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Efficacy and Safety of Adalimumab in Subjects With Moderately to Severely Active Ulcerative Colitis**This study has been completed.****Sponsor:**

Abbott

Information provided by:

Abbott

ClinicalTrials.gov Identifier:

NCT00408629

First received: December 5, 2006

Last updated: April 28, 2011

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[History of Changes](#)[Full Text View](#)[Tabular View](#)[Study Results](#)[Disclaimer](#)[? How to Read a Study Record](#) **Purpose**

This was a Phase 3, multicenter, randomized, double-blind, placebo-controlled trial designed to evaluate the efficacy and safety of the human anti-tumor necrosis factor (TNF) monoclonal antibody adalimumab (ADA) in patients with moderately to severely active ulcerative colitis (UC).

Condition	Intervention	Phase
Ulcerative Colitis	Biological: adalimumab Biological: placebo	Phase 3

Study Type: Interventional

Study Design: Allocation: Randomized

Endpoint Classification: Safety/Efficacy Study

Intervention Model: Parallel Assignment

Masking: Double Blind (Subject, Caregiver, Investigator, Outcomes Assessor)

Primary Purpose: Treatment

Official Title: A Multicenter, Randomized, Double-blind, Placebo-controlled Study of the Human Anti-TNF Monoclonal Antibody Adalimumab for the Induction and Maintenance of Clinical Remission in Subjects With Moderately to Severely Active Ulcerative Colitis

Resource links provided by NLM:[Genetics Home Reference](#) related topics: [ulcerative colitis](#)[MedlinePlus](#) related topics: [Ulcerative Colitis](#)[Drug Information](#) available for: [Adalimumab](#)[U.S. FDA Resources](#)**Further study details as provided by Abbott:**

Primary Outcome Measures:

- Proportion of Participants Who Achieved Clinical Remission Per Mayo Score at Week 8 [Time Frame: Week 8]
[Designated as safety issue: No]

Clinical remission per Mayo score is defined as a total Mayo score of at least 2 and no individual subscore greater than 1. The Mayo Score is a discrete ordinal scale ranging from 0 (normal or inactive disease) to 12 (severe disease) and is a composite of 4 subscores: Stool Frequency Subscore (SFS), Rectal Bleeding Subscore (RBS), Endoscopy Subscore, and Physician's Global Assessment Subscore (PGA), each of which ranges from 0 (normal) to 3 (severe disease).

- Proportion of Participants Who Achieved Clinical Remission Per Mayo Score at Week 52 [Time Frame: Week 52]
[Designated as safety issue: No]

Clinical remission per Mayo score is defined as a total Mayo score of at least 2 and no individual subscore greater than 1. The Mayo Score is a discrete ordinal scale ranging from 0 (normal or inactive disease) to 12 (severe disease) and is a composite of 4 subscores: SFS, RBS, Endoscopy Subscore, and PGA, each of which ranges from 0 (normal) to 3 (severe disease).

Secondary Outcome Measures:

- Proportion of Participants Who Achieved Sustained Clinical Remission Per Mayo Score at Both Week 8 and Week 52 [Time Frame: Week 8, Week 52] [Designated as safety issue: No]

Clinical remission per Mayo score is defined as a total Mayo score of at least 2 and no individual subscore greater than 1. The Mayo Score is a discrete ordinal scale ranging from 0 (normal or inactive disease) to 12 (severe disease) and is a composite of 4 subscores: SFS, RBS, Endoscopy Subscore, and PGA, each of which ranges from 0 (normal) to 3 (severe disease).

- Proportion of Participants Who Achieved Clinical Response Per Mayo Score at Week 8 [Time Frame: Week 8] [Designated as safety issue: No]

Clinical response per Mayo score is defined as a decrease in Mayo score of at least 3 points and at least 30% from Baseline, plus either a decrease in rectal bleeding subscore (RBS) of at least 1 point from Baseline or an absolute RBS of 0 or 1. The Mayo Score is a discrete ordinal scale ranging from 0 (normal or inactive disease) to 12 (severe disease) and is a composite of 4 subscores: SFS, RBS, Endoscopy Subscore, and PGA, each of which ranges from 0 (normal) to 3 (severe disease).

