Long-term sustained improvement of neurological symptoms in Wilson disease patients on tiomolybdate choline

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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.

Methods

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. The minimum clinically important difference (MCID) was determined for UWDRS Part II and Part III by calculating the standard error of measurement (SEM) of the baseline value in the efficacy dataset (n=255) using Cronbach's $\alpha = 0.94$.[1]

Results

ALXN1840 neurological benefit is sustained over 6 years

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

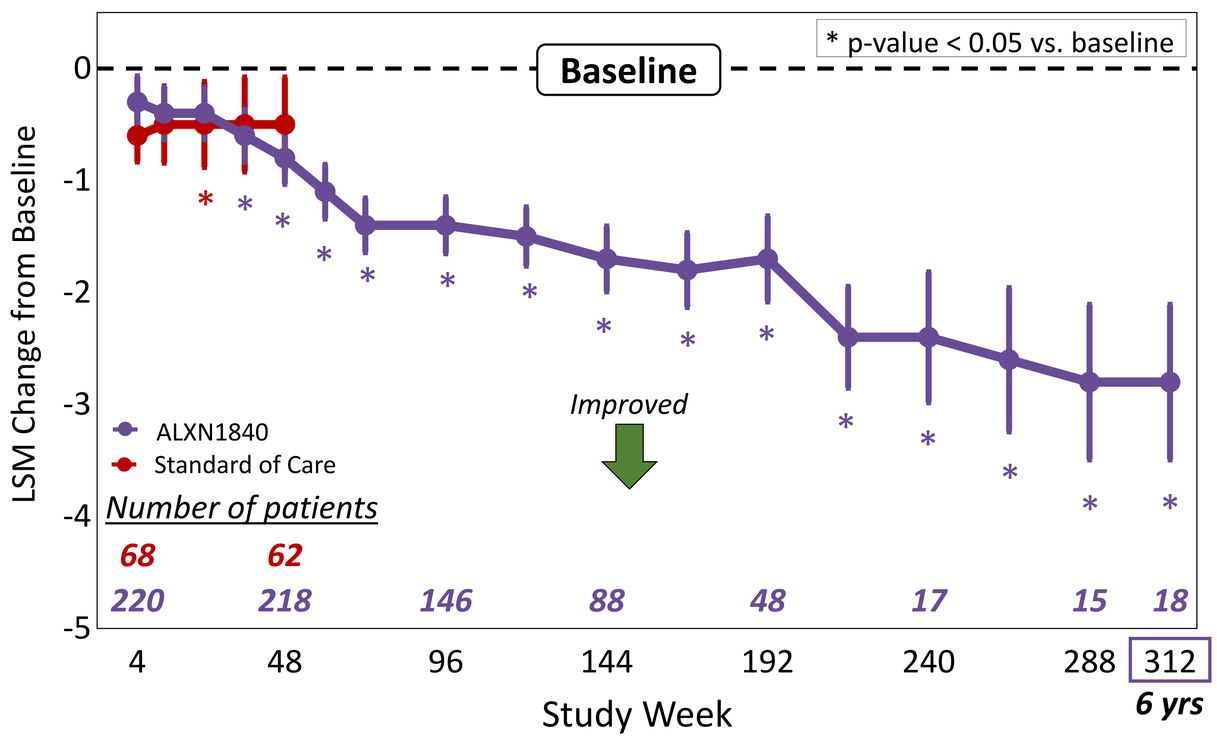
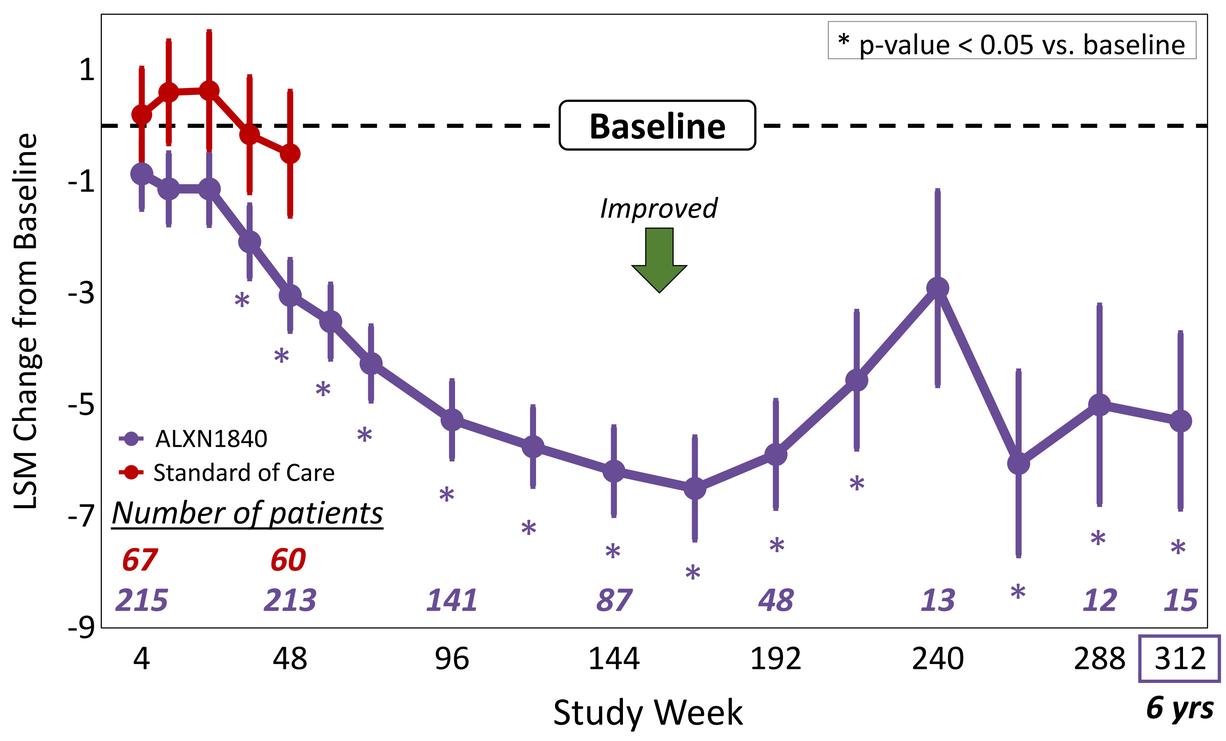


