History of bleeding and safety of abelacimab vs. rivaroxaban in patients with atrial fibrillation

An analysis of AZALEA – TIMI 71

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#ScientificSessions26

DISCLOSURES

- MMS, RPG, DAM, EG, MSS, CTR, SMP are members of the TIMI Study Group which has received institutional research grant support through Brigham and Women's Hospital from Abbott, Abiomed, Inc., Amgen, Anthos Therapeutics, ARCA Biopharma, Inc., AstraZeneca, Boehringer Ingelheim, Daiichi-Sankyo, Ionis Pharmaceuticals, Inc., Janssen Research and Development, LLC, MedImmune, Merck, Novartis, Pfizer, Regeneron Pharmaceuticals, Inc., Roche, Saghmos Therapeutics, Inc., Softcell Medical Limited, The Medicines Company, Verve Therapeutics, Inc., Zora Biosciences.

- AZALEA-TIMI 71 was sponsored by Anthos Therapeutics.

Background

- Patients with atrial fibrillation (AF) and history of bleeding pose a clinical challenge:
  - Remain at high risk for recurrent bleeding
  - Often discontinue anticoagulation, leaving them vulnerable to thromboembolism

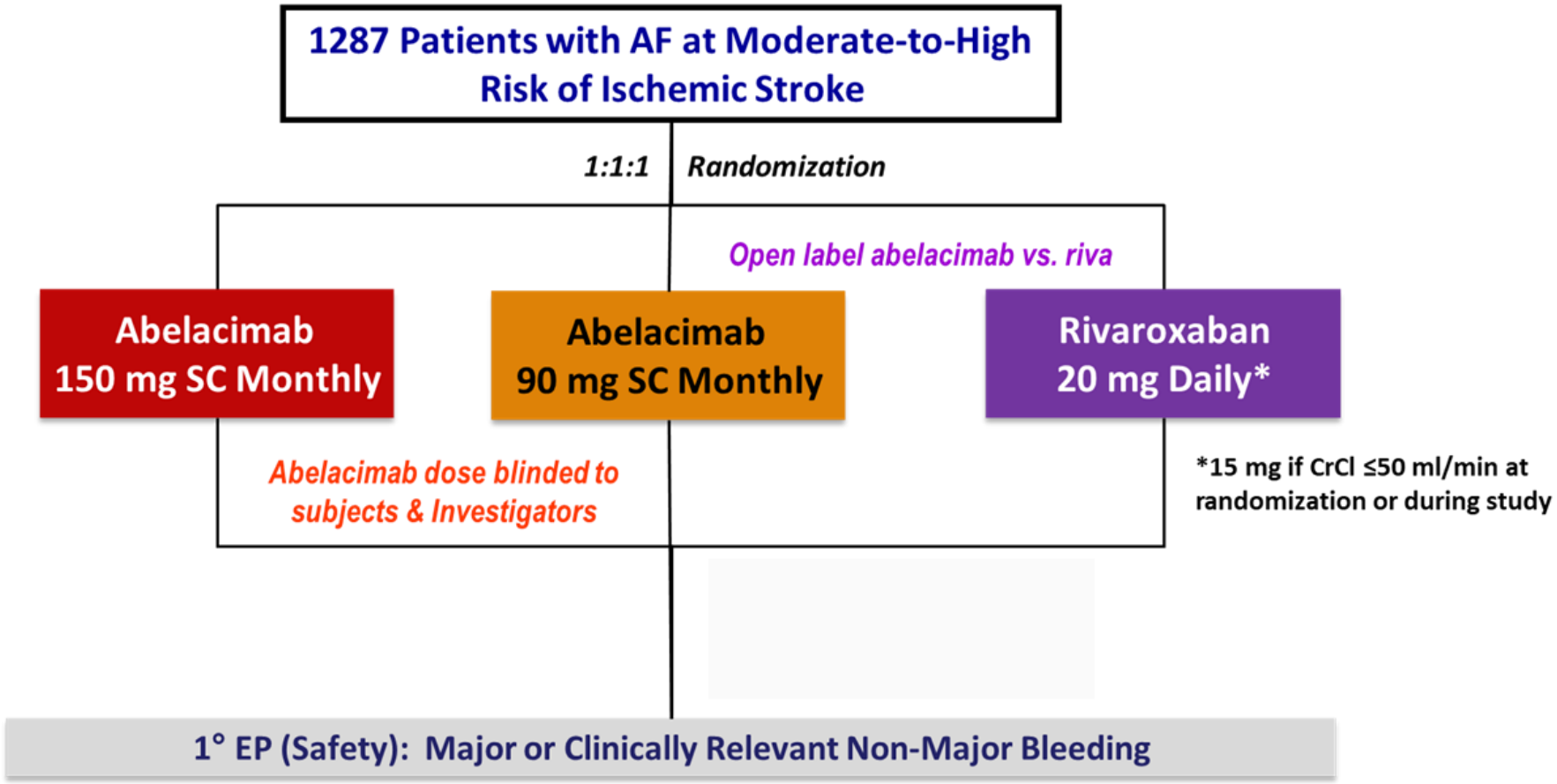
- Factor XI (FXI) inhibition may offer a safer alternative to currently approved anticoagulants.

