# Comparison of a new versus standard removable offloading device in patients with neuropathic diabetic foot ulcers:

# a French national, multicentre, open label randomized, controlled trial

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## SUPPLEMENTAL MATERIAL



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**Supplemental Table S1. Semi-quantitative survey for assessment of adherence to off-loading**

| Wearing off-loading device | Always | Most of the time | Sometimes | Rarely or never |
|---|---|---|---|---|
| **Outside** | 3 points | 2 points | 1 point | 0 point |
| **At home** | 4 points | 3 points | 1 point | 0 point |
| **Waking up at night** | 6 points | 5 points | 1 point | 0 point |



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**Supplemental Table S2. Key characteristics of subjects at baseline, study allocation, and primary outcome in each participant center**

| **Center** | Bichat | HEGP | Reims | Gonesse | Thionville | Corbeil | Nantes | Saint-Herblain | Bordeaux | Montpellier | Saint-Mandé | P-value |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Number** | 50 | 4 | 20 | 3 | 2 | 16 | 5 | 3 | 2 | 3 | 4 | |
| ***Orthèse Diabète*** | 24 | 2 | 10 | 1 | 0 | 9 | 3 | 1 | 1 | 1 | 2 | 0.97 |
| **Control** | 26 | 2 | 10 | 2 | 2 | 7 | 2 | 2 | 1 | 2 | 2 | |
| **Male** | 39 | 4 | 16 | 3 | 0 | 13 | 4 | 3 | 2 | 1 | 3 | 0.16 |
| **Age (years)** | 63±8 | 54±13 | 64±9 | 52±13 | 51±6 | 60±11 | 53±16 | 61±10 | 76±4 | 63±5 | 57±15 | 0.04 |
| **BMI (kg/m²)** | 30±5 | 26±4 | 31±6 | 30±5 | 32±16 | 33±7 | 32±4 | 30±5 | 29±1 | 26±7 | 30±6 | 0.75 |
| **SBP (mmHg)** | 136±23 | 140±6 | 133±13 | 125±5 | 130±14 | 136±10 | 129±21 | 130±1 | 147±4 | 135±7 | 138±17 | 0.94 |
| **DBP (mmHg)** | 72±12 | 77±10 | 75±9 | 77±5 | 85±7 | 82±3 | 75±12 | 70±16 | 83±11 | 65±21 | 79±10 | 0.24 |
| **Diabetes duration (years)** | 18±9 | 20±2 | 18±12 | 23±12 | 24±6 | 21±9 | 22±8 | 20±13 | 24±8 | 23±6 | 17±10 | 0.95 |
| **HbA1c (%)** | 7.9±1.9 | 8.4±1.6 | 7.8±1.5 | 10.2±2.2 | 7.8±2.3 | 9.7±2.1 | 8.6±0.4 | 9.1±0.9 | 6.5±0.8 | 7.7±0.3 | 7.0±1.7 | 0.19 |
| **Wound duration** | | | | | | | | | | | | |
| **<1 week** | 0 | 1 | 1 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0.07 |
| **1-2 weeks** | 10 | 0 | 4 | 0 | 0 | 2 | 1 | 0 | 0 | 0 | 0 | |
| **>2 weeks** | 35 | 2 | 9 | 1 | 2 | 8 | 4 | 3 | 1 | 2 | 4 | |
| **Infection** | 10 | 1 | 10 | 0 | 0 | 0 | 2 | 1 | 1 | 0 | 1 | 0.03 |
| **Soft tissue** | 6 | 1 | 9 | 0 | 0 | 0 | 2 | 1 | 1 | 0 | 1 | 0.01 |
| **Osteomyelitis** | 6 | 0 | 3 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0.81 |

| | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Lower-extremity artery disease** | 8 | 1 | 9 | 0 | 1 | 8 | 1 | 3 | 0 | 1 | 1 | 0.03 |
| **Primary outcome** | 23 | 0 | 4 | 2 | 0 | 5 | 1 | 3 | 1 | 0 | 1 | 0.22 |

Data are expressed as number of participants (categorical variables) or mean±SD (continuous estimates). Comparisons were performed using Chi-square or ANOVA tests. P<0.05 was significant.

Centers: Hôpital Bichat, Paris; Hôpital européen Georges-Pompidou (HEGP), Paris; Centre Hospitalier Universitaire de Reims; Centre Hospitalier de Gonesse; Centre Hospitalier Régional de Metz - Thionville; Centre hospitalier Sud Francilien, Corbeil-Essonne; Centre Hospitalier Universitaire de Nantes; Le Centre La Tourmaline, Saint-Herblain; CHU de Bordeaux, Haut Lévèque Hospital, Pessac; CHRU de Montpellier; Hôpital Bégin, Saint-Mandé.

