49th Annual New York Cardiovascular Symposium

STEMI vs. NSTEMI vs. STABLE CAD

Challenging Cases and Antithrombotic Approaches

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Disclosure

Relationships with Industry

Consultant to the following companies involved in developing antithrombotic drugs:

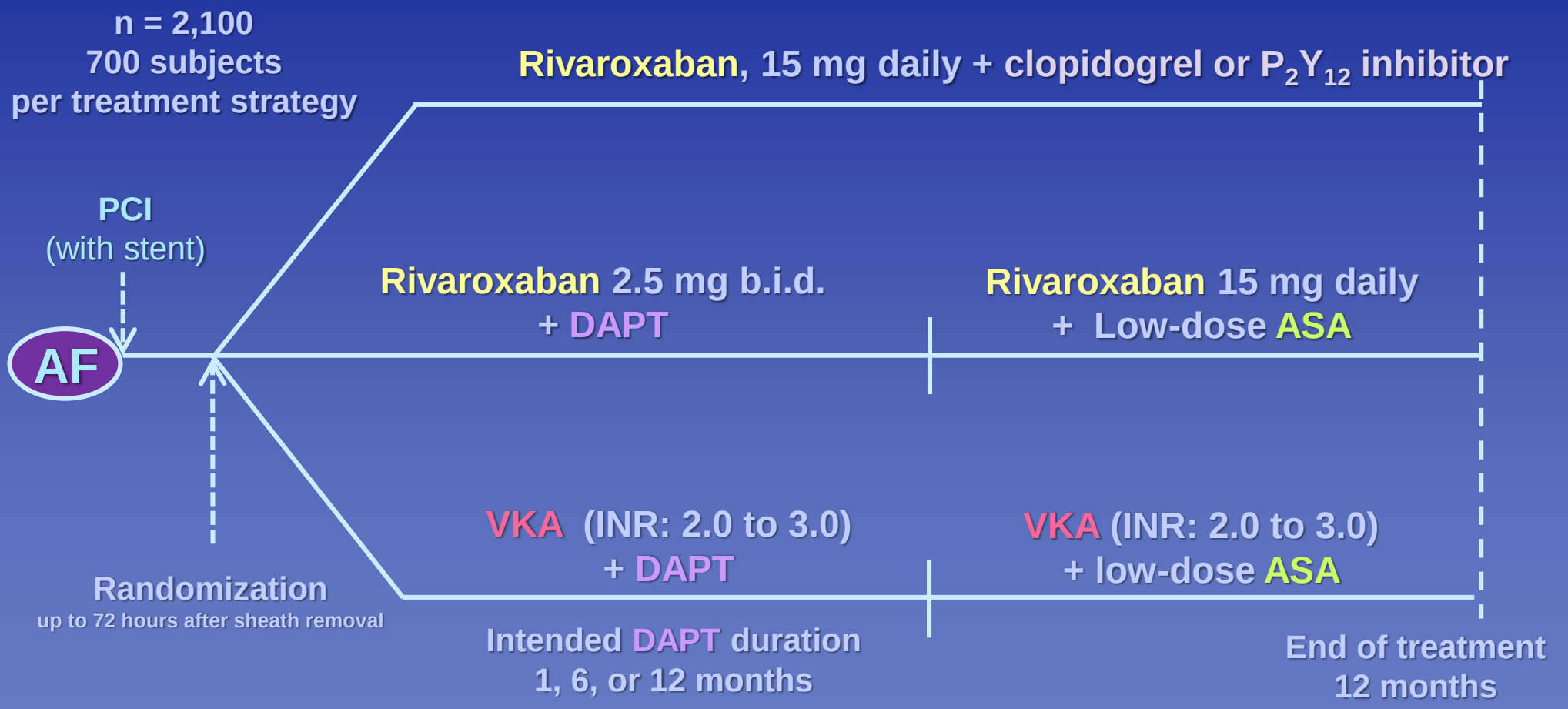
- AstraZeneca
- Bayer HealthCare
- Boehringer Ingelheim
- Bristol-Myers Squibb
- Daiichi Sankyo
- Janssen Ortho McNeil
- Johnson & Johnson
- Pfizer

Case 1

- 79 year-old woman with hypertension, hypothyroidism, and palpitation presented with sudden onset of chest pain, palpitation and dyspnea.
- ECG: AF with RVR (140-160 bpm) and ST-segment depressions; troponin 0.41 ng/ml (mildly elevated). Other lab values normal.
- Rate controlled with metoprolol, given aspirin and heparin and transferred for cardiac catheterization
- Angiography: 3-vessel CAD.
- Procedure: PCI with rotational atherectomy + DES of proximal LAD and DES of Cfx into OM1.

