Evaluating the efficacy of treatment for venous leg ulcers (VLU) is often difficult given the protracted study duration required before an endpoint of complete wound epithelialization can be achieved, thus intermediate outcomes may be necessary for more rapid evaluation of treatment safety and potential benefits. In patients receiving standard wound care it has been demonstrated that the percentage change in wound area at the fourth week of care can serve as an important surrogate measure of rapid evaluation of treatment status at 4 weeks, which may have confounded patient outcomes, these results confirm that the surrogate measure used in our initial study is a viable predictor of ultimate VLU healing.

We conducted a retrospective follow-up study of patients previously enrolled in an IRB approved multi-center RCT which evaluated the use of dHACM for the treatment of VLU.

We included 32 patients with complete healing during the initial study. Of these, 20 (45.4%) had reduced wound size of at least 40% and 24 (54.5%) <40% during the initial study. After complete healing occurred in 16/20 (80%) and 8/24 (33.3%), p=0.0027. Correct correlation between wound healing status at 4 weeks and complete healing occurred after a mean of 46 (n=16) or 103.6 (n=18) days for those with or without healing respectively. (Figure 2) Correct correlation between healing status at 4 weeks and complete healing within 24 weeks occurred in 32 of the 44 patients (72.7%). Although treatments received after the initial study period may have confounded patient outcomes, these results confirm that the surrogate measure used in our initial study is a viable predictor of ultimate VLU healing.

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Table 1. Comparison of clinical characteristics for patients with and without correct correlation of wound status at 4 weeks and complete healing within 24 weeks

<table>
<thead>
<tr>
<th></th>
<th>With Correct Correlation</th>
<th>Without Correct Correlation</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>62.9 ± 10.3</td>
<td>63.8 ± 11.7</td>
<td>0.87</td>
</tr>
<tr>
<td>Male gender</td>
<td>17 (35%)</td>
<td>31 (65%)</td>
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<tr>
<td>Non-Caucasian</td>
<td>8 (16%)</td>
<td>25 (53%)</td>
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<td>Body-mass index</td>
<td>38.0 ± 13.4</td>
<td>37.6 ± 12.9</td>
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<td>Wound size at end of RCT (cm²)</td>
<td>35.7 (17.3, 80.7)</td>
<td>37.5 (26.3, 51.2)</td>
<td>0.35</td>
</tr>
<tr>
<td>Duration of wound at RCT enrollment (weeks)</td>
<td>3.1 ± 1.8</td>
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Conclusions

Intermediate endpoints that can predict the ultimate outcome of treatment are beneficial for researchers of new wound healing products or techniques allowing for more rapid evaluation of potentially promising innovations.

The current analysis validates the intermediate outcome used in the initial RCT which showed that VLU treated with dHACM had greater reduction in wound size within the first 4 weeks of treatment than VLU treated with compression alone.

References


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

Poster # CR - 031

Abstract

The current analysis validates the intermediate outcome used in the initial RCT which showed that VLU treated with dHACM had greater reduction in wound size within the first 4 weeks of treatment than VLU treated with compression alone.

We conducted a retrospective follow-up study of patients previously enrolled in an IRB approved multi-center RCT which evaluated the use of dHACM for the treatment of VLU.

We included records from 55 patients at 5 study sites were reviewed. Forty-seven without complete healing during the initial study were eligible. Three patients were lost to follow-up, yielding 44 evaluable records (80%). Of these 44, 20 (45.4%) had reduced wound size of at least 40% and 24 (54.5%) <40% during the initial study. After complete healing occurred in 16/20 (80%) and 8/24 (33.3%), p=0.0027. Correct correlation between healing status at 4 weeks and complete healing occurred after a mean of 46 (n=16) or 103.6 (n=18) days for those with or without healing respectively. (Figure 2) Correct correlation between healing status at 4 weeks and complete healing within 24 weeks occurred in 32 of the 44 patients (72.7%). Although treatments received after the initial study period may have confounded patient outcomes, these results confirm that the surrogate measure used in our initial study is a viable predictor of ultimate VLU healing.

Correct correlation between wound healing status at 4 weeks (reduction in size by ≥40% yes or no) and healing within 24 weeks was determined. Patient characteristics were compared between those with and without correct correlation using parametric (Fisher’s Exact test, student’s t test) and non-parametric (Mann-Whitney U) statistics as necessary.

Evaluating the efficacy of treatment for venous leg ulcers (VLU) is associated with considerable morbidity and impaired quality of life with healing being a long and painful process.1,2 Annually in the United States, the economic burden to payers for healthcare costs related to VLU is $14.9 billion.3 Evaluating the efficacy of treatment for VLU is often difficult given the protracted study duration required before an endpoint of complete wound epithelialization can be achieved, thus intermediate outcomes may be necessary for more rapid evaluation of treatment safety and potential benefits. In patients receiving standard wound care it has been demonstrated that the percentage change in wound area at the fourth week of care can serve as an important surrogate marker of complete wound healing within 24 weeks of care.1,3 A proprietary PURION® Process of advanced tissue stabilization and preservation has allowed researchers of new wound healing products or techniques allowing for more rapid evaluation of potentially promising innovations.

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In that study (n=84), VLU treated with dHACM had a significant improvement in healing at 4 weeks compared to multi-layer compression therapy alone with 62% of wounds treated with dHACM and 32% of controls demonstrating a greater than 40% wound closure after 4 weeks (p=0.005).

Purpose

Our purpose is to evaluate long term outcomes of patients enrolled in the prior study and validate our use of a surrogate outcome.

Results

The current follow-up analysis validates the intermediate outcome used in the initial RCT which showed that VLU treated with dHACM had greater reduction in wound size within the first 4 weeks of treatment than VLU treated with compression alone.

Of the 44 patients, 20 (45.4%) had reduced wound size of at least 40% and 24 (54.5%) <40% during the initial study.

Correct correlation between healing status at 4 weeks and complete healing, occurred in 32 of the 44 patients (72.7%).

Wounds with reduction in size by at least 40% within the first 4 weeks of treatment were more likely to be completely healed within 24 weeks [16/20 (80%)] compared with those that did not have complete healing the first 4 weeks [8/24 (33.3%)], p=0.0027. (Figure 1)

Complete healing occurred after a mean of 46 (n=16) or 103.6 (n=18) days for those with or without healing respectively. (Figure 2) Complete healing occurred after a mean of 46 (n=16) or 103.6 (n=18) days for those with or without healing respectively. (Figure 2)

Comparison of clinical characteristics for patients with and without correct correlation of wound status at 4 weeks and complete healing within 24 weeks are presented in Table 1.

Conclusions

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Dye penetration mean ± standard deviation, median (minimum, maximum) or number (percent) as indicated. RCT = randomized controlled trial.