Sustained long-term clinical improvement in Wilson disease patients on tiomolybdate choline

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General Hepatology, Clinical Science
Rare liver diseases (including pediatric and genetic) – Clinical

Monopar Therapeutics

Introduction

Wilson disease (WD) is a rare disorder of copper disposition. ALXN1840 (tiomolybdate choline, TMC) is a novel copper binding agent under investigation for the treatment of WD. ALXN1840 rapidly forms inert tripartite complexes with copper and albumin to prevent toxicities associated with excessive free Cu. Monopar Therapeutics is advancing ALXN1840 toward an NDA filing.

Aim & Objectives

Long-term neurologic and hepatic outcomes of WD patients in ALXN1840 clinical trials were assessed to understand the effects of years-long ALXN1840 treatment.

Method

For efficacy, data from the Ph2 WTX101-201, Ph2 ALXN1840-WD-205, and Ph3 WTX101-301 trials were pooled and analyzed (**n=255**). For safety, data from the Ph2 ALXN1840-WD-204 trial was also included (**n=266**). Median duration on ALXN1840 treatment was **961 days** (2.63 years) and **943.5 days** (2.58 years) for the efficacy and safety datasets, respectively.

Results

ALXN1840 Demonstrates Sustained Copper Mobilization

Table 1: Cu Mobilization on ALXN1840

Study Week	N	Plasma dNCC (µmol/L)
0	250	1.199
48	214	2.949
312	18	3.302

dNCC: *directly measured non-ceruloplasmin-bound copper*

Efficacy

Unified Wilson Disease Rating Scale Results Show Long-term Benefit

Fig 1: UWDRS Part II (Patient-reported)
Least squares mean and standard error – Ph2 & Ph3

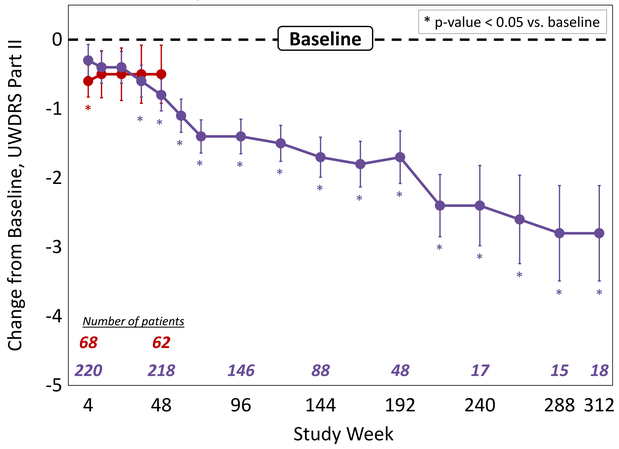
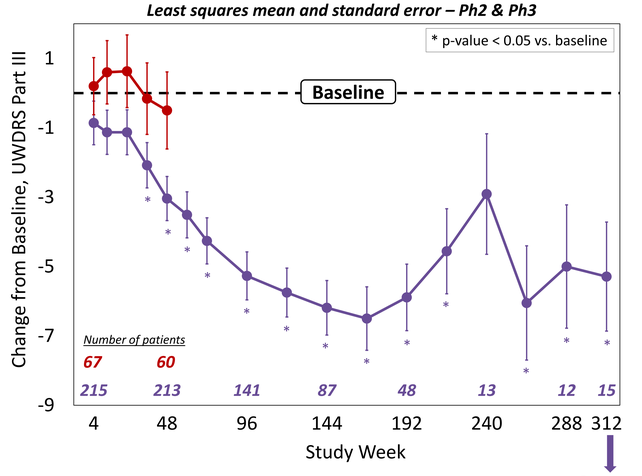