PIONEER AF-PCI

Trial Design

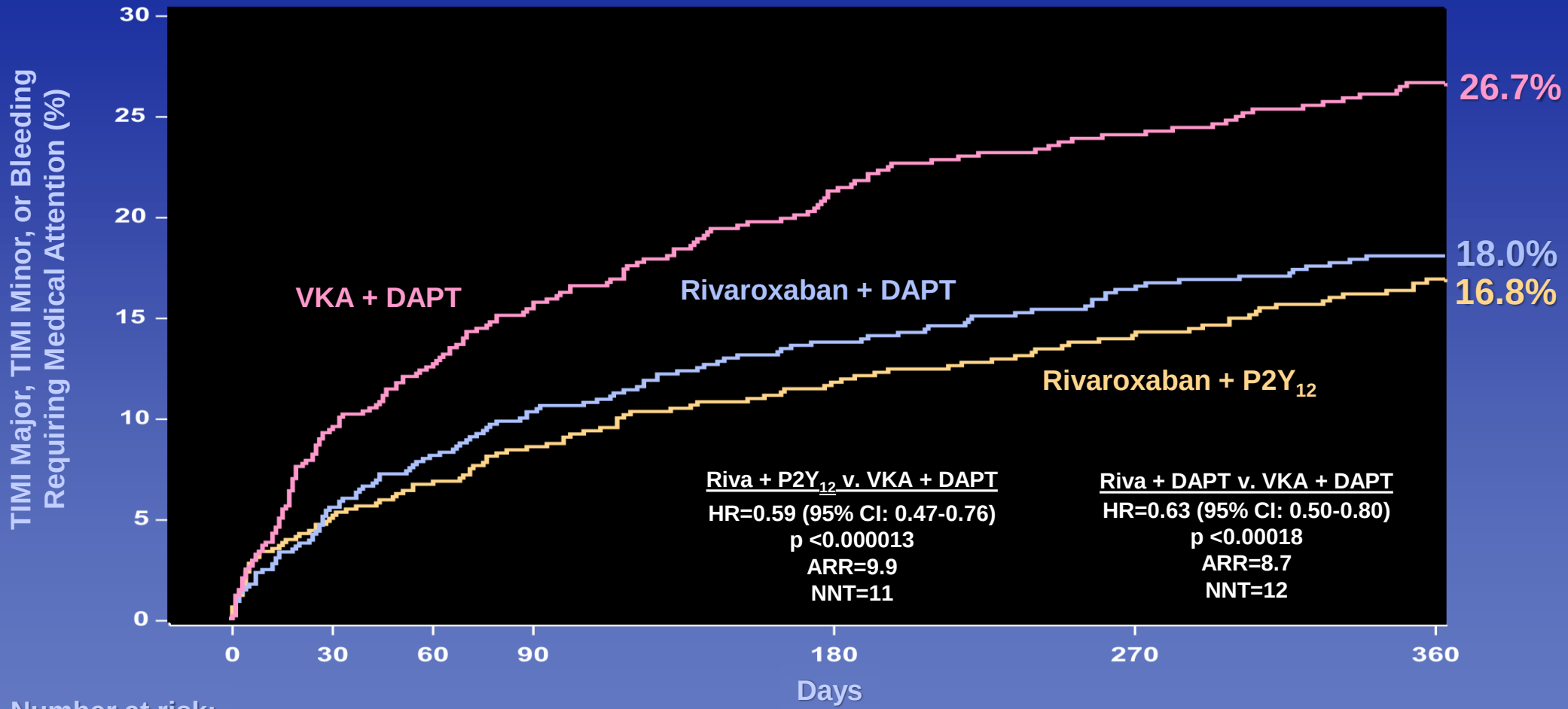


Primary endpoint
Clinically relevant bleeding

Gibson CM, et al. *Am Heart J* 2014; 169: 472.

