Presenter:
Aurelia Poujois, MD, PhD
apoujois@for.paris

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

A. Poujois[1], J. Bronstein[2], M. Lorincz[3], P. Hedera[4], D. Bega[5], C. Robinson[6], A. Cittadine[6], D. Tuffy[6], P. Dusek[7], I. Mohr[8], T. Litwin[9]

[1]Department of Neurology, Adolphe de Rothschild Foundation Hospital, Paris, France, [2]Department of Neurology, David Geffen School of Medicine at UCLA, Los Angeles, United States, [3]Department of Neurology, University of Michigan Health Systems, Ann Arbor, United States, [4]Department of Neurology, School of Medicine, University of Louisville, Louisville, United States, [5]Department of Neurology, Feinberg School of Medicine, Chicago, United States, [6]Monopar Therapeutics, Wilmette, United States, [7]Department of Neurology and Centre of Clinical Neuroscience, Charles University and General University Hospital, Prague, Czech Republic, [8]Department of Gastroenterology and Hepatology, Heidelberg University Hospital, Heidelberg, Germany, [9]Second Department of Neurology, Institute of Psychiatry and Neurology, Warsaw, Poland

Disclosures:

AP, ML, PH: Travel grants from Monopar Therapeutics
CR, AC, DT: Employees of Monopar Therapeutics
JB, DB, PD, IM, TL: Nothing to disclose

Introduction

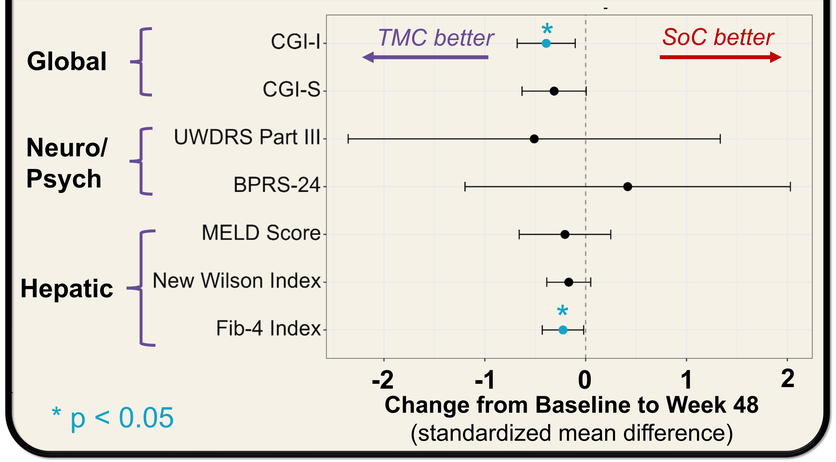
ALXN1840 (tiomolibdate choline, TMC), is a novel first-in-class Albumin Tripartite Complex (ATC) activator under investigation for the treatment of Wilson disease (WD). WD is a rare genetic disorder of copper overload. ALXN1840 rapidly mobilizes and tightly sequesters excess copper in ATCs, suppressing its redox reactivity, limiting oxidative damage, and blocking transport across the blood–brain barrier. Clinical data demonstrate that ALXN1840 improves copper balance by increasing fecal copper excretion. In the phase III pivotal trial, ALXN1840 demonstrated rapid and sustained copper mobilization significantly greater than standard of care (SoC) over 48 weeks in both previously treated and untreated patients. Durable clinical improvement and a favorable tolerability and safety profile were observed across > 6 years of treatment.

Methods

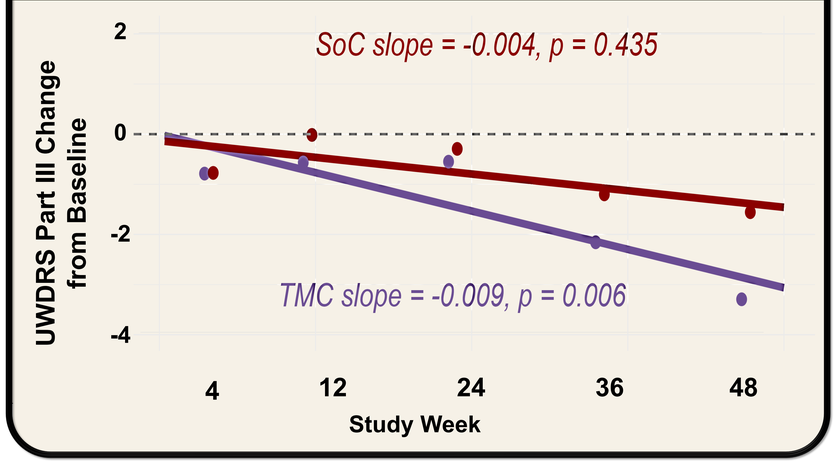
The Phase 3 FoCus RCT (NCT03403205) enrolled 207 patients with WD to TMC (n=137) or standard of care (SoC, n=70) for 48 weeks, with an optional 5-year extension on TMC. Over half of enrolled patients (TMC: n=77; SoC: n=35) demonstrated neurological symptoms at baseline, defined as baseline Unified WD Rating Scale (UWDRS) Part III score greater than the minimum clinically important difference (MCID) of 4.668. UWDRS Part III assessments during the trial were rater-blinded. Analyses were conducted on all patients with data available.

