Establishing the Safety and Effectiveness of ReCell® as an Autograft-sparing Technology for Definitive Closure of Burn Injuries

Friday, November 9, 2018
4:45 – 5:00 pm

Author and Co-authors:

James H. Holmes, IV, MD[1]; Joseph A. Molnar, MD, PhD[1]; Jeffrey E. Carter, MD[2]; James Hwang, MD[3]; Bruce A. Cairns, MD[4]; Booker T. King, MD[5]; David J. Smith, MD[6]; C. Wayne Cruse, MD[6]; Kevin N. Foster, MD[7]; Michael D. Peck, MD[7]; Rajiv Sood, MD[8]; Michael J. Feldman, MD[9]; Marion H. Jordan, MD[10]; Jeffrey W. Shupp, MD[10]; David W. Mozingo, MD[11]; David G. Greenhalgh, MD[12]; Tina L Palmieri, MD[12]; John A. Griswold, MD[13]; Sharmila Dissanaike, MD[13]; William L. Hickerson, MD[14]

[1]Wake Forest Baptist Medical Center, Winston-Salem, NC
[2]University Medical Center, New Orleans, LA
[3]University of Alabama, Birmingham, AL
[4]University of North Carolina, Chapel Hill, NC
[5]United States Army Institute of Surgical Research Burn Center, Fort Sam Houston, TX
[6]University of South Florida, Tampa, FL
[7]Maricopa Health, Phoenix, AZ
[8]University of Indiana, Indianapolis, IN
[9]Virginia Commonwealth University, Richmond, VA
[10]edstar Washington Hospital Center, Washington, DC
[11]University of Florida, Gainesville, FL
[12]UC-Davis, Sacramento, CA
[13]Texas Tech University Health Sciences Center, Lubbock, TX
[14]University of Tennessee, Memphis, TN

Objective:

Upon completion of the lecture, attendees should be better prepared to:
▪ Describe the use of autologous skin cell suspension for the treatment of burn injuries

Abstract:

Introduction: Split-thickness skin grafts (STSG) are standard care for the treatment of deep partial-thickness and full-thickness burn injuries. Although effective in achieving rapid and permanent closure of the burn injury, the donor site wound created during autograft harvest is often more troublesome for patients than the primary injury, as these wounds are a source of significant pain and are at a risk for infection, discoloration, and scarring.

The ReCell® Autologous Cell Harvesting Device is a point-of care, autograft-sparing technology that offers an alternative strategy to standard autografting. The device enables a clinician to process a small STSG sample into a non-cultured, autologous skin cell suspension (ASCS) for immediate application to the burn wound to achieve definitive closure. This technique allows for expansion of up to 80 times the area of STSG donor skin harvested, thereby minimizing the donor site wound created while maximizing wound coverage.

Methods: Two pivotal, prospective, randomized, within-patient controlled clinical trials were conducted under a US FDA Investigational Device Exemption (NCT01138917 and NCT02380612) evaluating the safety and effectiveness of ReCell® in the treatment of acute thermal burn injuries in a total of 131 subjects. The first trial evaluated 101 subjects at 12 clinical sites and investigated the effect of ASCS used as a primary intervention for the treatment of deep-partial thickness injuries compared to treatment with a 2:1 meshed STSG. The second pivotal trial evaluated the use of ASCS as an adjunct to widely meshed STSG for the treatment of mixed depth burns, inclusive of full-thickness, compared to a less widely meshed STSG in 30 subjects from 6 clinical sites. In these trials, the incidence of wound closure, donor site requirements, donor site healing, long-term scar and satisfaction outcomes, and adverse events were evaluated over 52 weeks.

Results: Collectively, the data from these 2 clinical trials demonstrate that the use of ASCS, either as a primary treatment or as an adjunct intervention to widely meshed STSG, significantly reduces the amount of donor skin required to achieve definitive closure, as compared to control-treated burn wounds, without compromising the quality of healing or long-term outcomes.

