Adaptive Design Clinical Trial: Dermacyte® Amniotic Wound Care Liquid for the Treatment of Non-Healing Venous Stasis Ulcers (VSU)

T. Christopher Broderick, CTBS, RAC[1,2]

[1]Merakris Therapeutics, Inc., Research Triangle Park, NC; [2]University of North Carolina State, Golden LEAF Biomanufacturing Training and Education Center, Raleigh, NC

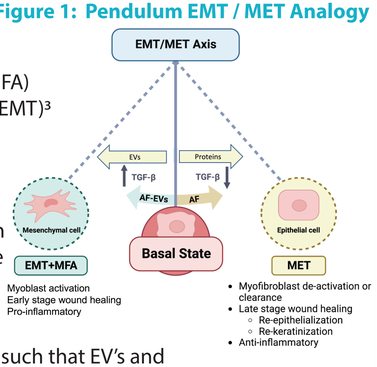
Background and Rationale

- Dermacyte® Amniotic Wound Care Liquid (Dermacyte Liquid) is full term amniotic fluid, clarified of cells and debris, and formulated to retain native insoluble exosome particles and soluble proteins
- US FDA issued Final Guidance in November 2017 that required amniotic fluid regenerative medicine products used in wound healing to be regulated under Section 351 of the PHS Act[1]
- Under the Guidance, FDA conveyed that by May 2021, all commercial amniotic fluid formulations were to be withdrawn from the market and subject to an approved Biological License Application[1]
- Wound healing safety and efficacy of Dermacyte Liquid was reported while marketed prior to FDA Guidance, and a Phase II adaptive design clinical trial to obtain controlled data was undertaken in May 2021[2]

Clinical Rationale

- EVs in Dermacyte Liquid have been shown to be necessary and sufficient for cell migration, and additionally stimulate myofibroblast activation (MFA) and induce epithelial to mesenchymal transition (EMT)[3]
- Required biological events for successful early-stage wound healing include MFA and EMT, which must resolve for the wound to progress to later stages of wound healing. Soluble proteins in Dermacyte Liquid have been shown to contribute to resolving EMT/MFA via mesenchymal to epithelial transition (MET)[3]
- Thus, the mechanism of action(s) are cumulative, such that EV's and proteins in Dermacyte Liquid collectively support wound healing by modulating EMT and MET (Figure 1)[4]

Figure 1: Pendulum EMT / MET Analogy



Target Indication

- For use in the treatment of non-infected VSU that fail to show improvement after a minimum of 4 weeks of standard wound therapy

Primary Objective

- Evaluate the safety and tolerability of Dermacyte Liquid for the treatment of a lower limb extremity VSU

Secondary Objectives

- Complete wound closure by Week 12 (confirmed by 2 visits 2 weeks apart)
- Assess percent reduction of surface area from Baseline to Weeks 4, 8 and 12
- Measure the change in ulcer-related pain from Baseline to Week 12
- Measure the Quality of Life change from Baseline to Week 12

Two Part, Adaptive Study Design

Part 1, n=10
Randomized 1:1 to weekly or bi-weekly injection.

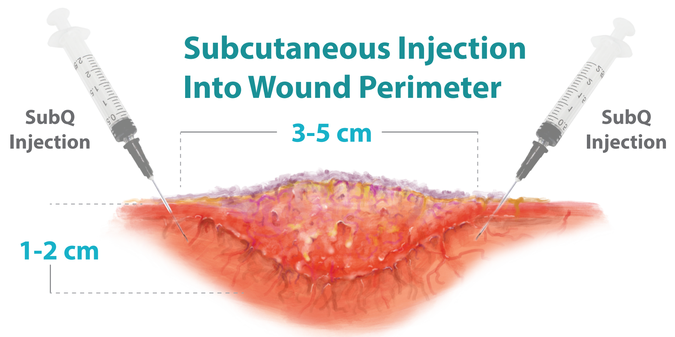
Part 2, n=30
Randomized 1:1 to active or placebo

Dosage Based on Ulcer Size

Small, 1.0 – 12.5 cm²
1.0 mL Dermacyte Liquid local injection

Large, 12.5 – 25.0 cm²
2.0 mL Dermacyte Liquid local injection

Route of Administration



Baseline & Follow Up

Surface Area: Baseline, Weeks 4, 8, and 12
Quality of Life Measures: Baseline and Week 12 (VAS, SF-36, DLQI, and Wound-QoL)

Inclusion Criteria

1. Males and female subjects aged 18 to 75 years at Screening
2. Subjects must have a full thickness ulcer that meets the following:
   A. Ulcer surface area (SA) > 1 cm² and < 25 cm²
   B. Ulcer SA has not changed by 25% within 14 days of Baseline
   C. Ulcer depth > 0.2 cm at the deepest point of the wound
3. Subjects must have received > 28 days of standard, conventional wound therapy with a high-compression prior to the Baseline visit
4. Subjects must have undergone venous hemodynamic correction
5. Adequate circulation to the affected extremity as demonstrated by ankle-brachial index >= 0.8 and <=1.2 triphasic or biphasic Doppler arterial waveforms
6. Must have venous reflux disease with physiological reflux > 500 milliseconds for superficial veins and > 1.0 seconds for deep veins
7. Agree to follow the specified precautions to avoid pregnancy

Exclusion Criteria

1. Subject must not be receiving topical antimicrobials and ulcer must not be infected as determined by clinical assessment rather than culture
2. Ulcer must not have exposed bone, tendon, or ligament
3. Subject must not have another ulcer within 3 cm from the ulcer receiving tx
4. Female subjects who are pregnant, lactating, or planning pregnancy
5. Subjects that received a skin graft substitute within 30 days prior to Baseline
6. Subjects receiving oral, systemically administered, or lower extremity injectable corticosteroid therapy within 60 days prior to Baseline
7. Subjects with angiographic or clinical signs of peripheral arterial disease or congestive heart failure with most previous echocardiogram demonstrating an ejection fraction less than 35%
8. Subjects with underlying osteomyelitis
9. An active infection/condition that would interfere with study assessments
10. Subjects with an HbA1c > 7.0%
11. Subjects with any other disease that would limit ambulation
12. History of alcohol or illicit drug abuse within 12 months of Baseline which, in the Investigator's opinion, would make inappropriate for enrollment

References

1. Center for Biologics Evaluation and Research; Center for Devices and Radiological Health. Regulatory Considerations for Human Cells, Tissues, and Cellular and Tissue-Based Products: Minimal Manipulation and Homologous Use. (2020)
2. Ditmars, Frederick S., et al. "Safety and efficacy of acellular human amniotic fluid and membrane in the treatment of non-healing wounds in a patient with chronic venous insufficiency." *SAGE Open Medical Case Reports 10* (2022)
3. Liu, Naiyou, et al. "Comparative Analysis of Co-Cultured Amniotic Cell-Conditioned Media with Cell-Free Amniotic Fluid Reveals Differential Effects on Epithelial–Mesenchymal Transition and Myofibroblast Activation." *J Biomedicines* (2022)
4. Merakris Therapeutics, Inc. (2021). Dermacyte® Amniotic Wound Care Liquid [INVESTIGATOR'S BROCHURE] (2021)

Actively Enrolling Patients | ClinicalTrials.gov Identifier: NCT04647240

Texas Podiatric Medical Association | June 23 - June 25, 2023 | Round Rock, TX
Merakris Therapeutics, Inc | 800 Park Offices Drive, Suite 403 | Research Triangle Park, NC