

AMELOGENINS (XELMA®) IN HARD-TO-HEAL VENOUS LEG ULCERS, AN OPEN REGIME INVESTIGATION

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Patient 211, duration 6 months and 12.2 cm² at baseline, received the 12-weeks treatment with amelogenin proteins



Final visit, 12 weeks after baseline, 0,7 cm²



Follow-up visit, 24 weeks after baseline, 0,1 cm²

Background:

This investigation investigated the optimal numbers of product applications for a novel extracellular matrix protein, amelogenin. Amelogenin proteins provide a temporary extracellular matrix protein for cells to attach to.

Aim:

The aim of this clinical investigation was to assess ulcer reduction by comparing 3 different application regimen of amelogenin protein: 3 weeks, 6 weeks and 12 weeks of applications.

Methods:

36 patients with persistent (>6 months) venous leg ulcer despite compression therapy were planned to be included in this open, randomised investigation. Patients judged to have inadequate compression were subject to a run-in period of 4 weeks; a patient healing more than 50% of the initial wound area was then excluded from further assessments.

Amelogenin in a propylene glycol alginate carrier was applied once weekly at the investigation visits. Compression therapy was maintained throughout the 12-week investigation period. Ulcer size reduction was measured by tracing and assessed by digital planimetry. A follow-up period of 12 weeks was scheduled after the observation period.

Patients with ulcers sized between 4-28 cm² were included. Highly exuding wounds or with clinical signs of infection was excluded.

The Ethics Committees in Tallinn and Pisa approved the investigation and patients were informed both orally and in writing before consent was signed.

Wound assessment was performed every second week up to week 8, at final visit (week 12) and at follow-up visit (12 weeks after the final visit). Secondary dressing were Mepilex® or Mepitel®/Mesorb®.

Results:

36 patients were included. 12 patients were randomised to each amelogenin protein application regimen, amelogenin for 3 weeks, 6 weeks and 12 weeks. Ulcers with an unrestrained area enlargement (>50% as compared to baseline/randomisation) were excluded from the per protocol analyses. Reported here are the results from the full analysis set (all 36 randomised) and the per protocol (PP):

- 10 patients who received 3 weeks treatment
- 7 patients who received 6 weeks treatment
- 9 patients who received 12 weeks treatment

There were some baseline differences with regard to ulcer age and size in the analysis populations (Table 1). Patients' demographic data was reasonably evenly distributed between the groups (Table 2). In total 4 patients suffered from diabetes.

The change in ulcer area, as measured in median values and expressed as percentage of the baseline ulcer area, was calculated for all patients. Patients who received the 12-weeks treatment had a larger ulcer reduction compared to patients who received the 3 or 6-weeks treatment with amelogenin protein (Table 3).

As can be seen from median tracing values per visit (Figure 1 and 2) both analysis populations show similar patterns in area changes.

The following adverse events were reported; in the 3-week group one patient had two episodes of erysipelas and later a small increase in ulcer area.

In the 6-week group one thrombophlebitis and one ulcer enlargement was reported. A third patient had oedematous legs in combination with influenza; later reported to have an ulcer enlargement.

In the 12-week group one urticaria and one ulcer infection were reported. A third patient reported ulcer infection followed by an ulcer enlargement. In addition, 2 patients in this group had ulcer enlargement alone.

Two patients experienced device related events; in the 3-week group an increase in ulcer area due to maceration and, in the 6-week group, an ulcer enlargement and pain.

One patient in the 12-week group experienced a Serious Adverse Events during the investigation. The patient was admitted to hospital due to deterioration of her diabetes. This patient later withdrew her consent.

Conclusion:

- This investigation indicates that a larger ulcer size reduction is obtained after 12 weeks treatment with amelogenin protein (compared to 3 and 6 weeks treatment), this despite the fact that ulcer reduction is close to 50% already after 6 weeks of treatment.
- Device-related adverse events were reported for two patients. One patient with ulcer enlargement and one with ulcer enlargement and pain. 7 out of 9 patients with an ulcer enlargement of more than 50% had this reported as an adverse event.

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Table 1. Legend: Ulcers age and size, median values, for PP

Regimen	Age of VLU in months Median (min/max)	Size of VLU in cm ² Median (min/max)
3 weeks n=10	18 (1-132)	6.8 (4.2-27.7)
6 weeks n=7	60 (12-180)	10.7 (3.8-22.2)
12 weeks n=9	12 (6-240)	10.0 (4.3-18.8)

Table 2. Legend: Demography, median values.

Regimen	Gender	Age (min/max)	Diabetes
3 weeks, n=10	6 F / 4 M	71y (57 - 86)	0
6 weeks, n=7	5 F / 2 M	64 y (48 - 84)	2
12 weeks, n=9	7 F / 2 M	65 y (43 - 84)	2

Table 3. Legend: Percentage change per regimen at 12-week assessment, median values with Q1 and Q3.

Regimen	Median	Q1	Q3
3w, n=10	-22.4	(-72.5	-15.3)
6w, n=7	-48.0	(-82.1	-31.3)
12w, n=9	-72.0	(-83.9	0.3)

Figure 1. Legend: Ulcer size reduction over time (median values) PP

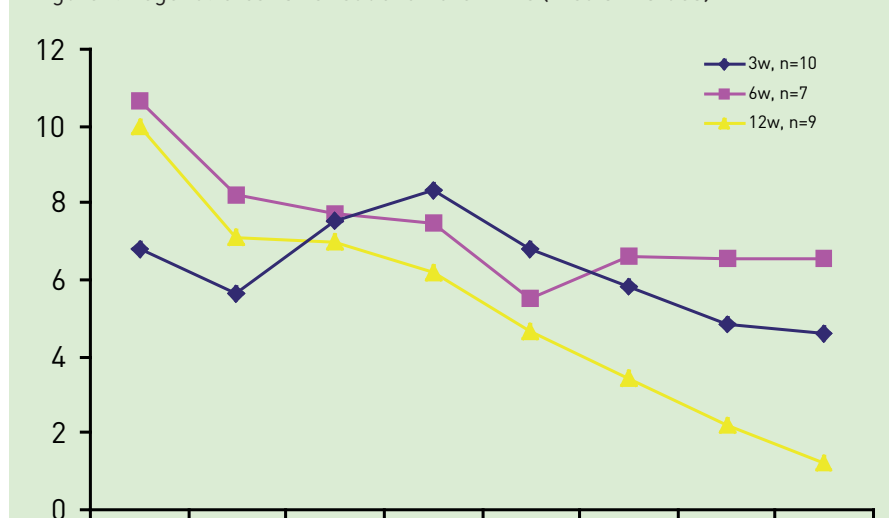


Figure 2. Legend: Ulcer size reduction over time (median values) ITT

