ISRCTN24783859 https://doi.org/10.1186/ISRCTN24783859

Clinical study to evaluate the effects of human microvascular tissue in diabetic foot ulcers

Submission date
12/09/2017

Recruitment status
No longer recruiting

Registration date
26/09/2017

Overall study status
Completed

Last Edited
02/09/2021

Condition category
Skin and Connective Tissue Diseases

[_] Prospectively registered
[_] Protocol
[_] Statistical analysis plan
[X] Results
[_] Individual participant data

Plain English summary of protocol

Background and study aims
Diabetic foot ulcers (DFU) occur as a result of various factors which occur with higher frequency and intensity in the diabetic population. This causes a broken area in the foot that is unable to heal due to uncontrolled blood sugar levels. DFU lesions are responsible for more hospitalisations than any other complication of diabetes. Diabetes is the leading cause of non-traumatic lower extremity amputations in the United States, with approximately 5% of diabetics developing foot ulcers each year and 1% requiring amputation. The management of diabetic foot ulcers requires offloading the wound by using appropriate therapeutic footwear, daily saline (cleaning) or similar dressings to provide a moist wound environment, debridement (removal) when necessary, antibiotic therapy, and controlling blood sugar.
Approximately 70% of DFUs are shown to heal with good standard of care, however, at least 30% become chronic wounds. These non-healing wounds are at greater risk for infection and lower extremity amputation. Consequently, more therapy is considered for patients with chronic DFUs to improve patient outcomes, lower treatment costs and reduce the risk of complications. There has been an increase in clinical trials evaluating the use of skin and tissue substitutes, including bioengineered skin, autografts (skin or tissue taken from the individual and put in another place), allografts (skin or tissue taken from another person) and xenografts on DFUs. These clinical studies have demonstrated improved healing rates and are fewer amputations of limbs. Additionally, retrospective studies and case reports have found that the application of microvascular (a minimally manipulated microvascular human tissue product) flaps and free tissue transfer to chronic and diabetic wounds result in enhanced patient outcomes. The aim of this study is to evaluate the effects of human mirovascular tissue in treating DFU.

Who can participate?
Adults aged 18 and older with chronic DFU.

What does the study involve?
Participants are randomly allocated to one of two groups. Those in the first group receive the standard level of care. Those in the second group receive the standard level of care as well as microvascular tissue on their wound. Participants are treated for 12 weeks. Participants undergo imaging and biopsies (samples taken) at baseline, six and 12 weeks to assess their healing.

What are the possible benefits and risks of participating?
Participants may benefit from having their chronic DFU healed. There are no direct risks with participation.

Where is the study run from?
This study is being run by Microvascular Tissues, Inc. (USA) and takes place in Foot and Ankle Associates of Southwest Virginia (USA).

When is the study starting and how long is it expected to run for?
April 2017 to September 2020

Who is funding the study?
Microvascular Tissues, Inc. (USA)

Who is the main contact?
Mrs Lael Pickett
lpickett@mvtissues.com

Contact information

Type(s)
Public

Contact name
Mrs Lael Pickett

Contact details
Microvascular Tissues, Inc.
6199 Cornerstone Court
Suite 109
San Diego
United States of America
92121
+1 858 522 0633
lpickett@mvtissues.com

Additional identifiers

Protocol serial number
VMV-DFU-01, Version 1.1

Study information

Scientific Title
A multi-center randomised controlled clinical trial evaluation the effect of allogenic microvascular tissue in the treatment of wagner one and two diabetic foot ulcers

Study objectives
The primary study hypothesis is that the proportion of wounds healed at 12 weeks, after up to 12 weeks of mVASC and SOC or SOC alone, will be equal for Groups 1 and 2. Formally, H0: I1–I2 =

0; HA: I1–I2 = D1≠0, where I1 is the proportion of wounds healed in Group 1, I2 is same metric for Group 2, D1 is the difference (I1–I2); assuming the alternative hypothesis and statistical test used is chi square/Fisher exact test.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Western IRB (WIRB), 08/31/2017, ref: 20171089

Primary study design
Interventional

Study design
Interventional randomised controlled trial

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Wagner 1 and 2 diabetic foot ulcers (DFUs)

Interventions
Randomisation is performed using envelopes that have be prepared prior to the randomisation visits.

Group 1: Standard of Care (SOC)
Group 2: SOC + mVASC. mVASC is a minimally manipulated microvascular human tissue product.

Study subjects are treated weekly for up to 12 weeks. Subjects receiving mVASC receive a quantity of mVASC appropriate to the size of their ulcer.

A subject of subjects undergo LUNA imaging and biopsy at selected time points (baseline, six and 12 weeks). All subjects undergo wound imaging.

Intervention Type
Biological/Vaccine

Phase
Not Applicable

Primary outcome(s)
Percentage of index ulcers healed is measured using photographs of the index ulcer at baseline and 12 weeks.