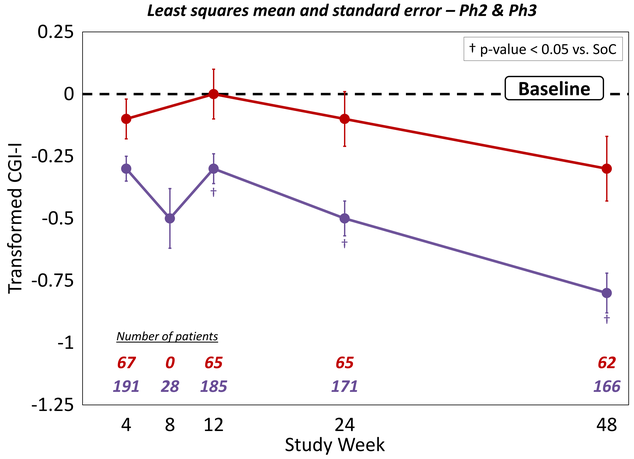
Fig 2: UWDRS Part III (Physician-assessed)
Least squares mean and standard error – Ph2 & Ph3



ALXN1840 Standard of Care

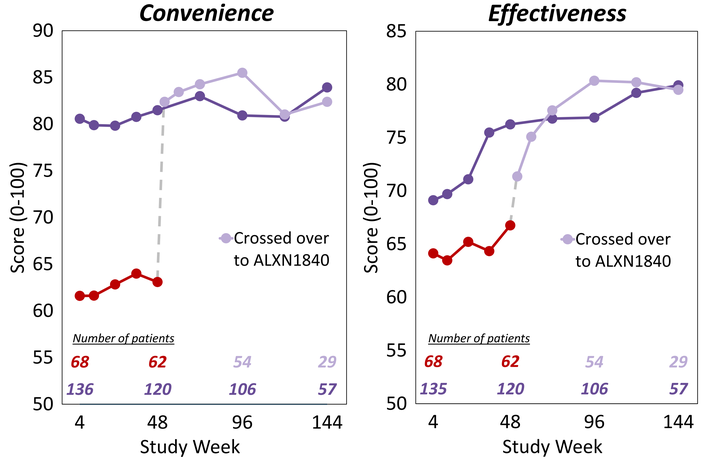
CGI-I & TSQM-9 Show Disease Improvement, Patient-Reported Benefit

Fig 3: Transformed CGI-I By Visit
Least squares mean and standard error – Ph2 & Ph3



Clinical Global Impression-Improvement 7-point Scale

Fig 4: TSQM-9 Treatment Satisfaction Scores – Ph3



Treatment Satisfaction Questionnaire for Medication-9

Safety

ALXN1840 has a Favorable Safety Profile

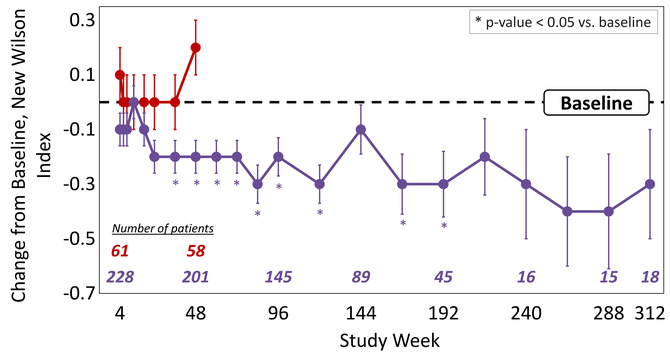
Table 2: Serious Adverse Events (SAEs) on ALXN1840
data thru 01-Sep-2022

N	266
Patient-years (PYs)	645.6
Patients with any ALXN1840-related SAEs	13 (4.9%)
Renal/Urinary System-related SAEs	0 (0%)
Liver-related SAEs	8 (3.0%)

- Only 2 patients (0.8%) had ALXN1840-related renal/urinary AE
- No deaths occurred due to ALXN1840

61 Ph3 cross-over patients from SoC to ALXN1840 had no change in psychiatric AE rate: 4.3% (3/70, 62.4 PYs) vs. 4.9% (3/61, 55.4 PYs)

Fig 5: New Wilson Index
Least squares mean and standard error – Ph2 & Ph3



New Wilson Index (based on bilirubin, AST, INR, leukocytes, albumin) improved for patients on ALXN1840 treatment over 6 years

Conclusions

Clinical data from 255 WD patients on ALXN1840 treatment show sustained clinical improvement over 6 years of treatment. Combined with long-term safety, this analysis supports the potential use of ALXN1840 as a treatment for Wilson disease.

References & Acknowledgements

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