Comparison of Negative Pressure Wound Therapy Utilizing Vacuum-Assisted Closure to Advanced Moist Wound Therapy in the Treatment of Diabetic Foot Ulcers—A Multicenter Randomized Controlled Trial

Peter A. Blume, DPM$^1$
Jodi Walters, DPM$^2$
Wyatt Payne, MD$^3$
Jose Ayala, MD$^4$
John Lantis, MD$^5$

$^2$Southern Arizona Veterans Affairs Medical Center, Surgery, Tucson, AZ
$^3$Institute for Tissue Regeneration, Repair, and Rehabilitation, Bay Pines VA Healthcare System, Bay Pines, FL and The University of South Florida, Division of Plastic Surgery, Tampa, FL
$^4$Valley Baptist Hospital, Brownsville, TX

Running Title: VAC NPWT: Diabetic Foot Ulcer RCT

Corresponding Author:
Dr. Peter A. Blume
North American Center for Limb Preservation
506 Blake Street, New Haven, CT 06515
peter.b@snet.net

Received for publication 19 November 2007 and accepted in revised form 18 December 2007
**ABSTRACT**

*Objective:* To evaluate safety and clinical efficacy of Negative Pressure Wound Therapy (NPWT) compared to Advanced Moist Wound Therapy (AMWT) to treat diabetic patients with foot ulcers.

*Research Design And Methods:* This multicenter randomized controlled trial enrolled 342 patients mean age 58 years; 79% male. Complete ulcer closure was defined as skin closure (100% re-epithelization) without drainage or dressing requirements. Patients were randomized to either NPWT (Vacuum-Assisted Closure) or AMWT (predominately hydrogels and alginites) and received standard off-loading therapy as needed. The trial evaluated treatment until Day 112 or ulcer closure by any means. Patients whose wound achieved ulcer closure were followed at 3 and 9 months. Each study visit included closure assessment by wound exam and tracings.

*Results:* A greater proportion of foot ulcers achieved complete ulcer closure with NPWT (73/169, 43.2%) than AMWT (48/166, 28.9%) within the 112-day Active Treatment Phase (p=0.007). Kaplan-Meier median estimate for 100% ulcer closure was 96 days (95% CI: 75.0, 114.0) for NPWT and not determinable for AMWT (p=0.001). NPWT patients experienced significantly (p=0.035) fewer secondary amputations. The proportion of home care therapy days to total therapy days for NPWT was 9471/10579 (89.5%) and 12210/12810 (95.3%) for AMWT. In assessing safety, no significant difference between the groups was observed in treatment-related complications such as infection, cellulitis, and osteomyelitis at 6 months.

*Conclusions:* NPWT appears to be as safe as, and more efficacious, than AMWT for the treatment of diabetic foot ulcers.

This study was registered with ClinicalTrials.gov as NCT00432965.
In 2005, the Centers for Disease Control estimated the prevalence of Diabetes in the United States to be 20.8 million people. A disabling complication with this disease is foot ulcer development, which leads to non-healing chronic wounds that are difficult to treat. Moreover, diabetic foot ulcers (DFUs) are a significant risk factor for nontraumatic foot amputations in persons with diabetes. Various DFU treatments have been reported in the literature, including advanced moist wound therapy (AMWT), bioengineered tissue or skin substitutes, growth factors, electric stimulation, and negative pressure wound therapy (NPWT). The treatment success is dependent on ulcer chronicity, patient compliance, appropriate off-loading of the appendage, and the therapy’s mechanisms of action.

NPWT is a non-invasive system that creates a localized controlled subatmospheric (negative) pressure environment. In this study NPWT was provided by the Vacuum-Assisted Closure Therapy System (KCI USA, San Antonio, Texas) which promotes wound healing by delayed primary or secondary intention through creating a moist wound environment, preparing the wound bed for closure, reducing edema, and promoting granulation tissue formation and perfusion. Vacuum-Assisted Closure Therapy is indicated for use in all care settings and in patients with a variety of wound types including diabetic foot ulcers.

This multicenter randomized controlled trial (RCT) evaluated the safety and efficacy of NPWT compared to AMWT (predominately hydrogels and alginates) for the treatment of DFUs. The cost benefit analysis will be reported in a future publication.