Key secondary outcome(s)
Current secondary outcome measures as of 18/03/2021:
1. Time to heal is measured using photographs at 6 and 12 weeks
2. Percent Area Reduction (PAR) measured using photographs at 6 and 12 weeks
3. Changes in peripheral neuropathy appendage area is measured using a probe and photographs at baseline and at 12 weeks

4. Difference in cellulitis and/or infection is measured using a visual scoring system at baseline and at 12 weeks

———

Previous secondary outcome measures:
1. Percentage of index ulcers healed is measured using photographs at baseline and at 6 weeks
2. Time to heal is measured using photographs at 6 and 12 weeks
3. Percent Area Reduction (PAR) measured using photographs at 6 and 12 weeks
4. Changes in peripheral neuropathy appendage area is measured using a probe and photographs at baseline and at 12 weeks
5. Changes in wound quality of life (per W-QoL) is measured using the validated W-QofL instrument at baseline and at 12 weeks
6. Change in pain levels during trial is measured using a visual analog scale (VAS) at baseline and at 12 weeks
7. Difference in cellulitis and/or infection is measured using a visual scoring system at baseline and at 12 weeks

Completion date
30/09/2020

Eligibility

Key inclusion criteria
1. At least 18 years old
2. Presence of a DFU, Wagner 1 or 2 grade, extending at least through the dermis or subcutaneous tissue and may involve the tendon, muscle, or bone, on any aspect of the foot, provided it is below the medial aspect of the malleolus
3. The index ulcer will be the largest ulcer if two or more DFUs are present with the same Wagner grade and will be the only one evaluated in the study. If other ulcerations are present on the same foot they must be more than 2 cm distant from the index ulcer
4. Index ulcer (i.e. current episode of ulceration) has been present for greater than four weeks prior to the initial screening visit and less than 1-year, as of the date subject consents for study
5. Index ulcer is a minimum of 0.75 cm2 and a maximum of 25 cm2 at first screening visit (SV1) and first treatment visit (TV1)
6. Adequate circulation to the affected foot as documented by a dorsal transcutaneous oxygen measurement (TCOM) or a skin perfusion pressure (SPP) measurement of ≥ 30 mmHg, or an Ankle Branchial Index (ABI) between 0.7 and 1.3 within 3 months of SV1, using the affected study extremity. As an alternative arterial Doppler ultrasound can be performed evaluating for biphasic dorsalis pedis and posterior tibial vessels at the level of the ankle or a Toe Brachial Index (TBI) of > 0.6 is acceptable
7. The index ulcer has been offloaded for at least 14 days prior to randomization
8. Females of childbearing potential must be willing to use acceptable methods of contraception (birth control pills, barriers or abstinence) during the course of the study and undergo pregnancy tests
9. Subject understands and is willing to participate in the clinical study and can comply with weekly visits

Participant type(s)
Patient

Healthy volunteers allowed

No

Age group
Adult

Lower age limit
18 Years

Sex
All

Total final enrolment
127

Key exclusion criteria
1. Index ulcer(s) deemed by the investigator to be caused by a medical condition other than diabetes
2. Index ulcer, in the opinion of the investigator, is suspicious for cancer and should undergo an ulcer biopsy to rule out a carcinoma of the ulcer
3. Subjects with a history of more than 2 weeks treatment with immune-suppressants (including systemic corticosteroids >10mg daily dose), cytotoxic chemotherapy or application of topical steroids to the ulcer surface within one month prior to SV1, or who receive such medications during the screening period, or who are anticipated to require such medications during the course of the study
4. Subjects taking a selective COX-2 inhibitor (e.g., celexocib) for any condition
5. Subjects on any investigational drug(s) or therapeutic device(s) within 30 days preceding SV1
6. History of radiation at the ulcer site (regardless of time since last radiation treatment)
7. Index ulcer has been previously treated or will need to be treated with any prohibited therapies. (See Section 7.3 of this protocol for a list of prohibited medications and therapies)
8. Presence of any condition(s) which seriously compromises the subject's ability to complete this study or has a known history of poor adherence with medical treatment
9. Osteomyelitis or bone infection of the affected foot near the site of the wound as verified by X-ray within 30 days prior to randomization. (In the event of an ambiguous diagnosis, the Principal Investigator will make the final decision)
10. Subject is pregnant or breast-feeding
11. Presence of diabetes with poor metabolic control as documented with an HbA1c > 12.0 within 90 days of randomization
12. Subjects with end stage renal disease as evidenced by a serum creatinine ≥ 3.0 mg/dL within 120 days of randomization
13. Index ulcer has reduced in area by 20% or more after 14 days of SOC from SV1 to the TV1 /randomization visit

Date of first enrolment
11/09/2017

Date of final enrolment
31/08/2020

Locations

Countries of recruitment

United States of America

Study participating centre
Foot and Ankle Associates of Southwest Virginia
1 Dudley Street
VA
Martinsville
United States of America
24112

Study participating centre
Foot and Ankle Associates of Southwest Virginia
222 Walnut Avenue
VA
Roanoke
United States of America
24016

Sponsor information

Organisation
Microvascular Tissues, Inc.

Funder(s)

Funder type
Industry

Funder Name
Microvascular Tissues, Inc.

Results and Publications

Individual participant data (IPD) sharing plan
The participant level data will be stored in the study database. Since this is a large study (approximately 100 subjects), the participant level data will be provided as demographic information and sub-analyses provided. Individual clinical sites may choose to publish participant level for their sites.

IPD sharing plan summary

Stored in repository

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article		01/09/2021	02/09/2021	Yes	No
Basic results		18/03/2021	19/03/2021	No	No