- Proportion of Participants Who Achieved Clinical Response Per Mayo Score at Week 52 [Time Frame: Week 52] [Designated as safety issue: No]

Clinical response per Mayo score is defined as a decrease in Mayo score of at least 3 points and at least 30% from Baseline, plus either a decrease in RBS of at least 1 point from Baseline or an absolute RBS of 0 or 1. The Mayo Score is a discrete ordinal scale ranging from 0 (normal or inactive disease) to 12 (severe disease) and is a composite of 4 subscores: SFS, RBS, Endoscopy Subscore, and PGA, each of which ranges from 0 (normal) to 3 (severe disease).

- Proportion of Participants Who Achieved Sustained Clinical Response Per Mayo Score at Both Week 8 and Week 52 [Time Frame: Week 8, Week 52] [Designated as safety issue: No]

Clinical response per Mayo score is defined as a decrease in Mayo score of at least 3 points and at least 30% from Baseline, plus either a decrease in RBS of at least 1 point from Baseline or an absolute RBS of 0 or 1. The Mayo Score is a discrete ordinal scale ranging from 0 (normal or inactive disease) to 12 (severe disease) and is a composite of 4 subscores: SFS, RBS, Endoscopy Subscore, and PGA, each of which ranges from 0 (normal) to 3 (severe disease).

- Proportion of Participants Who Achieved Mucosal Healing at Week 8 [Time Frame: Week 8] [Designated as safety issue: No]

Mucosal healing is defined as an Endoscopy Subscore of 0 or 1 as assessed by flexible sigmoidoscopy. Possible scores range from 0-3 as follows: 0 = Normal or inactive disease, 1 = Mild disease (erythema, decreased vascular pattern, mild friability), 2 = Moderate disease (marked erythema, absent vascular pattern, friability, erosions), 3 = Severe disease(spontaneous bleeding, ulceration).

- Proportion of Participants Who Achieved Mucosal Healing at Week 52 [Time Frame: Week 52] [Designated as safety issue: No]

Mucosal healing is defined as an Endoscopy Subscore of 0 or 1 as assessed by flexible sigmoidoscopy. Possible scores range from 0-3 as follows: 0 = Normal or inactive disease, 1 = Mild disease (erythema, decreased vascular pattern, mild friability), 2 = Moderate disease (marked erythema, absent vascular pattern, friability, erosions), 3 = Severe disease(spontaneous bleeding, ulceration).

- Proportion of Participants Who Achieved Sustained Mucosal Healing at Both Week 8 and Week 52 [Time Frame: Week 8, Week 52] [Designated as safety issue: No]

Mucosal healing is defined as an Endoscopy Subscore of 0 or 1 as assessed by flexible sigmoidoscopy. Possible scores range from 0-3 as follows: 0 = Normal or inactive disease, 1 = Mild disease (erythema, decreased vascular pattern, mild friability), 2 = Moderate disease (marked erythema, absent vascular pattern, friability, erosions), 3 = Severe disease(spontaneous bleeding, ulceration).

- Proportion of Participants Who Discontinued Corticosteroid Use Before Week 52 and Achieved Clinical Remission Per Mayo Score at Week 52 [Time Frame: Baseline to Week 52] [Designated as safety issue: No]

Clinical remission per Mayo score is defined as a total Mayo score of at least 2 and no individual subscore greater than 1. The Mayo Score is a discrete ordinal scale ranging from 0 (normal or inactive disease) to 12 (severe disease) and is a composite of 4 subscores: SFS, RBS, Endoscopy Subscore, and PGA, each of which ranges from 0 (normal) to 3 (severe disease).