**RESEARCH DESIGN AND METHODS**

The patient population consisted of diabetic adults ≥18 years with a Stage 2 or 3 (as defined by Wagner’s Scale) calcaneal, dorsal or plantar foot ulcer ≥ 2 cm² in area after debridement. Adequate blood circulation (perfusion) was assessed by Dorsum Transcutaneous Oxygen Test (TcPO₂) ≥ 30 mmHg, Ankle Brachial Index (ABI) ≥ 0.7 and ≤ 1.2 with toe pressure ≥ 30 mmHg, or Doppler arterial waveforms that were triphasic or biphasic at the ankle of the affected leg. Patients with recognized active Charcot disease; ulcers resulting from electrical, chemical or radiation burns; presence of untreated osteomyelitis, cellulitis, collagen vascular disease, or ulcer malignancy were excluded from the study. Patients with uncontrolled hyperglycemia (HbA₁c >12%) or inadequate lower extremity perfusion were not enrolled. Exclusion criteria also included ulcer treatment with normothermic or hyperbaric oxygen therapy; concomitant medications such as corticosteroids, immunosuppressive medications, or chemotherapy; recombinant or autologous growth factor products; skin and dermal substitutes within 30 days of study start; or use of any enzymatic debridement treatments. Pregnant or nursing mothers were excluded from study participation.

The NPWT system utilized in this study was Vacuum Assisted Closure Therapy. The system consists of 3 components: a negative pressure generating unit with a disposable canister, a pad with evacuation tube, and a reticulated, open cell sterile polyurethane or a dense open-pore polyvinyl alcohol foam dressing cut to fit the wound. The system unit is programmed to deliver controlled negative pressure ranging from 50 to 200 mmHg. NPWT was applied to the ulcer as specified by manufacturer’s guidelines and treated until ulcer closure, sufficient granulation tissue formation for healing by primary, secondary or surgical intention, or Day 112.
AMWT dressings were used according to Wound, Ostomy and Continence Nurses (WOCN) Society guidelines (6), and institutional treatment protocols, consistent with standards of care for treating DFUs. Skin substitutes, cytokines, recombinant human platelet-derived growth factors, or similar therapies as outlined in the exclusion criteria were not used in either group during the Active Treatment Phase (ATP).

The primary efficacy endpoint was incidence of complete ulcer closure. Secondary endpoints included reduction of ulcer surface area over time, time to achieve ulcer closure by either surgery or secondary intention, and reduction in complications, including secondary amputations. Complete ulcer closure was defined as skin closure (100% re-epithelization) without drainage or dressing requirements.

The sample size was based on a type I error probability set at 0.05, with 80% power. Detection of a 20% difference between treatment groups required 206 evaluable patients with a treatment-to-study ratio of 1:1. Sample size was set at 338 to account for subject withdrawal or loss to follow-up.

Randomization was accomplished by generating blocks of numbers through www.randomizer.org. Numbers were assigned to a treatment group and sealed in opaque envelopes containing black paper labeled with treatment and patient ID. Envelopes were sequentially numbered prior to clinical trial site distribution. At patient randomization, treatment was assigned based on the next sequentially labeled envelope.

FDA guidelines (15) state that in some devices, it is impractical or unethical to implement a control treatment that mimics the test product and allows masking. In this study, the physical differences between treatment regimens (eg, hydrogels and NPWT) can be so distinctive that it is not possible to blind either the patient or physician to the treatment post randomization.

**Study design.** This study was a prospective RCT initiated at 37 diabetic foot and wound clinics, and hospitals. A total of 342 patients were enrolled at 1 Canadian and 28 USA sites. Prior to randomization, patients were screened for neuropathy, adequate perfusion, and glycemic control. All foot ulcers were assessed and debrided as needed within two days of randomization.

Patients were examined weekly for the first 4 weeks (Day 28) then every other week until Day 112, or ulcer closure by any means. At each study visit, ulcers were assessed for area via wound tracing, ulcer closure, and/or adequate granulation tissue formation. NPWT dressing changes were performed every 48 to 72 hours, no less than 3 times per week. AMWT randomized patients were treated based on manufacturer’s guidelines. All patients received off-loading therapy as deemed necessary. Patients achieving ulcer closure were followed at 3 and 9 months.

**Statistical analysis.** The KCI Global Biometrics Group conducted the safety and effectiveness data analyses for this trial. Primary analysis was based on an intention-to-treat (ITT) dataset composed of all randomized patients who signed an informed consent and received at least one post-baseline treatment.

