FROM ARISTOTLE TO THE REAL WORLD

FOR MYSELF

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PP-ELI-HKG-1091 NOV 2022

This is not a real doctor but a model.

MY FATHER

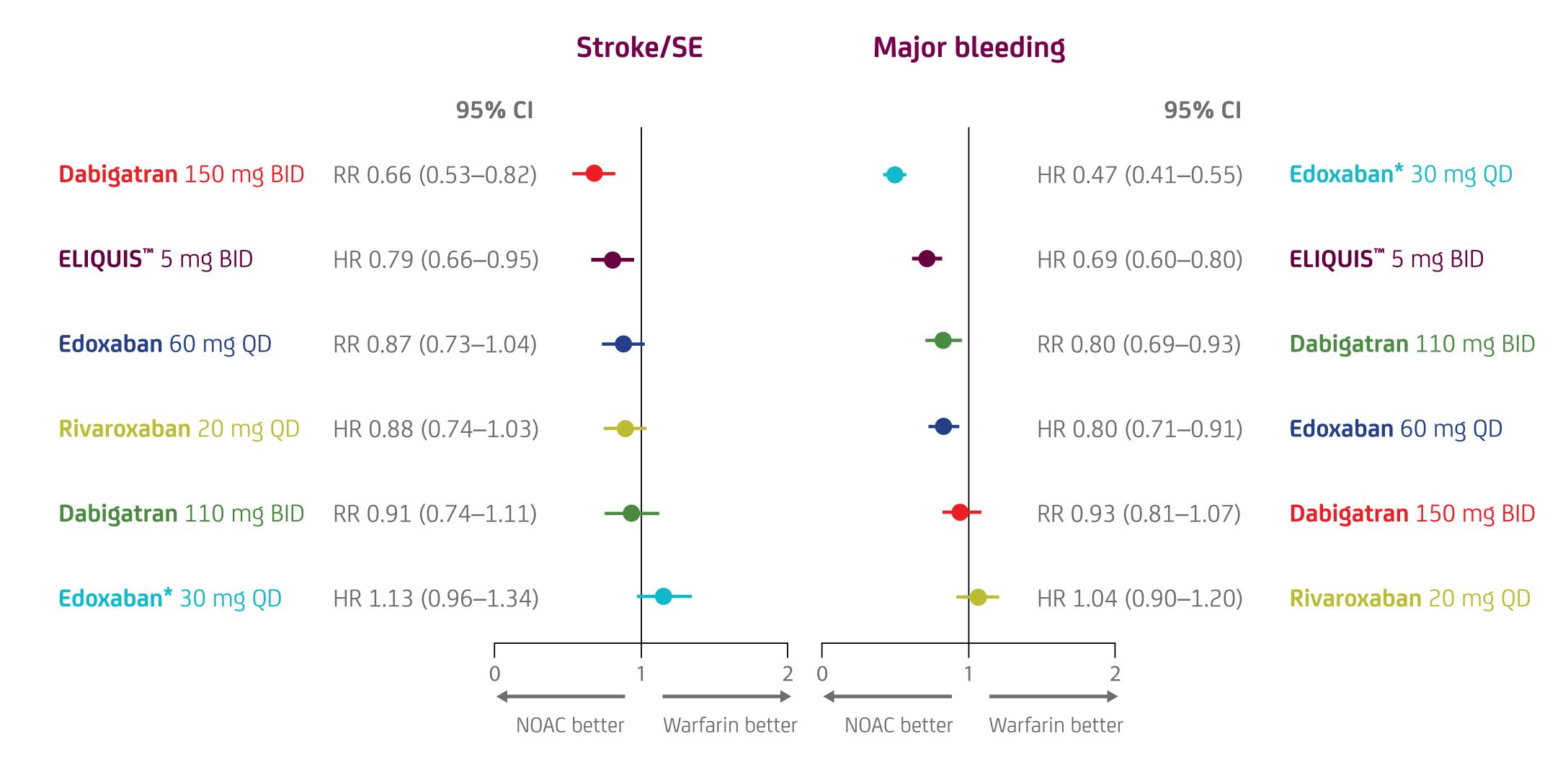
MY FRIENDS





ELIQUIS[™] provides superior stroke and bleeding protection vs warfarin in AF^{1-3*}

- is needed to assess causal relationships and treatment effect.⁴
- **bleeding (p<0.001)** vs warfarin.¹