Results

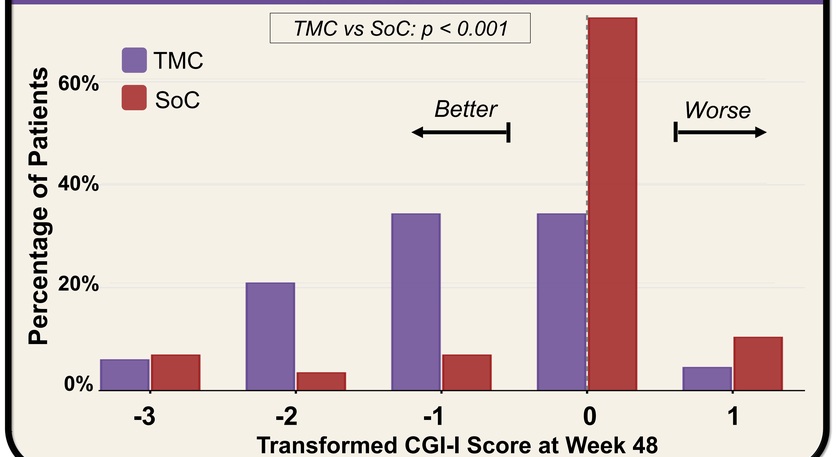
TMC was **same or better than SoC** across **neuro, psych, hepatic,** and **global** outcomes



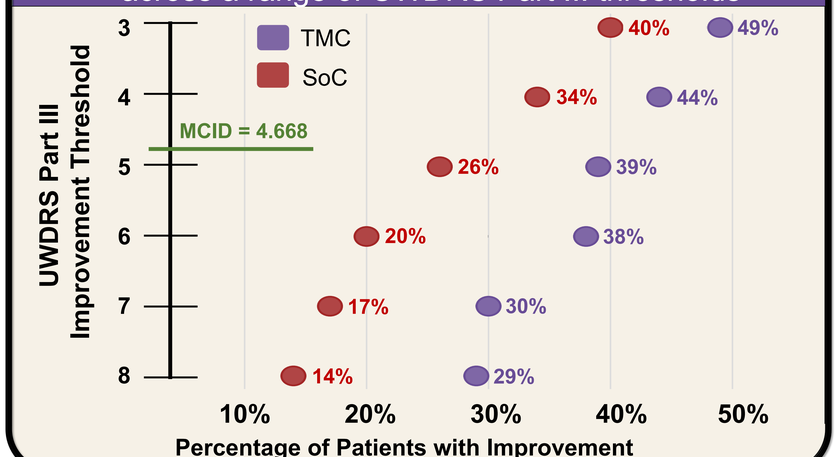
Significant continued neurologic improvement over time on TMC, but not SoC



Significantly greater **global clinical improvement** with TMC vs SoC



More neuro benefit on TMC vs SoC at Week 48, across a range of UWDRS Part III thresholds



Safety

TMC showed a favorable safety profile across all dosed patients with WD in Phase 2 & 3 studies.

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

Data through 01-Sep-2022.

Conclusions

In WD patients with neurologic symptoms at baseline, 48 weeks of treatment with TMC led to greater clinical and neurologic benefit and less worsening compared to SoC. Greater neurologic benefit was observed in the TMC group across both previously treated and treatment-naïve patient groups. Continued improvement was sustained through long-term follow-up. These findings demonstrate TMC improves outcomes in WD patients with neurologic symptoms and could serve as a valuable new treatment for this population in need.