- Proportion of Participants With Physician's Global Assessment Subscore Indicative of Mild Disease (a Score of 0 or 1) at Week 8 [Time Frame: Week 8] [Designated as safety issue: No]

The PGA includes the 3 other subscores (SFS, RBS, and Endoscopy), the participant's daily record of abdominal discomfort and functional assessment, and other observations such as physical findings and the participant's performance status. Possible scores range from 0-3 as

follows: 0 = Normal (other subscores are 0), 1 = Mild disease (other subscores are mostly 1), 2 = Moderate disease (other subscores are 1 to 2), 3 = Severe disease (other subscores are 2 to 3).

- Proportion of Participants With Stool Frequency Subscore Indicative of Mild Disease (a Score of 0 or 1) at Week 8 [Time Frame: Week 8] [Designated as safety issue: No]

SFS ranges from 0-3 as follows: 0 = Normal number of stools for this participant, 1 = 1-2 stools more than normal, 2 = 3-4 stools more than normal, 3 = 5 or more stools more than normal. The participant served as his/her own control.

- Proportion of Participants With Rectal Bleeding Subscore Indicative of Mild Disease (a Score of 0 or 1) at Week 8 [Time Frame: Week 8] [Designated as safety issue: No]

RBS ranges from 0-3 as follows: 0 = no blood seen, 1 = streaks of blood with stool less than half the time, 2 = obvious blood with stool most of the time, 3 = blood alone passed

- Proportion of Participants Who Discontinued Corticosteroid Use for At Least 90 Days and Achieved Clinical Remission Per Mayo Score at Week 52 [Time Frame: Baseline to Week 52] [Designated as safety issue: No]

Clinical remission per Mayo score is defined as a total Mayo score of at least 2 and no individual subscore greater than 1. The Mayo Score is a discrete ordinal scale ranging from 0 (normal or inactive disease) to 12 (severe disease) and is a composite of 4 subscores: SFS, RBS, Endoscopy Subscore, and PGA, each of which ranges from 0 (normal) to 3 (severe disease).

- Proportion of Participants Who Discontinued Corticosteroid Use and Achieved Clinical Remission Per Mayo Score (Sustained) at Both Weeks 32 and 52 [Time Frame: Week 32, Week 52] [Designated as safety issue: No]

Clinical remission per Mayo score is defined as a total Mayo score of at least 2 and no individual subscore greater than 1. The Mayo Score is a discrete ordinal scale ranging from 0 (normal or inactive disease) to 12 (severe disease) and is a composite of 4 subscores: SFS, RBS, Endoscopy Subscore, and PGA, each of which ranges from 0 (normal) to 3 (severe disease).

- Proportion of Inflammatory Bowel Disease Questionnaire Responders at Week 52 [Time Frame: Week 52] [Designated as safety issue: No]

Response per the Inflammatory Bowel Disease Questionnaire (IBDQ) was defined as at least a 16-point increase from Baseline in total IBDQ score. The IBDQ is a 32-item questionnaire consisting of 4 dimensions: bowel-related symptoms, systemic function, social function, and emotional status. The responses to questions within each domain range from 1 (significant impairment) to 7 (no impairment), with total score ranging from 32 (very poor) to 224 (perfect health-related quality of life).

- Proportion of Inflammatory Bowel Disease Questionnaire Responders at Week 8 [Time Frame: Week 8] [Designated as safety issue: No]

Response per the Inflammatory Bowel Disease Questionnaire (IBDQ) was defined as at least a 16-point increase from Baseline in total IBDQ score. The IBDQ is a 32-item questionnaire consisting of 4 dimensions: bowel-related symptoms, systemic function, social function, and emotional status. The responses to questions within each domain range from 1 (significant impairment) to 7 (no impairment), with total score ranging from 32 (very poor) to 224 (perfect health-related quality of life).

