A Multicenter, Open-Label Study of the Human Anti-TNF Monoclonal Antibody Adalimumab to Evaluate the Long Term Safety and Tolerability of Repeated Administration of Adalimumab in Subjects With Ulcerative Colitis

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To evaluate the long term maintenance of response, safety and tolerability of repeatedadministration of adalimumab in subjects with Ulcerative Colitis who participated in and successfullycompleted Protocol M06-826 or Protocol M06-827.The secondary...

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

Summary

ID

NL-OMON38090

Source
ToetsingOnline

Brief title
Adalimumab - Ulcerative Colitis - Long Term Administration

Condition

- Gastrointestinal inflammatory conditions

Synonym
inflamation of rectum and/or large intestine

Research involving

Human

Sponsors and support

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

Intervention

Keyword: adalimumab, ulcerative colitis

Outcome measures

Primary outcome

Efficacy will be evaluated by Partial Mayo Scores at each visit.

Additional efficacy variables will be analyzed at the following timepoints:

• Colectomy rates during the study

• Change from Baseline in Mayo Scores at Week 48; Week 96; Week 144; Week 192,

Week 240 and Week 292.

• Change from Baseline in Partial Mayo Scores at Week 48; Week 96; Week 144;

Week 192;

Week 240; Week 292 and other timepoints

• Change from Baseline in IBDQ Week 48; Week 96; Week 144; Week 192, Week 240,

Week 292.

• Change from Baseline in SF-36 Week 48; Week 96; Week 144; Week 192, Week 240,

Week 292.

• Change from Baseline in Work Productivity and Activity Impairment

Questionnaire Week 48;

Week 96; Week 144; Week 192, Week 240, Week 292.

• Cumulative number of unscheduled outpatient visits (physician visits,

emergency room visits,

hospital admissions, and days of hospitalization) at Week 48; Week 96; Week

144; Week 192, Week 240 and Week 292.

Safety: AEs, laboratory data, physical examinations and vital signs are the

safety parameters and these

will be assessed throughout the study

Secondary outcome

Summary statistics for adalimumab serum concentration at each time of scheduled

sampling will be calculated. In addition, pharmacokinetic model-based analyses

will be performed with the focus on clearance (CL) and volume of distribution

(V).

Study description

Background summary

Ulcerative colitis is one of the two primary forms of idiopathic inflammatory bowel disease. It is a chronic, relapsing inflammatory disease of the rectum and/or large intestine characterized by inflammation and ulceration of the mucosal and submucosal intestinal layers. The clinical course is marked by exacerbation and remission. The incidence in Europe is estimated at 1.5 to 20.3 cases per 100,000 person-years. The aim of medical treatment in ulcerative colitis is to induce and maintain remission.
Conventional pharmaceutical therapies do not completely abate the inflammatory process and have significant side effects. Conventional therapies for the induction of remission have included anti-inflammatory agents (5-ASA derivates and corticosteroids) and the immunomodulatory agent cyclosporine. 5-ASA derivates as well as immunomodulatory agents (azathiprine or 6-MP) have been used for the maintenance of remission. Most recently, infliximab (a chimeric monoclonal anti-TNF antibody) has demonstrated efficacy in subjects with

moderately to severely active ulcerative colitis and was approved in both Europe and the US for the induction and maintenance of remission in subjects with moderate to severe ulcerative colitis.

Study objective

To evaluate the long term maintenance of response, safety and tolerability of repeated
administration of adalimumab in subjects with Ulcerative Colitis who participated in and successfully
completed Protocol M06-826 or Protocol M06-827.
The secondary objective is to assess pharmacokinetics (PK) of adalimumab following subcutaneous adminstration.

Study design

The Day 1/Baseline visit for subjects entering M10-223 is Week 52 of studies M06-826 or M06-827.
Subjects who enter this study from a blinded cohort will be assigned to open-label adalimumab,
40 mg eow. Subjects who are inadequate responders (defined below) upon entering the study who do
not show response during the study, or who showed a response and then have a disease flare, may have
their adalimumab dose increased to 40 mg weekly, but no earlier than the Week 12 visit. If these
subjects continue to show inadequate response or continue to have a flare while on 40 mg weekly
dosing, they may be discontinued from the study. Subjects who are clinical responders or who are in
clinical remission and who subsequently experience a disease flare may have their adalimumab dose
increased to every week dosing, but no earlier than the Week 12 visit. If these subjects continue to have
a disease flare while on every week dosing, they may be discontinued from the study.
Subjects who enter this study from an open-label cohort will continue their previous dosing regimen of
every other week or weekly dosing. Subjects, entering the study who are inadequate responders while
receiving 40 mg eow of adalimumab and who continue to show inadequate response, may have their
dose frequency increased to 40 mg weekly at the Week 2 visit or thereafter. Those subjects who
continue to be inadequate responders while receiving 40 mg weekly dosing may be withdrawn from the

