Comparative Effectiveness of a Bilayered Living Cellular Construct and a Split Thickness Skin Graft for the Treatment of Venous Leg Ulcers

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Introduction

- Venous leg ulcers (VLUs) are the most common type of chronic leg wound, with 1% of adults expected to develop a VLU at some point in their lives.[1-3]
- VLUs are estimated to affect 0.05% to 1.52% of the US population.[4]
- VLU patients carry ~50% higher Medicare costs and >2x higher private insurance costs.[4]
- The economic burden of VLU's in the US is estimated at $14.9 billion annually[5].
- A bilayered living cellular construct, BLCC[(a)], is approved by the FDA for the treatment of VLUs and diabetic foot ulcers.
- BLCC is a bioengineered living skin substitute that contains living keratinocytes and fibroblasts that produce growth factors and cytokines.
- Skin substitutes eliminate the need for a donor site while reducing risk of infection, mortality, and morbidity.[6]
- Split thickness skin grafts (STSG) are widely used in the treatment of chronic wounds and regarded as the gold standard for treatment.[7,8]
- STSG incorporate the epidermis and a portion of the dermis and are indicated when simpler methods of wound closer do not suffice (secondary intention, primary closure, or negative pressure wound therapy).[9]

[(a)]Apligraf, Organogenesis Inc., Canton, MA

Objective

- Using real world evidence (RWE) from a deidentified, wound-specific, electronic medical record database (WoundExpert® Net Health®, PA, US), we compared the effectiveness of BLCC to STSG for the treatment of venous leg ulcers (VLUs) in a retrospective comparative effectiveness assessment (CEA) study.

*De-identified patient data released to Organogenesis, Inc. was consistent with the terms and conditions of Net Health's participating client contracts and the requirements of the Health Insurance Portability and Accountability Act of 1996 (HIPAA). Net Health was not involved in any way in the analysis, interpretation, or reporting of the data.

Methods

Study Population

- Data from 8,699 refractory VLUs, partial and full thickness, with surface areas between 1 and 20 cm^2 in size, treated between September 2011 and September 2021 at 477 wound care facilities across the US were analyzed.
- Exclusion criteria included lack of follow-up visits and lack of baseline wound measurements.
- VLUs between the knee and ankle joint that occurred in the presence of venous disease were included.
- All treated VLUs that closed by <40% within 28 days of the first treatment application were included.

Statistical Analyses

- Unadjusted time to event analyses were performed by the method of Kaplan-Meier (K-M), and adjusted analyses were performed using Cox's proportional hazards regression (Cox).

Summary of Results

- Patient baseline demographics and wound characteristics were comparable between groups.
- BLCC treatment significantly reduced the median time to wound closure by 18%, achieving healing 3.3 weeks sooner (14.7 vs. 18 weeks; p=0.0002). (Figure 1)
- Cox derived estimates of wound closure for BLCC (8,124 wounds) was significantly greater than STSG (575 wounds) at week 12 (43 vs. 37%), 24 (65 vs. 57%), and 36 (75 vs. 67%); (p=0.0002). (Figure 2)
- Cox regression analysis adjusting for multiple covariates including ulcer area, depth, and duration showed that treatment with BLCC increased the probability of healing by 24% compared with STSG throughout the period of observation. The Hazard Ratio (HR) = 1.24 [95% CI (1.11, 1.39)]; p=0.0002.

Figure 1. Median time to Wound Closure

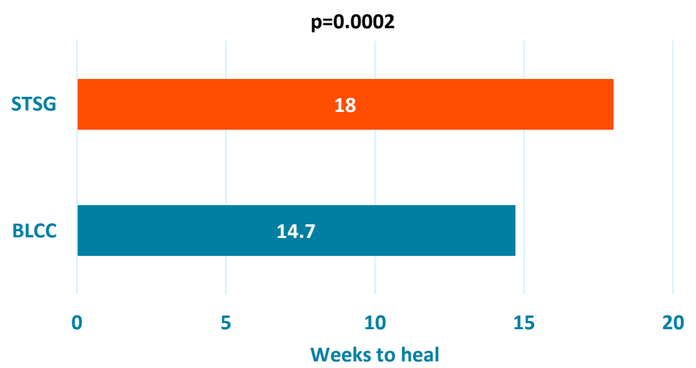
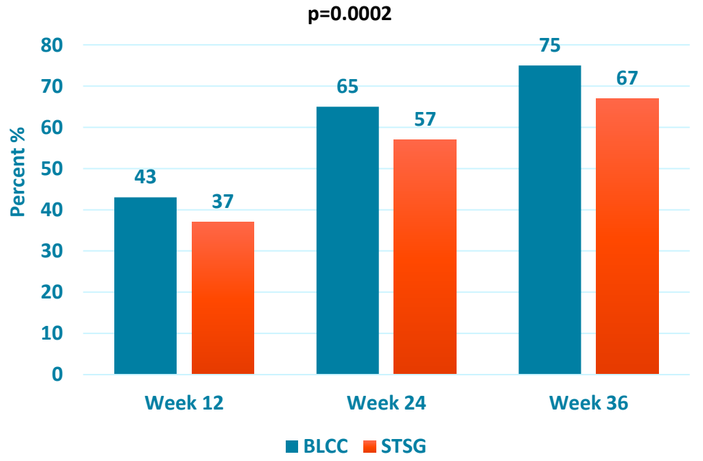


Figure 2. Percent Wounds Achieving Wound Closure



Conclusions

- RWE demonstrated that BLCC significantly improved VLU healing compared to STSG.
- Evidence based treatment algorithms for patients with refractory VLUs are needed to provide guidance to clinicians and payers.

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