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Efficacy of placental derived allografts and standard of care in the treatment of nonhealing diabetic foot ulcers using matched controls: a randomized controlled trial

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Abstract

Diabetic foot ulcers (DFUs) are a severe complication of diabetes, contributing to high morbidity, risk of amputation, premature mortality, and substantial healthcare costs. Standard of care (SOC), including debridement, offloading, infection control, and moisture balance, remains the foundation of DFU treatment; however, many ulcers fail to achieve complete closure with SOC alone. Placental-derived allografts, classified as cellular, acellular, and matrix-like products (CAMPs), provide a biologically active extracellular scaffold rich in growth factors and structural proteins that support angiogenesis, cellular migration, and control of inflammation. These properties suggest that CAMPs may overcome impaired healing pathways characteristic of chronic diabetic wounds. The RENEW trial is a multicenter, prospective, randomized controlled modified platform study designed to evaluate the effectiveness of multiple placental-derived allografts in combination with SOC using matched controls. Findings from RENEW aim to generate high-quality evidence to guide integration of biologic therapies into clinical practice, improve healing rates, and reduce long-term complications of DFU.

Introduction

Diabetes affects over 500 million people globally, with type 2 diabetes comprising the majority of cases.[1] A common and severe complication of diabetes is the development of diabetic foot ulcers (DFUs), which result from neuropathy, impaired circulation, and mechanical stress. These wounds are difficult to heal and frequently recur, often leading to limb amputation and premature death. Studies suggest that 19-34% of individuals with diabetes will develop a DFU in their lifetime, and the 5-year mortality rate following a DFU can range from 50%-70%.[2,3]

Current standard of care (SOC) for DFUs include sharp debridement, offloading, infection control, and moisture maintenance. While these interventions are foundational, many DFUs remain nonhealing, highlighting a critical unmet need for more effective treatment.[4] Chronic wounds impose significant burden on individuals in the form of pain, immobility, and reduced quality of life, in addition to the burden on healthcare systems. In the United States, the annual cost of diabetic foot care is estimated to exceed $80 billion, with a substantial portion related to chronic ulcer treatment and associated complications.[5]

In response, biologic wound therapies, such as cellular, acellular, and matrix-like products (CAMPs), have emerged as promising treatments. CAMPs, particularly those derived from placental tissues, offer a biologically active extracellular matrix scaffold that supports cell migration, angiogenesis, and control of inflammation, all of which are essential for wound healing.[6,7] Placental allografts are minimally immunogenic and contain structural proteins and growth factors that may accelerate closure in chronic wounds resistant to SOC.[8]

Despite growing clinical adoption, high-quality randomized controlled trials (RCTs) evaluating CAMPs in DFUs remain limited. Moreover, many studies focus on a single product, limiting generalizability. The RENEW trial addresses this gap through a novel, modified platform design that evaluates multiple CAMPs in parallel alongside matched controls drawn from the US Wound Registry database. The platform design provides the flexibility to add and remove products over time. This dynamic study structure increases efficiency, statistical power, and relevance to real-world clinical practice.

By generating robust comparative data across several CAMPs, RENEW aims to inform best practices for integrating biologic allografts into diabetic wound care. If effective, these therapies could reshape therapeutic approaches, reduce healing times, and alleviate the substantial economic and human burden of chronic DFUs.

Materials and methods

RENEW is a randomized controlled modified platform clinical trial evaluating placental derived allografts and standard of care (SOC) in the treatment of nonhealing DFUs (clinicaltrials.gov #NCT07086443). This study will be conducted at up to 30 SerenaGroup, Inc. or affiliated centers throughout the United States with up to 350 patients with nonhealing DFUs. This study is anticipated to be completed within 24 months. The study population will be drawn from patients suffering from chronic wounds who are attending wound clinics. The inclusion and exclusion criteria for the RENEW trial are discussed in this paper.

Objectives and endpoints

The primary objective for the RENEW clinical trial is to determine the between-arm difference in the proportion of subjects achieving complete closure of nonhealing DFUs with multiple CAMPs plus SOC versus matched controls over 12 weeks using a modified platform trial design. The primary endpoint is the percentage of target ulcers achieving complete wound closure in 12 weeks.

Additional important endpoints to evaluate will be time to closure for the target ulcer; percentage wound area reduction from TV-1 to TV-13 measured weekly with digital photographic planimetry, using an imaging device, and physical examination; the number of product- or procedure-related adverse events; change in quality-of-life (QoL) based on the Wound Quality of Life assessment; and change in pain in the target ulcer assessed using the Pain, Enjoyment of Life and General Activity Scale (PEG) scale.

