ASCENDING SINGLE DOSE STUDY OF THE SAFETY, TOLERABILITY, PHARMACOKINETICS, AND PHARMACO-DYNAMICS OF SRA-444 ADMINISTERED ORALLY TO HEALTHY ADULT SUBJECTS

Published: 18-12-2006
Last updated: 14-05-2024

Primary: to assess the safety and tolerability of ascending single oral doses of SRA-444 in healthy adult subjectsSecondary: to obtain preliminary PK and PD profiles of SRA-444 in healthy adult subjects to evaluate the effect of a high-fat meal on...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Cranial nerve disorders (excl neoplasms)
Study type	Interventional

Summary

ID

NL-OMON30387

Source
ToetsingOnline

Brief title
Clinical Trial Protocol 3197A1-100-EU

Condition

- Cranial nerve disorders (excl neoplasms)

Synonym
Dementia, neurological disorder

Research involving
Human

Sponsors and support

Primary sponsor: Wyeth
Source(s) of monetary or material Support: Wyeth Pharmaceuticals France

Intervention

Keyword: Alzheimer disease, first in men, safety, SRA-444

Outcome measures

Primary outcome

To assess the safety and tolerability of ascending single oral doses of

SRA-444 in healthy adult subjects.

Secondary outcome

To obtain preliminary PK and PD profiles of SRA-444 in healthy adult subjects.

To evaluate the effect of a high-fat meal on the PK of SRA-444 administered to

healthy adult subjects.

Study description

Background summary

Alzheimer disease (AD) is a progressive, neurodegenerative disorder that accounts for the majority of cases of dementia in the elderly. AD is currently estimated to afflict 18 million people worldwide, and by 2025 the prevalence is projected to increase to 34 million1. The therapeutic goal for patients with AD is to improve memory and cognition, or at least to slow the disease process. Most current treatments for AD act to modulate neurotransmitter function, primarily by augmenting cholinergic transmission through inhibition of acetylcholinesterase
activity. However, these agents have exhibited only modest efficacy, which is insufficient to reverse or substantially delay cognitive decline in patients with AD.
Recent preclinical studies have demonstrated a possible role for the serotonin subtype 1A (5-hydroxytryptamine1A [5-HT1A]) receptors in cognitive function. These receptors are localized in key brain regions associated with cognition, mediate events associated with synaptic plasticity, and affect cognitive

performance in animal models. SRA-444 (5-fluoro-8-{4-[4-(6-methoxyquinolin-8-yl)piperazin-1-yl]piperidin-1-yl}quinoline tri-succinate) is a selective, potent, full antagonist at the human 5-HT1A receptor being developed by Wyeth Research (WR) for the symptomatic treatment of mild to moderate dementia of the Alzheimer type.

Study objective

Primary: to assess the safety and tolerability of ascending single oral doses of SRA-444 in healthy adult subjects

Secondary: to obtain preliminary PK and PD profiles of SRA-444 in healthy adult subjects to evaluate the effect of a high-fat meal on the PK of SRA-444

Study design

a randomized study of ascending single oral doses of SRA-444 to be performed in 8 cohorts of 8 healthy young adult subjects. Part A will be a subject- and investigator-blinded, placebo-controlled, dose-escalation assessment. Part B will be an open-label pilot assessment of food effect with a dose previously tested in part A and expected to be well tolerated.

Intervention

Single oral doses of SRA-444 ranging from 0.5 mg to 40 mg will be evaluated in healthy adult subjects after an overnight fast of at least 10 hours. The following doses will be studied sequentially in ascending order: 0.5 mg, 1 mg, 2.5 mg, 5 mg, 10 mg, 20 mg, and 40 mg.

Study burden and risks

see flowcharts protocol, page 27-37

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

zie beneden

Exclusion criteria

zie beneden

Study design

Design

Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Placebo
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	03-02-2007
Enrollment:	64
Type:	Actual

Ethics review

Approved WMO Date:	18-12-2006
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	21-12-2006
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
EudraCT	EUCTR2006-005423-42-NL
CCMO	NL15656.056.06