A Phase 3, Randomized, Double-blind, Placebo-controlled, Parallel-group, Multicenter Study to Evaluate the Safety and Efficacy of Ustekinumab Maintenance Therapy in Subjects with Moderately to Severely Active Crohn*s Disease

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

Summary

ID

NL-OMON43994

Source
ToetsingOnline

Brief title
IMUNITI

Condition

- Gastrointestinal inflammatory conditions

Synonym
Crohn's Disease

Research involving

Human

Sponsors and support

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

Intervention

Keyword: Crohn's Disease, ustekinumab

Outcome measures

Primary outcome

The primary endpoint is clinical remission at Week 44, where clinical remission

is defined as a CDAI score of < 150 points.

Secondary outcome

The major secondary endpoints in order of importance are:

1. Clinical response at Week 44.

2. Clinical remission at Week 44 among subjects in clinical remission to

ustekinumab at Week 0.

3. Corticosteroid-free remission at Week 44.

4. Clinical remission at Week 44 in the subset of subjects who were refractory

or intolerant to TNF-antagonist therapy (ie, subjects from induction study

CNTO1275CRD3001).

Study description

Background summary

Ustekinumab is a fully human immunoglobulin G1 kappa (IgG1k) monoclonal antibody (mAb) to human interleukin (IL)-12/23p40 that binds with high affinity to human IL-12 and IL-23. Ustekinumab prevents IL-12 and IL-23 bioactivity by

preventing their interaction with their cell surface IL-12R*1 receptor protein. Through this mechanism of action, ustekinumab effectively neutralizes all IL-12 (Th1) and IL-23 (Th17) mediated cellular responses. Abnormal regulation of IL-12 and IL 23 has been associated with multiple immune-mediated diseases, including inflammatory bowel disease, and binding the IL 12/23p40 subunit may provide effective therapy in Crohn*s disease.

Study objective

The primary objectives are:
- To evaluate clinical remission for the 2 subcutaneous (SC) maintenance regimens of ustekinumab in subjects with moderately to severely active Crohn*s disease induced into clinical response with ustekinumab in the induction studies, CNTO1275CRD3001 and CNTO1275CRD3002.
- To evaluate the safety of 2 SC maintenance regimens of ustekinumab in subjects with moderately to severely active Crohn*s Disease.

The secondary objectives are:
- To evaluate the efficacy of ustekinumab in maintaining clinical response in subjects induced into clinical response.
- To evaluate the efficacy of ustekinumab in maintaining clinical remission in subjects induced into clinical remission.
- To evaluate the efficacy of ustekinumab in achieving corticosteroid free remission.
- To evaluate the pharmacokinetics, immunogenicity, and pharmacodynamics of ustekinumab therapy, including changes in CRP, fecal calprotectin, fecal lactoferrin, and other pharmacodynamic biomarkers.
- To evaluate the effect of ustekinumab on health related quality of life.

Study design

This is a randomized, double-blind, placebo-controlled, parallel-group multicenter study of the safety and efficacy of SC regimens of ustekinumab in maintaining disease control through Week 44 in subjects with moderately to severely active Crohn*s disease induced into clinical response with ustekinumab in the induction studies, CNTO1275CRD3001 or CNTO1275CRD3002. The maintenance portion of the
study continues to Week 44 and the subsequent study extension will continue up to Week 272. The number of subjects enrolling in this study will be dependent on the number of subjects from the induction studies eligible to enroll into the maintenance study.

Intervention

Subjects in the primary population will be randomized in a 1:1:1 ratio at Week 0 of this maintenance study to receive 1 of the following SC regimens:

- Group 1: Placebo
- Group 2: Ustekinumab 90 mg SC q12w (with final dose at Week 36)
- Group 3: Ustekinumab 90 mg SC q8w (with final dose at Week 40)

After the study is unblinded in the extension phase, Group 1 will be terminated. Patients in this group will not receive study medication anymore.

Study burden and risks

Please refer to section E9.

