A OPEN-LABEL EXTENSION STUDY OF CP-690,550 AS MAINTENANCE THERAPY IN PATIENTS WITH CROHN*S DISEASE

Published: 19-02-2013
Last updated: 26-04-2024

The primary objective of the study is to assess the safety and tolerability of long-term open-label CP-690,550 therapy in subjects with CD.Secondary objectives are to evaluate the effect of CP-690,550 maintenance therapy on clinical remission and on...

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

Summary

ID

NL-OMON43589

Source
ToetsingOnline

Brief title
A3921086 (9002/0097)

Condition

- Gastrointestinal inflammatory conditions

Synonym
Crohn's Disease, inflammatory bowel disease

Research involving
Human

Sponsors and support

Primary sponsor: Pfizer
Source(s) of monetary or material Support: Pfizer

Intervention

Keyword: 550, CP-690, Crohn's Disease, Open-Label Extension Study, Phase 2b

Outcome measures

Primary outcome

Safety

* Incidence and severity of adverse events, clinical laboratory abnormalities,

and change from baseline in clinical laboratory values

Efficacy

* As this is an open-label extension study, there will be no primary efficacy

endpoint. All efficacy endpoints will be exploratory. Sustained clinical

remission is defined as being in clinical remission at both Week 24 and Week 48

Health Outcome

* Absolute scores and change from baseline in Inflammatory Bowel Disease

Questionnaire (IBDQ) Total score and domain scores (Bowel Symptoms, Systemic

Symptoms, Emotional Function and Social Function) over time

Secondary outcome

Safety

* Incidence of clinically significant changes in physical examination from

baseline

Efficacy

* The proportion of all enrolled subjects in clinical remission and sustained

clinical remission at Week 48

* The proportions of subjects in clinical remission and sustained clinical remission among subjects in clinical remission at A3921086 baseline

* The proportion of subjects in clinical remission and sustained clinical remission among subjects in clinical response (CDAI-100 response from Study A3921083 baseline) or clinical remission at A3921086 baseline

Health Outcome

* The proportion of subjects with IBDQ total score *170 at Week 48 (clinical remission)

* The absolute scores for the Patient-Reported Treatment Impact Assessment (PRTI) at Week 48

For further information about safety, efficacy and health outcome secondary study parameters, see the protocol section 2 *study objectives and endpoints*.

Study description

Background summary

CP-690,550 is being developed for the treatment of adult patients with moderate-to-severe Crohn*s disease. At present, no current pharmacological therapy provides a cure for Crohn*s disease, and the treatment goal is to induce and then maintain remission. Despite available current treatment options, there is still a large unmet medical need with many patients failing to achieve clinical remission or experiencing apparent loss of initial efficacy with continued use. Surgery remains a treatment option of last resort, but is not curative and often is followed by disease recurrence. Thus, the need exists for a novel and more effective treatment for Crohn*s disease, with more convenient route of administration.

The clinical development program for CP-690,550 includes healthy volunteers and patients with Crohn*s disease and other diseases enrolled in 52 Phase 1, 2, and 3 studies; potentially important safety risks have been observed with the oral use of CP-690,550 in humans. It is not anticipated that treatment with CP-690,550 in CD patients will have new significant safety risks. However, the primary objective of the study is to assess the safety and tolerability of long-term open-label CP-690,550 therapy in subjects with CD. Please see chapter 1 of the protocol (introduction) for more details.

Study objective

The primary objective of the study is to assess the safety and tolerability of long-term open-label CP-690,550 therapy in subjects with CD.
Secondary objectives are to evaluate the effect of CP-690,550 maintenance therapy on clinical remission and on quality-of-life in subjects with CD, and also on biomarkers as measured by CRP and fecal calprotectin.

Study design

The patients participate in the study for approximately 1 year on average. During this period, the patient will visit the hospital 7 times (every 8 to 12 weeks). During these visits the following procedures will be performed:
* Discuss medical history, treatment and drug use complaints
* Measurement of blood pressure, pulse, temperature and weight and further physical examination
* Blood tests (around 10 ml withdrawn each time)
* Urine- and fecal analysis to assess the general health status
* Pregnancy test (if applicable)
* ECG (electrocardiogram)
* Completion of questionnaires on health, quality of life and daily activities

Four weeks after treatment, there is a final visit.

Intervention

* Oral intake of CP-690,550 5 mg or CP-690,550 10 mg study medication, in the form of CP-690,550 5 mg tablets
* Laboratory assessments (blood, urine and feces)
* Questionnaires

Study burden and risks

All medicines have side effects, as well as CP-690,550. Side effects often disappear when the drug is stopped. They can also remain for a longer period or permanently. Side effects can be mild, but also severe and even life threatening. Also, there may be not previously reported, potentially serious,

side effects. Furthermore, the patient may also experience an allergic reaction to the drug.
Most frequently mentioned side effects are: bowel complaints (nausea, diarrhea, constipation, and stomach ache), headache, fever, fatigue and upper respiratory inflammations.
Also less frequent side effects can be present, for example inflammations, decline in white blood cells or increased cholesterol values.

