PICO◇ Single Use Negative Pressure Wound Therapy System demonstrated greater reduction in wound area compared to Traditional Negative Pressure Wound Therapy in the treatment of Chronic Ulcers of the Lower Extremities

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Introduction

- Most leg ulcers (at least 70%) are the result of chronic venous insufficiency[1] and others are due to mixed venous and arterial disease.[2] Assuming good arterial blood supply, continuous compression therapy is the gold standard treatment for venous leg ulcers.[3]
- DFUs affect 15 – 25% of all diabetic subjects during their lifetime[1,4,5] and precede 84% of all lower leg amputations.[6] The management of DFUs is based in three principles: off-loading, appropriate local wound management (including surgical debridement) and infection control.[7]
- For DFUs that fail to improve (>50% wound area reduction) after 4 weeks of standard wound therapy, the Society for Vascular Surgery and others recommends to consider the use of adjunctive wound therapy options, which include Negative Pressure Wound Therapy (NPWT).[8]
- While many traditional Negative Pressure Wound Management (tNPWT) systems are available, comparative studies have demonstrated equivalent clinical outcomes.[9,10] tNPWT may be complicated to apply and use, require a skilled well trained technician, and the size of the pump and the canister may be intrusive and limit patient mobility.[3,10,11]
- Single Use Negative Pressure Wound Therapy (sNPWT) systems, which are smaller and disposable are now available. Based on the same principles of action of tNPWT systems,[10] single-use NPWT systems are expected to simplify the application and management of NPWT, at the same time making the therapy accessible to more patients, including active and homebound individuals.[12]

Materials and methods

- Randomized, controlled, multicenter study designed to compare the clinical effectiveness of two different types of NPWT (PICO sNPWT and tNPWT) to compare the percentage change in target ulcer dimensions in patients with chronic lower extremity wounds, either VLUs or DFUs
- Patients were screened and followed up for at least one week before being randomized to one of the two treatment groups, and were followed weekly for 12 weeks or until ulcer healed, whichever occurred first
- The study was performed in compliance with the ethical principles of the Declaration of Helsinki, Good Clinical Practice (GCP), ISO 14155:2011, and under governing IRB/IEC review and approval of the study protocol
- Eighteen wound care centers participated in the trial (16 in the USA and two in Canada)

Study endpoints

- The primary endpoint was to assess the percentage change in target wound area over a 12-week period from baseline for non-inferiority
- Secondary endpoints were the percentage change in the target ulcer depth and volume

Study device

- PICO is a single-use NPWT system indicated for patients who would benefit from a suction device as they may promote healing via removal of low to moderate levels of exudate and infectious materials. It is a battery powered system delivering continuous negative pressure at an average -80mmHg. This lightweight device is canisterless. The dressing incorporates a silicone interface, a patented AIRLOCK© Technology layer that transmits pressure evenly across the wound, wound margin, and periwound area, a superabsorbent core and a high MVTR top film layer, allowing evaporation of up to 80% of absorbed exudate. PICO dressings can be used with or without wound fillers (foams, gauze). The system can be used for up to 7 days, depending on the level of exudate
- The following tNPWT systems were used as comparators during this trial:
  - ActiV.A.C.™ Negative Pressure Wound Therapy (NPWT) System, Kinetic Concepts Inc., (KCI) an Acelity Company, San Antonio TX
  - Invia™ Liberty Negative Pressure Wound Therapy (NPWT) System, Medela Inc., McHenry IL
  - Avance™ Negative Pressure Wound Therapy (NPWT) System, Mölnlycke Health Care, Goteborg, Sweden
  - RENASYS© GO Negative Pressure Wound Therapy (NPWT) System, Smith & Nephew Inc., Fort Worth TX

PICO sNPWT

Patients

- Adults with either VLUs or DFUs present for more than four weeks, having provided signed consent, and being capable and willing to comply with protocol instructions

Wound management

- Ulcers were treated following good clinical practice and locally approved protocols including multilayer compression for all patients with VLUs and offloading for all patients with DFUs
- Patients were seen weekly for wound assessment and debridement if required, and the application/change of the corresponding NPWT dressings, then returned home with clear instructions about when to contact the center in case of problems between the visits
- Wound dimensions were confirmed using a Silhouette® wound assessment and management device (ARANZ Medical, Christchurch, New Zealand) at each study visit
- A survey designed to assess the impact of the NPWT devices on aspects of day living was completed by patients at the exit visit

Statistical analysis

For non-inferiority analysis, the primary analysis was performed using the per protocol (PP) population, so that drop-outs did not drive non-inferiority, and then the analysis was repeated using the intention-to-treat (ITT) population

Results

Baseline characteristics

- The ITT population included 161 subjects who were randomized, received trial treatment, and attended at least one follow-up post baseline visit
- The (PP) population included 115 subjects who were randomized, who continued treatment and had no significant protocol deviations
- Demography and relevant medical history of treatment groups were statistically similar in the ITT population. A majority of the ITT population had good mobility and no subjects were bed-bound
- No significant differences between the treatment groups were found regarding wound type, wound location, healing trajectories, Ankle-Brachial Index at baseline and baseline wound dimensions

