Prospective, Multi-site, Pilot Investigation of the Safety and Effectiveness of Microfocused Ultrasound with Visualization (MFU-V) for Correction of Moderate-to-Severe Atrophic Acne Scars

John H. Joseph, MD, Clinical Testing of Beverly Hills, Beverly Hills, CA; Corey S. Maas, MD, The Maas Clinic, San Francisco, CA

ABSTRACT

Background: Tissue remodeling created by micro-focused ultrasound with visualization (MFU-V) is hypothesized to improve the appearance of acne scars. Methods: Twenty subjects with moderate-to-severe acne scars were enrolled to receive three MFU-V treatments (30 lines per 2.5 X 2.5 cm square) at dual depths 30 days apart. Treatment squares were marked over acne scars in the cheek and/or temporal area and received treatment using the 10 MHz/1.5mm and 7 MHz/3.0 mm transducers. Delivery was 15 lines horizontally and 15 lines vertically with each transducer depth. Treatment pain was assessed using a validated numeric rating scale (NRS, 1-10). Standardized photographs were taken prior to each treatment and at 60, 90 and 180 days. A masked, qualitative assessment of photographs at 90 and 180 days post final treatment compared to baseline was completed. Efficacy was measured by Global Aesthetic Improvement Scores (GAIS) noting improvement in acne scar appearance by both physician and subject at all follow-ups compared to baseline images. Subjects completed a Patient Satisfaction Questionnaire (PSQ) at Day 90 after the third treatment. Safety data (AE incidence) were also collected. Results: Average age of acne scars was: 1-15 years (15%), 16-30 years (45%) and 30+ years (30%). Interim pain scores across all treatments averaged 4.5 and 5.4 with the 7 MHz/3.0 mm and 10 MHz/1.5mm transducers, respectively. Interim GAIS (n=14) was 79% 'Improved', 14% 'Much Improved', and 7% Very Much Improved physician reported and 50% 'Improved', 29% 'Much Improved', and 14% Very Much Improved subject reported at D90. Conclusion: Interim results suggest MFU-V is well tolerated. Final efficacy data will be presented as the last D180 is expected in June 2015.

BACKGROUND

Acne vulgaris is a common inflammatory disease which can adversely affects facial appearance. Facial acne can have a serious negative impact on psychosocial functioning leaving deep emotional scars (1). Severe acne may also lead to physical scars and disfigurement. Among patients with severe acne, facial scarring affects both genders equally and occurs to some degree in 95% of cases (2). The ultimate degree of scarring is correlated with initial acne grade and a delay between acne onset and adequate treatment. Among patients with acne scars, 80 to 90% have atrophic scars caused by the loss of collagen (3,4).

A micro-focused ultrasound with visualization MFU-V system (Ultherapy®, Ulthera, Inc., Mesa, AZ) delivers focused ultrasound energy to a specific soft tissue layer under the superficial layers of epidermis. The device is designed and configured to produce small (~1 mm^3) micro-coagulation zones in the mid-to-deep reticular layer of dermis and sub-dermis while sparing overlying papillary dermal and epidermal layers of skin. These micro-coagulation zones initiate a "wound-healing" response, thereby stimulating the formation of new tissue and collagen. The device also incorporates an ultrasound imaging capability to evaluate the skin tissue prior to treatment. This pilot study was performed to test the hypothesis that tissue remodeling stimulated by the treatment with MFU-V will improve the appearance of acne scars.

METHODS

Subjects

This prospective pilot study enrolled 20 healthy adult men and women at two clinical sites.

Key Inclusion Criteria:

- Presence of at least a 5.0 cm^2 area affected by moderate-to-severe atrophic acne scars on the cheeks and/or temples;
- Scars must be predominantly rolling and boxcar type scars with few or no icepick scars present and most should be distensible with tension applied to skin.

Key Exclusion Criteria:

- Active systemic or local skin disease that may affect wound healing;
- Severe solar elastosis;
- Significant scarring, other than acne scars, open wounds or lesions, or active severe or cystic acne in the proposed treatment area;
- Previous cosmetic treatments such as skin tightening, injectable fillers, neurotoxins, ablative or nonablative laser resurfacing or light treatment.

