NOAC´s across indications

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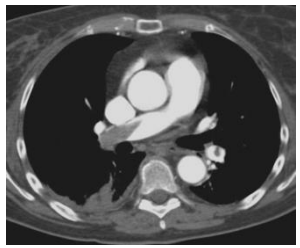
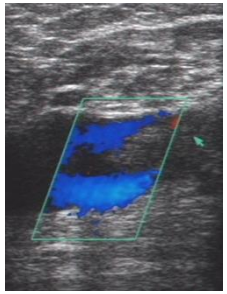
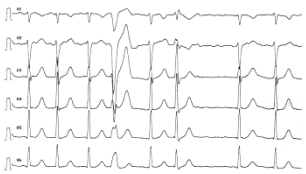






Disclosure

Speaker name: Ulrich Hoffmann

I have the following potential conflicts of interest to report:

- [x] Consulting & lecture fees (Bayer Health Care, Boehringer, Pfizer, BMS, Daiichi Sankyo, Leo, Aspen)
- [ ] Employment in industry
- [ ] Stockholder of a healthcare company
- [ ] Owner of a healthcare company
- [ ] Other(s)

- [ ] I do not have any potential conflict of interest

Pharmacology of NOAC´s

	Dabigatran[1]	Rivaroxaban[2,3]	Apixaban[4]	Edoxaban[5–9]
Target Molecule	IIa (Thrombin)	Xa	Xa	Xa
Bioavailability, %	3–7	80	50	62
Hrs to C_{max}	1–3	2–4	3–4	1–2
Halflife, hrs.	12–17	5–13	12	10-14
Renale Clearance, %	80	33	27	35*
Transporter	P-gp	P-gp	P-gp	P-gp
CYP-Metabolism, %	None	32 %	< 32 %	< 4 %
Proteinbinding, %	35	92–95	87	40–59
Dose regimen	bid	qd	bid.	qd

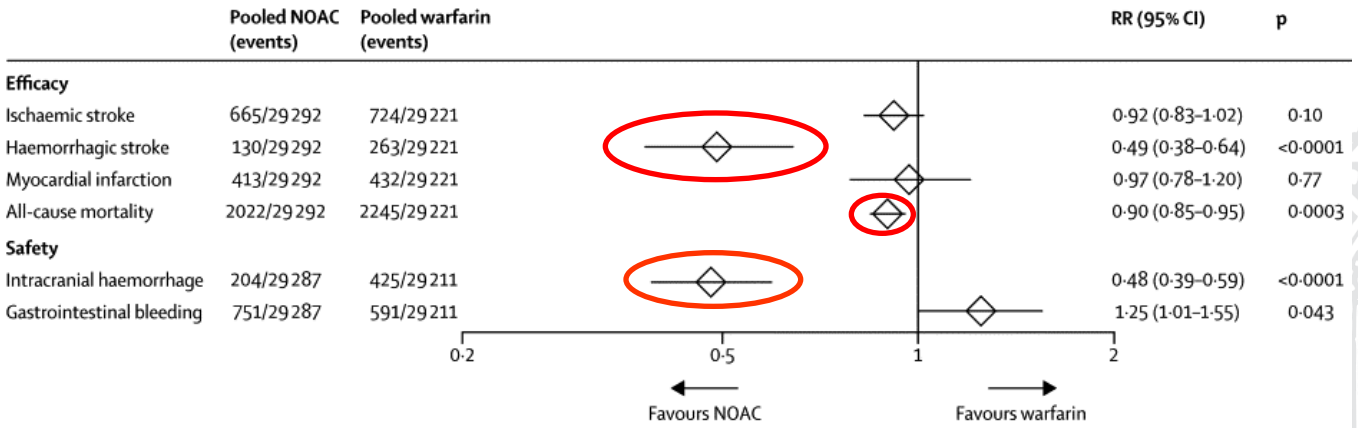
CYP: Cytochrom P450; P-gp: P-glycoprotein
*of the dosage applied

