

 ANTICOAGULATION THERAPY

Antidote to factor Xa inhibitors

“
... andexanet
alfa
significantly
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activity ...”

Andexanet alfa is “a potential universal antidote for both direct and indirect factor Xa inhibitors”. This conclusion comes from the ANNEXA trials, the results of which were presented at the AHA Scientific Sessions 2015 and published in *NEJM*. Andexanet alfa is a recombinant modified human factor Xa protein that binds to factor Xa inhibitors with high affinity, but which is catalytically inactive.

A total of 145 healthy participants (mean age 57.9 years, 39% women) were enrolled in the two studies. Individuals in the ANNEXA-A trial received apixaban (5 mg twice daily; $n = 65$); those in the ANNEXA-R trial received

rivaroxaban (20 mg daily; $n = 80$). Patients in both trials were randomly assigned to receive either administration of andexanet alfa as a 400 mg intravenous bolus (30 mg/min) or placebo. In participants receiving apixaban, andexanet alfa significantly reduced anti-factor Xa activity (94%) compared with placebo (21%). Similarly, in those receiving rivaroxaban, andexanet alfa reduced anti-factor Xa activity (92%) compared with placebo (18%). Thrombin generation was fully restored within 2–5 min with andexanet alfa in 100% of individuals receiving apixaban and in 96% of those receiving rivaroxaban, compared with 11% and 7% of

those who received placebo in each trial, respectively. The effects were sustained when andexanet alfa was administered as a bolus plus infusion, and no serious adverse or thrombotic events were reported.

The investigators conclude that “the rapid onset and offset of action of andexanet [alfa] and the ability to administer it as a bolus or as a bolus plus an infusion may provide flexibility with regard to restoration of haemostasis when urgent factor Xa inhibitor reversal is required”.

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ORIGINAL ARTICLE Siegal, D. M. Andexanet alfa for the reversal of factor Xa inhibitor activity. *N. Engl. J. Med.* doi:101056/NEJMoa1510991