A Phase II, Double-Blind, Randomized, Placebo-Controlled, Parallel Group Pilot Study to Evaluate the Safety and Efficacy of FFP104 in the Treatment of Subjects with Moderate to Severely Active Crohn*s Disease

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To evaluate the safety and efficacy of intravenously administered FFP104 in subjects with active Crohn*s disease following repeat doses of FFP104.

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

Summary

ID

NL-OMON43739

Source
ToetsingOnline

Brief title
Pilot study investigating safety and efficacy of FFP104 in Crohn's Disease.

Condition

- Gastrointestinal inflammatory conditions
- Autoimmune disorders

Synonym
Crohn's Disease; inflammatory bowel disease

Research involving

Human

Sponsors and support

Primary sponsor: Fast Forward Pharmaceuticals B.V.
Source(s) of monetary or material Support: Fast Forward Pharmaceuticals B.V.

Intervention

Keyword: Crohn's Disease, Inflammatory Bowel Disease

Outcome measures

Primary outcome

Evaluate the safety and efficacy of intravenously administered FFP104 in

subjects with active Crohn*s disease following repeat doses of FFP104.

Secondary outcome

Assess the clinical response (reduction of CDAI from baseline by 100 points and

by 70 points) and clinical remission (CDAI < 150) at 6 weeks (Day 42) and at

other time points in the trial

Assess effects of intravenously administered FFP104 in subjects with active

Crohn*s disease on the mucosa:

- Endoscopy using the Crohn*s Disease Endoscopy Index of Severity (CDEIS) (Day

42)

- Histology (including immune cell infiltration assessments) (Day 42)

- Faecal calprotectin (Dag 28, 42, 84)

- C-reactive protein (CRP) (all visits)

Characterize the pharmacokinetics (systemic exposure after i.v. dosing) of

FFP104 in subjects with active Crohn*s disease.

Assess the pharmacodynamics of intravenously administered FFP104 in subjects

with active Crohn*s disease

Study description

Background summary

Chronic inflammatory bowel disease (IBD) is a group of chronic inflammatory diseases of the intestine, of which Crohn's disease and ulcerative colitis, are the two main diseases. Despite scientific research, the exact cause of IBD is not yet known. It is also not yet possible to predict the disease course, or to predict how a person will respond to treatment. To obtain clarity on this is more research is needed.

FFP104 is a monoclonal antibody of the human immunoglobulin IgG4 subclass that antagonizes human CD40-CD154 cellular signaling. Antagonism of CD40 is anticipated to modify CD40-CD154 driven immune responses and may therefore have utility in immune-mediated and systemic inflammatory diseases including psoriatic arthritis, psoriasis, primary biliary cirrhosis and Crohn*s disease. There are good indications that the proposed medicinal product, FFP104, will interfere with the ongoing inflammation and pathogenic processes in Crohn*s disease. The chimeric predecessor of FFP104 showed positive results in patients with Crohn*s disease. This study will assess the effect of FFP104, as the humanized form the antibody.

Study objective

To evaluate the safety and efficacy of intravenously administered FFP104 in subjects with active Crohn*s disease following repeat doses of FFP104.

Study design

This study is a phase II, double-blind, randomized, placebo-controlled, parallel group pilot study

Intervention

Subjects will be randomized into one of the three treatment groups:

1. 2.5 mg/kg FFP104 administered three times over 15 days (Day 0, 7, 14) with option for up to 3 additional doses
at Day 21, 28 and 35
2. 5.0 mg/kg FFP104 administered three times over 15 days (Day 0, 7, 14) with option for up to 3 additional doses
at Day 21, 28 and 35
3. Placebo (0.9% saline) administered three times over 15 days (Day 0, 7, 14) with option for up to 3 additional doses
at Day 21, 28 and 35

Study burden and risks

Currently human data is limited for FFP104 and the rationale for dose selection in this study is based on the safety and tolerability observed in preclinical studies and three clinical Phase I/II studies: ch5D12 in Crohn*s patients and PG102 (former name of FFP104) in patients with active Psoriatic Arthritis (PsA) and the ongoing PG102 study in Normal Healthy Volunteer study.
There are good indications that the proposed medicinal product, FFP104, will interfere with the ongoing inflammation and pathogenic processes in Crohn*s disease. The chimeric predecessor of FFP104 showed positive results in patients with Crohn*s disease. This study will assess the effect of FFP104, as the humanized form the antibody.

