

## **Topical vascular endothelial growth factor (VEGF, telbermin) for neuropathic diabetic foot ulcers: Phase II randomized, double-blind, multi-dose trial**

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### **Purpose**

Topical application of telbermin 72  $\mu\text{g}/\text{cm}^2$  three times weekly for 6 weeks was well tolerated in a Phase I trial. We therefore evaluated wound healing efficacy and safety/tolerability of telbermin vs. placebo applied topically to neuropathic diabetic foot ulcers in a Phase II 12-week dose-ranging trial.

### **Methods**

At 40 U.S. sites, we enrolled ~170 patients with Type 1 or 2 DM, evidence of peripheral neuropathy, ABI >1.2, and a full thickness cutaneous ulcer at or below the malleolus. Patients were randomized to placebo gel or telbermin (24, 72, or 216  $\mu\text{g}/\text{cm}^2$ ) on top of standard of care (including offloading footwear and debridement). After instruction, patients applied study gel daily at home for up to 12 weeks. Outcome measures included the incidence of complete ulcer closure within 12 weeks (primary) and 24 weeks, time to complete closure, and change in ulcer surface area (secondary).

### **Results**

For the Intent-to-treat (ITT) population (all randomized patients), there were no significant differences between any of the telbermin dose groups versus placebo in the incidence of complete healing at 12 and 24 weeks (Table), or in other key secondary efficacy outcome measures. Overall adverse event rates, serious adverse event rates, and serum VEGF levels were similar across treatment groups.

### **Conclusion**

While telbermin overall appeared to be safe and well-tolerated with no evidence of significant systemic absorption, it failed to meet the primary efficacy endpoint of complete healing within 12 weeks for any dose.

Table: Ulcer Healing at 12 and 24 Weeks, Intent-to-Treat Population

	Placebo (N=42)	Telbermin 24 µg/cm <sup>2</sup> (N=43)	Telbermin 72 µg/cm <sup>2</sup> (N=43)	Telbermin 216 µg/cm <sup>2</sup> (N=42)
<b>Complete Healing at 12 weeks</b> N (%) p-value	17 (40.5) -	15 (34.9) 0.7	17 (39.5) 0.9	9 (21.4) 0.09
<b>Complete Healing at 24 weeks</b> N (%) p-value	21 (50.0) -	18 (41.9) 0.6	21 (48.8) 0.9	16 (38.1) 0.4

P-value based on logistic regression model with covariate = baseline ulcer area