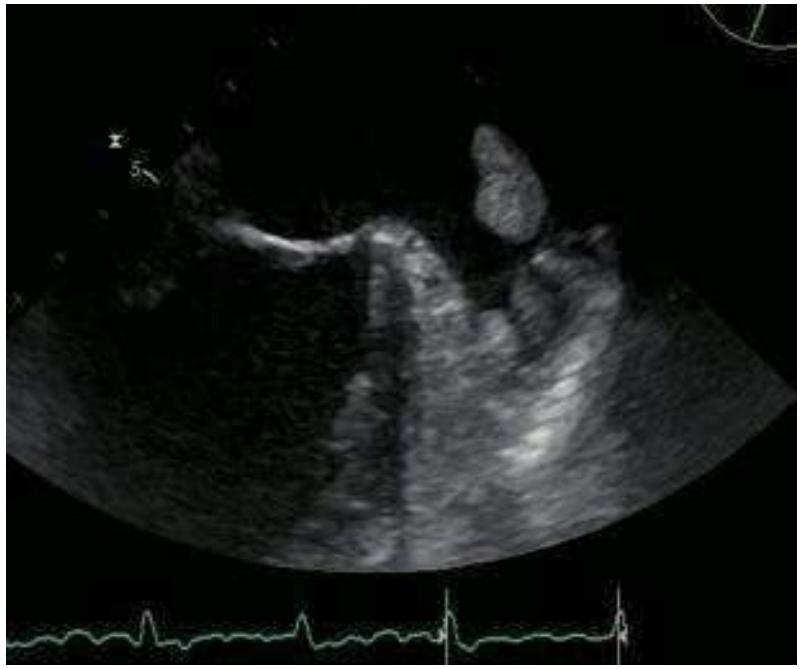
Vorhofflimmern 2018

Was empfiehlt der Kardiologe zur Antikoagulation?



D. Ropers

Medizinische Klinik

St. Theresien-Krankenhaus

Nürnberg

Bad Segeberg

06.06.2018

St. Theresien-Krankenhaus Nürnberg

Interessenskonflikt

Sprecher-Honorar	Advisory Board
Pfizer Pharma GmbH	Pfizer Pharma GmbH
Bristol-Myers Squibb	Amgen
Bayer Healthcare	Bayer Healthcare
Boehringer Ingelheim	Boehringer Ingelheim
Daiichi-Sankyo	Novartis
Sanofi Aventis	Daiichi-Sankyo
Berlin Chemie	Sanofi Aventis
AstraZeneca	
Siemens Healthengeers	
Novartis AG	

St. Theresien-Krankenhaus Nürnberg

Wie hätten Sie entschieden?

88jährige Patientin, 157 cm, 62 kg

Permanentes Vorhofflimmern

langjährige Hypertonie (4fach-Kombination)

fragliche TIA vor 3 Jahren

Kreatinin 1.4 mg/dl, GFR 57 ml/min.

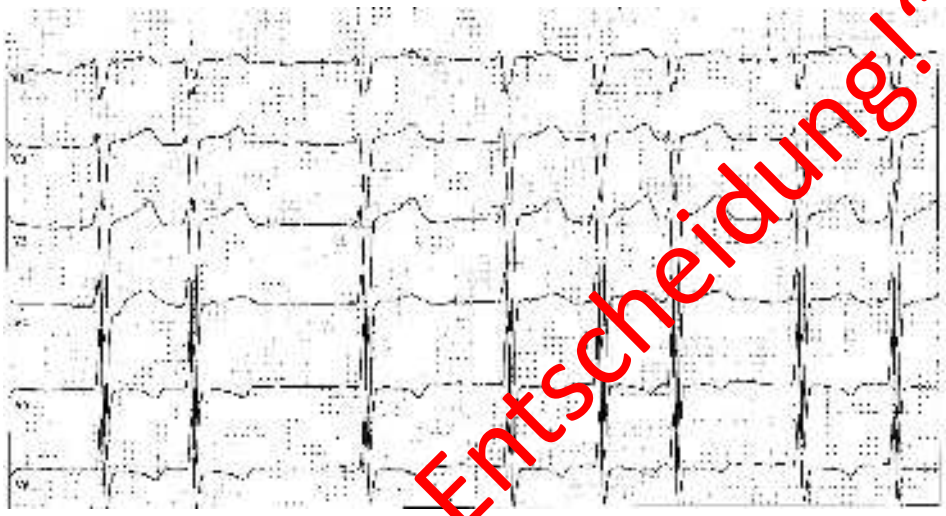
Sohn ist Belegarzt am Krankenhaus

Mehr als 10 Ärzte in der Familie (in ganz Deutschland)

Bisher keine Antikoagulation wegen Gebrechlichkeit („Frailty“)

Geri-REHA nach TEP nach Sturz

Entlassung ins betreute Wohnen



„Ihre Entscheidung!“

Wie hätten Sie entschieden?

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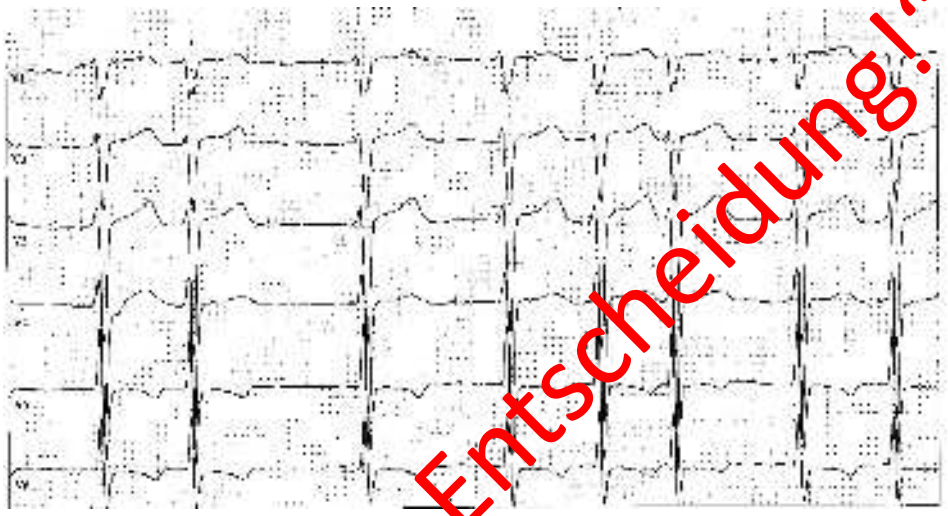


„Ihre Entscheidung!“

CHADS-VASc: 6 Punkte
TE-Risiko: 19.7%

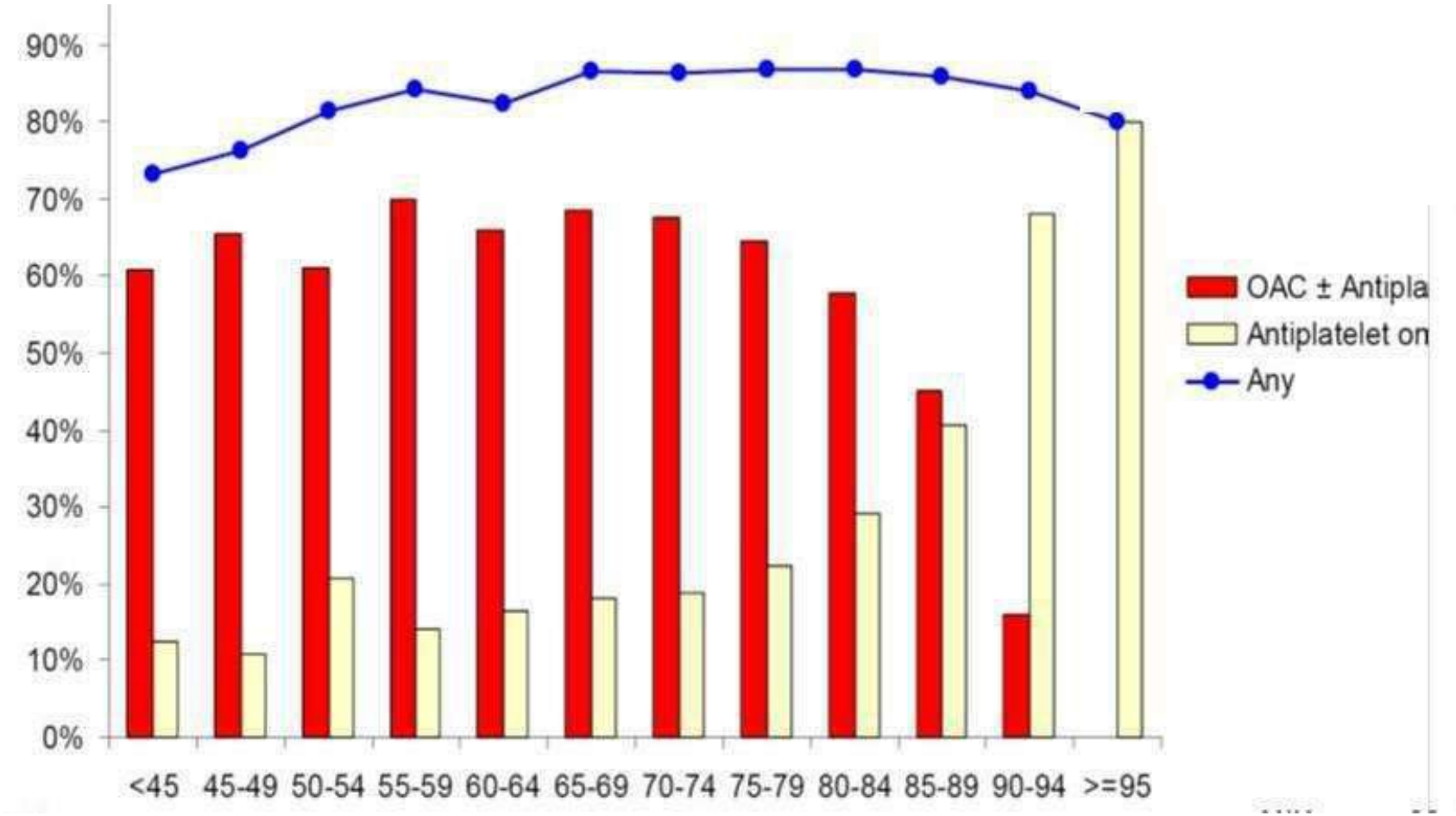
Blutungs-Risiko: 8.7%

St. Theresien-Krankenhaus Nürnberg

Wie hätten Sie entschieden?

