Long-acting Factor XI Inhibition and Periprocedural Bleeding

A Secondary Analysis from AZALEA-TIMI 71

Siddharth M. Patel, Robert P. Giugliano, David A. Morrow, Bruce Hug, Sanobar Parkar, Shih-Ann Chen, Shaun G. Goodman, Boyoung Joung, Robert G. Kiss, Jindrich Spinar, Wojciech Wojakowski, Jeffrey I. Weitz, Dan Bloomfield, Marc S. Sabatine, Christian T. Ruff on behalf of the AZALEA-TIMI 71 Investigators

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Procedures are Common in Patients with AF treated with Anticoagulation

- Management of perioperative anticoagulation is a commonly encountered clinical scenario among patients with AF.
- An estimated ~20% of patients with AF undergo invasive procedures per year, with frequent need for anticoagulation interruption.

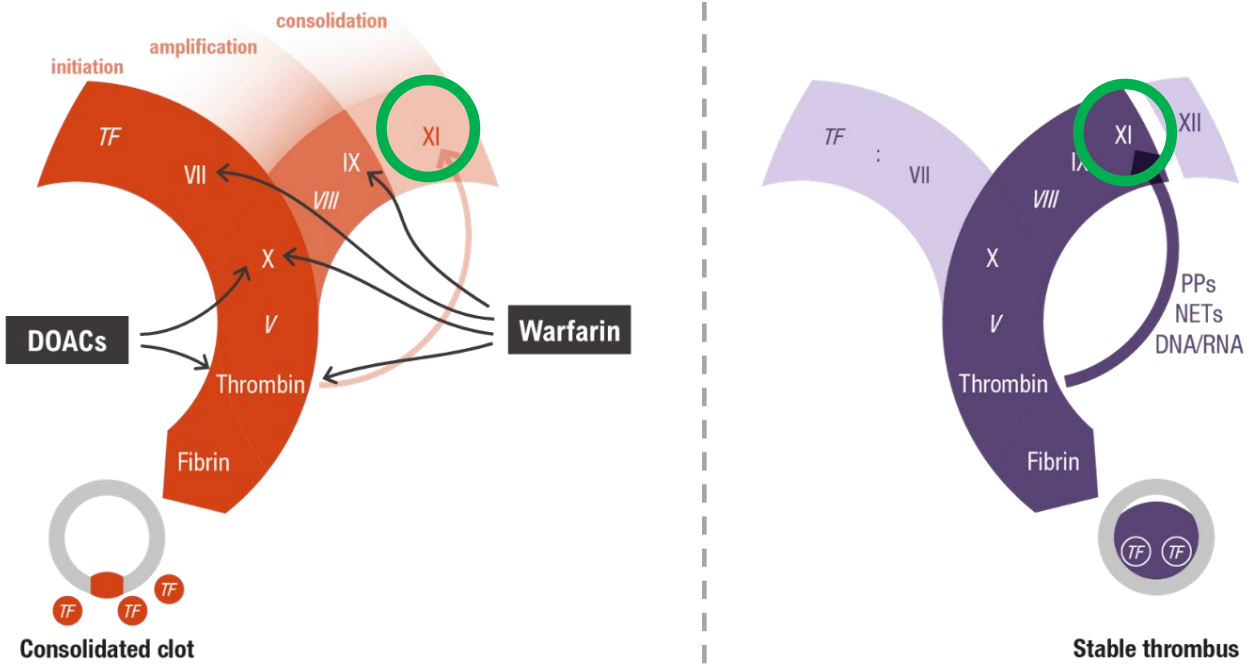
Douketis JD et al. *Chest.* 2022;162(5):e207-243.