- In AZALEA-TIMI 71, abelacimab, a mAb which inhibits FXI, substantially reduced bleeding risk vs. rivaroxaban in patients with AF

Ruff CT, et al. *N Engl J Med.* 2025;392(4):361–371. doi:10.1056/NEJMoa2406674.

Goal: In AZALEA – TIMI 71, we sought to evaluate the safety of abelacimab vs rivaroxaban among patients with and without a history of bleeding.

Methods: AZALEA-TIMI 71 Trial Design



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Methods

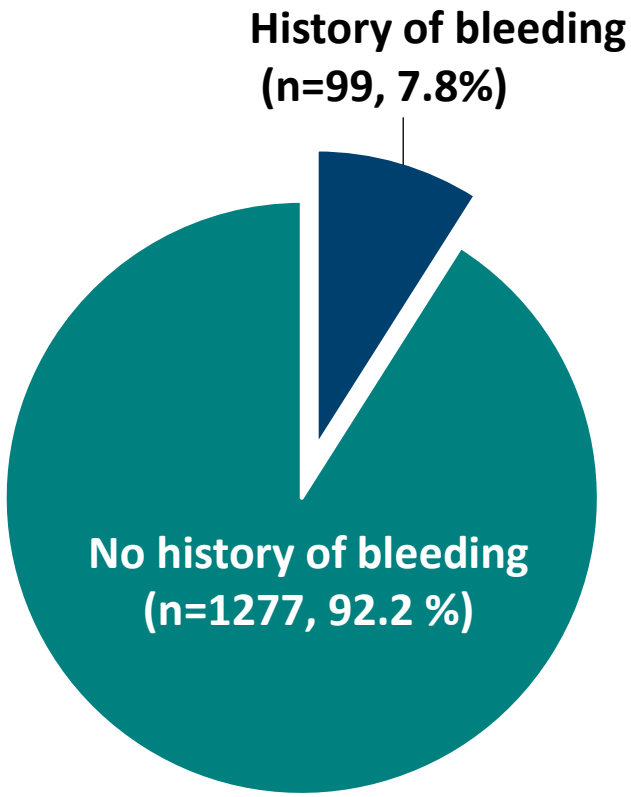
- History of bleeding was prospectively captured at in the eCRF at randomization.

- Outcomes of interest included
  - Major/CRNM bleeding (PEP)
  - Major bleeding
  - Major/CRNM/minor bleeding
  - GI bleeding

- Outcomes were adjudicated by blinded CEC.

- Analyses conducted on-treatment (including events w/in 60d of dosing).