Two centers (Henri Mondor hospital, Créteil and Nimes university hospitals) have screened 5 patients who were not included.

**Supplemental Table S3. Primary outcomes in adherent patients using the two definitions of offloading compliance**

| | **Conventional** | ***Orthèse Diabète*** | ***P* value** |
|---|---|---|---|
| **First definition of compliance (n)** | 38 | 25 | |
| Wound closure at 3 months | 14 (56%) | 11 (44%) | 0.57 |
| **Second definition of compliance (n)** | 21 | 15 | |
| Wound closure at 3 months | 7 (47%) | 8 (53%) | 0.23 |

First definition: patients were considered compliant if they replied at least at one visit the modality "Always" or "Most of the time" to the 3 items of the questionnaire. Second definition: adherence score ≥ 8 (as shown in Supplemental Table 1)

**Supplemental Table S4. Estimation of the offloading observance**

| | Conventional group | *Orthèse Diabète* | P value |
|---|---|---|---|
| **Overall*** | 38 (66) | 25 (46) | 0.04 |
| **At home** | | | |
| always | 28 (56) | 14 (33) | 0.06 |
| often | 3 (6) | 9 (21) | |
| rarely | 4 (8) | 4 (9) | |
| never | 15 (30) | 16 (37) | |
| **Outside** | | | |
| always | 29 (58) | 17 (39) | 0.22 |
| often | 3 (6) | 5 (12) | |
| rarely | 2 (4) | 5 (12) | |
| never | 16 (32) | 16 (37) | |
| **Overnight** | | | |
| always | 15 (30) | 10 (23) | 0.57 |
| often | 3 (6) | 5 (12) | |
| rarely | 6 (12) | 3 (7) | |
| never | 26 (52) | 25 (58) | |

Data, collected at 3-month visit, presented as number (percentage) and compared using Chi-2 test; *Participants who declared using the offloading device regularly (always or often) at home, outside, and overnight.

**Supplemental Table S5. Satisfaction of participants regrading offloading devices using QUEST 2.0 scale**

| | **Conventional group** | ***Orthèse Diabète*** | **P value** |
|---|---|---|---|
| **Device** | 3.9 (3.3 – 4.3) | 4 (3.5 – 4.5) | 0.50 |
| **Service** | 4.2 (3.6 – 4.7) | 4.5 (4.0 – 4.7) | 0.13 |
| **Total** | 3.9 (3.5 – 4.4) | 4.1 (3.7 – 4.6) | 0.31 |

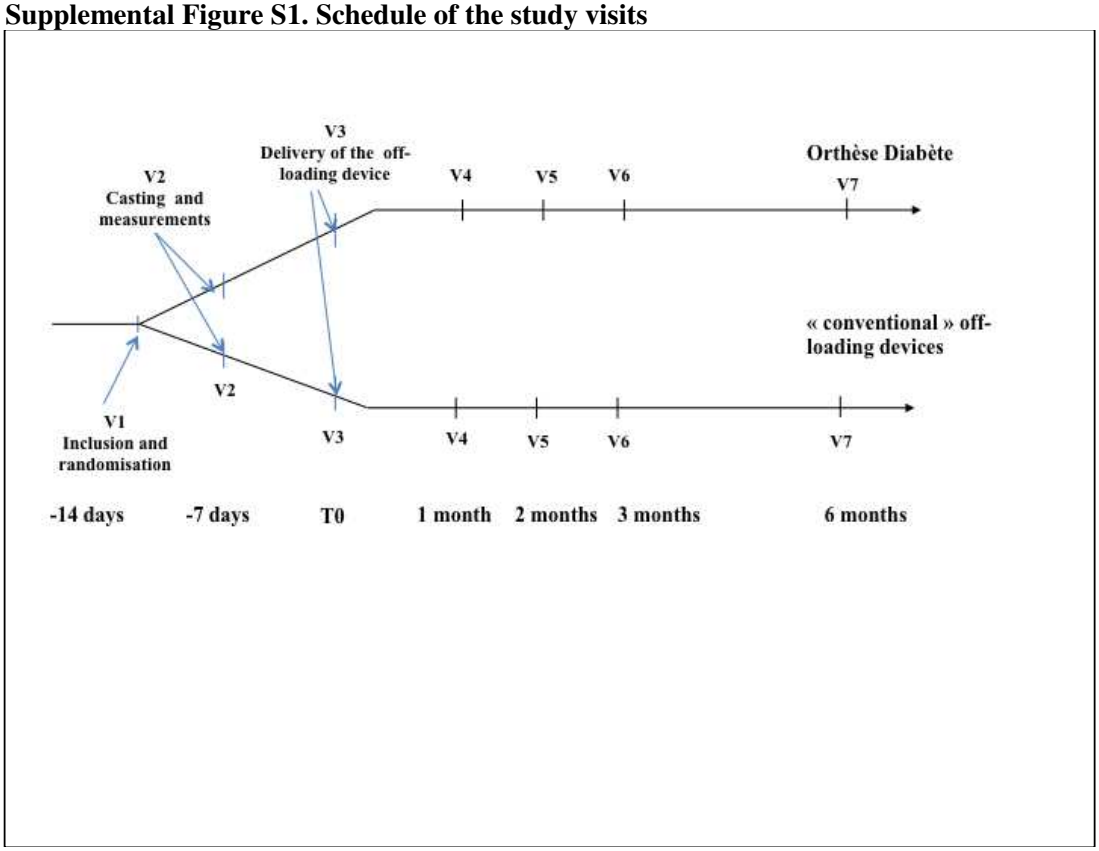
Data, collected at 3-month visit, presented as median ($25^{th}$ – $75^{th}$ percentiles) and compared using Wilcoxon test.

