Bleeding in Patients with Atrial Fibrillation and Acute Coronary Syndrome or PCI treated with Antithrombotic Therapy: Insights from the AUGUSTUS Trial

Duke Clinical Research Institute | FROM THOUGHT LEADERSHIP TO CLINICAL PRACTICE

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BACKGROUND / AIMS

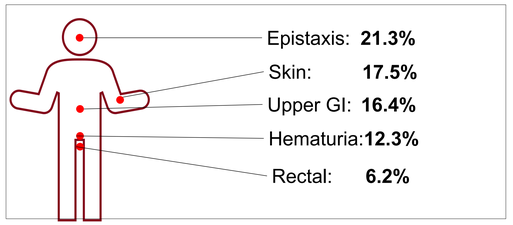
Bleeding is associated with higher risk of death, ischemic stroke, and MI in patients with atrial fibrillation (AF). However, less is known about the consequences of bleeding in patients with AF and concomitant acute coronary syndrome (ACS) and/or percutaneous coronary intervention (PCI).

Using data from AUGUSTUS, we characterized bleeding events by definition, number, and location; identified factors associated with bleeding; and evaluated the effect of Apixaban vs. vitamin K antagonist (VKA) and aspirin vs. placebo on bleeding.

METHODS

- AUGUSTUS used a 2 × 2 factorial design to compare Apixaban or VKA and aspirin or placebo, plus a P2Y12 inhibitor, in patients with AF and recent ACS and/or PCI.
- Major and CRNM bleeding were defined according to the ISTH criteria, GUSTO, and TIMI definitions.
- Patients were followed for 6 months.
- The association between randomized treatment and bleeding was compared using Cox proportional hazards models.

First ISTH Major/CRNM Bleeding Sites (N=578)



