Low-dose edoxaban in patients ≥80 years with atrial fibrillation who met dose-reduction criteria

Randomized analysis between edoxaban 15 mg and 30 mg

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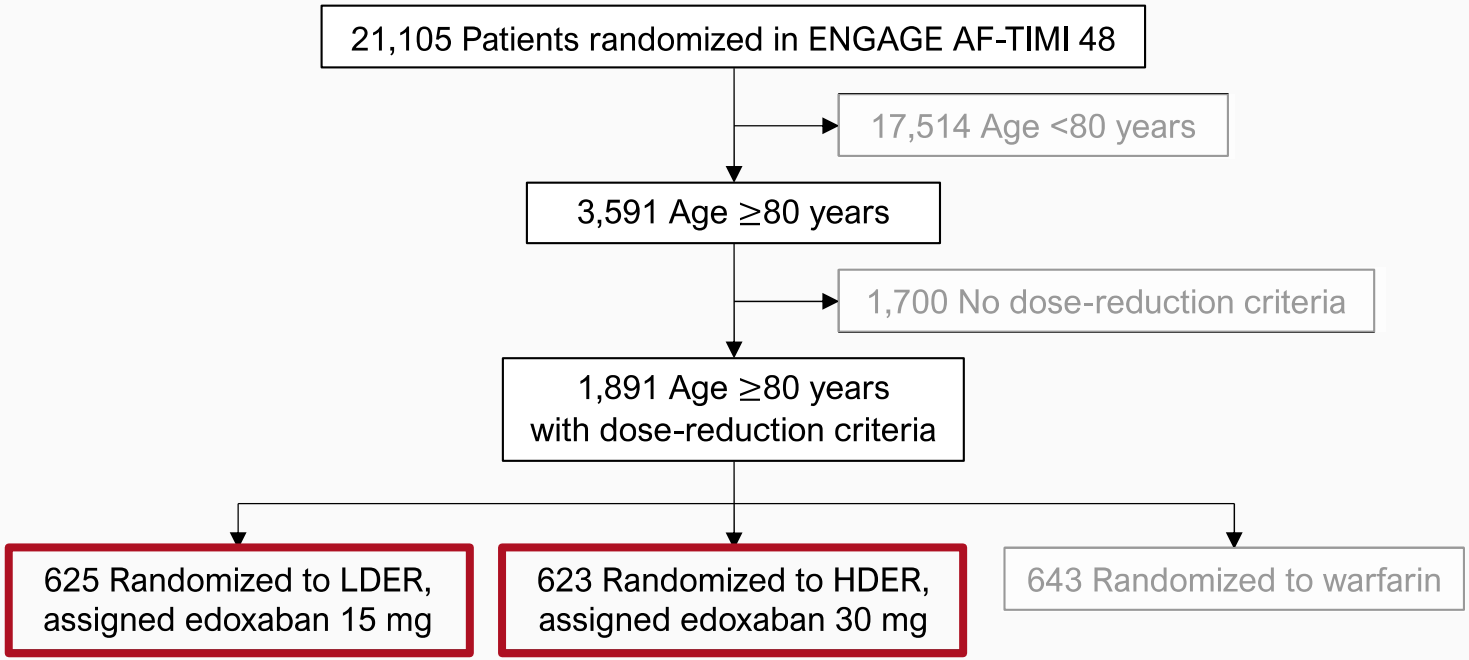
Background

- Dose-reduction (DR) criteria vary across DOACs
- Current edoxaban DR criteria (from 60 to 30 mg) do not consider age, but anticoagulants exhibit a stronger effect in older adults
- Patients meeting standard DR criteria plus advanced age may benefit from an edoxaban dose even lower than 30 mg
- **Purpose: to evaluate ischemic and bleeding outcomes in patients with AF ≥80 years who met DR criteria receiving edoxaban 15 mg or 30 mg**

Methods

- ENGAGE AF–TIMI 48 randomized 21,105 patients with AF to warfarin or one of two edoxaban regimens:
  - Higher-dose regimen: full dose 60 mg, reduced dose 30 mg
  - Lower-dose regimen: full dose 30 mg, reduced dose 15 mg
- Dose reduction was applied in patients meeting at least 1 DR criteria:
  - Creatinine clearance ≤50 mL/min
  - Weight ≤60 kg
  - Concomitant use of strong P-glycoprotein inhibitors
- Patients ≥80 years who met DR criteria were included in this analysis