Baseline Characteristics



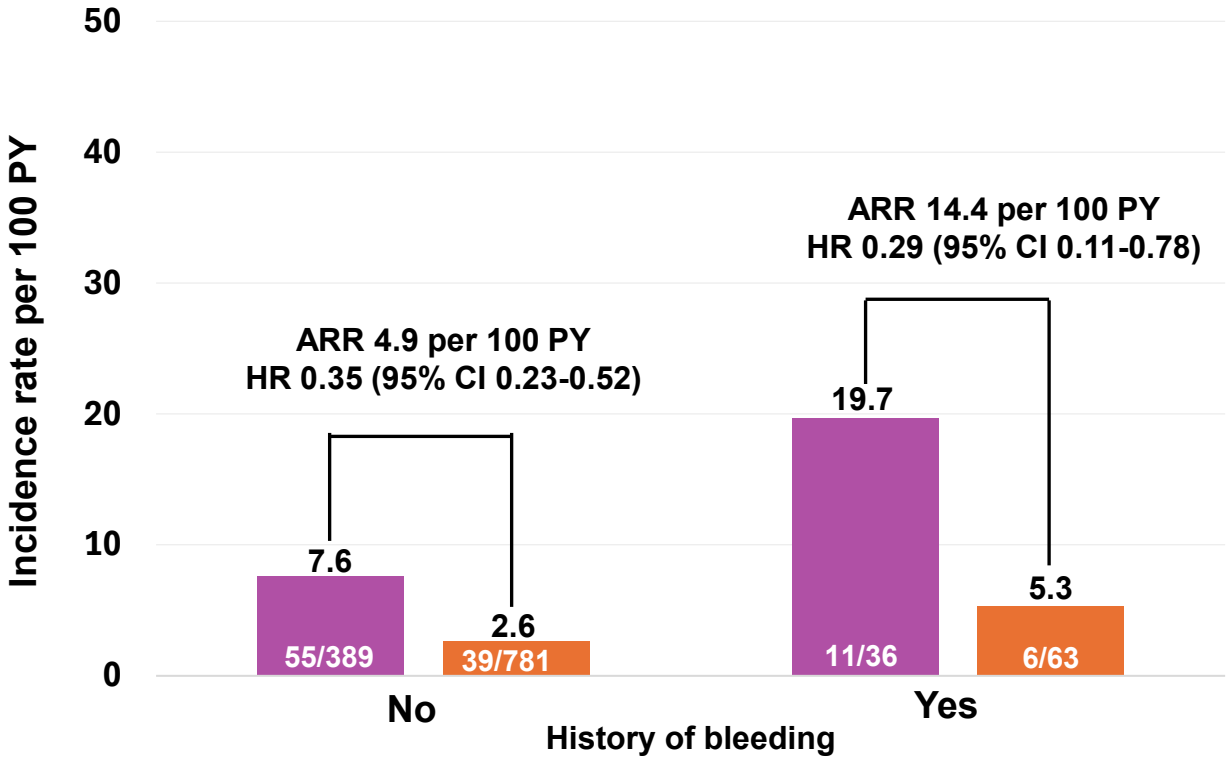
Clinical Characteristics	No History of Bleeding	History of Bleeding	P Value
Age, median, y	74	**77**	0.008
Male, %	56	**58**	0.69
Creatinine clearance ≤50 mL/min, %	20	**28**	0.044
Prior ischemic stroke, %	15	**17**	0.51
Concomitant Antiplatelet therapy, %	25	**17**	0.079
CHA_2DS_2-VASc ≥6, %	22	**40**	<0.001
HAS-BLED ≥3, %	46	**97**	*

* Not provided as history of bleeding is part of HAS-BLED score and will differ by design

