

Case Studies From A Pan European Randomised Controlled Trial

Xelma® -

extracellular matrix protein: a new treatment for hard-to-heal ulcers



Peter Vowden M.D.

Coordinating and Principal investigator
Vascular Surgeon at the Bradford Royal Infirmary Bradford
Teaching Hospitals, NHS Foundation Trust

Jerzy Wnorowski M.D. PhD

Dermatologist at the Department of Dermatology
Szpital Św. Łazarza, Warsaw, Poland

Anna Josefsson M.D.

Dermatologist at Örebro University Hospital, Sweden

Background – Pan European Randomised Controlled Trial

Hard-to-heal wounds

A review of over 20,000 venous leg ulcer cases by Margolis et al identified that a wound greater than 10 cm² in size and greater than 12 months old has only a 22% chance of healing by 24 weeks (Margolis et al 2000). Phillips et al (2000) came to a similar conclusion in a prospective study of 165 venous leg ulcers treated with compression and moisture retentive dressings but also established that the percentage reduction in ulcer size over the first three weeks of treatment were predictive of subsequent healing.

This and other supportive evidence was used as the basis for the patient population selection in a recent study (Vowden P 2006) on the role of Xelma, an extracellular matrix protein equivalent, in the management of "hard-to-heal" venous leg ulcers.

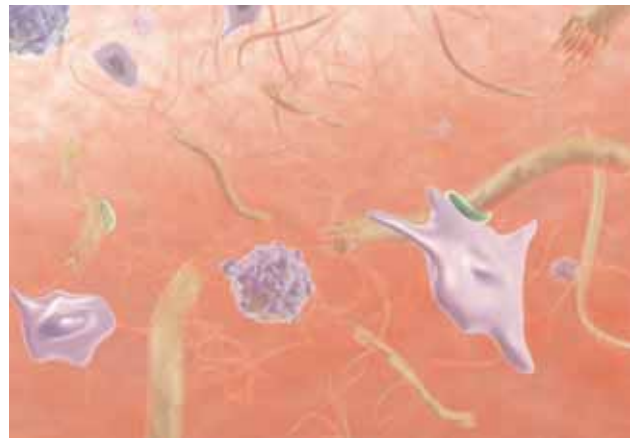
Extracellular matrix

Extracellular matrix (ECM) consists of a complex mixture of structural and functional proteins and serves an important role in the maintenance of cell and tissue structure and function during wound healing, particularly in the host response to injury (Badylak 2002). Disturbance in the balance between ECM production and degradation is known to lead to the formation of chronic ulcers (Ravanti and Kahari 2000). It seems likely, given the known importance of ECM deficiencies in the delayed healing of chronic wounds, that the application of Xelma extracellular matrix protein should improve healing.

The investigation

A single-blind, randomised, controlled investigation which compared a new extracellular matrix protein treatment, Xelma® to placebo treatment, in 123 patients with hard-to-heal venous leg ulcers, was conducted in 20 centres across Europe. This compendium contains four case examples from this pan European study.

Inclusion criteria included: a wound size between 5 and 25 cm², a wound duration of at least 6 months and controlled compression therapy for at least 1 month prior to inclusion.



Damaged extracellular matrix

The four cases presented are from the following centres: Örebro University Hospital, Sweden, Szpital Sw Lazarza, Warsaw, Poland and Bradford Royal Infirmary in UK.