Fig 2: UWDRS Part III (Physician-assessed)
Least squares mean (LSM) ± standard error – Ph2 & Ph3



Neurologic benefit reproduced across independent trials

UWDRS Minimum Clinically Important Difference (**MCID**)
- Previous studies have reported a Part III MCID of **4 - 6.9 pts**[2-4]
- Calculated UWDRS Part III MCID from Ph2 & Ph3 (n=255)**: 4.69 pts**

Table 1: UWDRS Part III (Physician-assessed)
MCID responder rate (change from baseline to Week 48) – Ph2 & Ph3

	ALXN1840				SoC
Study ID *(n enrolled)*	**201** (n=29)	**205** (n=31)	**301‡** (n=137)	**ISE** (n=255)	**301‡** (n=70)
Improved† *(%)*	94	57	45	50	32
Worsened *(%)*	5	4	8	7	13

† *Calculated from patients eligible to improve (baseline score ≥ MCID)*
‡ *Physician rater-blinded*

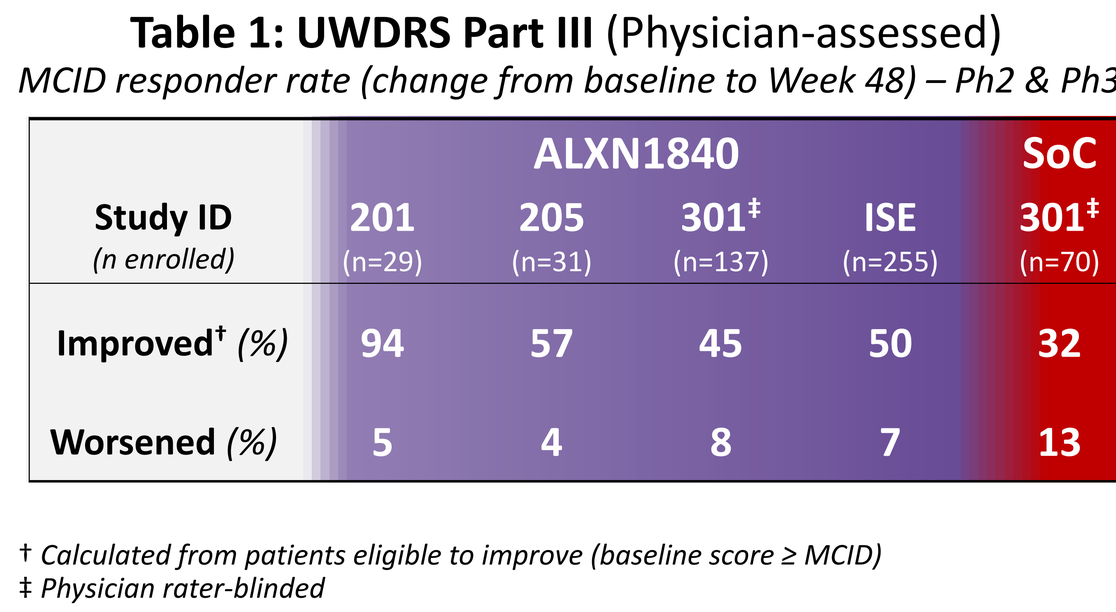
Patients who switch from SoC to ALXN1840 further improve

Fig 3: UWDRS Part III (Physician-assessed)
MCID responder rate – Ph3

† *Calculated from patients eligible to improve (baseline score ≥ MCID)*

Sustained psychiatric benefit

Fig 4: Brief Psychiatric Rating Scale (Clinician-assessed)
Least squares mean (LSM) ± standard error – Ph3



Favorable safety profile

Table 2: Adverse Events
Data through 01-Sep-2022 – Ph2 & Ph3

Drug-related Serious Adverse Events (SAEs)	
Number of patients	266
Total **patient-years** (PYs)	645.6
Patients with **any drug-related SAEs**	13 (4.9%)
Patients with **drug-related neurological SAEs**	2 (0.8%)
Patients with **drug-related psychiatric SAEs**	1 (0.4%)

Conclusions

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

References & Acknowledgments

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