A Phase 2b, Multicenter, Randomized, Double-blind, Placebo-controlled, Parallel-group, Dose-response Study Evaluating the Efficacy and Safety of JNJ-54781532 in Subjects with Moderately to Severely Active Ulcerative Colitis

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

Summary

ID

NL-OMON40180

Source
ToetsingOnline

Brief title
Niet van toepassing

Condition

- Gastrointestinal inflammatory conditions

Synonym
Bowel infection, Ulcerative Colitis

Research involving
Human

Sponsors and support

Primary sponsor: Janssen-Cilag
Source(s) of monetary or material Support: Janssen-Cilag NV

Intervention

Keyword: inflammatory bowel disease, JAK inhibitor, Ulcerative Colitis

Outcome measures

Primary outcome

Efficacy evaluations will include:

* Mayo score and partial Mayo score

* Inflammatory Bowel Disease Questionnaire (IBDQ)

* C-reactive protein (CRP)

* Fecal lactoferrin and fecal calprotectin

* Ulcerative Colitis Endoscopic Index of Severity (UCEIS)

Primary Endpoint

The primary endpoint is the change from baseline in the Mayo score at Week 8.

Secondary outcome

The secondary objectives are as follows:

1. To evaluate the efficacy of JNJ-54781532 in inducing clinical response at

Week 8.

2. To evaluate the efficacy of JNJ-54781532 in inducing clinical remission at

Week 8.

3. To evaluate the efficacy of JNJ-54781532 in inducing mucosal healing at Week

8.

Exploratory Objectives

The exploratory objectives are as follows:

1. To explore the optimal treatment duration of JNJ-54781532 for the primary

and major secondary endpoints.

2. To explore the response to treatment through Week 32 among subjects who are

in clinical response to JNJ-54781532 at Week 8.

3. To explore the efficacy of JNJ-54781532 in achieving partial Mayo score

response (or partial Mayo score remission) and eliminating corticosteroid use

at Week 32 among subjects who are in clinical response and receiving

concomitant corticosteroids at Week 8.

Study description

Background summary

JNJ-54781532, also known as JNJ-54781532-AAD and ASP015K, is an investigational oral immunosuppressant that acts by inhibiting Janus kinase (JAK), with moderate selectivity for JAK3, a key enzyme in the interleukin (IL)-2 signal pathway. ASP015K is being developed by Astellas Pharma Global Development, Inc. (Astellas) and has been studied in subjects with moderate to severe chronic plaque psoriasis, and for the prophylaxis of solid organ rejection in subjects receiving allogeneic kidney or liver transplants. ASP015K is currently being studied in subjects with rheumatoid arthritis (RA). The sponsor has entered into a codevelopment agreement with Astellas, and under this agreement the sponsor has acquired the rights to pursue the development of this compound for any additional indications. As such, the sponsor is currently developing JNJ-54781532 (ASP015K) for the treatment of subjects with moderately to severely active ulcerative colitis (UC).

Study objective

The primary hypothesis of this study is that a dose-response relationship exists between disease activity as measured by the change from baseline in the

Mayo score at Week 8 and JNJ-54781532 treatment regimens in subjects with moderately to severely active UC.

Study design

This is a Phase 2b, multicenter, randomized, double-blind, placebo-controlled, parallel-group, dose-response study of oral tablets of JNJ-54781532 in adult subjects with moderately to severely active UC, defined as a baseline Mayo score of 6 to 12, with an endoscopic subscore of *2. Eligible subjects will be randomized to 1 of 5 treatment groups (ie, 4 different dosages of JNJ-54781532 or placebo) at Week 0. At Week 8, subjects who are randomized to placebo and not in clinical response will receive treatment with JNJ-54781532 150 mg once daily; all the other subjects will continue to receive their original randomized dosage of study agent through Week 32. All subjects will have a final safety visit approximately 4 weeks after their last dose of study agent. The end of the study is defined as the date the last subject completes the final safety visit (ie, approximately 4 weeks after the last dose of study agent).