1.Pradaxa [Packungsbeilage]. Ridgefield, CT: Boehringer Ingelheim Pharmaceuticals, Inc. 2013
2. Xarelto [Packungsbeilage]. Titusville, NJ: Janssen Pharmaceuticals, Inc. 2011
3. Weinz et al. Drug Dispos Metab 2009;37:1056–1064
4. ELIQUIS Zusammenfassung der Merkmale des Arzneimittels. Bristol Myers Squibb/Pfizer EEIG, Vereinigtes Königreich
5. Matsushima et al. Am Assoc Pharm Sci 2011; Abstract; 6. Ogata et al. J Clin Pharmacol 2010;50:743–753
7. Mendell et al. Am J Cardiovasc Drugs 2013;13:331–342; 8. Bathala et al. Drug Metab Dispos 2012;40:2250–2255
9. Giugliano et. al. Am J Cardiovas Drugs; e-pub ahead of print

NOACs in nonvalvular Atrial Fibrillation

Compared to warfarin

- Better efficacy
  - **51 %** lower rate of hemorrhagic stroke
  - **10 %** lower mortality
- Better safety
  - **52 %** lower rate of intracranial bleeding



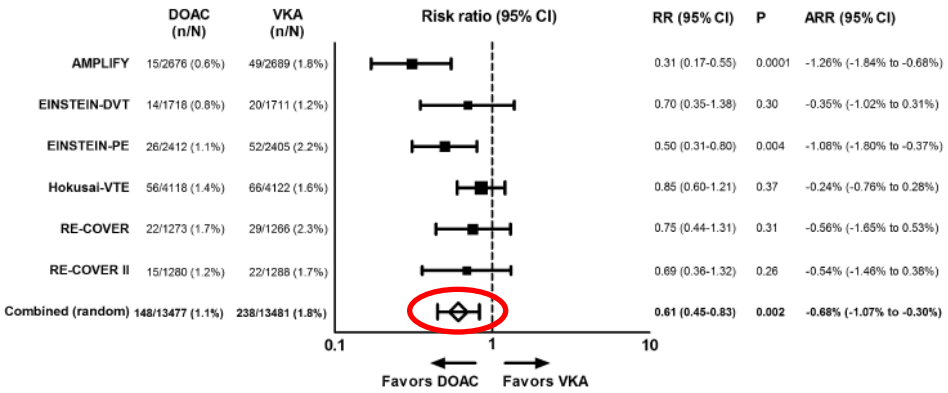
Ruff *et al.* Lancet. 2014;383:955-62
(Metaanalysis of all phase III studies) .

