

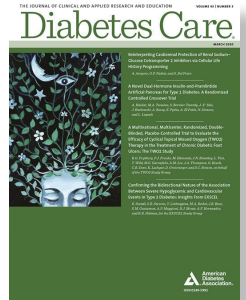


# RANDOMIZED CONTROLLED TRIAL

## A Multinational Multicenter, Randomized, Double-Blinded Placebo-Controlled Trial to Evaluate the Efficacy of Cyclical Topical Wound Oxygen Therapy (TWO<sub>2</sub>) in the Treatment of Chronic Diabetic Foot Ulcers: The TWO<sub>2</sub> Study

Robert G. Frykberg, Peter J. Franks, Michael Edmonds, Jonathan N. Brantley, Luc Teot, Thomas Wild, Matthew G. Garoufalos, Aliza M. Lee, Janette A. Thompson, Gerard Reach, Cyaandi R. Dove, Karim Lachgar, Dirk Grotemeyer, and Sophie C. Renton, on behalf of the TWO<sub>2</sub> Study Group

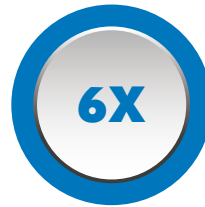
Study received perfect Cochrane Score for Quality of Research



## PROVEN SUSTAINED HEALING



**MORE LIKELY TO HEAL DFUs** in 12 weeks\*



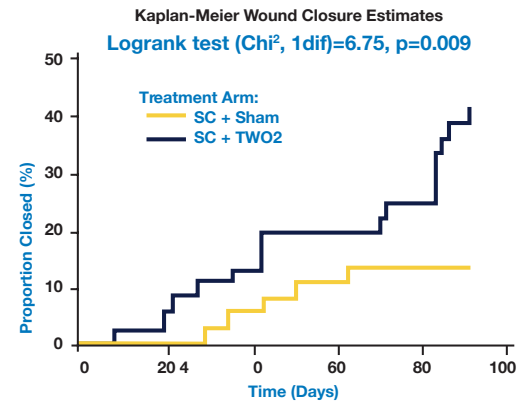
**LOWER RECURRENCE** rate at 12 months\*

\*Compared to Standard of Care (SOC) alone

## RESEARCH DESIGN:

Patients with diabetes and chronic DFUs were randomized (double-blind) to either active TWO<sub>2</sub> therapy or sham control therapy – both in addition to optimal Standard of Care (SOC).

- The study used a group sequential design with three predetermined analyses and hard stopping rules at 73, 146 and 220 patients on completing a 12-week intention-to-treat (ITT) 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 SOC alone.



## RESULTS:

- TWO<sub>2</sub> was shown to be 6 times more likely to heal a DFU at 12 weeks compared to optimal SOC alone, after adjusting for ulcer severity. At 12 months, 56% of Active arm ulcers were closed compared to 27% of the Sham arm ulcers ( $p=0.013$ ).
- TWO<sub>2</sub> demonstrated more durable healing with a 6 times lower recurrence rate compared to optimal SOC alone, with only 6.7% of Active TWO<sub>2</sub>-treated ulcers vs. 40% of Sham TWO<sub>2</sub>-treated ulcers recurring at 12 months.
- The wound-care-focused Quality of Life (QOL) index improved for patients whose ulcers healed with Active TWO<sub>2</sub> treatment in all functional domains, with the greatest improvement seen in the well-being component that improved 90-fold.
- TWO<sub>2</sub> therapy was shown to be safe and without complications.

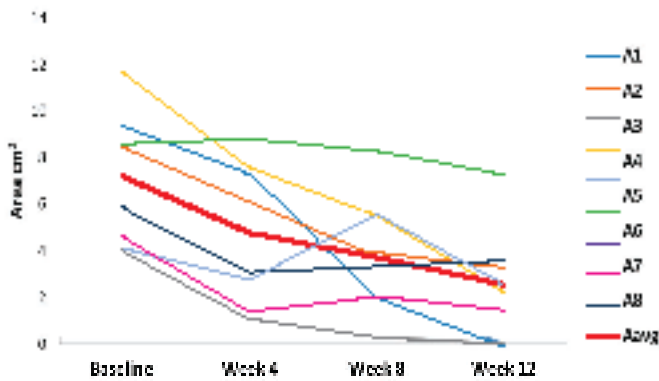
# PRIMARY ENDPOINT OF ULCERS 100% HEALED AT 12 WEEKS

- Active TWO<sub>2</sub> = 41.7% healed vs. Sham TWO<sub>2</sub> = 13.5% healed (Pearson Ch2 = 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

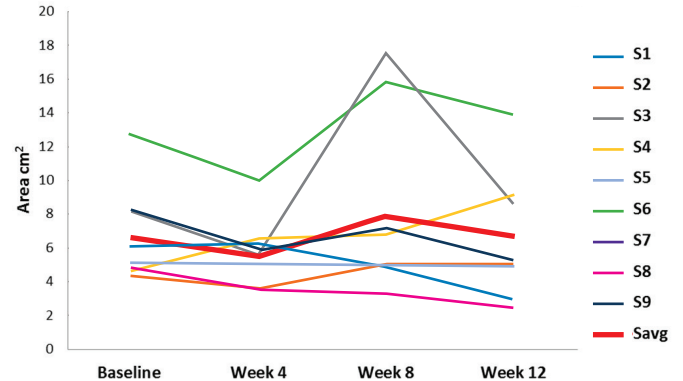


For the patients with larger open ulcers at the end of the 12-week active phase, the mean reduction in ulcer area from baseline was 4.12 cm for Active TWO<sub>2</sub> compared with a 1.34 cm *increase* for the Sham TWO<sub>2</sub>.

## TWO<sub>2</sub> ACTIVE ARM LARGER WOUND HEALING TRAJECTORIES



## TWO<sub>2</sub> SHAM ARM LARGER WOUND HEALING TRAJECTORIES



## CONCLUSION:

**This sham-controlled, double-blinded RCT demonstrates that, at 12 weeks and 12 months, adjunctive cyclical pressurized TWO<sub>2</sub> therapy was superior in healing chronic DFUs compared with optimal SOC alone.**

### REFERENCE:

1. Frykberg R, Franks P, et al. A multinational, multicenter, randomized, double-blinded, placebo-controlled trial to evaluate the efficacy of cyclical Topical Wound Oxygen (TWO<sub>2</sub>) therapy in the treatment of chronic diabetic foot ulcers: the TWO<sub>2</sub> study. *Diabetes Care*, 2020.



Visit [www.AOTInc.net](http://www.AOTInc.net) for more information.



3512 Seagate Way, Suite 100  
Oceanside, CA 92056, USA  
P: 1-760-431-4700 • F: 1-760-683-3063