Eligible subjects will be randomized in a 1:1:1:1:1 ratio to 1 of 5 treatment groups at Week 0:
* Placebo
* JNJ-54781532 25 mg once daily
* JNJ-54781532 75 mg once daily
* JNJ-54781532 150 mg once daily
* JNJ-54781532 75 mg twice daily
All subjects will receive their original randomized dosage of study agent through Week 8 and will be assessed for clinical response (ie, a decrease from baseline in the Mayo score by *30% and *3 points, with either a decrease from baseline in the rectal bleeding subscore of *1 or a rectal bleeding subscore of 0 or 1) at that timepoint. Treatment after Week 8 will be determined by clinical response status as follows:
* Subjects in clinical response at Week 8: These subjects will continue to receive their original randomized dosage of study agent through Week 32.
* Subjects not in clinical response at Week 8:
* Subjects randomized to placebo will begin treatment with JNJ-54781532 150 mg once daily.
* Subjects randomized to JNJ-54781532 will continue to receive their original randomized dosage of JNJ-54781532.
* At Week 16, subjects who do not achieve a partial Mayo score response (ie, a change from baseline of *3 in the partial Mayo score) at Week 16 will be discontinued from study agent. Subjects who achieve a partial Mayo score response at Week 16 can continue receiving JNJ-54781532 through Week 32. To maintain the blind, subjects randomized to a once daily dosage of JNJ-54781532 will receive a second daily administration of placebo. Study agent will be administered orally as 5 tablets (ie, all active drug, all matching placebo, or mixed active drug and matching placebo) given

twice daily according to treatment group assignment. Study agent should be taken with food and approximately 240 mL (8 oz) of water. Study agent should be taken at approximately the same time each day.

Intervention

There are 5 Treatment groups in this study. Four of the treatment groups include different doses of JNJ-54781532. One of the treatment groups is treatment with placebo.
The treatment groups for this study are:
*JNJ-54781532 25 mg once daily
* JNJ-54781532 75 mg once daily
* JNJ-54781532 150 mg once daily
* JNJ-54781532 75 mg twice daily
* Placebo
The chance that the subject will be placed in any one of these groups is 1 out of 5.

Study burden and risks

Number of visits:12x
Clinical laboratory assessments: 12x
PK samples at week 2: pre-dose, 0.5, 1 and 3 hour post-dose
Physical examination: 4x
ECG: 2x
X-ray:1x
Endoscopy: 2x (with biopsy)
Questionnaires:2x Inflammatory bowel disease questionnaire.
Diary: daily Mayo diary card + medication diary
Side effects:

Contacts

Public
Janssen-Cilag

Antwerpseweg 15-17
Beerse 2340
BE
Scientific
Janssen-Cilag

Antwerpseweg 15-17
Beerse 2340

BE

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

- Have a clinical diagnosis of ulcerative colitis (UC) at least 3 months prior to screening ;- Have moderately to severely active UC, defined as a baseline (Week 0) Mayo score of 6 to 12 ; including an endoscopy subscore greater than or equal to 2 as determined by a central read of the video endoscopy ;- Current treatment with oral corticosteroids or have a history of failure to respond to, or tolerate, at least 1 of the following therapies oral corticosteroids (including budesonide), 6-mercaptopurine (6-MP), azathioprine (AZA), or anti-tumor necrosis factor therapy or be corticosteroid dependent (ie, an inability to successfully taper corticosteroids without a return of the symptoms of UC ;- Must discontinue 6-MP/AZA for at least 1 week before the first dose of study medication

Exclusion criteria

- At imminent risk for colectomy ;- Have ulcerative colitis limited to the rectum only or to less than 20 centimeter of the colon ;- Presence of a stoma ;- Presence or history of a fistula ;- History or current diagnosis of active or latent tuberculosis (An exception is made for subjects who have a history of latent TB and are currently receiving treatment for latent TB) , human immunodeficiency virus, hepatitis C virus or hepatitis B virus infection ;- Have had more than 1 herpes zoster infection or have had any diagnosis disseminated herpes zoster;- Previous treatment with a janus kinase inhibitor (eg, tofacitinib)

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:	Recruitment stopped
Start date (anticipated):	04-03-2014
Enrollment:	8
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	JNJ-54781532
Generic name:	Peficitinib (ASP015K)

Ethics review

Approved WMO Date:	21-11-2013
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	23-01-2014
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	24-02-2014
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:	27-05-2014
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	04-06-2014
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	12-09-2014
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	22-09-2014
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	22-12-2014
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	09-01-2015
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	EUCTR2013-000263-88-NL
CCMO	NL46443.018.13