* Edoxaban 30 mg daily is not approved for stroke prevention in AF. Adapted from Schulman et al. 2014³

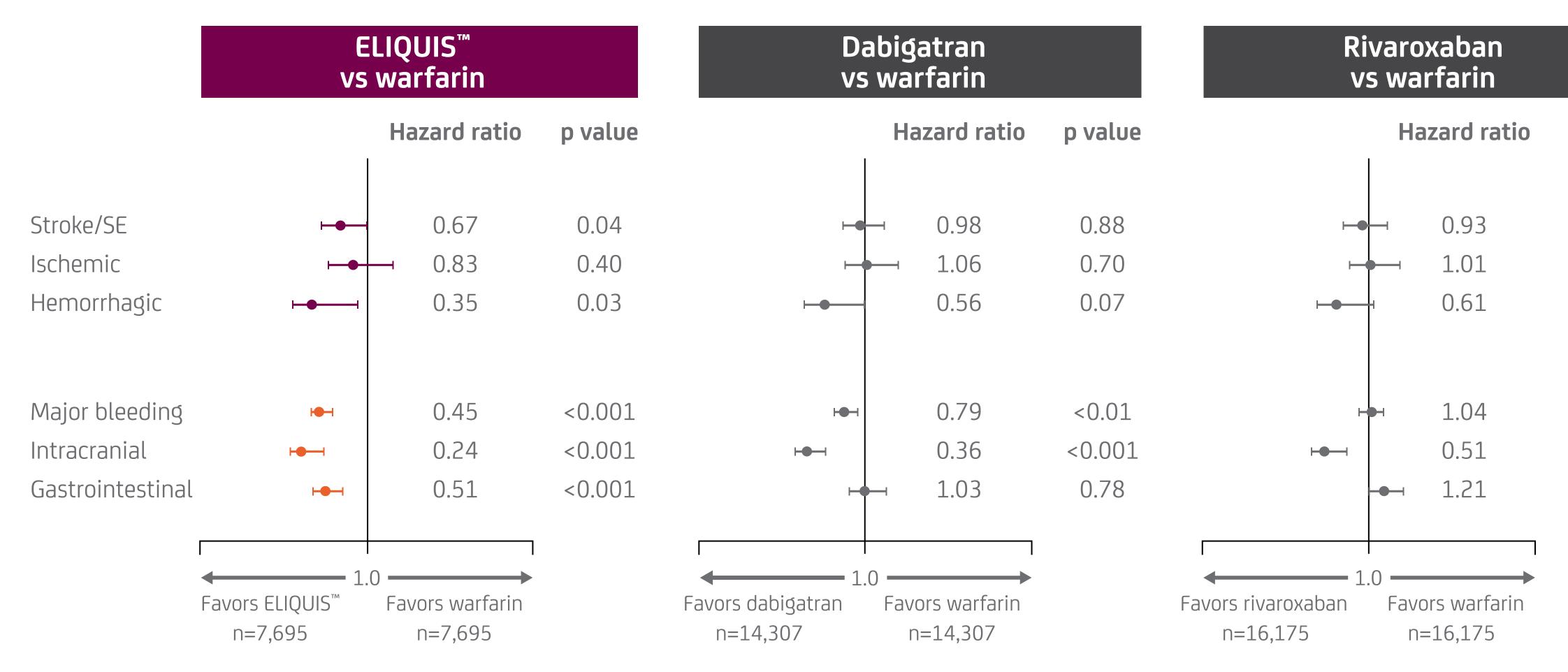
• Randomized controlled trials (RCTs) are the gold standard for assessing treatment efficacy and safety. Randomization

• In ARISTOTLE, ELIQUIS[™] demonstrated 21% superior RRR in stroke/SE (p=0.01) and 31% superior RRR in major



ELIQUISTM effectiveness and safety: Consistent results in a US real-world analysis (I)⁵

- **bleeding** compared with warfarin.



An independent retrospective analysis of a US Insurance database of more than 76,000 NVAF patients between October 2010 and June 2015 was carried out to evaluate the real-world effectiveness and safety of NOACs vs warfarin. Three matched cohorts using 1:1 propensity score matching was created.* * There are no head-to-head trials comparing NOACs.

Adapted from Yao et al. 2016⁵

• Consistent with ARISTOTLE, patients receiving ELIQUIS[™] had significantly lower risks of both stroke/SE and major

• Both dabigatran and rivaroxaban were associated with similar risks of stroke/SE vs warfarin. Dabigatran was associated with significantly lower risks of major bleeding while rivaroxaban was associated with similar risk of major bleeding vs warfarin.



