# Relative benefit of double versus triple antithrombotic therapy in patients with atrial fibrillation randomized earlier versus later after index coronary event: Insights from the AUGUSTUS Trial

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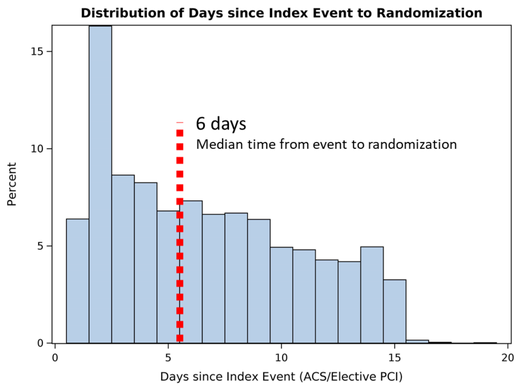
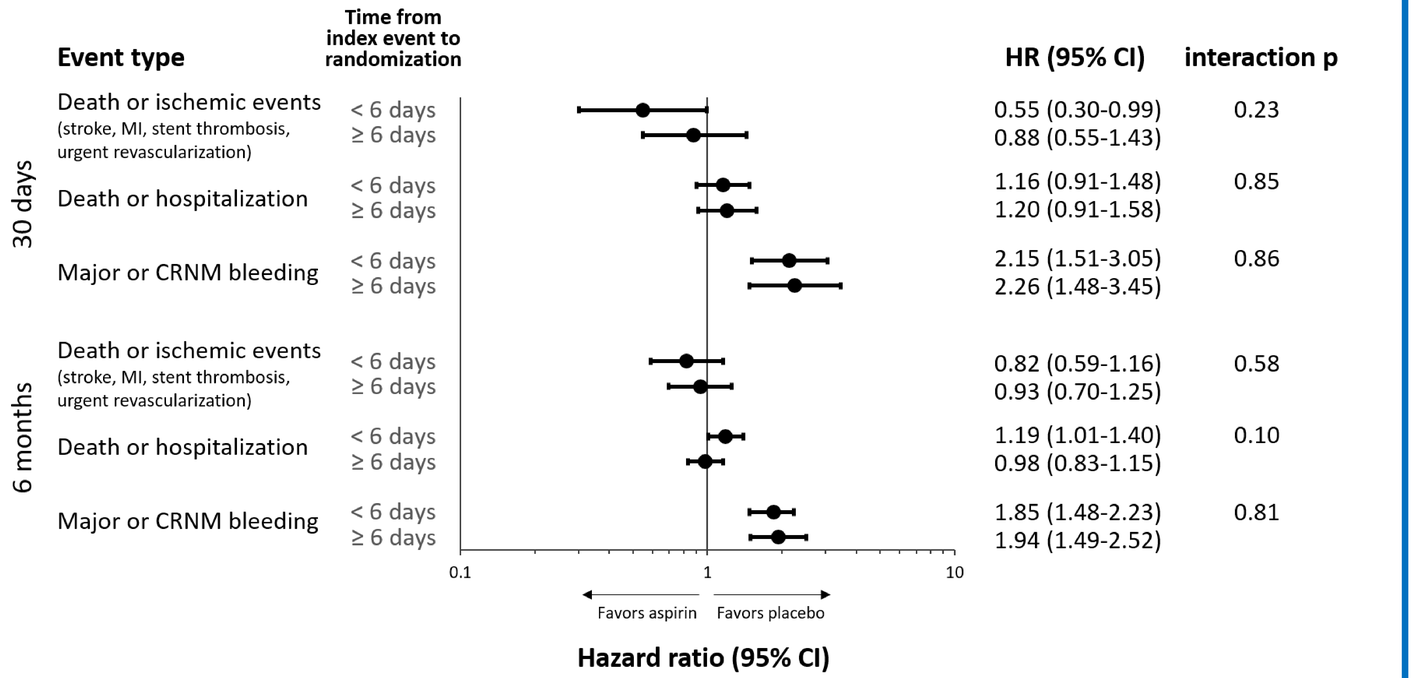
## BACKGROUND

