A Phase 1, Randomized, Placebo-Controlled Study to Investigate the Safety, Tolerability and Pharmacokinetics of Single and Multiple Doses Oral Doses of APX001, to Investigate the Effect of Food on APX001 and to Investigate the Drug-Drug Interaction Potential of APX001

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

Summary

ID

NL-OMON45345

Source
ToetsingOnline

Brief title
APX001 Safety, PK, Bioavailability, FE, DDI Study

Condition

- Fungal infectious disorders

Synonym
Fungal infection

Research involving
Human

Sponsors and support

Primary sponsor: Amplyx Pharmaceuticals, Inc.
Source(s) of monetary or material Support: Farmaceutische industrie

Intervention

Keyword: Fungal infections

Outcome measures

Primary outcome

Safety and tolerability: Evaluation of adverse events (AEs), physical

examinations (PE), vital signs (VS), laboratory safety tests.

Secondary outcome

Pharmacokinetics, APX001 and/or APX001A, urinalysis and 12-lead

electrocardiograms (ECG).

Study description

Background summary

APX001 is a new investigational compound that may eventually be used for the treatment of fungal infections. APX001 is a so-called prodrug, which is rapidly metabolized to APX001A after intake. APX001A is able to bind to an enzyme called GWT1, which is produced by fungi. By binding to GWT1, the cell wall of the fungus will be affected, biofilm formation by the fungus will be inhibited and the fungus will produce fungal growth defects. APX001 in development and is not registered as a drug but has been given to humans before.

The medication I the CYP substrates are known medications that are used for several indications.

Study objective

The study will be performed in 3 parts, Parts 1, 2 and 3. In all parts, the purpose is to investigate to what extent APX001 is tolerated. In addition, it will be investigated how quickly and to what extent APX001 is absorbed and eliminated from the body (this is called pharmacokinetics). The differences between the 3 parts are summarized below.

During Part 1, the effect of single doses of APX001 will be investigated. Also the effect of food on the pharmacokinetics of APX001 will be investigated.

During Part 2, the effect of multiple doses of APX001 will be investigated.

During Part 3, the potency of interaction between APX001 and other drugs during treatment with multiple doses of APX001 will be investigated.

This study will be performed in 46 healthy male or female volunteers, divided over 4 groups.

Study design

The pre-study screening will occur within 3 weeks before the start of the study.

Group 1a
For Group 1a, the actual study will consist of 4 periods during which the volunteer will stay in the clinical research center in Groningen (location Martini Hospital) for 4 days (3 nights) followed by one day during which the volunteer will visit the clinical research center in Groningen (location Martini Hospital) for a short visit. The time interval between the first days of each period is at least 13 days.

For each period, Day 1 is the first day of administration of the study compound. In each period, the volunteer is expected at the clinical research center at 14:00 h in the afternoon prior to the day of administration of the study compound. The volunteer will be required not to have consumed any food or drinks during the 4 hours prior to arrival in the clinical research center (with the exception of water).

In each of the 4 periods, the volunteer will leave the clinical research center on Day 3 and will come back for a short ambulant visit on Day 8.

The post-study screening will take place on 12 to 16 days after the last dosing. The appointment for the post-study screening will be made with you during the study.

For Group 1a, the participation to the entire study, from the pre-study

screening until the post study screening, will be approximately 11 weeks.

Group 1b
For Group 1b, the actual study will consist of 2 periods during which the volunteer will stay in the clinical research center in Groningen (location Martini Hospital) for 4 days (3 nights) followed by one day during which you will visit the clinical research center in Groningen (location Martini Hospital) for a short visit. The time interval between the first days of each period is at least 13 days.

For each period, Day 1 is the first day of administration of the study compound. In each period, the volunteer is expected at the clinical research center at 14:00 h in the afternoon prior to the day of administration of the study compound on Day 1. The volunteer will be required not to have consumed any food or drinks during the 4 hours prior to arrival in the clinical research center (with the exception of water).

In both periods, the volunteer will leave the clinical research center on Day 3 and will come back for a short ambulant visit on Day 8.

The post-study screening will take place on 12 to 16 days after the last dosing. The appointment for the post-study screening will be made with you during the study.

For Group 1b, the participation to the entire study, from the pre-study screening until the post study screening, will be approximately 7 weeks.

For Group 2 the pre-study screening will occur within 3 weeks before the start of the study.

The actual study will consist of 1 period during which the volunteer will stay in the clinical research center in Groningen (location Martini Hospital) for 17 days (16 nights), followed by one day during which the volunteer will visit the clinical research center in Groningen (location Martini Hospital) for a short visit.

Day 1 is the first day of administration of the study compound. The volunteer is expected at the clinical research center at 14:00 h in the afternoon prior to the day of administration of the study compound on Day 1. The volunteer will be required not to have consumed any food or drinks during the 4 hours prior to arrival in the clinical research center (with the exception of water).