**Supplemental Table S6. Detailed adverse events by study allocation**

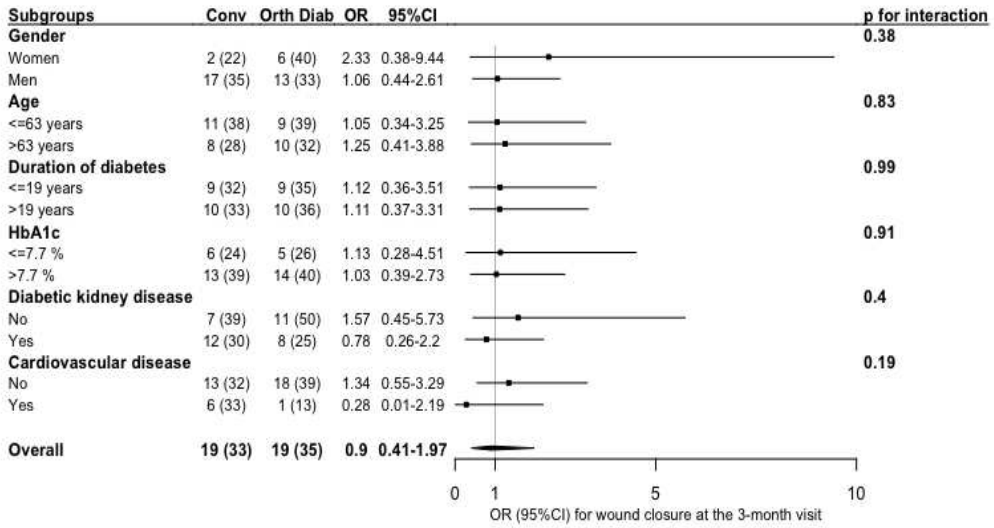
| | Conventional | *Orthèse Diabète* |
|---|---|---|
| **Foot wound** | 8 | 11 |
| **Foot infection** | 6 | 5 |
| **Osteitis or osteoarthritis** | 4 | 6 |
| **Skin infection** | 6 | 9 |
| **Systemic infection** | 5 | 2 |
| **Lower-extremity amputation** | 2 | 7 |
| **Foot surgery** | 8 | 3 |
| **Upper or lower-limb fracture** | 0 | 2 |
| **Upper or lower-limb fracture** | 0 | 2 |
| **Breakage of the orthosis** | 0 | 3 |
| **Pain** | 2 | 0 |
| **Hyperthermia** | 0 | 1 |
| **Sciatica** | 0 | 1 |
| **Leg oedema** | 0 | 1 |
| **Hypoglycemia** | 0 | 1 |
| **Severe diabetic retinopathy** | 0 | 2 |
| **Acute kidney failure** | 1 | 1 |
| **Acute heart failure** | 1 | 0 |
| **Iatrogenic hepatitis** | 0 | 1 |
| **Anemia** | 2 | 0 |
| **Cancer** | 1 | 0 |
| **Gastritis** | 1 | 0 |
| **Others** | 10 | 9 |

Data presented as numbers of adverse events.

**Supplemental Figure S1. Schedule of the study visits**



**Supplemental Figure S2. Primary endpoint in different subgroups**




Analyses performed in the intention to treat cohort using a multiplicative interaction in logistic regression model. Age, diabetes duration, and HbA1c subgroups were categorized as below or above medians.

**Supplemental Figure S3: Time to reach wound closure of the index ulcer by study arms**