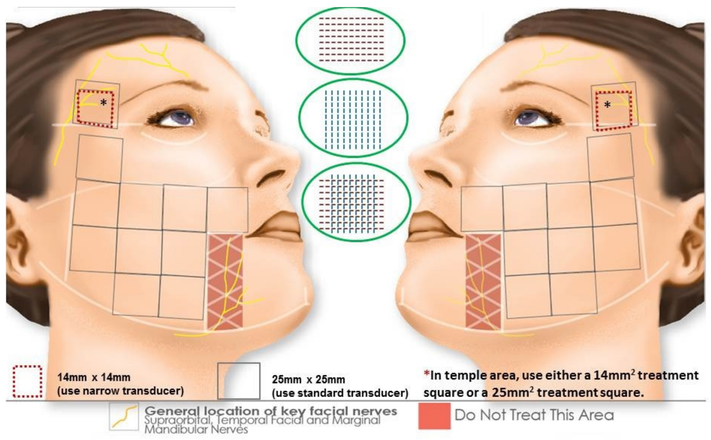
METHODS (CONT)

Procedures

- Pre-treatment medication was limited to ibuprofen 800mg and topical lidocaine 7%/tetracaine 7% cream taken or applied 30-60 minutes prior to treatment.
- Three (3) MFU-V treatments approximately 30 days apart .
- Transducer types: 7 MHz with 3.0mm focal depth and 10 MHz with 1.5mm focal depth.
- 2.5 X 2.5 cm^2 squares covered the desired treatment area marked on the skin; 14 mm x 14 mm treatment squares were used in the temple area (Figure 1).
- Narrow transducers with the same frequency and focal depth were used in the temple area if applicable.
- Thirty (30) treatment lines were delivered to each treatment square using a cross-hatched pattern. (Figure 1).

FIGURE 1.

The treatment area was identified and the number of 2.5 X 2.5 cm square squares required to cover the area was marked on the skin. Thirty treatment lines were delivered in each square using a cross hatch pattern (15 x 15 treatment lines). On the temple area, 14 mm x 14 mm treatment squares were treated using the narrow transducers with the same frequency and focal depth.



OUTCOME MEASURES

Primary Endpoint

Standardized images were obtained at baseline and each follow-up visit using a 2-dimensional digital imaging system. The primary endpoint was improvement in the appearance of acne scars as determined by blinded qualitative comparison of baseline images with those obtained 90 and 180 days after the final treatment using the following scale: Exacerbation (-1), No change (0), 1%-25% improvement (+1), 26%-50% improvement (+2), 51%-75% improvement (+3) and 76%-99% improvement (+4).

Secondary Endpoints

The secondary endpoints were a Physician Scar Improvement Scale (PSIS), Physician Acne Scar Assessment Scale (PASAS) and Physician Global Aesthetic Improvement Scale (PGAIS) 60, 90, and 180 days after the final treatment. Each subject completed a Self-Assessed Scar Improvement Scale (SASIS) and Subject Global Aesthetic Improvement Scale (SGAIS) 60, 90, and 180 days after the final treatment.

Safety

During the procedure, each subject rated their treatment discomfort using a validated 11-point (0-10) Numeric Rating Scale. The mean pain scores were determined for each treated region and each treatment depth. At each subsequent visit, subjects were queried about adverse events and changes in concomitant medications, and the treatment area was visually examined.

RESULTS

The baseline characteristics of enrolled subjects are summarized in Table 1. The available PGAIS and SGAIS scores are shown in Table 2 and PSIS and SAIS scores are shown in Table 3. Among subjects completing the Patient Satisfaction Questionnaire at the 90-day evaluation (*N*=14), all noted improvement (100%) and were Extremely Satisfied (n=3; 21.5%), Satisfied (n=7; 50%) or Slightly Satisfied (n=3; 21.5%) with the results they achieved (overall satisfaction, 93%). One subject (7.1%) was Slightly Dissatisfied. Twelve subjects (86%) would recommend treatment to family and friends.

