

DIABETIC WOUNDS – UPDATED STATISTICAL REPORT 29-JAN-2017

Statistical Methods

The analysis was performed on all participants using intention-to-treat principles. The primary outcome was the relative wound size at 12 weeks compared to baseline. Data of patients that withdrew before the end of the study was carried forward. The success criterion was defined as a difference of more than 50% in the mean %closure between the groups.

Wound sizes are reported as mean±SD or median [interquartile range (IQR)] because of the wide variety in wound sizes or as percent change. Categorical data including the number of patients with percent wound closure of 90% were analyzed using Fisher's exact test. Comparisons of baseline wound size between control and treated were performed by 2-sided exact Mann-Whitney-U (MWU) test, also called 2-sided Wilcoxon test. Comparisons between measurements of wound size, baseline vs endpoint, by group were performed by exact 2-sided Wilcoxon Sign Rank (WSR) test. Direct comparison of improvement by percent wound closure between the groups was performed by 2-sided exact MWU. $P < 0.05$ was considered significant. Analysis was performed using Systat Version 13 with the Exact test module.

Results

Original data presented in Table 3. Data is summarized in Tables 1-2 and Figure 1.

1. Baseline values of wound area were not significantly different between groups (wound size [cm²] at baseline, median[IQR]: Placebo vs B-cure: 4.5[12.0] vs 10.0[20.3], $p=0.92$ by exact Mann-Whitney U test) (**Table 1**).
2. A significant reduction in ulcer size over baseline was observed in the treated group but not in the placebo group (wound size [cm²] before vs post study, median[IQR] – Placebo: 4.5[12.0] vs 3.8[9.6], $p=0.301$; B-cure: 10[20.3] vs 0.2[2.4], $p=0.002$ by exact Wilcoxon Sign Ranks test) (**Table 1**).
3. Direct comparison of %wound closure showed a significant healing effect of laser treatment over the placebo group (%wound closure, median[IQR] – Placebo vs B-cure: 57.3[89.5] vs 97.3[20.0], $p=0.033$ by exact Mann-Whitney U test) (**Table 1**, **Figure 1**).
4. At the end of the study, 7 of 10 patients of the B-cure group had >90% wound closure, whereas only 1 of 9 of the placebo group had this degree of reduction ($p=0.019$ by Fisher Exact Probability Test) (**Table 2**).
5. Success criterion: Success was defined as a difference of 50% or more in the average healing rate (%closure **Table 1**) between the groups:

%Closure in Placebo group = 16%

%Closure in Active group = 84.6%

Difference between the groups = $84.6\% - 16\% = 68.7\% > 50\%$

Figure 1: %Wound Closure – B-Cure vs Placebo

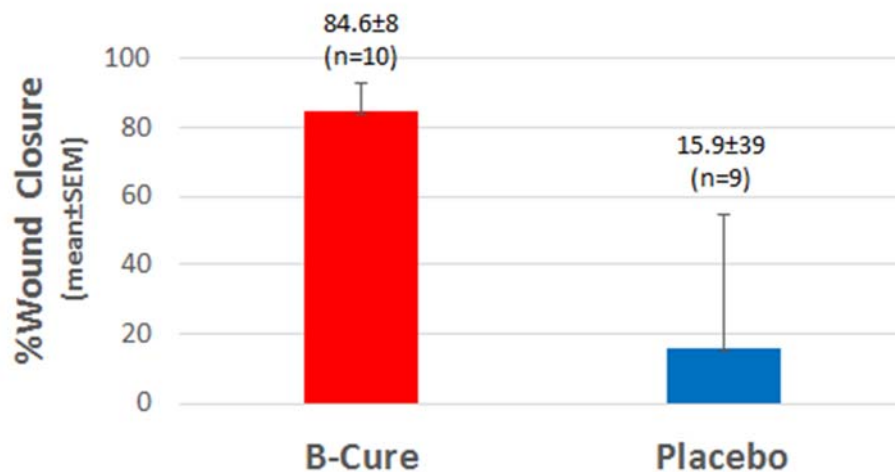


Table 1: Wound Size

	Placebo (n=9)				Active (n=10)			
	Baseline	Endpt.	Change	%Closure	Baseline	Endpt.	Change	%Closure
Mean±SD	11.2±11.1	6.5±7.3	-4.7±12.0	16±117	12.4±9.2	1.5±2.4	-10.9±9.6	84.6±24.4
Median [IQR]	4.5 [12.0]	3.8 [9.6]	-2.8 [8.6]	57.3 [89.5]	10 [20.3]	0.2 [2.4]	-5.8 [19.6]	97.3 [20.0]
Min	3.8	0.0	-32	-275	3.0	0.0	-24.9	31.3
Max	37.5	21	11	100	25	6.0	-2.4	100
Lower 95%CI	2.7	0.9	-13.9	-74.0	5.8	-0.2	-17.8	67.1
Upper 95% CI	19.8	12.0	4.5	67.1	19.0	3.2	-4.1	102.1

- Comparing baseline values – Placebo vs Active: p=0.92 by 2-sided exact Mann-Whitney U test
- Baseline vs Endpoint - Placebo: p=0.301 by 2-sided exact Wilcoxon Sign Ranks test
- Baseline vs Endpoint - Active: p=0.002 by 2-sided exact Wilcoxon Sign Ranks test
- Comparing %Closure – Placebo vs Active: p=0.033 by 2-sided exact Mann-Whitney U test

Table 2: improvement > 90%

Improvement	Placebo	Active	Total
Less than 90%	8 (42.1%)	3 (15.8%)	11 (57.9%)
More than 90%	1 (5.3%)	7 (36.8%)	8 (42.1%)
Total	9 (47.4%)	10 (52.6%)	19 (100%)

- Placebo vs Active baseline: P=0.019 by Fisher Exact Probability Test

Table 3: Original Data

PN	Group	Area at baseline [cm ²]	Area at termination [cm ²]	Absolute change [cm ²]	%Closure	Time [weeks]
1	Active	3	0	-3	100	.
3	Active	24	0	-24	100	.
4	Active	3	0.6	-2.4	80	8
7	Active	6	0.3	-5.7	95	10
8	Active	25	0.1	-24.9	99.6	12
11	Active	8	5.5	-2.5	31.3	12
13	Active	14.3	0	-14.3	100	8
14	Active	3.8	0	-3.8	100	10
16	Active	25	2.4	-22.6	90.4	12
19	Active	12	6	-6	50	.
5	Placebo	4	3.8	-0.3	6.3	4
6	Placebo	4.5	0	-4.5	100	10
9	Placebo	4	15	11	-275	8
10	Placebo	4	1.2	-2.8	70	12
12	Placebo	11.3	1.2	-10.1	89.3	12
15	Placebo	16	21	5	-31.3	8
17	Placebo	37.5	5.5	-32	85.3	12
18	Placebo	16	9.3	-6.7	41.6	12
20	Placebo	3.8	1.6	-2.1	57.3	.