Masupirdine (A Pure 5-HT$_6$ Antagonist): Updates from the Phase-3 Clinical Trial Program Targeting Agitation in Dementia of Alzheimer's Type

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Introduction:

The clinical phase of Alzheimer's disease (AD) is characterized by a spectrum of neuropsychiatric symptoms, with agitation particularly contributing to early institutionalization, increased morbidity, and functional impairment. Current pharmacological options for managing agitation are limited, and the associated side effects are substantial, underscoring the urgent need for effective and safe treatments. Blocking presynaptic 5-HT$_6$ receptors reduces the inhibitory influence exerted by GABAergic interneurons and enhances monoaminergic neurotransmission. This mechanism may restore cortical balance and, consequently, alleviate agitation. Masupirdine, a pure, potent, and orally active serotonin-6 (5-HT$_6$) receptor antagonist in clinical development for the treatment of agitation in dementia of Alzheimer's type.

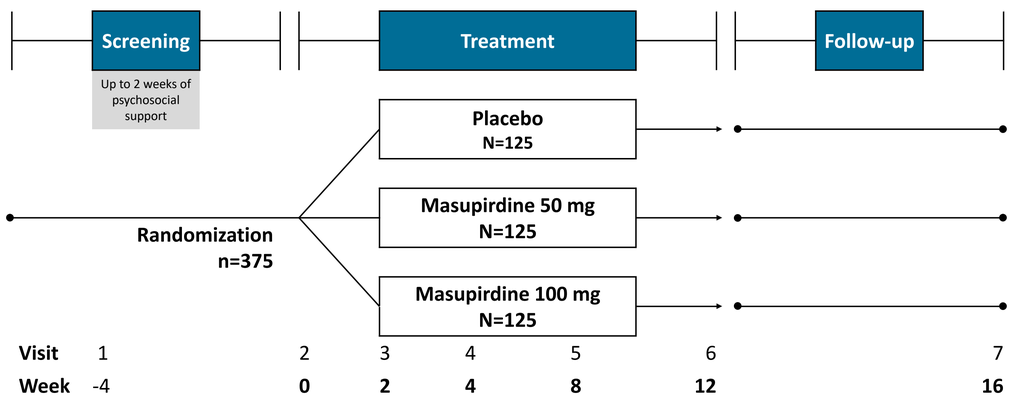
Objective:

To evaluate the potential utility of Masupirdine in treating agitation in dementia of Alzheimer's type.

Methods:

Phase-3 Study Design:

The study is a double-blind, randomized, placebo-controlled, parallel group, multicenter trial evaluating the efficacy, safety, tolerability and pharmacokinetics of Masupirdine.



Study countries: USA, Poland, Serbia & Croatia; **Total sites:** ~70;
Clinical Trial Identifier: NCT05397639; **EU CT Number:** 2024-513835-25-00.

Endpoints:

Primary:

Cohen-Mansfield Agitation Inventory (CMAI) - Change in the CMAI items score aligning to the International Psychogeriatric Association (IPA) agitation criteria domains from Baseline to Week 12.

Key Secondary:

Proportion of patients who were reported to have improved, according to the modified Alzheimer's Disease Cooperative Study-Clinical Global Impression of Change scale.

Key Eligibility Criteria:

Inclusion Criteria:

- Male or female at least 50 years old.
- Diagnosis of dementia of the Alzheimer's type, according to the NIA-AA criteria.
- Diagnosis of confirmed agitation using the IPA consensus provisional definition of agitation in cognitive disorders.
- Has an MRI or CT scan performed after onset of Alzheimer's disease symptoms with findings consistent with the diagnosis of dementia of the Alzheimer's type.

Exclusion Criteria:

- Diagnosis of dementia due to other causes.
- Has symptoms of agitation that are not secondary to AD.

Results:

Baseline Characteristics (at approximately 50% study completers):

Demographic Characteristics	Total (N=190)
Age (Years), Mean (SD)	71.7 (7.2)
Sex, n (%)	
Female	115 (60.5)
Ethnicity, n (%)	
Hispanic or Latino	131 (68.9)
Not Hispanic or Latino	59 (31.1)
Race, n (%)	
White	175 (92.1)
Black or African American	15 (7.9)
BMI (kg/m^2), Mean (SD)	27.5 (4.32)
Region, n (%)	
North America	141 (74.2)
Europe	49 (25.8)

Clinical Characteristics	Total (N=190)
CMAI Total Score, Mean (SD)	63.6 (14.88)
CMAI-IPA Score, Mean (SD)	39.4 (9.43)
NPI-12 Total Score, Mean (SD)	38.7 (16.13)
NPI-12 A/A Score, Mean (SD)	7.4 (1.76)
CGI-S Score, Mean (SD)	4.6 (0.59)
MMSE Total Score, Mean (SD)	18.5 (3.72)

Baseline characteristics are consistent with previous studies and representative of an AD population with agitation. No safety concerns identified until date.

Conclusion:

Phase-3 study results will inform the clinical utility of Masupirdine for the management of agitation in patients with dementia of the Alzheimer's type.

Last patient last visit is anticipated in January-2027,
Database lock and top-line results expected in Q2-2027.