ForPatients
by Roche

Ulcerative Colitis

A Clinical Trial to Compare Etrolizumab with Placebo and Adalimumab in Patients with Moderate to Severe Ulcerative Colitis Who Have not Received Treatment with Tumour Necrosis Factor Inhibitors (Hibiscus II)

A Study Comparing the Efficacy and Safety of Etrolizumab With Adalimumab and Placebo in Participants With Moderate to Severe Ulcerative Colitis (UC) in Participants Naive to Tumor Necrosis Factor (TNF) Inhibitors

Trial Status	Trial Runs In	Trial Identifier
Completed	19 Countries	NCT02171429 2013-004277-27 GA28949

The clinical trial information herein is sourced from public registries such as ClinicalTrials.gov, EuClinicalTrials.eu, and ISRCTN.com. Additional patient-friendly (lay) content has been prepared by Roche to support understanding.

Official Title:

Phase III, Randomized, Double-Blind, Double-Dummy, Placebo-Controlled, Multicenter Study to Evaluate the Efficacy (Induction of Remission) and Safety of Etrolizumab Compared With Adalimumab and Placebo in Patients With Moderate to Severe Ulcerative Colitis Who Are Naive to TNF Inhibitors

Trial Summary:

This Phase III, double-blind, placebo and active-comparator controlled, multicenter study will investigate the efficacy and safety of etrolizumab in induction of remission in participants with moderately to severely active ulcerative colitis (UC) who are naIve to tumor necrosis factor (TNF) inhibitors and refractory to or intolerant of prior immunosuppressant and/or corticosteroid treatment. In addition to this study, a second Phase III trial with identical study design (GA28948; NCT02163759) was independently conducted.

Hoffmann-La Roche	Phase 3
Sponsor	Phase

NCT02171429 2013-004277-27 GA28949
Trial Identifiers

Eligibility Criteria:

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Gender	Age	Healthy Volunteers
All	**# 18 Years & # 80 Years**	**No**

How does the Hibiscus II clinical trial work? This clinical trial is recruiting people who have ‘ulcerative colitis’, a condition that results in inflammation and ulcers in the large intestine or bowel (‘colon’) or back passage (‘rectum’). It is for people whose ulcerative colitis is categorised as moderately to severely active.

How do I take part in this clinical trial? To be able to take part in this clinical trial, you must not have already been given a type of medicine called a ‘tumour necrosis factor inhibitor’ for your ulcerative colitis and you must have been diagnosed with ulcerative colitis at least 3 months before the start of this trial.

If you think this clinical trial may be suitable for you and would like to take part, please talk to your doctor.

If your doctor thinks that you might be able to take part in this clinical trial, he/she may refer you to the closest clinical trial doctor who will give you all the information you need to make your decision about taking part in the clinical trial. You will also find the clinical trial locations at the top of this page.

You will have some further tests to make sure you will be able to take the treatments given in this clinical trial. Some of these tests and procedures may be part of your regular medical care and may be done even if you do not take part in the clinical trial. If you have had some of the tests recently, they may not need to be done again.

This clinical trial is divided into three parts or ‘phases’. These parts are called the:

- ‘Screening phase’ where the clinical trial doctor will check your suitability for the trial, this lasts for up to 5 weeks.
- ‘Treatment phase’ where you will be given the trial medicine, this lasts for up to 14 weeks. After the treatment phase, if you are eligible you may be asked if you would like to take part in an additional trial called the COTTONWOOD trial (also known as the ‘Open Label Extension Trial’) to receive the etrolizumab drug. If you do not qualify or choose not to join, then you would continue onto the next ‘Safety Monitoring’ phase.
- ‘Safety monitoring follow-up phase’ where the clinical trial doctor will check if you are having any side effects, this lasts for 12 weeks.

The maximum length of time you will be in this trial is 31 weeks.

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What happens during the screening phase? During the screening phase, you will be told about any risks and benefits of taking part in the trial and what other treatments are available so that you may decide if you still want to take part. While taking part in the clinical trial, both men and women (if you are not currently pregnant but can become pregnant) will need to either not have heterosexual intercourse or take effective contraceptive medications while taking part in the trial for safety reasons.

What treatment will I be given if I join this clinical trial? Everyone who joins this clinical trial will be split into three groups randomly (like flipping a coin) and given one of three different treatments in a blinded fashion.

