Systematic review of efficacy of anti–tumor necrosis factor (TNF) therapy in patients with psoriasis previously treated with a different anti–TNF agent

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Background: Tumor necrosis factor (TNF) antagonists have improved outcomes for patients with psoriasis, but some patients are unresponsive to treatment (primary failure) or lose an initially effective response (secondary failure).

Objective: We sought to systematically investigate the efficacy and safety of a second TNF antagonist after failure of a first TNF antagonist.

Methods: Published primary studies evaluating the efficacy of switching TNF antagonists after failure were systematically extracted.

Results: Fifteen studies were included. Although response rates to a second TNF antagonist were lower than for a first, a substantial proportion of patients in every study achieved treatment success. Week-24 response rates for a second antagonist were 30% to 74% for a 75% improvement in Psoriasis Area and Severity Index score and 20% to 70% for achieving a Physician Global Assessment score of 0/1; mean improvements in Dermatology Life Quality Index ranged from −3.5 to −13. In general, patients who experienced secondary failure achieved better responses than patients with primary failure. Adverse event incidences ranged from 20% to 71%, without unexpected adverse events; 0% to 11% of patients experienced serious adverse events.

Limitations: There was no common definition of treatment failure across these studies of varied design.

Conclusions: Some patients benefit from switching to a second TNF antagonist after failure of a first TNF antagonist, with improved quality of life. (J Am Acad Dermatol 2016;75:612-8.)

Key words: adalimumab; etanercept; failure; infliximab; psoriasis; switching; tumor necrosis factor antagonist.

Tumor necrosis factor (TNF) antagonists have dramatically improved outcomes for patients with moderate to severe psoriasis. TNF antagonists have been used in psoriasis therapy for over a decade and are extensively characterized.[1-6] These highly complex molecules differ structurally

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and functionally. Etanercept, the first TNF antagonist approved by the US Food and Drug Administration (in 2004) to treat plaque psoriasis, is a recombinant fusion protein combining soluble human TNF receptors linked to the fragment crystallizable portion of an IgG1 molecule. Infliximab (approved in 2006) and adalimumab (approved in 2008) are recombinant IgG1 monoclonal antibodies, but they differ in origin; infliximab is a human–murine chimeric molecule, whereas adalimumab is fully human. Certolizumab is a TNF inhibitor (humanized antibody fragment conjugated to polyethylene glycol) that is currently being evaluated in phase III studies of psoriasis; golimumab is a fully human monoclonal anti–TNF antibody that is approved for multiple indications but not psoriasis.

CAPSULE SUMMARY

- In patients with psoriasis, guidelines are needed for alternative treatment in patients who do not respond to anti–tumor necrosis factor agents.
- In this systematic review, some patients who failed treatment with 1 anti–tumor necrosis factor agent successfully responded to another.
- Switching to another anti–tumor necrosis factor agent may be considered in nonresponsive patients.

Despite the effectiveness of TNF antagonists in the treatment of psoriasis, some patients never achieve an initial response to treatment (primary failure), whereas others lose their initial response over time (secondary failure). Clinical observations, trials, and individual cases suggest that switching to a treatment with a different mechanism of action is sometimes unnecessary and that switching to a different TNF antagonist, specifically after secondary failure, is often successful in regaining a response. There is no consensus on the best approach for switching treatment after failure of an anti–TNF agent, partly because, to our knowledge, the data were never organized and systematically analyzed. Here, we systematically review data from clinical studies assessing the efficacy of switching to a TNF antagonist after failure with an initial TNF antagonist to help guide clinical treatment of patients with unsatisfactory response to prior anti–TNF therapy.

METHODS

Searches of the Cochrane Library, MEDLINE, EMBASE, EMBASE Alert, BIOSIS Previews, SciSearch, International Pharmaceutical Abstracts, and Derwent Drug File were conducted to identify clinical studies that evaluated TNF antagonists for the treatment of moderate to severe psoriasis in adults who previously experienced treatment failure with another TNF antagonist. The searches encompassed the literature through February 18, 2015. Search terms were based on specific agents ("adalimumab," "Humira," "certolizumab," "Cimzia," "etanercept," "Enbrel," "golimumab," "Simponi," "infliximab," and "Remicade") and mechanism of action ("anti TNF," "anti TNF agent*," "anti TNF alpha," "TNF alpha antagonist*," "TNF alpha antibody*," "TNF alpha blockade," "TNF alpha inhibitor*," "tumor necrosis factor antagonist*," "tumor necrosis factor blocker," "tumor necrosis factor inhibitor*," "tumour necrosis factor antagonist*," "tumour necrosis factor inhibitor*"). Case reports (but not case series), cost economic analyses, and reviews were excluded. Studies reporting results only in patients with psoriatic arthritis were manually removed, as were pediatric trials and studies in which most patients switched treatments for nonmedical reasons (eg, insurance reimbursement). Included studies must have reported the percentage of patients achieving a Physician Global Assessment (PGA) score of 0 or 1, 50% improvement in Psoriasis Area and Severity Index (PASI) score (PASI50), or 75% improvement in PASI score (PASI75).[7]

Overall, 334 articles were retrieved in the initial and follow-up searches; 2 additional related articles were subsequently found. After manually screening for the inclusion and exclusion criteria described above, 24 full-text articles were obtained. Nine additional articles were removed based on exclusion criteria (efalizumab treatment [n = 3], all patients having psoriatic arthritis [n = 2], lack of efficacy data [n = 1], lack of prior treatment with biologics [n = 1], overlapping study [n = 1], and review [n = 1]), leaving 15 full-text articles for the analysis.

RESULTS

Study designs and patients

Fifteen studies were analyzed (Table I; available at http://www.jaad.org). All patients from the included studies had moderate to severe plaque psoriasis. Most patients were men (range, 50%-80%; median, 65%). Studies differed by length, prevalence of concomitant psoriatic arthritis, duration of first TNF antagonist washout, and definitions of treatment failure. Six studies explicitly allowed concomitant methotrexate; however, the number of patients receiving concomitant methotrexate therapy was generally low (range, 3%-32%).[8-13]

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