In this study subjects will be evaluated after 3 to 6 doses of FFP104 at 2.5 mg/kg (for a total dose of 7.5 to 15 mg/kg) and 5.0 mg/kg (for a total dose of 15 to 30 mg/kg). These doses were selected based on considering all available information from non-clinical and clinical studies with PG102, and from the non-clinical and clinical evaluation of the closely related molecule ch5D12. These data demonstrate that the structural, functional and toxicological characteristics of FFP104 (PG102) are comparable to those of ch5D12.

An 84 day (Week 12) follow up has been selected in order to allow sufficient safety data to be collected based on the pharmacokinetic profile of FFP104, given its anticipated half-life.
Safety assessments have been selected to monitor subjects based on the current understanding of the mechanism of action of FFP104.
To be able to collect this information the trial subjects will visit the hospital 7 to 9 times over a period of 14 weeks. These visits vary in length from 1 to 5 hours, depending on study drug infusions and other procedures to be done. No long lasting therapeutic effect is to be expected in this study because the treatment period is relatively short. This study may however provide information which will lead to further clinical trials with FFP104 in patient with Crohn*s Disease.

In previous trials, the most common AEs observed with an occurrence of more than 5% and judged to be related to FFP104 by investigators, were: headaches (16%), fever (10%), ALT increase (8%), dizziness (8%) and AST increase (7%).

These side effects were temporary and mostly mild to moderate in nature. The changes in ALT and AST were temporary and all values returned to normal by the end of the study. Similar medications have shown these laboratory changes in liver transaminase values, but at this time it is not clear what caused these changes and what their significance is. These changes in liver transaminases were temporary, have not impacted liver function, and were not accompanied by changes in bilirubin.

Taking all this information in consideration we believe this clinical trial is justified.

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

1) Willing and able to provide written informed consent.
2) Male or female aged between 18 and 75 years, inclusive.
3) Clinical diagnosis of Crohn*s disease involving the colon and/or ileum for at least 3 months from Screening confirmed by radiological, endoscopic or histological evidence.
4) Active Crohn*s disease defined as a Crohn*s Disease Activity Index (CDAI) score between 220 and 450, inclusive, at Screening.
5) Active inflammatory disease as defined by CDEIS >= 8 or a CDEIS >= 4 in cases of isolated ileitis or postileocecal resection (as determined by a Central Blinded Reader).
6) TNF-naïve or previously exposed to anti-TNF therapy at a registered dose (such as infliximab, adalimumab or certolizumab pegol) with treatment discontinued at least 8 weeks prior to Baseline due to inadequate response, loss of response or intolerance as judged by the Investigator.
7) Previous exposure to one induction regimen of vedolizumab (maximum 5 infusions at a registered dose) is allowed if treatment has been discontinued for at least 75 days prior to Baseline (Day 0) due to inadequate response or intolerance.
8) Must have adequate renal and hepatic function as adjudged by the Investigator.

Exclusion criteria

1) Subjects who are pregnant, breastfeeding, or of child-bearing potential and not using a medically accepted form of contraception. Male participants, with their partners, unwilling to use medically accepted contraception throughout the study.
2) Presence of ileostomies, colostomies or rectal pouches or history of proctocolectomy or total colectomy. Subject has an ostomy or ileoanal pouch (subjects with a previous ileo-rectal anastomosis are not excluded).
3) Subject has short bowel syndrome as determined by the Investigator.
4) History of evidence of colonic mucosal dysplasia.
5) Subject currently has a significant mechanical obstruction (stenosis or stricture).
6) Subject has a current diagnosis of ulcerative or indeterminate colitis.
7) Immunization with a live vaccine within 4 weeks of Screening, with the exception of influenza vaccine and no planned immunizations within the period of the study.
8) Active or latent tuberculosis (TB) or tuberculosis infection; TB assessment and prophylaxis will be performed as per local biologicals regulations and guidelines.
9) Subjects with a history of or ongoing chronic or recurrent infectious disease within the 12 months prior to Screening.
10) Positive stool culture for Clostridium within the last 6 months prior to Screening.

Study design

Design

Study phase:	2
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Placebo
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	03-11-2016
Enrollment:	6
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	FFP104
Generic name:	FFP104

Ethics review

Approved WMO Date:	22-07-2015
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	16-10-2015
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	06-01-2016

Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	29-09-2016
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	20-10-2016
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	16-11-2016
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	14-12-2016
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	02-03-2017
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)

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	EUCTR2015-001678-17-NL
ClinicalTrials.gov	NCT02465944
CCMO	NL53289.078.15