Edoxaban Effects on Bleeding Following Punch Biopsy and Reversal by a 4-Factor PCC


Background and Objective: Edoxaban, a novel oral anticoagulant (NOAC), is an investigational, oral, once-daily anticoagulant that specifically and reversibly inhibits factor Xa. There are currently no specific reversal agents for the NOACs, although a 3-factor prothombin complex concentrate (PCC) has shown utility in reversing some biomarker effects. This two part study developed a punch biopsy model in healthy subjects to assess the anticoagulant effects of edoxaban and evaluated reversal by Beriplex®, a 4-factor prothombin complex concentrate (PCC). Bleeding duration (BD) was the primary endpoint, and key secondary endpoints were blood loss volume (BV), endogenous thrombin potential (ETP), and prothrombin time (PT).

Methods: This was a phase 1, single-dose, sponsor-unblinded, study. Part 1 was a two-way crossover with a 7 day washout between treatments (single dose of 60 or 180 mg edoxaban). Part 2 was a placebo-controlled, sequential descending PCC dose, two-way crossover with a =14-day washout between treatments. Healthy subjects, aged 18-45 y, were enrolled into part 1 (n=18) or into one of three PCC dose cohorts in part 2 (N=28-33 per cohort): 50 IU/kg, 25 IU/kg, or 10 IU/kg. Within each cohort in part 2, subjects received two treatments in random order: a single dose of edoxaban 60 mg followed by an infusion of PCC (treatment A) and a single dose of edoxaban 60 mg followed by an infusion of placebo (Treatment B). Infusions were started at approximately 1.75 h after edoxaban dosing and ended uniformly at 2.25 h after the edoxaban dose. For both parts, time matched punch biopsies were performed on Day -1 (baseline) and on Day 1, 2.75 h after edoxaban dosing. BD and BV were assessed after each biopsy. Serial sampling was performed for biomarkers (PT and ETP) and edoxaban pharmacokinetics. Treatment-emergent adverse events (TEAEs) were recorded throughout the study. The sample size for part 2 was determined based on the effect size and variability observed for BD following 60 mg edoxaban in Part 1.

Results: Results will be available in July 2014 and will be presented at the meeting.

Conclusions: This is the first trial to show an edoxaban effect on bleeding time following punch biopsy and assess the ability of a 4-factor PCC to reverse the effect of edoxaban on bleeding.
Disclosure: