ORIGINAL ARTICLE

A double-blind, randomized, multicenter, controlled trial of suspended polymethylmethacrylate microspheres for the correction of atrophic facial acne scars

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Background: Acne scarring remains a stubborn clinical problem. Few treatments have been shown to be definitely effective for this problem. Polymethylmethacrylate (PMMA) microspheres in collagen (ArteFill, Suneva Medical Inc, Santa Barbara, CA) have shown long-term benefit for nasolabial fold treatment. A pilot study has shown benefit for PMMA-collagen in atrophic acne scarring.

Objective: We sought to demonstrate the safety and effectiveness of PMMA-collagen for acne scarring in a controlled, blinded trial.

Methods: Subjects with at least 4 moderate to severe rolling, atrophic scars randomly received PMMA-collagen or saline injections. Subjects underwent up to 2 injection sessions and were followed up for 6 months. Efficacy was assessed using a validated rating scale for each scar.

Results: In all, 147 subjects underwent injections. Success was achieved by 64% of those treated with PMMA-collagen compared with 33% of control subjects ($P = .0005$). The treatment showed excellent safety with generally mild, reversible adverse events. No significant differences in efficacy or safety were noted between genders, for darker skin types, or in older age groups.

Limitations: Subjects were followed up for only 6 months.

Conclusion: PMMA-collagen demonstrates substantial effectiveness in the treatment of atrophic acne scars of the face while maintaining an excellent safety profile. Further follow-up should be undertaken to demonstrate longer-term benefit and safety. (J Am Acad Dermatol http://dx.doi.org/10.1016/j.jaad.2014.02.034.)

Key words: acne; acne scars; collagen; dermal filler; microspheres; polymethylmethacrylate.

Acne vulgaris affects approximately 40 million people in the United States and it is estimated that up to 90% of adolescents will have acne at some time.[1,2] The incidence of scarring from acne has been estimated to range from 1% to 12%.[3,4] Although somewhat difficult to classify, acne scars have been generally categorized into 3 types: icepick, boxcar, or rolling

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scars.[5,6] Most patients have a mix of several types of scars.

Treatments for acne scars are dependent on the type of scar. Icepick scars are generally amenable to punch excision.[7] Boxcar and rolling scars are broader and require other therapy such as subcision, resurfacing, or dermal filling. Although many therapeutic options are published, most are case reports, personal experiences, or small series from a single center. In the past, bovine collagen (Zyplast, Collagen Corporation, Palo Alto, CA) had been approved by the US Food and Drug Administration (FDA) for the treatment of acne scars but was subsequently removed from the US market. No other filler carries US FDA approval for treatment of acne scars. Several 510(k) medical devices are US FDA cleared for use in acne scarring but such clearance requires only modest evidence of clinical efficacy and safety.[8]

CAPSULE SUMMARY

- Acne scarring remains a common and difficult-to-treat condition.
- This study demonstrates safety, efficacy, and tolerability of polymethylmethacrylate microspheres in collagen for the treatment of acne scarring.
- Physicians may now offer a minimally invasive treatment to their patients with acne scarring.

Polymethylmethacrylate (PMMA) suspended in bovine collagen (ArteFill, Suneva Medical Inc, Santa Barbara, CA) has been US FDA approved for the treatment of nasolabial folds since 2006. It is similar to other filling materials in its ability to augment soft-tissue defects and is generally considered long lasting. A pilot trial in atrophic acne scars showed considerable benefit.[9] To demonstrate the efficacy and safety of PMMA-collagen for the treatment of atrophic acne scars for the purposes of US FDA registration, a multicenter clinical trial was undertaken.

METHODS

This study was a double-blind, randomized controlled trial and conducted at 10 investigative centers across the United States with expertise in dermatology and plastic surgery (Cintrials.gov identifier: NCT01559922). Before screening, subjects underwent an informed consent process and signed an institutional review board–approved informed consent form. The study was conducted in accordance with Good Clinical Practices and the principles that have their origins in the Declaration of Helsinki (revised Seoul, Korea, 2008).

Potential subjects with acne scars were selected from the investigators practices and solicited from advertisements. To be included, subjects must have met the inclusion and exclusion criteria shown in Fig 1. Each study center incorporated a treating investigator who performed the injections and a blinded investigator who performed subject evaluations only without knowledge of the treatment assignment.

Before treatment, all of a subject's facial acne scars were evaluated and each scar that met the inclusion and exclusion criteria and was within the treatment area was mapped and photographed. Skin testing consistent with the labeling for PMMA-collagen was performed before treatments were administered. Subjects were randomized to receive either PMMA-collagen or saline injections in a 2:1 fashion, respectively, using a randomization system that controlled for gender and Fitzpatrick skin type. Treatment centers had no access to randomization data. Four weeks after their first injections, subjects were re-evaluated and any scars that the blinded evaluator thought were not sufficiently corrected underwent a touch-up injection. Subjects were evaluated at 2 weeks, and 1, 3, and 6 months after their last injections.

Implant material or a saline control was placed at the reticular dermal level or dermal subcutaneous junction. Investigators were encouraged to perform injections using the retrograde linear threading technique but could also perform serial puncture based on actual scar response. For the linear threading, investigators made several passes in one direction and then several additional passes 90 degrees to the original direction. Because of the long-term nature of PMMA-collagen, overcorrection was specifically avoided and investigators were asked to rely on the touch-up injections to achieve the best overall appearance. Commercial PMMA-collagen and needles included with the packaging were used for the injections. Control injections were performed with preservative-free saline in a similar manner.

Scar severity was assessed using a proprietary Acne Scar Rating Scale (ASRS). This 4-point scale (1 = minimal, 2 = mild, 3 = moderate, and 4 = severe) was developed and validated specifically for this study (data on file). This is a photonumeric scale that yields a static score in which each scar receives an individual grade at a designated time point. In addition, assessment was conducted using Physician and Subject Global Aesthetic Improvement Scales (Fig 2). Lastly, subjects were asked to assess their level of satisfaction of scar correction using the scale