A Prospective Multicenter Randomized Controlled Open-label Trial to Assess the Clinical Effectiveness of a Decellularized Full-thickness Placental Membrane in Patients with Diabetic Foot Ulcers: Preliminary Results

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INTRODUCTION

Chronic wounds, such as diabetic foot ulcers (DFUs), impose substantial treatment and cost burdens on global healthcare systems, representing an estimated 1 to 4% of total healthcare spending in developed countries.[1] Placental membrane allografts obtained from consenting live-birth donors have emerged as an important treatment option for such chronic wounds.[2] The placenta consists of the amnion and chorion, which includes the trophoblast layer. For ease of cleaning and processing, these layers are often separated. They may or may not then be relaminated to produce an allograft that is amnion-only, amnion-chorion or other amnion-chorion combinations, such as amnion-chorion-amnion. This method of processing can adversely impact native growth factors and make the allograft difficult to handle and use due to the thinness of the graft, depending on the placental layers retained.[3]

To create a thick, easy-to-handle placental allograft while retaining growth factors, the first minimally manipulated, intact full-thickness placental membrane (FTPM) to include a decellularized trophoblast layer was developed (Figures 1A and B). Unlike other placental membrane allografts, the layers in FTPM are never separated during processing. FTPM undergoes processing with a validated proprietary decellularization technology (Matracell®; LifeNet Health®, Virginia Beach VA) resulting in at least 90% donor DNA removal,[4] indicative of thorough decellularization (Figures 1C and D). Further, in subsequent analyses, the trophoblast layer was found to retain more than 50% of 4 out of 5 biological factors tested.[4] This advance in placental membrane processing results in an FTPM allograft that minimizes the potential for patient inflammatory reaction, offers superior handling with four-times the thickness of other placental allografts, creates a better barrier to bacterial ingress, and provides a porous, biohospitable scaffold for host-cell migration, attachment, and neovascularization.

Here, we present preliminary results from an ongoing multicenter study that assesses the clinical effectiveness of this FTPM applied to DFUs.

METHODS

The protocol for this study was reviewed and approved by WCG IRB (Puyallup WA; IRB Tracking No. 20215452). Following screening and 30-day run-in to verify wound status and stability in this ongoing study, up to 120 patients who meet all inclusion criteria, no exclusion criteria, and who provide informed consent, are randomized at a 1:1 ratio to receive either FTPM or conventional care (CC; ie, moist-wound therapy). Baseline evaluations are conducted before and after thorough debridement of the wound bed. Treatment is then applied according to the patient's study arm and the treated wound is dressed until the next weekly study visit. Subsequent re-evaluation visits occur each week until 100% re-epithelialization is observed or up to 12 weeks following baseline treatment (ie, the treatment phase), whichever comes first. In the FTPM group, additional applications may be administered with or without additional debridement at the investigator's discretion at Weeks 1 through 11, or additional debridement may be performed in the CC group. Patients are required to off-load as appropriate with a boot, surgical shoe, or other device for the duration of the treatment phase.

If 100% re-epithelialization is observed at any time during the treatment phase, the patient returns to the site for 2 weeks following the initial observation for confirmation. If the wound remains closed upon the third weekly observation (defined as wound closure), the patient undergoes a termination visit and enters the follow-up phase, consisting of telephone visits at 2, 4, and 6 months. If 100% re-epithelialization is not observed by Week 12, the patient's participation in the study ends with a termination visit.

The primary endpoint of this preliminary analysis was the proportion of wounds closed by Week 12 in each group. Secondary endpoints included mean percent wound area reduction at Weeks 1 through 12 and mean number of FTPM applications.

