Submission Title: Improving Bioburden Control and Moisture Management: A Prospective Multi-Center Case Study Evaluating the Wound Healing Effectiveness of a Novel Pharmaceutical Ointment

Sponsor: Aspiera Medical
Primary Product Used: Terrasil Wound Care & Antiseptic Ointment

Aims/Objectives/Goal/Purpose:
Reducing bacterial bioburden and maintaining a moist wound healing environment are key elements in wound bed preparation. A novel pharmaceutical ointment* utilizes a basic law of physics: opposites attract. The ointment is formulated with a multiple-valent complex with positively-charged ions. The outer membrane of bacteria is negatively-charged. This technology was developed to facilitate faster, directed delivery of the active antiseptic to the wound bed. The ointment provides moisture management with jojoba seed oil and organic beeswax to achieve long-lasting moisturization without fear of maceration. This prospective multi-center case series assessed the effectiveness of the ointment in the promotion of wound healing.

Materials and Methods:
At four wound care centers in the United States, 30 adult patients with chronic, non-healing wounds of various etiologies, including diabetic foot, venous and arterial ulcers, traumatic and post-surgical wounds, received the ointment daily, except under compression therapy when it was applied 1-3 times weekly. Length, width, and depth measurements and physician assessments of the wound were taken during the initial visit and then weekly. The patients were followed for up to 12 weeks. Most of the patients self-administered the ointment.

Results:
The ointment controlled bioburden, evidenced by visual observation and random quantitative cultures. The natural emollients provided moisture management as reported by the principal investigators without periwound maceration (no reports of periwound maceration). All patients demonstrated a reduction in wound size with average of 89% surface area reduction in a mean of 26 days of treatment.

Conclusions:
This new topical antimicrobial and moisturizing ointment may be employed to promote faster wound closure through a reduction in bacterial bioburden and maintenance of a moist wound healing environment

*Terrasil Wound Care & Antiseptic Ointment

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Submission Title: Bacterial protease activity (BPA), an indicator of bacterial pathogenicity in chronic wounds even in the absence of clinical signs.

Primary Product Used: Diagnostic Testing

Background:
Excessive bacteria in chronic ulcers impairs wound healing and left untreated can progress to systemic infection. Chronic wounds are particularly challenging because they may not exhibit the clinical signs of infection. As a result, examination alone can under estimate wound bioburden. In addition, current culture techniques have limited reliability in chronic wounds. Bacterial protease activity (BPA) may represent an accurate method of detecting pathogenic bacteria even before clinical evidence of infection is present. Bacterial proteases are a type of virulence factor present when bacteria are in a pathogenic state. This study evaluates BPA as a diagnostic test for bacterial bioburden.

Materials and Methods:
186 patients with chronic wounds were assessed for the clinical signs of infection and underwent swabbing for BPA and quantitative bacteriology. BPA was assessed using a quantitative fluorometric assay for Casein modified with an inhibitor of the predominant host proteases (e.g. Human Neutrophil Elastase) to ensure that only BPA was detected

Results:
Only twenty percent (20%) of the wounds swabs exhibited clinical signs of infection. In contrast, 47% of wounds had elevated BPA; of these, 72% had no clinical signs of infection suggesting that although pathogenic bacteria were present the wounds had not progressed to overt infection (critical colonization). Interestingly, the majority of wounds analyzed (80%) had quantitative bacterial levels greater than 105 cfu/gm, currently the most frequently cited threshold for infection. In addition, of the samples with CFU > 105 42% were BPA positive and 39% BPA negative indicating that absolute bacterial counts did not correlate with levels of pathogenic bacteria.

Conclusions:
BPA detects pathogenic bacteria in chronic wounds prior to the clinical signs of infection. This diagnostic may be useful in determining excessive bioburden in wounds at the critical colonization stage permitting treatment prior to the onset of more invasive infection.

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Submission Title: A Prospective Multi-center Case Series Evaluating the Effectiveness of Sodium Hypochlorite as an Antiseptic in Chronic Wound Care

Sponsor: Angelini Pharma
Primary Product Used: ExSept Wound Wash

Background: It has long been known that excess bacterial bioburden impairs wound healing. Sodium hypochlorite, an electrolytically produced sodium hypochlorite solution*, has bactericidal properties and a favorable toxicity profile. This multi-center prospective case series assessed the in-vivo effectiveness of Sodium hypochlorite in promoting closure in chronic wounds by reducing bacterial bioburden.