Douketis JD et al. *JAMA.* 2024; doi:10.1001/jama.2024.12708

FXI Inhibition may offer safer anticoagulation

Potential to Uncouple

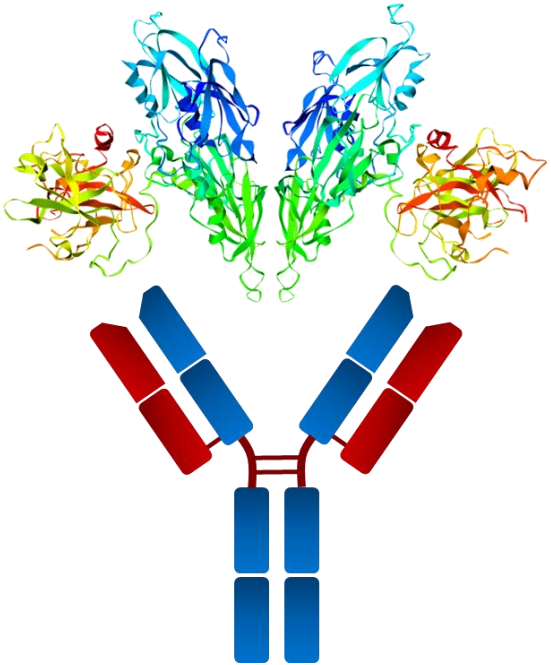
Hemostasis from Thrombosis



Hsu C, et al. *J Am Coll Cardiol* 2021;78:625-631

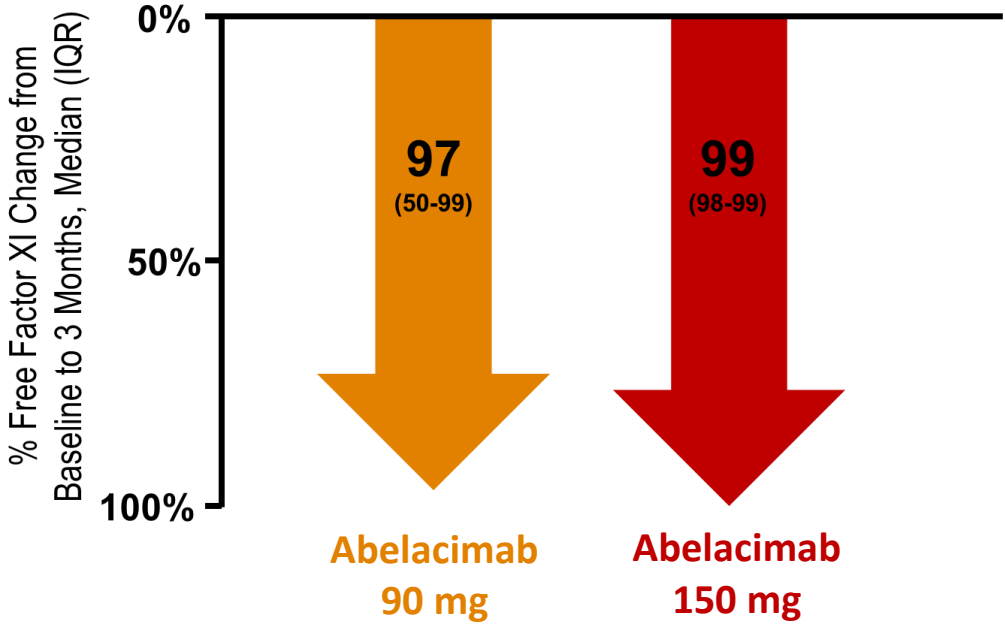
Abelacimab

Monoclonal Ab targeting factor XI



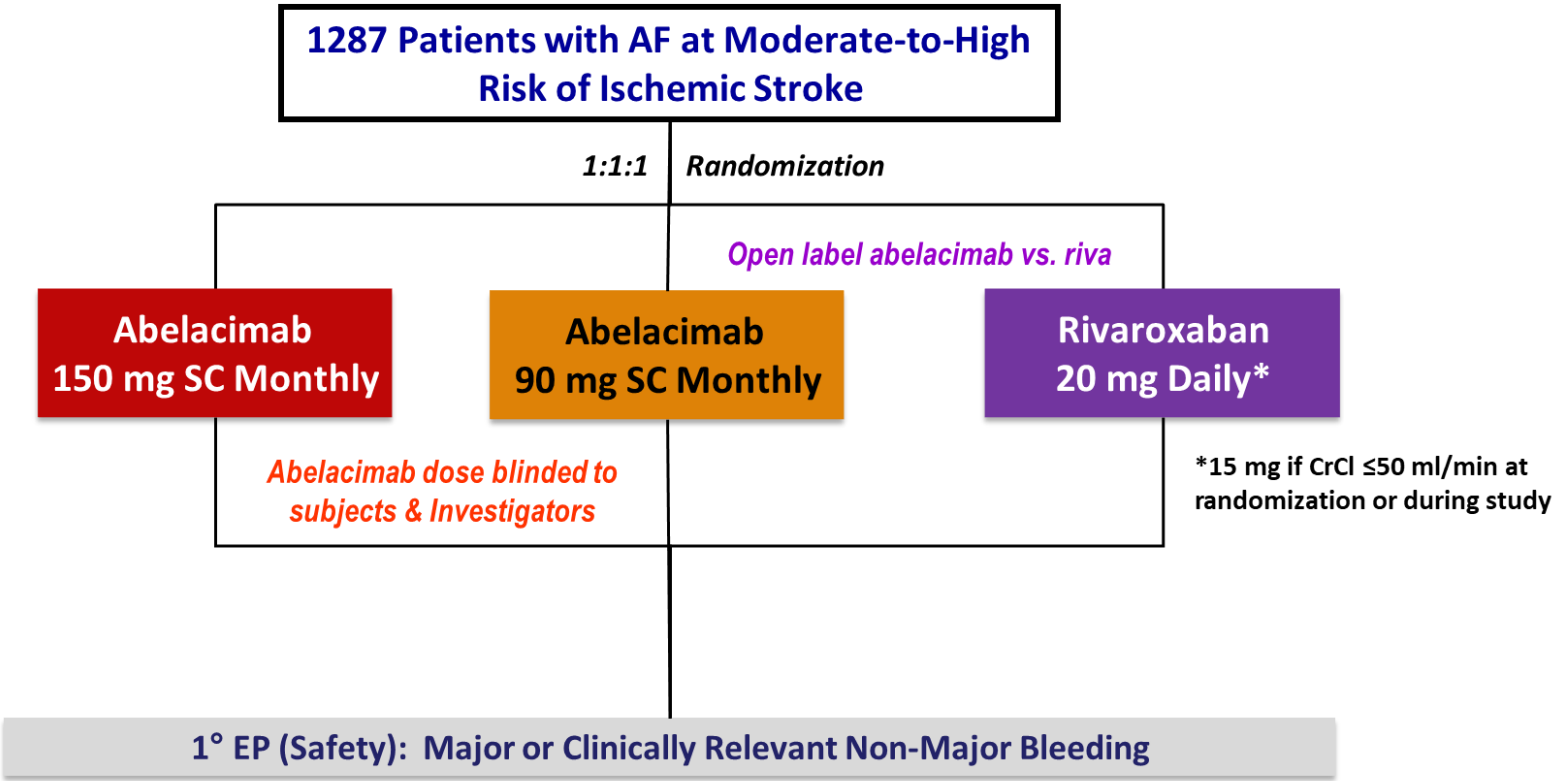
Papagrigoriou E, et al. *Nat Struct Mol Biol* 2006;13:557-558