Risk of procedures involved in this trial
Blood withdrawal: these risks include fainting, inflammation of the vein, pain, hemorrhage or a bleeding at the site of puncture. Also a small risk on inflammation is present
ECG: irritation of the skin or a rash of the gel/stickers used
Staying sober: a patient may experience dizziness, headache or stomach aches and could faint
Questionnaires: these may contain sensitive questions

The available data on the potential and identified risks of CP-690,550 are thus considered to not preclude clinical studies in Crohn*s disease patients and the risks are minimized through appropriate pre-enrolment screening and close safety monitoring. Therefore, the overall risk-benefit assessment for this study is considered to be favourable.

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

Subjects must meet all of the following inclusion criteria to be eligible for enrollment into the study:;
1. Subjects who complete 26-week maintenance treatment of the A3921084 study or subjects who withdraw early due to A3921084 study treatment failure;
2. Women of childbearing potential must test negative for pregnancy prior to study enrolment.;
3. Sexually active females of childbearing potential are required to use adequate contraceptive methods during the study period and until completion of the follow-up procedures. No specific contraceptive measures are required in male subjects during study participation.;
4. Subjects who are willing and able to comply with scheduled visits, treatment plan, laboratory tests, and other study procedures.;
5. Evidence of a personally signed and dated informed consent document(s) indicating that the subject (or a legal representative) has been informed of all pertinent aspects of the study.

Exclusion criteria

Subjects presenting with any of the following will be excluded from the study:;
1. Subjects who have been discontinued due to protocol violation(s) (as determined by the Sponsor) in the A3921084 study.;
2. Subjects who were discontinued from the A3921084 study due to an adverse event that was not related to Crohn's disease.;
3. Evidence of active (draining) fistulae, intrabdominal or perineal collection or abscess at Baseline (MRI imaging is not required for entry to this study unless clinically indicated).;
4. Subjects with evidence of or suspected liver disease ie, liver injury due to methotrexate or primary sclerosing cholangitis.;
5. Subjects with evidence of blood dyscrasias at Baseline visit (as assessed by the laboratory results from Week 26 or early discontinuation visit from the A3921084 study):;
* Hemoglobin levels * 9.0 g/dL.;
* An absolute white blood cell (WBC) count of <3.0 x 10 to the power of 9/L (<3000/mm3) or

absolute neutrophil count of <1.2 X 10 to the power of 9/L <1200/mm3) or absolute lymphocyte count of <0.5 x 109/L (<500/mm3).;
* Thrombocytopenia, as defined by a platelet count <100 x 10 to the power of 9/L (<100,000/mm3).;
6. Subjects who have been scheduled to receive any live or attenuated virus vaccination during study period and for 6 weeks after last dose of study drug.;
7. Women who are pregnant or breastfeeding, or planning pregnancy during the study period.;
8. Subjects with estimated GFR *40 mL/min based on Cockcroft-Gault calculation from Week 26 or early discontinuation visit from the A3921084 study.;
9. Subjects with total bilirubin, AST or ALT more than 1.5 times the upper limit of normal from Week 26 or early discontinuation visit from the A3921084 study.;
10. Subjects with current or recent history of severe, progressive, or uncontrolled renal, hepatic, hematological, gastrointestinal, metabolic (including uncontrolled hypercholesterolemia), endocrine, pulmonary, cardiac, or neurological disease.;
11. Baseline 12-lead ECG (from Week 26 or early discontinuation visit from the A3921084 study) that demonstrates clinically relevant abnormalities which may affect subject safety or interpretation of study results (ie, baseline QTcF >450 ms, complete LBBB, acute or indeterminate age myocardial infarction, 2nd-3rd degree AV block, or serious bradyarrhythmias or tachyarrhythmias).;
12. Subjects who are expected to receive prohibited concomitant medications including medications that are either moderate to potent CYP3A4 inducers or inhibitors during the study period.;
13. Subjects who, in the opinion of the investigator or Pfizer, will be uncooperative or unable to comply with study procedures.;
14. Subjects who are investigational site staff members or relatives of those site staff members or subjects who are Pfizer employees directly involved in the conduct of the trial.;
15. 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 for entry into this study.
16. Subjects who are participating in or interested in participating in other investigational studies during study A3921086.

Study design

Design

Study phase:	2
Study type:	Interventional
Intervention model:	Other
Allocation:	Non-randomized controlled trial

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

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	12-11-2014
Enrollment:	9
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Tofacitinib
Generic name:	-

Ethics review

Approved WMO Date:	19-02-2013
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	30-10-2013
Application type:	First submission
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	10-01-2014
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	31-01-2014
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)

Approved WMO Date:	10-06-2014
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	12-06-2014
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	31-07-2014
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	08-09-2014
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	24-04-2015
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	01-06-2015
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	29-09-2015
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	09-10-2015
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	19-05-2016
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO	

Date:	20-05-2016
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)

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	EUCTR2011-003622-27-NL
ClinicalTrials.gov	NCT01470599
CCMO	NL39793.091.12