Exploratory endpoints may be included provided they do not compromise the assessment of primary or secondary endpoints; they contribute to furthering knowledge in the treatment of chronic wounds. This study will evaluate percentage of target ulcers achieving complete wound closure in 12 weeks for subjects 65 years of age or older; and adherence to a prescribed offloading total contact casting (TCC) measured as % of time wearing the TCC as determined by digital technology.

Diagnosis

The diagnosis of DFUs is primarily clinical and is established through a combination of patient history, comprehensive physical examination findings, and targeted diagnostic testing. DFUs typically occur on weight-bearing areas of the foot, such as the plantar surface of the metatarsal heads or the tips of the toes, and are often preceded by signs of peripheral neuropathy and/or peripheral arterial disease (PAD). Neuropathic ulcers frequently present with a callused rim, punched-out appearance, and variable levels of granulation tissue, while ischemic or neuroischemic ulcers may have irregular margins, pale or necrotic wound beds, and minimal exudate. Pain is variable, often diminished or absent due to sensory neuropathy, but may be pronounced in ulcers complicated by ischemia or infection.

A detailed clinical history is critical to distinguish DFUs from other chronic wound types. This includes documentation of diabetes duration and glycemic control, prior ulcerations or amputations, history of peripheral vascular disease, neuropathic symptoms, mechanical or traumatic injury, prior treatments, and footwear habits. Differential diagnoses to consider include venous leg ulcers, arterial ulcers, pressure injuries, vasculitic ulcers, and malignancies, which must be excluded through careful evaluation.

Bedside neurological assessment should be performed to evaluate for loss of protective sensation. Vascular evaluation is essential, as ischemia significantly influences ulcer healing potential. An ankle-brachial index (ABI) should be measured in all patients; values between 0.9 and 1.3 suggest normal perfusion, whereas values <0.9 indicated PAD

and may warrant vascular imaging or consultation. In patients with diabetes who have calcified, noncompressible arteries, toe-brachial index (TBI) or transcutaneous oxygen measurement (TCOM) provides more accurate assessment of perfusion.

When ulcer features are atypical, nonhealing despite optimal care, or suggest neo-plastic transformation, a biopsy should be performed to rule out malignancy or other dermatoses masquerading as DFUs. Comprehensive evaluation of neuropathy, ischemia, infection, and mechanical factors remains the cornerstone of DFU diagnosis and guides both prognostication and therapeutic decision-making.

Vulnerable populations

Although vulnerable subjects will not specifically be recruited for this study, vulnerable subjects may be present in the potential subject pool. Vulnerable subjects are defined as patients who are pregnant, fetuses/children, or prisoners. Additional procedures will not be required to ensure protection for these human subjects.

Matched controls

This study will employ a matched-control design to enhance comparability between treatment and control groups and to minimize potential sources of bias. Subjects in the treatment arm will be prospectively enrolled as described and will receive the investigational product in combination with SOC. Outcomes will be compared to those of participants from the control database.

Each enrolled subject will be retrospectively matched with patients from the US Wound Registry (USWR) who received SOC alone, without exposure to CAMPs or other advanced therapeutics. Beginning with the initial repository of more than 30,000 DFUs, the inclusion and exclusion criteria specified for the RENEW trial will be applied to the registry data. The remaining eligible DFU cases will serve as the potential control pool.

Matched control participants will be carefully selected to ensure close similarity with the treatment cohort. Matching will be based on key demographic and clinical characteristics, such as age, sex, baseline wound characteristics, and other relevant prognostic factors that may influence outcomes. This approach is intended to ensure the groups are comparable at baseline and that observed differences can be attributed with greater confidence to the investigational intervention rather than underlying patient characteristics.

Standard of care

The SOC for DFUs is focused on addressing the underlying pathophysiological factors contributing to ulcer development, promoting wound healing, preventing infection, and reducing recurrence risk. Core components of SOC include effective offloading, wound bed preparation, infection control, optimization of metabolic and vascular status, and patient education.

Offloading therapy is the cornerstone of DFU management and is the most evidence-based intervention to redistribute pressure away from the ulcer site and facilitate healing. TCC is considered the gold standard for plantar DFUs, providing continuous pressure redistribution and protecting the wound from repetitive trauma.[9] When contraindications to casting exist, removable cast walkers or specialized offloading footwear are acceptable alternatives, although strict patient compliance is necessary to ensure effectiveness. Offloading should be applied promptly and maintained until full re-epithelialization is achieved to minimize delayed healing and risk of recurrence.

