Important RCTs for Venous Wound Healing

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Disclosures

• Scientific Consultant
  – Veniti
  – Factor Therapeutics
  – Tactile Medical
  – Volcano

VF001

• Factor Therapeutics
• Topical formulation
  – Vitronectin
  – Insulin-like GF-1

VF001

• Vitronectin facilitates adsorption of VF001 into wound tissue in animal studies
  – Complete uptake of IGF into wound tissue

• IGF-1 stimulates fibroblast and keratinocyte proliferation and accel wound healing in animal models

VF001 - Factor Therapeutics Phase II dosing trial

• Target enrollment: 168 at 20 centers
• Treatment arms:
  – VF001 high dose
  – VF001 low dose
  – Placebo

• Primary outcome measure
  – Complete healing at 12 weeks

VF001: % with complete healing at 12 weeks

![](chart.png)
VF001: Wound area reduction at 12 weeks

HP-802 “spray on skin”
- Allogeneic living cell therapy formulation
  - Epidermal keratinocytes
  - Dermal fibroblasts
  - 1:9 ratio in solution – sprayable
- Robust pre-clinical study supported acceleration of wound healing in animal models

HP-802 Phase 2

Phase 2: Signif higher healing in cell treated patients p = .04

HP-802 Phase 3 study
- 542 patients enrolled 55 centers
- Multinational
- Randomized optimal dose of cell therapy vs standard compression based care
- Failed to achieve primary outcome of more wounds closed at 12 weeks

VLU prospective trial failures
- Numerous growth factor therapies
  - PDGF, KGF, ILGF
- Connexin 43
- Cryopreserved human fibroblasts
- Platelet releasate
- Ultrasound therapy
Why is the VLU so difficult to heal?

- Inadequate therapies
- Inadequate trial design
- Poor control of underlying etiology of poor healing
- Lack of understanding of wound healing
- Inability to measure wound metrics

Wound metrics

- VLU does not heal due to
  - Uncontrolled inflammation
  - Uncontrolled venous hypertension
  - Bacterial overgrowth
  - Poor diagnosis (not actually a venous ulcer)

Wound study design

- Lack of detailed diagnosis of venous insufficiency
  - Is it really a venous ulcer?
  - Does healing vary based on whether there is obstruction?
  - Deep vs superficial disease?
  - Does overall severity of venous disease affect healing?

Compression management of venous insufficiency

- How do we measure whether compression is able to eliminate venous hypertension?
  - Can’t tell with duplex
- If we don’t know we don’t know whether patients will have a high chance of healing with compression alone

Clinical Trial Design needs to change for VLU

- Must do detailed venous evaluation in all VLU clinical trials
  - Increase knowledge of which patients will not heal without correction of venous disease
- Need method to understand when venous hypertension is corrected
- Probably topical therapies are irrelevant

Fix all abnormal venous function from heart to wound!