A MULTICENTER OPEN-LABEL EXTENSION STUDY TO ASSESS LONG-TERM SAFETY OF PF-00547659 IN SUBJECTS WITH CROHN*S DISEASE (OPERA II)

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The primary objective of this study is to monitor the safety and tolerability of PF 00547659 during long term treatment. Secondary objectives: * The secondary objective is to assess pharmacokinetics and immunogenicity of PF 00547659.* Exploratory…

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Gastrointestinal inflammatory conditions
Study type	Interventional

Summary

ID

NL-OMON43920

Source
ToetsingOnline

Brief title
OPERA II (A7281007 - 9002/0016)

Condition

- Gastrointestinal inflammatory conditions

Synonym
Crohns Disease, Inflammatory Bowel Disease

Research involving
Human

Sponsors and support

Primary sponsor: Pfizer

Source(s) of monetary or material Support: Farmaceutical industry

Intervention

Keyword: Crohn's Disease, Open-Label Extension, PF-00547659

Outcome measures

Primary outcome

* Frequency of on treatment AEs, AEs leading to withdrawal, and SAEs.

Secondary outcome

* Frequency of the development of anti-drug antibodies (ADAs).

* Plasma trough concentrations of PF 00547659 will be analyzed using Population

PK methodology.

Exploratory Efficacy Endpoints:

* Proportion of subjects in remission (HBI <5) at 6 and 12 months.

* Proportion of subjects with a decrease in HBI *3 points from baseline of

either this study or the source studies.

* Proportion of subjects who relapsed (relapse is defined as above).

* Proportion of subjects requiring dose escalation or de escalation.

* Proportion of subjects discontinued from the study at Week 16.

* Proportion of subjects remaining in the study at the end of the study.

* Time to relapse.

Exploratory Pharmacodynamics Endpoints

* Blood samples will be collected prior to dosing at baseline and every 4 weeks

to Week 24, Week 32 and Week 72 to measure hsCRP. Also, stool samples will be

collected at the timepoints noted above to measure fecal calprotectin. Blood

samples will be collected at baseline, and Week 12 to measure soluble MAdCAM.

Study description

Background summary

The rationale for conducting this open-label extension (OLE) study is primarily to evaluate long term safety of PF 00547659. This protocol also provides the opportunity for continued treatment for subjects responding to treatment from studies A7281006 and A7281008. It also provides an opportunity for initial treatment for subjects randomized to placebo in study A7281006.

Study objective

The primary objective of this study is to monitor the safety and tolerability of PF 00547659 during long term treatment.

Secondary objectives:
* The secondary objective is to assess pharmacokinetics and immunogenicity of PF 00547659.
* Exploratory objectives include an assessment of the durability of response with long term treatment with PF-00547659.
* To determine the effect of PF-00547659 on disease biology in lesional and non-lesional tissue obtained by endoscopy.
* To determine the effects of PF-00547659 on mucosal healing

An optional colonic sub study that will characterize the effect of PF-00547659 on mucosal healing and tissue biology.
Exploratory objectives:
* To determine the effect of PF-00547659 on disease biology in lesional and nonlesional tissue obtained by endoscopy.
* To determine the effects of PF-00547659 on mucosal healing

Study design

This is a multi center Phase 2, open label, safety extension study for studies A7281006. Subjects eligible for this study will have completed the 12 week double blind induction period in study A7281006 and will be stratified by responders or non responders based on change in CDAI in that study, without unblinding treatment assignment from study A7281006. All subjects entering this study must have discontinued immunosuppressant therapy.

Intervention

Subjects entering this study will be given a 75 mg SC dose at baseline and then every 4 weeks through Week 72. After the active treatment period, the subjects will enter a 6 month follow up period of 6 monthly visits. At Week 96, subjects will undergo an End of Study visit. Subjects entering from study A7281006 will be stratified based upon either whether or not they achieved a CDAI 70 response. Only subjects who were clinical responders in study A7281008 will be allowed to enter this study.

Study burden and risks

Pfizer considers that the results of the nonclinical toxicity and safety pharmacology studies, together with the clinical experience obtained to date with PF- 00547659, support the continued development of PF-00547659 for the treatment of Crohn*s Disease and support the initiation of phase 2 clinical study A7281006. Subjects will be monitored closely for neurologic symptoms, evidence of infection, evidence of allergy, and evidence of myocardial changes.