Wound bed preparation involves routine sharp debridement to remove devitalized tissue, callus, and biofilm, creating a healthy granulation tissue base and facilitating closure. Maintaining a moist wound environment is essential; this is typically achieved with modern dressings such as foam, hydrofiber, or alginate products, chosen according to exudate volume and wound depth.[10] Periwound skin should be protected to prevent maceration and breakdown during dressing changes.

Infection control strategies include regular assessment of the ulcer for local or systemic signs of infection. While chronic wounds are frequently colonized, true infection should be treated promptly with systemic antibiotics guided by deep tissue cultures obtained after debridement.[11] Topical antiseptics may be used for short periods during active infection but are not recommended for routine prolonged use due to potential cytotoxic effects on healthy tissue. Optimization of metabolic and vascular factors is an integral part of DFU management. Glycemic control should be closely monitored to support wound healing, and evaluation for PAD is essential, as ischemia significantly impairs closure rates. ABI or TBI should be performed in all patients, with revascularization considered for severe ischemia prior to or alongside wound care interventions.[12]

Patient education and multidisciplinary care are key to preventing recurrence and improving long-term outcomes.

Instruction on proper foot hygiene, daily inspection for new lesions, use of protective footwear, and compliance to offloading devices is essential. Engagement of a multidisciplinary team, including podiatrists, endocrinologists, vascular surgeons, and wound care specialists, facilitates comprehensive care and early intervention for complications.

Despite adherence to SOC, a subset of DFUs remains nonhealing due to complex underlying pathology. In these cases, advanced therapies, including cellular, acellular, and matrix-like products (CAMPs) may be considered in combination with SOC to enhance healing potential.[13]

Subject characteristics

Patients who suffer from DFUs were recruited for this study from participating wound clinics. Once patients agreed to adhere to the study schedule, and read and signed the IRB approved Informed Consent Form, screening was conducted to determine whether subjects were eligible based on inclusion and exclusion criteria, listed in Table 1.

Study procedures

Patients will undergo a structured series of clinical procedures spanning screening, treatment, and closure confirmation phases, designed to ensure eligibility assessment, standardized wound care, accurate data collection, and consistent application of study interventions. All subjects will complete a written informed consent form prior to the initiation of any study-related activity. Screening is conducted over a 14-day period and may include up to two visits. At the first screening visit (SV-1, Day -14 ±3 days), the investigator will review medical and medication history to assess eligibility against inclusion and exclusion criteria. Demographic information including height, weight, body mass index, sex, and ethnicity will be collected, and vital signs along with a general physical examination will be performed. Vascular testing (ABI, TBI, TCOM, or PVR) will be conducted unless valid results are available from the prior three months. The study ulcer will be evaluated for Wagner grade, Fitzpatrick skin type, and detailed wound characteristics including granulation tissue, non-viable tissue, depth, exudate, and condition of surrounding skin. Historical ulcer measurements from two weeks prior to SV-1 will be reviewed to determine the percentage area reduction (PAR); if the ulcer had reduced by more than 20%, the subject will be considered a screen failure. Pain will be assessed using the Pain, Enjoyment of Life and General Activity Scale (PEG), and participants will be counseled on avoidance of tobacco use. SOC wound management will be initiated, including cleansing with normal sterile saline (NSS), sharp debridement to remove non-viable tissue, photographic imaging and planimetric measurement of the ulcer using the study provided device, application of standardized calcium alginate or foam dressings, and initiation or continuation of offloading with a Defender boot or TCC.

At the second screening visit (SV-2, Day -7 ±3 days), the investigator will reassess for adverse events and any changes in concomitant medications, record updated vital signs, and document wound characteristics and PEG pain scores. SOC procedures will be repeated. Additional absorptive dressings will be permitted for highly exudative wounds only with medical monitor approval. Subjects who demonstrate less than a 25% reduction in ulcer area during the 2-week screening phase will remain eligible for enrollment.

On Day 0 (TV-1), a final eligibility review will be performed. The investigator will confirm that all inclusion criteria are met and that no exclusion criteria apply, reassess medications, adverse events, and vital signs, and document ulcer characteristics and PEG pain scores. Participants will complete the Forgotten Wound Score (FWS) and Wound Quality of Life (wQOL) questionnaires. If eligibility is confirmed, subjects will be randomized to receive one of seven CAMPS plus SOC treatments. The assigned treatment procedures will be performed following SOC wound cleansing, sharp debridement, ulcer imaging and measurement, and application of study dressings with investigational product based on treatment allocation. Adherence to prescribed offloading will be reviewed and documented.