The volunteer will leave the clinical research center on Day 16. The volunteer will return to the clinical research center for a short ambulant visit on Day 21.

The post-study screening will take place on Day 12 to 16 days after the last

dosing. The appointment for the post-study screening will be made with the volunteer during the study.

The participation to the entire study, from the pre-study screening until the post study screening, will be approximately 7 weeks.

For Group 3 the pre-study screening will occur within 4 weeks before the start of the study.

The actual study will consist of 1 period during which the volunteer will stay in the clinical research center in Groningen (location Martini Hospital) for 19 days (18 nights), followed by one day during which you will visit the clinical research center in Groningen (location Martini Hospital) for a short visit.

Day 1 is the first day of administration of the study compound. The volunteer are expected at the clinical research center at 14:00 h in the afternoon prior to the day of administration of the study compound on Day 1. The volunteer will be required not to have consumed any food or drinks during the 4 hours prior to arrival in the clinical research center (with the exception of water).

The volunteer will leave the clinical research center on Day 17. The volunteer will return to the clinical research center for a short visit on Day 22.

The post-study screening will take place on 12 to 16 days after the last dosing. The appointment for the post-study screening will be made with the volunteer during the study.

The participation to the entire study, from the pre-study screening until the post study screening, will be approximately 9 weeks.

Intervention

For Group 1a, the study will consist of 4 periods during which the volunteer will receive APX001 or placebo once per period. APX001 or placebo will be given as an intravenous infusion in the first period. In the other 3 periods, APX001 or placebo will be given as an oral tablet.

For Group 1b, the study will consist of 2 periods during which the volunteer will receive APX001 or placebo once per period. APX001 or placebo will be given as an oral tablet.

For Group 2, the study will consist of 1 period during which the volunteer will receive APX001 or placebo once daily for 14 consecutive days. APX001 or placebo will be given as an oral tablet. The dose for the next group will only be increased if the lower dose of the previous group was found to be well tolerated and after approval by the local Medical Ethics Review Committee.

For Group 3, the study will consist of 1 period during which the volunteer will receive once a cocktail of so-called CYP substrates (see also the Table below for details) on Day 1. Thereafter the volunteer will receive APX001 once daily for 13 consecutive days, followed by one day on which the volunteer will receive once APX001 combined with a cocktail of CYP substrates. APX001 will be given as an oral solution and the CYP substrate cocktail will be given as oral tablets and capsules.

Study burden and risks

The possible adverse effects of the investigational procedures (e.g. the use of the indwelling cannula) are described in Chapter 8 of the information booklet.

All potential drugs cause adverse effects; the extent to which this occurs differs. APX001 has been administered to man in a currently ongoing study. Thus far APX001 has been well tolerated with doses up to 350 mg administered via an intravenous infusion. There were no safety concerns arisen from this study. APX001 has been studied in animals. The most frequently observed adverse effects in animals were: vomiting, decreased activity, drowsiness, retching, decreased food consumption and increased reticulocyte (immature red blood cell) counts.

Because APX001 may react with light, protective measures will be taken to prevent exposure to direct sunlight.

The volunteer should be aware that the aforementioned adverse effects and possibly other, still unknown adverse effects, may occur during the study. However, with the doses used in this study no serious adverse effects are expected.

The possible adverse events of the CYP substrates can be found in the package leaflets that subjects will receive.

Contacts

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Scientific
Amplyx Pharmaceuticals, Inc.

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

Healthy male or female subjects
Age 18 to 55 years, inclusive
Body mass index (BMI) between 18.0 and 30.0 kg/m2, inclusive.

Exclusion criteria

Suffering from cardiovascular, pulmonary, gastrointestinal, metabolic, urogenital, neurological, immunological, psychiatric diseases, or neoplastic disorder with metastatic potential. Participation in a drug study within 60 days prior to (the first) drug administration in the current study. Pregnancy. Suffering from hepatitis B, hepatitis C, HIV/AIDS.

Study design

Design

Study type:	Interventional
Intervention model:	Crossover
Allocation:	Randomized controlled trial

Masking:	Double blinded (masking used)
Control:	Placebo
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	20-10-2016
Enrollment:	46
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Bupropion
Generic name:	Bupropion
Registration:	Yes - NL outside intended use
Product type:	Medicine
Brand name:	Caffeine
Generic name:	Caffeine
Registration:	Yes - NL outside intended use
Product type:	Medicine
Brand name:	Dextromethorphan
Product type:	Medicine
Brand name:	Flurbiprofen
Generic name:	Flurbiprofen
Registration:	Yes - NL outside intended use
Product type:	Medicine
Brand name:	Midazolam
Generic name:	Midazolam
Registration:	Yes - NL outside intended use

Ethics review

Approved WMO

Date:	29-09-2016
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	11-10-2016
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	03-01-2017
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	10-01-2017
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	20-02-2017
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	22-02-2017
Application type:	Amendment
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	EUCTR2016-003763-19-NL
CCMO	NL59228.056.16