≥97% Inhibition with $t_{1/2}$ of 28 days



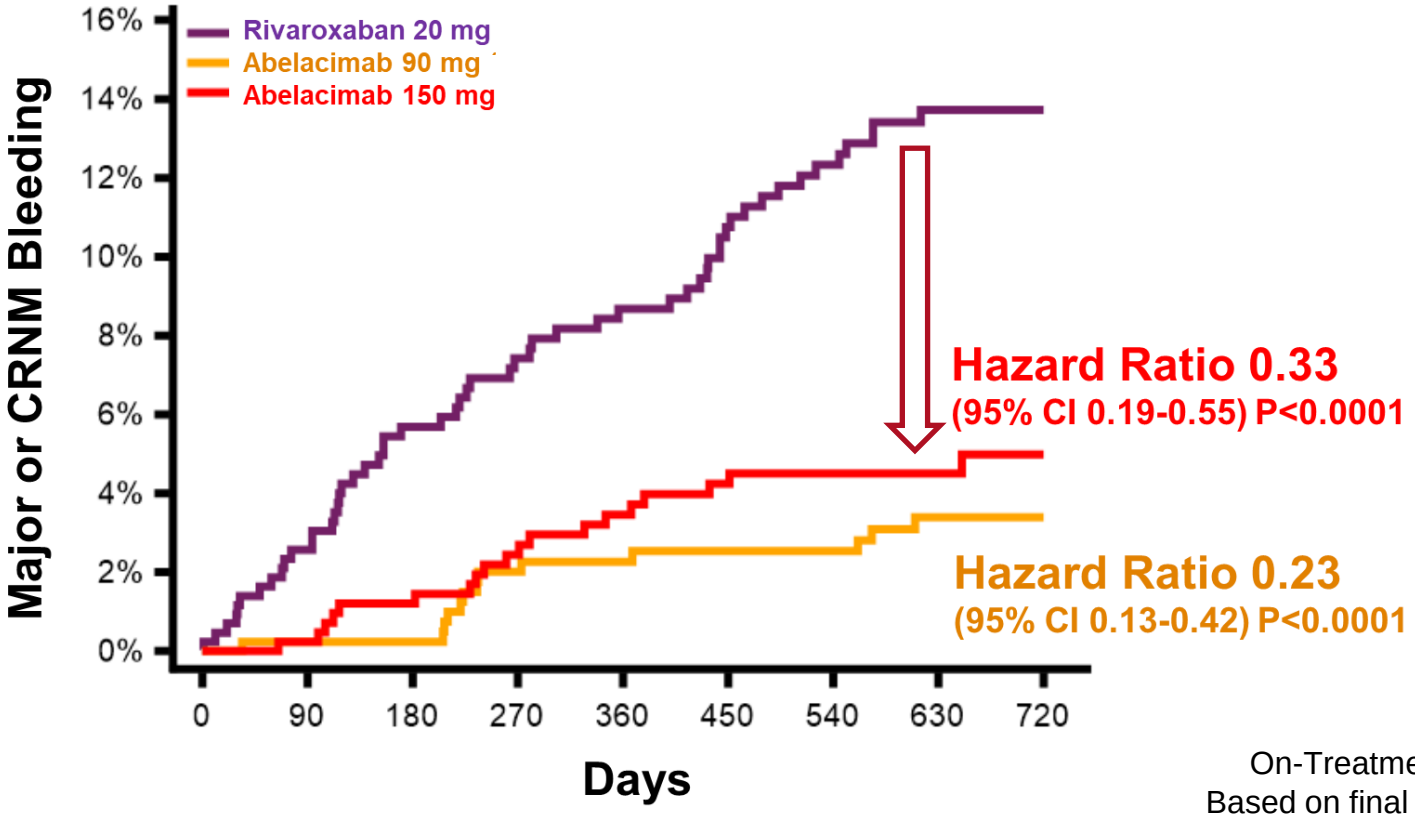
Ruff CT et al. *AHA Scientific Sessions* 2023, Late-breaking Clinical Trial