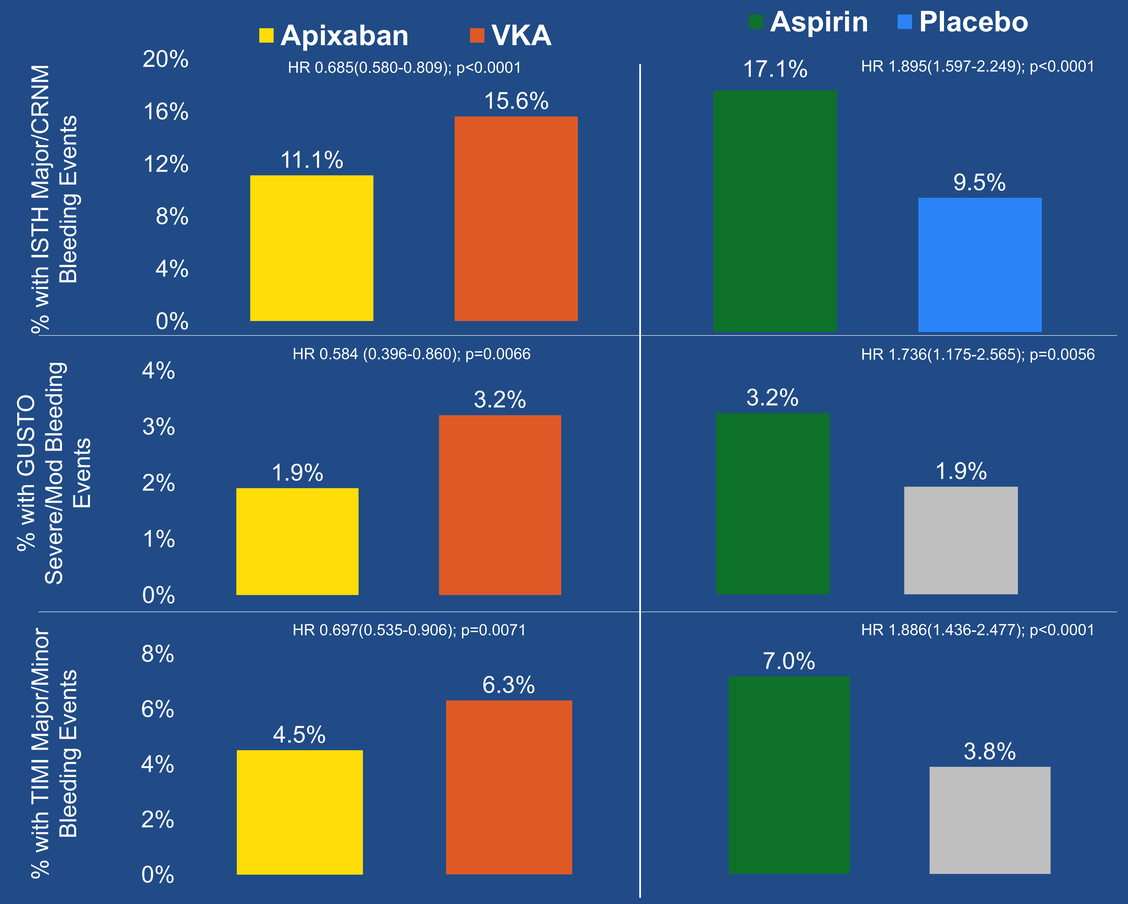
LIMITATIONS

Pre-specified secondary analysis so findings are observational in nature.

DISCLOSURES

JHA: Institutional research grants from Artivion/CryoLife, Bayer Bristol Myers Squibb, CSL Behring, Ferring, U.S. FDA, Humacyte, U.S. NIH, and XaTek. Advisory board or consulting payments or honoraria from AbbVie, Akros, Artivion/CryoLife, AtriCure, Bayer, Bristol Myers Squibb, Ferring, GlaxoSmithKline, Janssen, Pfizer, Portola, and Quantum Genomics. RM: Institutional research payments from Abbott, Abiomed, Alleviant Medical, AM-Pharma, Amgen, Applied Therapeutics, Arena, AstraZeneca, AtriCure, Bayer, Biosensors, Biotronik, Boston Scientific, Bristol-Myers Squibb, CardiaWave, CeloNova, Chiesi, Concept Medical, CSL Behring, Cytosorbents, Daiichi Sankyo, Element Science, Faraday, Humacyte, Idorsia, Janssen, Magenta, Medtronic, Novartis, OrbusNeich, PhaseBio, Philips, Pi-Cardia, RenalPro, Shockwave, Vivasure, Zoll; personal fees from Cine-Med Research, WebMD; Equity <1% in Applied Therapeutics, Elixir Medical, Stel, ControlRad (spouse); Scientific Advisory Board for AMA, ACC (BOT Member), SCAI (Women in Innovations Committee Member), JAMA Associate Editor: Faculty CRF (no fee). CBG: Institutional research grants: Boehringer Ingelheim, Bristol Myers Squibb, Daiichi Sankyo, US FDA, Janssen Pharmaceutical Products LP, Novartis, Pfizer, Philips Consulting fees/Honoraria: Abbvie, Abiomed, Alnylam Pharmaceuticals, Bayer, Boehringer Ingelheim, Boston Scientific, Bristol Myers Squibb, CeleCor Therapeutics, HengRui USA, Janssen Pharmaceutical Products LP, Medscape LLC, Medtronic, Merck, NIH, NovoNordisk, Novartis, PLX Pharma, Pfizer, Philips, REATA, NephroSynergy, Tenac.io SGG: RA: employee of Bristol Myers Squibb; SW:research, travel or educational grants to the institution from Abbott, Abiomed, Amgen, Astra Zeneca, Bayer, Biotronik, Boehringer Ingelheim, Boston Scientific, Bristol Myers Squibb, Cardinal Health, CardioValve, Corflow Therapeutics, CSL Behring, Daiichi Sankyo, Edwards Lifesciences, Guerbet, InfraReDx, Janssen-Cilag, Johnson & Johnson, Medicure, Medtronic, Merck Sharp & Dohm, Miracor Medical, Novartis, Novo Nordisk, Organon, OrPha Suisse, Pfizer, Polares, Regeneron, Sanofi-Aventis, Servier, Sinomed, Terumo, Vifor, V-Wave. Advisory board member and/or member of the steering/executive group of trials funded by Abbott, Abiomed, Amgen, Astra Zeneca, Bayer, Boston Scientific, Biotronik, Bristol Myers Squibb, Edwards Lifesciences, Janssen, MedAlliance, Medtronic, Novartis, Polares, Recardio, Sinomed, Terumo, V-Wave and Xeltis with payments to the institution but no personal payments. Steering/executive committee group of several investigator-initiated trials that receive funding by industry without impact on his personal remuneration. RDL:Research grants from Amgen, Bristol Myers Squibb, GlaxoSmithKline, Medtronic, Pfizer, and Sanofi-Aventis. Funding for educational activities or lectures from Pfizer. Consulting payments or honoraria from Bayer, Boehringer Ingelheim, Bristol Myers Squibb, Daiichi Sankyo, and Portola. The other authors have no relevant disclosures.

