



Long-acting Factor XI Inhibition and Periprocedural Bleeding

A Secondary Analysis from AZALEA-TIMI 71

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September 2, 2024

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

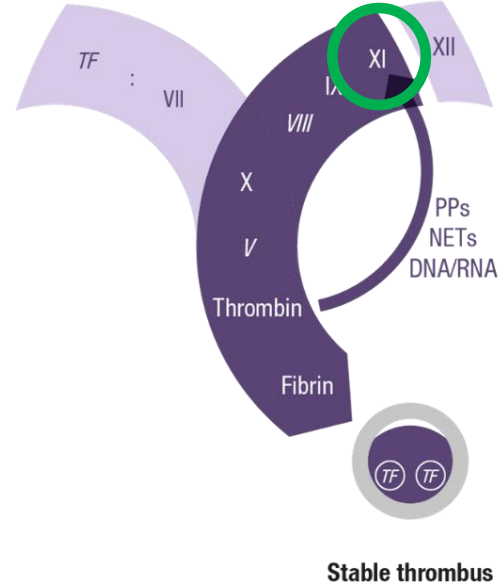
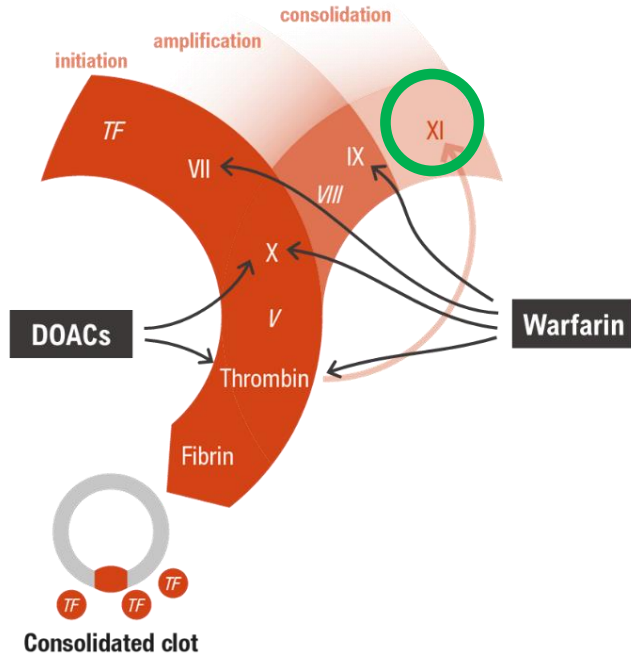
FXI Inhibition may offer safer anticoagulation

