

ZERVIMESINE SLOWS PROGRESSION OF SYMPTOMS IN MILD-TO-MODERATE DEMENTIA WITH LEWY BODIES

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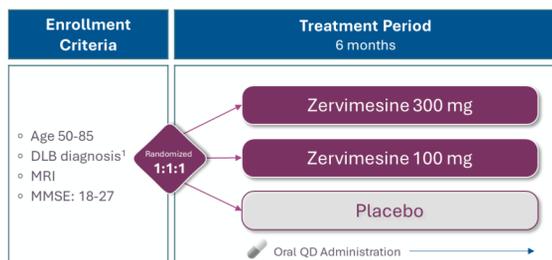
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Poster 2640

Aims:

- Zervimesine (CT1812) is an experimental, oral, brain-penetrant, small molecule therapeutic in development for age-related neurodegenerative diseases.
- Zervimesine was studied in a 6-month, double-blind, placebo-controlled Phase 2 trial in 130 adults with mild-to-moderate dementia with Lewy bodies (DLB) (NCT05225415; SHIMMER).

Figure 1



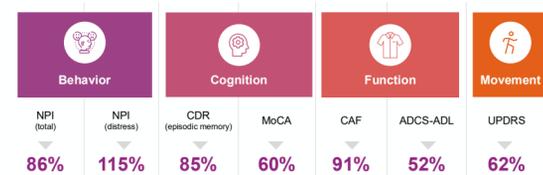
Results:

Zervimesine-treated participants progressed more slowly than those on placebo across neuropsychiatric, cognitive, motor, and global function domains.²



Published results: Galvin et al. Alz Dement. 2025

Figure 2
COG1201: Percent Slowing in Clinical Signals over 26 Weeks Pooled Zervimesine Arms Relative to Placebo



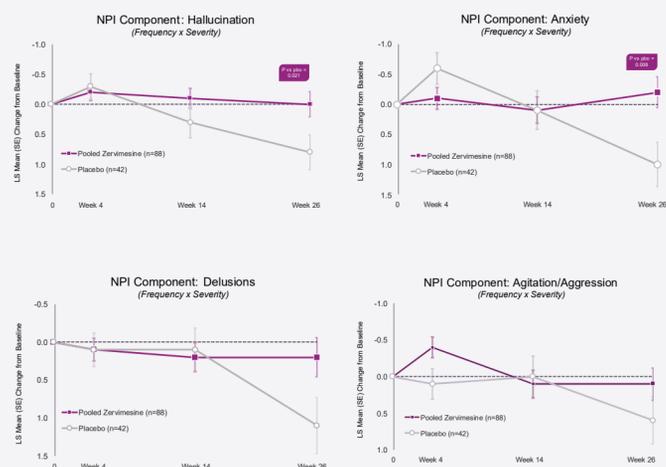
There is no single endpoint that captures DLB's diverse symptoms. Therefore, the Phase 2 SHIMMER study repurposed tools from other CNS conditions, including the:

- Neuropsychiatric Inventory (NPI),
- Cognitive Drug Research Battery (CDR),
- Montreal Cognitive Assessment (MOCA),
- Movement Disorder Society – Unified Disease Rating Scale III (MDS-UPDRSIII), and
- Alzheimer's Disease Cooperative Study – Activities of Daily Living (ADCS-ADL).

NPI-4 Core Symptoms:

Core DLB symptoms that improved relative to placebo included:

- Hallucinations (p=0.021),
- Anxiety (p=0.008),
- Delusions (p=0.061),
- Agitation/aggression (p=0.151)



In a Phase 2 trial, notable benefits were observed with zervimesine treatment in **neuropsychiatric symptoms, memory related items, and activities of daily living** relative to placebo.

Neuropsychiatric Inventory:

Zervimesine treatment resulted in an 86% slowing of decline on NPI-12 vs placebo (p=0.055; Figure 3). A forest plot of the NPI-12 results (below left) shows the four components of the NPI-4 in purple.

