A Prospective, Randomized, Controlled, Multi-Center Comparative Effectiveness Study of Healing Using Dehydrated Human Amnion/Chorion Membrane (dHACM) Allograft, Bioengineered Skin Substitute, or Standard of Care for Treatment of Chronic Diabetic Lower Extremity Ulcers

Charles M. Zelen, DPM, FACFAS; Thomas E. Sereno, MD, FACS; Lisa Gould, MD, PhD; Jennifer Keller, DPM; Marissa J. Carter, PhD, MA; William W. Li, MD

Background and Statement of Purpose

In 2012, more than 22.3 million people in the United States had a diagnosis of diabetes, with an attendant cost of approximately $245 billion, including $157 billion in direct medical cost and $69 billion in lost productivity.1

Approximately 25% of people with diabetes will develop a lower extremity ulcer over their lifetime.2

Diabetic ulcers precede 85% of lower-extremity amputations, and it is estimated that up to 85% of these amputations may be preventable.3

The desired goal of diabetic ulcer treatment is to promote rapid and complete healing in order to reduce the risk for infection and its limb- or even life-threatening complications.

The Wound Healing Society guidelines recommend consideration of advanced wound therapies if a diabetic ulcer does not reduce in size by 40% or more after 4 weeks of standard therapy.4

Randomized, controlled clinical trials have demonstrated that bioengineered skin substitutes (BSS) and dehydrated human amnion/chorion membrane (dHACM) both promote wound closure, resulting in more frequent and rapid healing of chronic diabetic ulcers when compared to standard therapy, yet there is little data available with which to assess differences in clinical and cost effectiveness between commercially available products.5,6

Rationale

A retrospective analysis of data collected in separate randomized trials suggests that dHACM may be superior to several products in promoting rapid healing.7

Study Design and Statement of Purpose

The purpose of this prospective, randomized, controlled, parallel group, multi-center clinical trial was to compare healing effectiveness of chronic lower extremity diabetic ulcers treated with either weekly application of BSS, dHACM, or standard wound care (SOC) with collagen-alginate dressing. The study was conducted at three outpatient centers in the state of Virginia (USA) and was approved by Western IRB (IRB) and pre-registered in ClinicalTrials.gov (NCT01921491).

Methodology

Type 1 or Type 2 diabetic patients presenting for care of a lower extremity ulcer.

Exclusion criteria included: patients under 18 years of age, patients with an infection at the ulcer site, patients with a prior history of non-healing ulcers, patients with severe arterial disease, patients with a history of allergy to the study product, and patients with a physical condition that contraindicated the use of the study product.


Inclusion/exclusion criteria were used to determine patients eligible to enter the two week study run-in period prior to study enrollment and randomization.

Type 1 or Type 2 diabetic patients presenting for care of a lower extremity ulcer.

Exclusion criteria included: patients under 18 years of age, patients with an infection at the ulcer site, patients with a prior history of non-healing ulcers, patients with severe arterial disease, patients with a history of allergy to the study product, and patients with a physical condition that contraindicated the use of the study product.

Study outcome was defined as complete wound closure within 6 weeks.4

Secondary outcomes included percent change in wound area per week, velocity of wound closure, and a calculation of amount used and cost of dHACM or BSS.

Data Analysis

The null hypothesis was that the proportion of wounds that achieve complete healing within 6 weeks is the same for dHACM or BSS treated subjects.

PARAMETRIC AND NON-PARAMETRIC TESTS WERE USED AS APPROPRIATE.

Conclusions

Wounds treated with dHACM were more likely to heal completely and reduce in size more rapidly, with less graft material used and at a lower cost compared to wounds treated with BSS, indicating that dHACM allografts are more clinically and cost effective than BSS for the treatment of chronic lower extremity ulcer patients with diabetes.

This is the first multi-center randomized comparative effectiveness study examining side by side the performance, outcomes, and utilization of two advanced wound care products as a treatment for chronic lower extremity diabetic ulcers.

References

BSS = Apligraf®. Apligraf® is a registered trademark of Novartis

dHACM = EpiFix®. EpiFix® is a registered trademark of MiMedx Group, Inc., Marietta, GA

Study sponsored by: MiMedx®, Marietta, GA

SAWC Spring Meeting, April 29-May 3, 2015 in San Antonio, TX

Poster C-09

Figure 1. Primary study outcome - rates of complete wound healing at 4 and 6 weeks.

Figure 2. Percent wound size reduction per week.

Figure 3. Product usage.

Figure 4. Costs of grafts.

Figure 5. Total cost of grafts applied in study.

Table 1. Clinical characteristics at study enrollment (all p>0.05).

<table>
<thead>
<tr>
<th></th>
<th>Total Care (n=20)</th>
<th>Standard Care (n=20)</th>
<th>BSS (n=20)</th>
<th>dHACM (n=20)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean HbA1c (SD)</td>
<td>8.0 (1.9)</td>
<td>7.4 (1.5)</td>
<td>8.0 (1.8)</td>
<td>8.0 (1.8)</td>
</tr>
<tr>
<td>Mean Age, in years (SD)</td>
<td>65.2 (11.7)</td>
<td>63.2 (13.0)</td>
<td>62.2 (12.8)</td>
<td>62.2 (12.8)</td>
</tr>
<tr>
<td>Mean Duration of Index Ulcer in weeks (SD)</td>
<td>15.6 (12.7)</td>
<td>11.3 (5.0)</td>
<td>9.6 (5.0)</td>
<td>9.6 (5.0)</td>
</tr>
<tr>
<td>Median (Min, Max)</td>
<td>13 (6, 54)</td>
<td>11 (5, 54)</td>
<td>9 (6, 52)</td>
<td>9 (6, 52)</td>
</tr>
<tr>
<td>HbA1c ≥ 9% (n, %)</td>
<td>11 (55.0%)</td>
<td>11 (55.0%)</td>
<td>9 (45.0%)</td>
<td>9 (45.0%)</td>
</tr>
<tr>
<td>Caucasian (n, %)</td>
<td>18 (90.0%)</td>
<td>19 (95.0%)</td>
<td>17 (85.0%)</td>
<td>17 (85.0%)</td>
</tr>
<tr>
<td>Median BMI (Min, Max)</td>
<td>32.3 (23.5)</td>
<td>32.9 (25.0)</td>
<td>31.2 (23.6)</td>
<td>31.2 (23.6)</td>
</tr>
</tbody>
</table>

Results

Clinical characteristics were similar between the study groups (Table 1).

The primary study outcome is presented in Figure 1, showing significantly higher rates of wound healing at 4 and 6 weeks in patients receiving dHACM.

Mean HbA1c in those wounds treated with dHACM had more rapid healing compared to wounds treated with BSS.

Mean number of grafts and amount of graft material used is shown in Figure 2. Descriptive statistics were used to compare groups. Without a correction for multiple comparisons the results are not statistically significant (all p>0.05).

A retrospective analysis of data collected in separate randomized trials suggests that dHACM may be superior to several products in promoting rapid healing.7

Study supported by: MiMedx®, Marietta, GA.