AZALEA-TIMI 71 Trial Design



Ruff CT et al. *AHA Scientific Sessions* 2023, Late-breaking Clinical Trial

AZALEA-TIMI 71 Primary Results



On-Treatment Population
Based on final DMC Datacut

Ruff CT et al. *AHA Scientific Sessions* 2023, Late-breaking Clinical Trial

Objective

To examine periprocedural bleeding among patients undergoing invasive procedures randomized to abelacimab, a long-acting factor XI inhibitor, vs. rivaroxaban in AZALEA-TIMI 71

AZALEA Peri-procedural Guidance

Bleeding Risk	Low Risk	Intermediate-High Risk	Very High Risk	
Procedure example	Coronary angiography	Colonoscopy w/ polypectomy	Spinal surgery, open thoracic or abdominal surgery	
Abelacimab guidance	No interruption or therapy	No interruption; consider anti-fibrinolytic (e.g., TXA) pre-procedurally	**Elective** Interrupt abelacimab	**Non-elective** Consider anti-fibrinolytic + low-dose rVIIa
Rivaroxaban guidance	Interruption per SoC (~24-48h prior to procedure based on CrCl)			

Application of guidance & perceived procedural bleeding risk based on local site's judgement

Classification of Procedural and Bleeding Events

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- **Procedural bleeding risk was categorized as per the 2017 ACC Periprocedural Management Expert pathway as low, intermediate, or high.**

- **Periprocedural bleeding events were identified as:**

  - **Major or CRNM bleeds adjudicated by an independent CEC blinded to treatment assignment**

  - **Within 30 days of the procedure and classified as related to the procedure**

Proportion of Patients with Invasive Procedures

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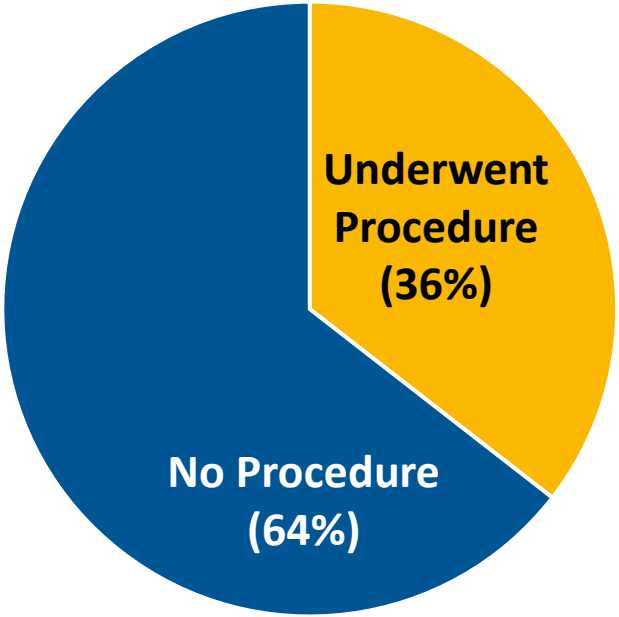
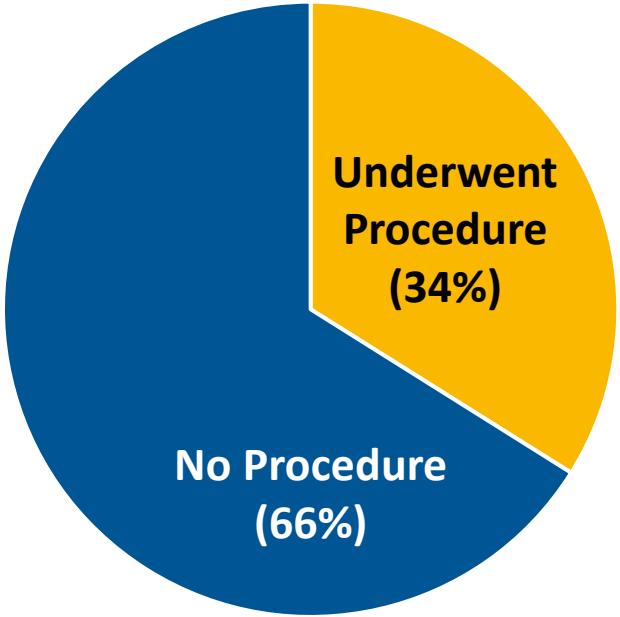
Rivaroxaban (n=428)