Potential to Uncouple

Hemostasis

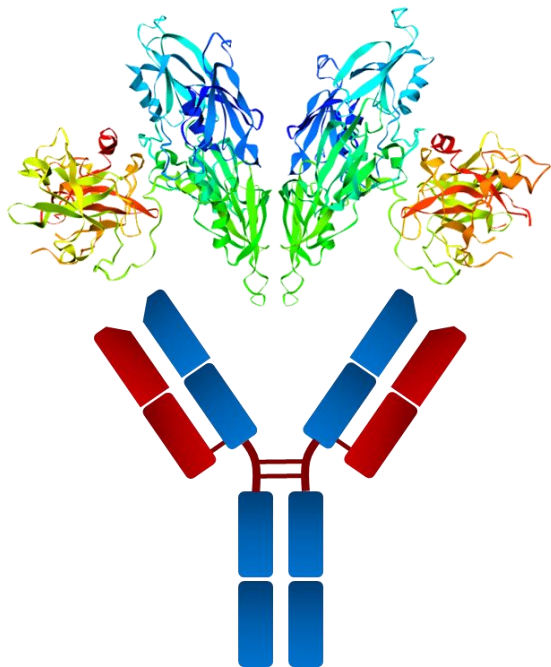
from

Thrombosis

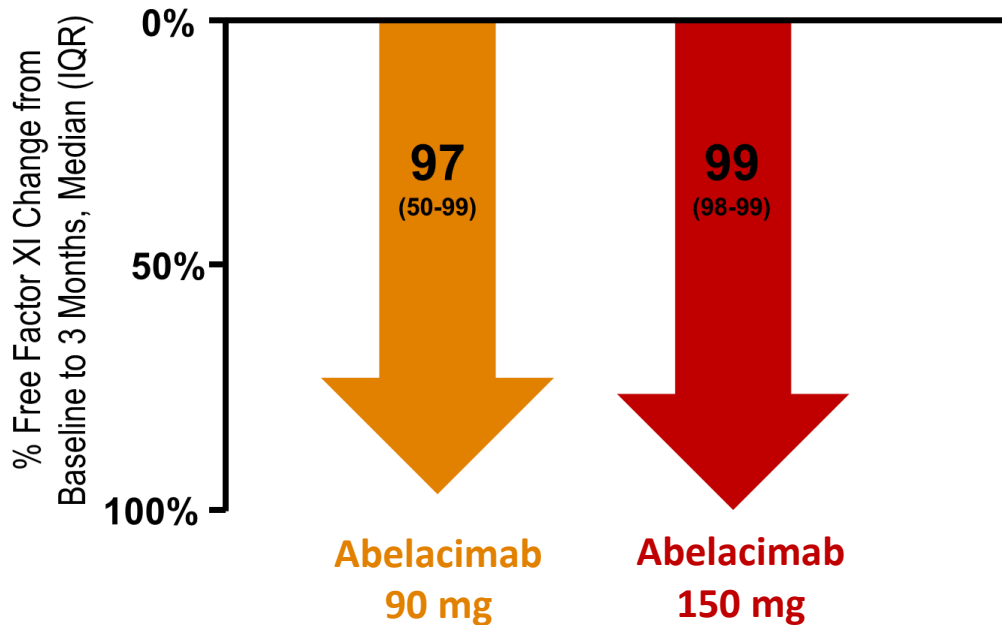


Abelacimab