First Occurrence of Clinically Significant Bleeding

PIONEER AF-PCI



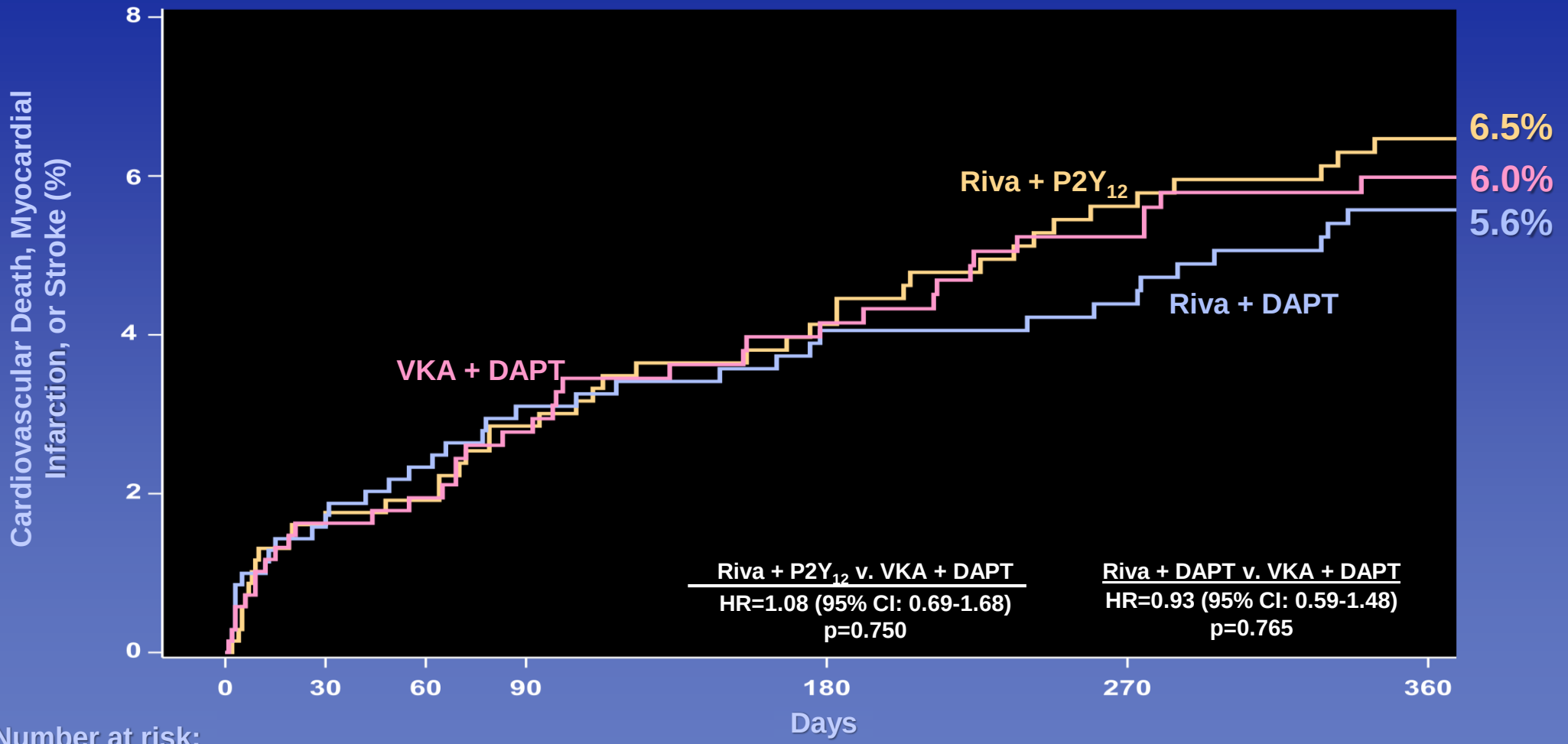
Number at risk:

