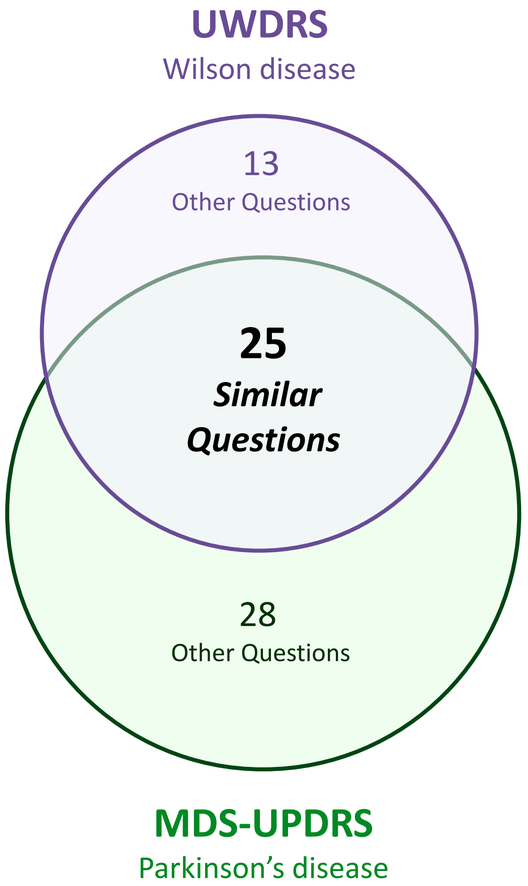
FoCus Phase 3 RCT in WD Patients

- The Phase 3 FoCus RCT enrolled 207 patients with WD onto **TMC (n=137)** or standard of care **(SoC, n=70)** for **48 weeks**, with optional 5-year extension on TMC

- Over half of enrolled patients (56% TMC; 50% SoC) demonstrated **neurologic symptoms at baseline**

  - Defined as baseline **Unified WD Rating Scale (UWDRS) Part III** score greater than minimum clinically important difference (**MCID**) of 4.668