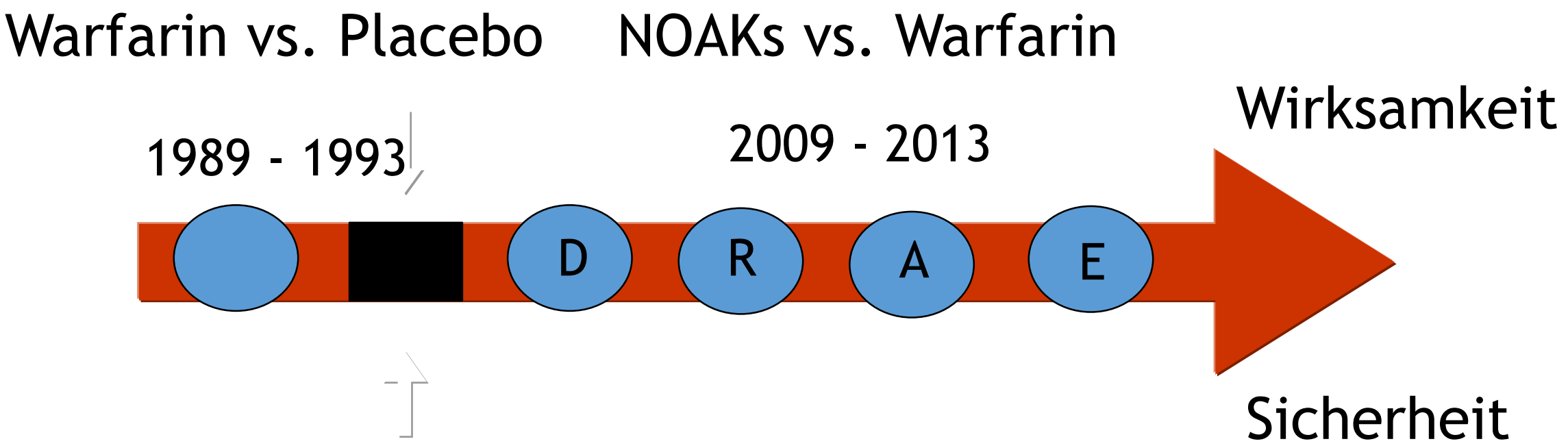
A. Bloß nix geben. Keine orale Antikoagulation, kein ASS
B. Nur ASS
C. Enoxaparin 0.4 ml s.c. 1x/Tag
D. Dabigatran 2 x 150 mg
E. Rivoroxaban 1 x 15 mg
F. Apixaban 2 x 2.5 mg
G. Edoxaban 1 x 30 mg 1x
H. Vorhofsohrverschluß, keine OAK
I. Nichts von alledem

Orale Antikoagulation 2010



Gerth A. et al. Nervenheilkunde 2012

Neue orale Antikoagulation (NOAK)



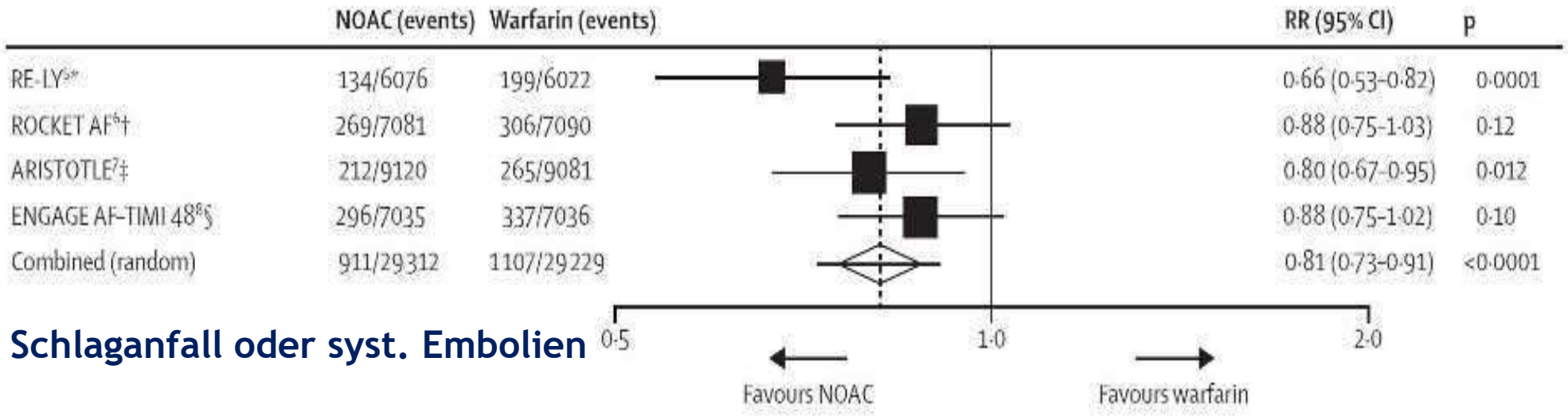
D = Dabigatran; Connolly SJ, et al. NEJM 2009

R = Rivaroxaban; Patel MR, et al. NEJM 2011

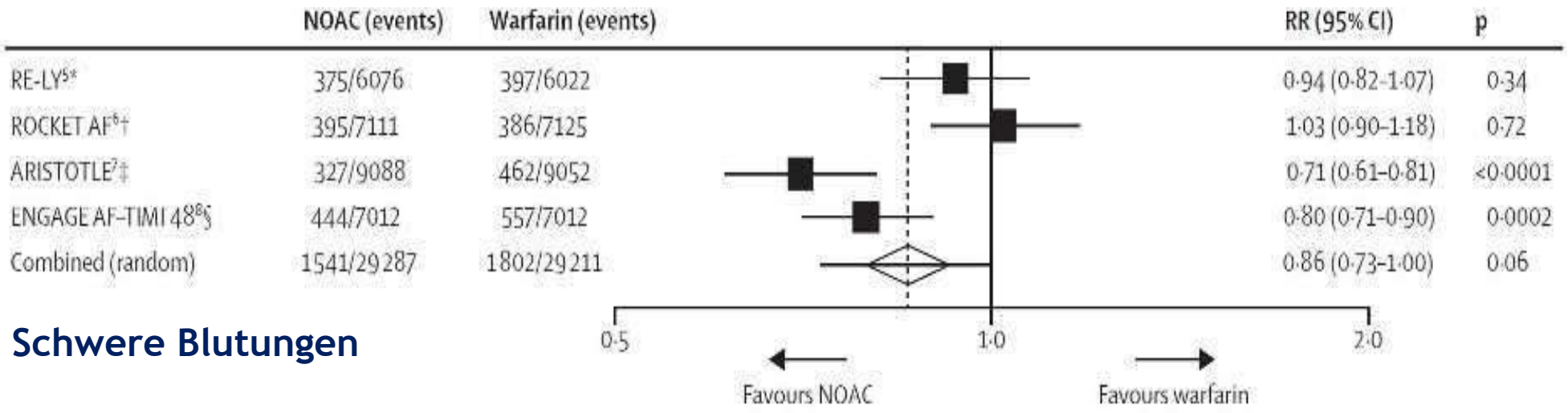
A = Apixaban; Granger CB, et al. NEJM 2011

E = Edoxaban; Giugliano RP, et al. NEJM 2013

NOAK Studien – Meta-Analyse (n > 58.000)



Schlaganfall oder syst. Embolien



Schwere Blutungen

Ruff et al. Lancet 2013

St. Theresien-Krankenhaus Nürnberg

Neue orale Antikoagulation (NOAK)

Mindestens vergleichbare Effizienz im Hinblick auf ischämische Ereignisse

Geringeres Risiko für schwere Blutungen

- Reduktion intrazerebraler Blutungen
- Intrazerebrale Blutungen unter NOAK „benigner“
- Weniger PPSB / EKs

Keine Spiegelkontrollen. Weniger Wechselwirkungen

Schnelleres On-/Off der Wirkung

Antidot (Idarucizumab für Dabigatran/Andexanat alfa für Apixaban/Rivaroxaban, FDA)

Höhere Adhärenz, z.B. 83% vs. 65% Vit.K-Pat.

Akiyama et al. PLoS One 2015, Martinez et al. Thromb Haemost 2015; Hylek et al. JACC 2014

ESC-Leitlinien zum nicht-valvulären Vorhofflimmern

Empfehlungen für die Prophylaxe von Thromboembolien bei VHF § – NOAK	Klasse*	Grad†
Dort, wo eine OAK empfohlen wird, sollte ein NOAK, und zwar entweder • ein direkter Thrombin-Inhibitor (Dabigatran); oder • ein oraler Faktor-Xa-Inhibitor (z. B. Rivaroxaban, Apixaban) … erwogen werden anstelle eines dosisangepassten VKA (INR 2–3), basierend auf dem klinischen Nettonutzen.	IIa	A

Camm et al. EHJ 2012

Empfehlungen für die Prophylaxe von Thromboembolien bei VHF § – NOAK	Klasse*	Grad†
Wenn zur Schlaganfallprävention eine OAK begonnen wird, der ein NOAK (Apixaban, Dabigatran, Edoxaban, Rivaroxaban) erhalten kann, wird ein NOAK vor einem Vitamin-K-Antagonisten empfohlen.	I	A

Kirchhof et al. EHJ 2016

DGN-Leitlinie 2015: Sekundärprophylaxe nach Schlaganfall und TIA

Empfehlung 3.10	Empfehlungsgrad/ Evidenzebene
Patienten mit ischämischem Schlaganfall oder TIA und nicht valvulärem Vorhofflimmern sollen eine orale Antikoagulation erhalten (siehe Empfehlung 3.1). Die neuen Antikoagulantien (d. h. Dabigatran, Rivaroxaban und Apixaban) stellen eine Alternative zu den Vitamin-K-Antagonisten dar und sollten aufgrund des günstigeren Nutzen-Risiko-Profils zur Anwendung kommen.	*Empfehlungsgrad B* *Evidenzebene Ib*

