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ORIGINAL ARTICLE

Full Study Report of Andexanet Alfa for Bleeding Associated with Factor Xa Inhibitors

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Background

- Andexanet alfa is a modified recombinant inactive form of human factor Xa developed for reversal of factor Xa inhibitors.
- Andexanet was approved by the Food and Drug Administration (FDA) in May 2018, under its Accelerated Approval Program, for patients treated with apixaban or rivaroxaban, when reversal of anticoagulation is needed owing to life-threatening or uncontrolled bleeding.

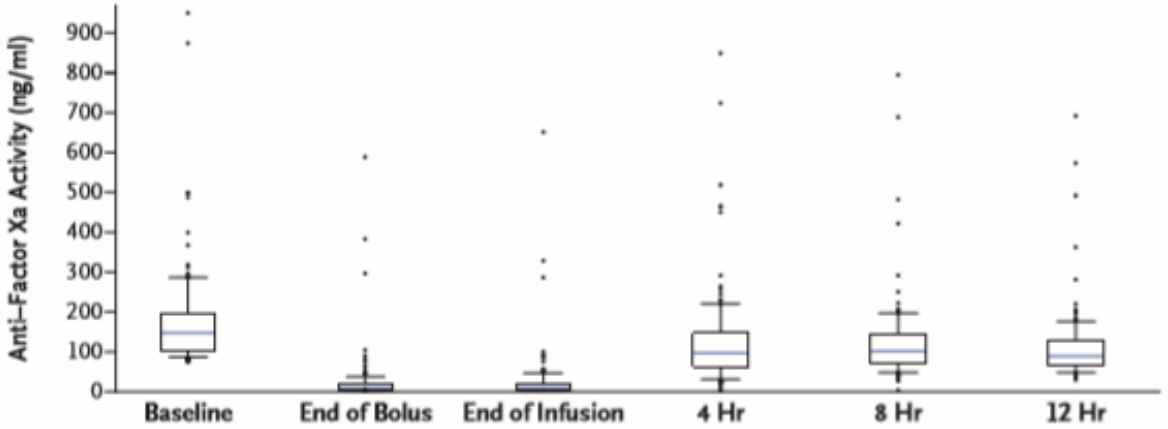
Methods

- The Andexanet Alfa, a Novel Antidote to the Anticoagulation Effects of Factor Xa Inhibitors (ANNEXA-4) study is a single-group cohort study designed to assess the efficacy and safety of andexanet in patients with acute major bleeding occurring while taking a factor Xa inhibitor.
- 352 patients who had acute major bleeding within 18 hours after administration of a factor Xa inhibitor.
- The co-primary outcomes were the percent change in anti–factor Xa activity after andexanet treatment and the percentage of patients with excellent or good hemostatic efficacy at 12 hours after the end of the infusion, with hemostatic efficacy adjudicated on the basis of prespecified criteria.

Results

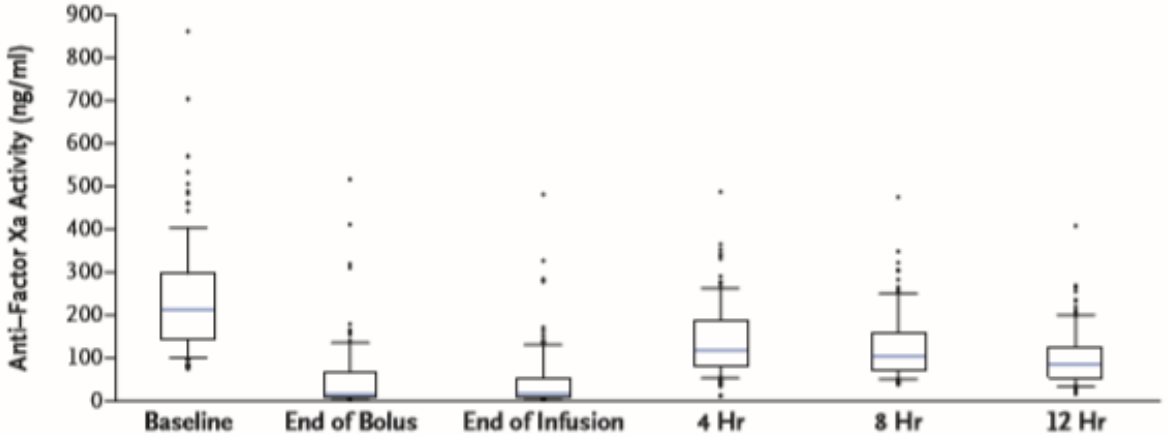
- Patients had a mean age of 77 years, and most had substantial cardiovascular disease.
- Bleeding was predominantly intracranial (in 227 patients [64%]) or gastrointestinal (in 90 patients [26%]).
- In patients who had received apixaban, the median anti–factor Xa activity decreased from 149.7 ng per milliliter at baseline to 11.1 ng per milliliter after the andexanet bolus (92% reduction); in patients who had received rivaroxaban, the median value decreased from 211.8 ng per milliliter to 14.2 ng per milliliter (92% reduction).
- Excellent or good hemostasis occurred in 204 of 249 patients (82%) who could be evaluated.
- Within 30 days, death occurred in 49 patients (14%) and a thrombotic event in 34 (10%).