  - UWDRS Part III assessment was **rater-blinded**



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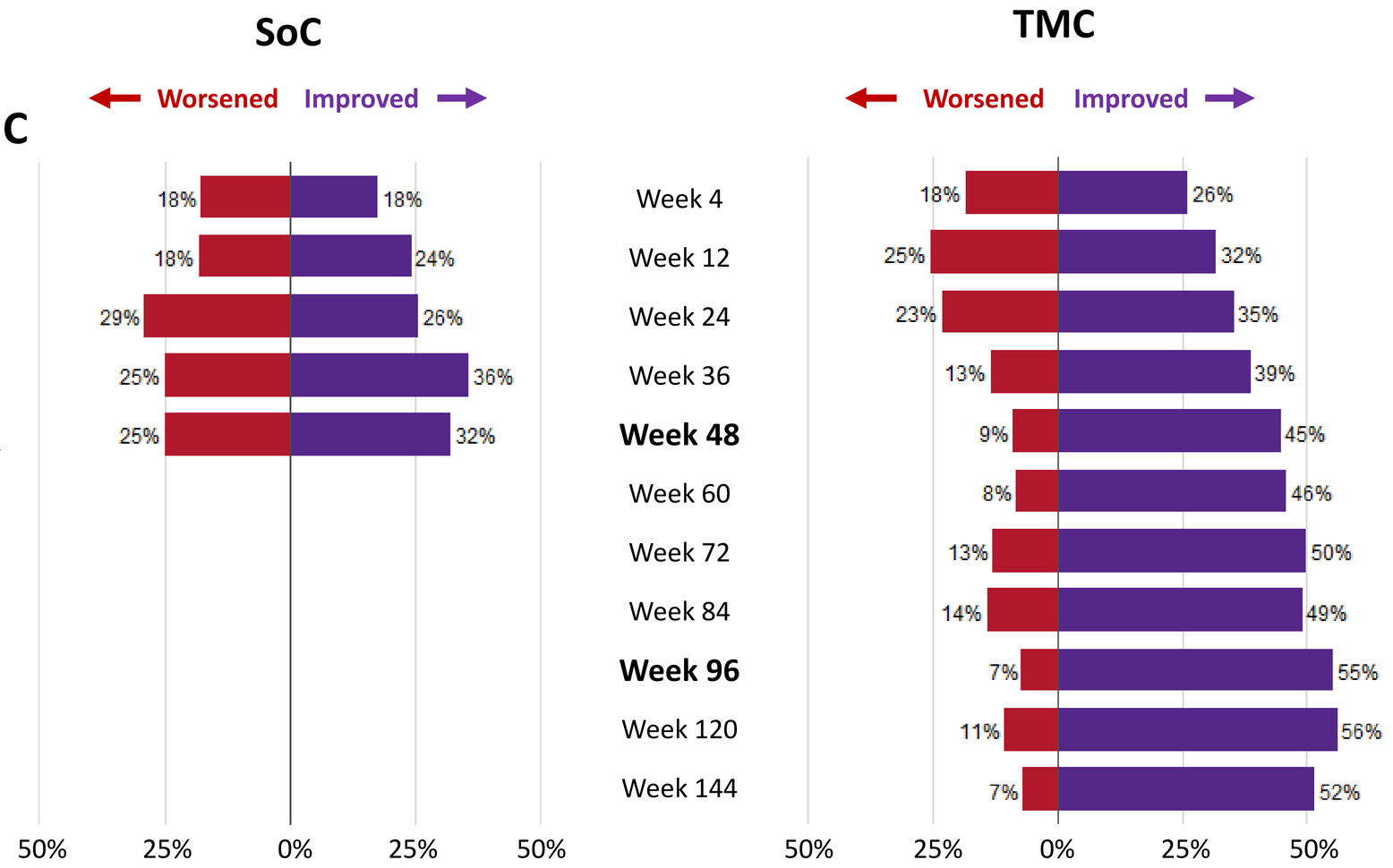
More Patients with Neurologic Symptoms Improved and Fewer Worsened with TMC vs. SoC

Durable neuro benefit with TMC sustained over time (shown out to ~3 years at the right)

Significantly more likely to worsen on SoC vs TMC at Week 48 (p = 0.038)

UWDRS III at 48 weeks:

