Infliximab therapy for patients with moderate to severe hidradenitis suppurativa: A randomized, double-blind, placebo-controlled crossover trial

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Background: Biologic therapies with anti–tumor necrosis factor agents are promising treatments for hidradenitis suppurativa (HS).

Objective: We assessed the efficacy and safety of infliximab (IFX) for the treatment of moderate to severe HS.

Methods: A prospective double-blind treatment phase of 8 weeks where patients received IFX or placebo was followed by an open-label phase where patients taking placebo were given the opportunity to cross over to IFX, and an observational phase. Primary treatment efficacy was based on HS Severity Index. Secondary end points included Dermatology Life Quality Index, visual analog scale, and Physician Global Assessment scores. Inflammatory markers erythrocyte sedimentation rate and C-reactive protein were also assessed.

Results: More patients in the IFX than in the placebo group showed a 50% or greater decrease from baseline HS Severity Index score. In addition, statistically and clinically significant improvement from baseline was observed at week 8 in Dermatology Life Quality Index score, visual analog scale score, erythrocyte sedimentation rate, and C-reactive protein compared with placebo. Patients in the placebo group treated with IFX after week 8 (crossover) responded similarly to the original IFX group. Many patients withdrew during the observational phase to continue anti–tumor necrosis factor-alfa therapy. No unexpected serious adverse events were observed.

Limitations: Results are representative of a single center, patients were treated by a single physician, some patients did not return after their last infusion, and the HS Severity Index requires validation.

Conclusions: This clinical study represents the first formal assessment of IFX for treatment of moderate to severe HS. IFX was well tolerated, no unexpected safety issues were identified, and improvements in pain intensity, disease severity, and quality of life were demonstrated with concomitant reduction in clinical markers of inflammation. (J Am Acad Dermatol 2010;62:205-17.)

Key words: hidradenitis suppurativa; infliximab; tumor necrosis factor.

Hidradenitis suppurativa (HS) is a chronic, inflammatory, relapsing, often debilitating dermatologic disease for which there is no approved medical therapy.[1-3] HS is often hereditary and usually appears after puberty with a higher incidence observed in women and African Americans.[1,4-6] Current findings suggest the primary sequence of events leading to HS to be

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Supported by Centocor Inc.

Disclosure: Dr Kerdel, Ms Grant, and Ms Cardenas have received research support from Centocor Inc. Drs Gonzalez and Montgomery are employees of Centocor Inc.

Presented at the 2008 Conference of the American Academy of Dermatology, San Antonio, TX, March 2008; the 2009 Conference of the American Academy of Dermatology, San Francisco, CA, March 2009; and the 2007 Annual Conference of the British Association of Dermatologists, Birmingham, UK, June 2007.

Accepted for publication June 10, 2009.

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0190-9622/$36.00

doi:10.1016/j.jaad.2009.06.050

hyperkeratosis of the follicular epithelium with subsequent occlusion and rupture of the follicle resulting in an inflammatory response that is associated with bacterial infection of the apocrine sweat glands.[7] In moderate to severe cases, further tissue destruction leads to draining pustules, subcutaneous sinus tracts, and extensive fibrous scars.[8-10] HS predominately occurs in skin folds bearing terminal hairs and apocrine glands, typically affecting the axillae, genitofemoral region of female patients, and anogenital region of male patients.[1,8] The lesions are invariably painful, unsightly, odorous, and can have a devastating effect on the patient's quality of life both as a physical ailment and social concern.[11,12] The reported prevalence of HS varies widely depending on whether only clinically confirmed cases are included or whether self-reports by patients are considered. Available information from larger population-based studies indicates prevalence rates that range from 0.2% to 1%[13,14] to as high as 4% in a population subset.[1,3] Challenges in estimating the prevalence are that early symptoms can be analogous to other skin disorders, patients are often seen by many different specialties, embarrassment results in delays to seek medical attention, and it can be difficult to diagnose the disease in its early stages.[8,15] It is possible that the prevalence of HS may actually be somewhat higher than available estimates.

Current treatment modalities for HS have failed to provide a consistently effective treatment strategy. Depending on extent of the disease, medical treatment with topical antiseptics, topical or systemic anti-inflammatory antibiotics, intralesional steroid and hormonal therapy, oral retinoids, immunosuppressive drugs, or radiation have achieved varying degrees of success.[8,15,16] Incision and draining of pustules and tracts can be helpful at earlier stages, whereas surgical intervention for more severe disease can be extensive, involving skin grafts, extended periods for recovery, and significant postsurgical complications with potential for disfigurement.[3,8,17,18] Because currently available medical treatments are minimally effective in cases of moderate to severe HS, there is a clear need to identify new therapies for this serious, disabling, and chronic disease.

CAPSULE SUMMARY

- We assessed the efficacy and safety of infliximab for the treatment of moderate to severe hidradenitis suppurativa in a prospective double-blind treatment phase of 8 weeks where patients received infliximab or placebo followed by an open-label phase and an observational phase.
- Infliximab was well tolerated, no unexpected safety issues were identified, and improvements in pain intensity, disease severity, and quality of life were demonstrated with concomitant reduction in clinical markers of inflammation.

Biologic therapies with anti–tumor necrosis factor (TNF)-alfa agents are promising treatments for HS. These agents have demonstrated efficacy in other chronic inflammatory disorders such as psoriasis, Crohn disease (CD), ulcerative colitis, and rheumatoid arthritis.[19-24] Patients with HS often present with comorbidities of CD and arthridities indicating a possible mechanistic connection among these diseases.[22,25] After treatment with infliximab (IFX), a monoclonal antibody directed against TNF-alfa, patients with simultaneous CD and HS showed dramatic improvement of HS symptoms, suggesting that TNF-alfa may have a central role in HS.[21,26,27] These findings are supported by the observation that during the proinflammatory phase of HS, neutrophilic infiltration is accompanied by the release of TNF-alfa, which may mediate HS-associated keratinocyte proliferation.[9,16,26,28-30] Observational data, case reports, and limited nonrandomized studies in the literature highlight the potential clinical use of IFX in patients with moderate to severe HS and underscore the need for a controlled, randomized prospective clinical trial.[26,28,31-35]

We report here the results of a single-center, prospective, randomized double-blind, placebo-controlled, open-label crossover trial to examine the efficacy and safety of IFX and placebo on patients with moderate to severe HS.

METHODS

Trial design

The safety and efficacy of IFX for the treatment of HS was investigated in a phase-II, randomized, single-center, prospective clinical trial, which included a double-blind placebo-controlled treatment phase, an open-label crossover parallel treatment phase, and an observational phase. Institutional review board approval (protocol No. 20060449) and written informed consent from patients were obtained for this investigator-initiated study before any protocol-related procedures were undertaken. The trial was submitted to the Food and Drug Administration as an investigator-sponsored investigational new drug and registered on the clinical trials World Wide Web site (clinicaltrials.gov, identifier No. NCT00795574).