A Phase IIb Randomized, Placebo-Controlled Study to Evaluate the Clinical Efficacy and Safety of Induction and Maintenance Therapy with BMS-936557 in Subjects with Active Ulcerative Colitis (UC)

Published: 15-03-2011
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Primary objective:Compare the efficacy of BMS-936557 versus placebo for induction of clinical remission (defined as Mayo score * 2 points with no individual subscore > 1 point) at Week 7 (IP-50).Secondary objective* Compare the efficacy of BMS-...

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

Summary

ID

NL-OMON35771

Source
ToetsingOnline

Brief title
IM129-005

Condition

- Gastrointestinal inflammatory conditions

Synonym
Ulcerative Colitis

Research involving

Human

Sponsors and support

Primary sponsor: Bristol-Myers Squibb
Source(s) of monetary or material Support: Pharmaceutical industry

Intervention

Keyword: BMS-936557, Inadequate clinical response, Ulcerative colitis

Outcome measures

Primary outcome

Compare the proportion of the subjects with clinical remission (defined as Mayo score * 2 points with no individual subscore > 1 point) of BMS-936557 with that of the placebo at IP-50 (Week 7).

Secondary outcome

* Compare the proportion of the subjects with clinical response (defined as reduction from baseline in Mayo score * 3 points and * 30%, and decrease from baseline in rectal bleeding subscore * 1 point or absolute rectal bleeding subscore * 1 point) of BMS-936557 with that of the placebo at IP-50 (Week 7)
* Compare the proportion of subjects with mucosal healing (defined as endoscopy subscore of * 1 point) of BMS-936557 with that of the placebo at IP-50 (Week 7).

Study description

Background summary

Induction of clinical response and remission over a 6 to 8 week period, followed by long-term maintenance of response is a well-accepted treatment paradigm in Inflammatory Bowel Disease (IBD). Upon successful induction

therapy, with decreased burden of acute inflammation, less intensive therapy can usually be used in the maintenance setting. Consistent with the IBD treatment paradigm, the current study is designed with an induction and a maintenance period. While dose selection in the induction period is based on an exposure response model constructed from the data of the Phase IIa study, there is insufficient information available to determine the dose required to obtain maintenance of response. As such, the maintenance period is an exploratory study designed to gain information on the exposure-response relationship in the maintenance setting. The open label period is available as an option to ensure that subjects who enrolled into the clinical study are guaranteed to receive the potential clinical benefit offered by the study drug and for subjects who have experienced clinical benefit from the study drug at any point in time, that they can continue to receive the study drug upon disease relapse or at the end of the maintenance period.

Study objective

Primary objective:
Compare the efficacy of BMS-936557 versus placebo for induction of clinical remission (defined as Mayo score * 2 points with no individual subscore > 1 point) at Week 7 (IP-50).

Secondary objective
* Compare the efficacy of BMS-936557 versus placebo for induction of clinical response (defined as reduction from baseline in Mayo score * 3 points and * 30%, and decrease from baseline in rectal bleeding subscore * 1 point or absolute rectal bleeding subscore * 1 point) at Week 7 (IP-50)
* Compare the efficacy of BMS-936557 versus placebo for induction of mucosal healing (defined as endoscopy subscore of * 1 point) at Week 7 (IP-50)
* Assess health-related quality of life outcome (IBDQ) of BMS-936557 and placebo in the induction period
* Assess the safety of BMS-936557 in the induction period.

Study design

This study includes three periods (Screening, Induction, and Maintenance) and an Open Label Extension period (OL). Following the brief Screening Period, eligible subjects will enter a 7-week placebo-controlled Induction Period with staged cohort design. The placebo controlled Induction Period (IP) will serve as a dose-finding study and is adequately powered to demonstrate with statistical rigor the efficacy of BMS-936557 for the induction of clinical response, remission, and mucosal healing in subjects with moderate to severely active UC.
Subjects from all 3 cohorts who are responders at Day IP-50 (Week 7) during the Induction Period will enter the randomized, double-blind, and placebo-controlled Maintenance Period (MP). The MP will serve as an exploratory

dose-finding study and is not statistically powered.
Subjects who complete the IP or MP, or who experience Disease Relapse during the first year of MP, or who are not in remission or have unsatisfactory clinical response after the first year of MP, have the option to enter the OL.