study.
Subjects entering the study on eow adalimumab dosing who are clinical responders or who are in clinical remission may have their adalimumab dose increased to every week dosing if they subsequently experience a disease flare (defined below). This dose increase may not occur earlier than the Week 12 visit. If these subjects are still in disease flare while on every week dosing, they may be discontinued from the study. Subjects who enter the study on every week adalimumab dosing and who subsequently experience a disease flare may be withdrawn from the study.
Inadequate responder definition:
• Subjects with a Day 1/Baseline (M06-826 or M06-827 study) Partial Mayo Score of 4-7 who present with a score greater than or equal to their Baseline score on 2 consecutive visits at least 14 days apart
• Subjects with a Partial Mayo Score of 8 or 9 at Day 1/Baseline (M06-826 or M06-827 study) who present with a score of >= 7 on 2 consecutive visits at least 14 days apart
Disease Flare definition:
• Subject who present with a Partial Mayo Score difference of >= 3 compared to the Day 1/Baseline (extension study) Partial Mayo Score on 2 consecutive visits at least 14 days apart

Intervention

The Day 1/Baseline visit for subjects entering M10-223 is Week 52 of studies M06-826 or M06-827.

Subjects who enter this study from a blinded cohort will be assigned to open-label adalimumab, 40 mg eow. Subjects who are inadequate responders (defined below) upon entering the study who do not show response during the study, or who showed a response and then have a disease flare, may have their adalimumab dose increased to 40 mg weekly, but no earlier than the Week 12 visit. If these subjects continue to show inadequate response or continue to have a flare while on 40 mg weekly dosing, they may be discontinued from the study. Subjects who are clinical responders or who are in clinical remission and who subsequently experience a disease flare may have their adalimumab dose increased to every week dosing, but no earlier than the Week 12 visit. If these

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who present with a score of >= 7 on 2 consecutive visits at least 14 days apart
Disease Flare definition:
• Subject who present with a Partial Mayo Score difference of >= 3 compared to the Day
1/Baseline (extension study) Partial Mayo Score on 2 consecutive visits at least 14 days apart.

Beginning from week 96 in subjects who are in clinical response per Partial Mayo Score compared to baseline for at least 2 consecutive visits at least 14 days apart the dose of adalimumab may be decreased to 40mg every other week, at the discretion of the investigator using the IVR system.

Subjects who experience a disease flare or inadequate response may re-increase

their dose of adalimumab to 40 mg ew using the IVR system.

Study burden and risks

The subject may experience adverse events when the study drug is used. The most common adverse events of Adalimumab injections were reactions at the injection site. Subjects suffered from redness, itching, bruising, pain and/or swelling of the injection site. Most injection site reactions were described as mild, transient, and most of them disappeared without having to stop using the medication. Other frequently reported site effects (rate of >=5%) of adalimumab in subjects participating in the clinical studies in order of decreasing frequency are: nasopharyngitis, upper respiratory infection, headache, nausea, bronchitis, diarhea, cough, sinusitis, influenza, hypertension, urinary tract infection, back pain, and rash.

Endoscopy risks
Preparation for the endoscopy may involve a limitation on the kinds of food you may eat for 1-2 days prior to the test. Preparation for the endoscopy may also involve the use of laxatives that may produce loose stools. Possible risks during the endoscopy are getting a puncture (or hole) in the colon wall, which may require surgery to correct, and bleeding that requires getting blood from donors. The risk of the sedation medication, usually given during a colonoscopy to help you relax, may cause allergic reactions such as nausea, skin rash, dizziness with a drop in blood pressure, a slowing down of your breathing.