SoC	TMC
32% improved	45% improved
25% worsened	9% worsened



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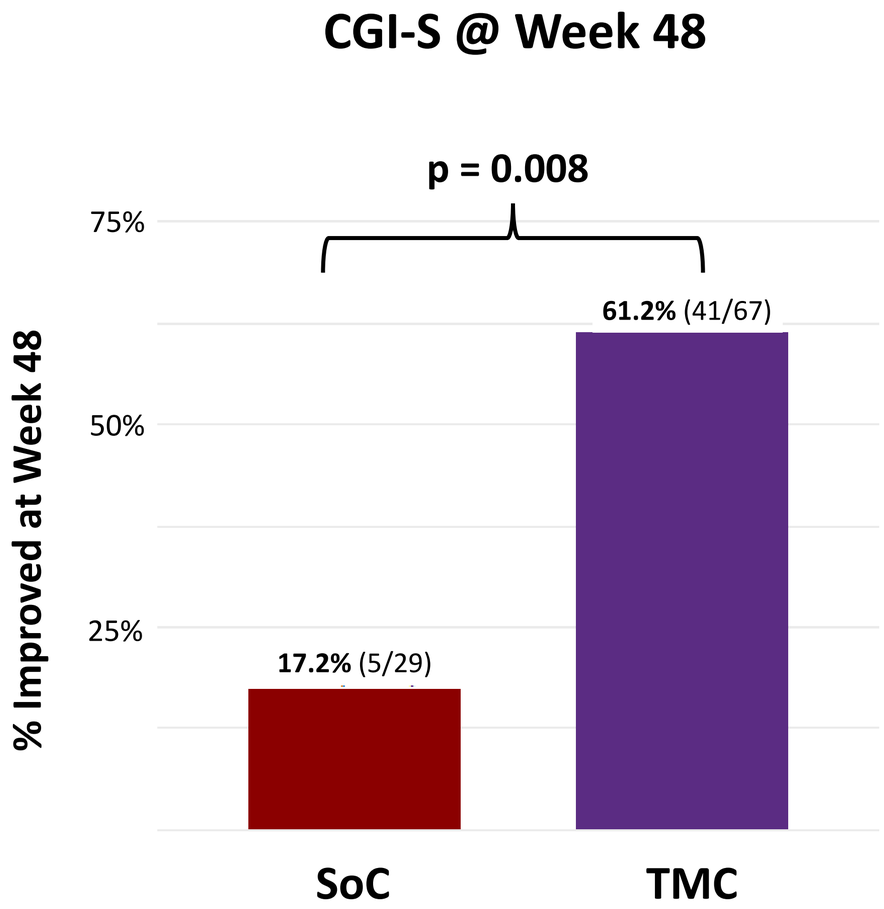
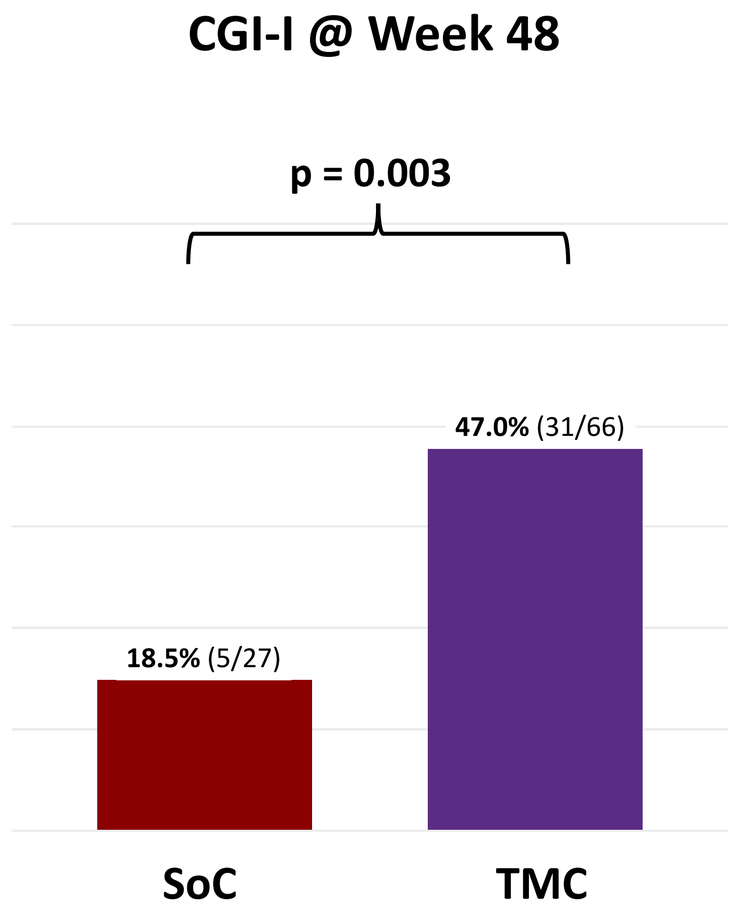
Patients with Neurologic Symptoms Achieved Greater Global Clinical Improvement on TMC vs. SoC





P-value for comparison of mean change from baseline in score.