Enrollment: 518
 Study Start Date: November 2006
 Study Completion Date: March 2010
 Primary Completion Date: March 2010 (Final data collection date for primary outcome measure)

Arms	Assigned Interventions
Experimental: adalimumab group	Biological: adalimumab Prefilled syringe, 40 mg, 160 mg at Week 0, 80 mg at Week 2, and 40 mg every other week between Weeks 4 and 50. Other Names: - ABT-D2E7 - adalimumab - Humira
Experimental: placebo group	Biological: placebo Matching Placebo for prefilled syringe, 40 mg, Other Name: placebo

Detailed Description:

This was a Phase 3, multicenter, randomized, double-blind, placebo-controlled trial designed to evaluate the efficacy and safety of adalimumab (ADA) in patients with moderately to severely active ulcerative colitis (UC).

The duration of the study was up to 65 weeks, including a Screening Period of up to 3 weeks, a double-blind (DB) placebo-controlled treatment period of up to 52 weeks, and a 70 day follow-up phone call for participants who prematurely discontinued or who did not enroll in the extension study NCT# 00573794 (M10-223).

Adult participants with moderate to severe UC (Mayo score of 6 to 12 points with endoscopy subscore of 2 to 3 points), confirmed by colonoscopy with biopsy or flexible sigmoidoscopy with biopsy, were to be enrolled at approximately 120 sites worldwide. Planned enrollment was 500 participants.

Participants were to be stratified by prior exposure to infliximab and/or other anti-TNF agents, and randomized in a 1:1 ratio to receive ADA or placebo by subcutaneous injection. Participants assigned to the ADA treatment arm were to receive an induction dose of 160 mg at Week 0 and 80 mg at Week 2, and 40 mg every other week (eow) starting at Week 4. Participants assigned to the placebo treatment arm were to receive matching placebo during the same period of time. At or after Week 10, participants who met the criteria for inadequate response could be switched to open-label (OL) ADA 40 mg eow beginning at Week 12. Inadequate response was defined as:

- Partial Mayo score greater than or equal to Baseline score on 2 consecutive visits at least 14 days apart (for participants with a partial Mayo score of 4 to 7 at Baseline).
- Partial Mayo score greater than or equal to 7 on 2 consecutive visits at least 14 days apart (for participants with a partial Mayo score of 8 or 9 at Baseline).

Participants who demonstrated inadequate response at 2 consecutive visits at least 14 days apart while on OL administration ADA 40 mg eow were permitted to dose escalate to ADA 40 mg weekly (ew). Participants with persistent inadequate response while on ADA 40 mg ew may have been discontinued from the study at the Investigator's discretion. Upon completion of the study, participants had the option to enroll into the OL extension Study M10-223 in which they could receive ADA treatment.

Efficacy and safety measurements were performed throughout the study. A follow-up phone call was made 70 days after the last dose of study drug to obtain information on any ongoing or new adverse events (AEs) for all participants who terminated early or who did not enroll in the OL extension study.

► Eligibility

Ages Eligible for Study: 18 Years and older
 Genders Eligible for Study: Both
 Accepts Healthy Volunteers: No

Criteria

Inclusion Criteria:

1. Participants ≥ 18 years of age and in good health (Investigator discretion) with a recent stable medical history
2. Diagnosis of UC for greater than 90 days prior to Baseline
3. Diagnosis of active UC confirmed by colonoscopy with biopsy or flexible sigmoidoscopy with biopsy during the Screening Period, with exclusion of infection
4. Active UC with a Mayo score of 6 to 12 points and endoscopy subscore of 2 to 3 points, despite concurrent treatment with at least 1 of the following (oral corticosteroids or immunosuppressants or both as defined below):
 - Stable oral corticosteroid dose (prednisone ≥ 20 mg/day or equivalent) for at least 14 days prior to Baseline or maintenance, corticosteroid dose (prednisone < 20 mg/day or equivalent) for at least 40 days prior to Baseline

and/or

- At least a 90 day course of azathioprine (AZA) or 6-mercaptopurine (6-MP) prior to Baseline, with a dose of AZA ≥ 1.5 mg/kg/day or 6-MP ≥ 1 mg/kg/day (rounded to the nearest available tablet formulation), or a dose that is the highest tolerated by the participant (e.g., due to leukopenia, elevated liver enzymes, nausea) during that time. Participant must be on a stable dose for at least 28 days prior to Baseline.