Riva + P2Y$_{12}$	696	628	606	585	543	510	383
Riva + DAPT	706	636	600	579	543	509	409
VKA + DAPT	697	593	555	521	461	426	329

Gibson CM, et al. *N Engl J Med 2016;* E-published November 14, 2016

Cardiovascular Death, MI or Stroke

PIONEER AF-PCI



Number at risk:

Riva + P2Y$_{12}$	694	648	633	621	590	562	430
Riva + DAPT	704	662	640	628	596	570	457
VKA + DAPT	695	635	607	579	543	514	408

Gibson CM, et al. *N Engl J Med 2016;* E-published November 14, 2016

Case 1, continued

- In the cath lab, received bivalirudin, aspirin + clopidogrel.
- The following day aspirin stopped; discharged on clopidogrel, 75 mg/d + rivaroxaban, 15 mg/d (24 hours after sheath removal).
- The next day developed an expanding groin hematoma. Duplex arterial ultrasound: common femoral artery pseudoaneurysm and A-V fistula. Rivaroxaban stopped.
- Pseudoaneurysm and AV fistula closed via ultrasound-guided thrombin injection. Stability confirmed by duplex sonography 2 days later.
- Hemoglobin stable; hematoma resolving.
- Continued clopidogrel; rivaroxaban resumed a week later.
- Staged PCI of rPDA planned.

Case 2

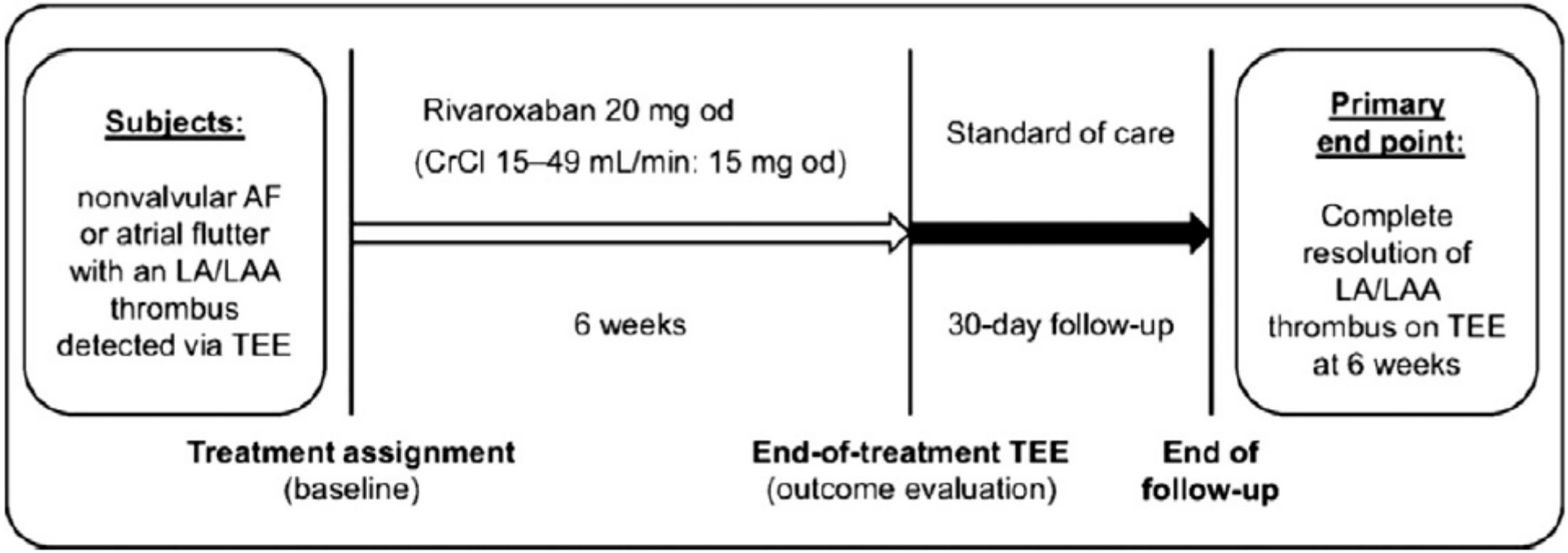
- 68 year old man with arrhythmogenic right ventricular cardiomyopathy, VT and ICD, admitted to an outside hospital after falling at home. He was febrile, a urine culture grew *E. coli,* and he improved on antibiotic therapy.
- Over the next 48 hours, he developed progressive dyspnea, the ECG showed nonspecific ST-T wave changes in a paced rhythm, and serum troponin increased to 8.3 ng/ml. He was given aspirin, clopidogrel, 300 mg, furosemide IV and nebulizers, and symptoms resolved.
- A TTE after this episode was technically limited, and he was transferred for further evaluation and management.
- On arrival he was hemodynamically stable. Interrogation of the ICD found that AF started around the time of the fall at home that prompted hospitalization; the ventricular rhythm was paced.

