Effect of Amelogenin Extracellular Matrix Protein (Xelma) as an Adjunct Treatment to High Compression in Hard-to-Heal Venous Leg Ulcers: a Multi-Centre, Randomised Controlled Trial.

Peter Vowden MD, FRCS
Vascular Unit, Bradford Royal Infirmary, Bradford, United Kingdom

Marco Romanelli MD PhD
Department of Dermatology, University of Pisa, Pisa, Italy

Patricia Price PhD
Wound Healing Research Unit, Cardiff, United Kingdom

Poster presented at the European Wound Management Association Conference, Glasgow, United Kingdom, 2-4 May 2007
Effect of Amelogenin Extracellular Matrix Protein (Xelma®) as an Adjunct Treatment to High Compression in Hard-to-Heal Venous Leg Ulcers: a Multi-Centre, Randomised Controlled Trial.

INTRODUCTION

Extracellular matrix (ECM) proteins define the extracellular environment of living cells. Inappropriate matrix remodelling in chronic wounds results from the imbalance of proteinases and their endogenous inhibitors; this may compromise the function of the ECM, especially with respect to the sequence of filling the dermal defect. Xelma® (Molnlycke Health Care) is an advanced wound care product containing amelogenin, an ECM biocompatible protein. When applied to the wound bed it provides a temporary matrix for cell attachment and promotes wound healing.

Therapy using amelogenin has already been shown to be successful in the treatment of periodontal wounds. Furthermore, clinical evaluations (a randomised controlled trial and case studies) have indicated the potential for amelogenin to assist in the healing of ‘hard-to-heal’ venous leg ulcers (VLUs).

OBJECTIVE

A comparison of hard-to-heal venous leg ulcers (VLUs) treated with high compression therapy alone versus high compression therapy with amelogenin protein.

METHODS

An open, randomised, comparative, parallel group multi-centre investigation with a 3-week run-in period. Patient eligibility for inclusion included adult, mobile patients with ‘hard-to-heal’ VLUs that had been treated with compression therapy for at least 1 month prior to screening. The ulcers had to be at least 6 months old, with a surface area at inclusion of at least 10cm², but not exceeding 30cm², and not demonstrating excessive exudate or signs of infection. At the end of the run-in period, additional criteria for eligibility, e.g. change in wound area of at least 50% and a wound area < 8 and > 36 cm² were applied. Patients were randomly assigned to treatment with amelogenin plus compression bandaging, or high compression bandaging alone. All participants received a secondary bandaging combination of Mepilex® and Mepore®, high compression bandaging therapy one month prior to, during the investigational period of 3 weeks in run-in and throughout the following 12 weeks of active treatment.

Investigational Product: Xelma® is a sterile extracellular matrix protein for topical application, consisting of amelogenin proteins dissolved in a propylene glycol matrix protein for topical application, consisting of amelogenin proteins dissolved in a propylene glycol matrix protein. When applied to wounds, it provides a temporary matrix for cell attachment and promotes wound healing.

Statistical Analysis

The primary endpoint was the percent change in ulcer size from baseline to the last visit. The results showed a statistically significant improvement in ulcer size from baseline to the last visit for the amelogenin group compared to 18.5% in the control group. The percentage of improved ulcers at the last visit was statistically significantly higher, 47.5% in the amelogenin group compared to 19.5% in the control group.

RESULTS AND DISCUSSION

A total of 83 of the 101 screened patients were randomised and entered the treatment phase (see Table 1). The Intention To Treat (ITT) population included all the patients that received at least one treatment. In total, 62 patients were treated with amelogenin plus compression therapy, and 41 patients with compression alone.

Statistical Analysis

The primary efficacy analysis was the difference, although the difference was not significant, in the percent change ulcer size from baseline to the last visit between the two treatment groups. The results showed a statistically significant improvement in ulcer size from baseline to the last visit for the amelogenin group compared to 18.5% in the control group. The percentage of improved ulcers at the last visit was statistically significantly higher, 47.5% in the amelogenin group compared to 19.5% in the control group. No consistent pattern of AEs was observed in either treatment group. No consistent pattern of AEs was observed in either treatment group.

CONCLUSION

The results from this investigation, carried out over 24 weeks including 3 months of follow-up, are in agreement with other clinical studies which have demonstrated that the addition of amelogenin to high compression bandaging is statistically and clinically significantly beneficial to the healing of hard-to-heal VLUs, in the following areas:

- Reduction in ulcer size
- Improvement in the state of ulcers
- Reduction in pain at dressing change
- Larger proportion of ulcers with no/excellent levels of exudate
- Improved patients, and comparisons of exudate levels were also analysed between the groups at the final time point using Fishers Exact Test. Multiple Logistic Regression was also calculated on the primary efficacy variable.

The total number of AEs in the two groups was similar; vital signs, weight and BMI did not reveal any safety issue in the investigational period of 12 months. The results showed a statistically significant improvement in ulcer size from baseline to the last visit for the amelogenin group compared to 18.5% in the control group. The percentage of improved ulcers at the last visit was statistically significantly higher, 47.5% in the amelogenin group compared to 19.5% in the control group.

CONCLUSION

The results from this investigation, carried out over 24 weeks including 3 months of follow-up, are in agreement with other clinical studies which have demonstrated that the addition of amelogenin to high compression bandaging is statistically and clinically significantly beneficial to the healing of hard-to-heal VLUs, in the following areas:

- Reduction in ulcer size
- Improvement in the state of ulcers
- Reduction in pain at dressing change
- Larger proportion of ulcers with no/excellent levels of exudate
- Improved patients, and comparisons of exudate levels were also analysed between the groups at the final time point using Fishers Exact Test. Multiple Logistic Regression was also calculated on the primary efficacy variable.

The total number of AEs in the two groups was similar; vital signs, weight and BMI did not reveal any safety issue in the investigational period of 12 months. The results showed a statistically significant improvement in ulcer size from baseline to the last visit for the amelogenin group compared to 18.5% in the control group. The percentage of improved ulcers at the last visit was statistically significantly higher, 47.5% in the amelogenin group compared to 19.5% in the control group.

CONCLUSION

The results from this investigation, carried out over 24 weeks including 3 months of follow-up, are in agreement with other clinical studies which have demonstrated that the addition of amelogenin to high compression bandaging is statistically and clinically significantly beneficial to the healing of hard-to-heal VLUs, in the following areas:

- Reduction in ulcer size
- Improvement in the state of ulcers
- Reduction in pain at dressing change
- Larger proportion of ulcers with no/excellent levels of exudate
- Improved patients, and comparisons of exudate levels were also analysed between the groups at the final time point using Fishers Exact Test. Multiple Logistic Regression was also calculated on the primary efficacy variable.

The total number of AEs in the two groups was similar; vital signs, weight and BMI did not reveal any safety issue in the investigational period of 12 months. The results showed a statistically significant improvement in ulcer size from baseline to the last visit for the amelogenin group compared to 18.5% in the control group. The percentage of improved ulcers at the last visit was statistically significantly higher, 47.5% in the amelogenin group compared to 19.5% in the control group.