



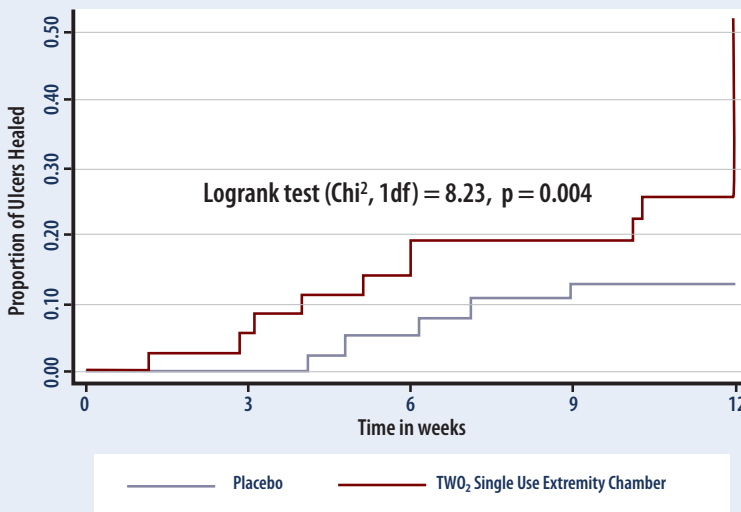
# Breakthrough Randomized Controlled Trial Demonstrating TWO<sub>2</sub> Efficacy in Healing Diabetic Foot Ulcers

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full abstract available online at <https://doi.org/10.2337/db18-43-LB1>



## Kaplan-Meier Healing Estimates



Tier 1A study with the highest level of scientific rigor\*:

- Multi-center
- Multi-national
- Double-blinded
- Placebo-controlled

\*The study protocol included a 2 week run-in of gold standard-of-care (SOC) for all subjects meeting enrollment eligibility criteria that included gold-standard offloading and sharp debridement. This ensured that only those wounds that had truly failed to heal with SOC alone would be randomized into the active phase of the study.

### At 12 weeks the study demonstrated:

- 41.7% of TWO<sub>2</sub> treated ulcers were completely healed compared to just 13.5% of ulcers treated with gold standard-of-care alone. *Pearson  $\chi^2 = 7.2707, p = 0.007$ .*
- TWO<sub>2</sub> showed nearly 4 times the likelihood to completely heal ulcers compared to gold standard-of-care alone: *HR 3.88 (95% CI 1.4, 10.71), p = 0.009.*

***“This breakthrough study unequivocally demonstrates at the highest scientific level the efficacy of Cyclical Pressure Topical Wound Oxygen Therapy in healing Diabetic Foot Ulcers.”***

*-Dr. Robert Frykberg, Chief Principal Investigator*



## Multi-National, Multi-Center, Prospective, 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

### Authors:

ROBERT FRYKBERG, PETER J. FRANKS, MICHAEL E. EDMONDS, JONATHAN N. BRANTLEY, LUC TÉOT, THOMAS WILD, MATTHEW G. GAROUFALIS, ALIZA M. LEE, JANETTE THOMPSON, GERARD REACH, CYAANDI R. DOVE, KARIM LACHGAR and DIRK GROTEMEYER

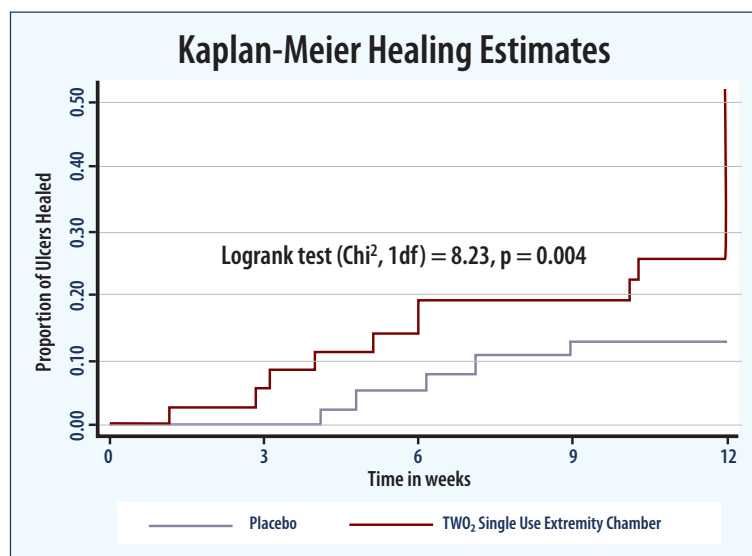
### Author Affiliations:

