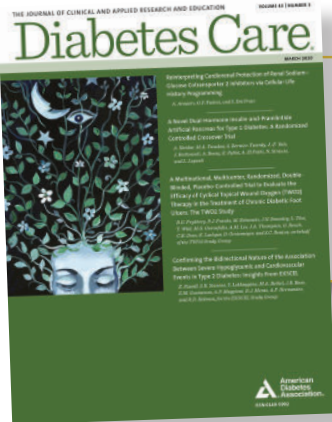


RANDOMIZED CONTROLLED TRIAL



A Multinational Multicenter, Randomized, Double-Blinded Placebo-Controlled Trial to Evaluate the Efficacy of Cyclical Topical Wound Oxygen Therapy (TWO₂) in the Treatment of Chronic Diabetic Foot Ulcers: The TWO₂ Study

Study Received Perfect Cochran Score for Quality of Research

6X

**MORE LIKELY TO HEAL
in 12 weeks**

6X

**LOWER RECURRENCE
rate at 12 months**

RESULTS:

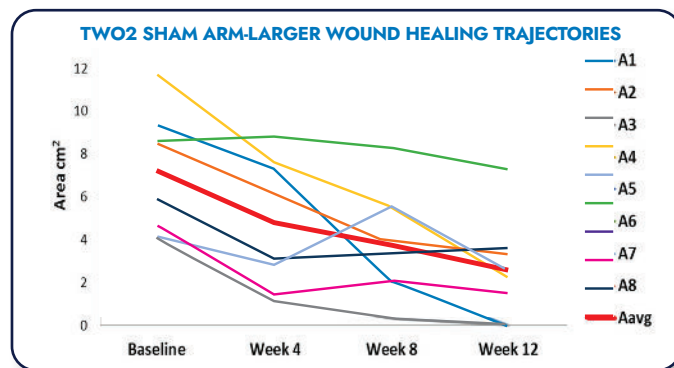
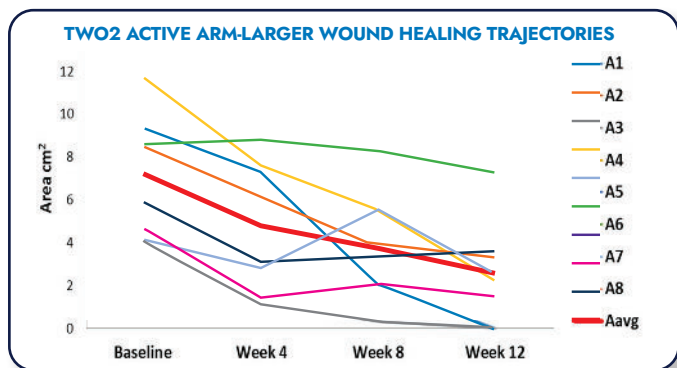
- TWO₂ was shown to be 6 times more likely to heal a DFU at 12 weeks compared to optimal SOC after adjusting for ulcer severity.
- TWO₂ demonstrated more durable healing with a 6 times lower recurrence rate compared to optimal SOC with only 6.7% of Active TWO₂ vs 40% of Sham TWO₂ ulcers recurring at 12 months.
- The wound care–focused QOL index improved for patients whose ulcers healed with Active TWO₂ in all functional domains, with the greatest improvement seen in the Well-Being component that improved 90-fold.



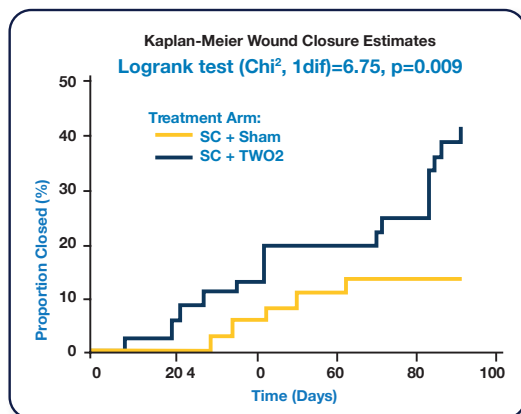
PRIMARY ENDPOINT OF ULCERS 100% HEALED AT 12 WEEKS:

- Active TWO₂ = 41.7% vs Sham TWO₂ = 13.5%
- (Pearson $\chi^2 = 7.27$, $p = 0.007$)
- Odds ratio (OR) of 4.57 (97.8% CI 1.19, 17.57), $p = 0.010$, after adjustment for University of Texas Classification (UTC) ulcer grade
- Odds ratio (OR) increased to 6.00 (97.8% CI 1.44, 24.93), $p = 0.004$

For the patients with larger open ulcers at the end of the 12-week active phase, the mean reduction in ulcer area from baseline was 4.12 cm for Active TWO₂ compared with a 1.34 cm increase for the Sham TWO₂.



RESEARCH DESIGN:



A state-of-the-art, level 1A evidence, Randomized Controlled Trial (RCT) demonstrating the efficacy of multi-modality cyclical pressure Topical Wound Oxygen (TWO₂) therapy in healing and reducing recurrence of Diabetic Foot Ulcers (DFU).

A Group Sequential Design was utilized for the study with three predetermined analyses and hard stopping rules at 73, 146 and 220 on completing a 12-week treatment phase ($p < 0.022$ at each analysis point). All data analysis utilized an Intention-to-treat (ITT) approach.

Patients meeting eligibility criteria were enrolled into a 2-week run-in with defined optimal standard-of-care (SOC) Only hard-to-heal ulcers were included in the study, 25% of run-in patients were excluded prior to randomization due to achieving 30% wound area reduction on SOC alone.

CONCLUSION: This sham-controlled, double-blind RCT demonstrates that, at 12 weeks and 12 months, adjunctive cyclical pressurized TWO₂ therapy was superior in healing chronic DFUs compared with optimal SOC.

TWO₂ therapy was shown to be safe, without complications, and provided more durable healing for those who had wound closure compared to optimal Standard care alone.

Additionally, TWO₂ can be easily administered by the patient at home without the expense and difficulties of daily travel to a specialized center and can also be combined with other advanced wound care modalities.



FIND OUT WHAT TWO₂ CAN DO FOR YOUR PATIENTS.
Visit www.AOTInc.net for more information.

AOTI, Inc. is recognized as a leader in wound care technology around the world.

AOTI is an FDA QSR, ISO 13485 2016 and ACHC accredited company, which demonstrates our commitment to quality in all that we do.



Health
Canada



REFERENCE:

- A Multinational, Multicenter, Randomized, Double-Blinded, Placebo-Controlled Trial to Evaluate the Efficacy of Cyclical Topical Wound Oxygen (TWO₂) Therapy in the Treatment of Chronic Diabetic Foot Ulcers; The TWO₂ Study; *Diabetes Care* 2020;43:616-624 | <https://doi.org/10.2337/dc19-0476>.

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