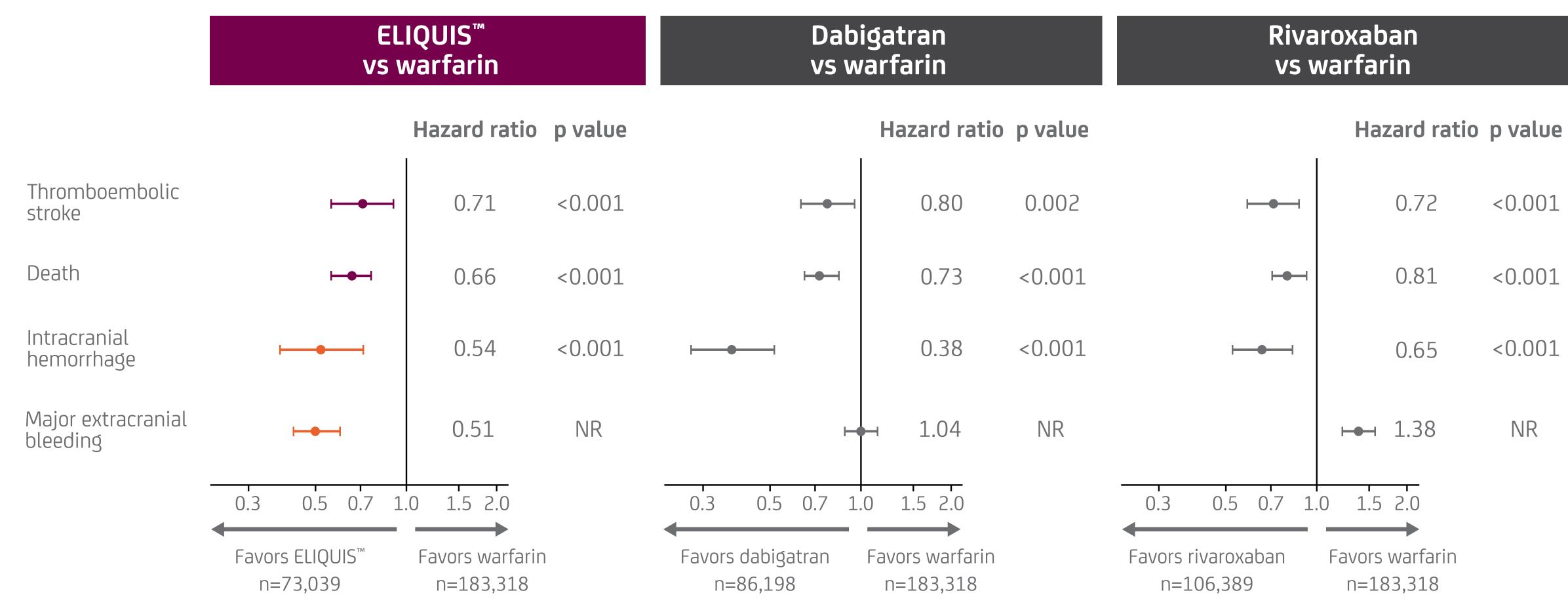
p value

0.56 0.95 0.08

0.60 < 0.001 0.03

ELIQUIS[™] effectiveness and safety: Consistent results in a US FDA-initiated real-world analysis (II)⁶

• ELIQUIS[™] demonstrated superior risk reduction in stroke, ICH, major bleeding and death vs warfarin.*



* There are no head-to-head trials comparing NOACs.

A retrospective new-user cohort study was conducted on patients with NVAF enrolled in US Medicare who initiated on warfarin, or standard-dose ELIQUIS[®], dabigatran or rivaroxaban between October 2010 and September 2015. Study outcomes were hospitalized thromboembolic stroke, intracranial hemorrhage, major extracranial bleeding and all-cause mortality.