Phoenix, AZ, London, United Kingdom, Richmond, VA, Montpellier, France, Dessau, Germany, Chicago, IL, Salem, VA, Washington, DC, Bobigny, France, Las Vegas, NV, Eaubonne, France, Luxembourg, Luxembourg

### Abstract:

Non-healing DFUs lead to increased mortality, morbidity & health economic burden. Our RCT (NCT02326337) was undertaken to explore the efficacy of Topical Wound Oxygen (TWO<sub>2</sub>) homecare therapy in healing DFUs that had failed to heal with Standard of Care (SOC) alone. A Group Sequential Design was utilized with 2 interim analyses, requiring a significance of  $p < 0.022$  at each. All subjects meeting the incl/excl criteria were enrolled into a run-in of SOC that included gold-standard offloading and sharp debridement. Only DFUs not on a proven healing trajectory with SOC alone (<30% wound area reduction) were randomized into the active phase of the study, where they were assigned (double blind) to either active, or sham (placebo), TWO<sub>2</sub> device treatment arms. The primary endpoint of the study was ulcers healed at 12 weeks. At the first interim analysis point of 73 subjects, the active TWO<sub>2</sub> arm was shown to be significantly superior to the sham arm (Pearson  $\chi^2 = 7.2707$ ,  $p = 0.007$ ). Multivariable analysis using logistic regression and Cox proportional hazards modelling of the secondary outcome measure of time to heal showed no other covariates achieved significance. The active TWO<sub>2</sub> arm showed nearly 4 times the likelihood to heal DFUs in 12 weeks compared to the sham arm HR 3.88 (95%CI 1.40 to 10.71),  $p = 0.009$

Table 1. Results by randomized group using ITT Analysis				
	Placebo	TWO2	Total	p Value
<b>N</b>	37	36	73	
<b>Gender</b>				
Female	6 (16.2%)	4 (11.1%)	10 (13.7%)	
Male	31 (83.8%)	32 (88.9%)	63 (86.3%)	
<b>UT Scale</b>				
1A	29 (78.4%)	25 (69.4%)	54 (74.0%)	
1B	2 (5.4%)	2 (5.6%)	4 (5.5%)	
1C	1 (2.7%)	0 (0)	1 (1.4%)	
2A	5 (13.5%)	8 (22.2%)	13 (17.8%)	
2B	0 (0)	1 (2.8%)	1 (1.4%)	
<b>Neuropathic</b>				
Yes	29 (78.4%)	28 (77.8%)	57 (78.1%)	
No	8 (21.6%)	8 (22.2%)	16 (21.9%)	
<b>Infection</b>				
Yes	3 (8.1%)	1 (2.8%)	4 (5.5%)	
No	34 (91.9%)	35 (97.2%)	69 (94.5%)	
<b>Age (years)</b>				
mean	61.9	64.6	63.3	0.410
sd	9.5	10.3	9.9	
<b>Wound area (cm<sup>2</sup>)</b>				
mean	3.22	3.02	3.13	0.756
sd	2.54	2.66	2.59	
<b>Duration (days)</b>				
mean	174.6	157.9	166.4	0.625
sd	94	96.3	94.8	
<b>Hgba1c</b>				
mean	8.07	8.43	8.25	0.308
sd	1.5	1.75	1.64	
<b>Ulcers 100% Healed at 12 weeks</b>	5 (13.5%)	15 (41.7%)	20 (27.4%)	<b>0.007</b>



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