A Randomized, Double-Blind, Placebo-Controlled Study to Determine Safety and Tolerability of LX6171 Oral Suspension Dosed for 28 Days in Subjects Exhibiting Age Associated Memory Impairment (AAMI) with a Lead-in, Open-Label, Single-Dose Relative Bioavailability Study of LX6171 Oral Suspension in Healthy Elderly Subjects

Published: 25-10-2007
Last updated: 10-05-2024

Stage AThe primary objective is:• To compare the relative bioavailability of a single dose of 300 mg LX6171 using a 40mg/mL and an 80mg/mL formulated suspension;• To evaluate plasma concentrations of LX6171 and its major metabolite LP-523122 after a...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Neurological disorders NEC
Study type	Observational invasive

Summary

ID

NL-OMON31580

Source
ToetsingOnline

Brief title
NA

Condition

- Neurological disorders NEC

Synonym
amnesia, memory impairment

Research involving
Human

Sponsors and support

Primary sponsor: Lexicon Pharmaceuticals Inc.
Source(s) of monetary or material Support: zoals is opgegeven bij vraag B7

Intervention

Keyword: AAMI, bioavailibility, memory imparement, proof-of-concept

Outcome measures

Primary outcome

Stage A:

The primary objective is:

• To compare the relative bioavailability of a single dose of 300 mg LX6171

using a 40mg/mL and an 80mg/mL formulated suspension;

• To evaluate plasma concentrations of LX6171 and its major metabolite

LP-523122 after a single 300 mg administration of LX6171 oral suspension at two

concentrations (40 mg/mL and 80 mg/mL), in order to determine doses to be

utilized over a 28 day period (see stage B).

Stage B:

The primary objective is:

• To evaluate the safety and tolerability of 2 dose levels LX6171 oral

suspension when administered for 28 days, in subjects exhibiting AAMI

Secondary outcome

Stage A:

The secondary objective is:

• To evaluate the safety and tolerability of single doses of 300 mg of LX6171

utilizing two different concentrations of oral suspension (40 mg/mL and 80

mg/mL) in healthy elderly subjects

Stage B:

The secondary objectives are:

• To evaluate effects of multiple doses of LX6171 oral suspension on cognition

in subjects exhibiting AAMI;

• To evaluate plasma concentrations of LX6171 and its major metabolite

LP-523122 after administration of LX6171 oral suspension for 28 days, in

subjects exhibiting AAMI

Study description

Background summary

LX6171 is a new drug for the treatment cognitive disorders involving learning and memory impairment. LX6171 inhibits an enzyme in the brain. Animal studies in mice showed that by inhibiting the enzyme the animals could learn specific tasks more easily. These animal studies indicate that LX6171 might have a positive effect on memory in humans.

Study objective

Stage A
The primary objective is:
• To compare the relative bioavailability of a single dose of 300 mg LX6171 using a 40mg/mL and an 80mg/mL formulated suspension;
• To evaluate plasma concentrations of LX6171 and its major metabolite LP-523122 after a single 300 mg administration of LX6171 oral suspension at two concentrations (40 mg/mL and 80 mg/mL), in order to determine doses to be utilized over a 28 day period (see stage B).

The secondary objective is:
• To evaluate the safety and tolerability of single doses of 300 mg of LX6171 utilizing two different concentrations of oral suspension (40 mg/mL and 80 mg/mL) in healthy elderly subjects

Stage B
The primary objective is:
• To evaluate the safety and tolerability of 2 dose levels LX6171 oral suspension when administered for 28 days, in subjects exhibiting AAMI
The secondary objectives are:
• To evaluate effects of multiple doses of LX6171 oral suspension on cognition in subjects exhibiting AAMI;
• To evaluate plasma concentrations of LX6171 and its major metabolite LP-523122 after administration of LX6171 oral suspension for 28 days, in subjects exhibiting AAMI

Study design

Stage A:
16 healthy male and female volunteers will participate in this study of an investigational drug. The study will include a medical screening, one admission period of 4 days, and two follow-up visits.

Stage B:
120 healthy male and female volunteers will participate in this study of an investigational drug. The study will include a medical screening, 6 visits and finally a follow-up.

Study burden and risks

Stage A:
16 healthy male and female volunteers will participate in this study of an investigational drug. The study will include a medical screening, one admission period of 4 days, and two follow-up visits.

Stage B:
120 healthy male and female volunteers will participate in this study of an

investigational drug. The study will include a medical screening, 6 visits and finally a follow-up.

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

Stage A:
Subjects must meet all of the following criteria to be considered eligible to participate in Stage A of the study:;1. Males or females 60-80 years old;
2. Females must be post-menopausal (defined as two years without menses) or surgically sterile (defined by surgical sterilization, hysterectomy or bilateral salpingo-oophorectomy);
3. Vital signs (after at least 3 minutes resting in a supine position) which are within the following ranges or considered not clinically significant if outside these ranges:
• Systolic blood pressure, 80-140 mmHg

• Diastolic blood pressure, 60-100 mmHg
• Heart rate, 60-100 bpm
4. Non-smokers or very light smokers (less than or equal to 10 cigarettes per day) who are able to abstain from smoking during the residential part of the study;
5. Body weight between 50 and 100 kg and body mass index (BMI) between 18 and 30 kg/m2 or, if outside the range, not clinically significant and agreed with Sponsor and Investigator;
6. Negative urine screen for drugs of abuse at screening and on the day of admission (Day 1);
7. Negative hepatitis B surface antigen (HBsAg), hepatitis C antibody (HCV Ab), and HIV 1 and HIV 2 antibody test results must be obtained within the last 21 days prior to study admission;
8. Ability to provide written, informed consent.;Stage B:
Subjects must meet all of the following criteria to be considered eligible to participate in Stage B of the study:

1. Adult males and females 60-80 years (inclusive) old;
2. Females must be post-menopausal (defined as two years without menses) or surgically sterile (defined by surgical sterilization, hysterectomy or bilateral salpingo-oophorectomy);
3. Complaints of memory loss in everyday life as reflected by a score of 25 or more on the Memory Complaint Questionnaire (MAC-Q);
4. Memory test performance of one standard deviation below the mean established for young adults on the Logical Memory I Subtest of the Wechsler Memory Scale-Revised (WMS-R) , but not more than a standard deviation below the age-adjusted mean on the test (score of 11 to 19, inclusive);
5. Vital signs (after at least 3 minutes resting in a supine position) which are within the following ranges or considered not clinically significant if outside these ranges:
• Systolic blood pressure, 100-140 mmHg
• Diastolic blood pressure, 60-100 mmHg
• Heart rate, 60-100 bpm
6. Body weight between 50 and 100 kg and BMI between 18 and 30 kg/m2 or, if outside the range, not clinically significant and agreed with Sponsor and Investigator;
7. Negative urine screen for drugs of abuse at screening and on Day -1;
8. Negative hepatitis B surface antigen (HBsAg), hepatitis C antibody (HCV Ab), and HIV 1 and HIV 2 antibody test results must be obtained within the last 28 days prior to study admission;
9. Non-smokers or very light smokers (less than or equal to 10 cigarettes per day) who are able to abstain from smoking during the residential part of the study
10. Ability to provide written, informed consent;

Exclusion criteria

Stage A:
Candidates are not allowed to participate in Stage A of the study if any of the following exclusion criteria apply:
1. A need for or having taken any medication within five days of dosing, with the exception of hormone replacement therapy and those approved by the Investigator;
2. Administration of any investigational agent within 12 weeks of study entry;
3. Existence of any surgical or medical condition that, in the judgment of the Investigator,

might interfere with the absorption, distribution, metabolism, or excretion of LX6171;
4. Clinically significant abnormal physical findings;
5. Clinically significant laboratory abnormality;
6. Clinically significant abnormalities on resting Electrocardiogram (ECG);
7. Donation or loss of greater than 400 mL of blood within 12 weeks of study entry;
8. Serious adverse reaction or hypersensitivity to any drug;
9. Known history of hepatic disease or significantly abnormal liver function tests (greater than 1.5 times the upper limit of normal) on study entry;
10. History of alcoholism or substance abuse within three years prior to study entry;
11. Known history of significant hematological abnormalities;
12. Concurrent conditions that could interfere with the safety and/or tolerability measurements;
13. Inability to communicate or cooperate with the study staff for any reason;Stage B: Candidates are not allowed to participate in Stage B of the study if any of the following exclusion criteria apply:;1. Any neurological disorder that could produce cognitive deterioration as determined by history, clinical neurological examination, and, if indicated neuroradiologic examinations. Such disorders include Alzheimer*s Disease, Mild Cognitive Impairment, Parkinson's disease, stroke, intracranial hemorrhage, local brain lesions including tumors, and normal pressure hydrocephalus;
2. History of any infective or inflammatory brain disease, including those of viral, fungal, or syphilitic etiologies;
3. Evidence of dementia as determined by a score of 26 or less on a Mini-Mental State Examination (MMSE);
4. Evidence of depression as determined by a score of 11 or higher on the Geriatric Depression Scale (GDS);
5. Evidence of delirium, confusion, or other disturbances of consciousness;
6. Clinically significant cardiovascular, hepatic, renal, endocrine, neurological, or psychiatric disorders that could be responsible for memory loss in the judgment of the investigator;
7. Current psychiatric diagnosis according to DSM-IV criteria of depression, mania, or any major psychiatric disorder;
8. Evidence of significant cerebral vascular pathology as determined by a Hachinski Ischemic Score of 4 or more, or by neuroradiologic examination;
9. History of repeated minor head injury (e.g. in boxing) or a single injury resulting in a period of unconsciousness for 20 minutes or more;
10. Baseline laboratory values indicative of clinically significant co morbidity;
11. History of myocardial infarction within the past 12 months or evidence of recent infarction on ECG;
12. Current diagnosis or history of alcoholism or drug dependence, and not able/willing to commit to alcohol restrictions;
13. A need for or having taken any medication within 21 days of dosing, with the exception of hormone replacement therapy, ibuprofen, paracetamol, daily vitamins and aspirin;
14. Use of dietary supplements containing Huperzine A, gingko biloba, phosphatidylserine or docosahexanoic acid (DHA) within 15 days of baseline evaluation or reasonably expected to use these supplements during the course of the study.
15. Administration of any investigational agent within 12 weeks of study entry;
16. Donation or loss of greater than 400 mL of blood within 12 weeks of study entry;
17. Concurrent conditions that could interfere with the safety and/or tolerability

measurements;
18. Inability to communicate or co-operate with the study staff for any reason.

Study design

Design

Study phase:	2
Study type:	Observational invasive
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):	29-11-2007
Enrollment:	136
Type:	Actual

Ethics review

Approved WMO Date:	25-10-2007
Application type:	First submission
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)

Approved WMO Date:	12-11-2007
Application type:	First submission
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)

Approved WMO

Date:	08-02-2008
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	11-02-2008
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	26-03-2008
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	31-03-2008
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	09-04-2008
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	19-05-2008
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	21-05-2008
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)

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	EUCTR2007-005241-38-NL
CCMO	NL20162.040.07