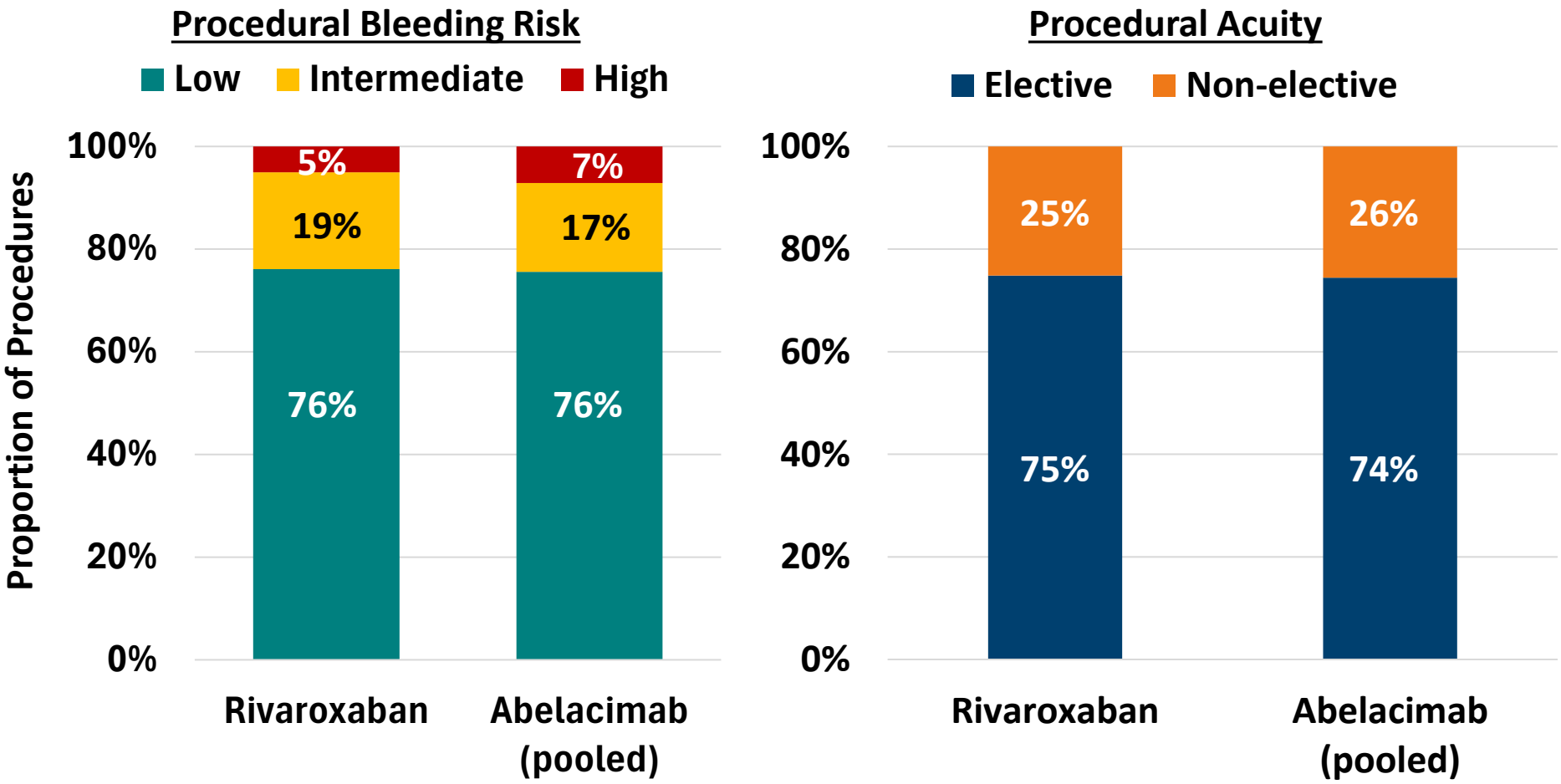


Pooled Abelacimab (blinded to dose; n=852)