DGN Deutsche Gesellschaft für Neurologie

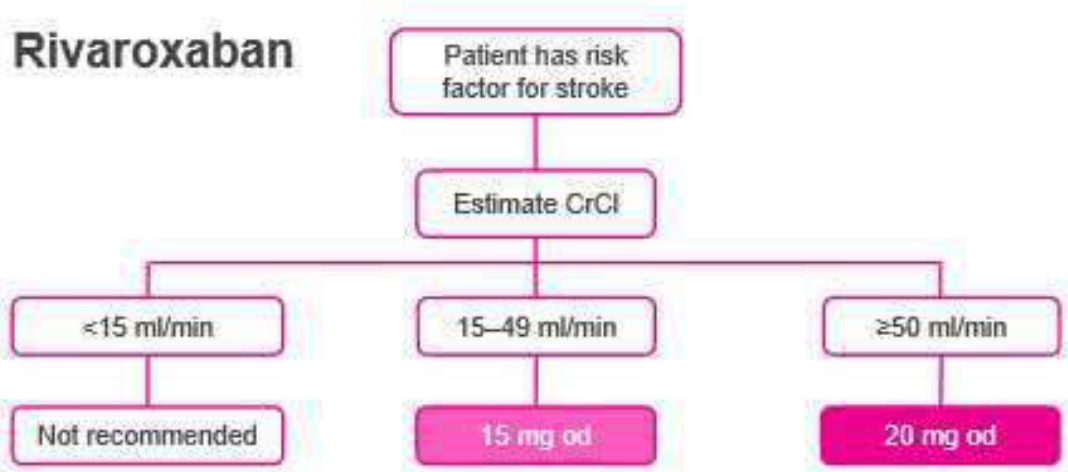
http://www.dgn.org/leitlinien/11-leitlinien-der-dgn/3024-ll-23-ll-sekundaerprophylaxe-ischaemischer-schlaganfall-und-transitorische-ischaemische-attacke

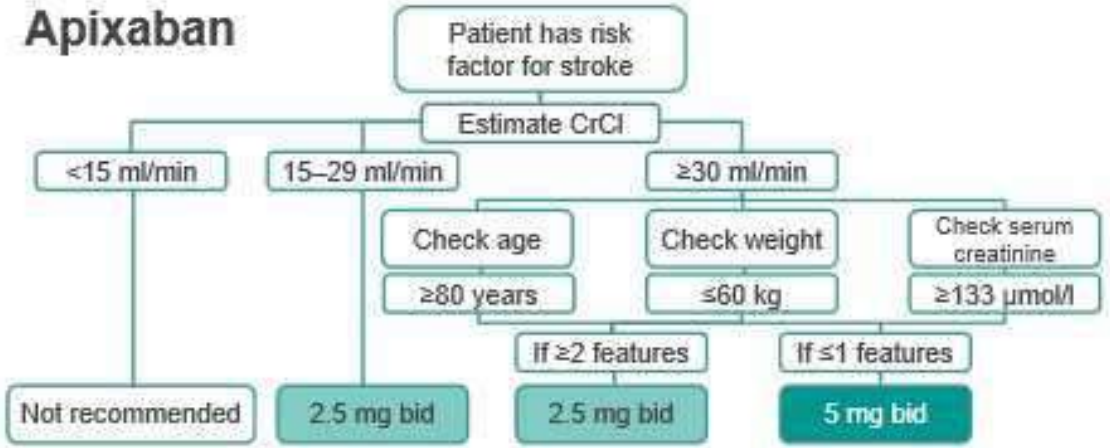
St. Theresien-Krankenhaus Nürnberg

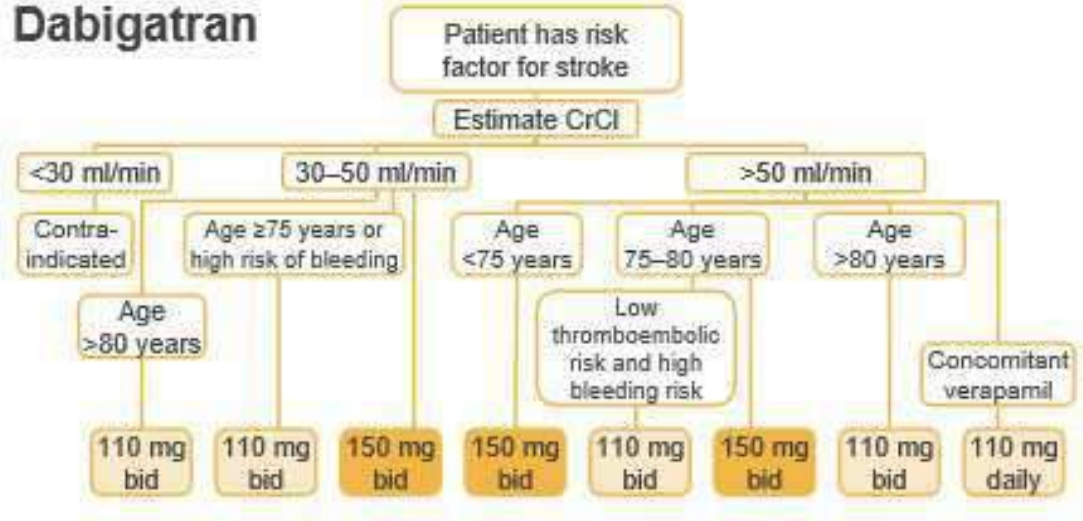
„Nicht-Vit.-K. abhängige orale Antikoagulation (NOAK)

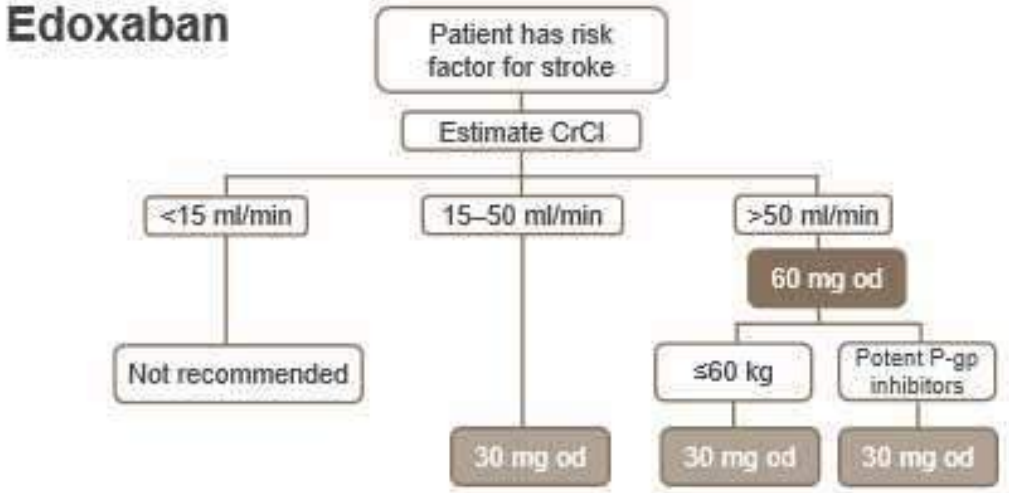
	Prophylaxe	Vorhofflimmern	LE/BVT	ACS
Rivaroxaban	2008	2011	2011	2013
Dabigatran	2008	2011	2014	
Apixaban	2011	2012	2014	
Edoxaban		2015	2015	

