Clinical trial results support adalimumab treatment for painful skin condition

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The results of two phase 3 clinical trials that led to FDA approval of adalimumab for treatment of the chronic inflammatory skin disease hidradenitis suppurtiva (HS) are being published in the August 4 *New England Journal of Medicine*. An inhibitor of the inflammatory protein tumor necrosis factor (TNF), adalimumab is the first such medication approved to treat the painful skin disorder.

"HS is a devastating disease affecting young women and men with painful, disfiguring boils and abscesses, primarily in the armpits and groin," says Alexa Kimball, MD, MPH, lead and corresponding author of the New England Journal report and until recently a member of the Massachusetts General Hospital Department of Dermatology. "Both physical functioning and quality of life are severely affected, and while many treatments are used to relieve symptoms and try to get the disease under control, this largest set of placebo-controlled information to date clearly shows that improvement can result for patients."

Conducted at institutions in six countries, the PIONEER I and PIONEER II trials were sponsored by AbbVie, which markets adalimumab for a number of inflammatory conditions under the brand-name Humira. Affecting the skin in regions containing apocrine sweat glands, HS is believed to be caused by immune system abnormalities, and elevated levels of the inflammatory factors called cytokines - including TNF - have been detected in HS lesions. Adalimumab acts by suppressing TNF activity, and its potential to treat HS was supported by phase 2 trial results showing that weekly injections of the drug were

more effective than placebo in reducing symptoms and relieving pain. The two phase 3 trials were designed to better investigate the drug's safety, compare dosage frequency and determine whether improvement would persist after treatment was discontinued.

Both trials enrolled more than 300 patients with moderate to severe HS, who were originally randomized into two nearly equal groups. During the first 12-week stage of each trial, one group received weekly 40 mg adalimumab doses, and the other received a placebo. In the PIONEER I trial, participants in the placebo group received adalimumab in the second 24-week stage, while those originally receiving the active drug were randomized into three subgroups - one continuing to receive weekly adalimumab, one receiving the drug every other week and the third receiving a placebo. The design of PIONEER II was similar, except that first-stage placebo group continued to receive the placebo during the second stage. Several participants dropped out because of worsening symptoms, lack of improvement or other reasons, with 170 completing PIONEER I and 116 completing PIONEER II.

For both trials, results at the end of the first stage confirmed the phase 2 trials result - that adalimumab provided significantly greater symptom relief than placebo, with no unexpected serious adverse events. While second-stage results showed no significant differences between participants continuing to receive weekly doses of the active drug, those receiving biweekly doses and those shifted to placebo, Kimball notes that, since it is typical for the severity of HS symptoms to increase and decrease and because the study protocol required treatment discontinuation for participants whose symptoms stopped responding to the drug, larger scale studies will be required to better define the ideal length and frequency of treatment.

"These results are exciting because they open up a whole new era for HS research and treatment," she says. "HS has been underappreciated and

understudied, and this kind of research - showing not only that these studies can be done well but also that we can improve our patients' symptoms - can only lead to further advances."

More information: *New England Journal of Medicine*, DOI: 10.1056/NEJMoa1504370

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