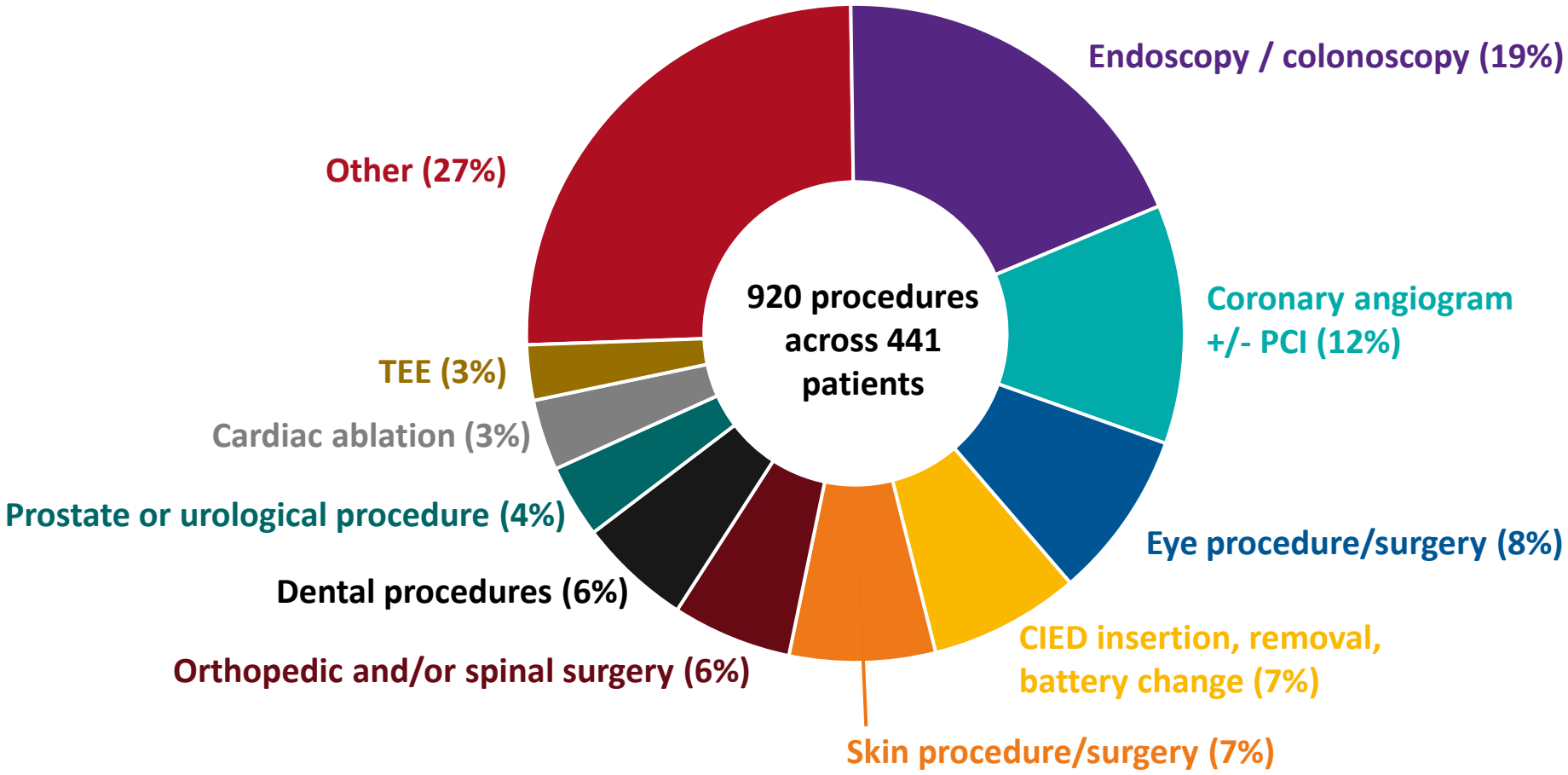


Similar proportion in each treatment arm undergoing procedures, with similar baseline characteristics

