

# Randomised, Placebo-controlled Study of OPAL A for the Treatment of Chronic Venous and Pressure Ulcers

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# BACKGROUND AND OBJECTIVES

## Chronic Venous and Pressure Ulcers

- Common in developed countries, particularly among the elderly.
- Challenging and expensive to treat: healing may take considerable time and rates of recurrence are high<sup>1,2</sup>; \$285 to \$655 million per year in Australia.<sup>3,4</sup>
- May lead to serious complications and increased mortality<sup>5,6</sup>: can have a significant impact on quality of life.<sup>3</sup>

## OPAL A

- Derivative of the inner flesh of the paw paw fruit *Carica papaya*: topically administered filtrate and cream.
- Treatment with OPAL A was associated with wound healing in 9 patients with quadriplegia with hard-to-heal chronic pressure ulcers<sup>7</sup>, 4 patients with pressure, diabetic foot, or venous ulcers<sup>8</sup>, and 1 patient with paraplegia with a sacral pressure ulcer.<sup>9</sup>

## Objectives

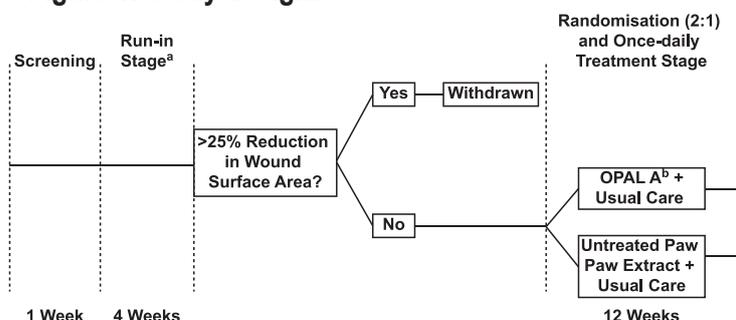
- Primary: To evaluate the safety and tolerability of the topical application of OPAL A to hard-to-heal chronic venous and pressure ulcers.
  - Assessed by examining the frequency and severity of adverse events.
- Secondary: To evaluate the effect of OPAL A on the healing of hard-to-heal chronic venous or pressure ulcers.
  - Assessed by examining wound healing using the Advanced Medical Wound Imaging System<sup>®</sup>.

## METHODS

### Study Population

- Inclusion Criteria:
  - Age: ≥ 18 years; a venous leg ulcer or Stage II or III pressure ulcer present ≥4 months (or recurrent).
- Exclusion Criteria:
  - Any dermatologic condition / disorder that may interfere with treatment / assessment.
  - Participants using immunosuppressants, cytotoxins, anti-inflammatory agents, or antibiotics, unless intending to remain on stable doses of these medications during the study (any topical medication must not be applied within 10cm of the ulcer under study treatment).
  - Known hypersensitivity to paw paw products.

Figure 1. Study design.



<sup>a</sup> Treatment with untreated paw paw extract and usual care. <sup>b</sup> OPAL A filtrate and cream.

## PRELIMINARY RESULTS

- Note: the trial is ongoing and the results have not been unblinded.

### Participant Disposition

- 15 participants screened to date; 3 ineligible; 12 entered run-in stage.
- 6 participants (50%) experienced a >25% reduction in wound surface area during the run-in stage and were excluded from the treatment stage.
- 5 of 6 participants completed the treatment stage.
  - 1 participant withdrew due to hospitalisation for a condition unrelated to the treatment of his / her ulcer.
  - 1 participant who completed the study was excluded from the efficacy analyses because the participant's ulcer had decreased in size by >25% in the run-in stage.
  - 1 participant died due to cardiogenic shock after completing the study (this death was considered unrelated to study treatment).

### Participant Characteristics

- All participants were in poor health (many had comorbidities).
- Mean time ulcer(s) had been present: 26 months.
- Mean ulcer size at screening: 11.8 cm<sup>2</sup>.

