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Dramatic Responses in Cutaneous Sarcoidosis With JAK Inhibitor

— More than 80% reduction in disease activity in case series of tofacitinib treatment

by [Charles Bankhead](#), Senior Editor, MedPage Today

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NEW YORK CITY -- Patients with longstanding sarcoidosis and skin involvement had dramatic improvement after 6 months of treatment with the Janus kinase (JAK) inhibitor tofacitinib (Xeljanz), a small open-label clinical series showed.

Disease activity declined by an average of 82.7% in 10 patients, six of whom had complete clinical resolution of inflammation. Improvement was evident within 30 days and continued to increase with ongoing treatment.

Imaging and laboratory results showed improvement in internal organ involvement and changes in molecular markers that correlated with the skin improvement, reported William Damsky, MD, PhD, of Yale School of Medicine in New Haven, Connecticut, at the [Inflammatory Skin Disease Summit](#).

"Patients typically came into therapy on combination immunosuppressive regimens, although some were not on therapy," he said. "All 10 patients improved and they commonly were able to discontinue or significantly taper their baseline immunosuppressive therapy. We saw an average reduction in cutaneous sarcoidosis activity of about 80% and six patients had nothing left in their skin at the end of the study, a complete response."

"All patients completed the study, tofacitinib was well tolerated, and there were no adverse effects," Damsky added. "There's a great need for better treatments other than prednisone, and our trial and prior work have now shown that JAK inhibition appears to be a highly efficacious treatment. It really seems that randomized, controlled studies are not only warranted but need to further define its efficacy."

A systemic inflammatory condition involving T-cell activation, sarcoidosis can affect almost any organ in the body, although the lungs and lymph nodes are the most common sites, Damsky pointed out. About a third of patients have cutaneous manifestations, and occasionally, the skin is the only involved site. The only FDA-approved therapy is prednisone, which is limited to patients with lung involvement. Cutaneous sarcoidosis has no approved therapies.

Sarcoidosis pathogenesis involves multiple cytokines regulated through the JAK/STAT, prompting speculation that JAK inhibition might be effective treatment for the condition, he continued. Damsky said that a colleague and mentor of his suggested tofacitinib for a female patient, age 48, who had longstanding sarcoidosis with extensive cutaneous involvement, and lack of response to multiple therapies that included methotrexate and a tumor necrosis factor (TNF) inhibitor.

"The patient had a really remarkable response [to tofacitinib treatment], such that all that was left after a number of months was post-inflammatory hyperpigmentation," said Damsky, who along with several colleagues [published a case report](#). "Biopsy on treatment showed that, whereas there were well-defined sarcoidosis granulomas at baseline, they went away on therapy...We treated other patients with off-label tofacitinib and had equally dramatic responses."

Imaging of patients suggested the treatment effect extended beyond the cutaneous manifestations of the disease to affected internal organs, he added.

A subsequent [literature review](#) turned up multiple case reports about use of tofacitinib to treat sarcoidosis. The accumulation of evidence led to a prospective evaluation of the JAK inhibitor in patients with cutaneous sarcoidosis.

The 10-patient open-label study included nine patients with active internal-organ disease. All patients received tofacitinib 5 mg twice-daily for 6 months. The primary outcome was change in the Cutaneous Sarcoidosis Activity and Morphology Instrument (CSAMI). At the end of the study period, patients could continue, taper, or discontinue concomitant immunosuppressive therapy.

The patients ranged in age from 53 to 63, and disease duration ranged from 1 to 31 years. All of the patients were being treated with methotrexate and prednisone at enrollment, and some were also receiving infliximab (Remicade), hydroxychloroquine, or azathioprine.

Baseline CSAMI ranged from 20 to about 60. At 6 months, the reduction in CSAMI from baseline averaged 82.7% and six patients had complete resolution of cutaneous disease.

Laboratory work has implicated multiple cytokines in the pathogenesis of sarcoidosis, said Damsky. The studies led to a working hypothesis that interferon-gamma is the key driver of the disease process, which is consistent with the known effects of tofacitinib. TNF-alpha and interleukin-6 appear to be secondary signaling molecules.

In a post-presentation discussion, an attendee asked Damsky to speculate about the relative importance of blocking different JAK tyrosine kinases (TKs). After briefly discussing different cytokines affected by the different TKs, Damsky said "the short answer is we don't know."

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Disclosures

Damsky disclosed relationships with Pfizer, Advanced Cell Diagnostics/Bio-Techne, AbbVie, Eli Lilly, Twi Biotechnology, Incyte, and EMD/Millipore/Sigma.

Primary Source

Inflammatory Skin Disease Summit

Source Reference: [Damsky W, et al 'Treatment of sarcoidosis with cutaneous involvement with tofacitinib: Results of an open-label clinical trial with mechanistic insight' ISDS 2021; Abstract 46.](#)