Weekly treatment visits (TV-2 through TV-12, Days 7-77 ±3 days) will be conducted according to protocol. At each visit, the investigator will assess adverse events, review concomitant medications, record vital signs, and document wound characteristics and PEG pain scores. The FWS and wQOL questionnaires will be administered at TV-4, TV-8, and TV-12 or final visit. SOC procedures will be repeated at each visit, in addition to investigational product application based on treatment allocation. Adherence to the offloading protocol will be evaluated and recorded weekly.

At the final treatment visit (TV-13, Day 84 ±3 days or 7 days after initial wound closure), comprehensive evaluations will be performed including adverse event assessment, medication review, PEG pain scoring, FWS, and wQOL questionnaires. If the ulcer remains unhealed, wound characteristics will be documented, imaging will be performed, and participants will be referred for continued wound care outside of the study. An End of Study (EOS) form will be completed for every participant.

TABLE 1 | Inclusion and exclusion criteria

Inclusion criteria	Exclusion criteria
• Must be at least 18 years of age or older. • Must have a diagnosis of type 1 or 2 diabetes. • At enrollment, must have a target ulcer with a mini-mum surface area of 1.0cm^2 and a maximum surface area of 15.0cm^2 measured post-debridement with the imaging device length times width. • Must have a target ulcer that has been present for a minimum of 4 weeks of SOC prior to the initial screening visit. • Must have a target ulcer located on the foot with at least 50% of the ulcer below the malleolus. • Must have a target ulcer that is Wagner 1 or 2 grade, extending at least through the dermis or subcutaneous tissue and may involve the muscle, provided it is below the medial aspect of the malleolus. The ulcer may not include exposed tendon or bone. • Must have adequate perfusion confirmed by vascular assessment. Any of the following methods performed within 3 months of the first screening visit are acceptable: o ABI between 0.7 and ≤1.3; o TBI ≥0.6; o TCOM ≥ 40mmHg; o PVR: biphasic • If the potential subject has two or more ulcers, they must be separated by at least 2cm. The largest ulcer satis-fying the inclusion and exclusion criteria will be des-ignated as the target ulcer. • Must have a target ulcer located on the 50% below the malleolus and not on the dorsal toes. • Must be offloaded for at least 14 days prior to enrollment. • Must consent to using the prescribed offloading method for the duration of the study. • Must agree to attend the weekly study visits required by the protocol. • Must be willing and able to participate in the informed consent process.	• Known to have a life expectancy of <6 months. • Target ulcer is not secondary to diabetes. • Target ulcer is infected or there is cellulitis in the surrounding skin. • Target ulcer exposes tendon or bone. • Evidence of osteomyelitis complicating the target ulcer • Receiving immunosuppressants (including systemic corticosteroids at doses greater than 10 mg of prednisone per day or equivalent) or cytotoxic chemotherapy or is taking medications that the PI believes will interfere with wound healing (e.g., biologics). • Has applied topical steroids to the ulcer surface within one month of initial screening. • Previous partial amputation on the affected foot that results in a deformity that impedes proper offloading of the target ulcer. • Has glycated hemoglobin (HbA1c) greater than or equal to 12% within 3 months of the initial screening visit. • Surface area has reduced in size by more than 20% in the 2 weeks prior to the initial screening visit ('historical' run-in period). • The surface area measurement decreases by 25% or more during the active 2-week screening phase: the 2 weeks from the initial screening visit (S1) to the TV-1 visit during which time the potential subject received SOC. • Has an acute Charcot foot, or an inactive Charcot foot, which impedes proper offloading of the target ulcer. • Pregnant or considering becoming pregnant within the next 6 months. • Has end stage renal disease requiring dialysis. • Has participated in a clinical trial involving treatment with an investigational product within the previous 30 days. • Has a medical or psychological condition that may interfere with study assessments. • Treated with hyperbaric oxygen therapy (HBOT) or a Cellular, Acellular, Matrix-like Product (CAMP) in the 30 days prior to the initial screening visit. • Has a malnutrition. • Has a known allergy or sensitivity to PBS, IPA, pro-cessing solutions, reagents, or latex.