Methods



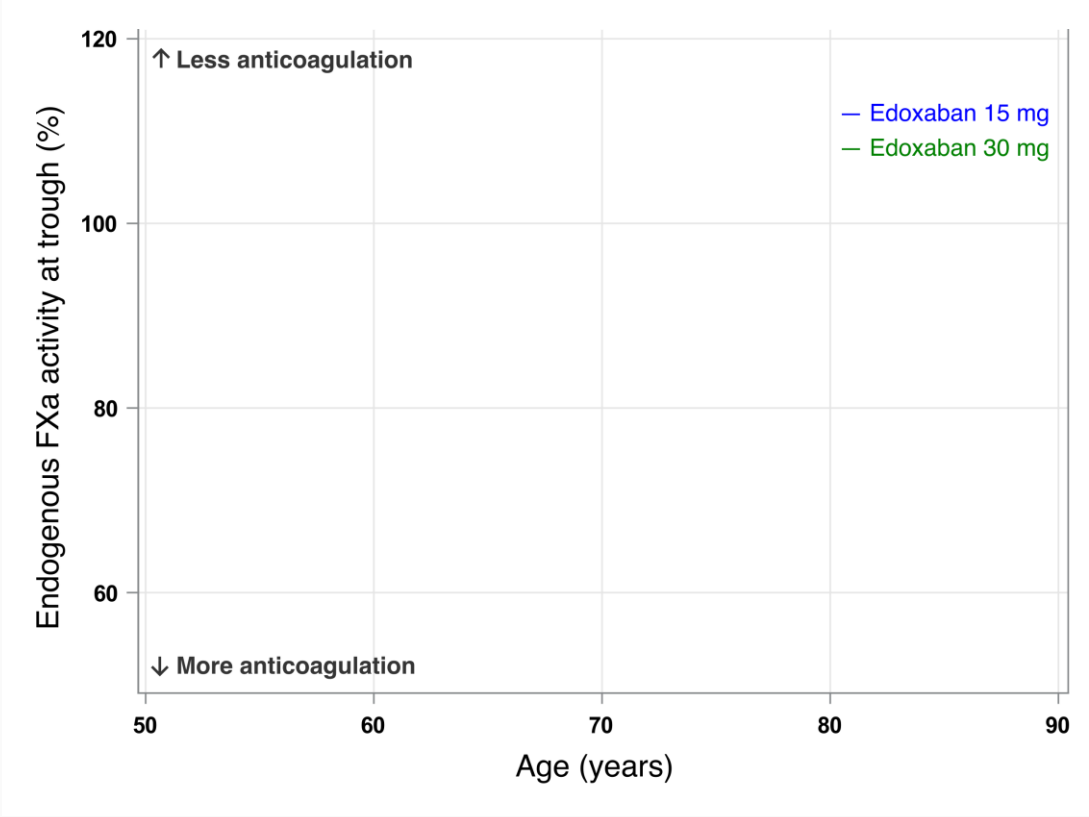
HDER, higher-dose edoxaban regimen (full dose 60 mg, reduced dose 30 mg).
LDER, lower-dose edoxaban regimen (full dose 30 mg, reduced dose 15 mg).

Results

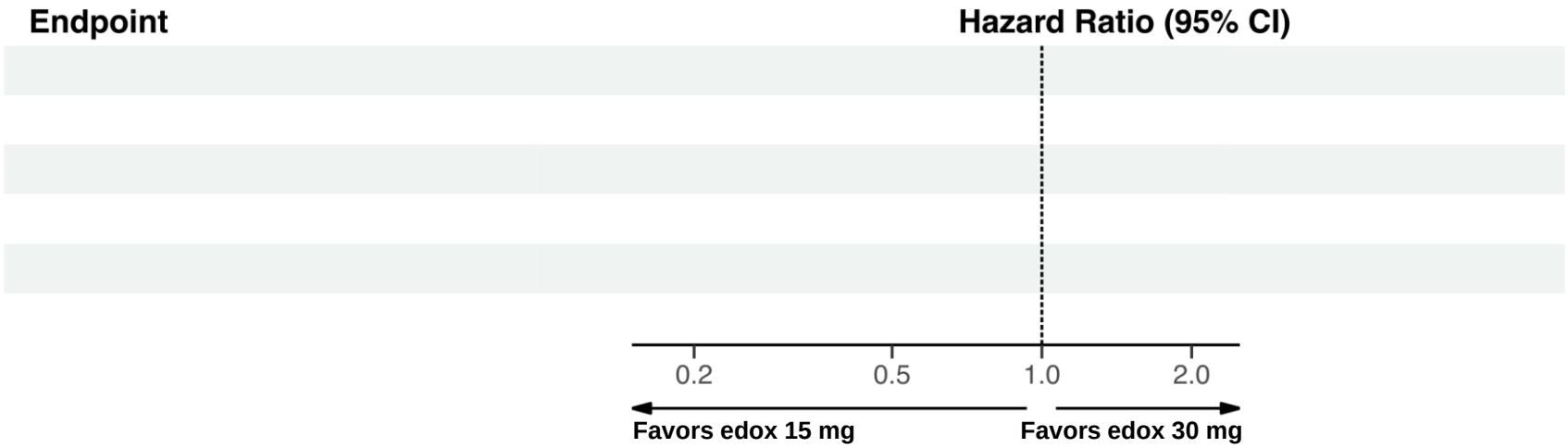
Characteristics	Edoxaban 15 mg (N=625)	Edoxaban 30 mg (N=623)
Age (years)	83 (81-85)	83 (81-85)
Female sex	57	55
CHA_2DS_2-VASc score ≥4	91	92
Prior stroke or TIA	30	27
Dose-reduction criteria	100	100
CrCl ≤50 mL/min	81	84
Weight ≤60 kg	32	32
Use strong P-gp inhibitors	8	5

Data are shown as % or median (IQR). Characteristics are shown at the time of randomization.
CrCl, creatinine clearance; P-gp, P glycoprotein; TIA, transient ischemic attack.

Pharmacodynamic Analysis



Efficacy and Safety Outcomes



The primary net outcome is a composite of all-cause death, stroke, systemic embolic event, and major bleeding.

Conclusions

- In a randomized comparison of AF patients ≥80 years meeting DR criteria, edoxaban 15 mg resulted in comparable rates of stroke or systemic embolism relative to 30 mg
- Edoxaban 15 mg resulted in a trend toward more ischemic strokes and fewer major and intracranial bleeding events
- These findings illustrate the trade-off between ischemic and bleeding risk when determining optimal anticoagulation strategy in older adults