Evaluation of E7050 Pharmacokinetics after 100 mg Single Oral Doses Under Fed and Fasted Conditions and Characterization of E7050 Pharmacokinetics after 100 mg, 200 mg and 400 mg Single Oral Doses Under Fasted Condition in Healthy Subjects

Published: 05-10-2010
Last updated: 04-05-2024

Primary: * To determine the effect of food on the bioavailability of E7050 following oral administration of a tablet containing 100 mg E7050 with and without a standard low- or high-fat breakfast (Part A)* To characterize E7050 pharmacokinetics...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Miscellaneous and site unspecified neoplasms malignant and unspecified
Study type	Interventional

Summary

ID

NL-OMON34518

Source
ToetsingOnline

Brief title
Food effect study of E7050

Condition

- Miscellaneous and site unspecified neoplasms malignant and unspecified

Synonym

cancer, solid tumors

Research involving
Human

Sponsors and support

Primary sponsor: Eisai
Source(s) of monetary or material Support: Farmaceutische industrie

Intervention

Keyword: Cancer, Food Effect

Outcome measures

Primary outcome

Pharmacokinetics:

plasma and urine E7050 concentrations, pharmacokinetic parameters

Secondary outcome

Safety:

adverse events, vital signs, ECG-parameters, laboratory parameters, physical

examination

Study description

Background summary

E7050 is a new, investigational drug that may eventually be used for the treatment of different types of cancer. The study drug is expected to stop the cell growth of certain cancer cells; this action has been shown in early animal studies.

E7050 is a new chemical entity, an inhibitor of multi-targeted receptor tyrosine kinase that potently inhibits c-Met kinase. E7050 selectively inhibits cell growth of c-Met amplified cancer cell lines and HGF-induced proliferation of cancer cell lines, in which c-Met kinase signal is activated. E7050 also inhibits VEGFR-2 kinase and VEGF-induced cell growth of human umbilical vein

endothelial cells at slightly higher IC50 compared to inhibition of c-Met.

Study objective

Primary:
* To determine the effect of food on the bioavailability of E7050 following oral administration of a tablet containing 100 mg E7050 with and without a standard low- or high-fat breakfast (Part A)
* To characterize E7050 pharmacokinetics after single doses at 200 mg and 400 mg under fasted conditions (Part B)

Secondary:
* To evaluate the safety in healthy subjects with single doses of 100 mg E7050 (formulated as a tablet) administered with and without a standard low- or high-fat breakfast (Part A) and after single doses of 200 and 400 mg administered in the fasted state (Part B).

EXPLORATORY OBJECTIVE(S)
* To evaluate the role of DNA sequence variability on ADME.

Study design

Design:

The study will consist of two parts:
Part A (Food Effect) and Part B (E7050 PK characterization after a single oral dose of 200 or 400 mg E7050)

Part A will be a randomized, single-dose, open-label, three period crossover study. It will consist of 2 phases: Prerandomization and Randomization. The Prerandomization Phase will have two periods: Screening and Baseline. The Randomization Phase will have 5 periods: Period 1, Baseline + Period 2, and Baseline + Period 3. Just prior to the Randomization Phase, 18 subjects will be randomized to one of six possible sequences (ABC, ACB, BAC, BCA, CAB and CBA). In each period, subjects will receive a single tablet containing 100 mg E7050 either following an overnight fast (A), with a standard low-fat meal (B), or with a standard high-fat meal (C). There will be a 2-week washout between the periods.

Part B will begin approximately 2 weeks after Period 1 of Part A is complete and once all safety data has been evaluated. It will be conducted as a randomized, open-label, two-period parallel study design with two phases: a Prerandomization Phase consisting of a Screening and Baseline period and a Randomization Phase with 1 period (Treatment Period). Just prior to the Randomization Phase, 24 subjects will be randomized equally to receive either 200 mg (D) or 400 mg (E) of E7050 under fasted conditions.

Procedures and assessments
Screening and follow-up:
clinical laboratory, vital signs (including respiratory rate and body temperature), physical examination, 12-lead ECG, serum pregnancy test (females only; at eligibility screening: medical history, genomic DNA sample, urine drug screen, urine alcohol screen, HBsAg, anti HCV, anti-HIV 1/2; physical examination, vital signs (including respiratory rate and body temperature), 12-lead ECG, urine drug screen, urine pregnancy test and clinical laboratory to be repeated upon (each) admission; follow-up on Day 37 (Part A) and Day 9 (Part B)

Part A (FE):
observation period:
3 periods, first period in clinic from -17 h up to 168 h after drug administration on Day 1, second period in clinic from -17 h up to 168 h after drug administration on Day 15 and third period in clinic from -17 h up to 168 h after drug administration on Day 29