- On a background of oral anticoagulation plus a P2Y12 inhibitor, placebo (versus aspirin) reduced major and clinically relevant non-major bleeding without increasing ischemic events in the AUGUSTUS trial of antithrombotic therapies in patients atrial fibrillation and acute coronary syndrome or undergoing PCI
- In AUGUSTUS, patients were randomized within 14 days after their index event and received triple therapy (OAC + P2Y12 inhibitor + aspirin) until randomization. Guidelines therefore recommend a short course (7-30 days) of triple antithrombotic therapy after ACS or PCI
- In AUGUTUS, patients randomized **early** after their index event had a shorter duration of triple therapy than those randomized later; we leveraged this variability to study the risks and benefits of a short course of triple therapy immediately following ACS or PCI

## METHODS

- We divided patients into two groups based on time from index event to randomization (< and ≥ 6 days, the median for the study cohort)
- We used Cox proportional hazards models to determine randomized treatment effect (aspirin vs. placebo) stratified by time from index event to randomization and performed interaction testing




**There was no difference in the relative benefit of aspirin versus placebo when patients were randomized early versus later after their index event.**

**Background:** On a background of oral anticoagulation (OAC) plus $P2Y_{12}$ inhibitor, placebo (versus aspirin) reduced the risk of bleeding without increasing ischemic events among patients with atrial fibrillation (AF) with acute coronary syndrome (ACS) and/or undergoing percutaneous coronary intervention (PCI) in the AUGUSTUS trial. However, there may be a benefit to triple antithrombotic therapy very early after a coronary event, which would manifest as a reduction in ischemic events for patients randomized to aspirin (versus placebo) earlier after their index ACS or PCI.

**Methods:** In this secondary analysis of AUGUSTUS, we tested for an interaction between aspirin vs. placebo, time from index event to randomization, and clinical outcomes using a Cox proportional hazards model.

**Results:** Among 4605 patients enrolled in AUGUSTUS, median time from index event to randomization was 6 days (range 0-14 days). There were no significant interactions between time from index event, aspirin vs. placebo, and clinical outcomes at 30 days or 6 months (**Figure**), though patients with time from index event <6 days had a nominally significant reduction in the composite of all-cause death or ischemic events at 30 days with aspirin (HR 0.55, 95% CI 0.30-0.99) and patients with time from index event ≥6 days did not (HR 0.88, 95% CI 0.54-1.43) (interaction p = 0.23).

**Conclusion:** Among patients with AF with ACS and/or undergoing PCI, there was no difference in the relative benefit of aspirin versus placebo when patients were randomized early versus later after their index event.



## BASELINE CHARACTERISTICS

| | Time from index event < 6 days (n = 2136) | Time from index event ≥ 6 days (n = 2469) |
|---|---|---|
| Age | 71 (65, 77) | 70 (64, 77) |
| Female sex, n (%) | 521 (24.4%) | 813 (32.9%) |
| CHADS2-VASc score, mean (SD) | 3.8 (1.5) | 4.0 (1.6) |
| Hypertension, n (%) | 1872 (87.6%) | 2194 (88.9%) |
| Diabetes, n (%) | 800 (37.5%) | 875 (35.4%) |
| Heart failure, n (%) | 758 (35.5%) | 1212 (49.1%) |
| Prior stroke/TIA, n (%) | 266 (12.5%) | 365 (14.9%) |
| Index event, n (%) | | |
| ACS plus PCI | 895 (41.9%) | 819 (33.3%) |
| Medically-managed ACS | 272 (12.7%) | 825 (33.6%) |
| PCI without ACS | 969 (45.4%) | 815 (33.1%) |

## DISCUSSION/LIMITATIONS

- This is a post-hoc analysis of a randomized controlled trial, though it is hypothesis-driven. However, it may be underpowered
- Treatment prior to randomization in AUGUSTUS was not systematically reported
- Though there was no suggestion that a 6-14 day course of triple therapy was superior to a 0-5 day course for prevention of ischemic events, a longer duration of triple therapy (i.e. 30 days) following ACS or PCI may be beneficial
- These results indicate that a short (7-day) course of triple therapy followed by OAC + P2Y12 alone best balances bleeding and ischemic risks in patients with AF and ACS or PCI