RESULTS

In this preliminary analysis, 25 patients had completed the treatment phase (FTPM = 14 patients, CC = 11 patients). Mean (SEM) patient ages were similar between groups (FTPM = 62.3 [2.7] years, CC = 56.2 [3.3] years; p = 0.1636). The proportion of wounds closed at Week 12 was significantly higher in the FTPM group (64.3%) vs the CC group (27.3%; p < 0.0001; Figure 2A). Mean percent wound area reduction trended higher in the FTPM group beginning at Week 3, reaching significance at Weeks 9 (p = 0.0157), 10 (p = 0.0039), and 11 (p = 0.0348; Figure 2B). The mean (SEM) number of FTPM applications was 8.4 (1.1). Representative photographs depict a 61-year-old male patient presenting with a chronic (4 months) dorsal Wagner 2 DFU measuring 13.7 cm^2 (Figure 3A). Previous failed treatments included compression and bioengineered tissue/skin substitutes. The wound was considered closed by Week 10 following 6 applications of FTPM (Figure 3B).

REFERENCES

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CONCLUSIONS

Preliminary results from this ongoing study suggest that FTPM as a protective barrier provides better support for wound closure and wound area reduction when compared to CC in the treatment of chronic DFUs.

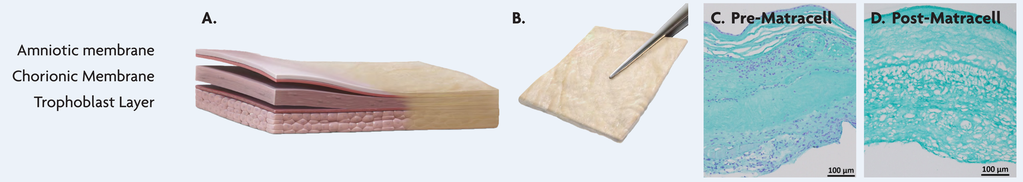

Figure 1. (A) The decellularized full-thickness placental membrane (FTPM) retains all 3 major structural layers, including the amniotic and chorionic membranes and trophoblast layer. (B) Representative photograph of FTPM in its final form. (C) Feulgen staining identified intact nuclei in FTPM prior to Matracell processing, (D) which were at least 90% removed following processing.[4]

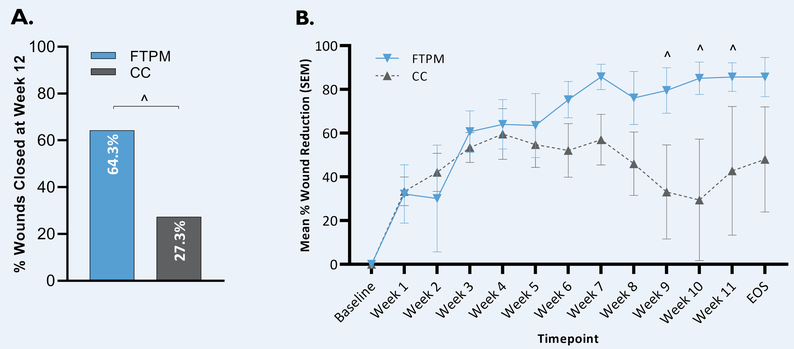

Figure 2. (A) In this preliminary analysis (N = 25), the proportion of wounds closed at Week 12 was significantly higher in the FTPM group (64.3%) vs the CC group (27.3%; p < 0.0001). (B) Mean percent wound area reduction trended higher in the FTPM group beginning at Week 3, reaching significance at Weeks 9 (p = 0.0157), 10 (p = 0.0039), and 11 (p = 0.0348).

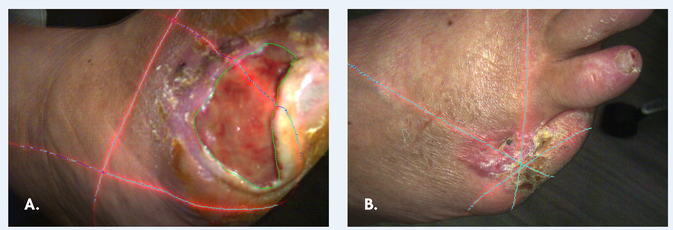

Figure 3. Representative photographs of a 61-year-old male patient (A) presenting with a chronic (4 months) dorsal Wagner 2 DFU measuring 13.7 cm^2. Previous failed treatments included compression and bioengineered tissue/skin substitutes. (B) The wound was considered closed by Week 10 following 6 applications of FTPM.

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