Table 1. Adverse events. The majority of adverse events were mild or moderate and not related to study treatment.

| Parameter                        | Run-in Stage<br>n (%) | Treatment Stage<br>n (%) |
|----------------------------------|-----------------------|--------------------------|
| Participants                     | N = 12                | N = 6                    |
| At least 1 AE                    | 8 (66.7)              | 6 (100.0)                |
| At least 1 severe AE             | 1 (8.3)               | 3 (50.0)                 |
| At least 1 SAE                   | 0 (0.0)               | 2 <sup>a</sup> (33.3)    |
| Discontinuation because of an AE | 0 (0.0)               | 1 (16.7)                 |
| Total AEs                        | N = 19                | N = 28                   |
| Mild AEs                         | 3 (15.8)              | 12 (42.9)                |
| Moderate AEs                     | 15 (78.9)             | 10 (35.7)                |
| Severe AEs                       | 1 (5.3)               | 6 (21.4)                 |
| SAEs                             | 0 (0.0)               | 3 (10.7)                 |
| Not related AEs                  | 13 (68.4)             | 25 (89.3)                |
| Possibly related AEs             | 6 (31.6)              | 3 (10.7)                 |
| Probably related AEs             | 0 (0.0)               | 0 (0.0)                  |
| Definitely related AEs           | 0 (0.0)               | 0 (0.0)                  |

AE = adverse event; SAE = serious adverse event. <sup>a</sup> Participant #603 experienced SAEs of anaemia (secondary to a gastrointestinal tract bleed) and malaena, and withdrew from the study due to the SAE of malaena. Participant #804 experienced an SAE of gastric ulcer bleeding. All SAEs were considered unrelated to study treatment.

Table 2. Common adverse events. Wound infection, wound pain, and redness / inflammation were the most common adverse events.

| AEs Experienced by ≥2 Participants             | Number of Participants<br>n (%)<br>(N = 12) | Number of Events<br>n (%)<br>(N = 50) |
|--|---|---------------------------------------|
| Infection, wound <sup>a</sup>                  | 6 (50.0)                                    | 8 (16.0)                              |
| Wound pain <sup>b</sup>                        | 3 (25.0)                                    | 6 (12.0)                              |
| Redness / inflammation, increased <sup>c</sup> | 4 (33.3)                                    | 4 (8.0)                               |
| Venous eczema                                  | 3 (25.0)                                    | 3 (6.0)                               |
| Cellulitis                                     | 2 (16.7)                                    | 3 (6.0)                               |
| Hypotension                                    | 2 (16.7)                                    | 2 (4.0)                               |
| Nausea   | 2 (16.7)                                    | 2 (4.0)                               |

AE = adverse event. <sup>a</sup> Infection of the ulcer wound. <sup>b</sup> The AEs "wound pain" and "ulcer pain" were combined, with the assumption that "wound" refers to the participant's ulcer. <sup>c</sup> Increased redness includes skin redness and wound / ulcer redness and inflammation.

Figure 2. Wound surface area during the run-in stage. A high proportion (50%) of participants who entered the run-in stage experienced a >25% reduction in wound surface area.

