

Fibroblast injection improves depressed acne scars, study shows

Dermatology Times

January 2012

By: Cheryl Guttman Krader

In study of off-label use of autologous fibroblasts for acne scars, responder rate was significantly higher for fibroblast treatment compared with control; Injections were well tolerated; Injections performed under topical anesthesia or with local anesthesia using a ring block

Washington — Injection of autologous cultured fibroblasts (azficel-T; Laviv, Fibrocell Science) is safe and effective for improving the appearance of distensible, depressed acne scars, according to the results of a prospective, double-blind, placebo-controlled clinical trial reported by Girish "Gilly" Munavalli, M.D., at the 2011 annual meeting of the American Society for Dermatologic Surgery.

"Injection of autologous fibroblasts represents an exciting and promising new paradigm," Dr. Munavalli says. "Not only does it appear to correct the dermal defect underlying distensible, depressed acne scars, but the treatment appears to have a broader field effect and provides a more global improvement in regional skin contour."

The off-label use of autologous fibroblasts was investigated in a randomized, phase 2/3 study conducted at eight sites. Eligible patients had bilateral facial acne scars involving an area of at least 9 cm² on each cheek that were moderate to severe based on subject and investigator ratings. The patients in the study ranged in age from 19 to 65 years (mean 42) and were predominantly female and white.

One cheek of each patient was randomized to treatment with autologous fibroblasts or vehicle (cell culture media), and the alternate treatment was administered on the contralateral side. Each patient received a series of three injections at intervals of about two weeks and was evaluated for safety and scarring severity monthly until four months after the last injection.

Ninety-nine patients were evaluated for efficacy based on a responder endpoint for both the subjects' and investigators' ratings.



Dr. Munavalli

Study results

At one month after the last injection, treatment with the autologous fibroblast injection was associated with a significantly higher responder rate compared with control in both the subject and investigator ratings. Responder rates for treatment with the autologous

fibroblasts continued to increase throughout follow-up and reached a plateau after three months with the vehicle injection.

At the study's conclusion, the responder rate was significantly higher for the autologous fibroblast treatment compared with the control in both the subject (43.1 vs. 18.3 percent) and investigator assessments (58.7 vs. 42.2 percent).

The autologous fibroblast injections were well tolerated, and there were no serious adverse events or study withdrawals related to a treatment emergent adverse event, says Dr. Munavalli, medical director of Dermatology, Laser & Vein Specialists of the Carolinas, Charlotte, N.C., and clinical assistant professor of dermatology, Wake Forest University School of Medicine, Winston-Salem.

The process

The autologous fibroblasts are harvested by taking three 4-mm postauricular punch biopsies. The tissue is sent overnight to the manufacturer, where the fibroblasts are isolated, expanded in culture, and packaged in vials containing 10 million to 20 million cells/mL.

The injections are performed either under topical anesthesia or with local anesthesia using a ring block. The cells are withdrawn from the manufacturer's vial into 0.5 mL tuberculin syringes equipped with a 28 gauge to 30 gauge needle and delivered into the upper papillary dermis in a grid approach under and around the scars, administering 0.1 mL/cm² and a maximum a total volume of 2 mL per session.



A patient with distensible, depressed acne scarring before (left) and three years after three treatments with azficel-T, administered about three weeks apart. (Photos: Gilly Munavalli, M.D.)

Assessing severity

In the clinical trial, patients rated the severity of their scarring using a five-point Subject Live Acne Scarring scale that asked them to describe how they felt about the appearance of their cheek (-2 = very dissatisfied, 0 = somewhat satisfied, +2 = very satisfied). Investigators used the five-point Evaluator Live Acne Scar Assessment (ELASAS; 0 = clear, 4 = severe) that was developed and validated for the study.

For the subject ratings, patients were defined as responders if they achieved a two-point improvement from baseline; a one-point improvement was used to define responders for the evaluators' ratings.

"There are few validated instruments for assessing the severity of acne scarring. The ELASAS was developed to address this issue, and in testing it was shown that a one-point change in score was indicative of a clinically meaningful change in acne scarring severity," Dr. Munavalli says.

Adverse events in the study were generally limited to injection site reactions, with erythema and swelling the only events that occurred in 5 percent or more of patients. The overall rate for both types of reaction was 11 to 12 percent for both treatments, although the reactions were mild to moderate in severity following the fibroblast injections and only mild after vehicle injection.

Dr. Munavalli says the improvement seen with the vehicle control treatment is not surprising, since acne scarring also improves with skin needling and subcision, presumably through stimulation of collagen synthesis.

The progressive improvement during follow-up after the last fibroblast injection and the global type of improvement achieved suggest that the cells remain viable for some time after injection and are continuing to produce collagen, as well as perhaps also stimulating neighboring native fibroblast activity through paracrine effects, Dr. Munavalli says.

Disclosures: Dr. Munavalli is an investigator and consultant for Fibrocell. He is on the speakers bureaus and is a consultant for Merz and Medicis.