This is a 'placebo-controlled' clinical trial, which means that one of the groups will be given only injections with no active drug (also known as a placebo). At the start of the treatment phase, a computer will randomly choose your treatment group. This will be one of:

- Treatment with active etrolizumab (and an adalimumab placebo).
- Treatment with active adalimumab (and an etrolizumab placebo).
- Treatment with placebo only (an etrolizumab placebo and an adalimumab placebo).

You will have a 2 in 5 chance of being given etrolizumab and the placebo, a 2 in 5 chance of being given adalimumab and the placebo, and a 1 in 5 chance of being given only placebo treatment.

To allow a fair comparison between etrolizumab and adalimumab, you and your clinical trial doctor will be 'blinded' to treatment. This means that neither you nor your clinical trial doctor will know which treatments you are taking. If your safety is at risk, your clinical trial doctor can find out which drug you are being given.

How often will I be seen in follow-up appointments, and for how long? During the treatment phase, you will be asked to keep an electronic diary at home to record how you are feeling and managing with day-to-day activities. You will also come to the hospital every 2 weeks to be given your medicine. The clinical trial doctor will ask you about how your ulcerative colitis is responding to the treatment and about any side effects that you may be having.

At the Week 10 visit, you will be assessed by the clinical trial doctor to see if your ulcerative colitis has responded to treatment.

If, at Week 10 your ulcerative colitis has responded to treatment, you will continue for another 4 weeks and be given one more dose of etrolizumab or placebo at the Week 12 visit. No more doses of adalimumab will be given after Week 8. You will be assessed at Week 14 to see if you are still responding to treatment. After this assessment, you will either enter the safety monitoring follow-up phase of this clinical trial or your doctor will talk to you about entering the Open Label Extension Trial COTTONWOOD where you will

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be given long-term treatment with etrolizumab. The clinical trial doctor will give you all the information you need to make your decision about taking part in this other clinical trial.

If you have not met the required response at the Week 10 visit, you will either enter the 12-week safety monitoring follow-up phase, or if suitable, your doctor will talk to you about entering the Open Label Extension Trial COTTONWOOD where you will be given long-term treatment with etrolizumab. The clinical trial doctor will give you all the information you need to make your decision about taking part in this other clinical trial.

What happens during the safety monitoring follow-up phase? All patients who leave this trial and do not enter the other clinical trial of long-term treatment with etrolizumab will be asked to complete a 12#week safety monitoring follow-up phase. This will include one safety monitoring telephone call at Week 6 and one clinic visit at Week 12.

What happens if I'm unable to take part in this clinical trial? If this clinical trial is not suitable for you, you will not be able to take part. Your doctor will suggest other treatments for you that you can be given or other clinical trials that you may be able to take part in. You will not lose access to any of your regular care.

For more information about this clinical trial see the **For Expert** tab on this page or follow this link to ClinicalTrials.gov https://clinicaltrials.gov/ct2/show/NCT02171429

Trial-identifier: NCT02171429

Inclusion Criteria:

- Diagnosis of ulcerative colitis (UC) established at least 3 months prior to randomization (Day 1)
- Moderately to severely active UC as determined by the MCS
- Naive to treatment with TNF inhibitor therapy
- An inadequate response, loss of response, or intolerance to prior corticosteroid and/or immunosuppressant treatment
- Background UC therapy may include oral 5-aminosalisylate (5-ASA), budesonide, oral corticosteroids, probiotics, azathioprine (AZA), 6-mercaptopurine (6MP), or methotrexate (MTX) if doses have been stable for:
- AZA, 6-MP, MTX: 8 weeks immediately prior to randomization
- 5-ASA: 4 weeks immediately prior to randomization
- Corticosteroids: 4 weeks immediately prior to randomization; if corticosteroids are being tapered, dose has to be stable for at least 2 weeks prior to randomization
- Use of highly effective contraception method as defined by the protocol
- Have received a colonoscopy within the past year or be willing to undergo a colonoscopy in lieu of a flexible sigmoidoscopy at screening

Exclusion Criteria:

Exclusion Criteria Related to Inflammatory Bowel Disease:

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- Prior extensive colonic resection, subtotal or total colectomy, or planned surgery for UC
- Past or present ileostomy or colostomy
- Diagnosis of indeterminate colitis
- Suspicion of ischemic colitis, radiation colitis, or microscopic colitis
- Diagnosis of toxic megacolon within 12 months of initial screening visit
- Any diagnosis of Crohn's disease
- Past or present fistula or abdominal abscess
- A history or current evidence of colonic mucosal dysplasia
- Patients with any stricture (stenosis) of the colon
- Patients with history or evidence of adenomatous colonic polyps that have not been removed