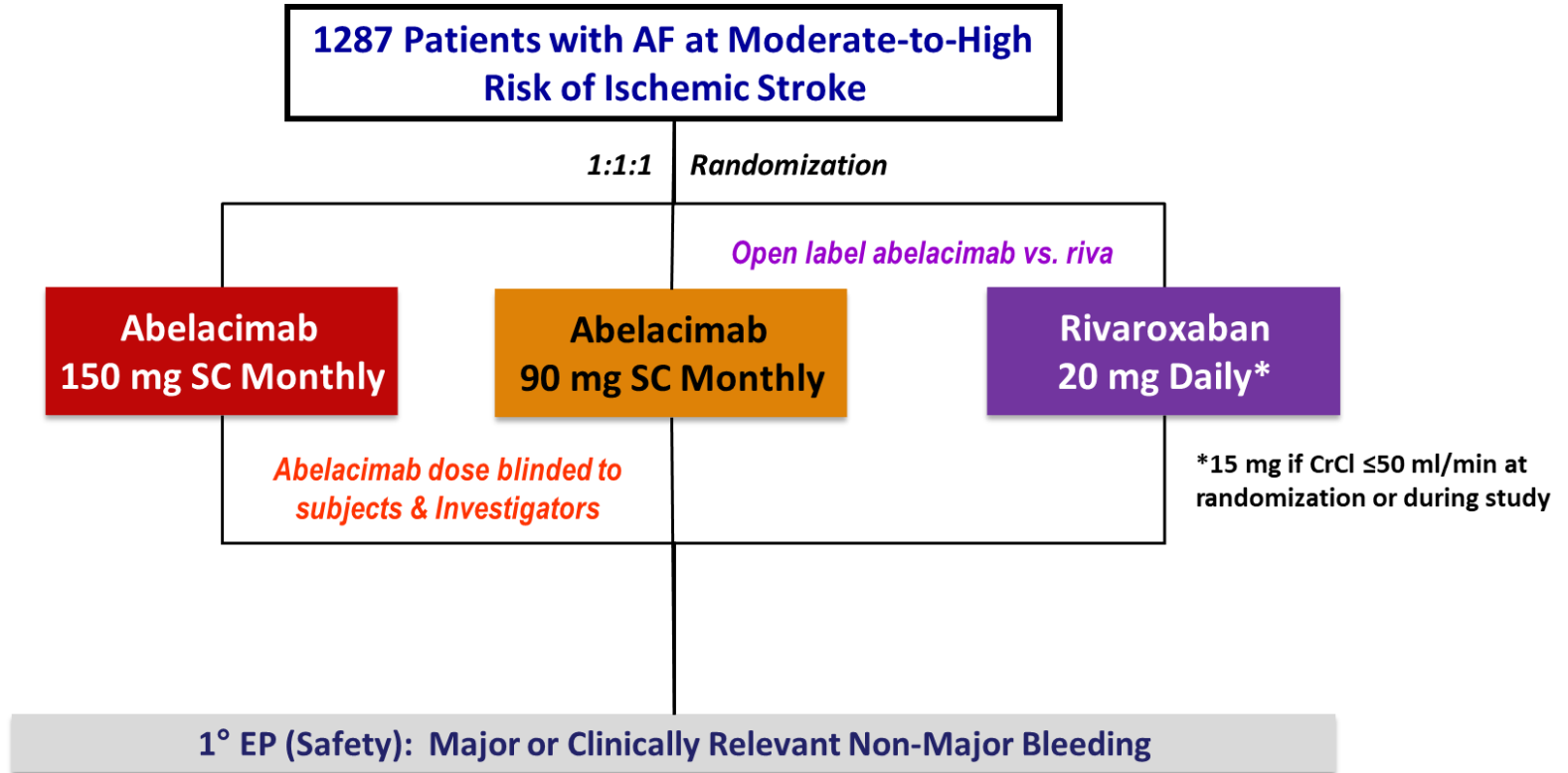
Monoclonal Ab targeting factor XI



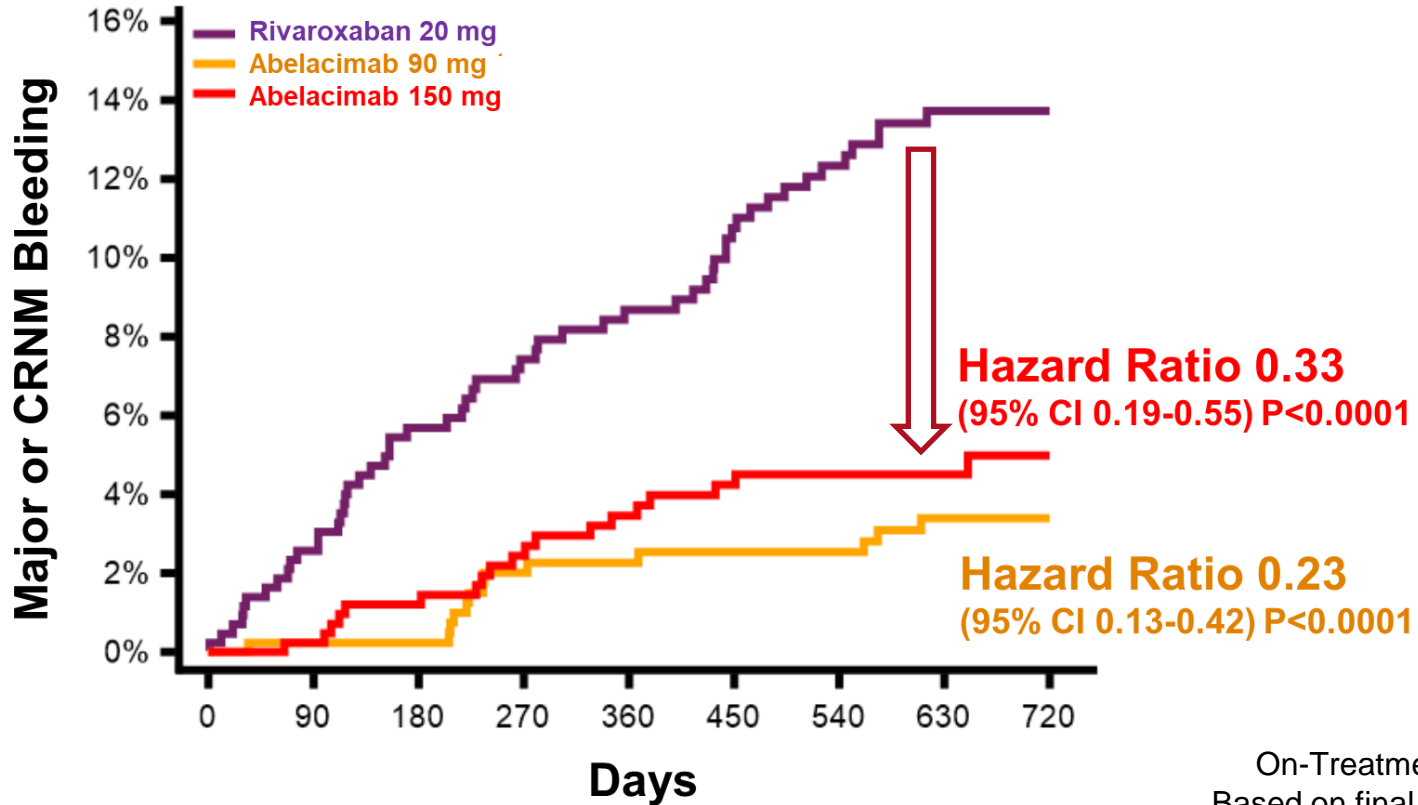
$\geq 97\%$ Inhibition with $t_{1/2}$ of 28 days



