A Phase II Randomized Double-Blind, Placebo Controlled Study in Patients with Critical Limb Ischemia to Evaluate the Safety and Efficacy of hSDF-1 plasmid (JVS-100) Post Open or Endovascular Revascularization (STOP-PAD Trial)

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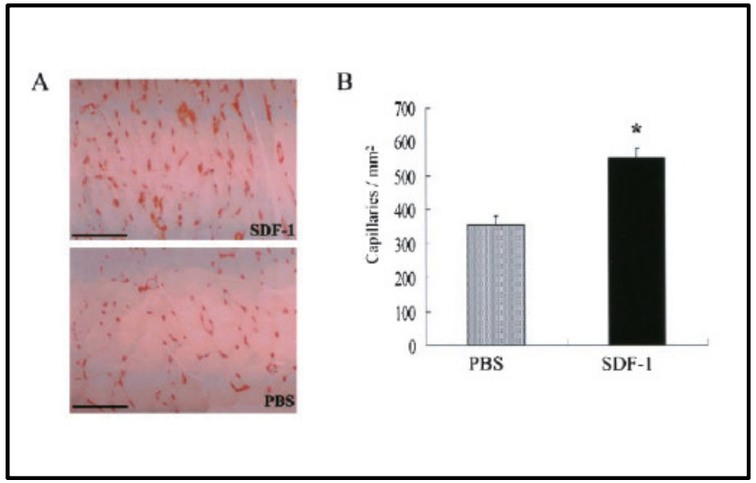
Background – Critical Limb Ischemia

- After over 20 yrs of research we are left with bypass and angioplasty alone to treat this disease.
- However:
  - Only 20-30% of wounds heal within 3 months
  - Wounds are associated with:
    - Low quality of life
    - Depression
    - Increased health care cost
    - Amputations
    - Death

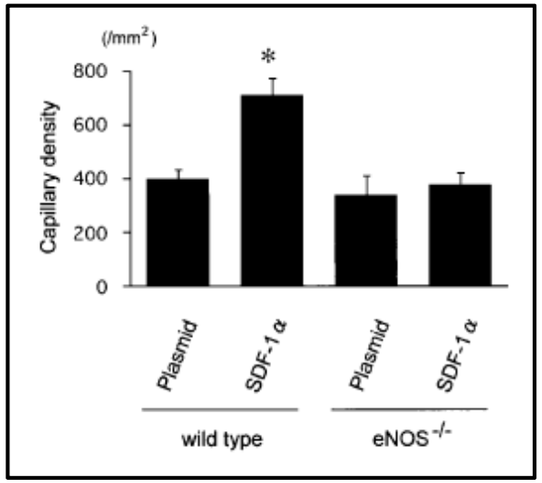
Shishehbor et al. J Am Coll Cardiol 2016;68:2002-15

- **JVS-100** is a non-viral DNA plasmid based therapy that encodes stromal cell-derived factor-1(SDF-1)



Yamaguchi, J. Circulation 2003;107:1322

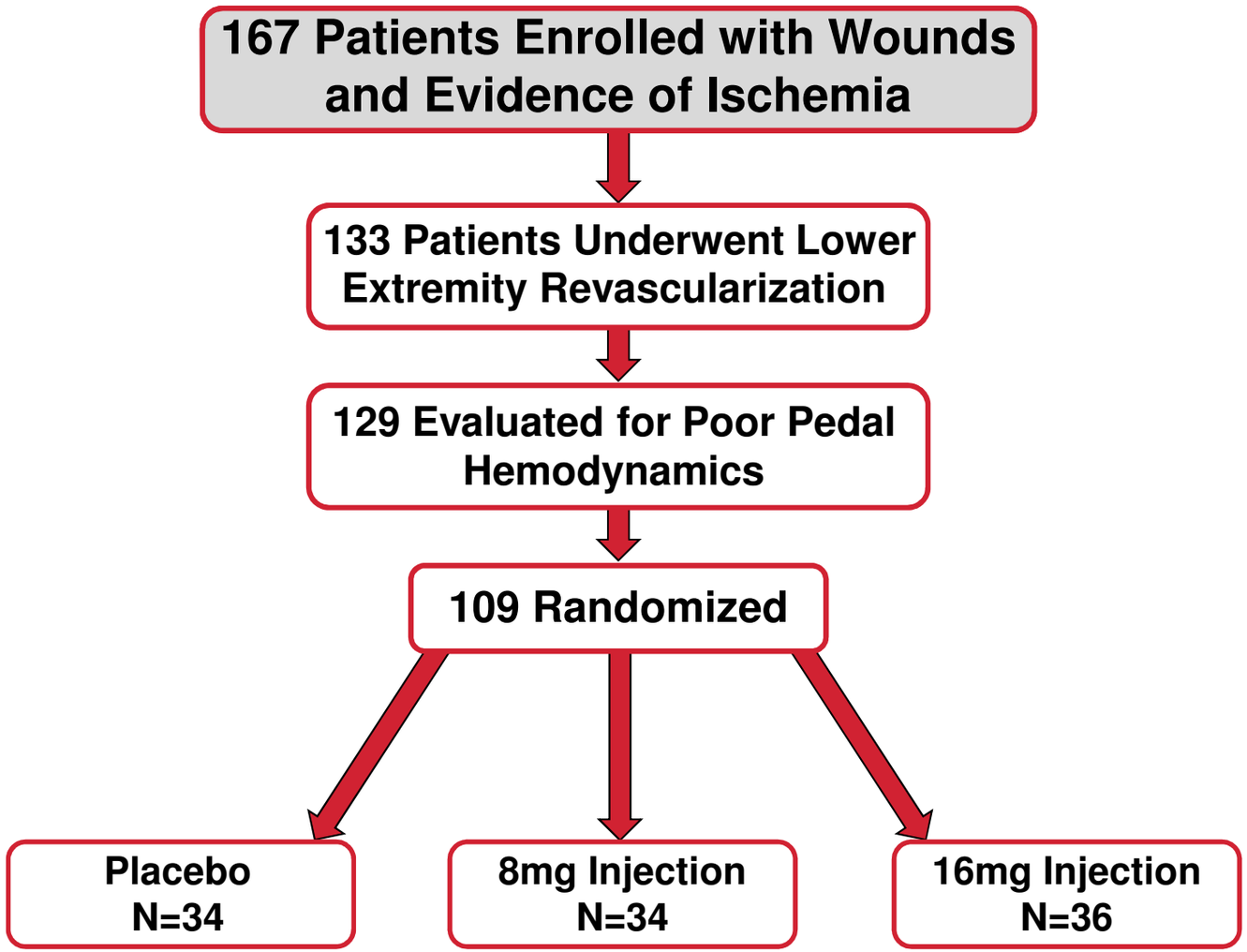
- **SDF-1** through binding of the CXCR-4 receptor activates:
  - Endogenous regenerative repair pathways
  - Promotes new blood vessel growth
  - Prevents cell death
  - Causes remodeling of scar tissue