NOAC´s in Venous Thromboembolism

Compared to **LMWH/Wafarin**

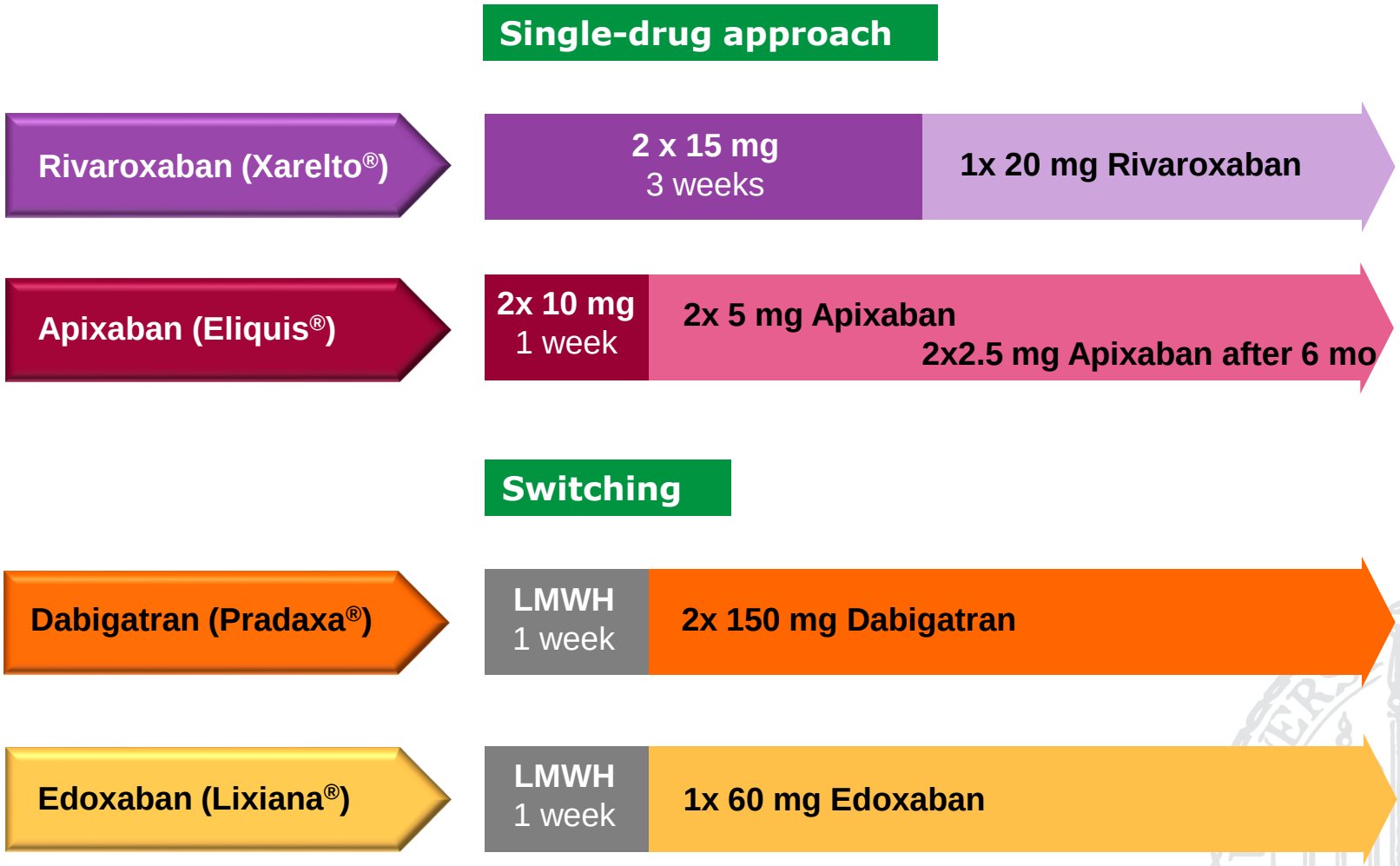
- Non inferior efficacy
- Better safety
  - **40 %** reduction of major bleedings

Safety (major bleeding)