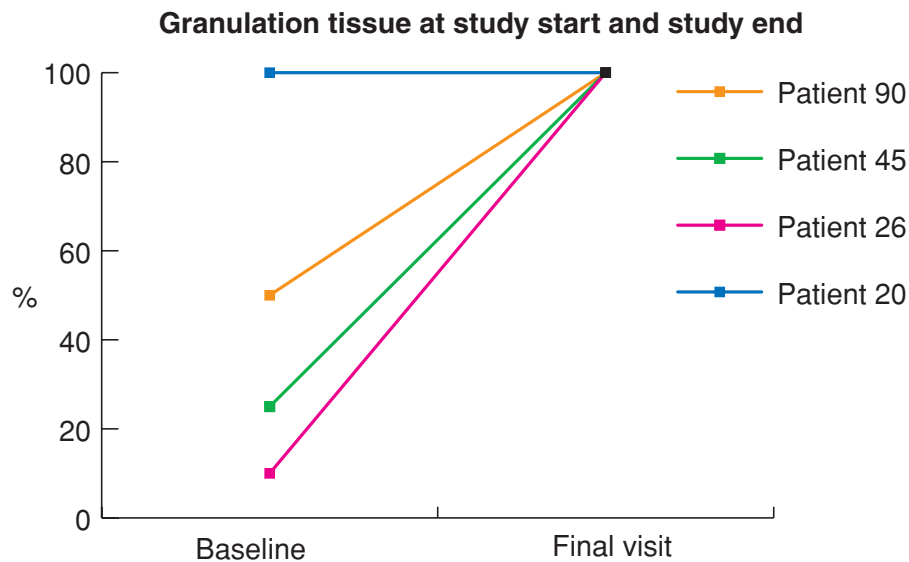
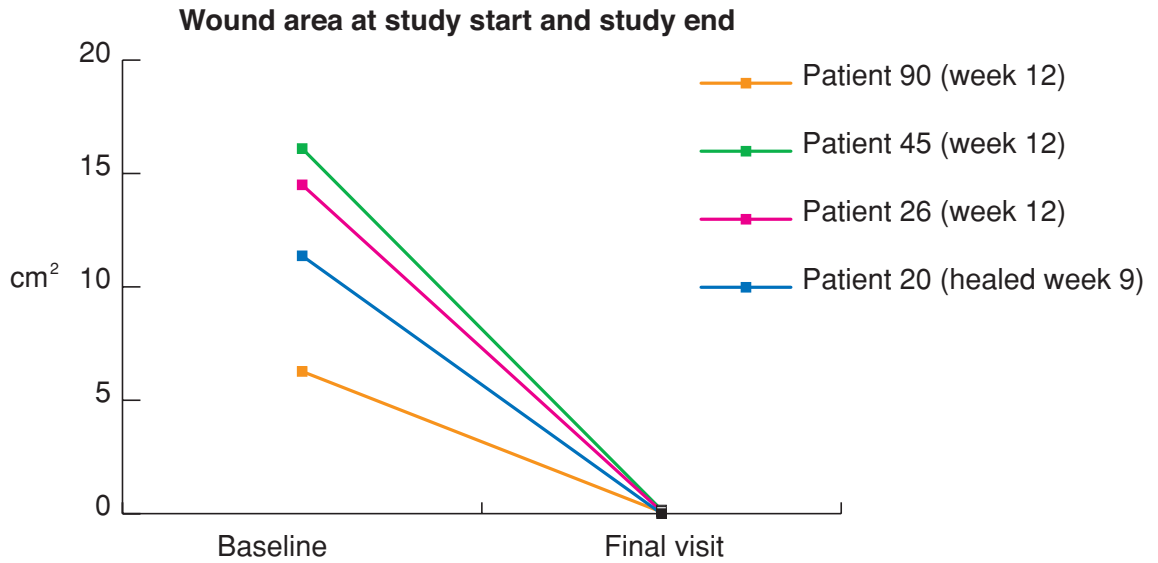
The clinical investigation showed therapeutic benefits for Xelma with an improved rate of healing for larger ulcers and ulcers with long duration (Margolis's criteria for hard-to-heal venous ulceration). Xelma was well tolerated with a trend towards less pain, exudates and maceration than in the control group.

Certainly the research team in Bradford felt that this product (Xelma) has a role to play in the management of the non-healing or slow healing venous leg ulcer. To obtain the maximum cost benefit this and similar products must be introduced early into the treatment plan and their use must be related to either the baseline ulcer characteristics in terms of size and ulcer duration or to measurement of ulcer healing rates.

Peter Vowden M.D.
Coordinating and Principal Investigator
Vascular Surgeon at the Bradford Royal Infirmary



Xelma – extracellular matrix treatment is a suitable treatment for hard-to-heal ulcers. Xelma is intended for topical application and applied once a week.



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Patient 20

An 81 year old woman with a pre tibial venous ulcer of 9 months' duration. She received ongoing treatment for hypertension and atrial fibrillation. Before commencing the trial her leg ulcer management involved standard good practice of moist wound healing using an advanced dressing (Mepilex, Mölnlycke Health Care) together with compression bandaging (Profore, Smith and Nephew).

Patient 20 entered the trial with a baseline assessment on August 22nd 2003, her venous insufficiency was confirmed by a hand-held Doppler assessment and she had an ankle brachial pressure index (ABI) value of 1.

The clinician made the following baseline assessment of the ulcer. The ulcer showed 100% viable tissue, produced moderate amounts of yellow/green exudates, with no odour and no signs of clinical infection. The ulcer was surrounded by healthy intact skin. A tracing was performed giving a baseline wound size of 11.37cm². The patient rated pain in the wound as 2 on a scale where 10 was the highest value.

Over the following 9 weeks she received treatment with Xelma once a week. During the trial treatment continued with Mepilex and 4-layer compression.

Outcome

The patient ulcer size decreased rapidly during the trial. By week 9 her ulcer had healed. Her pain ratings also declined rapidly during the trial. From visit 5 she no longer reported any pain at dressing removal and scored 1 for ulcer pain. From visit 7 and for the rest of the trial she reported no pain at all. Exudate levels showed a steady decrease from moderate to none during the trial. The patient experienced no adverse events during the trial.



Baseline photograph of ulcer Aug 22nd 2003 – wound size 11.37cm²



Photograph week 3



Photograph week 8.
Week 9 the ulcer was healed

Patient 26

A 67 year old woman with an ulcer of 8 months' duration located above the lateral malleolus in the gaiter area. She received ongoing treatment for hypertension.

Before commencing the trial her leg ulcer management involved standard good practice of moist wound healing (NU-gel, J&J and Mepilex), together with compression bandaging (short stretch, Comprilan, BSN). One week prior to inclusion she was treated with antibiotics for a wound infection, however, she no longer had a clinical wound infection when she was included in the trial.

Patient 26 entered the trial with a baseline assessment on April 3rd 2003, her venous insufficiency was confirmed by a hand-held Doppler assessment and she had an ABI value of 1.

The clinician made the following assessment of the ulcer: 10% viable tissue, 90% non-viable tissue (fibrin). The ulcer showed moderate amounts of yellow/ green exudates, with no odour and no signs of clinical infection. Redness could be observed on the surrounding skin. A tracing was performed giving a baseline wound size of 14.50cm²

The patient rated both pain in the wound and pain at dressing removal as 8 out of 10.

Over the following 12 weeks she received treatment with Xelma once a week. During the whole trial Mepilex and short stretch compression with Comprilan were used.

Outcome

The patient's skin condition improved remarkably during the trial. By week 4 the ulcer area had reduced in size by more than 50%. On her final visit after 12 weeks of treatment the investigation wound had almost healed having reduced in size by 99.3% it only measured 0.1cm²

The patient's pain ratings decreased during the trial. At final visit she rated both ulcer pain and pain at dressing removal as 2 out of 10.

No adverse reactions were reported. The exudates levels had decreased from moderate to low. At visit 7 the ratio non-viable/viable tissue had improved to a 100% viable tissue.



Baseline photograph of ulcer April 3rd 2003 – wound size 14.50 cm²



Photograph week 3



Photograph week 9.
Week 12 wound area reduced by 99.3%

Patient 45

An 85 year old man with a venous ulcer of 7 months' duration located above the lateral malleolus in the gaiter area. He suffered from chronic venous insufficiency.

Before commencing the trial his leg ulcer management involved silver nitrate solution (25%) and Gauze together with a compression with (short stretch, Polpress).

Patient 45 entered the trial with a baseline assessment on March 25th 2004. Clinical signs confirmed his venous insufficiency and he had an ABI value of 1.

The clinician made the following assessment of the ulcer: 25% viable tissue, 75% non-viable tissue. The ulcer was surrounded by healthy intact skin. A tracing was performed giving a baseline wound size of 16.10cm²

The patient rated pain in the wound as 3 out of 10, and pain at dressing removal as 2.