Female must be either not of childbearing potential, defined as postmenopausal for at least 1 year
prior to the previous study (M06-826 study or M06-827 study), or surgically sterile (bilateral tubal
ligation, bilateral oophorectomy or hysterectomy), or is of childbearing potential and practicing an
approved method of birth control throughout the study and for 150 days after last dose of study drug.
Examples of approved methods of birth control include the following: Condoms, sponge, foam, jellies, diaphragm or intrauterine device, oral, parenteral or intravaginal contraceptives or a vasectomized partner.

Contacts

Public
AbbVie

Wegalaan 9

Hoofddorp 2132 JD
NL
Scientific
AbbVie

Wegalaan 9
Hoofddorp 2132 JD
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

1. Subject must have successfully enrolled in and completed either the M06-826 study or the M06-827
study.
2. Female must be either not of childbearing potential, defined as postmenopausal for at least 1 year
prior to the previous study (M06-826 study or M06-827 study), or surgically sterile (bilateral tubal
ligation, bilateral oophorectomy or hysterectomy), or is of childbearing potential and practicing an
approved method of birth control throughout the study and for 150 days after last dose of study drug.
Examples of approved methods of birth control include the following:
• Condoms, sponge, foam, jellies, diaphragm or intrauterine device
• Oral, parenteral or intravaginal contraceptives
• Vasectomized partner.
3. Subject has voluntarily signed and dated an informed consent approved by and compliant with the
requirements of this study protocol which has been approved by an Institutional Review Board

(IRB)/Independent Ethics Committee (IEC).
4. Subject must be able to self-inject study medication or have a designee or healthcare professional
who can inject the study medication.
5. Subject is judged to be in generally good health as determined by the principal investigator based
upon clinical evaluations performed during the preceding adalimumab ulcerative colitis study (M06-826 study or the M06-827 study).

Exclusion criteria

1. For any reason, subject is considered by the investigator to be an unsuitable candidate for participation in the M10-223 study.
2. Female who is pregnant will be excluded from this study.
3. Has not responded to weekly adalimumab therapy from Study M06-826 or M06 827.
4. Female subject considering becoming pregnant during the study. There should be at least a 150-day
period between the last dose of study drug and conception.
5. History of malignancy other than a successfully treated non-metastatic cutaneous squamous cell,
basal cell carcinoma and/or localized carcinoma in situ of the cervix. If the Week 52 (Study M06-826 or M06-827) colonoscopy/flexible sigmoidoscopy shows evidence of dysplasia or a malignancy, subject must not be enrolled in the study.
6. History of listeriosis, histoplasmosis, chronic or active hepatitis B infection, human immunodeficiency virus (HIV) infection, immunodeficiency syndrome, central nervous system (CNS) demyelinating disease, or untreated tuberculosis (TB) (active and latent).
7. Currently receiving total parenteral nutrition (TPN).
8. Subject is not in compliance with prior and concomitant medication requirements.
9. Subjects with a poorly controlled medical condition, such as uncontrolled diabetes, unstable
ischemic heart disease, moderate or severe congestive heart failure, recent cerebrovascular accidents
and any other condition which, in the opinion of the investigator or sponsor, would put the subject at
risk by participation in this study.
10. Received cyclosporine, tacrolimus, or mycophenolate mofetil within 30 days prior to Baseline.
11. Subjects with known hypersensitivity to the excipients of adalimumab as stated in the label.
12. Current diagnosis of fulminant colitis and/or toxic megacolon.

Study design

Design

Study phase:	3
Study type:	Interventional
Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	26-03-2009
Enrollment:	2
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Humira
Generic name:	adalimumab
Registration:	Yes - NL intended use

Ethics review

Approved WMO Date:	12-09-2008
Application type:	First submission
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	12-11-2008
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	09-12-2008
Application type:	First submission

Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	20-05-2009
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	10-06-2009
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	10-12-2009
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	06-08-2010
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	20-08-2010
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	09-06-2011
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	14-07-2011
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)

Approved WMO

Date:	28-09-2011
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	10-10-2011
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	21-05-2012
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	22-05-2012
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	10-07-2012
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	04-09-2012
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	17-09-2012
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	27-11-2012
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United

	(Nieuwegein)
Approved WMO Date:	29-11-2012
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	21-06-2013
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	27-06-2013
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)

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	EUCTR2007-004157-28-NL
ClinicalTrials.gov	NCT00573794
CCMO	NL23080.060.08