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LB003

## Raps (rivaroxaban in antiphospholipid syndrome): a prospective randomised controlled phase II/III clinical trial of rivaroxaban vs. warfarin in patients with thrombotic antiphospholipid syndrome, with or without SLE

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**Background:** Rivaroxaban has been shown to be effective and safe compared with warfarin for the treatment of venous thromboembolism (VTE) in major phase III prospective randomised controlled trials (RCT), but the results may not be directly generalisable to patients with antiphospholipid syndrome (APS).

**Aims:** The primary aim of RAPS (http://www.isrctn.com/ISRCTN68222801) is to demonstrate, in patients with APS and previous VTE, that the intensity of anticoagulation achieved with rivaroxaban is not inferior to that of warfarin. Secondary aims are to compare rates of recurrent thrombosis and bleeding, and the quality of life in patients on rivaroxaban with those on warfarin.

**Methods:** RAPS is a phase II/III prospective, non-inferiority RCT in which eligible patients with APS, who are on warfarin, target International Normalised Ratio (INR) 2.5 for previous VTE, are randomised either to continue warfarin (standard of care) or to switch to rivaroxaban 20 mg daily. Intensity of anticoagulation is assessed using thrombin generation (TG), with the endogenous thrombin potential (ETP) as the key parameter. The primary outcome is the percentage change in ETP from randomisation to day 42. Markers of *in vivo* coagulation activation, prothrombin fragment 1.2, thrombin-antithrombin complex and D-dimer, will also be measured.

**Results:** Results will be submitted as soon as available, and presented at the meeting.

**Conclusion:** If RAPS demonstrates that i) that the anticoagulant effect of rivaroxaban is not inferior to that of warfarin using the TGT; and ii) the absence of any adverse effects that cause concern with regard to the use of rivaroxaban, this would provide sufficient supporting information to make rivaroxaban a standard of care for the treatment of APS patients with previous VTE, requiring a target INR of 2.5.

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LB004

## ANNEXA™-A PART 2: A phase 3 randomized, double-blind, placebo-controlled trial demonstrating sustained reversal of apixaban-induced anticoagulation in older subjects by andexanet ALFA (PRT064445), a universal antidote for factor XA (FXA) inhibitors

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**Background:** Direct FXa inhibitors appear to have superior or comparable anticoagulant efficacy and safety relative to warfarin. However, a specific antidote for these agents is lacking in case of major bleeding. Andexanet alfa (AnXa) is a modified, recombinant human FXa molecule under clinical development as a specific antidote for FXa inhibitors. We have recently reported data for Part 1 of the Phase 3 registration study in older subjects anticoagulated with apixaban, where an AnXa IV bolus rapidly and significantly reversed anti-FXa activity and restored thrombin generation. Here we report data from Part 2 of this study where AnXa was administered as a bolus *plus* an infusion regimen in a similar study population.

**Aims:** To demonstrate immediate and sustained reversal of apixaban anticoagulation following administration of AnXa.

**Methods:** ANNEXA™-A is a Phase 3, double-blind, placebo-controlled study of AnXa in older subjects treated with apixaban. Part 2 investigated a bolus of AnXa followed by a 2-hr continuous infusion. In Part 2, 34 subjects age 50 to 75 were randomized to receive either AnXa or placebo in a 3:1 ratio. All subjects received apixaban 5 mg PO BID for 4 days to achieve steady state plasma levels. AnXa (400 mg IV bolus followed by a 2-hr infusion at 4 mg $min^{-1}$) or placebo was administered on Day 4, 3 h after the last apixaban dose (~ apixaban Cmax). Safety data were collected through Day 43. The primary efficacy endpoint is the percent change from baseline in anti-FXa activity at its nadir between 10 min prior to and 5 min after the end of the continuous infusion. Additional efficacy endpoints included reduction in plasma free fraction of apixaban and restoration of thrombin generation.

**Results:** Part 2 of the study has been completed. Efficacy and safety results will be presented and discussed.

**Conclusion:** This study continues our investigations of AnXa as an antidote for reversing the anticoagulant effects of apixaban and other FXa inhibitors.