Over the following 12 weeks he received treatment with Xelma once a week. During the whole trial period he used Mepilex and short stretch compression with Polpress.

Outcome

At final assessment on, June 17th 2004, the ulcer had almost healed with a wound size of 0.16cm² a wound area reduction of 99%. Exudate levels decreased from low to none during the trial.

The patient's pain ratings (wound and dressing removal) decreased rapidly during the trial. From visit 2 he no longer reported pain at dressing removal and only 1 for ulcer pain. From visit 6 and for the rest of the trial he reported no pain at all.

His wound improved rapidly. By visit 3 the ulcer area had been reduced to a third of its original size. The non-viable/viable tissue ratio had improved to 100% viable tissue.

The patient experienced no adverse events during the trial. However it should be noted that he experienced a temporary increase to moderate exudate levels during his fourth week in the trial. This continued for two weeks after which the exudate levels returned to a low level.



Baseline photograph of ulcer March 25th 2004 – wound size 16,10cm²



Photograph week 3



Week 12 the wound area reduced by 99%

Patient 90

An 80 year old woman with an ulcer of 2 years' duration located above the lateral malleolus in the gaiter area. She received treatment for both rheumatoid arthritis and hypertension. She also suffered from varicose veins.

She had previously been treated with Mepilex together with 4-layer compression with Profore.

She was included in the investigation on October 6th 2003. Her venous insufficiency was confirmed by hand-held Doppler assessment and Duplex scanning and she had an ABI value of 1.2.

The clinician made the following assessment of the ulcer: 50% viable tissue, 50% non-viable tissue. Redness could be observed on the surrounding skin. A tracing was performed giving a baseline wound size of 6.27cm² and she received her first treatment of Xelma.

The patient rated pain in the wound as 2, but did not experience pain at dressing removal.

Over the following 12 weeks she received treatment with Xelma once a week. During the whole trial she used Mepilex and 4-layer compression with Profore.

Outcome

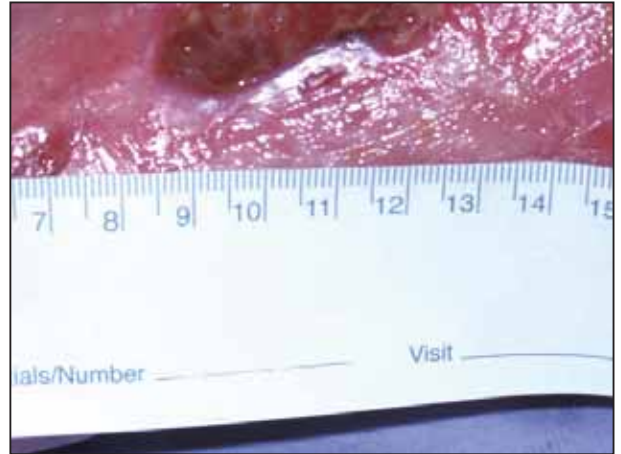
The ulcer showed a good healing rate during the trial. By visit 3 the ulcer had been reduced to two thirds of its original size. At final visit, December 29th 2003, the ulcer had almost healed having reduced to 0.07cm² a reduction of 98.9%.

The patient's pain ratings decreased during the trial. From visit 7 she no longer reported pain.

During week 7 in the trial the patient developed cellulites and received a one-week course of antibiotics. The cellulites was reported as an adverse event although it was not related to the study ulcer. The patient continued to use Xelma in the investigation wound during the antibiotic treatment period.

The viable/ non-viable tissue ratio also improved and by visit 7 the ulcer showed 100% viable tissue. Exudate levels showed a steady decrease from moderate to none during the trial.

The condition of the surrounding skin went from 'redness' to 'healthy intact' during the trial.



Baseline photograph of ulcer Oct 6th 2003 – wound size 6.27cm²



Photograph week 3



Photograph week 8.
Week 12 the wound area reduced by 98.9%



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Mölnlycke Health Care AB (publ)
Box 13080, SE-402 52 Göteborg, Sweden
Phone: + 46 31 722 30 00
www.molnlycke.com

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