Nick van Es et al., Blood 2014;124:1968-1975

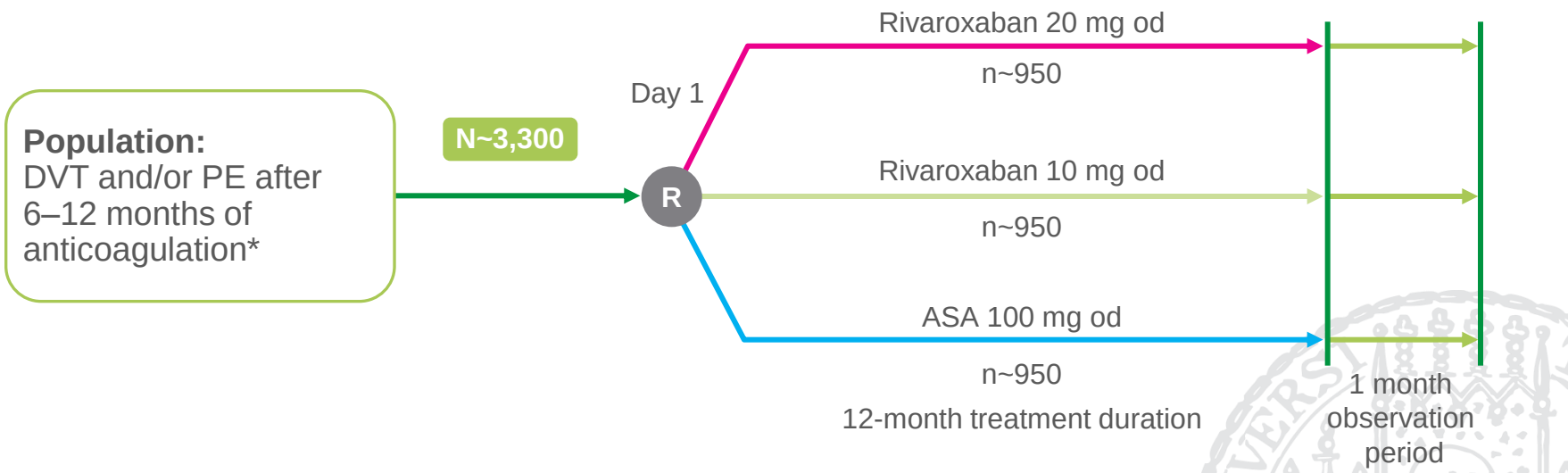
Concepts tested in Phase III VTE Trials



EINSTEIN CHOICE
LONG-TERM SECONDARY VTE PREVENTION STUDY

Official study title: Reduced-dosed Rivaroxaban and Standard-dosed Rivaroxaban Versus ASA in the Long-term Prevention of Recurrent Symptomatic Venous Thromboembolism in Patients With Symptomatic Deep-vein Thrombosis and/or Pulmonary Embolism

Objective: efficacy and safety of reduced-dosed rivaroxaban, standard-dosed rivaroxaban versus ASA for the long-term secondary prevention of recurrent symptomatic VTE in patients with symptomatic DVT and/or PE



Short design: Multicentre, randomized, double-blind, double-dummy, active-comparator, event-driven, superiority study

Indication: VTEx

FPFV: Q1-14
LPLV: Q4-16

*Completed 6–12 months (±1 month) with interruption of anticoagulation ≤1 week at randomization

www.clinicaltrials.gov/ct2/show/NCT02064439 Weitz JI et al. Thromb Haemost 2015

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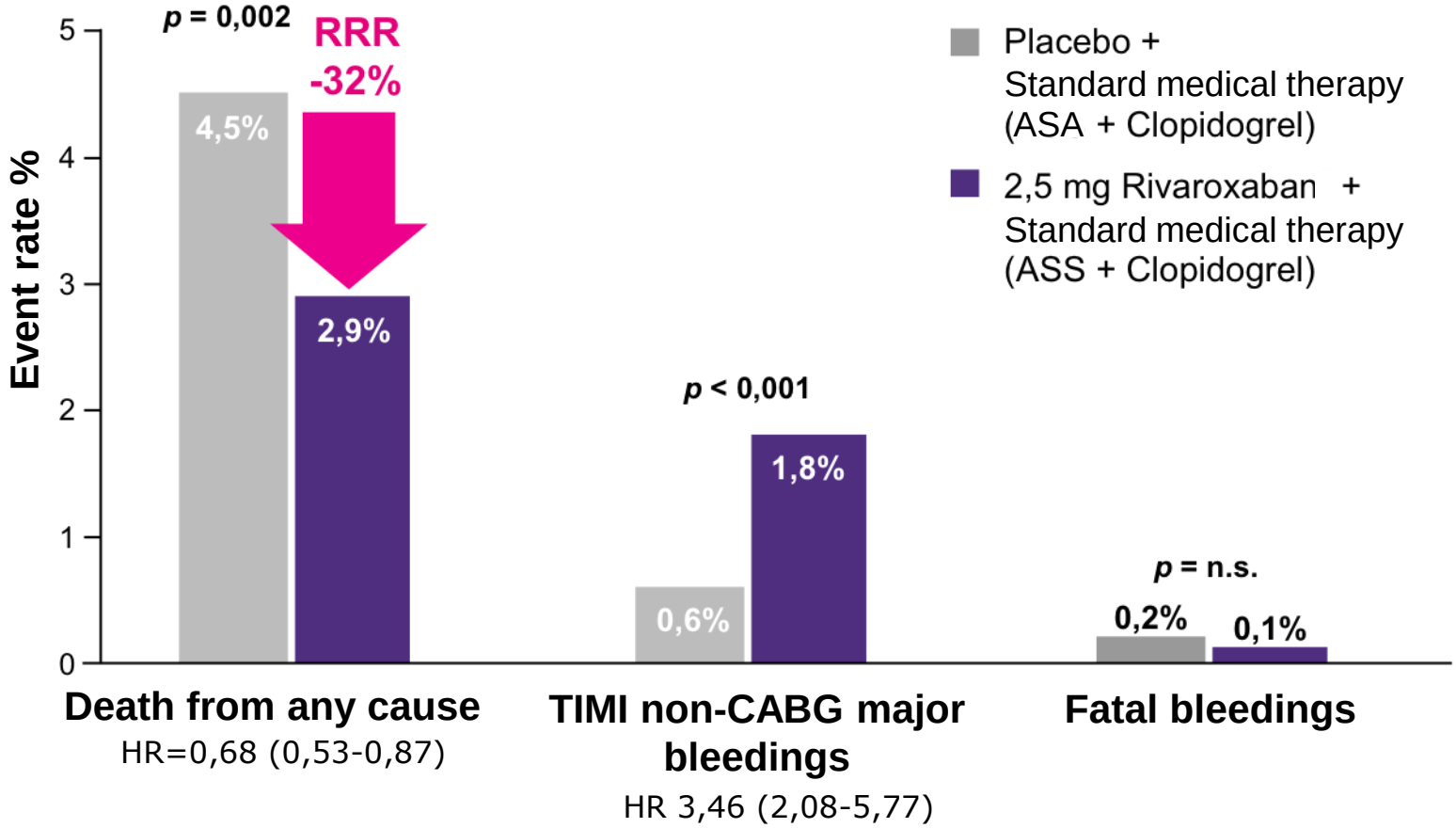
EINSTEIN CHOICE