CGI-S = Clinical Global Impression – Severity , CGI-I = Clinical Global Impression – Improvement

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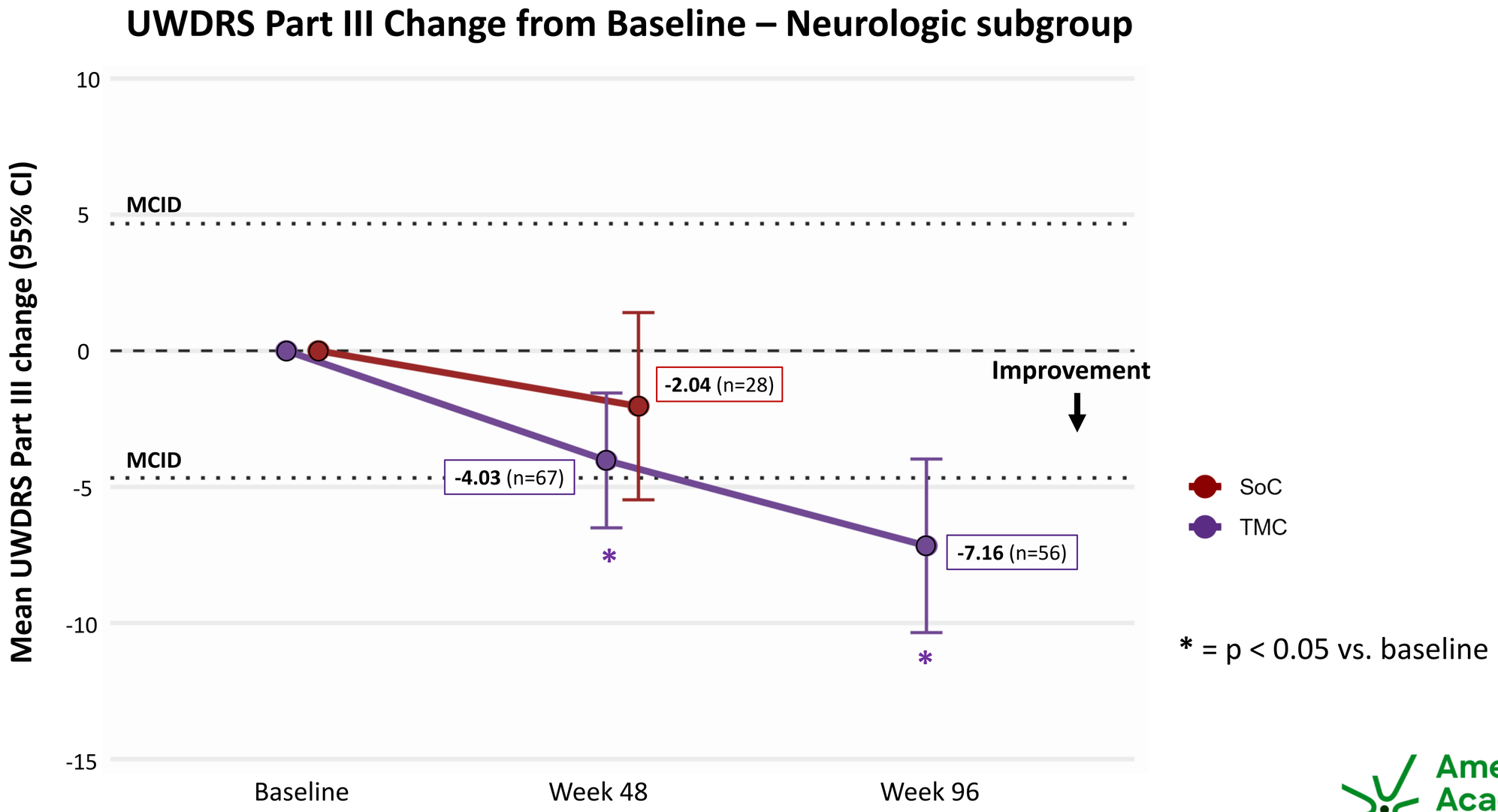
TMC Neurologic Benefit Increased Over Time



