A Randomized Clinical Pilot Evaluating The Efficacy For Two Application Regimens Of A Unique Keratin Based Graft In The Treatment Of Non-Healing Diabetic Foot Ulcers

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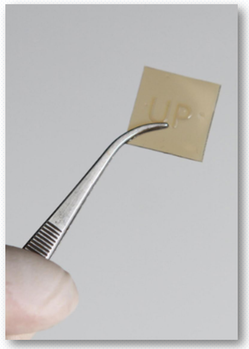
Introduction: The diabetic foot presents a significant challenge for the entire global healthcare system. Complications from non healing diabetic foot ulcers (DFU) such as infection, hospitalization, and amputation continue to rise at an alarming rate. Thus, there is a great need to develop wound care modalities that improve outcomes in this complex patient population. ProgenaMatrix is a novel, advanced wound care product constructed from human keratin and is the only human keratin matrix commercially available. The human keratin technology in ProgenaMatrix is hydrated, non-cellular, not tissue-based, non-resorbing, and supports the body's own healing process. The matrix is made from all-natural components with no synthetic ingredients. It is a monolithic biomaterial made of protein and water. Keratin is the predominant protein with several keratin subtypes. It also contains other non-keratin proteins. ProgenaMatrix™ is 510K approved for application on DFUs and has been shown in case studies to assist in wound healing. A study published by Tang and Kirsner showed that keratin stimulates human keratinocyte migration and types IV and VII collagen expression (Tang, et al., Experimental Dermatology, 2012). Therefore, based on this early promising data, a larger pilot is necessary to further validate these results and identify the likelihood of wound healing with weekly versus bi-weekly application.

Methods: A randomized clinical pilot study of 26 patients with a history of a chronic DFU was performed in which two groups were treated with ProgenaMatrix (applied either weekly or bi-weekly), in addition to standard of care (SOC). SOC included offloading with CAM boot or TCC (if subject's foot too large for boot), appropriate sharp or surgical debridement, infection management (systemic antibiotics only in conjunction with debridement), and application of a Human Keratin Graft, ProgenaMatrix, applied either weekly or bi-weekly, followed by a 3-layer dressing. Patients with nonhealing DFUs (full thickness on the foot or ankle that does not probe to bone), present for more than 4 weeks, and refractory to SOC therapies were included in the study. Subjects with HbA1c greater than or equal to 13% taken at or within 3 months of the initial screening visit and Serum creatinine ≥ 3.0mg/dL within 6 months of randomization or end stage renal disease requiring dialysis were excluded, as well as those wounds with infection, osteomyelitis or exposed bone, probes to bone or joint capsule. Wounds were treated with either weekly or bi-weekly application of ProgenaMatrix, and then followed weekly for up to 12 weeks, or until the wounds were completely epithelialized and determined to be fully healed.

Primary endpoint: Proportion of subjects that obtain complete closure over the 12-week treatment period.

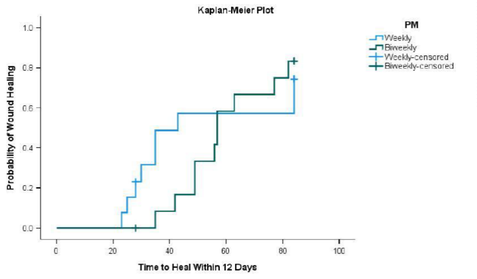
Secondary endpoints: Time to achieve complete wound closure of the target ulcer by the end of 12 weeks, percentage wound area reduction (PAR) during the treatment, measured weekly, change in weekly peripheral neuropathy of the target foot, change in weekly pain in the target ulcer, and change in quality of life.

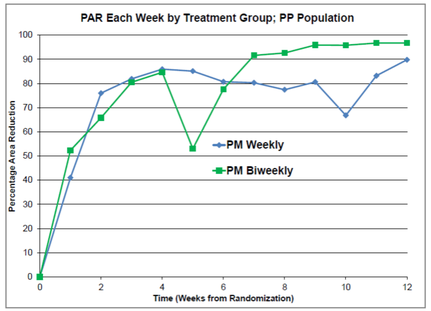


Results (ITT population)

- 77% (10/13) of DFUs treated with bi-weekly application of ProgenaMatrix healed compared with 69% (9/13) treated with weekly application
- The mean time to heal within 12 weeks in the bi-weekly group was 61 days and in the weekly group was 54 days
- The mean PAR at 12 weeks was 94.7% in the bi-weekly group compared with 84.8% in the weekly group
- Number of grafts used in the bi-weekly group was 3.9 compared with 6.2 in the weekly group

	ProgenaMatrix WEEKLY	ProgenaMatrix BI-WEEKLY
Healing rate	9/13 (69%)	10/13 (77%)
Time to heal (days)	54	61
PAR	84.8	94.7
Number of grafts used	6.2	3.9





Case example 1

WEEKLY application

Ulcer history: 7 weeks
Area: 1.0 cm2
HbA1c: 6.6%

Healed: 4 weeks

Case example 2

BI-WEEKLY application

Ulcer history: 4 weeks
Area: 1.1 cm2
HbA1c: 11.8%

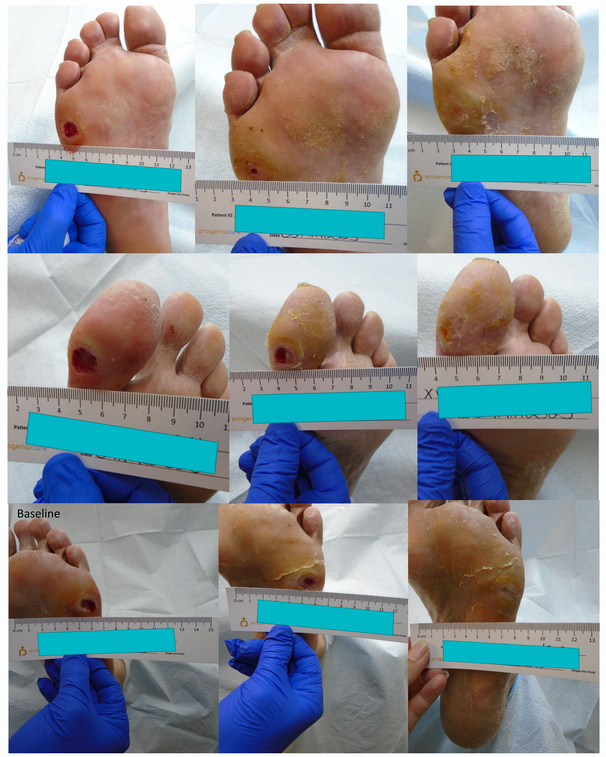
Healed: 8 weeks

Case example 3

WEEKLY application

Ulcer history: 8 weeks
Area: 1.1 cm2
HbA1c: 7.5%

Healed: 3 weeks



Conclusions: In this randomized clinical pilot, 77% (10/13) of patients with a chronic DFU treated with bi-weekly application of ProgenaMatrix healed as compared with 69% (9/13) treated with weekly application. Wound closure was achieved in an average of 61 days in the bi-weekly group and 54 days in the weekly group. The mean PAR at 12 weeks was 94.7% in the bi-weekly group compared with 84.8% in the weekly group, and the number of grafts used in the bi-weekly group was 3.9 compared with 6.2 in the weekly group. Based on the success of this pilot, future studies should be conducted to further investigate the use of a Human Keratin Graft, ProgenaMatrix, for the treatment of chronic DFUs.