Concurrent therapy was not required for participants who were previously treated with corticosteroids or immunosuppressants (AZA or 6-MP) during the past 5 years and in the judgment of the Investigator have failed to respond to, or could not tolerate, their treatment.

5. Participants may have been included if they had previously used an anti-tumor necrosis factor (TNF) agent (except ADA) and discontinued its use due to a loss of response or intolerance to the agent.
6. Had to be able to self-administer or had caregiver who could reliably administer subcutaneous (SC) injections.
7. Had to be able and willing to give written informed consent and to comply with the requirements of the study protocol.
8. Female had to be either not of childbearing potential, defined as postmenopausal for at least 1 year or surgically sterile (bilateral tubal ligation, bilateral oophorectomy, or hysterectomy), or of childbearing potential and practicing an approved method of birth control throughout the study and for 150 days after the last dose of study drug. Examples of approved methods of birth control included the following:
 - Condoms, sponge, foams, jellies, diaphragm, or intrauterine device
 - Oral, parenteral, intravaginal contraceptives for 90 days prior to study drug administration

- A vasectomized partner The results of the serum pregnancy test performed at the Screening Visit and urine pregnancy test performed at the Baseline Visit must have been negative.

9. Judged to be in generally good health as determined by the Investigator

Exclusion Criteria:

1. History of subtotal colectomy with ileorectostomy or colectomy with ileoanal pouch, Koch pouch, or ileostomy for UC, or planned bowel surgery.
2. Received previous treatment with ADA or previous participation in an ADA clinical study.
3. Received cyclosporine, tacrolimus, or mycophenolate mofetil within 30 days of Baseline.
4. Received intravenous (IV) corticosteroids within 14 days of Screening or during the Screening Period.
5. Received therapeutic enema or suppository, other than required for endoscopy, within 14 days of the Screening endoscopy and during the remainder of the Screening Period.
6. Current diagnosis of fulminant colitis and/or toxic megacolon.
7. Disease limited to the rectum (ulcerative proctitis).
8. Current diagnosis of indeterminate colitis.
9. Current diagnosis and/or history of Crohns disease (CD).
10. Currently receiving total parenteral nutrition.
11. Used aminosalicylates for < 90 days before Baseline or not on a stable dose for at least 28 days before Baseline or discontinued use within 28 days of Baseline.
12. Positive Clostridium difficile stool assay.
13. Previously used infliximab or any anti-TNF agent within 56 days of Baseline.
14. Previously used infliximab or any anti-TNF agent without clinical response at any time ("primary non-responder") unless subject experienced a treatment-limiting reaction.
15. Infections requiring treatment with IV antibiotics, antivirals, or antifungals within 30 days of Baseline or oral antibiotics, antivirals, or antifungals within 14 days of Baseline.
16. History of malignancy other than a successfully treated non-metastatic cutaneous squamous cell or basal cell carcinoma and/or localized carcinoma in situ of the cervix. If the Screening colonoscopy/flexible sigmoidoscopy showed evidence of dysplasia or a malignancy, subject was not to be enrolled in the study.
17. History of listeria, histoplasmosis, chronic or active hepatitis B infection, human immunodeficiency virus (HIV), immunodeficiency syndrome, central nervous system demyelinating disease, or untreated tuberculosis (TB).
18. Female subject who was pregnant or breast-feeding or considering becoming pregnant during the study (there should be at least 150 days between the last dose of study drug and either conception or initiation of breast-feeding in women of childbearing potential).
19. Poorly controlled medical condition(s), such as uncontrolled diabetes, unstable ischemic heart disease, moderate to severe congestive heart failure (CHF), recent cerebrovascular accident, and any other condition, which in the opinion of the investigator, put the subject at risk by participation in the protocol.
20. Received any investigational agent within 30 days or 5 half lives prior to Baseline (whichever was longer).
21. History of clinically significant drug or alcohol abuse during the past year.
22. Known hypersensitivity to the excipients of ADA as stated in the label.
23. Any prior exposure to Tysabri® (natalizumab), or Orencia® (abatacept) or any other biological therapy [other than Kineret® (anakinra) and anti-TNF agents].
24. Currently taking both budesonide and prednisone (or equivalent) simultaneously.