Case 2, continued

- Echocardiogram: Technically limited; segmental LV dysfunction (EF 40%), worse than 2 years earlier; normal RV systolic function.
- Coronary angiography: Thrombotic occlusion of mid-LAD, partly recanalized; 80-90% stenosis of 1st diagonal branch; diffuse, non-obstructive disease of other vessels.
- PCI performed in diagonal artery (DES); thrombectomy and balloon PTCA of LAD (no stent). Aspirin and clopidogrel continued.
- Subsequent echo (with contrast for endocardial border enhancement): LV apical akinesis, EF 40%, apical mural thrombus. Heparin added.
- Antithrombotic regimen at discharge?

Trials of NOACs for Intracardiac Thrombus

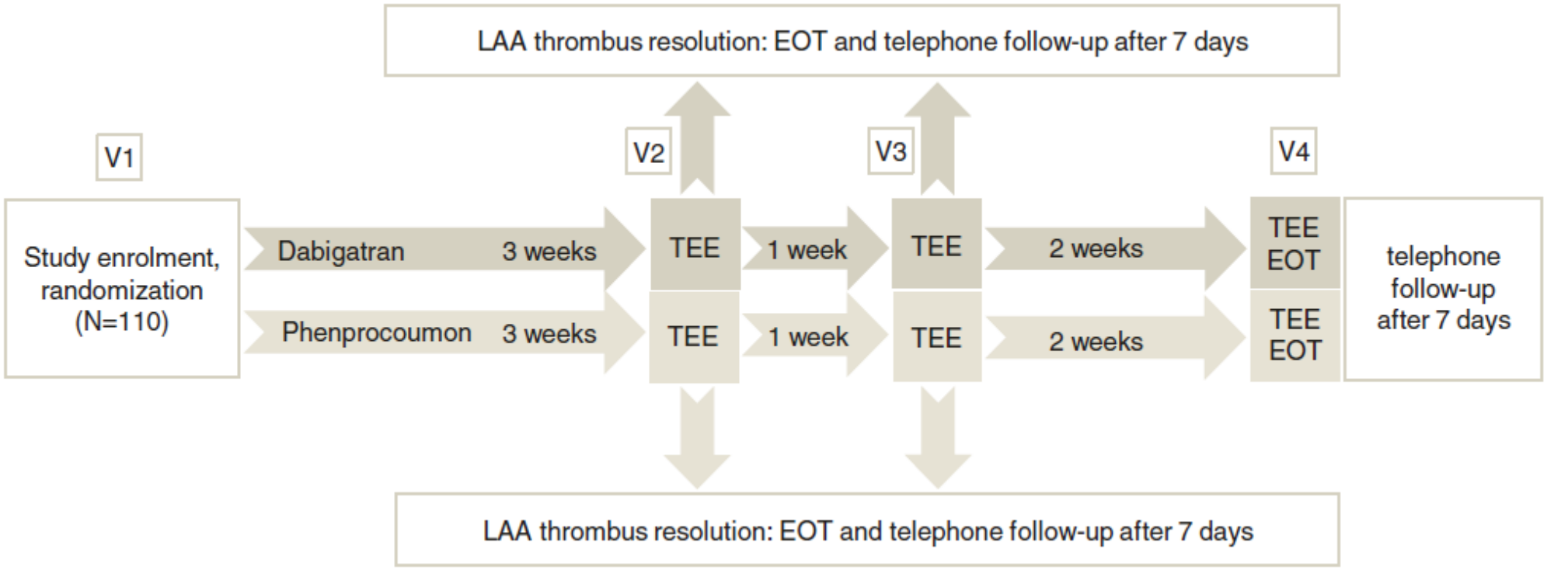
X-TRA



Lip GYH, et al. *Am Heart J* 2015; 169: 464

Trials of NOACs for Intracardiac Thrombus

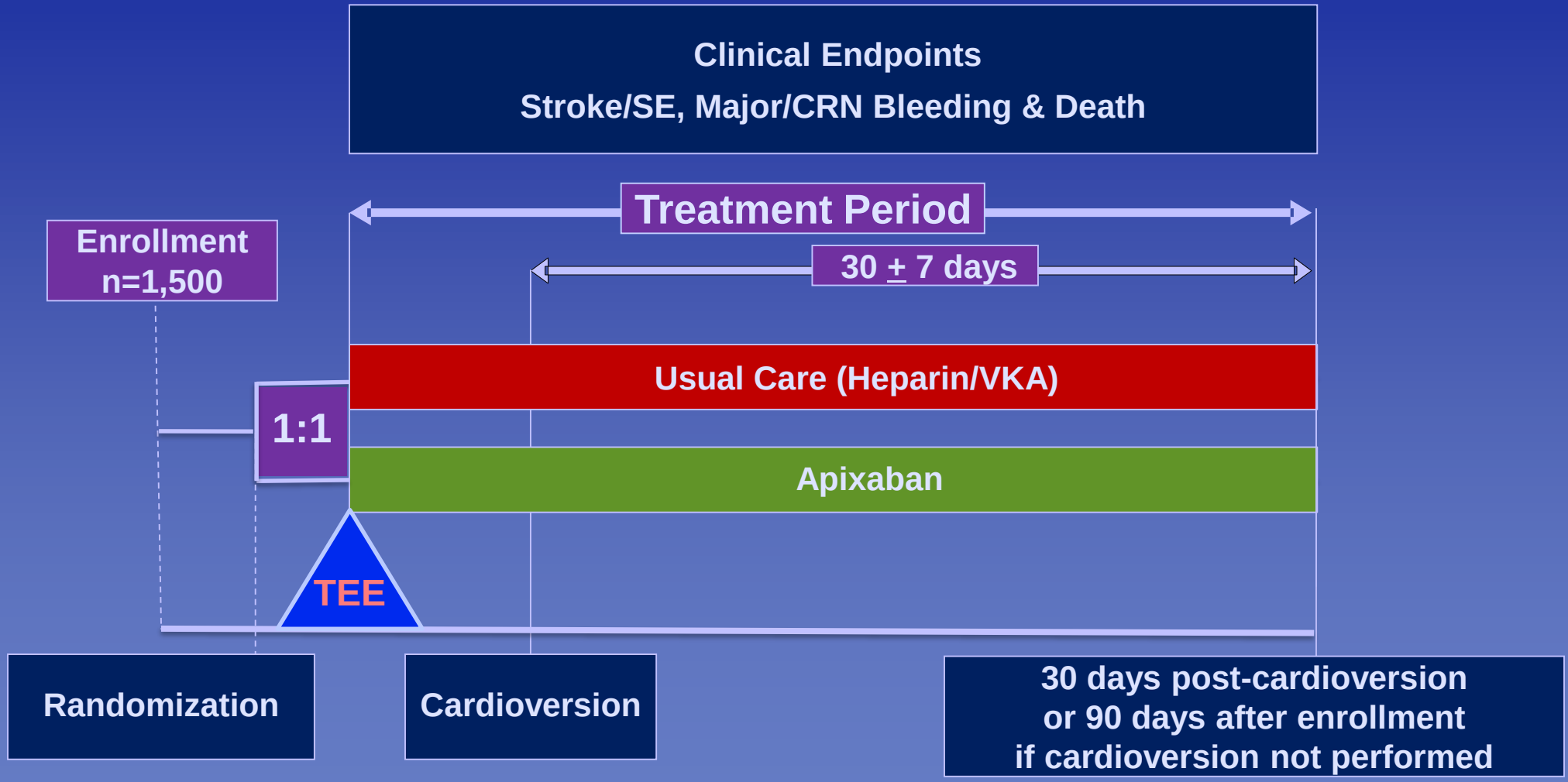
RE-LATED AF - AFNET 7



Ferner M, et al. *Clin Res Cardiol* 2016; 105: 29.