ASSOCIATION BETWEEN RANDOMIZED TREATMENT AND BLEEDING ENDPOINTS

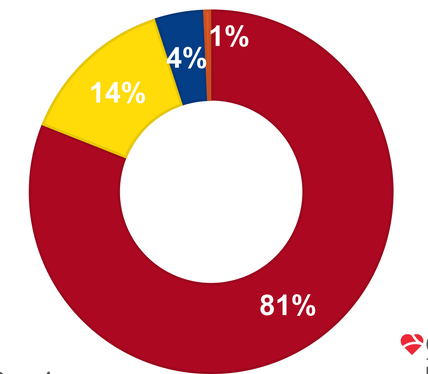


IN PATIENTS WITH AF AND RECENT ACS AND/OR PCI, VKA (COMPARED WITH APIXABAN) AND ASPIRIN (COMPARED WITH PLACEBO) BOTH CONTRIBUTED TO HIGHER RATES OF BLEEDING

RESULTS

Characteristic	ISTH Major/CRNM Bleeding during Follow-Up	
	Yes (N=578)	No (N=3990)
Age, yrs (median, 25th-75th)	73.1, 66.8-79.0	70.3, 63.8-76.9
Female sex -- no. (%)	167 (28.9%)	1160 (29.1%)
White Race	512/562 (91.1%)	3628/3949 (91.9%)
Black Race	7/562 (1.2%)	51/3949 (1.3%)
Asian Race	13/562 (2.3%)	126/3949 (3.2%)
Other	30/562 (5.3%)	144/3949 (3.6%)
Serum Creatinine -- no./total no. (%)		
<1.5 mg/dl	515/575 (89.6%)	3637/3957 (91.9%)
≥1.5 mg/dl	60/575 (10.4%)	320/3957 (8.1%)
Ever Smoked -- no./total no. (%)	303/574 (52.8%)	1950/3967 (49.2%)
CHA_2DS_2-VASc Score (mean (SD))	4.2 (1.5)	3.9 (1.6)
HAS-BLED Score (mean (SD))	2.9 (0.9)	2.8 (0.9)
Hypertension leading to medication use -- no.(%)	504 (87.2%)	3533 (88.5%)
Diabetes mellitus -- no.(%)	233 (40.3%)	1421 (35.6%)
Stroke, TIA, or thromboembolism -- no./total no.(%)	96/576 (16.7%)	526/3963 (13.3%)
Congestive Heart Failure -- no./total no.(%)	248/578 (42.9%)	1705/3990 (42.7%)
Prior Bleeding -- no./total no.(%)	13/576 (2.3%)	36/3967 (0.9%)
Concomitant P2Y12 inhibitor -- no.(%)		
Clopidogrel	504 (87.2%)	3621 (90.8%)
Ticagrelor	52 (9.0%)	225 (5.6%)
Prasugrel	9 (1.6%)	42 (1.1%)
None	13 (2.2%)	102 (2.6%)
Previous use of oral anticoagulant -- no.(%)	287 (49.7%)	1961 (49.1%)
On Beta Blockers at Randomization -- no.(%)	417 (72.1%)	2888 (72.4%)
On ACE Inhibitors/ARBs/ARNI -- no.(%)	368 (63.7%)	2579 (64.6%)
On Diuretics -- no.(%)	215 (37.2%)	1202 (30.1%)
Qualifying index event -- no./total no.(%)		
Acute coronary syndrome and PCI	218/575 (37.9%)	1481/3977 (37.2%)
Medically managed acute coronary syndrome	93/575 (16.2%)	1002/3977 (25.2%)
Elective PCI	264/575 (45.9%)	1494/3977 (37.6%)
No. of days from ACS or PCI to randomization (mean (SD))	5.7 (4.2)	6.8 (4.2)

NUMBER OF ISTH MAJOR/CRNM BLEEDING AMONG PATIENTS WITH AT LEAST ONE BLEEDING



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