A One-Way Drug-Drug Interaction Study to Assess the Effect of Ritonavir-boosted Atazanavir on the Pharmacokinetics, Safety and Tolerability of BMS-790052 in Healthy Subjects

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Primary Objective: To assess the effect of multiple oral doses of atazanavir 300 mg + ritonavir 100 mg once daily on the PK of BMS-790052 at steady state in healthy subjects.Secondary Objective(s): To assess the safety of multiple oral doses of BMS-...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Viral infectious disorders
Study type	Interventional

Summary

ID

NL-OMON36726

Source
ToetsingOnline

Brief title
BMS-790052/ritonavir-boosted atazanavir drug-drug interaction study

Condition

- Viral infectious disorders

Synonym
Hepatitis C, viral liver inflammation

Research involving
Human

Sponsors and support

Primary sponsor: Bristol-Myers Squibb
Source(s) of monetary or material Support: Farmaceutische industrie

Intervention

Keyword: atazanavir, BMS-790052, Hepatitis C, ritonavir

Outcome measures

Primary outcome

- Pharmacokinetics

Secondary outcome

- Safety

Study description

Background summary

The drug to be given, BMS-790052, is a new, investigational compound that may eventually be used for the treatment of Hepatitis C. The current standard of care for treating Hepatitis C fails more frequently in individuals co-infected with HIV. In addition, current therapies are unpleasant to administer and are associated with significant side effects. The study medication is being developed for the treatment of Hepatitis C, also in patients co-infected with HIV, and to address some of the shortcomings of the current treatments. The study medication inhibits a multifunctional protein that plays an important role in the replication and functioning of the Hepatitis C virus. This new compound is not registered as a drug, but has been given to humans before. During this study you will also receive Ritonavir and Atazanavir. Ritonavir and Atazanavir have been registered as drugs for the treatment of HIV/AIDS. The combination of both drugs is used in the treatment of patients with HIV/AIDS and is frequently used in patients co-infected with Hepatitis C

Study objective

Primary Objective:
To assess the effect of multiple oral doses of atazanavir 300 mg + ritonavir 100 mg once daily on the PK of BMS-790052 at steady state in healthy subjects.

Secondary Objective(s):
To assess the safety of multiple oral doses of BMS-790052 given alone and together with multiple doses of atazanavir plus ritonavir.

Study design

This will be an open-label, two-treatment, single-sequence crossover, multiple-dose, one-way interaction study in healthy subjects. Subjects will be screened and enrolled into the study up to 21 days prior to Day 1. All subjects will receive 2 treatments, A and B, sequentially.
Treatment A: multiple doses of BMS-790052 60 mg (2 x 30 mg tablets), orally, QD, administered after a light breakfast on Days 1 to 4.
Treatment B: multiple doses of BMS-790052 20 mg (2 x 10 mg tablets), orally, QD, simultaneously with atazanavir 300 mg + ritonavir 100 mg, orally, QD, administered after a light breakfast on Days 5 to 14. Subjects will be discharged on Day 15.

Procedures and assessments:
Screening and follow-up: clinical laboratory, full physical examination, Vital signs (BP, HR, OBT, RR), ECG and pregnancy test (females only).; at eligibility screening: medical history, drug screen, HBsAg, anti HCV, anti-HIV1/2, and HIV viral load.

Observation period:
in clinic from -17 h up to 24 h after first drug administration(Day -1 to Day 15)

Blood sampling:
for pharmacokinetics of BMS-790052: pre-dose on Days 8, 10, 12 and 13, pre-dose and 0.5, 1, 1.5, 2, 4, 6, 8, 12, 16, and 24h after dosing on Days 4 and 14 for pharmacokinetics of atazanavir: pre-dose and 1, 2, 4, 6, 12, 16, and 24h after dosing on Day 14

Safety assessments:
Safety assessments: adverse events throughout the study; vital signs, ECG: pre dose on Days 1, 5, and 10, and on Day 15; clinical laboratory: predose on Day 4 and 10, and on Day 15

Bioanalysis:
analysis of BMS 790052 samples using a validated LC-MS/MS method by the sponsor, analysis of atazanavir samples using a validated LC-MS/MS method by the sponsor if deemed necessary

Intervention

Active substance: BMS-790052, atazanavir, ritonavir

Study burden and risks

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

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

Age: 18-49 years, inclusive
BMI: 18.0 - 32.0 kg/m2, inclusive
Women of child bearing potential should use adequate contraception (e.g., double barrier method) until at least 4 weeks after last dose of study medication

Exclusion criteria

- Any significant acute or chronic medical illness.
- Current or recent (within 3 months of study drug administration) gastrointestinal disease indicated as clinically relevant by the Medical Investigator.
- Any major surgery within 4 weeks of study drug administration.
- Any gastrointestinal surgery that could impact upon the absorption of study drug.
- Donation of blood or plasma to a blood bank or in a clinical study (except a screening visit) within 90 days of study drug administration.
- Blood transfusion within 90 days of study drug administration.
- Inability to tolerate oral medication.
- Inability to swallow oral medication in the form of tablets or capsules.
- Inability to be venipunctured and/or tolerate venous access.
- Smoking more than 5 cigarettes per day.
- Recent (within 6 months of study drug administration) drug or alcohol abuse as defined in DSM IV, Diagnostic Criteria for Drug and Alcohol Abuse (see Appendix 1).
- History of cardiac conduction abnormalities.
- History of nephrolithiasis.
- Any other sound medical, psychiatric and/or social reason as determined by the investigator.
- Evidence of organ dysfunction or any clinically significant deviation from normal in physical examination, vital signs, ECG or clinical laboratory determinations beyond what is consistent with the target population.
- Positive urine screen for drugs of abuse.
- Positive blood screen for hepatitis C antibody, hepatitis B surface antigen, HIV viral load, or HIV-1, -2 antibody
- History of any significant drug allergy (such as Stevens-Johnson Syndrome, anaphylaxis or hepatotoxicity).
- Pregnancy or lactation (females only).
- Prisoners or subjects who are involuntarily incarcerated.
- Subjects who are compulsorily detained for treatment of either a psychiatric or physical (eg, infectious disease)
illness.

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):	16-03-2011
Enrollment:	14
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Norvir
Generic name:	Ritonavir
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	Reyataz
Generic name:	Atazanavir
Registration:	Yes - NL intended use

Ethics review

Approved WMO Date:	20-01-2011
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	24-01-2011
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	EUCTR2010-023213-60-NL
CCMO	NL35264.056.11