Methods: Seventeen patients with chronic wounds of varying etiologies were followed for up to 12 weeks. Wound etiologies included diabetic foot and venous leg ulcers, wounds complicated by osteomyelitis, and surgical wounds; treatment regimens included hyperbaric oxygen, skin grafting, silver and collagen dressings, and multilayer compression. Sodium hypochlorite solution was used as a wound cleansing solution at each dressing change and prior to any debridement. Length, width, and depth measurements as well as percent granulation tissue were measured at each patient visit. The trial continued until in the physician's opinion antiseptics were no longer required or until complete wound healing had been achieved.

Results: Fifteen patients had decreased wound size with an average of 51.7% ± 53.7% surface area reduction and an average treatment length of 35.8 ± 19.9 days. Three patients experienced total wound closure in 30.0 ± 10.2 days. One patient had complete wound healing after 18 days but returned with a recurrence and underwent a successful second treatment. Physician assessments revealed an increase in healthy granulation tissue in 70% of the patients evaluated with an average increase of 187%. A decrease in slough and fibrin was also reported.

Conclusion: An Electrolytically produced sodium hypochlorite wound antiseptic may result in increased granulation tissue and improved wound closure.

*ExSept Plus Wound Cleanser - Angelini Pharma

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Submission Title: Indocyanine Green Angiography (ICGA) Performed in the Wound Care Center as a Guide to Excisional Debridement in Diabetic Foot Ulcers

Sponsor: Novadaq
Primary Product Used: Fluorescence Angiography

Background:
Indocyanine Green Fluorescence angiography (ICGA) assesses perfusion at the microvascular level. It has become an essential tool in the operating theater reducing post-operative complications in coronary artery bypass grafting, plastic and reconstructive surgery, abdominal wall component separation, colorectal and other surgical procedures. The use of ICGA can be expanded beyond the operating room to the wound care center. The Fluorescence Angiography system* evaluates perfusion in lower extremity wounds, such as diabetic foot ulcers.

Materials and Methods:
Five patients with Wagner III diabetic foot ulcers under consideration for hyperbaric oxygen therapy (HBOT) underwent evaluation of perfusion to the foot using ICGA. 2.5ml indocyanine green followed by 10ml flush of saline is injected through an intravenous line in a peripheral vein. The fluorescence is noted on the monitor 10 to 20 seconds after injection. The foot is imaged using the system over the next five minutes and perfusion percentages are measured. It is important to note that operates on the principles of near infrared light therefore ambient light may affect the quality of the image.

Results:
The flurescence angiography system permitted the wound care physician to evaluate the perfusion to the angiosome in which the wound is located. The procedures were performed in the wound clinic without adverse events. The five patients had adequate flow. They were deemed to be appropriate candidates for HBOT. The investigators observed that in the majority of the patients there were areas in the periwound that did not have adequate perfusion indicating non-viable tissue was present. These areas were then excised sharply. All of the wounds improved with a reduction in wound surface area over four week follow-up period.

Conclusions:
Fluorescence angiography measures skin perfusion. In addition, it can be used to guide debridement of diabetic foot ulcers.

*LUNA® - Novadaq

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Submission Title: A Multi-center Randomized Controlled Clinical Trial Evaluating Two Application Regimens of Dehydrated Human Amniotic Membrane and Standard of Care vs. Standard of Care Alone in the Treatment of Venous Leg Ulcers.

Sponsor: MiMedx
Primary Product Used: Epifix

Background:
Venous leg ulcers pose significant clinical, humanistic and economic burdens on society. Standard of care (SOC), multi-layer compression, results in healing of only 50% of venous leg ulcers in 12 weeks. Dehydrated Human amniotic membrane* (dHAM) promotes healing by replacing damaged extracellular matrix and providing cytokine growth factors. This randomized controlled clinical trial was designed to evaluate the efficacy of dHAM in the treatment of venous leg ulcers.

Materials and Methods:
A multi-center, randomized, controlled open-label clinical trial evaluating the safety and efficacy of dHAM (1 application or 2 applications two weeks apart) plus multi-layer compression versus multi-layer compression alone (Coban-2, 3M) in the treatment of venous leg ulcers was conducted at six geographically distinct sites in the United States. The trial utilized a surrogate endpoint which is known to be a predictor of healing at 12 weeks: The primary outcome measure was the proportion of ulcers achieving 40% wound closure at 4 weeks comparing SOC alone to one or two applications of dHAM.