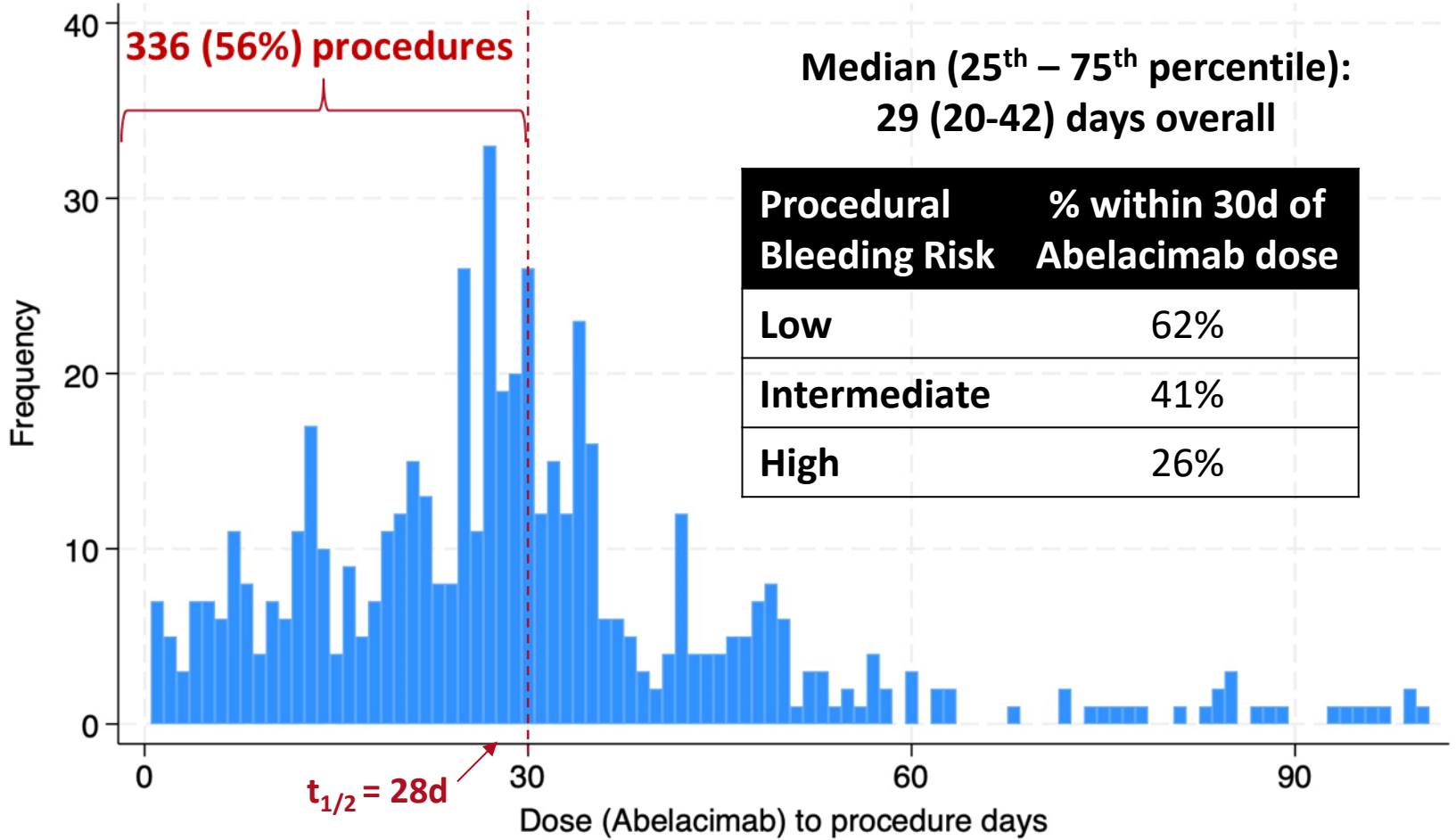
Procedural Bleeding Risk and Acuity



Breakdown of Procedure Types



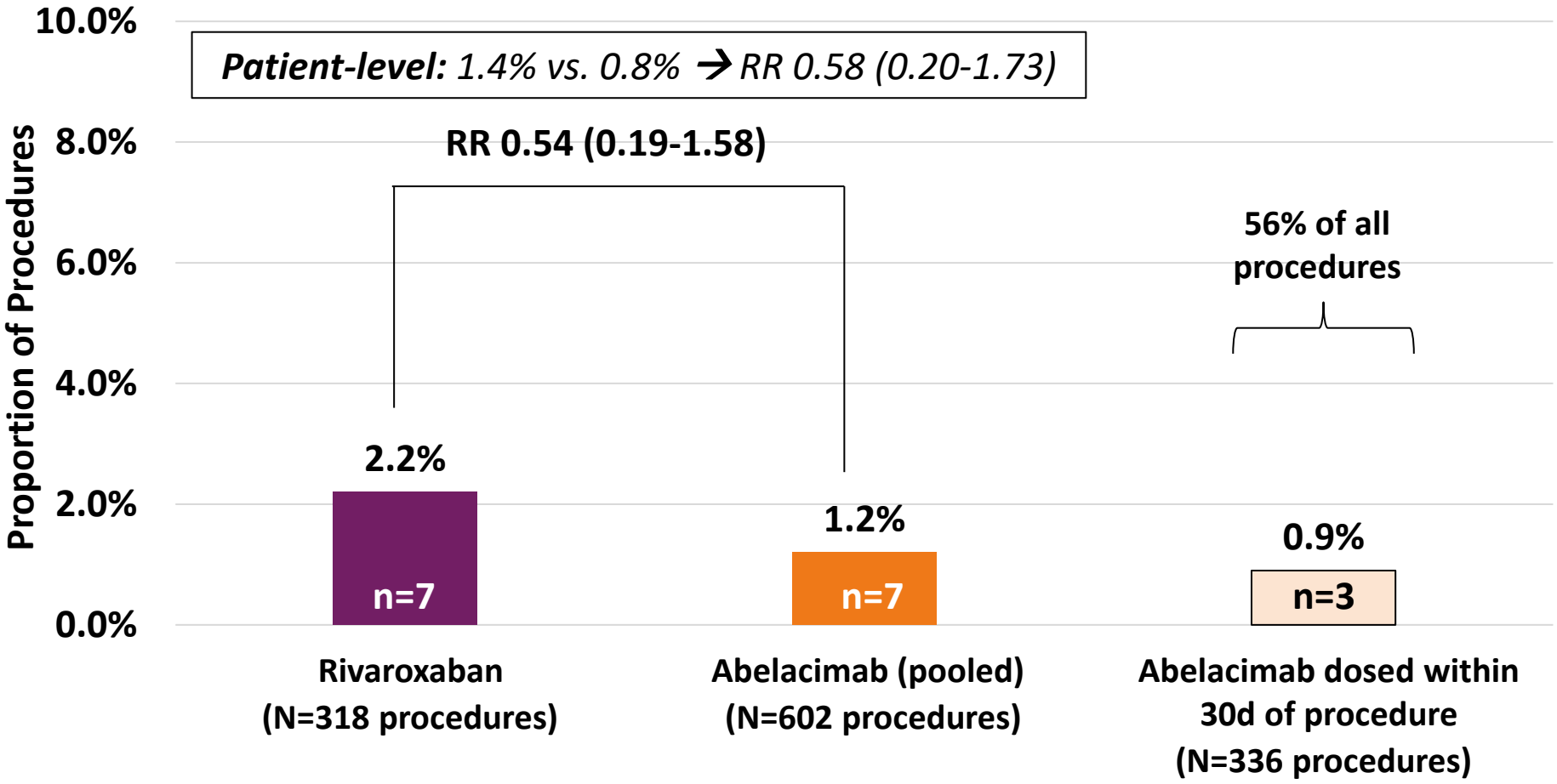
Time from Last Abelacimab Dose to Procedure



Median (25th – 75th percentile):
29 (20-42) days overall

Procedural Bleeding Risk	% within 30d of Abelacimab dose
Low	62%
Intermediate	41%
High	26%

Major or CRNM Bleeding (Procedure-level)



Major or CRNM Bleeding by Procedural Risk & Acuity (Procedure level)

	Proportion (n/N), Rivaroxaban	Proportion (n/N), Abelacimab
Overall	**2.2% (7/318)**	**1.2% (7/602)**
Procedural Bleeding Risk		
Low	1.2% (3/241)	0.4% (2/455)
Intermediate	6.6% (4/61)	2.9% (3/104)
High	0.0% (0/16)	4.7% (2/43)
Procedural Acuity		
Elective	2.5% (6/238)	0.9% (4/448)
Non-elective	1.3% (1/80)	2.0% (3/154)

Hemostatic Therapies and Transfusions

Hemostatic Therapy	Proportion of Procedures	
	Rivaroxaban (N=318)	Abelacimab (N=602)
Hemostatic Therapies	**2.5%**	**6.6%**
Anti-fibrinolytic (e.g., tranexamic acid)	0.9%	5.1%
Topical hemostatic agent	0%	0.8%
Fresh frozen plasma	0.9%	0.2%
Recombinant factor VIIa	0%	0%
Other	0.6%	0.5%
Blood Transfusions	**5.3%**	**1.2%**

Represents therapies used both pre-/intra-procedurally (>95%) or for bleeding

Summary

- Invasive procedures are frequent in a contemporary patient population with AF treated with anticoagulation
  - ~1 in 3 patients over median follow-up of 2.1 years
  - Majority (76%) are low bleeding risk
- Very low rates of procedural bleeding overall (<2% of all procedures)
  - Similar rates for abelacimab vs. rivaroxaban (1.2% vs. 2.2%)
- These data suggest routine interruption of anticoagulation may not be necessary for all procedures in the context of FXI inhibition
  - Further data in non-elective/high bleeding risk procedures are necessary