A Patients Who Received Apixaban

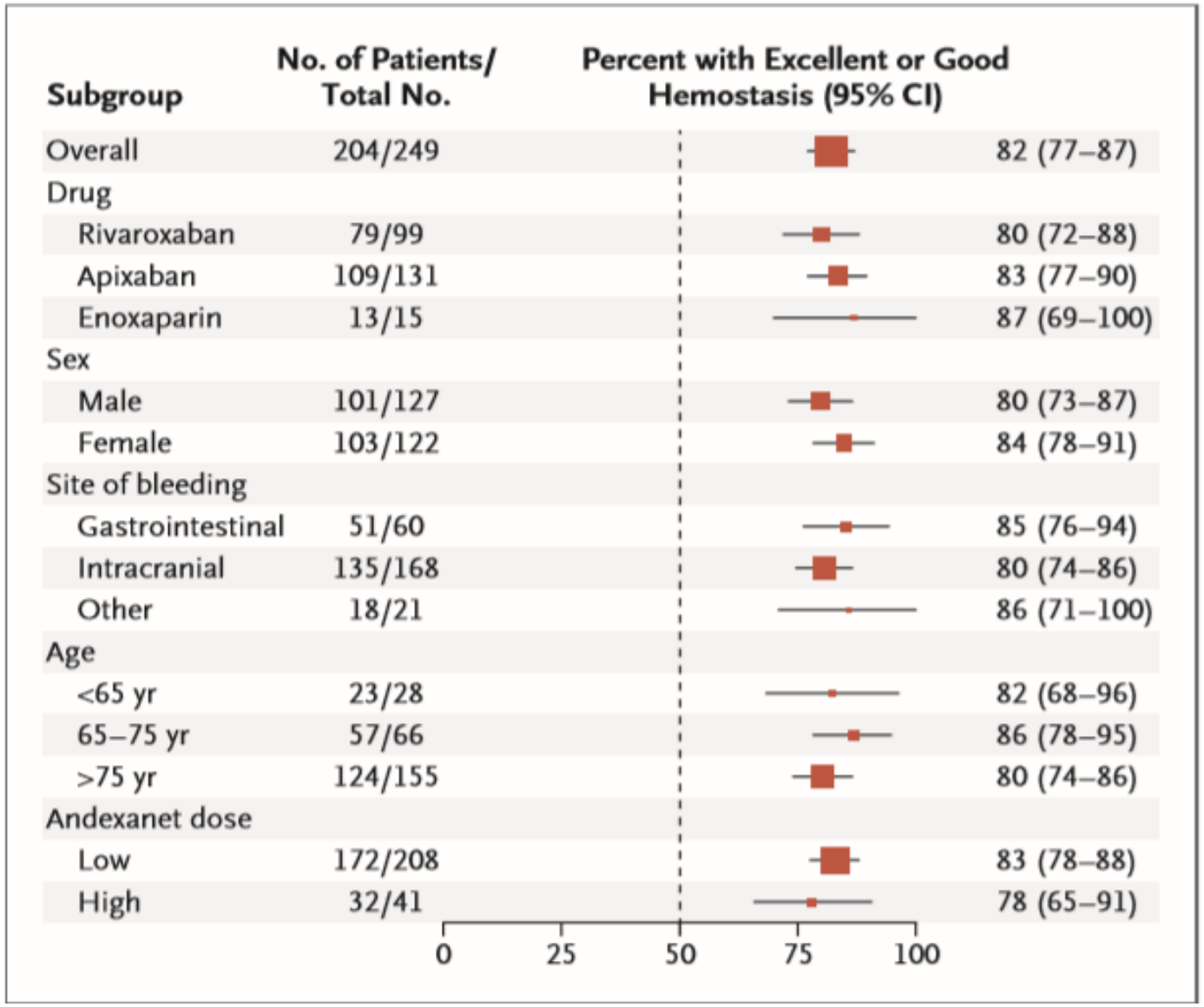


	Baseline	End of Bolus	End of Infusion	4 Hr	8 Hr	12 Hr
Median	149.7	11.1	11.5	97.2	104.6	91.2
Percent Change (95% CI)		–92 (–93 to –91)	–92 (–93 to –91)	–32 (–38 to –29)	–34 (–36 to –27)	–38 (–41 to –34)

B Patients Who Received Rivaroxaban



	Baseline	End of Bolus	End of Infusion	4 Hr	8 Hr	12 Hr
Median	211.8	14.2	16.5	121.7	101.4	85.5
Percent Change (95% CI)		–92 (–94 to –88)	–90 (–93 to –87)	–42 (–45 to –36)	–48 (–52 to –45)	–62 (–65 to –58)


Subgroup
No. of Patients/ Total No.
Percent with Excellent or Good Hemostasis (95% CI)
Overall 204/249 82 (77–87)
Drug
Rivaroxaban 79/99 80 (72–88)
Apixaban 109/131 83 (77–90)
Enoxaparin 13/15 87 (69–100)
Sex
Male 101/127 80 (73–87)
Female 103/122 84 (78–91)
Site of bleeding
Gastrointestinal 51/60 85 (76–94)
Intracranial 135/168 80 (74–86)
Other 18/21 86 (71–100)
Age
<65 yr 23/28 82 (68–96)
65–75 yr 57/66 86 (78–95)
>75 yr 124/155 80 (74–86)
Andexanet dose
Low 172/208 83 (78–88)
High 32/41 78 (65–91)
0
25
50
75
100

Conclusions

- In patients with acute major bleeding associated with the use of a factor Xa inhibitor, treatment with andexanet markedly reduced anti–factor Xa activity, and 82% of patients had excellent or good hemostatic efficacy at 12 hours, as adjudicated according to prespecified criteria.