Safety and hemostatic efficacy of fibrin pad in partial nephrectomy: results of an open-label phase I and a randomized, standard-of-care-controlled phase I/II study.

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Abstract:

BACKGROUND: Bleeding severity, anatomic location, tissue characteristics, and visibility are common challenges encountered while managing intraoperative bleeding, and conventional hemostatic measures (suture, ligature, and cautery) may sometimes be ineffective or impractical. While topical absorbable hemostats (TAH) are useful hemostatic adjuvants, each TAH has associated disadvantages.

METHODS: We evaluated the safety and hemostatic efficacy of a new advanced biologic combination product-fibrin pad-to potentially address some gaps associated with TAHs. Fibrin pad was assessed as adjunctive hemostat in open partial nephrectomy in single-center, open-label, Phase I study (N=10), and as primary hemostat in multicenter, single-blind, randomized, standard-of-care (SOC)-controlled Phase I/II study (N=7) in Israel. It was used to control mild-to-moderate bleeding in Phase I and also spurting arterial bleeding in Phase I/II study. Phase I study assessed safety and Phase I/II study, proportion of successes at 10min following randomization, analyzed by Fisher exact tests at 5% significance level.

RESULTS: Phase I (N=10): All patients completed the study. Hemostasis was achieved within 3-4min (average=3.1min) of a single application in all patients. Fibrin pad was found to be safe for human use, with no product-related adverse events reported. Phase I/II (N=7): Hemostatic success

at 10min (primary endpoint) was achieved in 3/4 patients treated with fibrin pad versus 0/3 patients treated with SOC. No clinically significant change in laboratory or coagulation parameters was recorded, except a case of post-procedural hemorrhage with fibrin pad, which was considered serious and related to the fibrin pad treatment, and required re-operation. Although Data Safety Monitoring Board authorized trial continuation, the sponsor decided against proceeding toward an indication for primary treatment of severe arterial hemorrhage as a replacement for sutures. The study was suspended after 7/30 planned subjects were enrolled.

CONCLUSIONS: The first-in-man trial of fibrin pad demonstrated its safety and efficacy as an adjunctive hemostatic technique for mild-to-moderate bleeding in partial nephrectomy. The study also suggested that the product should not replace sutures or meticulous surgical techniques for the treatment of severe arterial hemorrhage.

TRIAL REGISTRATION: Phase I/II trial, NCT00598130.