AZALEA-TIMI 71 Trial Design



AZALEA-TIMI 71 Primary Results



On-Treatment Population
Based on final DMC Datacut

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	<u>Elective</u> Interrupt abelacimab	<u>Non-elective</u> 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

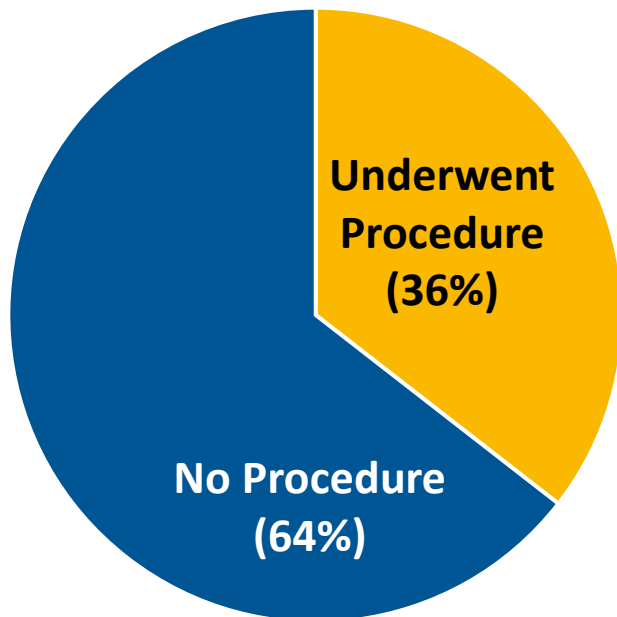
Classification of Procedural and Bleeding Events

- 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

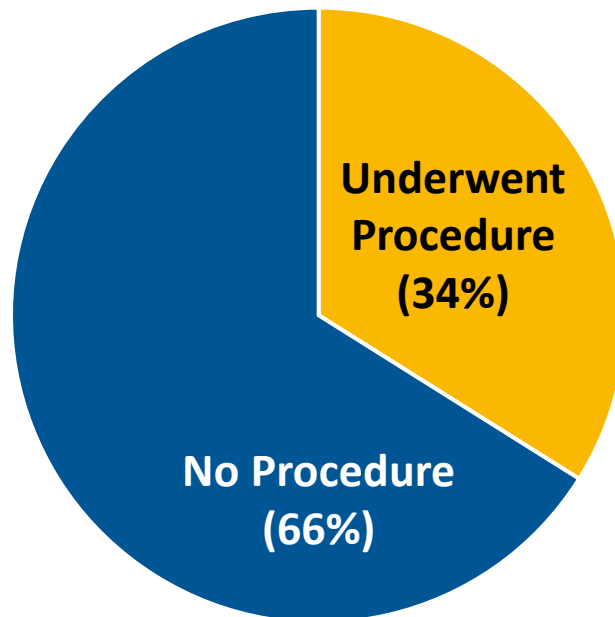
Proportion of Patients with Invasive Procedures



Rivaroxaban (n=428)



Pooled Abelaclimab (blinded to dose; n=852)