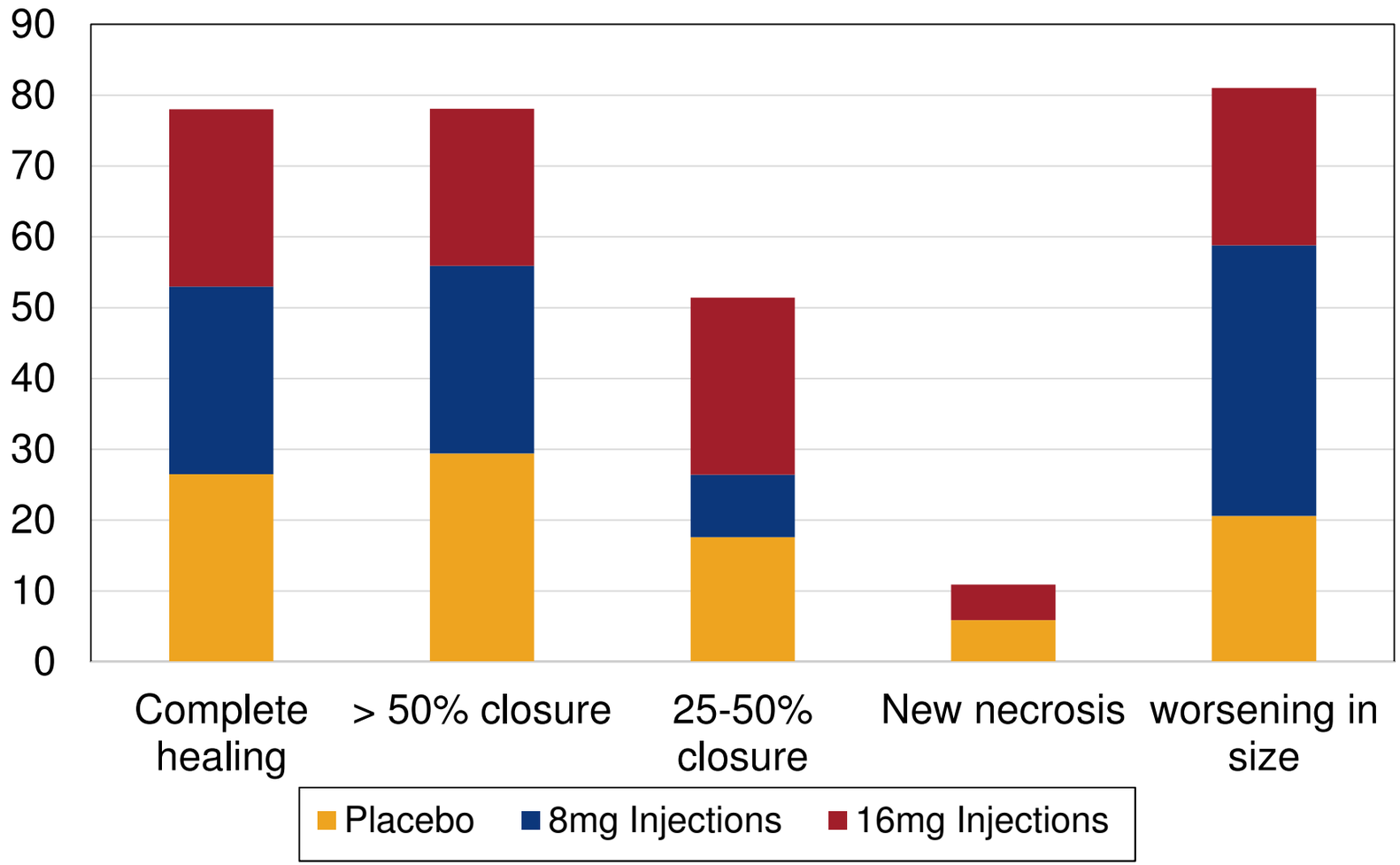
Hiasa, K. Circulation 2004;109:2454

Askari AT et al, Lancet 2003;362:697-703

STOP-PAD Trial Design and Patient Disposition



Primary Efficacy (P = 0.93)



Conclusions

- Adjunctive injection of JVS-100 failed to impact wound healing or rates of MALE in patients with Rutherford class V and VI CLI
- Only 25% of wounds healed within 3 months despite advanced revascularization and rigorous follow-up
- A quarter of the wound actually got bigger over 3 months
- Will anxiously await 6 months results; however, future biologic therapies may require addressing multiple pathways