A Study of Infliximab for Treatment Resistant Major Depression

This study is currently recruiting participants.

Verified by Emory University, December 2008
First Received: April 19, 2007 Last Updated: April 6, 2010 History of Changes

Sponsor:	Emory University
Information provided by:	Emory University
ClinicalTrials.gov Identifier:	NCT00463580

Purpose

Major depression is increasingly recognized to be a chronic and highly recurrent condition, which results in significantly increased health problems. One possible mechanism that may contribute to treatment resistance is increased production and release of chemicals called proinflammatory cytokines in patients with major depression. These chemicals mediate the body's response to infectious agents like bacteria and have been shown to be increased by psychological stress. They produce the symptoms that we associate with being sick, including fever, malaise and changes in sleep and appetite. Several lines of evidence indicate that proinflammatory cytokines may contribute to the development of major depression and may thus represent a novel target for the pharmacological treatment of the disorder.

The TNF-alpha antagonist, Infliximab(Remicade®), is an infusion style drug approved by the FDA for the treatment of inflammatory conditions like Crohns disease and rheumatoid arthritis. We are conducting a study to see if the infliximab (Remicade®) is more effective than placebo in acutely reducing symptoms of depression in patients who have elevated proinflammatory markers and have not responded to, or been unable to tolerate, at least two previous treatments in the current depressive episode. Proinflammatory markers are measured by a simple blood test for C-Reactive Protein(CRP)levels in the body.

After appropriate screening to determine eligibility, 64 subjects with treatment resistant depression will be randomized to receive three infusions of either infliximab(Remicade®)or placebo(salt water) in the Emory Infliximab Infusion Center in the Division of Digestive Diseases, Emory University School of Medicine. Subjects will

be followed for 12 weeks with evaluations at weeks 0 (baseline), 1, 2, 3, 4, 6, 8, 10 and 12. The first infliximab(Remicade®)infusion will occur at the first (Baseline) visit. The second infusion will occur at Study Week 2 (the third visit). The third infusion will occur at Study Week 6 (Visit 6). The choice of three infusions, and the infusion schedule, is based on current recommendations for the use of infliximab(Remicade®)in conditions for which it has received FDA approval. Subjects will be evaluated for twelve weeks by trained clinicians for changes in depression symptoms and improvements in quality of life. In addition, a physician will evaluate subjects each visit to make sure they are remaining healthy. Blood will be withdrawn at baseline prior to infusion and all subsequent visits to check labs for safety but also to evaluate potential relationships between changes in inflammatory activity and therapeutic response. After Study Week 12, participants will be monitored by phone, every 4 weeks during the 22-Week Post Study Follow-up Phase to assess physical and psychiatric symptoms in the period following the final infusion. At the baseline and Week 8 visits, subjects will be admitted to the Atlanta Clinical Translational Science Institute(ACTSI),a research unit in the Emory Hospital, for an extended evaluation. The purpose of coming to the ACTSI will be for researchers to evaluate whether treatment with infliximab improves endocrine function, inflammation, sleep and thinking abilities in people who are depressed. For all other visits (Week 1, 2, 4, 6, 10 and 12), participants will come for an office visit in the Winship Cancer Institute.

Condition	Intervention	Phase
Treatment Resistant **Depression** Current Diagnosis: Major **Depressive Disorder** or Bipolar Disorder I or II: Current Episode, **Depressed**	Drug: infliximab (remicade)	Phase IV

Study Type: Interventional

Study Design:
Allocation: Randomized
Control: Placebo Control
Endpoint Classification: Efficacy Study
Intervention Model: Parallel Assignment
Masking: Double Blind (Subject, Caregiver, Investigator, Outcomes Assessor)
Primary Purpose: Treatment

Official Title: An Evaluation of the Efficacy of the Tumor Necrosis Factor-alpha Antagonist Infliximab in Treatment Resistant Major **Depression**: Mechanisms and Mediators

Resource links provided by NLM:

MedlinePlus related topics: Bipolar Disorder Cancer Depression

Drug Information available for: Infliximab

U.S. FDA Resources

Further study details as provided by Emory University:

Primary Outcome Measures:

- (Study Endpoint): Between-group differences (mean ±SD) at all post-baseline time points in HDRS scores. [Time Frame: Study endpoint] [Designated as safety issue: No]

Secondary Outcome Measures:

- Between group difference in percentage of patients with a 30% and a 50% reduction in HDRS scores at any study point
  [Time Frame: At any study point]
  [Designated as safety issue: No]
- Between group difference in percentage of remitted patients during treatment (HDRS ≤7 or CGI of 1) [Time Frame: At any study point]
  [Designated as safety issue: No]
- Between group differences in self-reported depression scores measured by the IDS—SR [Time Frame: At any study point]
  [Designated as safety issue: No]
- Between group differences in quality of life post-infusion quality of life measured by the SF-36. [Time Frame: At any study point]
  [Designated as safety issue: No]
- The correlation coefficient between changes in HDRS symptom score(measured numerically and as the ratio of change score to baseline score) and changes in the plasma concentrations of TNF-alpha, IL-6 and CRP. [Time Frame: Between baseline and any study point] [Designated as safety issue: No]
- Between-group differences (mean ±SD) in the change of cortisol and ACTH slope, p.m. cortisol, diurnal plasma cytokine and cytokine receptor concentrations and sleep efficiency between baseline and study week 8. [Time Frame: Between baseline and study week 8.] [Designated as safety issue: No]
- Correlation coefficients between changes in HDRS symptom score and changes in diurnal slope of cortisol and ACTH, p.m. cortisol plasma concentrations, diurnal plasma concentrations of inflammatory cytokines and their receptors and sleep efficiency

[Time Frame: Measured numerically and as the ratio of change score to baseline score] [Designated as safety issue: No]

Estimated Enrollment:	64
Study Start Date:	November 2008
Estimated Study Completion Date:	December 2010
Estimated Primary Completion Date:	December 2010 (Final data collection date for primary outcome measure)

Arms	Assigned Interventions
Normal saline: Placebo Comparator Normal saline Intervention: Drug: infliximab (remicade)	Drug: infliximab (remicade) Three infusions across a 12 week period. (Baseline, week 2 and week 6)

Show Detailed Description

Eligibility

Ages Eligible for Study: 25 Years to 60 Years
Genders Eligible for Study: Both
Accepts Healthy Volunteers: No

Criteria

Inclusion Criteria:

1. Males or females ages 25-60. Must be able to read and understand English.
2. Currently meets DSM-IV criteria for a major depressive episode. (History of either unipolar major depression (depressive episodes only) or bipolar I disorder (history of manias and depressions) or bipolar II disorder (hypomanias and depressions), current episode depressed acceptable).
3. Must meet criteria for "treatment resistant" depression defined by failure to respond to, or intolerance of, at least 2 treatment trials (antidepressants or ECT) during the current episode.
4. All subjects will be fully ambulatory and in good medical health.
5. Are required to either be antidepressant free for 2 weeks prior to study entry (4 weeks for fluoxetine secondary to long half-life) or be on a fixed psychotropic medication regimen for at least 4 weeks.

Subjects and their primary care providers must agree to continue their status (i.e. without antidepressant or on a fixed regimen) until the 12-week assessment is complete.

6. Pre-menopausal female subjects must not be pregnant and must be willing to use adequate contraception during the study period.

Exclusion Criteria:

1. Current or history of psychotic symptoms.
2. Active suicidal ideation (defined as a score of ≥3 on HDRS suicide item).
3. Prior use of a TNF-alpha antagonist (i.e. etanercept, infliximab, adalimimub) and use of any other immunosuppressant agent (i.e. systemic corticosteroids or anti-proliferative agents such as methotrexate) within one year of study entry.
4. Current use of aspirin, non-steroidal anti-inflammatory agents (NSAIDs) or COX-2 inhibitors during the study. Acetaminophen will be allowed.
5. History of any of the following conditions: Congestive heart failure, abnormal electrocardiogram, malignancy, schizophrenia, neurological disease, auto-immune condition (e.g. rheumatoid arthritis, inflammatory bowel disease, multiple sclerosis, lupus), chronic infection (e.g. human immunodeficiency virus, hepatitis B or C), and hematologic, renal or hepatic abnormality.
6. Subjects will be excluded for a positive anti-double stranded DNA antibody test.

Contacts and Locations

Please refer to this study by its ClinicalTrials.gov identifier: NCT00463580

Contacts

Contact: Bobbi J. Woolwine, MSW	404-712-9620	bwoolwi@emory.edu
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Locations

United States, Georgia

Emory University School of Medicine, Department of Psychiatry and Behavioral Sciences — **Recruiting**

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Sub-Investigator: Ebrahim Haroon, MD

Sponsors and Collaborators
Emory University

Investigators

Principal Investigator: Charles Raison, MD Emory University

Principal Investigator: Andrew H Miller, MD Emory University

More Information

No publications provided

Responsible Party:	Emory University School of Medicine, Department of Psychiatry and Behavioral Sciences (Charles L. Raison, MD)
ClinicalTrials.gov Identifier:	NCT00463580 History of Changes
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Study First Received:	April 19, 2007
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Keywords provided by Emory University:

depression
TNF-alpha antagonist
infliximab
treatment resistant **depression**
major **depressive disorder** (MDD)
bipolar I disorder
bipolar II disorder

Additional relevant MeSH terms:

Depression
Depressive Disorder
Depressive Disorder, Major
Bipolar Disorder
Affective Disorders, Psychotic
Mood Disorders
Mental Disorders
Behavioral Symptoms
Infliximab
Dermatologic Agents
Therapeutic Uses
Pharmacologic Actions
Gastrointestinal Agents
Antirheumatic Agents
Anti-Inflammatory Agents

ClinicalTrials.gov processed this record on January 20, 2011

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Links to all studies - primarily for crawlers