SOC=standard of care

A Closure Confirmation Visit (CCV) will take place 14 days (±3 days) after the first assessment of 100% re-epithelialization, even if closure occurs at TV-13. At this visit, the investigator will reassess adverse events, review medications, perform PEG pain scoring, and confirm wound closure by physical examination and imaging. Independently blinded reviewers will verify closure images to determine the primary endpoint. Participants who withdraw early or are withdrawn by the investigator will undergo a final evaluation equivalent to the EOS visit whenever possible. Unscheduled visits will be permitted for additional dressing changes, with reasons documented in the case report form. All study procedures will be performed consistently to ensure protocol adherence, patient safety, and reliable endpoint evaluation. Table 2 details the schedule of events for the study.

Statistical methods

A minimum total sample size of 350 patients will be needed to detect a difference of 35% between treatment groups. In total, 50 patients will be recruited to receive one of 7 CAMPs + SOC and matched from a sample size of 1,050 control patients (1:3 match ratio) to achieve 80% statistical power.

Once the sample size for the CAMPs + SOC have been met, the enrolled patients will be matched using a database of controls. Patients will be matched on the following variables initially: wound type (DFU), wound age, wound area at

baseline, patient sex, patient age (within the range of 5-10 years), and diabetes status.

The primary endpoint is the proportion of wounds achieving complete wound closure in 12 weeks. The primary endpoint will be analyzed using Chi-square test with the null hypothesis stating the proportion of wounds achieving complete wound closure in 12 weeks is equal between treatment arms.

The secondary endpoints will be analyzed using Kaplan-Meier, Mann-Whitney, and linear mixed models. Summary statistics on all demographics, time to wound closure, and adverse and serious adverse events will be described. All analysis will be completed using the most recent versions of R Studio and Python.

Subject withdrawals

All participants have the right to withdraw from the study at any time during the treatment period without prejudice. The completion status of each participant's involvement in the clinical trial will be documented. In the event that study treatment or protocol-required observations are discontinued for any participant, the reason(s) for discontinuation will be recorded. The investigator will have the authority to withdraw a participant from the study at any time if deemed medically necessary.

Participant withdrawal from the study is not expected to compromise their safety. Should a participant choose to withdraw consent or be withdrawn by the investigator, efforts will be made to obtain permission to continue collecting survival data through the end of the follow-up period as defined by the study protocol. Whenever feasible, the reason for withdrawal or early termination will be documented.

A participant will be classified as lost to follow-up if they cannot be reached after five telephone contact attempts and three written communications.

Subject compensation

Participants will receive a nominal compensation of $50 USD upon completion of each study visit. This compensation is intended to offset expenses associated with participation, including travel, parking, and the additional time required for study-specific procedures and data collection.

Anticipated risks/risk mitigation

Anticipated risks associated with the study procedures are listed below, along with the applicable risk mitigation. Adverse events related to the treatment are unlikely. The potential risks are listed in *Table 3*.

Discussion

DFUs continue to pose a significant challenge in clinical practice, often resulting in prolonged healing times, high recurrence rates, and substantial risk of lower-limb amputation despite well-established SOC interventions. Emerging evidence suggests that adjunctive biologic therapies, particularly placental-derived cellular, acellular, and matrix-like products (CAMPs) may enhance healing outcomes in chronic DFUs compared to SOC alone. These products provide an extracellular matrix scaffold enriched with growth factors and cytokines that support angiogenesis, modulate inflammation, and facilitate tissue regeneration, addressing many of the biological deficits that contribute to impaired healing in diabetes.[14,15]

Several recent randomized controls trials (RCTs) and systematic reviews have demonstrated the potential benefit of placental-derived biomaterials in management of DFUs. A 2024 meta-analysis of 12 RCTs reported that the odds of complete ulcer healing were more than six-fold higher in patients treated with placental-derived products compared to SOC alone.[14] Another systematic review concluded that amniotic membrane allografts consistently reduced healing time and improved closure rates across multiple studies, supporting their use as an effective adjunctive therapy in chronic wound care.[15]

Real-world data also reinforce these findings. A retrospective analysis of over 333,000 Medicare beneficiaries found that patients receiving placental allografts has significantly lower recurrence rates, fewer amputations, and reduced all-cause mortality compared with those treated with SOC alone.[16] Furthermore, clinical evidence highlights that optimal outcomes with CAMPs depend on combining biologic therapy with high-quality wound bed preparation, particularly thorough debridement, to maximize bioactivity and healing potential.[17]