In the first pivotal trial (n=101), co-primary endpoints for the incidence of recipient site wound closure and donor site wound healing were established for deep-partial thickness burns treated with ASCS vs. 2:1 meshed STSG. The proportion of subjects with recipient site wound healing at 4 weeks was 98% for ASCS-treated and 100% for control STSG-treated burns. Non-inferiority was established for the incidence of recipient site wound closure, as the lower bound of the 95% CI for the difference of the proportions between the ASCS and control treatments was greater than the pre-defined -10% non-inferiority margin. Superiority was achieved for donor site wound healing as a significantly greater proportion of the donor sites harvested to prepare ASCS were healed at one week compared to donor sites harvested for conventional STSG ($p<0.05$). A significant difference was also seen at week 2, with 90% of the ASCS donor sites being healed as compared to 67% of the control donor sites ($p<0.001$). Additionally, the donor sites harvested to prepare ASCS were significantly smaller ($p<0.001$), were significantly less painful at weeks 1 - 8 ($p<0.001$), had significantly improved long-term appearance as assessed by the patient at week 52 ($p=0.0018$), and were associated with significantly improved scar outcomes as assessed by the investigator at week 52 ($p=0.0025$). The use of ASCS did not introduce any safety risks, as all adverse events were consistent with a patient population undergoing autografting for the treatment of burn injuries.

In the second pivotal trial (n=30), co-primary endpoints for the incidence of recipient site wound closure by 8 weeks and the comparison of expansion ratios were established for mixed depth burns treated with ASCS in conjunction with a widely meshed STSG as compared to conventionally meshed STSG alone. The proportion of subjects with recipient site wound closure by 8 weeks, as assessed by a blinded

evaluator, was 92% for ASCS-treated and 85% for control STSG-treated burn wounds. Non-inferiority was established for the incidence of recipient site wound closure, as the upper bound of the 97.5% CI for the difference of the proportions between the ASCS and control treatments was less than the pre-defined 10% non-inferiority margin. Superiority was achieved for the relative reduction in donor area requirements, calculated as the ratio of measured treatment area to measured donor area. The average reduction for ASCS-treated sites compared to control-treated sites was 32% ($p<0.001$). Furthermore, comparable long-term patient satisfaction, scar outcomes, and safety profiles were observed over the 52-week study.

Conclusion: These data establish the safety and effectiveness of the ReCell® device as an autograft-sparing technology indicated for use at the patient's point-of-care for preparation of ASCS in treating acute thermal burn injuries. When used as a primary treatment for deep partial-thickness burns or as an adjunct to widely meshed STSG for full-thickness burns, ASCS-treated wounds achieve epidermal regeneration using significantly less donor skin with comparable healing and long-term outcomes to conventional STSG. These findings have potential implications for a paradigm shift in the approach used to achieve rapid and permanent closure of burn injuries. Furthermore, achieving definitive closure using less skin compared to standard autografting has the potential to decrease the number of surgical procedures required to achieve wound closure as well as reducing hospital length of stay, thus decreasing the overall costs related to the treatment of burn injuries.

Disclosure:

James H. Holmes – Dividends: Abbott Labs, AbbVie, Merk; Stock: PermeaDerm; Honorarium: Mallinckrodt
Joseph A. Molnar – No Relevant Financial Relationships to Disclose
Jeffrey E. Carter – Stock: PermeaDerm
James Hwang – No Relevant Financial Relationships to Disclose
Bruce A. Cairns – No Relevant Financial Relationships to Disclose
Booker T. King – No Relevant Financial Relationships to Disclose
David J. Smith – No Relevant Financial Relationships to Disclose
C. Wayne Cruse – No Relevant Financial Relationships to Disclose
Kevin N. Foster – No Relevant Financial Relationships to Disclose
Michael D. Peck – No Relevant Financial Relationships to Disclose
Rajiv Sood – Consultant: Avita
Michael J. Feldman – Research grant funding: PolarityTE
Marion H. Jordan – No Relevant Financial Relationships to Disclose
Jeffrey W. Shupp – No Relevant Financial Relationships to Disclose
David W. Mozingo – No Relevant Financial Relationships to Disclose
David G. Greenhalgh – No Relevant Financial Relationships to Disclose
Tina L Palmieri – No Relevant Financial Relationships to Disclose
John A. Griswold – No Relevant Financial Relationships to Disclose
Sharmila Dissanaike – No Relevant Financial Relationships to Disclose
William L. Hickerson – Stock: PermeaDerm, Avadim; Honorarium: PolyNovo, Vericel, Avita, Medline