Continuous demographic variables (age, gender, etc.) were summarized for the study population as descriptive statistics (number, mean, Standard Deviation [SD]), median, minimum, and maximum values, and 95% two-sided confidence limits and compared between groups with a two-sample *t*-test or Wilcoxon Rank-Sum test.

An interim ITT analysis of the primary endpoint was conducted at the enrollment of 275 patients to confirm the consistency of trial design assumptions with observed data. The Lan-Demets group sequential boundaries (two-sided symmetric boundaries) were calculated.
using the alpha-spending function of O’Brien-Fleming.

Data were analyzed based on differences in incidence of closure between treatment groups and assessed with a test of proportions, using chi-square or Fisher’s Exact test, as appropriate. Treatment differences in ulcer area (cm$^2$) were calculated (ulcer area [cm$^2$] = ulcer length [cm] x ulcer width [cm] x π/4) and analyzed using Analysis of Covariance (ANCOVA) with baseline area used as a covariate. Median time to closure was based on number of days from baseline until closure via Kaplan-Meier (KM) survival analysis. Patients not achieving closure were censored using last date of observation.

RESULTS

Figure 1 describes the patient flow through each stage of this RCT including discontinued patients. During the course of the study, 384 patients were consented and screened for inclusion. Of these, 42 patients were excluded due to inclusion/exclusion criteria, patient refusal to participate, or withdrawal of consent, and 342 were enrolled. Seven patients did not receive treatment and 335 patients were analyzed. All patient data collected during ATP were included in the ITT analyses.

The data suggest that no statistically significant demographic differences existed between treatment arms (Table 1). The mean patient population age was 58 years and predominantly male (78.5%). Percentages of patients treated for study ulcer infections at baseline were 29.6% (50/169) for NPWT and 27.1% (45/166) for AMWT. The randomization method resulted in an even distribution of characteristics between treatment groups.

Patients receiving off-loading were 164/169 (97.0%) for NPWT and 162/166 (97.6%) for AMWT. Patients were treated in both acute and home care settings. The proportion of home care therapy days to total therapy days was 9471/10579 (89.5%) for NPWT and 12210/12810 (95.3%) for AMWT.

Efficacy. Complete ulcer closure was defined as skin closure (100% re-epithelization) without drainage or dressing requirements. Within ATP, the NPWT group proportion was significantly (p=0.007) greater for complete ulcer closure than the AMWT group (73/169, 43.2% vs. 48/166, 28.9%). For patients completing ATP, completers analysis significantly (p=0.001) confirmed that a greater percentage of NPWT treated ulcers (60.8%, 73/120) achieved ulcer closure compared to AMWT (40.0%, 48/120). After sufficient wound bed preparation, 9.5% (16/169) NPWT-treated ulcers and 8.4% (14/166) AMWT-treated ulcers were surgically closed by split thickness skin grafts, flaps, sutures, or amputations. KM median time to complete ulcer closure was 96 days (95% CI: 75.0, 114.0) for NPWT (p=0.001). AMWT median time to complete ulcer closure could not be estimated. (Figure 2). The NPWT mean duration of therapy was 63.6 days (SD 36.57) versus 78.1 days (SD 39.29) for AMWT.

To further evaluate NPWT effects, 75% ulcer closure, degree of granulation tissue formation, and ulcer area reduction were assessed. Significantly more NPWT patients (105/169, 62.1%) achieved 75% ulcer closure than AMWT patients (85/166, 51.2%; p=0.044). NPWT KM median estimate for 75% ulcer closure was 58 days (95% CI: 53.0, 78.0) and 84 days (95% CI: 58.0, 89.0) for AMWT (p=0.014). In assessing ulcer area, a significant difference between NPWT (-4.32 cm$^2$) and AMWT (-2.53 cm$^2$) from baseline was achieved on Day 28 (p=0.021).

The clinical treatment effect on wound bed preparation was assessed in 46 patients (24 NPWT, 22 AMWT), who presented with 0-10% granulation at baseline and achieved 76-100% granulation. Of these, 17/24 (70.8%) NPWT and 8/22 (36.4%) AMWT patients achieved 76-100% granulation tissue formation.
NPWT KM median estimates for 76-100% granulation tissue formation were 56 days (95% CI: 42.0, 84.0) and 114 (95% CI: 44.0, -) for AMWT (p=0.022).