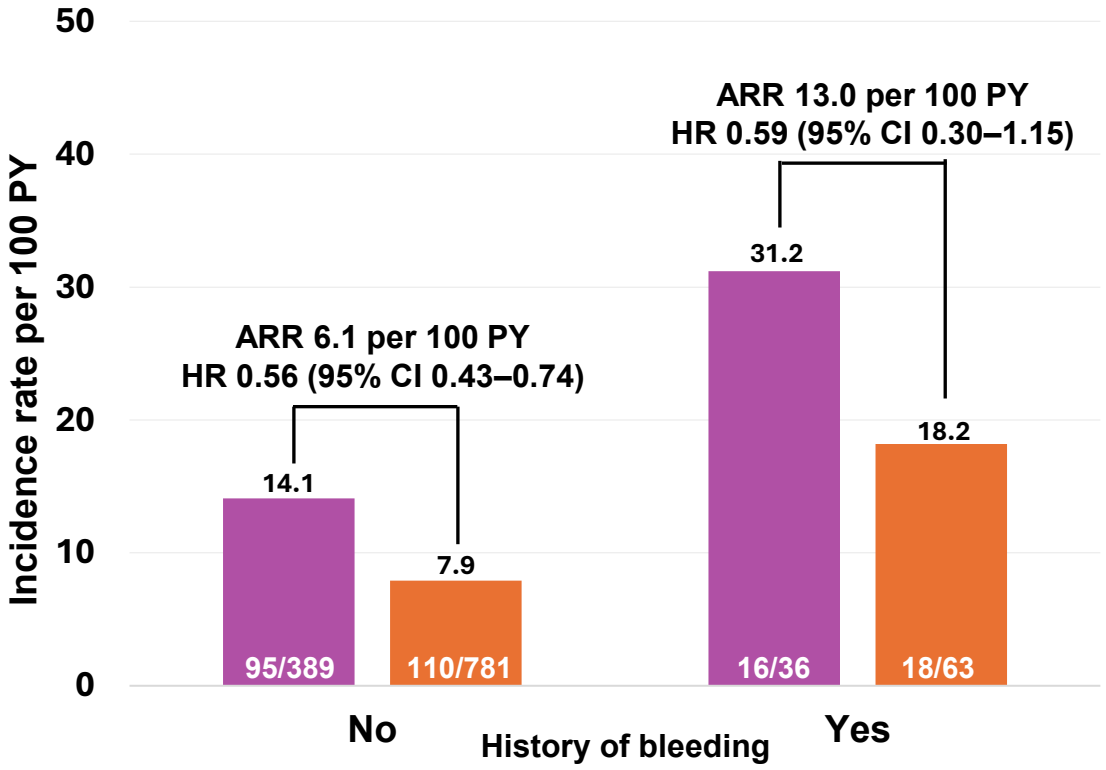
RESULTS

Rivaroxaban Abelacimab

Major / CRNM bleeding



Major, CRNM, or minor bleeding

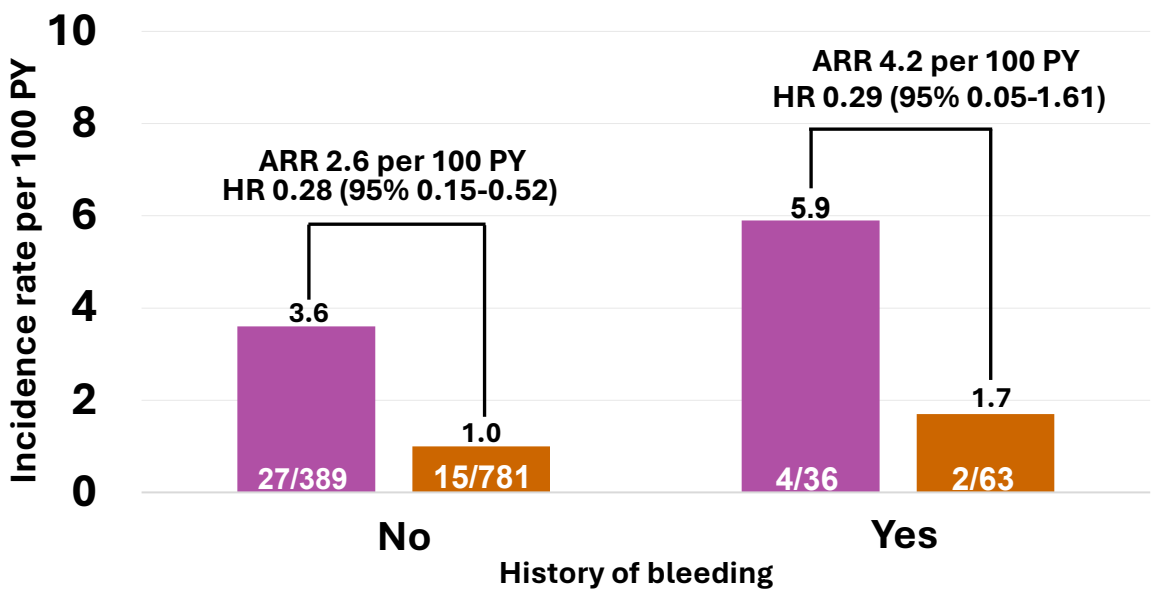


All p-interaction > 0.10

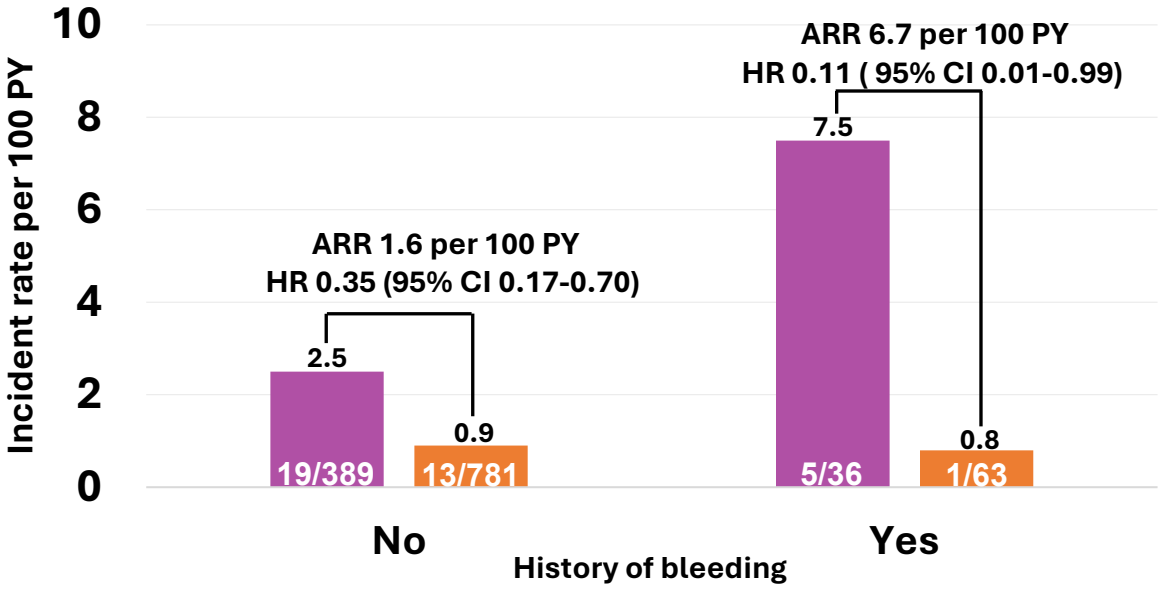
RESULTS

Rivaroxaban Abelacimab

Major bleeding



Major / CRNM GI bleeding



Results were consistent across the individual abelacimab doses for the same endpoints

All p-interaction > 0.10

Conclusion

- Patients with a history of bleeding were at ~2x increased risk of bleeding compared to those w/o such a history
- Abelacimab, compared with rivaroxaban, significantly reduced the relative risk of bleeding in patients with and without history of bleeding
- Given the higher risk of bleeding in subjects with a prior history, the absolute risk reductions in bleeding with abelacimab tended to be twice as high in these patients
- If proven to be effective for stroke prevention in AF, FXI inhibition with abelacimab may be particularly advantageous in high-risk patients with AF and history of bleeding

Thank you