Masupirdine (A Pure 5-HT$_6$ Receptor Antagonist): Clinical Development Program Targeting Agitation in Alzheimer's Dementia – Phase-3 Study Updates

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Introduction

Alzheimer's disease (AD) is a progressive neurodegenerative disorder characterized by the manifestation of neuropsychiatric symptoms. Agitation is among the most distressing symptoms for both patients and caregivers. There remains a void in the available treatment options for managing agitation.

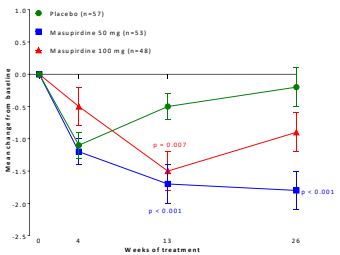
Masupirdine, a pure, potent, and orally active serotonin-6 (5-HT$_6$) receptor antagonist in clinical development for the treatment of agitation.

Methods & Results

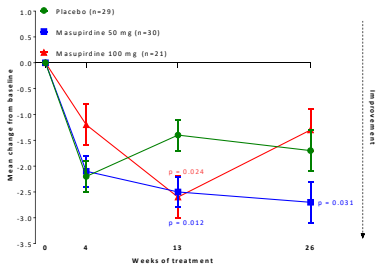
NPI-Agitation/Aggression

Subgroup analyses of Masupirdine trial (NCT02580305, Phase-2 study) were carried out on the agitation/aggression (NPI-A/A) domains of the 12-item neuropsychiatric inventory scale (NPI-12).

Baseline NPI-A/A score ≥1



Baseline NPI-A/A score ≥3



Masupirdine significantly reduced agitation/aggression in patients having baseline symptoms.

Phase-3 Study (NCT05397639 & EudraCT 2021-003405-22)

A double-blind, randomized, placebo-controlled, parallel group, multicenter study to evaluate the efficacy, safety, tolerability and pharmacokinetics of Masupirdine for the treatment of agitation in patients with dementia of the Alzheimer's type is currently ongoing.

Endpoints

Primary

Cohen-Mansfield Agitation Inventory (CMAI) - Change in the CMAI items score aligning to the 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 (mADCS-CGI-C), with a focus on agitation

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 International Psychogeriatric Association 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.

Baseline Characteristics

At ~50% of enrollment target achieved, following are the baseline demographic and clinical characteristics

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

Conclusion

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

The study is currently recruiting patients across USA, Poland, Serbia and Croatia