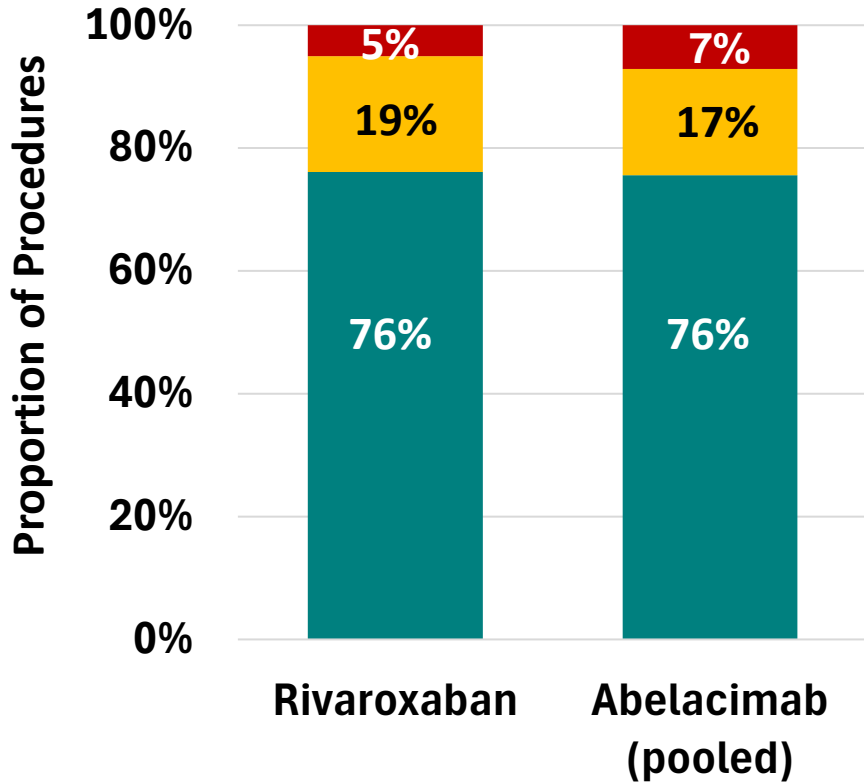


Similar proportion in each treatment arm undergoing procedures, with similar baseline characteristics

