Etanercept for Treatment of Hidradenitis

This study is currently recruiting patients.

Sponsors and Collaborators: University of Pennsylvania
Amgen

Information provided by: University of Pennsylvania

Purpose

This study is being done to test a drug called etanercept (Enbrel®). Etanercept has been approved by the U.S. Food and Drug Administration (FDA) for the treatment of chronic moderate to severe plaque psoriasis (PsO), for use in reducing the signs and symptoms of moderately to severely active rheumatoid arthritis (RA) in adults and children, and psoriatic arthritis (PsA) and ankylosing spondylitis (AS) in adults. It is available by prescription for the treatment of PsO, RA, PsA, and AS. Etanercept is approved for injection under the skin at a dose of 50 mg per week in patients with psoriasis.

The purpose of this study is to determine whether etanercept is safe and effective for the treatment of hidradenitis. Another purpose of this study is to determine the impact of etanercept treatment of hidradenitis on skin related to quality of life. The skin lesions typically associated with hidradenitis are thought to be partly due to a blockage that occurs in sweat glands, called apocrine ducts, which become inflamed and eventually destroyed. A protein found in the body called tumor necrosis factor alpha, or TNF-α, is a hormone that causes this inflammation or swelling. The study drug, etanercept, blocks the action of TNF-α. By blocking the action of TNF-α, etanercept may provide a reduction in the signs and symptoms of hidradenitis.

This study will take place at the University of Pennsylvania and will involve up to 21 participants ages 18 and up. Approximately 21 subjects will participate at the University of Pennsylvania. Each patient will participate in this study for a maximum of 6 months. The study consists of a screening visit, baseline assessment visit (Day 1), a treatment period (Week 2 – Week 14), and a one month follow-up visit (Week 18 visit). The total duration of the study will be approximately 2 years.

<table>
<thead>
<tr>
<th>Condition</th>
<th>Treatment or Intervention</th>
<th>Phase</th>
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<tr>
<td>Hidradenitis Suppurativa</td>
<td>Drug: etanercept</td>
<td>Phase II</td>
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MedlinePlus related topics: Bacterial Infections; Skin Diseases

Study Type: Interventional
Study Design: Treatment, Non-Randomized, Open Label, Uncontrolled, Single Group Assignment, Safety/Efficacy Study

Official Title: A Phase II Open Label Clinical Trial of Etanercept for the Treatment of Hidradenitis Suppurativa
Further Study Details:

Primary Outcomes: The primary objective of this study is to determine the safety and estimate the efficacy of etanercept for the treatment of hidradenitis suppurativa.

Secondary Outcomes: The secondary objective of this study is to determine the impact of etanercept treatment of hidradenitis suppurativa on skin related quality of life.

Expected Total Enrollment: 21

Study start: April 2005; Expected completion: April 2007
Last follow-up: August 2006; Data entry closure: October 2006

Purpose: The primary objective of this study is to determine the safety and estimate the efficacy of etanercept for the treatment of hidradenitis suppurativa. The secondary objective of this study is to determine the impact of etanercept treatment of hidradenitis suppurativa on skin related quality of life.

Duration: Each patient will participate in this study for a maximum of 6 months. The study consists of a screening visit, baseline assessment visit (Day 1), a treatment period (Week 2 – Week 14), and a one month follow-up visit (Week 18 visit). The total duration of the study will be approximately 2 years.

Subject Recruitment and Selection: It is planned that enrollment will be 12-21 patients.

Background: Hidradenitis suppurativa is a physically, psychologically, and socially disabling disease characterized by inflammatory, cystic papules and nodules affecting the underarms, groin, perineum, and breasts. Lesions can become erosive and often develop deep abscesses and sinus tracts and drain foul smelling pus. Left untreated, hidradenitis can result in permanent scarring. In the most severe cases, characterized by chronic ulceration and granulation, there may be an increased risk of aggressive squamous cell carcinoma.

Current treatment of hidradenitis consists of intra-lesional injections of steroids, topical and/or systemic antibiotics, hormonal therapy, and isotretinoin. For many patients with severe hidradenitis (stage II and III), these therapies are often ineffective. Patients with stage II and III hidradenitis often require surgical excision of the affected area (a highly morbid procedure) to control the disease. Unfortunately, for most patients with hidradenitis, existing therapies are ineffective and there is an unmet medical need for therapies that control this disabling and destructive disease.

The pathophysiology of hidradenitis is unknown. The leading hypothesis is that occlusion of apocrine ducts leads to severe dilatation, apocrine gland inflammation, with ensuing bacterial growth and neutrophilic infiltration and destruction of the duct. The importance of the immune dysregulation in hidradenitis is further demonstrated by its association in many individuals with inflammatory bowel disease.

The pathologic immune reaction to follicular occlusion in hidradenitis suggests a strong rationale for the use of treatments that may neutralize this inflammatory reaction. In fact, the existing standard treatment of hidradenitis is intra-lesional injections of steroids, in the effort to minimize the destructive nature of the immune response. Medications that are broadly immuno-suppressive, such as cyclosporine, have also been used to successfully treat hidradenitis, but are limited by organ toxicity. This rationale is further supported by case reports of dramatic and rapid (e.g. within days) improvement in hidradenitis treated with infliximab, a monoclonal antibody that blocks TNF-alpha.
Etanercept is a TNF-alpha inhibitor currently FDA approved to treat various inflammatory disorders including rheumatoid arthritis, psoriatic arthritis and psoriasis. By inhibiting TNF-alpha, etanercept stops the inflammatory cascade by binding directly to circulating TNF-alpha and inhibiting its binding to cell surface receptors.