Intervention

BMS-936557 will be administered intravenously. During the Induction Period on Days IP-1, IP-8, IP-22 and IP-36, subjects will receive placebo or BMS-936557 at a dose of 15 mg/kg or 25 mg/kg. After randomization in the Maintenance Period, subjects will receive placebo or BMS-936557 at a dose of 5 mg/kg, 10 mg/kg or 20 mg/kg on Days MP-1, MP-8 and every 14 days thereafter up to MP-757. In the Open-label Period, subjects will receive 15 mg/kg BMS-936557 until marketed in local country or study is discontinued.

Study burden and risks

There is a possibility that BMS-936557 may be an effective treatment for colitis ulcerosa. However, it is not known if individual patients entering this trial will benefit directly. The information gained from this study may help future patients with colitis ulcerosa. Patients will have the inconvenience of more frequent interventions/procedures and longer visits to the hospital than would be usual for routine clinical care. They will also have to undergo additional procedures. Potential side effects are known from research studies in a small number of subjects. Additional unforeseen side effects could occur and some side effects could be life threatening or fatal. Safety monitoring is included throughout the protocol. At all times throughout the study, the patient has the right to withdraw consent without their usual standard of care being affected.

Contacts

Public
Bristol-Myers Squibb

Vijzelmolenlaan 9
3447 GX Woerden
NL
Scientific
Bristol-Myers Squibb

Vijzelmolenlaan 9
3447 GX Woerden
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

1. Signed Written Consent
2. Have had ulcerative colitis (UC) for at least 6 months from the time of initial diagnosis.
3. In the past have failed or intolerant t at least one convential therapy or currently receiveing at least one convential therapy
*Inadequate response and/or intolerant response
-Oral aminosalicylates for at least 6 weeks
- Prednisone * 40 mg/day for at least 2 weeks
- Immunosuppressants for at least 12 weeks
- Intravenous hydrocortisone * 400 mg/day for at least 1 week
- Approved anti-TNF agent for at least 8 weeks.
*Currently receiving:
- Oral aminosalicylates for at least 6 weeks
- Prednisone * 20 mg/day for at least 4 weeks
- Immunosuppressants for at least 12 weeks.
4. Mayo score * 6 with an endoscopic subscore of * 2
5. Drug Stabilization Requirements
- Oral corticosteroid treatment must have been * 30 mg/day prednisone at a stable dose for at least 2 weeks prior to randomization into the Induction Period
-Oral aminosalicylates should be at a stable dose for at least 2 weeks prior to randomization into the Induction Period
- Azathioprine or 6-mercaptopurine should be at a stable dose for at least 8 weeks prior to randomization into the Induction Period
6. Men and women * 18 years of age
7. Women of childbearing potential (WOCBP) must have a negative serum or urine pregnancy test

Exclusion criteria

1. Diagnosis of Crohn*s Disease or Indeterminate Colitis
2. Diagnosis of ulcerative colitis that is limited to the rectum
3. Current evidence of fulminant colitis, toxic megacolon or bowel perforation
4. Current need for colostomy or ileostomy
5. Previous total or subtotal colectomy or any surgical resection for UC
6. Surgical bowel resection within 6 months before screening for any reason other than UC
7. Primary sclerosing cholangitis (PSC)
8. Current evidence of colonic dysplasia or past evidence of definite colonic dysplasia that has not been definitively treated
9. Current symptoms of severe, progressive, or uncontrolled renal, hepatic, hematological, pulmonary, cardiac, neurological, ophthalmologic or cerebral disease. Concomitant medical conditions that in the opinion of the Investigator might place the subject at unacceptable risk for participation in this study
10. Subjects with a history of or current evidence of malignancies
11. Subjects at risk for active tuberculosis (TB).
12. Subjects with any serious bacterial infection within the last 3 months
13. Subject who have received any live vaccines within 3 months of the anticipated first dose of study medication or who will have need of a live vaccine at any time following randomization into the study

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):	22-11-2011

Enrollment:	12
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	BMS-936557
Generic name:	BMS-936557

Ethics review

Approved WMO Date:	15-03-2011
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	26-09-2011
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	13-12-2011
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	25-06-2012
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:	09-12-2013
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO	

Date:	21-01-2014
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	24-06-2014
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	EUCTR2010-022506-41-NL
ClinicalTrials.gov	NCT01294410
CCMO	NL35656.018.11