Procedural Bleeding Risk and Acuity

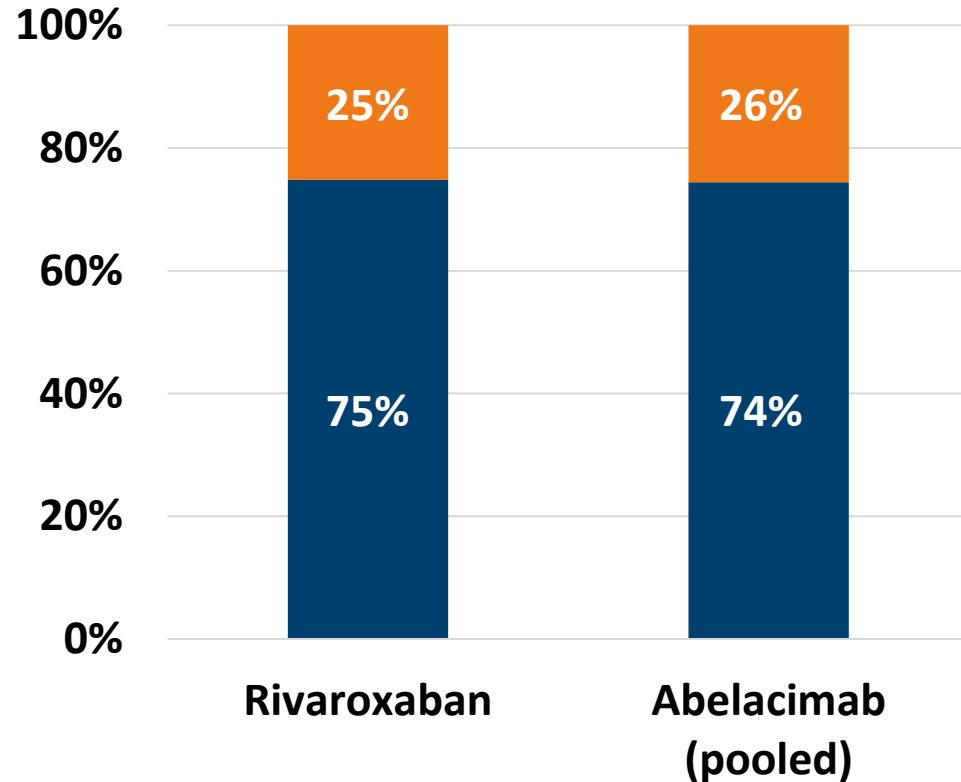
Procedural Bleeding Risk

■ Low ■ Intermediate ■ High

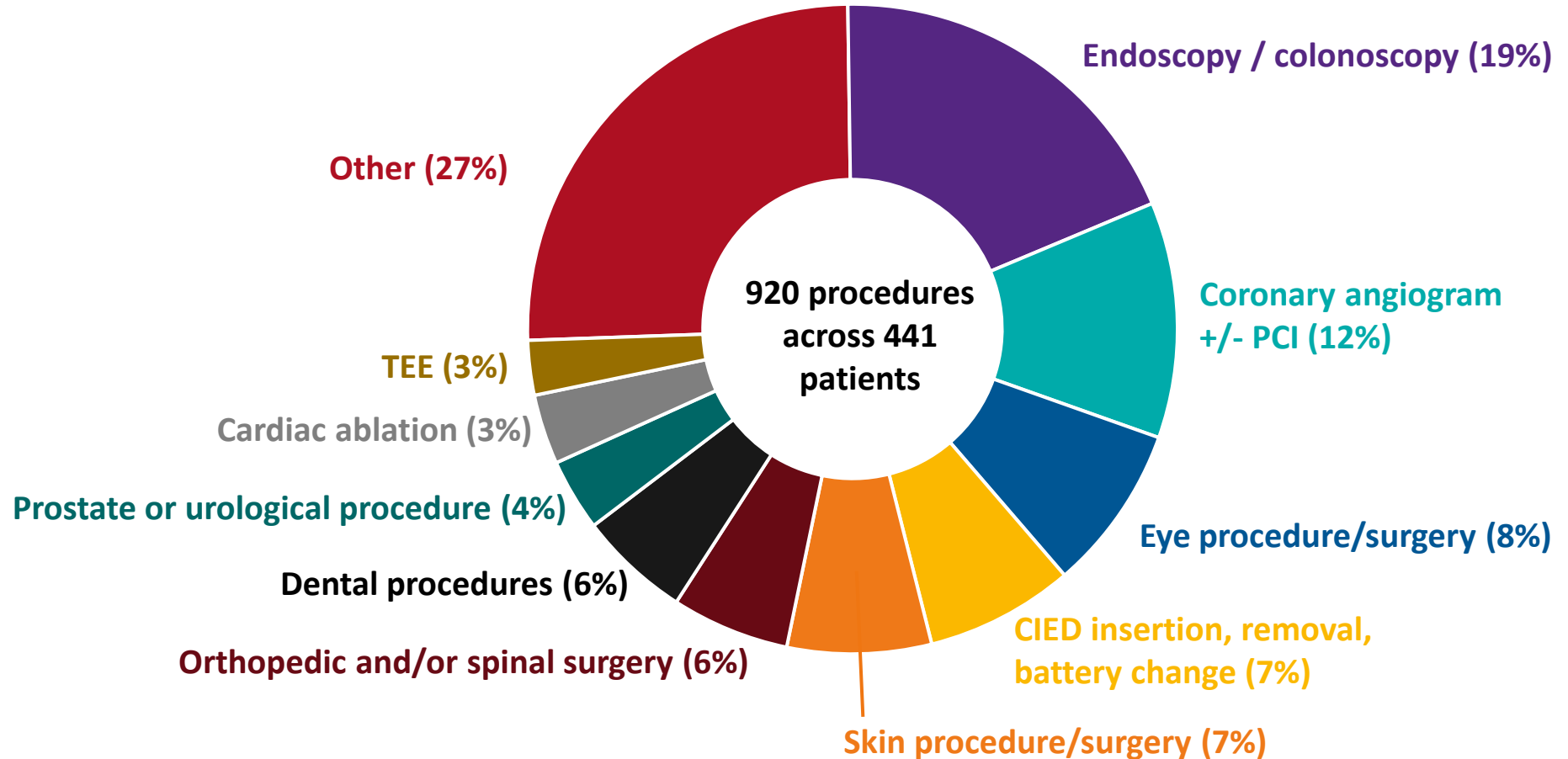


Procedural Acuity