TABLE 1. Baseline Demographics, *N*=20

	Mean (SD) (Min, Max)
Mean Age	45.0 (11.5) (24, 64)
Mean BMI	24.4 (3.9) (18.6, 35.2)
Gender	***N* (%)**
Female	12 (60)
Male	8 (40)
Race/Ethnicity	***N* (%)**
Asian	4 (20)
American Indian/ Alaskan Native	1 (5)
White	15 (75)
Hispanic or Latino	7 (35)
Fitzpatrick Skin Type	***N* (%)**
I	2 (10)
II	3 (15)
III	9 (45)
IV	4 (20)
V	2 (10)
Acne Scar Satisfaction	***N* (%)**
Slightly Dissatisfied	1 (5)
Dissatisfied	7 (35)
Very Dissatisfied	12 (60)
Age of Acne Scar, years	***N* (%)**
1-5	1 (5)
6-10	1 (5)
11-15	3 (15)
16-20	5 (25)
21-25	1 (5)
26-30	3 (15)
31-35	3 (15)
36-40	2 (10)
41-45	1 (5)

TABLE 2. Physician Global Aesthetic Improvement Scale (PGAIS) and Subject Global Aesthetic Improvement Scale (SGAIS)

	Day 60 (*N*=18)		Day 90 (*N*=14)		Day 180 (*N*=8)	
	PGAIS n (%)	SGAIS n (%)	PGAIS n (%)	SGAIS n (%)	PGAIS n (%)	SGAIS n (%)
Very Much Improved (VMI)	0 (0)	0 (0)	1 (7)	2 (14)	0 (0)	1 (13)
Much Improved (MI)	2 (11)	7 (39)	2 (14)	4 (29)	1 (13)	5 (63)
Improved (I)	16 (89)	11 (61)	11 (79)	7 (50)	7 (88)	1 (13)
No Change	0 (0)	0 (0)	0 (0)	1 (7)	0 (0)	1 (13)
Worse	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
ANY IMPROVEMENT (VMI + MI + I)	18 (100)	18 (100)	14 (100)	13 (93)	8 (100)	7 (88)

TABLE 3. Physician Scar Improvement Scale (PSIS) and Self-Assessed Scar Improvement Scale (SAIS)

	Day 60 (*N*=18)		Day 90 (*N*=14)		Day 180 (*N*=8)	
	PGAIS n (%)	SGAIS n (%)	PGAIS n (%)	SGAIS n (%)	PGAIS n (%)	SGAIS n (%)
Execerbation (-1)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
No Change (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
1-25% Improvement (+1)	5 (28)	8 (44)	6 (43)	6 (43)	4 (50)	3 (37.5)
26-50% Improvement (+2)	12 (67)	5 (28)	7 (50)	2 (14)	3 (37.5)	0 (0)
51-75% Improvement (+3)	1 (6)	4 (22)	1 (7)	5 (36)	1 (12.5)	4 (50)
76-99% Improvement (+4)	0 (0)	1 (6)	0 (0)	1 (7)	0 (0)	1 (12.5)

CONCLUSION

The preliminary results of this pilot study indicate MFU-V is a safe and effective means for improving the appearance of atrophic acne scars. Additional studies are warranted.

REFERENCES

1. Lee IS, Lee AR, Lee H, et al. Psychological distress and attentional bias toward acne lesions in patients with acne. *Psychol Health Med*. 2014;19:680-6.
2. Layton AM, Henderson CA, Cunliffe WJ. A clinical evaluation of acne scarring and its incidence. *Clin Exp Dermatol*.1994;19:303-308.
3. Fabbrocini G, Annunziata MC, D'Arco V, et al. Acne scars: pathogenesis, classification and treatment. *Dermatol Res Pract*. 2010;2010:893080.
4. Goodman G. Post acne scarring: a review. *J Cosmet Laser Ther*. 2003;5:77-95

ACKNOWLEDGEMENT

This study was sponsored by Ulthera, Inc., Mesa, AZ.