Safety. Table 2 reports treatment-related rates for secondary amputations, edema, wound infection, cellulitis, osteomyelitis, staphylococcal infection, and infected skin ulcers at 6 months. Significantly (p=0.035) fewer amputations were observed in NPWT patients (7/169, 4.1%) compared to AMWT patients (17/166, 10.2%). The majority of these amputations (2 and 13, respectively) were minor amputations. In all other categories, no significant differences were observed.

CONCLUSIONS

Results of the largest NPWT RCT to date demonstrate that NPWT is as safe as, and more efficacious, than AMWT in the treatment of DFUs. A significantly greater number of NPWT patients achieved complete ulcer closure and granulation tissue formation compared to AMWT patients. This was supported by a significant reduction in median time needed to heal DFUs. Approximately 90% of therapy days occurred in the home care setting for both treatments.

No significant difference was observed in ulcer related complications such as infection, cellulitis, and osteomyelitis. However, the study showed that AMWT patients had more than twice as many secondary amputations than those receiving NPWT.

Chronic DFUs present a significant challenge to treating physicians.(16) Treatment involves multiple modalities including debridement, assessment and treatment of infection, revascularization if indicated, and sufficient off-loading of the foot.(17) A key component of the healing process is debridement because it enables removal of devitalized and necrotic tissue. Debridement is critically important to the initiation of healing. NPWT and other wound healing technologies work in conjunction with debridement as the foundation upon which the wound healing process can begin.(18) As observed in this clinical trial, the use of NPWT in concurrence with debridement of the affected foot increases the number of DFUs healed and decreases the length of time required for ulcer healing as compared to AMWT. In addition, the prescription of off-loading may have also contributed to positive results in both groups. Therefore, it appears that NPWT in addition to established standards of care enhances successful healing and closure of DFUs.

In this study, 14.3% more NPWT patients achieved complete ulcer closure in less median time to closure than those treated with AMWT. This parallels the findings by Argenta and Morykwas in 1997, in which they reported that the success of NPWT in chronic wounds is associated with removal of excess interstitial fluid, an increase in vascularity and associated decrease of bacterial colonization, and stimulation of granulation tissue formation through the response of wound tissue to the mechanical forces exerted by the application of negative pressure through the foam dressing.(10) In separate studies, Saxena (18) and Greene (19) have further elucidated the role of open pore foam dressing in the creation of micromechanical deformations of the wound surface. These micromechanical deformations are caused when negative pressure draws tissue into the foam pores. This stretches cells and promotes cell division that stimulates granulation tissue formation.(18)

As NPWT use has grown, the use of NPWT for wound bed preparation in conjunction with either delayed primary or secondary wound closure has also increased. In 2005, Armstrong and Lavery reported that the use of NPWT may be an alternative therapy to achieve an improved granulating wound bed in diabetic foot wounds in order to prepare the wound bed...
for other closure techniques. As shown in these data and previous studies, NPWT promotes granulation tissue formation, thereby allowing the clinician to determine course of closure.

DFUs are a significant risk for amputation. In this study, the incidence of secondary amputations was significantly less (p=0.035) for NPWT (4.1%) compared to AMWT (10.2%). This finding substantiates other reports, in which diabetic foot wounds treated with NPWT trended towards fewer secondary amputations (p=0.060) than those treated with AMWT. While the exact mechanism of the decrease in secondary amputations remains unclear, treatment of DFUs with NPWT appears to promote significant healing.

This study of 342 patients with DFUs showed that NPWT is as safe as and more efficacious than AMWT for the treatment of diabetic foot ulcers.