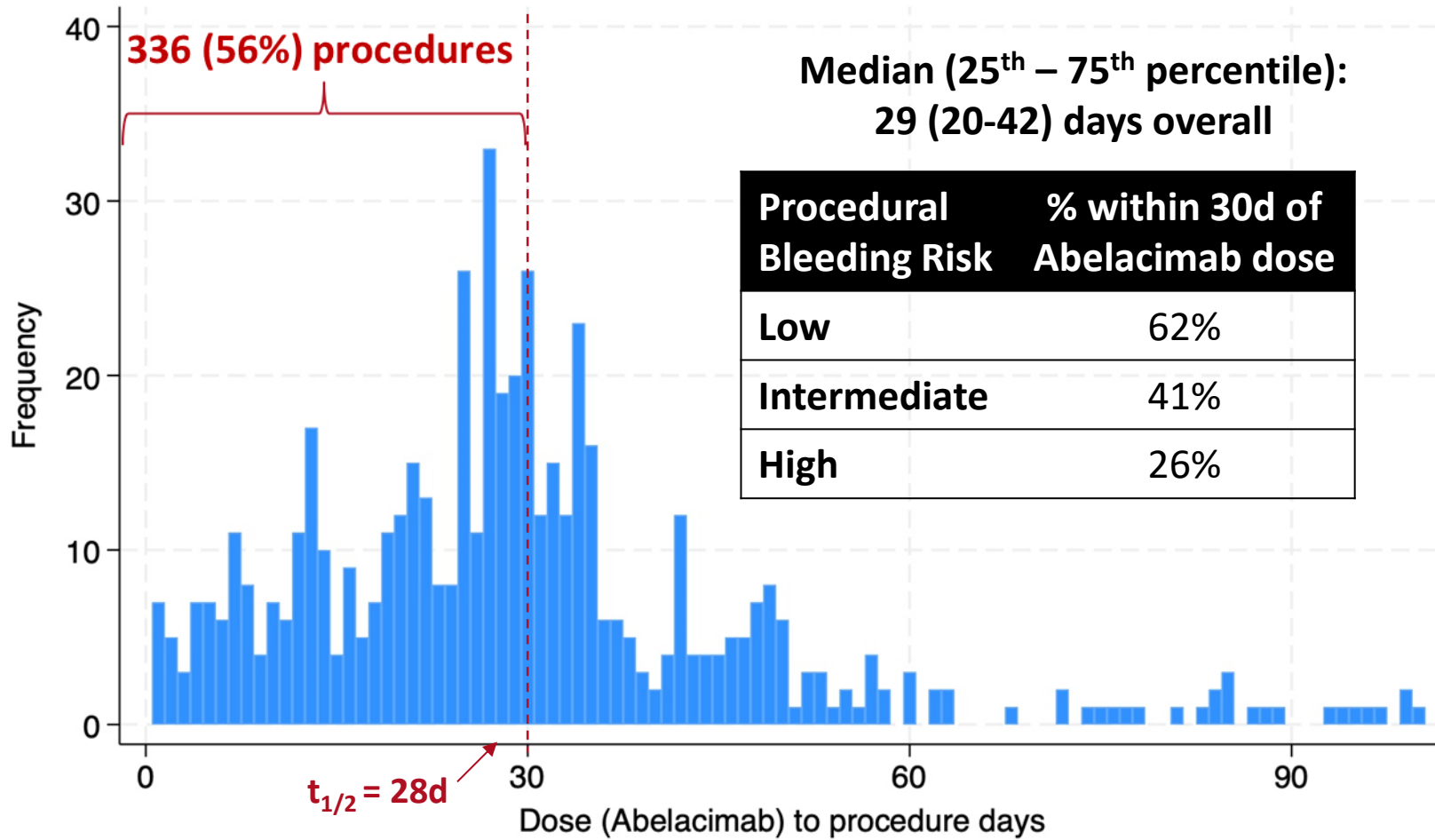
■ Elective ■ Non-elective



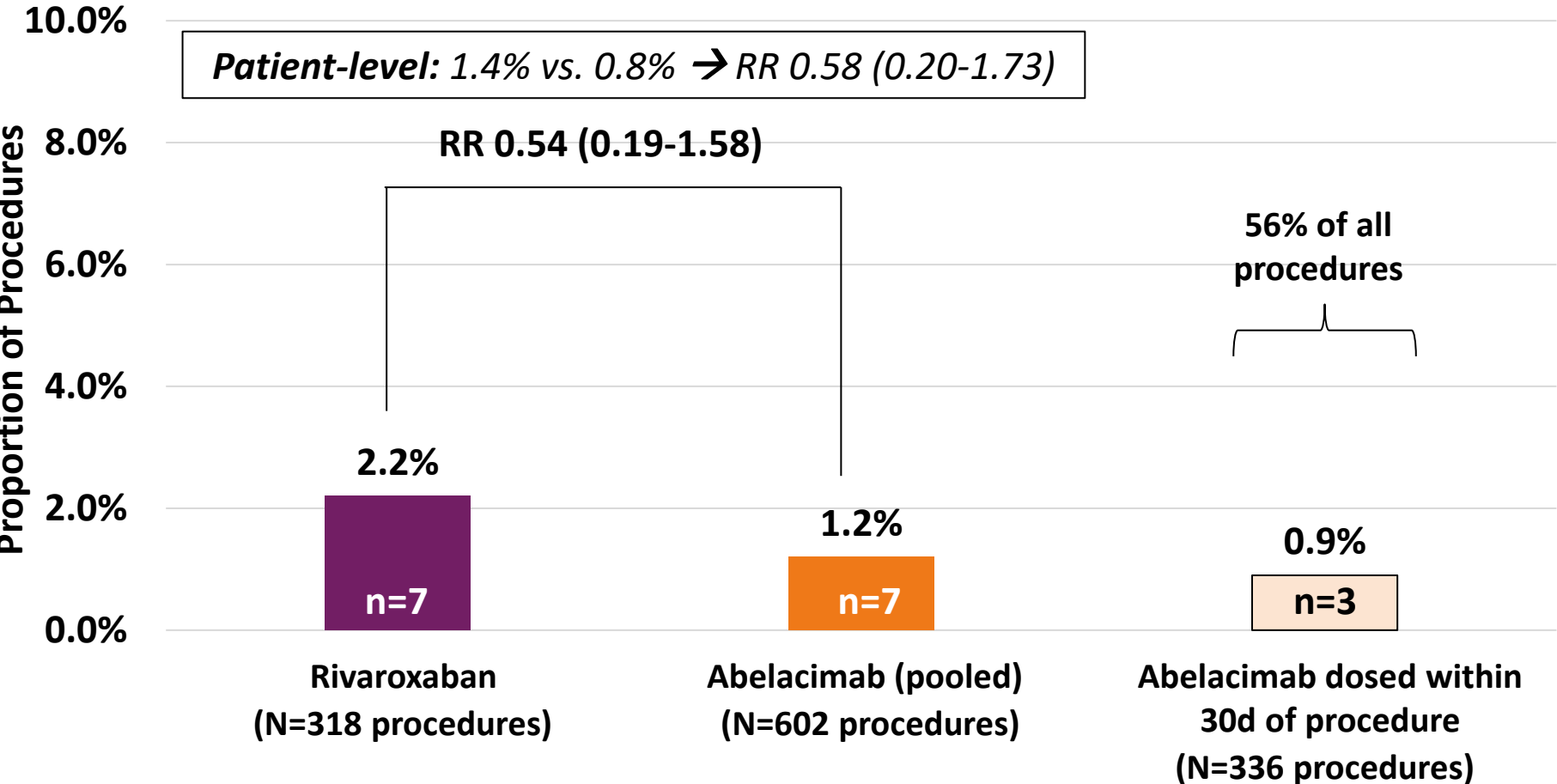
Breakdown of Procedure Types



Time from Last Abrelacimab Dose to Procedure



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%

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

Blood Transfusions	5.3%	1.2%
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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**