Nicht-Vitamin-K-abhängige Antikoagulation bei Vorhofflimmern

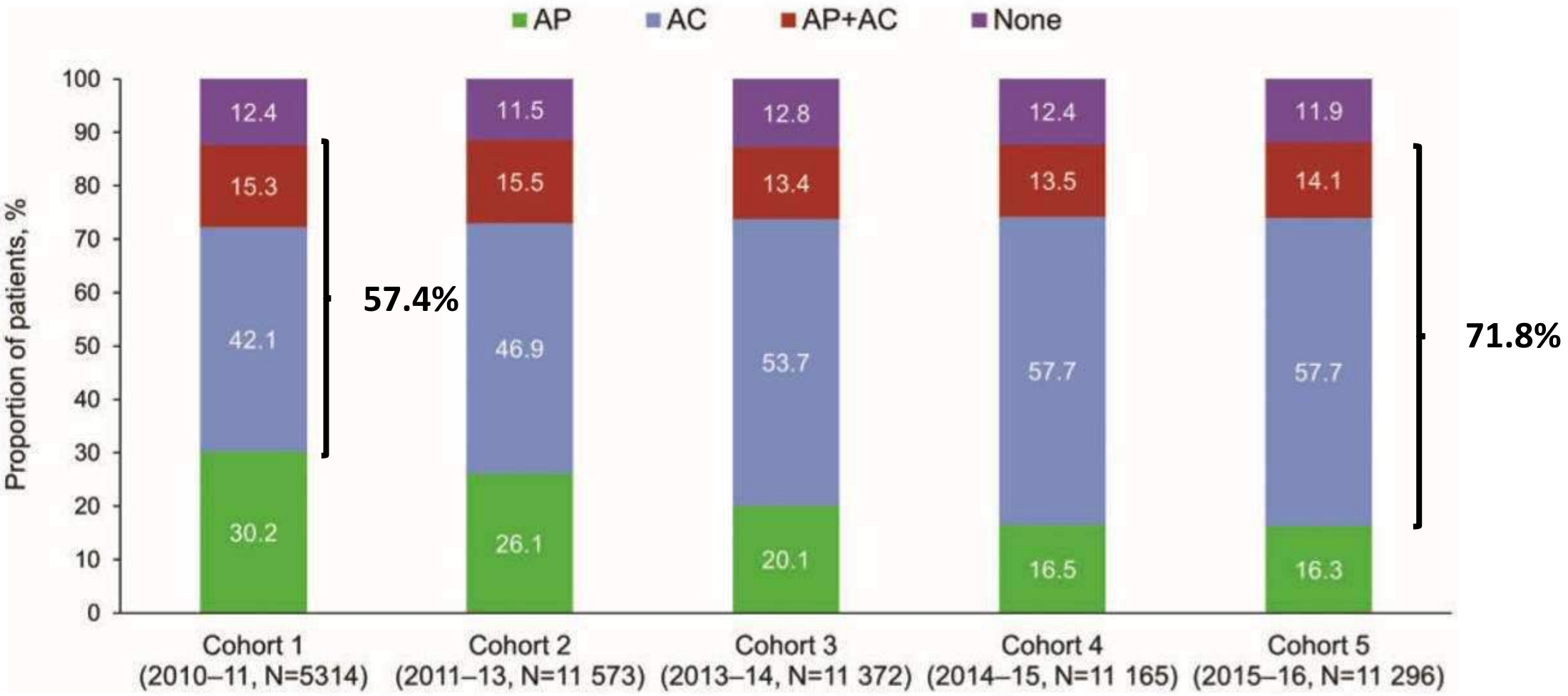






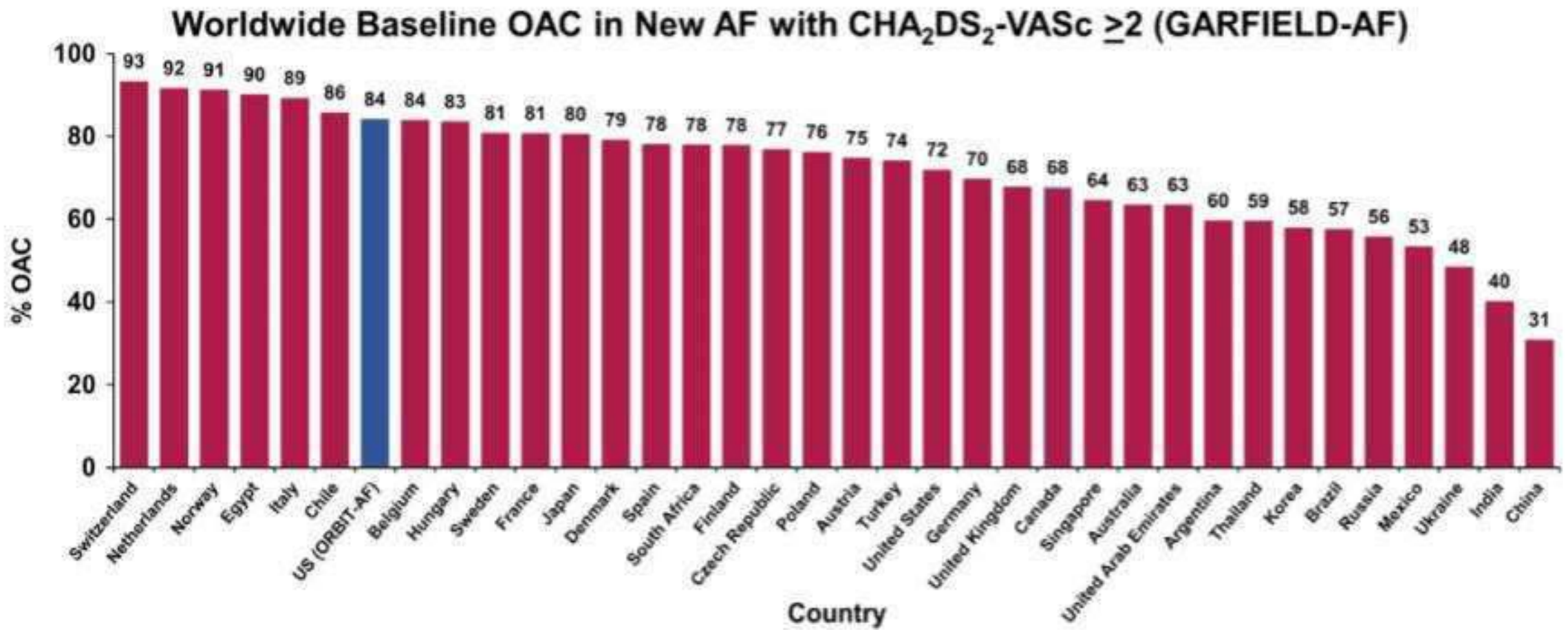


GARFIELD-AF (n = 50.720)



Verheugt FWA et al. EHJ 2018

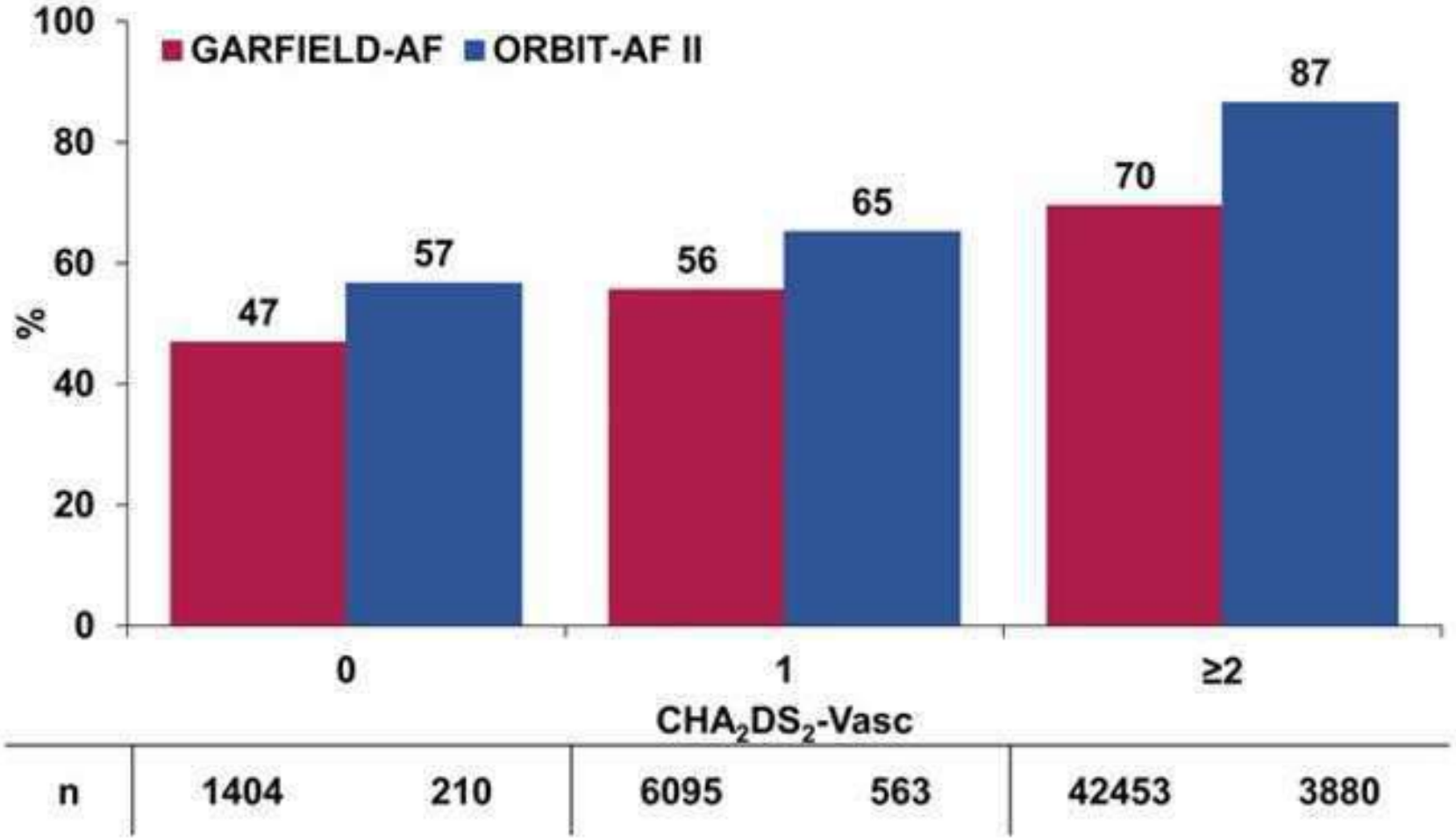
GARFIELD-AF / ORBIT-AF II (n = 54.605)



Steinberg BA et al. AHJ 2017

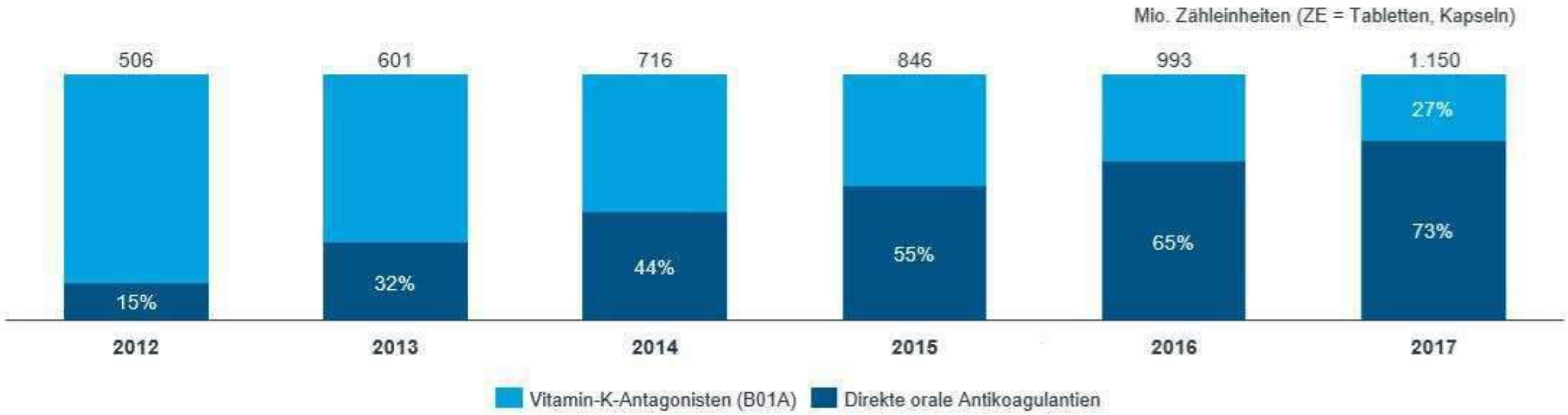
St. Theresien-Krankenhaus Nürnberg

GARFIELD-AF / ORBIT-AF II (n = 54.605)