Primary efficacy endpoint – wound area improvement

- In the PP population, by the end of the 12-week treatment period, the mean percentage reduction in area was 88.7% for PICO sNPWT and 58.6% for t-NPWT (p=0.003)
- After adjustment for baseline wound area, pooled site, wound type (DFUs/VLUs) and wound duration at baseline in the PP population, the difference in least-squares (LS) mean area reduction of 27% was in favor of PICO s-NPWT, (p=0.003 Figure1) which met the pre-established definition of non–inferiority using a 12.5% margin
- The ITT population showed difference of 39.1% in favor of PICO sNPWT (p<0.001 Figure 1)
- Subset analyses were performed using data from VLU and DFU subjects separately and showed that the differences between treatment groups in wound area reduction in both subsets were statistically significant. (VLUs p=0.007, DFUs (p=0.031)

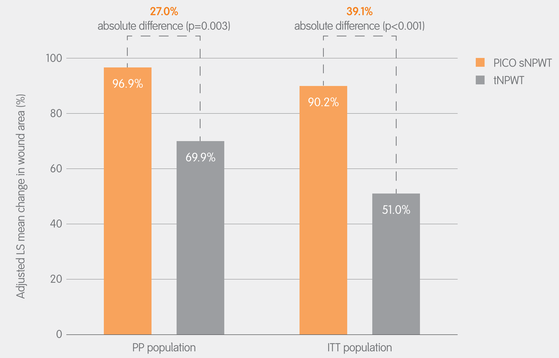


Figure 1: Adjusted LS mean change in wound area (%) in patients with VLUs and DFUs (PP and ITT populations)

Key secondary efficacy endpoints – wound depth variation and volume variation

- In the PP population, the mean percentage change in depth was a 68.8% reduction for PICO sNPWT and a 38.8% reduction for tNPWT (p=0.018)
- In the ITT population, the mean percentage change in depth was a 48.1% reduction in the PICO sNPWT group and a 12.7% reduction in the tNPWT group (p=0.014)
- In the PP population, the average percentage change in wound volume favored PICO sNPWT (98% reduction) compared with tNPWT (10% reduction) with a statistically significant difference of 79.5% (p=0.01; Figure 2)
  - Results from the ITT population showed a reduction of volume in the PICO sNPWT group (–61%) and an increase in volume in the tNPWT group (+30%)
- The LS-mean percentage change in the PP population was a 77.9% reduction for PICO sNPWT and a 1.6% increase for tNPWT after adjustment for baseline wound volume, pooled site, wound type and wound duration at baseline.
  - In the ITT population, there was a percentage reduction of 48.6% with PICO sNPWT and a 42.5% increase with tNPWT (p=0.013; Figure 2)

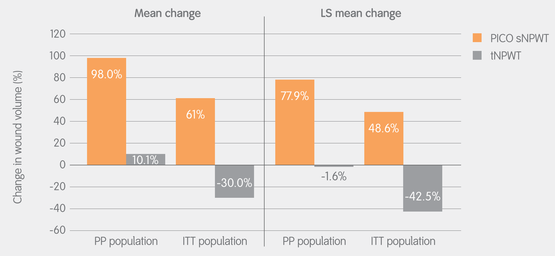


Figure 2: Mean and adjusted LS mean change in wound volume (%) in patients with VLUs and DFUs (PP and ITT populations)

Patient satisfaction

- Forty-seven patients (64.4%) in the PICO sNPWT group stated they would "strongly agree" with using the device on another wound in future compared with 26 (33.8%) patients in the tNPWT group (p=0.003)

Adverse events

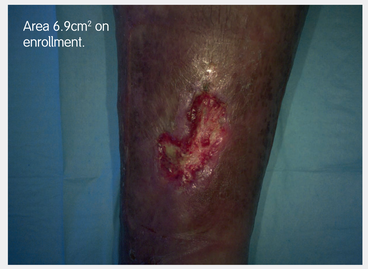
- Eleven subjects reported 12 AEs on the target ulcers, which were considered as related to the study treatments (three with sNPWT and nine with tNPWT), and resulted in subject discontinuation from the study
  - These included an increase in the target ulcer size, inability to tolerate NPWT, and periwound skin maceration
- Adverse events described as wound area increasing and considered treatment-related were responsible for the discontinuation of eight patients in the tNPWT group versus one in the PICO sNPWT group

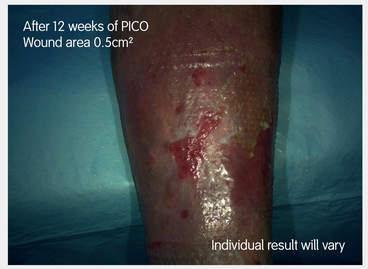
Conclusions

- In this study, PICO sNPWT met non-inferiority, and further achieved statistical superiority versus tNPWT in terms of reductions in wound dimensions (area, depth, volume) over the treatment period of 12 weeks
- PICO sNPWT performed well in a community care setting in patients under compression for VLUs or offloading for DFUs
- The results from this study support the use of sNPWT for the management of chronic leg ulcers (VLUs and DFUs) and when NPWT is being considered, PICO sNPWT may be an option

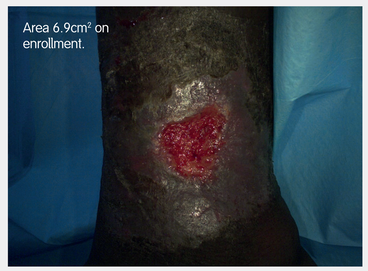
Examples of venous leg ulcer patients enrolled in the study and treated with PICO sNPWT

Patient 1: 50 years old. Venous ulcer on left leg





Patient 2: 80 years old. Venous ulcer on left shin



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