Adapted from Graham et al. 2019⁶

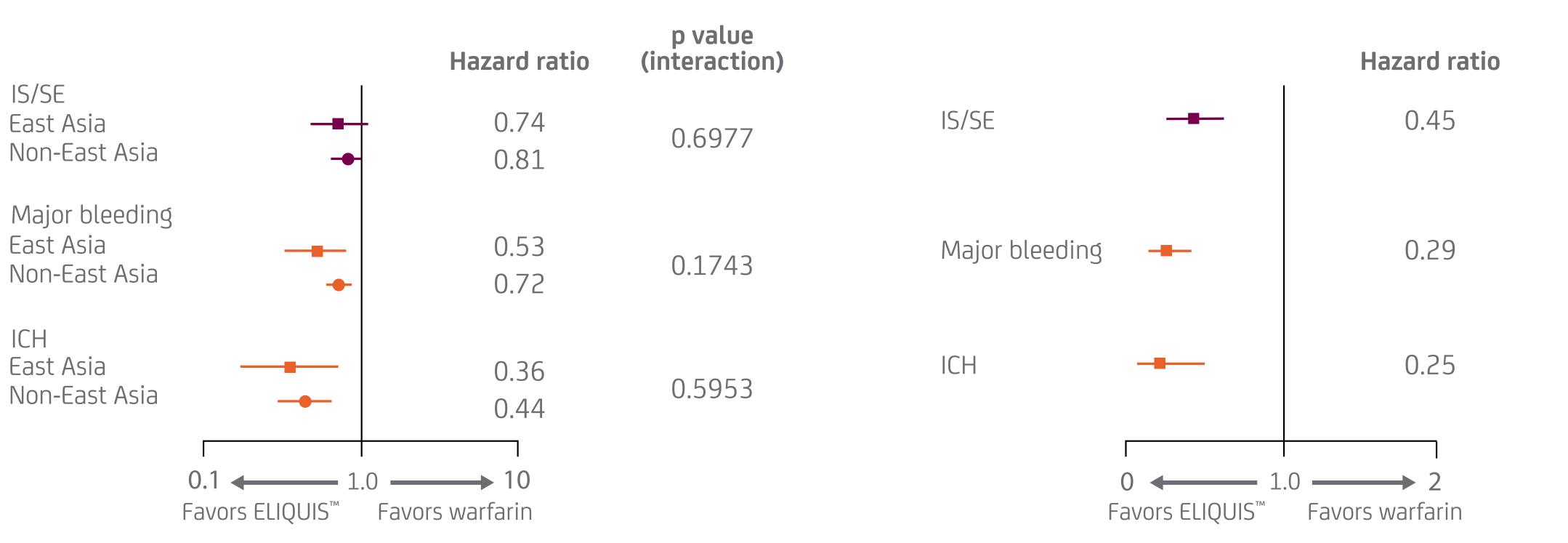


< 0.001 < 0.001 < 0.001

NR

ARISTOTLE data translate well into the real-world setting in an Asian cohort^{7,8}

ARISTOTLE East Asia⁷



Adapted from Goto et al. 2014⁷

In both ARISTOTLE East Asia and the Taiwan cohort study, ELIQUIS[™] resulted in reductions in IS/SE, ICH and major bleeding compared with warfarin in Asian patients. ARISTOTLE East Asia: ELIQUISTM (n=988), warfarin (n=1,005); Taiwan Cohort: ELIQUISTM (n=5,843), warfarin (n=19,375); ARISTOTLE non-East Asia: ELIQUISTM (n=8,132), warfarin (n=8,076).

ELIQUISTM in real-world settings: consistent superior stroke and bleeding reductions vs warfarin across different studies.⁵⁻⁸

The Taiwan Cohort⁸

Adapted from Chan et al. 2018⁸



p value < 0.0001

< 0.0001

< 0.0005



AF, atrial fibrillation; AMI, acute myocardial infarction; CI, confidence interval; HR, hazard ratio; FDA, Food and Drug Administration; ICH, intracranial hemorrhage; IS, ischemic stroke; NOAC, non-VKA oral anticoagulant; NR, not reported; NVAF, nonvalvular atrial fibrillation; OAC, oral anticoagulant; RCT, randomized controlled trial; RRR, relative risk reduction; RWD, real-world data; SE, systemic embolism

References 1. Granger CB, et al. N Engl J Med 2011;365:981-992. 2. Ruff CT, et al. Lancet 2014;383:955-962. 3. Schulman S. Thromb Haemost 2014;111:575-582. 4. Fanaroff AC, et al. Eur Heart J 2018;39:2932-2941. 5. Yao X, et al. J Am Heart Assoc 2016;5:e003725. 6. Graham D, et al. Am J Med 2019;132:596-604.e11. 7. Goto S, et al. Am Heart J 2014;168:303-309. 8. Chan YH, et al. J Am Heart Assoc 2018;7:e008150.

Apixaban (2.5 mg)



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