Steinberg BA et al. AHJ 2017

VKA / NOAKs



	2012	2017
VKA:	85 %	27%
NOAK:	15%	73%

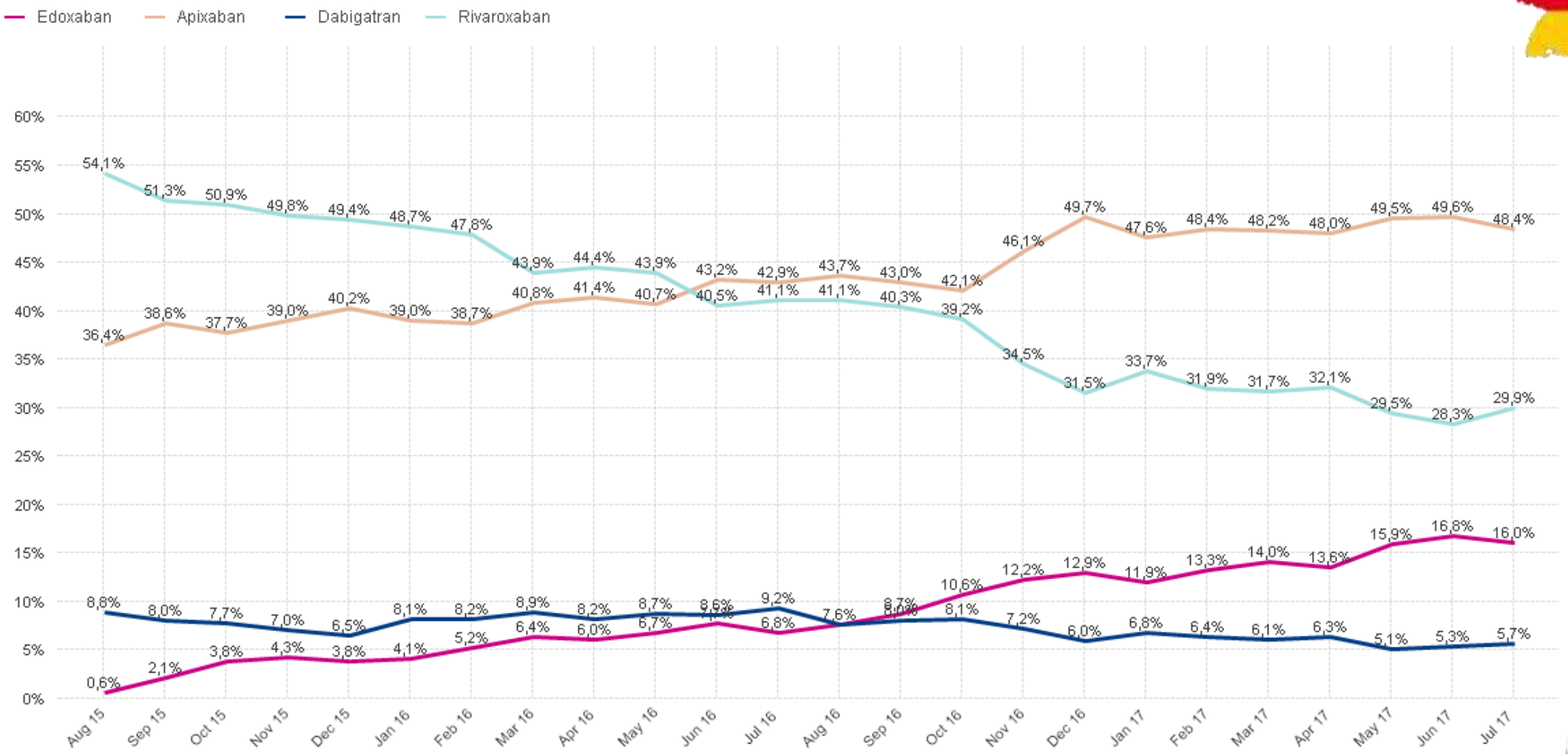
Umsatzstärkste Präparategruppen 2017

	Jahr 2017*	Veränderungsrate zum Vorjahr
L04B ANTI-TNF PRODUKTE	1.904,0	8,1 / 11,2
N07A PROD.G.MULTIPLE SKLEROSE	1.469,3	-1,2 / 3,2
L01H PROTEINKIN.HEMM.A.NEOPL.	1.394,0	14,7 / 19,0
L01G MAB** ANTINEOPLASTIKA	1.200,6	14,0 / 16,7
B01F DIREKTE FAKTOR XA HEMMER	1.141,1	25,9 / 23,8
A10C HUMANINSULIN UND ANALOGA	1.006,1	-2,4 / 0,2
L04X SONST.IMMUNSUPPRESSIVA	898,7	13,0 / 0,2
J05C VIRUSTATIKA GEGEN HIV	819,6	-2,8 / 2,8
N02A BETAEUBUNGSMITTEL	802,3	1,5 / 2,3
L02B CYTOSTAT.HORMONANTAGON.	612,7	9,8 / 3,9
SUMME TOP 10	**11.248,2**	9,2 / 4,4
GESAMT	**34.114,4**	-0,2 / 4,6

+/- % Umsatz +/- % Absatz

NOAKs 2017: + 25,9% (Umsatz)

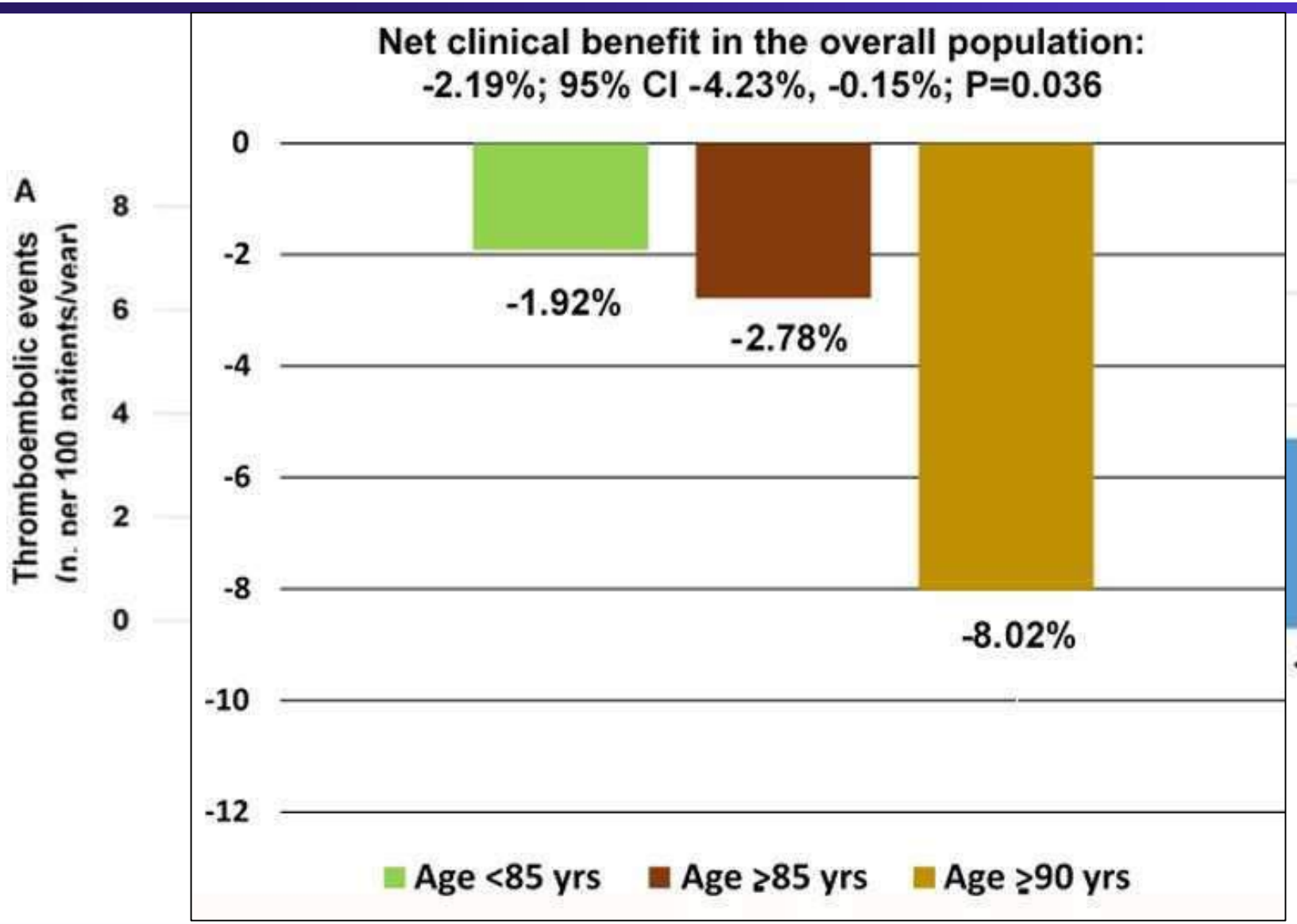
Neuverschreibungen



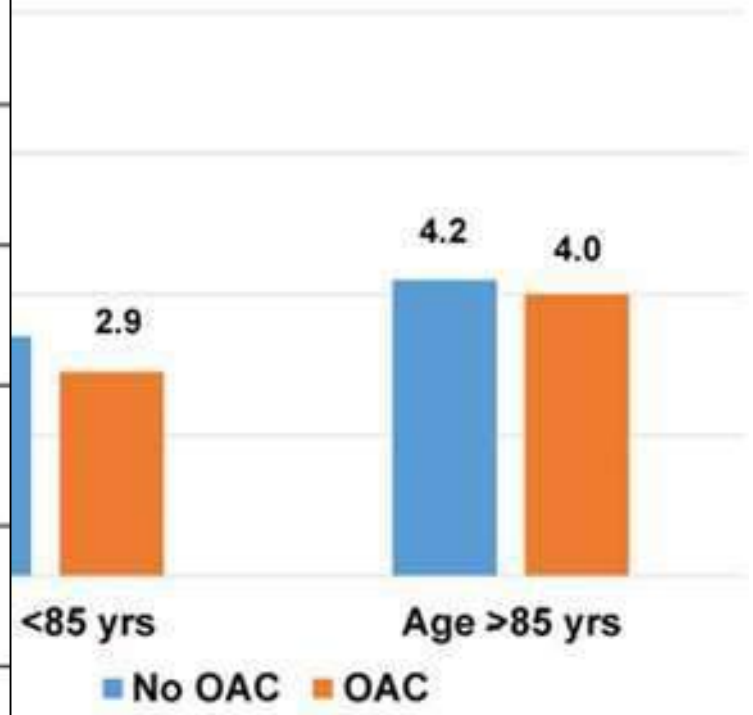
IMS Health, Pharmascope 2017

Patienten > 75/80 Jahre

PREFER in AF (n = 6412; 2012 – 2013)



Blutung



Patti et al. JAHA 2017

NOAK bei Älteren

	Schlaganfall / Embolie	Blutung	
Apixaban (n = 5678)	0.71 (0.53;0.95)	0.64 (0,52;0,79)	≥ 75 J.
	0.72 (0.54;0.96)	0.71 (0.56;0.89)	65-74 J.
	1.16 (0.77;1.73)	0.78 (0.55;1.11)	< 65 J.
Rivaroxaban (n = 3110)	0.80 (0.63;1.02)	1.11 (0.91;1.34)	≥ 75 J.
	0.95 (0.76;1.19)	0.96 (0.78;1.19)	< 75 J.
Dabigatran (n = 7258) 110 mg	0.88 (0.66;1.17)	1.01 (0.83;1.23)	≥ 75 J.
	0.93 (0.70;1.22)	0.62 (0.57;0.86)	< 75 J
150 mg	0.67 (0.49;0.90)	1.18 (0.98;1.42)	≥ 75 J.
	0.63 (0.46;0.86)	0.70 (0.70;0.93)	< 75 J.
Edoxaban (n = 8474)	0.83 (0.66;1.04)	0.83 (0.70;0.99)	≥ 75 J.
	0.89 (0.68;1.19)	0.75 (0.60;0.94)	65-74 J.
	0.94 (0.65;1.37)	0.81 (0.58;1.12)	< 65 J.

Halvorsen et al. EHJ 2014, Halperin et al. Circulation 2014, Eikelboom et al. Circulation 2011, Kato et al. JAHA 2016

Choosing a particular oral anticoagulant and dose for stroke prevention in individual patients with non-valvular atrial fibrillation: part 2

Non-vitamin K oral anticoagulants and age

First choice	In patients older than 75 years, we suggest apixaban 5 mg twice daily [2.5 mg if ≥2 of the following: age ≥80 years, body weight ≤60 kg, or creatinine ≥1.5 mg/dL (133 μmol/L)] *
Second choice	Dabigatran 110 mg twice daily, rivaroxaban 20 mg once daily, or edoxaban 60 mg once daily

* Oder bei einer Kreatinin-Clearance von 15 – 29 ml/min.

