CONTINUED ACCESS PROTOCOL: Demonstration of the Safety and Effectiveness of ReCell® combined with Meshed Skin Graft for Reduction of Donor Area in the Treatment of Acute Burn Injuries

Investigational Plan

Study Number: CTP001-7

Device: ReCell Autologous Cell Harvesting Device

Study Type: IDE Study (IDE 13053)

Date: August 25, 2016

Sponsor: Avita Medical Americas, LLC
9221 Corbin Ave
Suite 220
Northridge, CA 91324-2494

PRINCIPAL INVESTIGATOR'S STATEMENT

This statement is to certify that I have received the above-referenced investigational plan, which has been approved for initiation at my investigational site by the Institutional Review Board on the date of _____. As Principal Investigator, I will ensure that all personnel who have been delegated responsibilities for this study will be trained on the investigational plan and associated responsibilities prior to study participation. I agree to conduct this clinical study in compliance with the investigational plan and applicable requirements of the U.S. Code of Federal Regulations (21 CFR Parts, 50, 54, 56, 812 and 45 CFR Part 46).

Signature: _____ Date: _____
Principal Investigator

PROTOCOL SYNOPSIS

Title	**CONTINUED ACCESS PROTOCOL:** Demonstration of the Safety and Effectiveness of ReCell® combined with Meshed Skin Graft for Reduction of Donor Area in the Treatment of Acute Burn Injuries
Purpose	The overall purpose of this is study to provide continued access to the ReCell device following completion of protocol CTP001-6, and to allow for collection of supplementary clinical outcome data for the ReCell device when used as an adjunct to meshed grafts in subjects with acute thermal burn injuries requiring skin grafting for closure of burn injuries
Design	This is a prospective, randomized, multicenter, evaluator blinded, within-subject controlled study. Patients 5 years or older with a total body surface area (TBSA) thermal burn injury between 5 and 50% (inclusive) will be considered for participation in this study. Following burn excision and confirmation of eligibility, a grafting plan will be developed and documented in accordance with investigators' standard of care. Among the excision sites, two comparable contiguous or non-contiguous areas (i.e., similar in burn injury depth, graft plan and size) at least 300 cm^2 in size will be identified and labeled as Area A and Area B. The wound regions will be randomly assigned to receive grafting consistent with the Investigator's pre-identified graft plan (control) or to receive application of the ReCell- generated cell suspension applied over a graft more widely meshed than identified in the pre-specified graft plan (ReCell-treated). For example, if the graft plan called for a 2:1 mesh graft, for the ReCell-treated wounds, the area will be treated with 3:1 mesh graft and over-sprayed with the ReCell-generated cell suspension. The donor area for skin allocated to ReCell and control treatment areas will be measured and documented. The two treatment areas will be compared with respect to healing characteristics and the amount of donor skin harvesting required. Follow-up visits will be performed at 1, 2, 4, 6, 8, 10, 12, 24, 36 and 52 weeks post treatment. Acute healing and pain outcomes will be evaluated in the early post-operative period (i.e., through 12 weeks). Pain, healing durability and scar outcomes will be evaluated in the longer-term follow-up visits (i.e., 24, 36 and 52 week visits). Treatment-related and serious adverse events will be captured throughout the duration of the study. Treatment-area closure will be evaluated via direct visualization by the treating investigator and by a qualified clinical investigator blinded to treatment allocation (i.e., Blinded Evaluator). The blinded assessment will serve as the primary healing assessment. At all visits, all subjects' study treatment areas will be documented photographically using standardized digital photography. Scar outcomes will be measured using the Patient and Observer Scar Assessment Scale (POSAS) questionnaire which includes components for both the Blinded Evaluator and the patient.

Co-Primary Effectiveness Endpoints	1.Confirmed treatment area closure at (or prior to) the Week 8 visit. Complete wound closure is defined as skin re-epithelialization without drainage, confirmed at two consecutive study visits at least 2 weeks apart by direct visualization by a qualified clinician. Blinded Evaluator assessment of wound closure will be performed at Weeks 4, 6, 8, 10 and 12. 2.The actual expansion ratios (treatment area to donor site area, inclusive of donor skin needed for secondary treatments) will be calculated separately for the ReCell and control treatments. Treatment area and donor area will be based on measurements of the treatment and donor site wound bed at the time of the grafting procedure (obtained intra-operatively). Calculation of expansion ratios will include any donor skin required for re-treatments performed to achieve wound closure, if applicable.
Additional Effectiveness Endpoints	The following additional effectiveness endpoints will be investigated: Subject Satisfaction at Week 24 (evaluating whether there is a preference for the ReCell treatment), 24 Week Observer POSAS Overall Opinion Score and 24 Week Patient POSAS Overall Opinion Score
Safety	Safety will be assessed with evaluation of the following: 1. Delayed healing (all visits) 2. Infection (all visits) 3. Allergic response to trypsin (all visits) 4. Treatment area durability, in terms of any evidence of recurrent wound breakdown following initial complete closure (Week 12, 24, 36 and 52) 5. Scars necessitating surgical intervention 6. Treatment-area pain via numeric rating scale (1-10, where 1 represents no pain and 10 represents worst possible pain) will be evaluated at all visits, and incorporated as a component of the POSAS beginning at Week 12 7. Treatment-related and serious adverse events (all visits)
Other Evaluations	1. Healing assessment by treating investigator (all visits) 2. POSAS and Subject Satisfaction evaluations at Week 12, 36 and 52 3. Subject and Blinded Evaluator blinding effectiveness
Enrollment	Up to 60 patients enrolled at up to 18 investigational sites in the United States
Analysis	Data will be analyzed and summarized in an interim analysis at a time to coincide with the submission of the ReCell marketing application. At that time all available data will be presented. Data will be analyzed consistent with the statistical plan develop for the CTP001-6 protocol; however, there are no formal statistical hypotheses to be investigated.

Statistical Consideration	It is anticipated that up to 60 subjects may be accrued in the period between the time the protocol is approved and receipt of FDA marketing approval for the ReCell device. Primary effectiveness will be assessed on the following two analysis sets: Intent to treat population (ITT) – All those enrolled into the study who are randomized; and Per protocol population (PP) – ITT subjects who receive both study treatments and have no major protocol deviations. For the co-primary effectiveness endpoint for confirmed treatment area closure, the hypothesis test of non-inferiority will be one-sided with a 5% significance level; for the endpoint of relative reduction in donor site area, the hypothesis test of superiority will be one-sided with a 2.5% significance level, all other statistical tests will be two-sided at the 5% significance level, unless otherwise noted. Data will be analyzed and summarized in an interim analysis at a time to coincide with the submission of the ReCell marketing application. For evaluation of the co-primary effectiveness endpoints, it is anticipated that there will be minimal missing data. However, multiple imputation and sensitivity analyses (e.g., pattern mixture models) will be performed if appropriate to account for missing data.