

Dermatomyositis-Etanercept trial

A commentary from *Neurology*

**A pilot trial illustrates the challenges of studying therapies for rare diseases but suggests that etanercept may be well tolerated and have some efficacy.**

Dermatomyositis (DM), a subtype of inflammatory myopathy, is a rare disease; estimates of its prevalence range from about 1 to 6 per 100,000. Patients with DM are typically treated with prednisone.

Searching for more-effective and less noxious therapies, researchers undertook this randomized, double-blind pilot trial of etanercept, a soluble tumor necrosis factor alpha (TNF- $\alpha$ ) receptor fusion protein that inactivates TNF- $\alpha$ .

Selection criteria initially targeted newly diagnosed and treatment-naive patients, but were subsequently modified (because of slow recruitment) to also include those with refractory and steroid-dependent disease. After screening 153 patients, 16 patients were enrolled (5 newly diagnosed and 11 with refractory disease); 11 received etanercept (50 mg subcutaneously) and 5 received placebo weekly for 52 weeks.

Participants also received high-dose steroids (typically 60 mg/day) for 2 months before randomization, after which they underwent a forced steroid taper aimed at discontinuing prednisone by week 25. Primary outcome measures included the frequency of adverse events, average dose of prednisone after week 24, and time to treatment failure.

The treatment groups did not differ significantly in adverse-event rates. Between weeks 25 and 52, the median prednisone dose was significantly lower in the etanercept group (1.2 mg/day; range, 0.0–31.1 mg/day) than in the placebo group (29.2 mg/day; range, 9.9–62.6 mg/day).

Treatment failure rates were significantly higher in the placebo group. The authors cautiously conclude that the absence of safety concerns and the finding of a steroid-sparing effect suggest that further investigation of etanercept as a treatment for DM is warranted.

Comment: This trial highlights the challenges of developing new treatments for patients with rare diseases such as DM. The public health impact of rare diseases is evident from the estimated 25 to 30 million Americans with a rare disease (defined by the U.S. Orphan Drug Act as a prevalence of <200,000, or unlikely to attract investment in drug research), making such research highly valuable despite the challenges.

The authors are to be commended for conducting this trial, but caution is warranted in interpreting the results. The unplanned modification of trial selection criteria and the small sample size preclude firm conclusions about the safety and efficacy of etanercept in DM.

— Michael Benatar, MD, MS, PhD

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