FibrocapsTM, a novel fibrin sealant, for bleeding during hepatic resection: Results of a phase 2, randomized, controlled study.

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Abstract:

Introduction: Fibrin sealants mimic the final stage of the clotting cascade and are used when control of bleeding by surgical technique is difficult. Diffuse bleeding of the hepatic resection surface can be a problem due to the vascularity of the liver, for which fibrin sealants have been used. FibrocapsTM (ProFibrix, Leiden, The Netherlands) is a ready-to-use, premixed powder blend of human plasma-derived fibrinogen and thrombin. We conducted a study of the efficacy and safety of Fibrocaps in liver surgery. Methods: Study FC-002 NL was a Phase 2, randomized, single-blind, controlled, comparative efficacy and safety study of Fibrocaps in subjects with diffuse bleeding during hepatic resection at 5 centers in The Netherlands. 56 subjects were randomized (2 : 1) during surgery to Fibrocaps (n = 39) or gelatin sponge (n = 17). Treatment was followed by a 10-min observation period where hemostasis was evaluated every minute, with failure defined as lack of hemostasis by 10 min. The primary efficacy endpoint was the mean time to hemostasis (TTH), and the secondary was the incidence of hemostasis at 10, 5 and 3 min. Overall safety was determined by treatment-emergent adverse events, clinical labs and antithrombin antibodies monitored for 4 weeks after treatment. Results: Subject demographics were similar across both treatment groups (64% male, mean age of 61 yrs). The mean +/- SD dose of Fibrocaps was 1.4 +/- 0.5 g used for a mean +/- SD bleeding surface area of 58 +/- 29 cm². There was a statistically significant reduction on the intent-to-treat analysis of the mean TTH of Fibrocaps 2.2 +/- 1.2 min vs. gelatin sponge 4.4 +/- 3.1 (p = 0.004). There were no treatment failures in the Fibrocaps arm and 3

in the control arm (p = 0.025). The incidence of hemostasis at 5 min was also statistically significant for Fibrocaps (p = 0.022). The safety was comparable across both treatments, with most AEs gastrointestinal, and classified mild or moderate and unrelated to treatment. No neutralizing anti-thrombin antibodies were detected. Conclusion: These efficacy results with Fibrocaps in liver surgery demonstrate a significant reduction in mean bleeding time across patients and in the incidence of treatment failure. The safety profile of Fibrocaps in this study was very good and consistent with events expected in subjects with multiple diseases undergoing major hepatic resection under general anesthesia. The observed benefit: risk profile strongly supports the conduct of a Phase 3 study in surgical hemostasis.