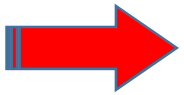
Diener et al. EHJ 2016

NOAK bei Älteren

Appropriateness of Oral Anticoagulants for the Long-Term Treatment of Atrial Fibrillation in Older People: Results of an Evidence-Based Review and International Consensus Validation Process (OAC-FORTA 2016)

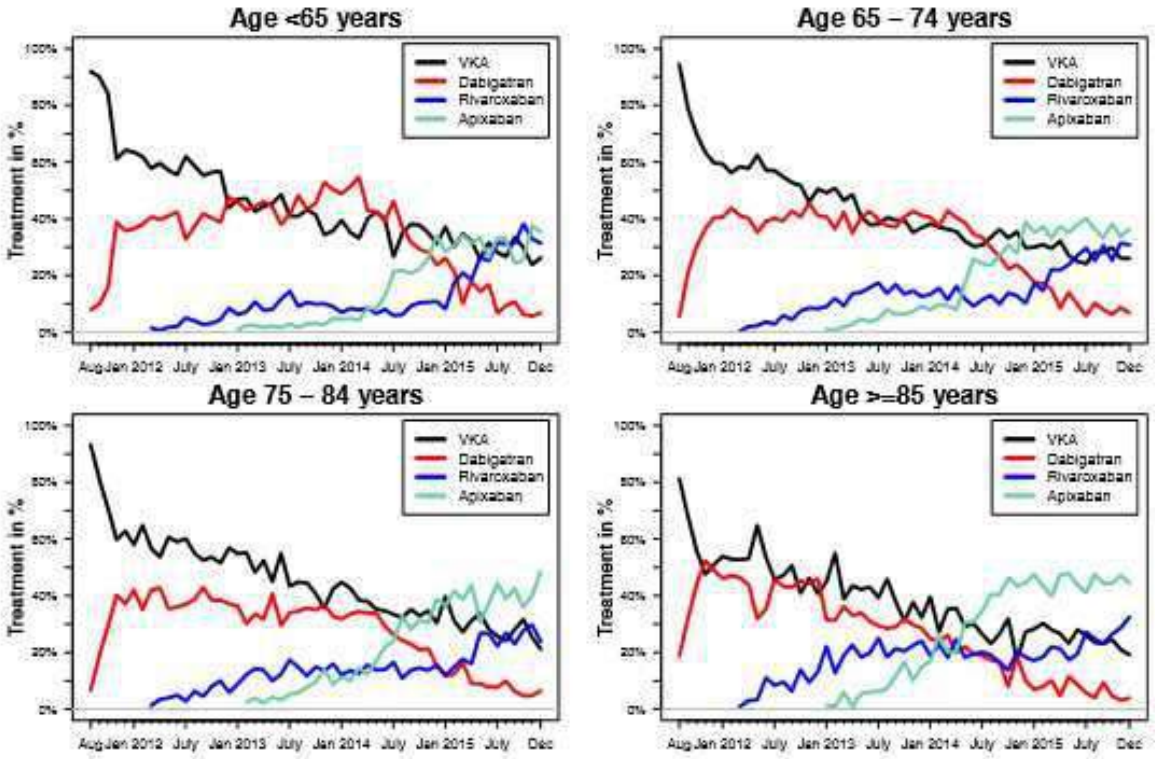
Table 1: Recommendations for FORTA classification

Drug	FORTA class	Comments relevant for FORTA classification
Acenocoumarol	C	No clinical data, efficacy/safety unknown, high risk of interactions
Fluindione	C	No clinical data, efficacy/safety unknown, high risk of interactions
Phenprocoumon	C	No clinical data, efficacy/safety unknown though high exposure of large patient groups, high risk of interactions
Warfarin	B	Well studied, efficacy highly likely in the elderly, safety concerns, monitoring need, evidence on geriatric syndromes still limited, inferiority to NOACs in certain conditions, high risk of interactions
Dabigatran (low dose)	B	Large study in the elderly, efficacy/safety established with limited indications for superiority, low risk of interactions, significant renal problem, antidote available
Dabigatran (high dose)	B	Large study in the elderly, efficacy/safety established with limited indications for superiority, low risk of interactions, significant renal problem, antidote available
Edoxaban	B	Large study in the elderly, efficacy/safety established with limited indications for superiority, low risk of interactions
Rivaroxaban	B	Large study in the elderly, efficacy/safety established with the least indications for superiority, low risk of interactions
Apixaban	A	Two large studies in the elderly, efficacy/safety established with convincing data on superiority in multiple major endpoints including mortality, low risk of interactions



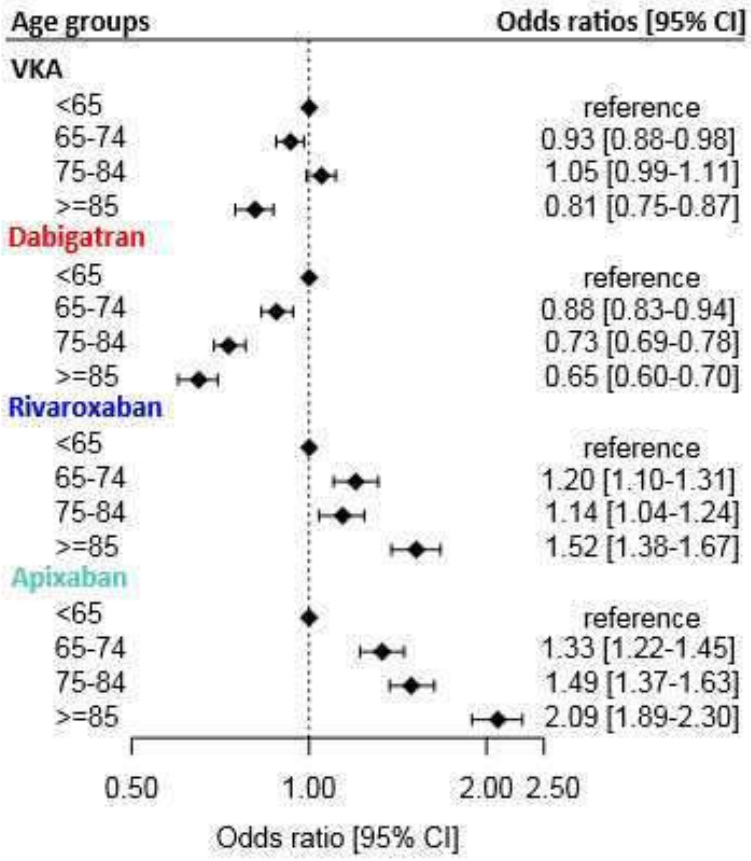
Wehling M, . . .Ropers D, . . et al. Drugs and Aging 2017

Temporal trends of initiation patterns 2011-2015



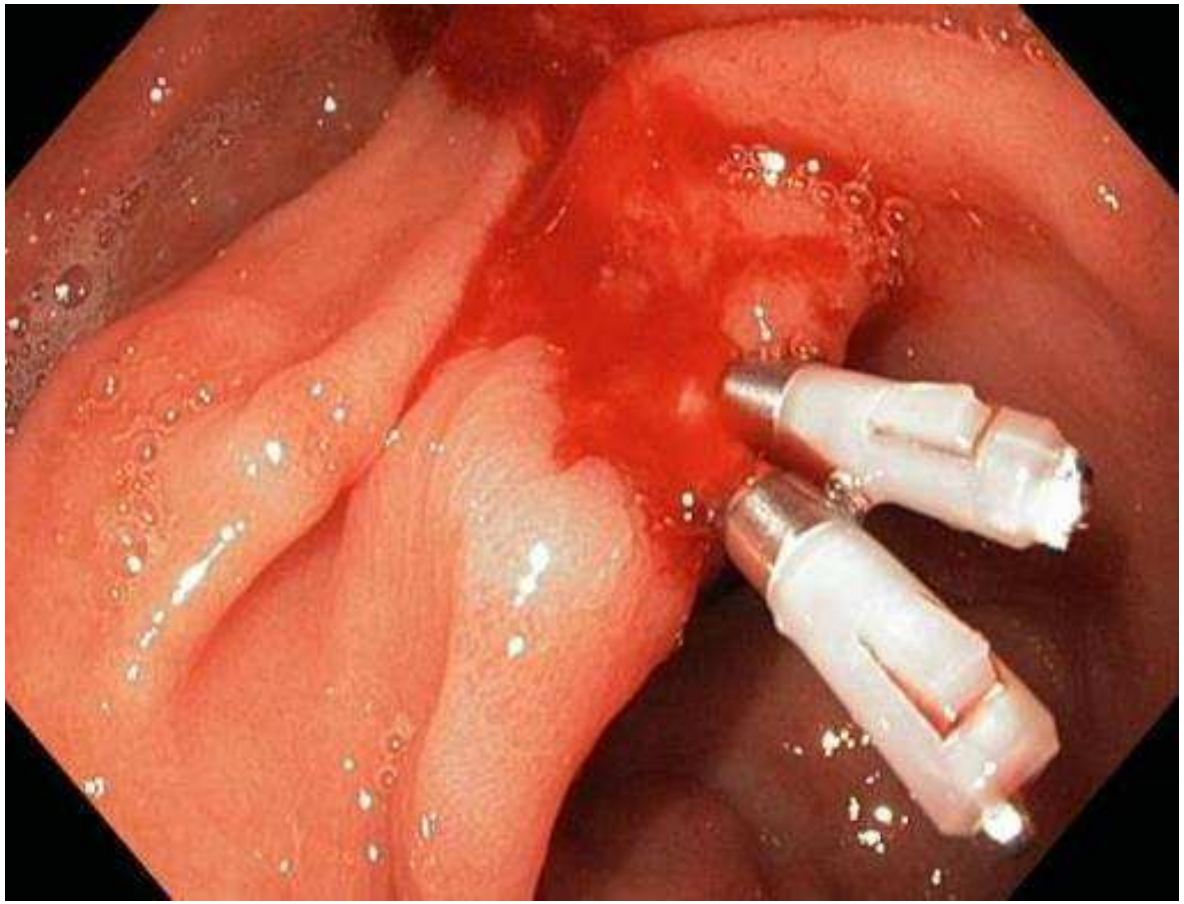
n = 43.299

Odds ratios of initiation related to age



Staerk L. et al. EHJ 2016

Patient mit Blutungsanamnese



„Real-Life“ (US Versicherungsdaten): n = 125.243

	Schlaganfall / Systemische Embolie	Ischämischer SA	Hämorrhagischer SA
Apixaban gg. Warferin (2 x 7695)	1.33 vs. 1.66 , p = 0.04	1.03 vs. 1.05, p = 0.4	0.19 vs. 0.46, p = 0.03
Dabigatran gg. Warferin (2 x 14307)	1.18 vs. 1.22 , p = 0.88	0.92 vs. 0.88, p = 0.7	0.16 vs. 0.29, p = 0.07
Rivaroxaban gg. Warferin (2 x 16175)	1.26 vs. 1.29 , p = 0.56	0.95 vs. 0.88, p = 0.95	0.21 vs. 0.32, p = 0.08