Apixaban For Cardioversion of AF

EMANATE Trial



Ezekowitz MD, et al. *Am Heart J* 2016; 179: 59.

Case 3

- 29 year-old man with a Hx of PE 2 years ago and “multiple MI’s” presents with chest pain.
- Medications: ticagrelor, metoprolol
- Quit smoking 1 month ago.
- Family history: mother had multiple miscarriages
- Past coronary interventions: 9/2014: mLAD PCI (aspirin + clopidogrel)
  3/2015: PTCA
  5/2016: mLAD PCI x 2 for stent thrombosis
  A total of 6 procedures and 3 stents

Case 3, continued

- ECG: mid-precordial T-wave inversions
- Troponin 3.3 ng/ml; INR = 1
- Urine toxic screen: negative for cocaine; positive for cannabinoids
- Coronary angiography:
  - Mid-LAD -- thrombotic total occlusion of multilayered stents, distal vessel supplied collaterals from the RCA
  - D1 -- 80-90% stenosis, jailed stent
- Interventions: thrombectomy; PCI with DES
- INR did not rise after 7 days of warfarin at 10 mg daily
- Discharged on aspirin + ticagrelor + rivaroxaban

Case 3, continued

Thrombophilia Testing

- Antinuclear antibody – negative
- Antiphospholipid studies:
  - Anticardiolipin IgM – normal
  - Lupus Inhibitor – normal
  - B-2 glycoprotein – normal
  - Anti-P-serine IgG – normal
- Factor V Leiden – wild type
- Homocysteine – normal
- Factors VII, VIII, IX, X, XI – normal
- Plasminogen – normal
- Plasminogen activator inhibitor – normal
- Thrombin time – normal
- PFA-100 ADP/collagen – normal
- PFA-100 EPI/collagen – normal
- D-dimer – normal
- Fibrinogen – normal
- Prothrombin allele – wild type
- Protein C – normal
- Protein S – normal
- Antithrombin-III – normal
- 5,10, MTHFR – wild type
- APC-resistance – normal
- PAI-1 polymorphism gene wild type
- Platelet inhibitory responses to aspirin and ticagrelor – responsive

Case 3, continued

- 1 month after discharge, the patient presented with recurrent chest pain and similar ECG changes
- Angiography: stent thrombosis
- Referred for CABG: LIMA -> LAD
- Discharged on aspirin and enoxaparin
- 1 month later, recurrent chest pain
- Angiography: thrombosis of the mid-LAD and LIMA graft
- Pain resolved, discharged without intervention on aspirin + ticagrelor + enoxaparin
- Advised to quit using marijuana

Potential Thrombogenicity of Marijuana

- Marijuana use associated with thrombotic arterial occlusion causing acute MI (over a dozen reported cases linking marijuana to acute MI).
- Principal biological effects attributed to Δ-9-tetrahydrocannabinol (THC) and other cannabinoids, mediated by activation of CB-receptors, which occur in the CNS, peripheral and myocardial vessels
- While at lower doses, effects of THC on human platelet aggregation are mixed, higher concentrations cause irreversible platelet aggregation, apparently due to release of endogenous inducers but have little effect on thrombin-induced platelet aggregation.
- THC enhances platelet $GP_{IIb\text{-}IIIa}$ and P-selectin expression on platelet membranes and induces an inflammatory response in the arterial wall (oxidative stress, platelet activation, deformation of oxidized LDL and hyper-activation of factor VII), leading to endothelial dysfunction and thrombus formation in coronary artery preparations *in vitro*.

Grambow E, et al. *Biofactors* 2016; PMID: 27151562
Dahdouh Z, et al. *Platelets* 2012; 23: 243.
Galan AM, et al. *Thromb Haemost* 2009; 102:511.


Thank you !