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

Each potential subject must satisfy all of the following criteria to be enrolled in the study. Each subject must:
1. Have received study agent at Week 0 in study CNTO1275CRD3001 or CNTO1275CRD3002 and completed the Week 8 CDAI score evaluation.;2. Be able to complete the Week 0 visit in study CNTO1275CRD3003 within 4 days of the Week 8 visit in study CNTO1275CRD3001 or CNTO1275CRD3002. At the discretion of the investigator, the window may be extended to 8 days to allow appropriate treatment and/or recovery of nonserious infections (eg, acute upper respiratory tract infection, simple urinary tract infection).;3. Be able and willing to adhere to the study visit schedule and comply with other protocol requirements;4. Be capable of providing informed consent, which must be obtained prior to any study-related procedures

Exclusion criteria

Any potential subject who meets any of the following criteria will be excluded from participating in the study. The subject will be excluded if he or she:
1. Had any of the following changes to their concomitant medications due to Crohn*s disease (ie, lack of efficacy) since Week 0 of studies CNTO1275CRD3001 and CNTO1275CRD3002
a. Increase in physician-prescribed daily dose of oral corticosteroids of more than 5 mg or more of prednisone (or equivalent increase in prednisone-equivalent dose of other corticosteroids),
b. Initiation of oral budesonide or increase in daily dose
c. Initiation of parenteral, and oral corticosteroids for Crohn*s disease, except for dose equivalent substitutions among oral corticosteroids
d. Initiation or increased physician-prescribed daily dose of methotrexate (MTX), 6-MP, or azathioprine (AZA), except for dose equivalent substitutions;2. Initiated a protocol prohibited medication since Week 0 of studies CNTO1275CRD3001
and CNTO1275CRD3002:
a. Immunomodulatory agents other than 6-MP/AZA or MTX (including but not limited to 6-TG, cyclosporine, tacrolimus, sirolimus, mycophenolate mofetil)
b. Immunomodulatory biologic agents (including but not limited to TNF-antagonists, natalizumab, abatacept, commercial ustekinumab)
c. Experimental Crohn*s disease medications (including but not limited to thalidomide, briakinumab, vedolizumab, traficet, AMG-827);3. Underwent a Crohn*s disease related surgery since Week 0 of induction study CNTO1275CRD3001 or CNTO1275CRD3002. Seton placement and recent cutaneous and perianal abscesses which have been drained and adequately treated at least 3 weeks prior to receiving baseline study agent are not exclusionary provided that there is no anticipated need for any further surgery;4. Subjects from countries with high multidrug-resistant TB burden (eg, South Africa, Bulgaria, and the Russian Federation) diagnosed with latent TB during induction study CNTO1275CRD3001 or CNTO1275CRD3002, or any subject who has discontinued or is noncompliant with appropriate therapy for the treatment of latent TB.;5. Are diagnosed with any medical

condition (or signs or symptoms thereof) which would have precluded enrollment in induction studies CNTO1275CRD3001 and CNTO1275CRD3002. This includes any lymphoproliferative disorder or malignancy (other than basal cell carcinoma of the skin), opportunistic or other significant infection, or other severe, progressive, or uncontrolled medical (eg renal, hepatic, hematological, endocrine, pulmonary, cardiac, neurologic, or autoimmune) or psychiatric disease,
including recent significant instability in a previous condition.;6. Have signs and symptoms of latent or active granulomatous infection, including TB, histoplasmosis, or coccidioidomycosis.;7. Is a woman who is pregnant, or breast-feeding, or planning to become pregnant or is a man who plans to father a child while enrolled in this study or within 20 weeks after the last dose of study agent.

Study design

Design

Study phase:	3
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):	17-10-2012
Enrollment:	36
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	ustekinumab
Generic name:	Stelara
Registration:	Yes - NL outside intended use

Ethics review

Approved WMO Date:	11-07-2011
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	08-03-2012
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	04-04-2012
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	08-03-2013
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	10-04-2013
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	30-08-2013
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	31-10-2013
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO	

Date:	11-02-2014
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	13-03-2014
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	31-07-2014
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	07-11-2014
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	13-07-2015
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	18-09-2015
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	09-10-2015
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	17-11-2015
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam

	(Rotterdam)
Approved WMO Date:	20-06-2016
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	08-07-2016
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	02-08-2016
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	31-08-2016
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	10-11-2016
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	03-07-2017
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	21-07-2017
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	14-11-2018

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	EUCTR2010-022760-12-NL
ClinicalTrials.gov	NCT01369355
CCMO	NL37124.078.11