A Novel Skin Graft to Accelerate Wound Healing

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Introduction

One of the most prevalent complications of type 2 diabetes is limb amputation caused by diabetic foot ulcer (DFU). The exposure to high glucose changes the normal cell physiology, decreases cell proliferation and migration, promotes the abnormal expression of growth factors, and impairs immune function. These changes make the treatment of DFU to be a constant challenge in diabetes care.

This study evaluated a novel skin graft (TRV-01) developed to improve the wound healing process in a glycated microenvironment.

TRV-01 is a dermal substitute formulated as a cellular sheet for cutaneous use that is applied directly to diabetic foot ulcers. The manufacturing process allows the differentiation of HaLow cells into a stratified semipermeable epidermis intended as a temporary wound cover. It is genetically modified using a no replicative type 5 adenovirus to express two important growth factors: Human insulin and $VEGF_{165}$. TRV-01 reduces advanced glycation end products (AGEs) and enhances the formation vascular network to supply the area of healing.

Acknowledgments

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References

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Methods and Study Design

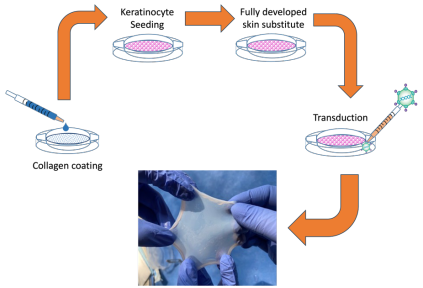

Figure 1. TRV-01 Dermal substitute manufacturing Process.

Chronic diabetic wound model

A standard streptozotocin (STZ)-induced diabetic model was used to evaluate safety and efficacy in rats and pigs. Diabetes was confirmed 48 hours after a single dose of STZ and animals were monitored for 8 weeks prior the administration of TRV-01. Fasting blood glucose range in rats was 350-540 mg/dL (control 55-125) following a standard full thickness model, a 1cm diameter wound was made in the scapular region of the rats and TRV-01 was applied to cover the wound.

Fasting blood glucose range in pigs was 300-500 mg/dL (control 80-120 mg/dL), three 12cm^2 wounds were made on the back of the pigs following a standard full thickness model and one TRV-01 was applied to each wound to cover them. Wounds of animals in control groups were covered with sterile gauzes.

Healthy model

Following a standard full thickness model, a 1cm diameter wound was made in the scapular region of the rats and either TRV-01 or Algisite M® (control) was applied to cover the wound. Biodistribution of the virus was evaluated and key factors were assessed at five different times from day 0 to day 60.

Results

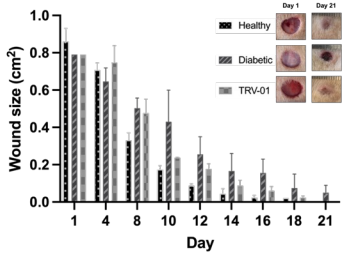

Figure 2. Wound closure, diabetic rats.

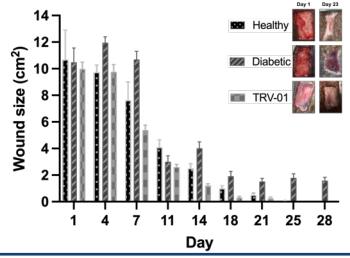

Figure 3. Wound closure, diabetic pigs.

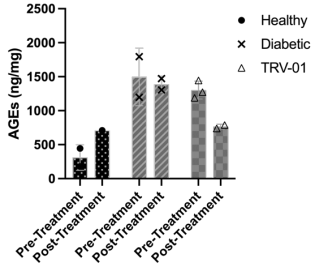

Figure 4. Levels of Advanced Glycation End Products

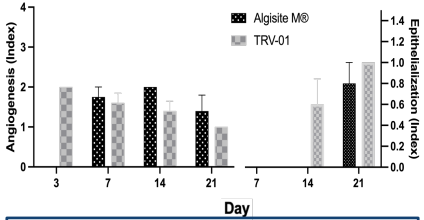

Figure 5. Angiogenesis and epithelialization, healthy rats.

In healthy animals, angiogenesis was observed at day 3 and full epithelialization in 60% of the animals was observed at day 14.

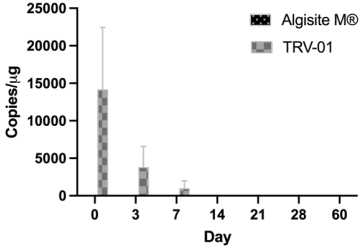

Figure 6. Detection of E4, healthy rats

Safety results showed no viral genomes from TRV-01 in the site of the wound after day 7.

Conclusions

In diabetic animals, this new dressing seems to favor local angiogenesis and has not shown abnormal cell growth, a reduction of AGEs was observed at day 28 and wound closure was similar to healthy animals at day 23. Whilst wounds treated with standard of care didn't fully close at day 28. TRV-01 helps to restore the microenvironment of the wound, improve inflammatory response, and increases the migration of fibroblast and keratinocytes. We must wait for the clinical phase to have better clarity in results .