## DISCLOSURES

Dr. Fanaroff reports research grants from the American Heart Association, National Institutes of Health, and Boston Scientific, and consulting fees from Intercept Pharmaceuticals. Dr. Granger reports research grants from Bayer, Boehringer Ingelheim, Bristol-Myers Squibb, Daiichi Sankyo, Janssen, Pfizer, Armetheon, AstraZeneca, US Food and Drug Administration, GlaxoSmithKline, The Medicines Company, Medtronic Foundation, Medtronic Inc, and Novartis, as well as consulting fees from Bayer, Boehringer Ingelheim, Boston Scientific, Bristol-Myers Squibb, Daiichi Sankyo, Janssen, Pfizer, Abbvie, Armetheon, AstraZeneca, Eli Lilly, Gilead, GlaxoSmithKline, Hoffmann-La Roche, The Medicines Company, National Institutes of Health, Novartis, Sirtex, Verseon, Apple, Medscape, LLC, Merck, Novo Nordisk, Roche Diagnostics, and Rbo Pharmaceuticals. Dr. Goodman reports research grant support and/or speaker/consulting honoraria from Amgen, AstraZeneca, Bayer, Boehringer Ingelheim, Bristol-Myers Squibb, CSL Behring, Daiichi-Sankyo, Eli Lilly, Esperion, Fenix Group International, Ferring Pharmaceuticals, GlaxoSmithKline, HLS Therapeutics, Janssen/Johnson & Johnson, Luitpold Pharmaceuticals, Matrizyme, Merck, Novartis, Novo Nordisk A/C, Pfizer, Regeneron, Sanofi, Servier, Tenax Therapeutics, Heart and Stroke Foundation of Ontario/University of Toronto, Canadian Heart Research Centre and MD Primer, Canadian VIGOUR Centre, Duke Clinical Research Institute, and PERFUSE. Dr. Aronson is an employee of Bristol-Myers Squibb. Dr Windecker reports institutional research and educational grants from Abbott, Amgen, Bayer, BMS, CSL Behring, Boston Scientific, Biotronik, Edwards Lifesciences, Medtronic, Polares, and Sinomed. Dr. Mehran reports institutional research grants from AstraZeneca, Bayer, Beth Israel Deaconess, Bristol-Myers Squibb/Sanofi, CSL Behring, Eli Lilly/Daiichi Sankyo, Medtronic, Novartis, and OrbusNeich; consulting fees from Boston Scientific, Abbott Vascular, Medscape, Siemens Medical Solutions, Roivant Sciences Inc, and Sanofi; consulting (no fees) to Regeneron Pharmaceuticals Inc; institutional consulting fees from Abbott Vascular, Spectranetics/Phillips/Volcano Corporation, Bristol-Myers Squibb, Novartis, and Watermark Research; serving as an executive committee member for Janssen Pharmaceuticals and Bristol-Myers Squibb; and <1% equity in Claret Medical and Elixir Medical. Dr. Alexander reports research grants from Bristol-Myers Squibb, Boehringer Ingelheim, AstraZeneca, CryoLife, CSL Behring, US Food and Drug Administration, National Institutes of Health, Sanofi, and VoluMetrix, as well as consulting fees from Pfizer, Bristol-Myers Squibb, AbbVie Pharmaceuticals, CSL Behring, Novo Nordisk, Portola Pharmaceuticals, Quantum Genomics, Teikoku Pharmaceuticals, VA Cooperative Studies, and Zafgen.. Dr. Lopes reports research grants from Bristol-Myers Squibb, Pfizer, Amgen, Inc, GlaxoSmithKline, Medtronic PLC, and Sanofi Aventis, as well as consulting fees from Bristol-Myers Squibb, Pfizer, Boehringer Ingelheim, and Bayer AG. The other authors report no conflicts.