Pharmacokinetic study of a new formulation of elacridar

Published: 01-10-2013
Last updated: 22-04-2024

To determine the pharmacokinetic properties of a new elacridar formulation

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Other condition
Study type	Interventional

Summary

ID

NL-OMON38922

Source
ToetsingOnline

Brief title
Pharmacokinetic study of a new formulation of elacridar

Condition

- Other condition

Synonym
na

Health condition

gezonde vrijwiliggers

Research involving
Human

Sponsors and support

Primary sponsor: Antoni van Leeuwenhoek Ziekenhuis
Source(s) of monetary or material Support: startgeld voor dr N. Steeghs toegekend door NKI-AvL

Intervention

Keyword: elacridar, Pharmacokinetics

Outcome measures

Primary outcome

pharmacokinetic properties of a new elacridar formulation

Secondary outcome

na

Study description

Background summary

Elacridar:
Elacridar is the most potent oral PgP/BCRP inhibitor, but unfortunately no longer available for clinical trials. Therefore our pharmacy developed a new elacridar formulation.

Purpose of elacridar development:
We need a potent PgP/BCRP inhibitor with high systemic exposure to ensure maximal inhibitory effects at the site of the blood brain barrier. We hypothesize that, when tyrosine kinase inhibitor (TKI; class of anticancer agents) treatment is combined with an inhibitor of PgP and BCRP, such as elacridar, TKI concentrations in the central nervous system (CNS) will increase and the development of brain metastases may be prevented.

Ultimately, this healthy volunteer study will result in the possibility to conduct a study combining elacridar with C11-labeled erlotinib. Using PET scans we can study whether erlotinib (or other TKIs) can pass the blood brain barrier and enter the brain when elacridar is given as an auxiliary drug. This can then be used in the treatment of brain metastases and brain tumors.

Study objective

To determine the pharmacokinetic properties of a new elacridar formulation

Study design

Phase I pharmacokinetic exploration study

Subjects will receive a single oral dose of elacridar.
Pharmacokinetic samples will be drawn after dosing at
T= 0, 0.5, 1, 1.5, 2, 3, 4, 5, 8, 12, 24, 48 hours.

PK curves of the new elacridar formulation will be compared with historic PK curves of the GSK elacridar tablets from earlier trials in our department and from the literature.

Dosing will start with 25 mg in three healthy volunteers. After the first 3 healthy volunteers the following dose levels will be discussed by an internal expert board. Dose will not exceed 1000 mg (which is known to be safe in humans using the GSK tablet formulation)
The internal expert board at least consists of a preclinical elacridar expert (Dr O. van Tellingen), a pharmacist/clinical pharmacologist and pharmacokinetics expert (Dr. A. Huitema), and a medical oncologist/clinical pharmacologist (Dr N. Steeghs).
The dose level defining the dose used for future studies will be expanded to a total of 6 healthy volunteers.

The study is stopped when the target exposure is reached, when further dose-increase does not result in further increase in systemic exposure (as in the case of non-linear oral PK), or when dose limiting toxicity is observed.

Intervention

Tablets containing 25 mg of a new elacridar formulation are used. All subjects will receive one single administration of one or multiple tablets(depending on dose level). Starting dose level is 25 mg. The maximum dose is set at 1000 mg.

Study burden and risks

Elacridar
Elacridar can be safely given in doses up to 1000 mg without side effects. Elacridar shows very limited side effects in animal as in human studies (data GSK on file). Elacridar is given in over 300 healthy volunteers and over 2000 cancer patients. Adverse events were predominantly mild in nature and all resolved. The most common events were neurological (headache, somnolence, dizziness, and tiredness) and gastrointestinal (diarrhea, gas, dyspepsia, nausea and vomiting, abdominal discomfort). No serious adverse events were seen in the healthy volunteer studies.

Blood samples:
Several blood samples will be drawn. Risks of this procedure is low. Some pain, bruising and hematoma formation may occur. In rare ocasions an vein infection or collaps may occur.

Contacts

Public
Antoni van Leeuwenhoek Ziekenhuis

Plesmanlaan 121
Amsterdam 1066 CX
NL
Scientific
Antoni van Leeuwenhoek Ziekenhuis

Plesmanlaan 121
Amsterdam 1066 CX
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

1. Healthy volunteer;
2. Age >=18 years;
3. Able and willing to give written informed consent;
4. Able and willing to undergo blood sampling for pharmacokinetic sampling;
5. Able and willing to swallow and retain oral medication;
6. Willing to comply to the protocol

Exclusion criteria

1. Any treatment with investigational drugs within two weeks prior to receiving the first dose of investigational treatment;

Study design

Design

Study type: Interventional

Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	25-10-2013
Enrollment:	15
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Elacridar
Generic name:	Elacridar

Ethics review

Approved WMO Date:	01-10-2013
Application type:	First submission
Review commission:	METC Slotervaartziekenhuis en Reade (Amsterdam)
Approved WMO Date:	02-10-2013
Application type:	First submission
Review commission:	METC Slotervaartziekenhuis en Reade (Amsterdam)

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	EUCTR2013-001131-47-NL
CCMO	NL45639.048.13

Study results

Date completed:	01-12-2014
Actual enrolment:	12