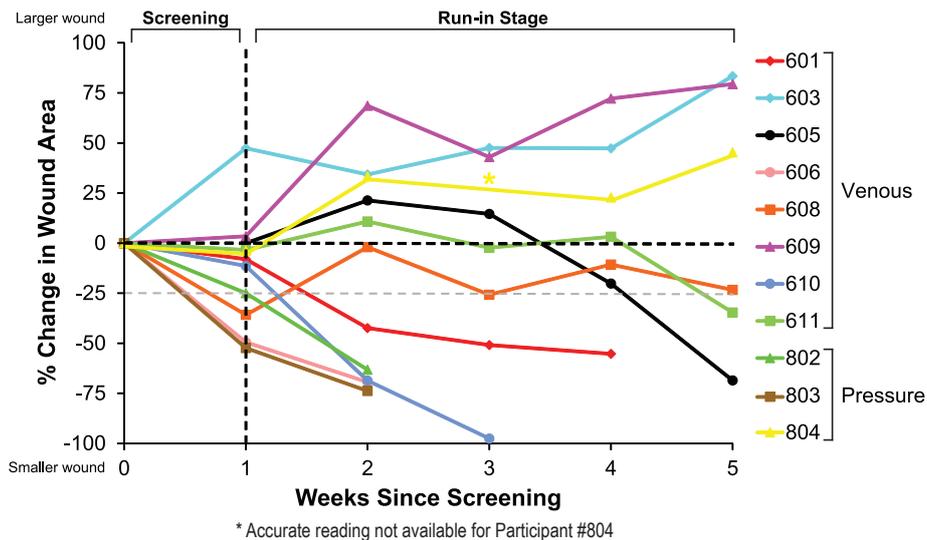
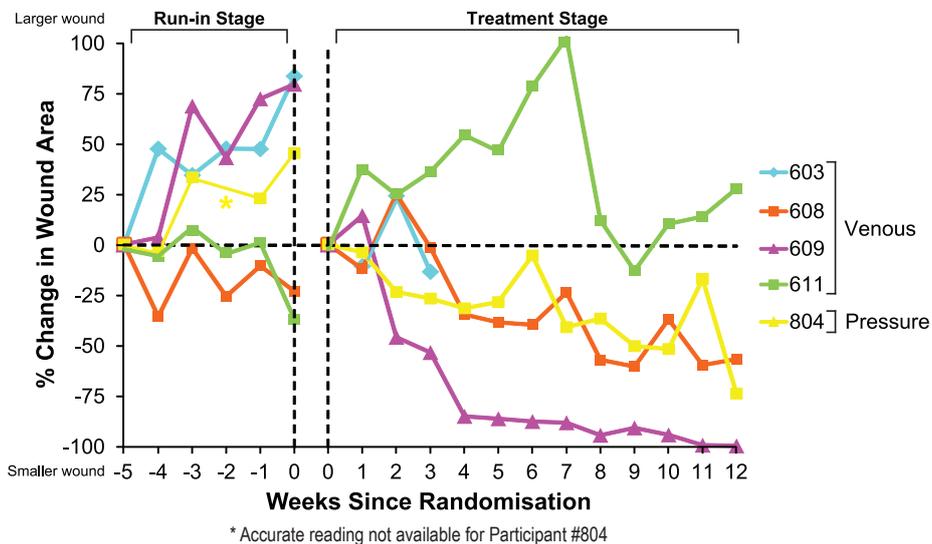


Figure 3. Wound surface area during the run-in and treatment stages. Three of four participants who completed the treatment stage had a 50% to 100% reduction in wound surface area.



## CONCLUSIONS

- The results of the run-in stage suggest that:
  - Many of the ulcers would have been healed by best clinical practice and that daily ulcer care is an important component of ulcer management.
  - Untreated paw paw extract may have wound healing properties.
- These preliminary, unblinded data suggest that:
  - OPAL A has an acceptable safety and tolerability profile in patients with chronic venous or pressure ulcers.
  - OPAL A may promote wound healing.
- In contrast to many studies of chronic wound healing, this ongoing study has a robust design, including a run-in stage and randomisation to an active or control treatment.
  - An independent National Health and Medical Research Council assessor has noted "This is a well-designed and thorough study, which is logical in the approach that is being taken. If successful, it will be well received both nationally and internationally, particularly since the trial is designed in line with FDA recommendations. Given the preliminary clinical results, this study is likely to demonstrate proof of principle that the use of OPAL A is beneficial in treating ulcers."
  - The final results will provide important information on the safety and efficacy of OPAL A for treating chronic ulcers.

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