Contacts

Public
Pfizer

Arcola Road 500
Collegeville PA 19426
US
Scientific
Pfizer

Arcola Road 500
Collegeville PA 19426
US

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

Subject eligibility should be reviewed and documented by an appropriately qualified member of the investigator*s study team before subjects are included in this study. Subjects must meet all of the following inclusion criteria to be eligible for enrollment into this study:;1. Subjects previously enrolled in study A7281006 who have completed the blinded 84 day (12 week) induction period or in study A7281008 who have completed week 12 and have demonstrated a clinical response as defined by that protocol.;2. Evidence of a personally signed and dated informed consent document indicating that the subject (or a legally acceptable representative) has been informed of all pertinent aspects of the study.;3. All women of childbearing potential (WOCBP) as determined during the feeder study (data must be available as source documents for this study) must have a negative urine pregnancy test result at the Baseline visit and throughout the duration of this study (defined as the time of the signing of the ICD through the end of this study).
* Women of non childbearing potential (WONCBP) as determined during the previous study do not require urine pregnancy tests in this study.;4. WOCBP who have sexual intercourse with a non surgically sterilized male partner must agree and commit to the use one of the following highly effective methods of contraception for the duration of the study (defined as the time of the signing of the ICD through the conclusion of subject participation or for approximately 6 months from the last dose of investigational product for any subject who discontinues early from the study). Contraceptive methods considered acceptable for use in this study include:
a. Established use [*2 months prior to the screening visit] of oral, injected, transdermal or implanted hormonal methods of contraception. Subjects who have used such methods for less than 2 months at the screening visit are required to use one of the methods described under b) or c) until the establishment of hormonal contraception methods.;b. Double barrier contraception: use of occlusive diaphragm (cap or cervical/vault caps) with spermicidal foam/gel/film/cream/suppository. In countries that spermicidal condoms are not allowed ordinary condoms could be used in combination with spermicidal creams. Appropriate measures are to be determined by the investigator together with the subject, in accordance with the standard of care in the country where treatment is administered. A female condom and a male condom should not be used together as friction between the two can result in either, or both product(s) failing. Appropriate measures are to be determined by the investigator together with the subject, in accordance with the standard of care in the country where treatment is administered.;c. An intrauterine device or system.;5. All men (unless surgically sterile, as defined below) who have sexual intercourse with a WOCBP must agree and commit to use a highly effective method of contraception as described under WOCBP for the duration of this study (defined as the time of the signing of the ICD through the conclusion of subject participation or for 6 months from the last dose of investigational product for any subject who terminates early from this study). Highly effective methods of contraception include properly used spermicidal condom.;6. To be considered surgically sterilized, a male partner must have had a vasectomy at least 24 weeks or bi lateral

orchiectomy >30 days before the Baseline visit of this study.;7. Subjects who are willing and able to comply with scheduled visits, treatment plan, laboratory tests, and other study procedures.

Exclusion criteria

Subjects presenting with any of the following will not be included in this study:;1. Subjects that have completed Day 84 (Week 12) of study A7281006 or completed Day 85 (Week 12) of study A7281008 but have experienced serious event(s) related to the investigational product, an unstable medical condition, or any other reason, in the opinion of the investigator, would preclude entry or participation in this study.;2. Subjects who are taking any dose of AZA, 6 MP or MTX.;3. Pregnant or breastfeeding women.;4. Entero vesicular (ie, between the bowel and urinary bladder) fistulae are prohibited. Other fistulae are allowed (e.g., enterocutaneous fistulae). Documentation of active and inactive fistulae are required.;5. Evidence of right or left heart failure based on echocardiographic assessments conducted as part of a prior study of PF-00547659.;6. Other severe acute or chronic medical or psychiatric condition or laboratory abnormality that may increase the risk associated with study participation or investigational product administration or may interfere with the interpretation of study results and, in the judgment of the investigator, would make the subject inappropriate entry into this study.;7. Received any prohibited treatment during the feeder study that, in the opinion of the investigator, compromised the safety or efficacy of this study.;8. Planned live (attenuated) vaccination during the course of this study.;9. Subjects with known allergy or hypersensitivity to PF-0547659 or its components.;10. Planned major elective medical or surgical procedure during the course of this study.;11. Participation in other interventional studies during participation in this study.;12. The inability to complete any of the five neurological assessments.

Study design

Design

Study phase:	2
Study type:	Interventional
Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	15-06-2012
Enrollment:	16
Type:	Actual

Ethics review

Approved WMO Date:	07-06-2011
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	09-11-2011
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	11-11-2011
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	23-02-2012
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	11-04-2012
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	25-07-2012
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	21-02-2013
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO	

Date:	26-02-2013
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	16-05-2013
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	25-07-2013
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	04-10-2013
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	07-10-2013
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	07-02-2014
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	27-02-2014
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	20-05-2014
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	27-05-2014
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO	

Date:	03-03-2016
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	21-04-2016
Application type:	Amendment
Review commission:	METC Amsterdam UMC

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	EUCTR2010-024638-48-NL
ClinicalTrials.gov	NCT01298492
CCMO	NL36946.018.11