Yao X et al. JAHA 2016

„Real-Life“ (US Versicherungsdaten): n = 125.243

	Schwere Blutung	GI-Blutung	ICB
Apixaban gg. Warferin (2 x 7695)	2.33 vs. 4.46 , p < 0.001	1.78 vs. 3.04, p < 0.001	0.29 vs. 1.06, p < 0.001
Dabigatran gg. Warferin (2 x 14307)	2.37 vs. 3.03 , p < 0.01	1.97 vs. 1.95, p = 0.78	0.28 vs. 0.79, p < 0.001
Rivaroxaban gg. Warferin (2 x 16175)	4.04 vs. 3.64 , p = 0.60	3.26 vs. 2.53, p = 0.03	0.44 vs. 0.79, p < 0.001

Yao X et al. JAHA 2016

Meta-Analyse von Real World Daten

	GI-Blutung	Signifikante Blutung	Hirnblutung	Tod
Apixaban	HR 0.63 (p = 0.03) [n = 14.201]	HR 0.55 (p < 0.00001) [n = 27.514]	HR 0.45 (p < 0.00001) [n = 25.183]	HR 0.65 (p < 0.00001) [n = 6349]
Dabigatran	HR 1.20 (p = 0.003) [n = 169.730]	HR 0.83 (p = 0.12) [n = 98.049]	HR 0.42 (p < 0.00001] [n = 201.532]	HR 0.63 (p < 0.00001) [n = 107.111]
Rivaroxaban	HR 1.24 (p = 0.002) [n = 27.046]	HR 1.00 (p = 0.92) [n = 55.575]	HR 0.64 (p 0.004] [n = 50976]	HR 0.67 (p = 0.24) [n = 11.108]

Ntaios G. et al. Stroke 2017

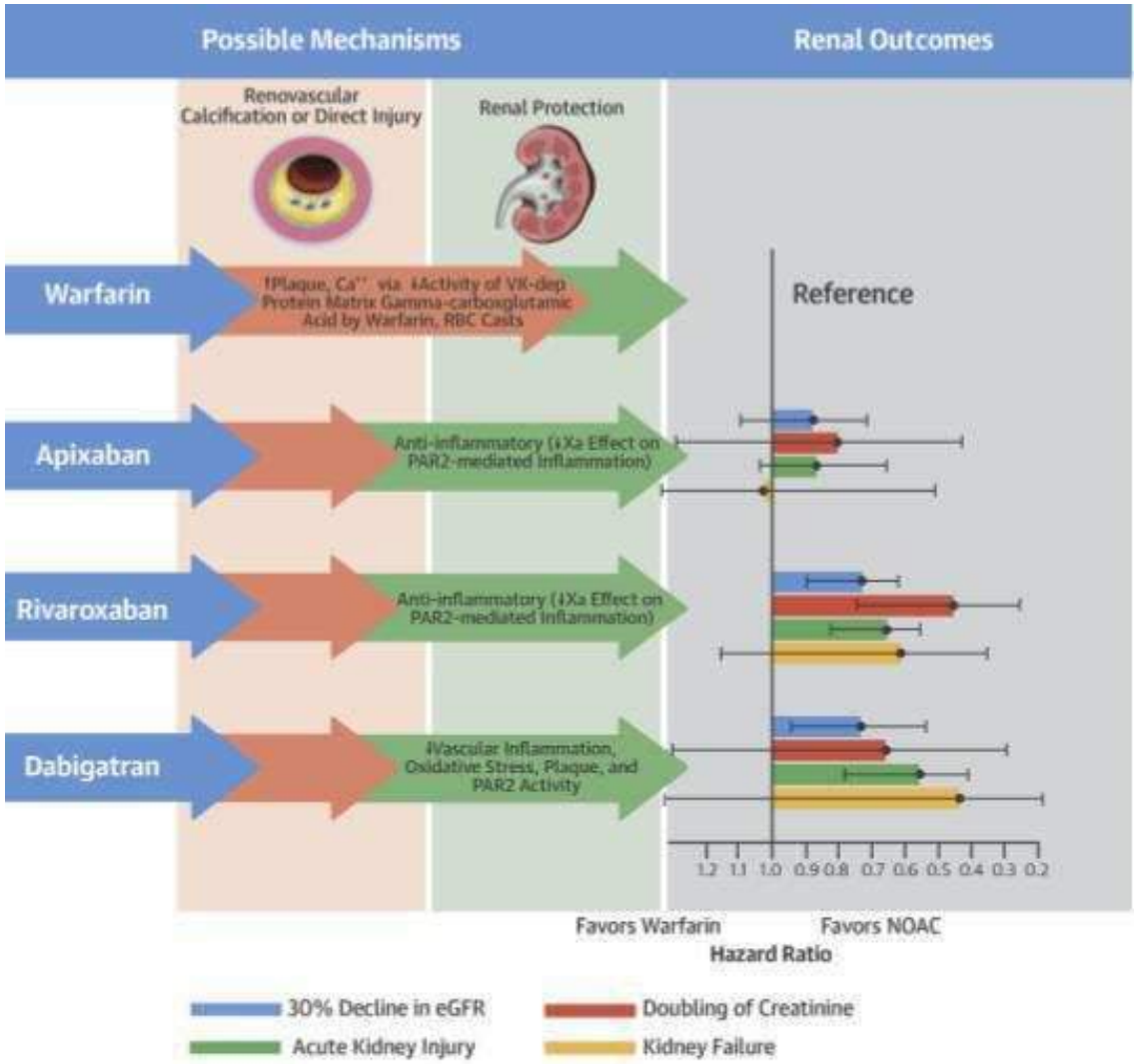
„Real-Life“ (Deutsche Krankenkassen; 2013–2015): n = 61.205

	Schwere Blutungen	GI-Blutung	Jegliche Blutung
Apixaban gg. Phenprocoumon (10117 vs. 23823)	1.40 vs. 2.30 , p < 0.001	1.70 vs. 2.40, p < 0.001	7.7 vs. 9.8, p = 0.001
Dabigatran gg. Phenprocoumon (5122 vs. 23823)	1.50 vs. 2.30 , p = 0.001	2.2 vs. 2.4, p = 0.940	7.9 vs. 9.8; p = 0.006
Rivaroxaban gg. Phenprocoumon (22143 vs. 23823)	2.30 vs. 2.30 , p = 0.932	2.9 vs. 2.4, p < 0.001	10.1 vs. 9.8, p = 0.039

Hohnloser et al. Thrombosis Haemost 2018

Patienten mit Niereninsuffizienz

„Real-Life“ (US Datenbank): n = 9769



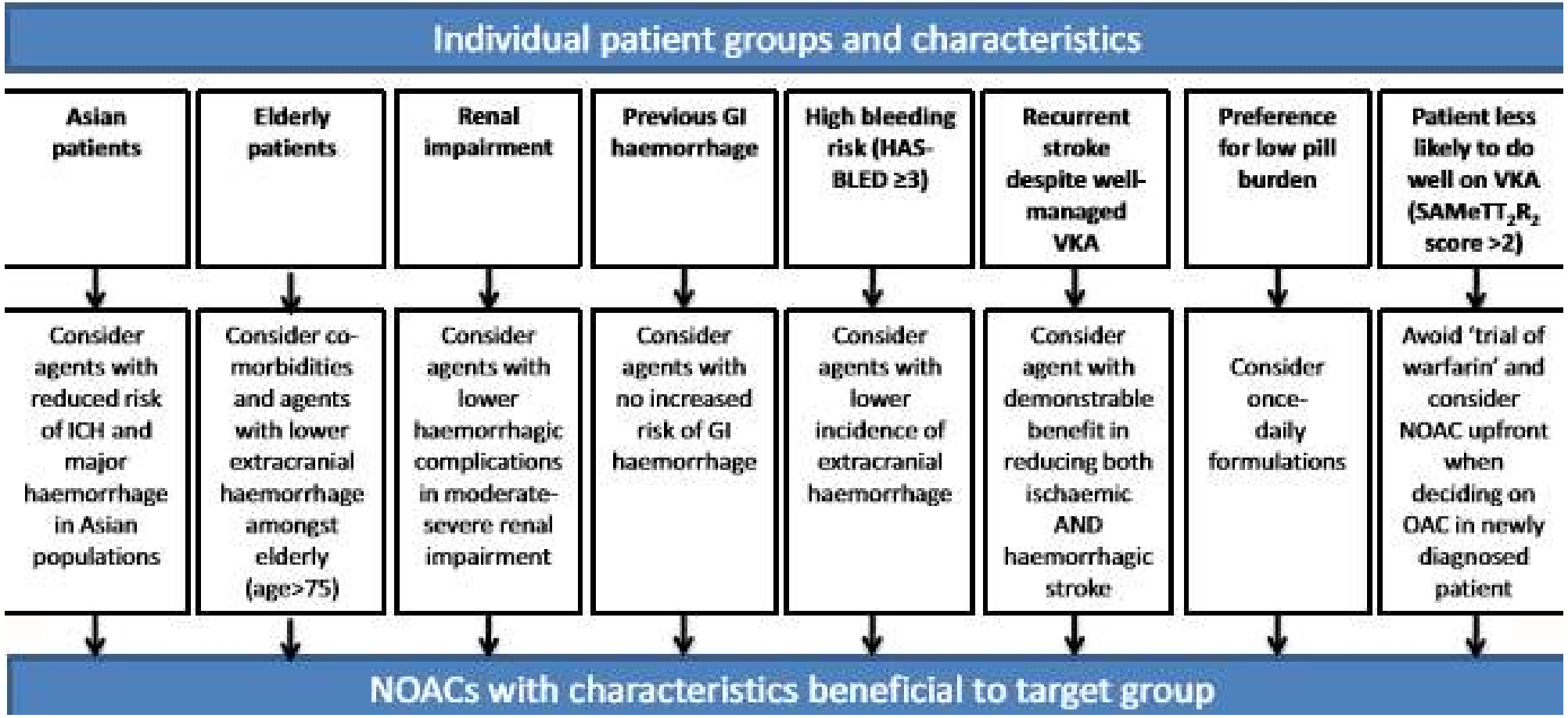
<u>Nach 2 Jahren:</u>

Abnahme der GFR um 30%:	24.4%
Verdoppelung des Kreatinins:	4%
Akute Nierenschädigung:	14.8%
Nierenversagen:	1.7%