Etanercept has been used in over 200,000 patients worldwide for more than 5 years and has a well established safety record. The most common adverse effect of etanercept is injection site reaction which is typically mild and self-limited. Currently, laboratory monitoring for patients being treated with etanercept is not recommended according to its label since the drug has not been associated with a significant incidence of laboratory abnormalities.

The well established safety profile of etanercept and its potent role in suppressing pathologic immune responses through TNF-inhibition make it a promising agent for the treatment of hidradenitis suppurativa. In this phase II clinical trial, we will determine preliminary evidence of safety and estimate the efficacy of etanercept in the treatment of hidradenitis. This study will provide critical preliminary data for planning larger pivotal trials.

Research Design: This is a phase II, open label, two-stage clinical trial of etanercept for the treatment of hidradenitis. This design is a widely accepted method for early investigations of safety and efficacy of medications for new indications. Etanercept 50 mg will be administered subcutaneously once a week for 12 weeks in an open label manner. At week 12, the etanercept dose will be tapered to 25 mg subcutaneously once a week for 2 weeks.

This is an 18 week study. Subjects will be screened to determine eligibility. Day -95 to -3 will be a screening period which will allow washout of concurrent therapies if necessary.

Potential Risks: Etanercept was generally well tolerated in patients with rheumatoid arthritis, psoriatic arthritis, and ankylosing spondylitis. Adverse events that were reported in at least 3% of all patients with higher incidence in patients treated with etanercept than placebo are: *Injection site reaction; *Infection; *Headache; *Nausea; *Rhinitis; *Dizziness; *Pharyngitis; *Cough; *Asthenia; *Abdominal pain; *Rash; *Peripheral edema; *Respiratory disorder; *Dyspepsia; *Sinusitis; *Vomiting; *Mouth ulcer; *Alopecia

Potential Benefits: No direct benefits from participation in the study can be guaranteed. The study medication will be provided by the Financial Sponsor at no charge.

Eligibility

Ages Eligible for Study: 18 Years and above, Genders Eligible for Study: Both

Criteria

Inclusion Criteria:

- Subjects must be able to give informed consent.
- Severe hidradenitis suppurativa clinically confirmed by the investigator and defined as recurrent abscesses, with 4 or more lesions (e.g. nodules or abscesses) with sinus track and scar formation (e.g. Stage II or III disease) that has not responded to previous standard therapies such as topical or oral antibiotics, or intralesional injections of steroids.
- Age 18 or older.
- Willingness to use at least one form of effective contraception during the study period and
for one month after discontinuation of etanercept if female and of child bearing capacity or
if male. If the patient elects to use a hormonal form of contraception then the patient must
be on the same form of hormonal contraception for 90 days prior to the start of Etanercept
and must plan to continue using the same form of hormonal contraception for the duration
of the study (e.g. until week 18).

Exclusion Criteria:

- Use of oral or topical antibiotics, isotretinoin, or intralesional steroids within 30 days prior
to day 0 or at any time during the study treatment period.
- Use of systemic immunosuppressants within 90 days prior to day 0 of this study.
- Use of an investigational medication 90 days prior to day 0 of this study.
- Use of a live vaccine 90 days prior to day 0 of this study.
- Any previous use of TNF- α inhibitors.
- If using a hormonal form of contraception, the patient will be excluded if they have not
  used the same form of hormonal contraception for 90 days prior to the start of the
etanercept (e.g. day 0) or are not willing to continue the use of the same form of hormonal
contraception for the duration of the study.
- Active infection within 30 days of day 0 of the study that is moderate (discomfort sufficient
to reduce or affect normal daily activity) or severe (incapacitating with inability to work or
perform normal daily activities) or requires treatment with antibiotics.
- History of tuberculosis or other mycobacterial disease or positive screening visit PPD (≥ 5
mm).
- Known history of an immuno-suppressing disease (e.g. HIV)
- Clinically significant abnormality in liver function, renal function, chemistry panel or CBC
  (AST or ALT ≥ 2 times the laboratory’s upper limit of normal, hemoglobin < 10.0 g/dL,
  platelet count <125,000/cm3, white blood count <3,500 cells/cm3 or > 15,000 cells/cm3,
or serum creatinine ≥ 2.0 mg/dL) or severe co-morbidities defined as diabetes mellitus
  requiring insulin, congestive heart failure, history of myocardial infarction, unstable angina,
  uncontrolled hypertension (systolic blood pressure > 180 mmHg or diastolic blood pressure
>110 mmHg), severe pulmonary disease (requiring oxygen therapy), history of cancer
within 5 years (other than resected basal cell or squamous cell carcinoma and in situ
cervical cancer), known history of active hepatitis B or C or HIV infection, history of
demyelinating diseases or lupus.
- Pregnancy or lactation
- History of alcohol or drug abuse within 12 months of screening visit

Location and Contact Information

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More Information