ACKNOWLEDGMENTS
KCI USA Incorporated (San Antonio, TX) supported this study. Conference abstracts reporting preliminary and interim study data were presented at the 2003 Symposium on Advanced Wound Care, 2004 World Union of Wound Healing Societies meeting, 2007 Symposium on Advanced Wound Care, and 2007 American Podiatric Medicine Association meeting. Investigators who enrolled patients for the V.A.C.® Therapy Diabetic Foot Ulcer Study were: Charles Anderson, MD, Madigan Army Hospital, Tacoma, WA; David Armstrong, DPM, North Chicago VA Medical Center and Rosalind Franklin University, North Chicago, IL; Jose Ayala, DPM, Valley Baptist Hospital, Brownsville, TX; John Bennett, DPM, Des Moines University, Des Moines, IA; Scott Berman, MD, Tucson Vascular Surgery, Tucson, AZ; Peter Blume, DPM, North American Center for Limb Preservation, New Haven, CT; Milton Boden, MD, Aim Research, Atlanta, GA; William Bogey, MD, East Carolina University, Greenville, NC; Marc Dolce, DPM, Cleveland Foot and Ankle Clinic, Cleveland, OH; Kenneth Dolynchuk, MD, Saint Boniface General Hospital, Manitoba, Winnipeg, Canada; Tamara Fishman, DPM, Primary Foot Care Center, Incorporated, North Miami Beach, FL; Gabriel J. Halperin, DPM, Innovative Medical Technologies, Los Angeles, CA; Allen Holloway, MD, Maricopa Medical Center, Phoenix, AZ; John Lantis, MD, Saint Luke's Roosevelt, New York, NY; Brock Liden, DPM, Circleville Foot and Ankle, LLC, Circleville, OH; Jeffrey Page, DPM, Carl T. Hayden VA Medical Center, Podiatry Section, Phoenix, AZ; Marc Passman, MD, Vanderbilt University Clinical Trials Center, Nashville, TN; Wyatt Payne, MD, Bay Pines Veterans Affairs Medical Center, Bay Pines, FL; Alexander Reyzelman, DPM, Bay Area Foot Care, Castro Valley, CA; Bret Ribotsky, DPM, Podiatric Success, Inc., Boca Raton, FL; Kathleen Satterfield, DPM, Texas Diabetes Institute - University of Texas Health Science Center San Antonio, San Antonio, TX; Bhavesh Shah, DPM, South Texas Foot Institute, Poth, TX; David Skrobot, DPM Genesis Health Care System, Zanesville, OH; Rodney Stuck, DPM, Hines Veterans Affairs Hospital, Hines, IL; Arthur Tallis, DPM, Hope Research Institute, Phoenix, AZ; Mike Vaardahl, DPM, Banner Health at North Colorado Medical Center, Greeley, CO; Jodi Walters, DPM, Southern Arizona Veterans Affairs Medical Center, Department of Surgery, Tucson, AZ; Robert Wunderlich, DPM, San Antonio, TX.
REFERENCES

9. Robson MC, Payne WG, Garner WL, Biundo J, Giacalone VF, Cooper DM, Ouyang P: Integrating the results of phase IV (postmarketing) clinical trial with four previous trials reinforces the position that Regranex (becaplermin) gel 0.01% is an effective adjunct to the treatment of diabetic foot ulcers. J Appl Res 5: 35-45, 2005
### TABLE 1. Patient demographics

