Poster #

Residual Hepatic, Neurologic, And Psychiatric Disease Burden In Treatment-Experienced Patients with Wilson Disease: Baseline Findings from the FoCus Phase 3 Trial

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BACKGROUND

- Wilson disease (WD) is a rare, progressive, autosomal-recessive disorder of copper accumulation that drives hepatic, neurologic, and psychiatric morbidity[1,2]
- Patients have persistent disease across these domains despite long-term treatment with penicillamine, trientine, and/or zinc, the current standard-of-care (SoC) therapies[3,4]

OBJECTIVE

To characterize the residual disease burden among patients receiving SoC, we analyzed baseline data from the FoCus trial (NCT03403205), the largest and longest randomized controlled WD trial conducted to date

METHODS

- The ALXN1840 Phase 3 FoCus Trial was a multicenter trial evaluating tiomolibdate choline (TMC; ALXN1840) against SoC
- Patients aged ≥12 years with a diagnosis of WD were enrolled in 22 countries, including North America, Europe, and Asia
- Patients were categorized based on prior WD treatment history as treatment-naïve (TN, ≤28 days) or treatment-experienced (TE, >28 days)

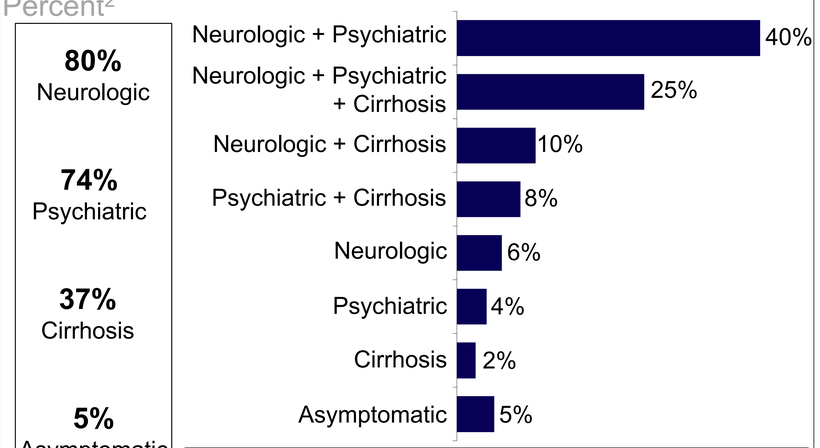
RESULTS

- Across all patients, approximately 73% had symptoms in two or more domains **(Figure 1)**
- Majority of patients despite SoC treatment (median ~9.5 years) had hepatic, neurologic, and/or psychiatric symptoms **(Figure 2)**
- Only 5.4% of patients had no symptoms **(Figure 2)**
- In patients on SoC >12 months, 31% had baseline 24-hour urinary copper excretion (UCE) above guideline-directed maintenance targets

Table 1. Overall Patient Demographics

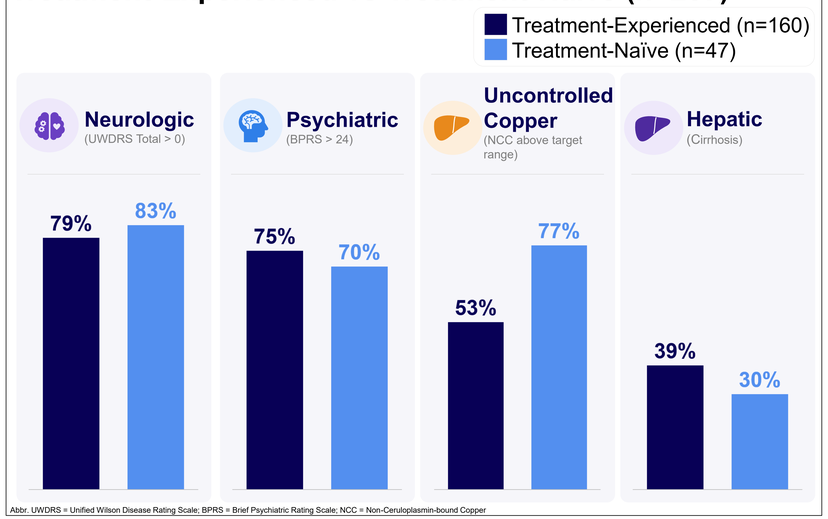
Variable		Treatment Experienced (n = 160)	Treatment Naïve (n = 47)
Sex	Male, n (%)	84 (52.5)	35 (74.5)
	Female, n (%)	76 (47.5)	12 (25.5)
Race	White, n (%)	121 (75.6)	39 (83.0)
	Asian, n (%)	32 (20.0)	5 (10.6)
	Black or African American, n (%)	3 (1.9)	0 (0.0)
	Other / Not Reported, n (%)	4 (2.5)	3 (6.4)
Age (Years)	Mean (SD)	35.3 (14.1)	27.8 (9.5)
	Min-Max	12-71	15-56

Figure 1. Patient Distribution Across Individual and Overlapping Disease Domains (n=207[1])



1 For overlapping disease domains, n was 204 since 1 patient without Unified Wilson Disease Rating Scale (UWDRS) & Brief Psychiatric Rating Scale (BPRS) score and 2 patients without BPRS scores were excluded
2 Percentages are rounded to the nearest whole number

Figure 2. Proportion of Patients with Baseline Morbidity – Treatment-Experienced vs Treatment-Naïve (n=207)



Abbr. UWDRS = Unified Wilson Disease Rating Scale; BPRS = Brief Psychiatric Rating Scale; NCC = Non-Ceruloplasmin-bound Copper

CONCLUSIONS

Disease burden across treatment experienced patients was comparable to treatment naïve patients. After nearly 10 years on SoC, TE patients with WD continued to exhibit substantial multi-system disease, including cirrhosis in nearly 40%, persistent neurologic or psychiatric symptoms in the majority, fewer than half within the guideline-recommended NCC target range, and approximately one-third with 24-hour UCE above guideline-directed maintenance targets

IMPLICATIONS

These data underscore the inability of existing WD therapies to fully address the disease burden of WD and the need for novel therapeutic approaches

References:
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Acknowledgments:
- The clinical study was sponsored by Alexion, AstraZeneca Rare Disease
- Writing support was provided by Xelay Acumen Group, Inc., and funded by Monopar Therapeutics