► Contacts and Locations

Choosing to participate in a study is an important personal decision. Talk with your doctor and family members or friends about deciding to join a study. To learn more about this study, you or your doctor may contact the study research staff using the Contacts provided below. For general information, see [Learn About Clinical Studies](#).

Please refer to this study by its ClinicalTrials.gov identifier: NCT00408629

✚ Show 108 Study Locations

Sponsors and Collaborators

Abbott

Investigators

Study Director: Roopal B Thakkar, M.D. Abbott

More Information

No publications provided by Abbott

Additional publications automatically indexed to this study by ClinicalTrials.gov Identifier (NCT Number):

[Wolf D, D'Haens G, Sandborn WJ, Colombel JF, Van Assche G, Robinson AM, Lazar A, Zhou Q, Petersson J, Thakkar RB. Escalation to weekly dosing recaptures response in adalimumab-treated patients with moderately to severely active ulcerative colitis. Aliment Pharmacol Ther. 2014 Sep;40\(5\):486-97. doi: 10.1111/apt.12863. Epub 2014 Jul 15.](#)

[Feagan BG, Sandborn WJ, Lazar A, Thakkar RB, Huang B, Reilly N, Chen N, Yang M, Skup M, Mulani P, Chao J. Adalimumab therapy is associated with reduced risk of hospitalization in patients with ulcerative colitis. Gastroenterology. 2014 Jan;146\(1\):110-118.e3. doi: 10.1053/j.gastro.2013.09.032. Epub 2013 Sep 22.](#)

[Sandborn WJ, Colombel JF, D'Haens G, Van Assche G, Wolf D, Kron M, Lazar A, Robinson AM, Yang M, Chao JD, Thakkar R. One-year maintenance outcomes among patients with moderately-to-severely active ulcerative colitis who responded to induction therapy with adalimumab: subgroup analyses from ULTRA 2. Aliment Pharmacol Ther. 2013 Jan;37\(2\):204-13. doi: 10.1111/apt.12145. Epub 2012 Nov 23.](#)

Responsible Party: Roopal B Thakker, M.D./Project Director, Abbott
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 Other Study ID Numbers: M06-827, 2006-002782-40
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 Health Authority: Canada: Health Canada
 United States: Food and Drug Administration
 Argentina: Administracion Nacional de Medicamentos, Alimentos y Tecnologia Medica
 Australia: Department of Health and Ageing Therapeutic Goods Administration
 Austria : Federal Ministry for Labour, Health, and Social Affairs
 Belgium: Federal Agency for Medicinal Products and Health Products
 Czech Republic: State Institute for Drug Control
 Denmark: Danish Medicines Agency
 France: Afssaps - Agence française de sécurité sanitaire des produits de santé (Saint-Denis)
 Germany: Paul-Ehrlich-Institut
 Hungary: National Institute of Pharmacy
 Israel: Ministry of Health
 New Zealand: Medsafe
 Norway: Norwegian Medicines Agency
 Poland: Ministry of Health
 Portugal: National Pharmacy and Medicines Institute
 Spain: Agencia Española de Medicamentos y Productos Sanitarios
 Switzerland: Swissmedic

Keywords provided by Abbott:

Ulcerative Colitis
 Adalimumab
 TNF Antagonist
 Mayo Score

Additional relevant MeSH terms:

Colitis	Intestinal Diseases
Colitis, Ulcerative	Pathologic Processes
Ulcer	Adalimumab
Colonic Diseases	Anti-Inflammatory Agents
Digestive System Diseases	Antirheumatic Agents
Gastroenteritis	Pharmacologic Actions
Gastrointestinal Diseases	Therapeutic Uses
Inflammatory Bowel Diseases	

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