ATLAS ACS 2-TIMI 51
EFFICACY AND SAFETY ENDPOINTS

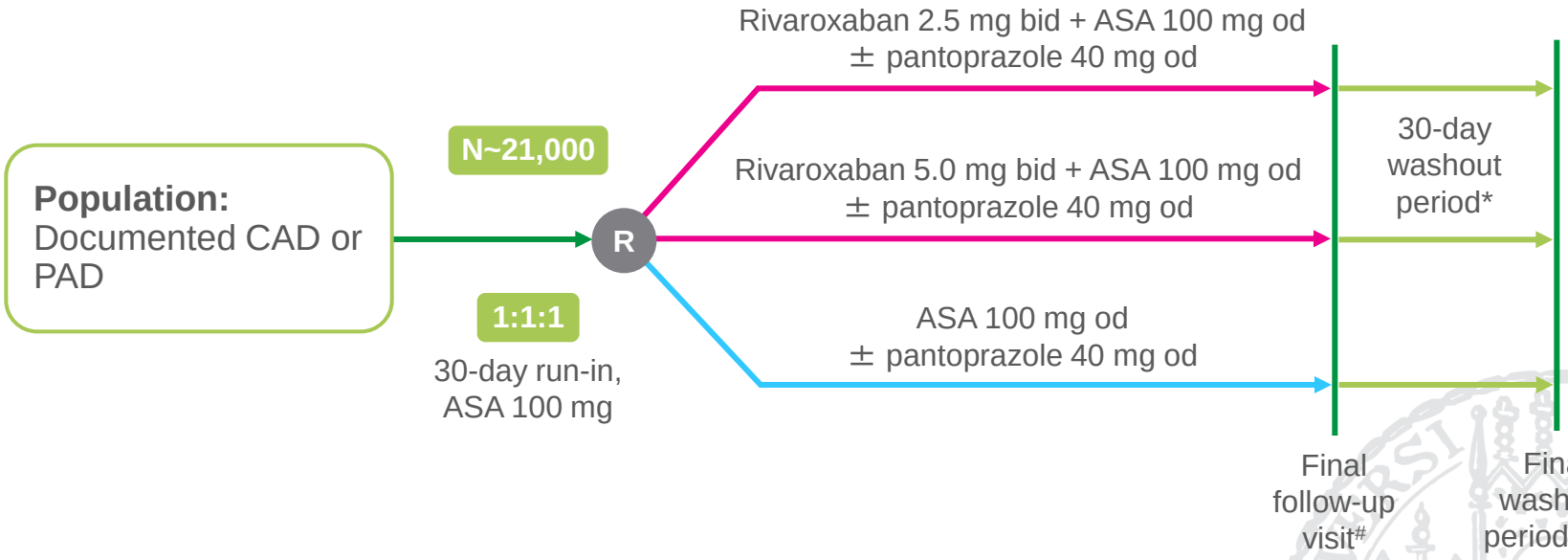


Mega et al. N Engl J Med 2012;366:9–19.

