Bleeding with the FXI Inhibitor Abelacimab Compared with Rivaroxaban in Older Individuals with Atrial Fibrillation: Analysis of the AZALEA-TIMI 71 Trial

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BACKGROUND

- Older age is a strong risk factor for bleeding with currently available anticoagulants.
- In AZALEA-TIMI 71, the novel factor XI inhibitor abelacimab reduced the risk of bleeding compared with rivaroxaban (riva) in pts with atrial fibrillation (AF). In this analysis, we examined the safety of abelacimab vs. riva by age.

METHODS

- AZALEA-TIMI 71 randomized 1,287 pts with AF to abelacimab (90 or 150 mg SC monthly) or riva (20/15mg orally daily) with median f/u of 2.1 [2.0, 2.3] yrs.
- Cox proportional hazards model was used to examine the primary outcome of major/clinically relevant non-major (CRNM) bleeding with an interaction term for treatment*age (≥75 vs <75 yrs) and across key subgroups: CrCl, BMI and concomitant antiplatelet therapy (APT).

RESULTS

Of 1,287 pts, 625 (49%) were ≥75 years at baseline.

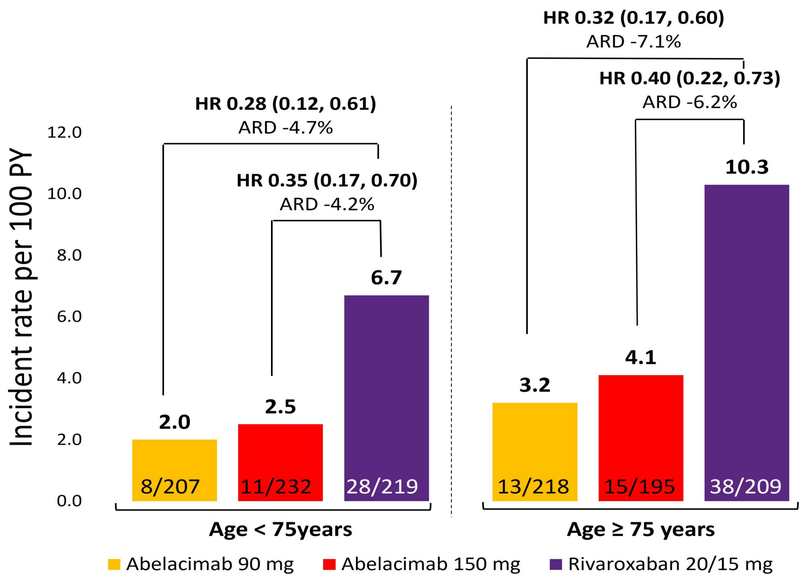
Table 1: Baseline Characteristics by Age

Characteristic	<75 years (N = 662)	≥75 years (N = 625)
Age, years	69 (66, 72)	79 (77, 82)
Male sex	59	52
Body mass index, kg/m^2	32 (28, 36)	28 (26, 33)
Concomitant antiplatelets	32	17
Creatinine clearance ≤ 50 ml/min	8	33
Diabetes mellitus	63	45
Heart failure	52	38
Coronary artery disease	51	46
Ischemic stroke	19	11

Data shown as median (IQR) for continuous variables and % for categorical variables.
IQR denotes interquartile range. P<0.05 for all except for coronary artery disease.

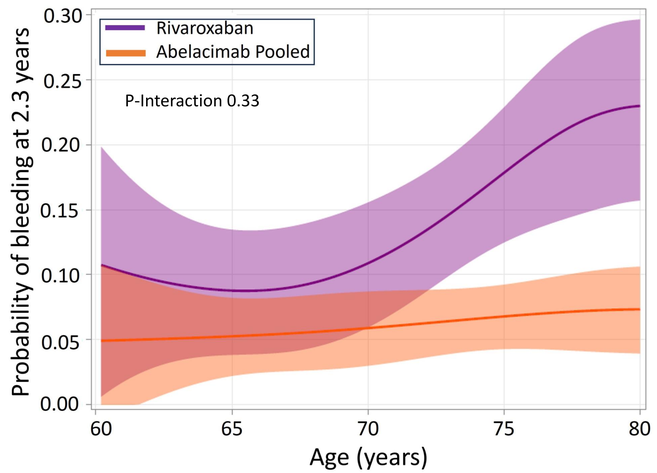
RESULTS

Fig 1: Major or CRNM Bleeding: Abelacimab vs. Riva by Age (≥75 vs. <75 years)



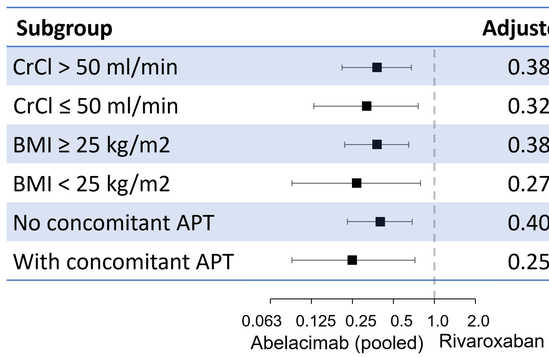
P-interaction HR Abelacimab 90mg vs. Riva = 0.85, Abelacimab 150mg vs. Riva = 0.84
P-interaction ARR for pooled abelacimab doses vs. Riva = 0.33

Fig 2: Probability of Major/CRNM Bleeding at 2.3 years: Abelacimab vs. Riva by Age



RESULTS

Fig 3: Major/CRNM Bleeding in Key Subgroups of Pts Age ≥ 75 years



Subgroup	Adjusted HR (95% CI)	P-interaction
CrCl > 50 ml/min	0.38 (0.21, 0.68)	0.74
CrCl ≤ 50 ml/min	0.32 (0.13, 0.76)	
BMI ≥ 25 kg/m2	0.38 (0.22, 0.65)	0.67
BMI < 25 kg/m2	0.27 (0.09, 0.79)	
No concomitant APT	0.40 (0.23, 0.69)	0.44
With concomitant APT	0.25 (0.09, 0.72)	

KEY FINDINGS

- Compared with riva, both abelacimab doses significantly reduced the risk of major/CRNM bleeding irrespective of age (Fig 1).
- Pts ≥75 yrs tended to have greater ARR in bleeding with abelacimab than those <75 yrs (Fig 1).
- Abelacimab consistently reduced relative bleeding risk in pts ≥75 yrs vs. riva, with no significant interactions across CrCl, BMI and concomitant antiplatelet therapy subgroups (Fig 3).

CONCLUSIONS

- Inhibition of factor XI with abelacimab significantly reduced the relative risk of bleeding compared with riva regardless of age, with potential for greater absolute reductions with older age.
- The factor XI inhibitor abelacimab may be especially attractive in minimizing bleeding in older patients with AF.

DISCLOSURES

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