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>NPWT* n=169</th>
<th>AMWT n=166</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>58 ± 12</td>
<td>59 ± 12</td>
</tr>
<tr>
<td>Sex (M/F)</td>
<td>141/28 (83/17)</td>
<td>122/44 (73/27)</td>
</tr>
<tr>
<td>Race</td>
<td></td>
<td></td>
</tr>
<tr>
<td>African American</td>
<td>28 (16.6)</td>
<td>22 (13.3)</td>
</tr>
<tr>
<td>Caucasian</td>
<td>95 (56.2)</td>
<td>100 (60.2)</td>
</tr>
<tr>
<td>Hispanic</td>
<td>41 (24.3)</td>
<td>40 (24.1)</td>
</tr>
<tr>
<td>Other</td>
<td>2 (1.2)</td>
<td>1 (0.6)</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>99.2 ± 25.1</td>
<td>93.8 ± 25.6</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>175.0 ± 9.6</td>
<td>175.0 ± 12.4</td>
</tr>
<tr>
<td>Current Smoker</td>
<td>34 (20.1)</td>
<td>32 (19.4)</td>
</tr>
<tr>
<td>Currently Use Alcohol</td>
<td>37 (21.9)</td>
<td>45 (27.1)</td>
</tr>
<tr>
<td>Type of Diabetes</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Type 1</td>
<td>15 (8.9)</td>
<td>14 (8.4)</td>
</tr>
<tr>
<td>Type 2</td>
<td>154 (91.1)</td>
<td>152 (91.6)</td>
</tr>
<tr>
<td>Pre-albumin (g/L)</td>
<td>21.1 ± 7.6</td>
<td>19.9 ± 7.9</td>
</tr>
<tr>
<td>Albumin (g/L)</td>
<td>3.4 ± 0.6</td>
<td>3.4 ± 0.8</td>
</tr>
<tr>
<td>Characteristics</td>
<td>NPWT* n=169</td>
<td>AMWT n=166</td>
</tr>
<tr>
<td>----------------------------------------</td>
<td>-------------</td>
<td>------------</td>
</tr>
<tr>
<td>HbA1c</td>
<td>8.3 ± 2.0</td>
<td>8.1 ± 1.9</td>
</tr>
<tr>
<td>ABI (mmHg)</td>
<td>1.0 ± 0.2</td>
<td>1.0 ± 0.2</td>
</tr>
<tr>
<td>Transcutaneous oxygen tension (TcPO2; mmHg)</td>
<td>43.2 ± 10.4</td>
<td>43.3 ± 12.5</td>
</tr>
<tr>
<td>Loss of Protective Sensation†</td>
<td>150 (90.4)</td>
<td>143 (88.8)</td>
</tr>
<tr>
<td>Ulcer Duration Prior to Treatment (days)</td>
<td>198.3 ± 323.5</td>
<td>206.0 ± 365.9</td>
</tr>
<tr>
<td>Baseline Wound Area (cm²)</td>
<td>13.5 ± 18.2</td>
<td>11.0 ± 12.7</td>
</tr>
<tr>
<td>Received Off-Loading Therapy</td>
<td>164 (97.0)</td>
<td>162 (97.6)</td>
</tr>
<tr>
<td>Treated for Ulcer Infection Prior to Randomization</td>
<td>50 (29.6)</td>
<td>45 (27.1)</td>
</tr>
</tbody>
</table>

Therapy Received at Treatment Initiation

- NPWT: 169 (100)
- Hydrogel: 78 (47.0)
- Alginate: 31 (18.7)
- Other: 28 (16.9)
- Saline: 17 (10.2)
- Collagen: 11 (6.6)
- Hydrocolloid: 1 (0.6)

*Data are means ± SD or n (%) †Percentage based on available data
## TABLE 2. Results of safety analysis

<table>
<thead>
<tr>
<th>MeDRA System Organ Class</th>
<th>NPWT n=169 (%)</th>
<th>AMWT n=166 (%)</th>
<th>P-Value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Secondary Amputations</td>
<td>7 (4.1)</td>
<td>17 (10.2)</td>
<td>0.035</td>
</tr>
<tr>
<td>Edema</td>
<td>5 (3.0)</td>
<td>7 (4.2)</td>
<td>0.571</td>
</tr>
<tr>
<td>Wound Infection</td>
<td>4† (2.4)</td>
<td>1‡ (0.6)</td>
<td>0.371</td>
</tr>
<tr>
<td>Cellulitis</td>
<td>4 (2.4)</td>
<td>1 (0.6)</td>
<td>0.371</td>
</tr>
<tr>
<td>Osteomyelitis</td>
<td>1 (0.6)</td>
<td>0 (0.0)</td>
<td>--</td>
</tr>
<tr>
<td>Staphylococcus Infection</td>
<td>1 (0.6)</td>
<td>0 (0.0)</td>
<td>--</td>
</tr>
<tr>
<td>Infected Skin Ulcer</td>
<td>1 (0.6)</td>
<td>2 (1.2)</td>
<td>0.620</td>
</tr>
</tbody>
</table>

*Fisher’s Exact Test
†1 moderate, 3 mild
‡1 moderate
FIGURE 1

VAC NPWT: Diabetic Foot Ulcer RCT

Lost to Follow-up (n=1)
Reasons:
Did not return for next visit
Discontinued (n=54)

Allocated NPWT (n=172)
Received NPWT (n=169)
Did Not Receive NPWT (n=3)

Lost to Follow-up (n=5)
Reasons:
3 Did not return for next visit
1 Developed gangrene of foot
1 Incarcerated

Discontinued (n=43)
Reasons:
8 Self Withdrawal
10 Withdrawals by Investigator
5 Ineffective Therapy
15 Adverse Events
3 Death
1 Exclusionary Methods
Incomplete Data (n=1)

Allocated AMWT
(n=169)
Received AMWT
(n=166)
Did Not Receive AMWT
(n=3)

Intent to Treat (n=169)

Intent to Treat (n=166)