Despite these promising results, limitations in the current evidence base persist. Many published studies have small sample sizes, limited follow-up periods, heterogenous patient populations, and focus on single products, making it difficult to directly compare therapies or establish standardized treatment algorithms. The RENEW trial addresses these limitations through its multicenter, prospective, randomized, modified platform design. This structure allows for the evaluation of multiple CAMPs under a unified protocol, improves statistical efficiency, and provides flexibility to

TABLE 2 | Schedule of events

	SV	TV-1	TV-2, TV-3	TV-4	TV-5, TV-6 TV-7	TV-8	TV-9, TV-10, TV11	TV-12	TV-13	CCV
Window period	-14	Day 0	Week 1, week 2	Week 3	Week 4, week 5, week 6	Week 7	Week 8, week 9, week 10	Week 11	Week 12	+14
Record medical history and demographic information	X									
Assessment of eligibility	X	X								
Sign informed consent form	X									
Vascular screening test	X									
Physical exam	X	X								
HbA1c	X									
Fitzpatrick Scale	X									
Historical measurement	X									
Randomization		X								
Assessment for AE and SAE		X	X	X	X	X	X	X	X	X
Review medication for changes		X	X	X	X	X	X	X	X	X
Vital signs	X	X	X	X	X	X	X	X		
Wound assessment	X	X	X	X	X	X	X	X	X	X
Pain assessment (PEG)	X	X	X	X	X	X	X	X	X	X
wQOL		X		X		X		X	X	
FWS		X		X		X		X	X	
Study ulcer cleaning, debridement (if applicable)	X	X	X	X	X	X	X	X	X	X
Study ulcer area with imaging device		X	X	X	X	X	X	X	X	
Treatment based on randomization	X	X	X	X	X	X	X	X		
Apply dressing	X	X	X	X	X	X	X	X	X	

TABLE 2 | Anticipated risks and mitigations

Study procedure	Anticipated risks	Risk mitigation
Wound debridement	Pain	Procedures to be performed by trained clinical staff
Wound measurements	None anticipated	N/A
Pain assessments	None anticipated	N/A
Wound photos	None anticipated	N/A
CAMP/skin substitute application	This allograft has the potential to transmit infectious disease to the recipient.	Strict donor screening and laboratory testing, along with dedicated processing and sterilization methods, are employed to reduce the risk of any disease transmission. However, as with all biological implants, an absolute guarantee of tissue safety is not possible.
Dressing placement	Potential allergic reaction/ skin irritation	Patients with a known sensitivity to aminoglycoside antibiotics are excluded from participating in the study.
	None anticipated	N/A
TCC	None anticipated	N/A
Ankle-Brachial Index (ABI)	Discomfort in area of skin break-down secondary to pressure from cuff	Topical lidocaine
CGM	Local skin irritation, failure of the CGM to function properly, and inaccurate glucose measurements.	Patient education and weekly monitoring. Obtain serum glucose and or fingerstick glucose if inaccu-racy of the CGM is suspected.

incorporate new biologic therapies as they emerge. Additionally, RENEW will incorporate a matched-control design, in which control participants are selected from a database to closely resemble treated subjects on key demographic and clinical variables. This matching strategy is designed to enhance validity by minimizing confounding and ensuring that observed treatment effects can be more confidently attributed to the CAMP interventions.

If RENEW demonstrates that one or more CAMPs significantly improve healing outcomes compared with SOC alone, these findings could inform clinical guidelines, support reimbursement decisions, and broaden patient access to advanced wound care products. Moreover, the inclusion of matched controls will provide high-quality comparative data that more accurately reflect real-world patient populations, bridging the gap between randomized trial conditions and routine clinical practice. Beyond the immediate trial results, the platform design of RENEW offers a scalable framework for conducting rigorous comparative effectiveness research in chronic wound management, potentially transforming the way biologic therapies are evaluated and adopted in clinical practice.[18]

Conclusion

RENEW is a multicenter, prospective, randomized, modified platform clinical trial. The study will evaluate the efficacy of placental derived allografts and SOC in the treatment of nonhealing DFUs using matched controls.

Conflicts of interest

The authors declare no conflicts of interest. The funders of the RENEW study had no role in the design of the study; in the writing of this manuscript, or in the decision to publish the results.

Data availability statement

The data is proprietary, but is available on request to the corresponding author.

Author contributions

Conceptualization, TS; methodology, TS, BT and EK; writing—original draft preparation, TS, BT and EK; writing—review and editing, TS, BT and EK; supervision, BT. All authors have read and agreed to the published version of the manuscript.

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