Results:
71 participants have been enrolled to date in this ongoing trial: 24 ulcers were randomized to one application of dHAM; 23 to two applications of dHAM and 24 received SOC alone. At 4 weeks, 66.7% of wounds in the single dHAM application group, 57.1% in the double dHAM application group and 26.7% of the standard of care group demonstrated greater than 40% wound closure at 4 weeks. The combined dHAM groups had a 62.1% wound closure rate at 4 weeks. There was a significant difference in wound area reduction between the dHAM groups and standard of care at the 4-weeks.

Conclusions:
Dehydrated human amniotic membrane resulted in more rapid healing of venous leg ulcers compared to standard of care at the surrogate endpoint of percentage of wound area reduction at four weeks.

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Submission Title: Human Placental Connective Tissue Matrix in the Treatment of Chronic Wounds A Prospective Multi-Center Case Series

Primary Product Used: Dermavest

Background: In recent years, application of amniotic membrane has expanded to the treatment of diabetic and venous stasis ulcers, postsurgical wound dehiscence and chronic wounds. In this case series, we evaluated the efficacy of a Human Placental Connective Tissue Matrix Graft*.

Methods: This prospective, multicenter case series evaluated wound healing time and wound characteristics of fifteen patients with various etiologies. Up to two, six cm2 pieces of the Graft* were used per application on wounds ranging up to 44 cm2. The average number of applications was 2 with a max of 4. Length, width, and depth measurement as well as percent granulation tissue were measured at each weekly visit using a wound imaging camera. The wounds were cleaned and debrided based on the physician's discretion.

Results: All patients demonstrated a decrease in wound size and depth. There were no graft-related adverse events. The age of the ulcers ranged from 3 weeks to 4 years. There was also a notable decrease in would exudate and odor in all ulcers treated.
For the diabetic and venous ulcer cases:

- The week 4 PAR (Percent Area Reduction) was 59% (71% diabetic and 50% venous).
- 62% (80% diabetic and 50% venous) of the cases had a week 4 PAR > than 40%.

For the diabetic and venous ulcer cases that started with a wound size < 20 cm2 and where one six cm2 Graft* was used per application:

- The week 4 PAR was 70% (82% diabetic and 62% venous).
- 80% (100% diabetic and 67% venous) of the cases had a week 4 PAR > than 40%.

Conclusion: The Graft* was effective in reducing wound size and improving wound bed characteristics in chronic wounds.

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Submission Title: A Prospective, Multi-center Cooperative Group Study to Evaluate the Effectiveness of Epidermal Grafting

Primary Product Used: Cellutome Epidermal Grafting

Introduction: Epidermal grafting is an evidenced-based reconstructive option to promote healing in acute and chronic wounds. However, until recently, its use was limited to a few investigational trials because of the laborious and arduous harvesting techniques. Introduced in 2013 an automated epidermal harvesting device* produces more than 100 epidermal grafts at the bedside with minimal patient discomfort in 20 to 40 minutes.

Methods: This prospective, multi-center cooperative group study evaluated the effectiveness of epidermal grafting in the treatment of acute and chronic wounds of various origins (diabetic, venous, traumatic, pyoderma and post-surgical). Patients with granulating wounds, free of non-viable tissue, underwent one epidermal graft application. Wound assessment and planimetric measurements were performed weekly in the wound center for a total of four weeks.

Results: 24 patients from three geographically distinct wound centers with a variety of chronic ulcers underwent epidermal grafting with micrografts harvested using the System*, 87.5% of the wounds demonstrated improvement with decreased wound surface area with four wounds achieving complete closure in four weeks. There were three wounds that either did not improve or worsened. All of the grafts were harvested from the inner thigh without anesthesia. There were no donor site adverse events with 100% healed during the trial. The one patient with pyoderma gangrenosum did not suffer from pathergy at the donor site. Approximately 50% of the wounds treated exhibited "graft take" to some degree. Those that did not, healed from the margins as is seen with other cellular and tissue-based products (CTP).

Conclusions: Epidermal grafting was effective in promoting healing of XX patient's chronic wounds. The results of this prospective series informed the ongoing randomized controlled clinical trial evaluating the efficacy of epidermal grafting in venous leg ulcers.

* CelluTome® - Epidermal Grafting

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