Blood sampling:
for pharmacokinetics of E7050: pre-dose and 0.5, 1, 2, 3, 4, 8, 12, 16, 24, 48, 72, 96, 120, 144 and 168 h post-dose on Days 1, 15 and 29

Urine Sampling:
for pharmacokinetics of E7050: pre-dose and intervals 0-4, 4-8, 8-12 and 12-24 h post-dose on Days 1, 15 and 29

Safety Assessments:
adverse events: throughout the study; physical examination: once on Days 1, 15 and 29; vital signs (including respiratory rate and body temperature): pre-dose and 1, 2, 3, 4, 8 and 16 h post-dose on Days 1, 15 and 29

Part B (SAD)
Observation period:
one period in clinic from -17 h up to 168 h after drug administration

Blood sampling
for pharmacokinetics of E7050: pre-dose and 0.5, 1, 2, 3, 4, 8, 12, 16, 24, 48, 72, 96, 120, 144 and 168 h post-dose

Urine sampling:
for pharmacokinetics of E7050: pre-dose and intervals 0-4, 4-8, 8-12 and 12-24 h post-dose

Safety assessments:
adverse events: throughout the study; physical examination: once on Day 1; vital signs (including respiratory rate and body temperature): pre-dose and 1,

2, 3, 4, 8 and 16 h post-dose on Day 1.

Bioanalysis:
analysis of plasma and urine E7050 samples using validated methods by Sponsor
genotyping by Sponsor

Intervention

Part A
Treatment A: a single oral dose of 100 mg E7050 in the fasted state
Treatment B: a single oral dose of 100 mg E7050 in the fed state (low fat breakfast)
Treatment C: a single oral dose of 100 mg E7050 in the fed state (high-fat breakfast)

Part B
Treatment D: a single oral dose of 200 mg E7050 in the fasted state
Treatment E: a single oral dose of 400 mg E7050 in the fasted state

Study burden and risks

Procedures:
Pain, light bleeding, heamatoma, possibly an infection.

Contacts

Public
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Scientific
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Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

* between 18 and 45 years of age
* BMI between 18 and 32 kg/m2
* non-smoker
* at screening state of health must satisfy the entry requirements

Exclusion criteria

1. Evidence of clinically significant cardiovascular, hepatic, gastrointestinal, renal, respiratory, endocrine, hematological, neurological, or psychiatric disease or abnormalities or a known history of any gastrointestinal surgery that could impact the pharmacokinetics of study drug.
2. Clinically significant illness within 8 weeks or a clinically significant infection within 4 weeks of dosing.
3. Evidence of organ dysfunction or any clinically significant deviation from normal in their medical history.
4. Evidence of clinically significant deviation from normal in physical examination, vital signs, or clinical laboratory determinations at Screening or Baseline.
5. A QTcF interval > 450 msec at Screening or Baseline, or 30 seconds before administration of study drug.
6. Females who are either pregnant or lactating.
7. A known or suspected history of drug or alcohol abuse within 6 months prior to screening, or who have a positive urine drug test or alcohol test at Screening or Baseline.
8. Positive results for Hepatitis B surface antigen (HBsAg) or Hepatitis C antibody (HCV) screen.
9. Diagnosis of acquired immune deficiency syndrome (AIDS), or positive test for human immunodeficiency virus (HIV).
10. Participation in another clinical trial less than 4 weeks prior to dosing or current enrollment in another clinical trial.
11. Receipt of blood products within 4 weeks, or donation of blood within 8 weeks, or donation of plasma within 1 week prior to dosing.
12. Hemoglobin level < 12.0 g/dL.

13. Known history of any significant drug or food allergy or an ongoing seasonal allergy.
14. Use of prescription drugs within 2 weeks prior to Screening (unless drug has a long t*, i.e., 5x t* exceeds 2 weeks).
15. Use of over-the-counter (OTC) medications within a minimum of 2 weeks prior to dosing.
16. Requiring a special diet or taking dietary aids known to modulate drug metabolizing enzymes, or who have consumed foods/beverages or herbal preparations containing Kava root, Ginkgo Biloba Extract (GBE), or St John*s Wort within 4 weeks of Baseline Period 1.
17. Known intolerance to the study drug (or any of the excipients).
18. Any medical or other condition which, in the opinion of the investigator, would preclude participation in a clinical trial.

Study design

Design

Study type:	Interventional
Intervention model:	Crossover
Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	15-11-2010
Enrollment:	42
Type:	Actual

Ethics review

Approved WMO Date:	05-10-2010
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	11-10-2010

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	EUCTR2010-022185-27-NL
CCMO	NL33785.056.10