

Multicenter, phase 2, randomized evaluation of topical recombinant human thrombin (rhThrombin) for hemostasis in subjects undergoing vascular surgery

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Up to 40-80% of patients exposed intraoperatively to commercial bovine thrombin preparations develop antibodies to bovine thrombin and bovine factor V. Some of these acquired antibodies may cross-react with the corresponding native human proteins and increase the risk of severe postoperative bleeding diatheses and/or thrombotic events. To minimize these risks, rhThrombin has been produced from cell culture and evaluated in randomized, double-blinded, multicenter phase 2 studies in subjects undergoing vascular surgery. Subjects undergoing infrainguinal arterial bypass surgery or arteriovenous graft formation using synthetic conduits were treated with either rhThrombin (1000 U/mL) or placebo in combination with an absorbable gelatin sponge applied to each anastomotic site requiring a topical hemostatic agent. The primary objective of the studies was to evaluate the safety of rhThrombin as determined by incidence and severity of adverse events. A total of 60 subjects, age range 32-89 years, were enrolled; 38 subjects were exposed to rhThrombin. The most common adverse events (AEs) were postprocedural pain, nausea, pyrexia, vomiting, hypotension, peripheral edema, ecchymosis, insomnia, and graft thrombosis. Nausea, vomiting, and insomnia were reported more frequently in subjects receiving rhThrombin. Most AEs were mild to moderate in severity and were typical for the postoperative period in this surgical population. There were no serious AEs considered related to rhThrombin treatment. One of 37 subjects (2.7%) developed non-neutralizing antibodies to rhThrombin 4 weeks following treatment. Most subjects (88%) were treated with study drug at both anastomotic sites. Hemostasis occurred within 10 minutes at 52 of 58 (90%) anastomoses treated with rhThrombin and 41 of 55 (75%) anastomoses treated with placebo. The mean time to hemostasis was 3.2 minutes with rhThrombin treatment versus 4.5 minutes with placebo (29% relative improvement). rhThrombin appeared to be safe and well tolerated in subjects undergoing vascular surgery, and may provide a valuable alternative to bovine thrombin for use in surgical hemostasis.