Exclusion Criteria Related to Prior or Concomitant Therapy:

- Prior treatment with TNF-alpha antagonists
- Any prior treatment with etrolizumab or other anti-integrin agents
- Any prior treatment with rituximab
- Any treatment with tofacitinib during screening
- Any prior treatment with anti-adhesion molecules
- Use of intravenous (IV) steroids within 30 days prior to screening with the exception of a single administration of IV steroid
- Use of agents that deplete B or T cells
- Use of anakinra, abatacept, cyclosporine, sirolimus, or mycophenolate mofetil (MMF) within 4 weeks prior to randomization
- Chronic nonsteroidal anti-inflammatory drug (NSAID) use
- Patients who are currently using anticoagulants including, but not limited to, warfarin, heparin, enoxaparin, dabigatran, apixaban, rivaroxaban
- Patients who have received treatment with corticosteroid enemas/suppositories and/or topical (rectal) 5-ASA preparations within 2 weeks prior to randomization
- Apheresis (i.e., Adacolumn apheresis) within 2 weeks prior to randomization
- Received any investigational treatment including investigational vaccines within 5 half lives of the investigational product or 28 days after the last dose, whichever is greater, prior to randomization
- History of moderate or severe allergic or anaphylactic/anaphylactoid reactions to chimeric, human, or humanized antibodies, fusion proteins, or murine proteins or hypersensitivity to etrolizumab (active drug substance) or any of the excipients (L histidine, L-arginine, succinic acid, polysorbate 20)
- Patients administered tube feeding, defined formula diets, or parenteral alimentation/nutrition who have not discontinued these treatments within 3 weeks prior to randomization

Exclusion Criteria Related to General Safety:

- Pregnant or lactating
- Lack of peripheral venous access
- Hospitalization (other than for elective reasons) during the screening period
- Significant uncontrolled comorbidity, such as cardiac (e.g., moderate to severe heart failure New York Heart Association Class III/IV), pulmonary, renal, hepatic, endocrine, or gastrointestinal disorders
- Neurological conditions or diseases that may interfere with monitoring for PML
- History of demyelinating disease
- Clinically significant abnormalities on screening neurologic examination (PML Objective Checklist)
- Clinically significant abnormalities on the screening PML Subjective Checklist
- History of alcohol, drug, or chemical abuse less than 6 months prior to screening
- Conditions other than UC that could require treatment with >10 mg/day of prednisone (or equivalent) during the course of the study
- History of cancer, including hematologic malignancy, solid tumors, and carcinoma in situ, within 5 years before screening

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Exclusion Criteria Related to Infection Risk

- Congenital or acquired immune deficiency
- Patients must undergo screening for HIV and test positive for preliminary and confirmatory tests
- Positive hepatitis C virus (HCV) antibody test result
- Positive hepatitis B virus (HBV) antibody test result
- Evidence of or treatment for Clostridium difficile (as assessed by C. difficile toxin testing) within 60 days prior to randomization or other intestinal pathogens (as assessed by stool culture and ova and parasite evaluation) within 30 days prior to randomization
- Evidence of or treatment for clinically significant cytomegalovirus (CMV) colitis (based on the investigator's judgment) within 60 days prior to randomization
- History of active or latent TB
- History of recurrent opportunistic infections and/or history of severe disseminated viral infections
- Any serious opportunistic infection within the last 6 months prior to screening
- Any current or recent signs or symptoms (within 4 weeks before screening and during screening) of infection
- Any major episode of infection requiring treatment with IV antibiotics within 8 weeks prior to screening or oral antibiotics within 4 weeks prior to screening
- Received a live attenuated vaccine within 4 weeks prior to randomization
- History of organ transplant

Exclusion Criteria Related to Laboratory Abnormalities (at Screening)

- Serum creatinine >2 x upper limit of normal (ULN)
- ALT or AST >3 x ULN or alkaline phosphatase >3 x ULN or total bilirubin >2.5 x ULN
- Platelet count <100,000/uL
- Hemoglobin <8 g/dL
- Absolute neutrophil count <1500/uL
- Absolute lymphocyte count <500/uL

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