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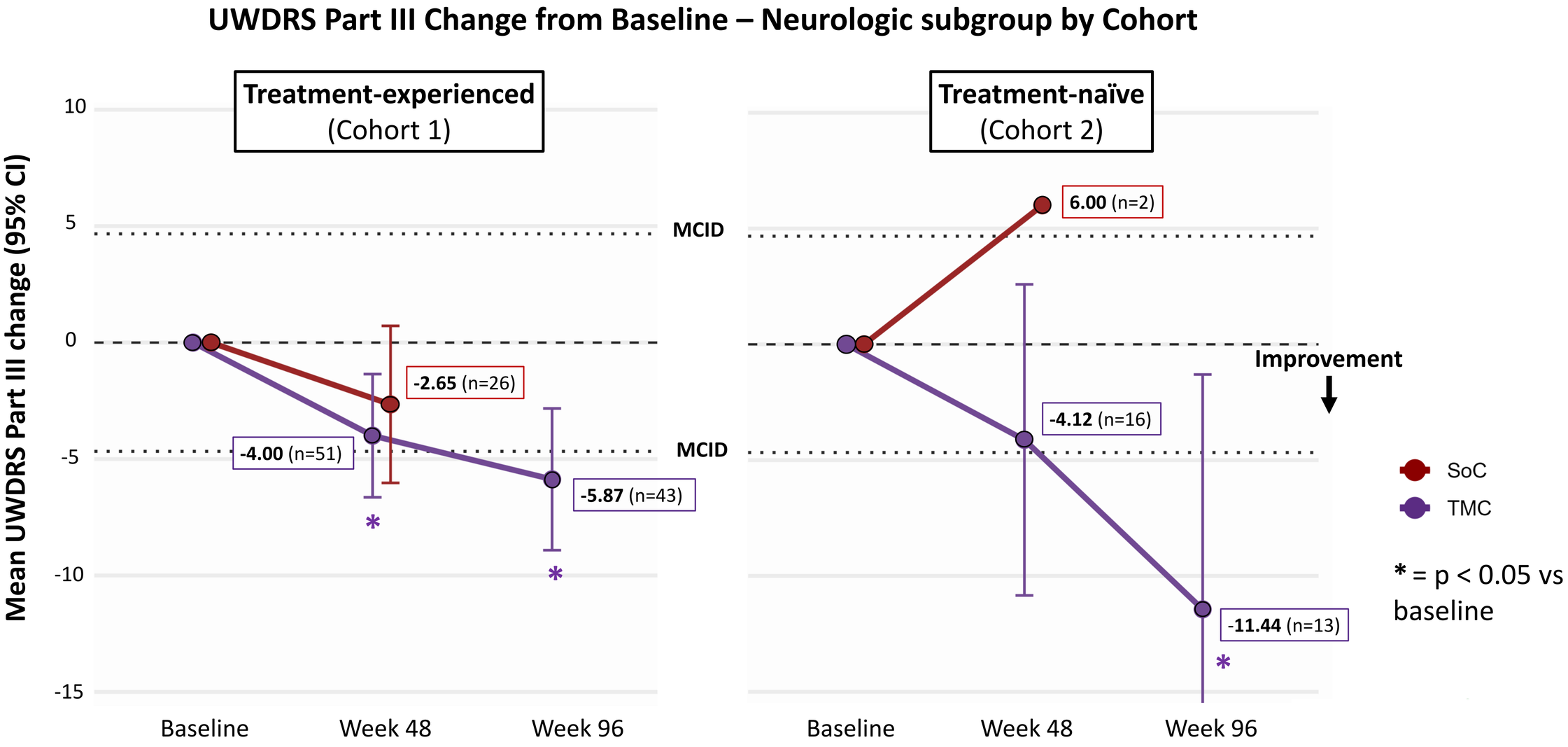
Consistent Neurologic Benefit with TMC Regardless of Cohort



Favorable Safety Profile Across All Treated WD Patients in Ph 2 & Ph 3 Studies

Serious Adverse Events (SAEs) on TMC	
Number of patients	266
Median time on treatment (years)	2.58
Total **patient-years** (PYs)	645.6
Patients with **any drug-related SAE**	13 (4.9%)
Neurologic	2 (0.8%)
Psychiatric	1 (0.4%)

No deaths occurred that were deemed related to TMC. Data through 01-Sep-2022.

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Questions?