COMPASS
CAD/PAD STUDY

Official study title: A Randomized Controlled Trial of Rivaroxaban for the Prevention of Major Cardiovascular Events in Patients With Coronary or Peripheral Artery Disease (COMPASS - Cardiovascular OutcoMes for People Using Anticoagulation StrategieS)

Objective: efficacy and safety of rivaroxaban, low-dose rivaroxaban plus ASA or ASA alone for reducing risk of MI, stroke or cardiovascular death in CAD or PAD



Short design: Randomized, double-blind, controlled trial

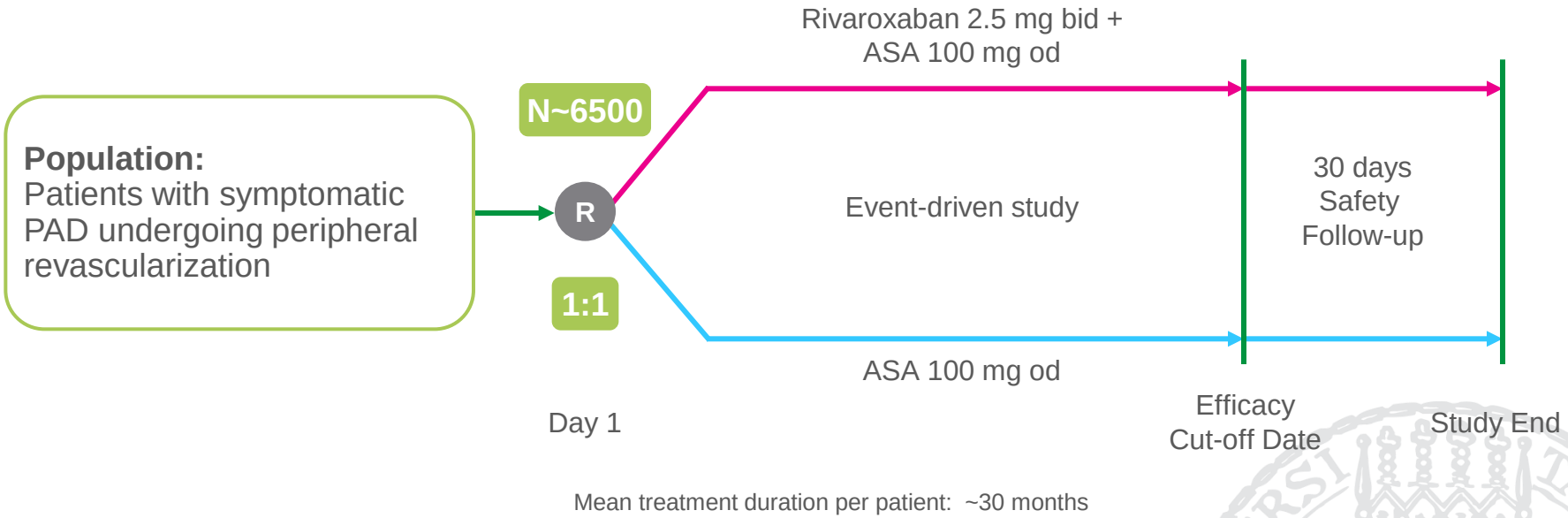
Indication: CAD/PAD

Start: Q2-13
LPLV: Q1-18

*Patients treated according to local standard of care; #≤30 days of the required pre-specified number of events having occurred
www.clinicaltrials.gov/show/NCT01776424

VOYAGER PAD STUDY

Objective: Efficacy and Safety of Rivaroxaban for the Reduction of Thrombotic Vascular Events in Subjects with PAD Undergoing Peripheral Revascularization Procedures



Mean treatment duration per patient: ~30 months

Short design: Randomized, multicenter, prospective, double-blind, double-dummy, parallel-group, placebo-controlled, event-driven

Indication:
PAD

FPFV: Q2-2015
LPLV: Q1-2019

www.clinicaltrials.gov/ct2/show/NCT02504216

NOAC´s across indications
Ongoing non-cardiac phase III vascular studies

- Cerebrovascular
  - Acute nondisabling cerebrovascular events
  - Embolic stroke of undetermined source
- VTE
  - Long term prevention of VTE (prophylactic dosage)
  - Cancer related venous thromboembolism
  - VTE in children
  - Thrombembolism in anti-Phospholipid AB Syndrome
  - Medically ill patients at risk for VTE
- PAD
  - Major CV events in CAD and PAD patients
  - Thrombotic vascular events in PAD patients undergoing peripheral artery interventions

Thank you for your attention

NOAC´s across indications

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