Figure 3

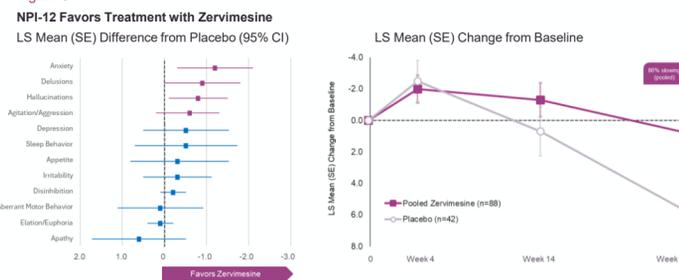
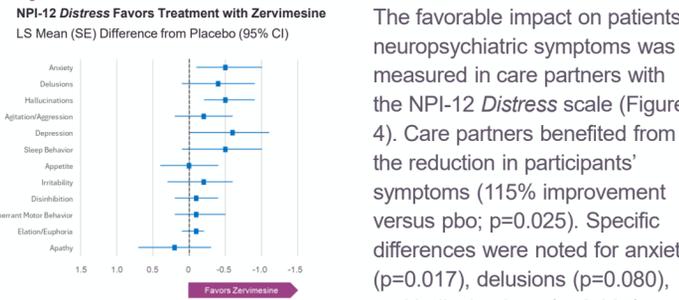


Figure 4

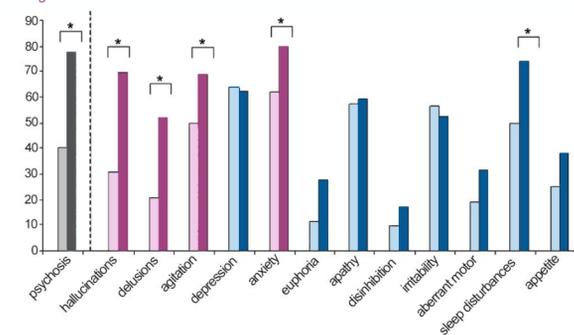


Discussion:

In DLB, while all patients may present differently, there are common neuropsychiatric symptoms that are more likely to progress during the course of disease.

Behavioral and psychological symptoms are frequently associated with DLB and typically worsen over the disease course³ (Figure 5) and are reported by patients as some of the most troublesome symptoms.⁴

Figure 5



Modified from Borroni et al 2008
Light bars: mild DLB patients (MMSE>19, CDR<1)
Dark bars: moderate-severe DLB patients (MMSE<19, CDR>1). p < 0.05
Original modified to highlight psychoses that are components of NPI-4 (purple)

A regulatory strategy for zervimesine focusing on a neuropsychiatric outcome is under consideration.

Notably, the favorable impact on neuropsychiatric symptoms observed during the Phase 2 study was not at the expense of other symptom domains. This has been reported with some medications such as antipsychotics, which can worsen symptoms (e.g. motor function) in other domains.

Rather, zervimesine had a directionally favorable impact on cognitive fluctuations, memory, movement symptoms, and activities of daily living.

A strategy focusing on a global composite endpoint that captures changes in multiple symptom domains in DLB could also be considered.

See AD/PD poster 3026 for discussion of a proposed composite endpoint.

Conclusions:

- Zervimesine treatment effects were particularly large for the psychiatric symptoms most commonly associated with DLB.
- Development of zervimesine for DLB's psychiatric symptoms may be an efficient path to approval.
- This development strategy also has the potential to address symptoms that have been identified as important to patients and care partners.

Disclosures:

Jl and AC are employees of Cognition Therapeutics; MG is a paid consultant and shareholder in Cognition Therapeutics; JG is a consultant for Alpha Cognition, Biogen, Bristol Meyers Squibb, DiagnaMed, Eisai, Eli Lilly, GE Healthcare, Genentech, Lundbeck, Roche, and Thema Medical; chief scientific officer for Cognivue, Inc; a clinical trial investigator for Cognition Therapeutics, Cervomed, and CND Life Sciences; and member of the BoD for the Lewy Body Dementia Association, Lewy Body Dementia Resource Center, and So FL Chapter of Alzheimer Association

References:

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