Yao X et al. JACC 2017

St. Theresien-Krankenhaus Nürnberg
Fachkompetenz mit Kopf, Herz & Hand

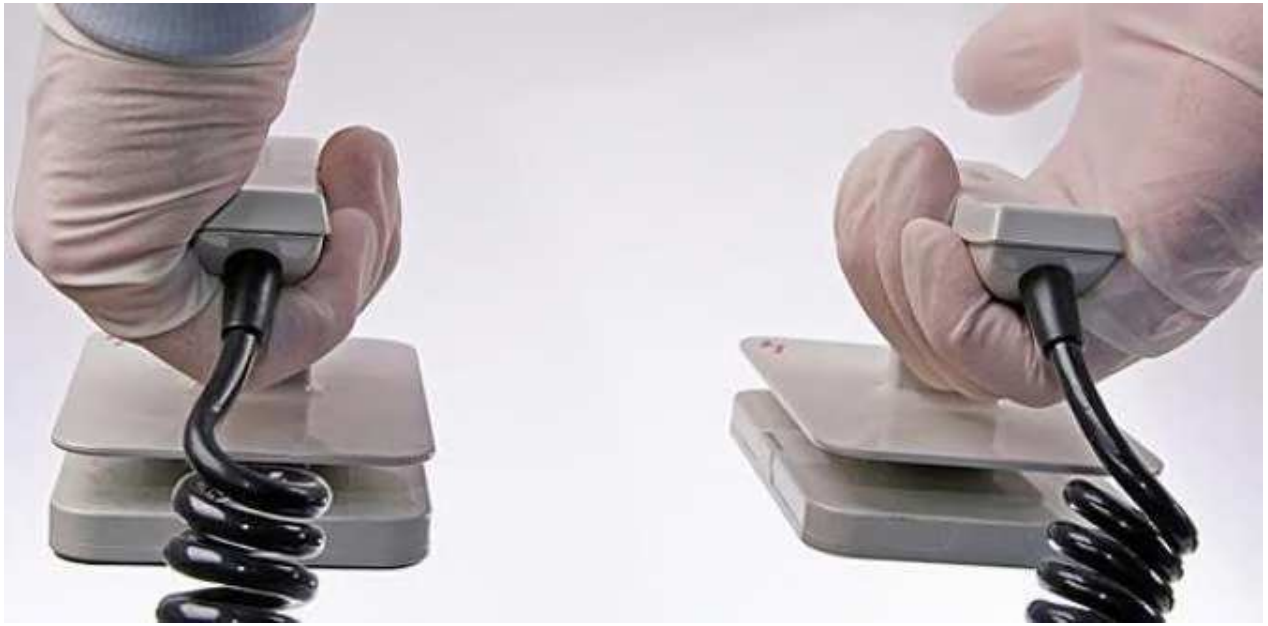
Choosing the right drug to fit the patient when selecting oral anticoagulation for stroke prevention in atrial fibrillation



Apix Riva Apix Apix/Edox Dabig Riva/Edox

Modifiziert nach Shields AM and Lip GYH. J Intern Med 2016

Patienten vor Cardioversion

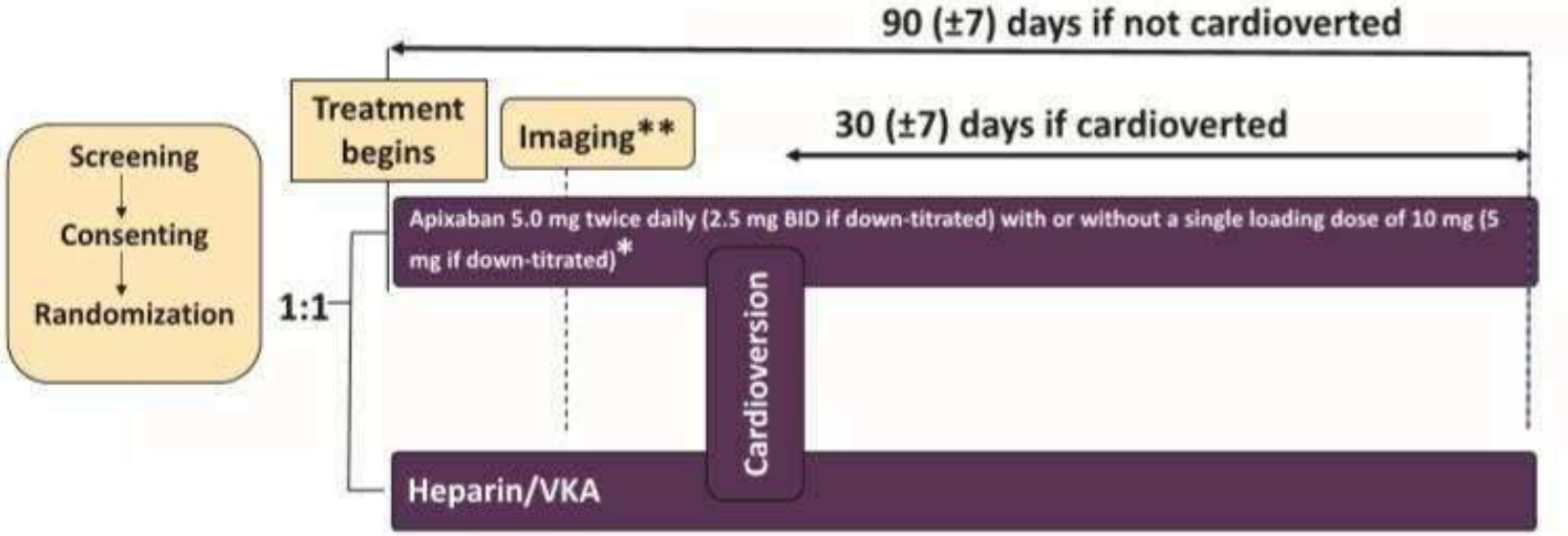


NOAK und Cardioversion: EMANATE

Patienten mit Vorhofflimmern und Indikation zur Cardioversion

Rasche Cardioversion innerhalb von 48 Stunden

Apixaban 2 x 5 mg vs. Heparin/VKA



X-VeRT-Studie (Rivaroxaban):
1-5 Tage od. 3-8 Wochen

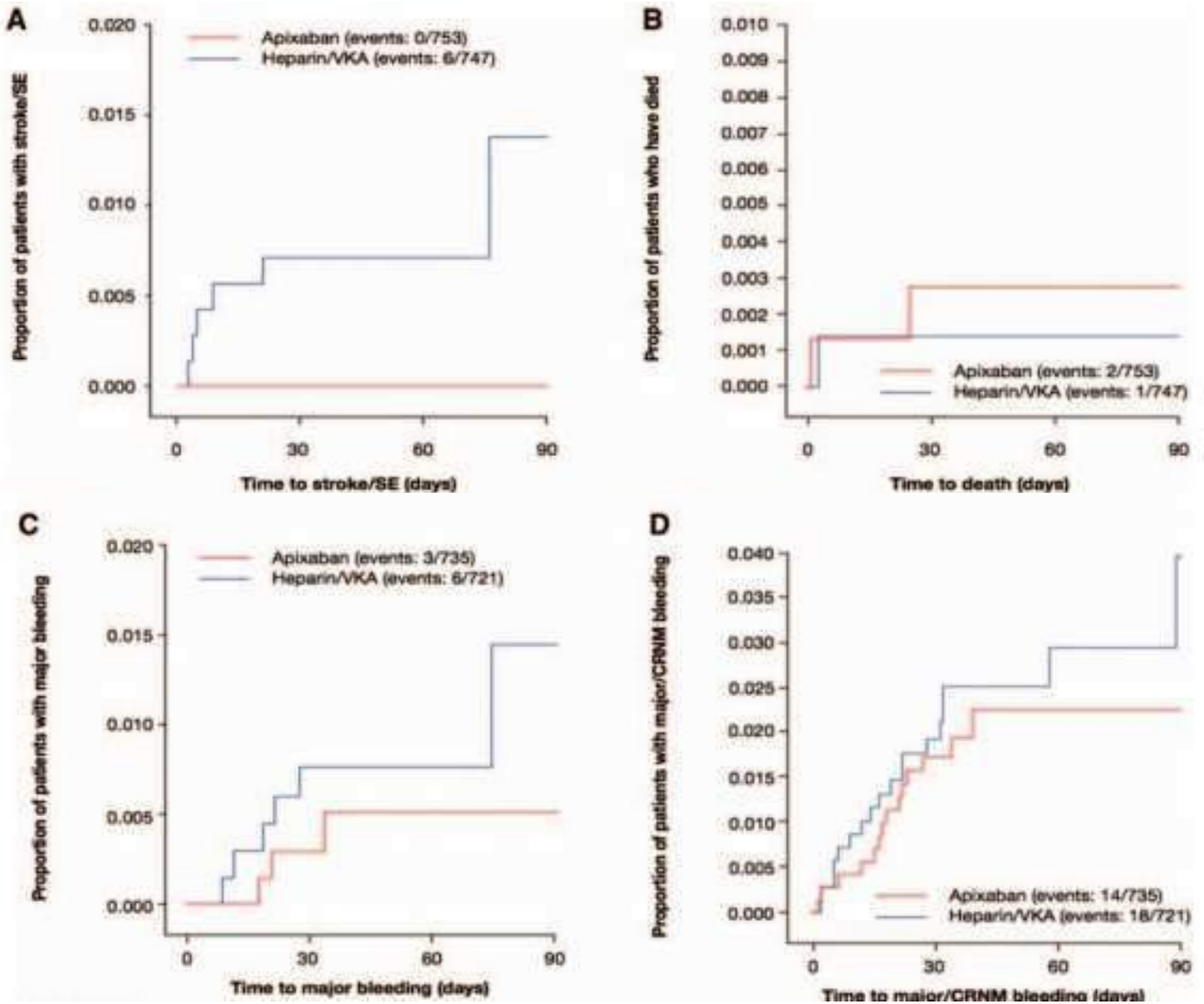
Cappato et al.
EHJ 2014

ENSURE AF (Edoxaban):
TEE: bis 3 Tage
Non-TEE: 21 Tage

Goette et al.
Lancet 2016

Ezekowitz MD et al. EHJ 2018

NOAK und Cardioversion: EMANATE



Ezekowitz MD et al. EHJ 2018

St. Theresien-Krankenhaus Nürnberg

NOAK und Cardioversion: EMANATE

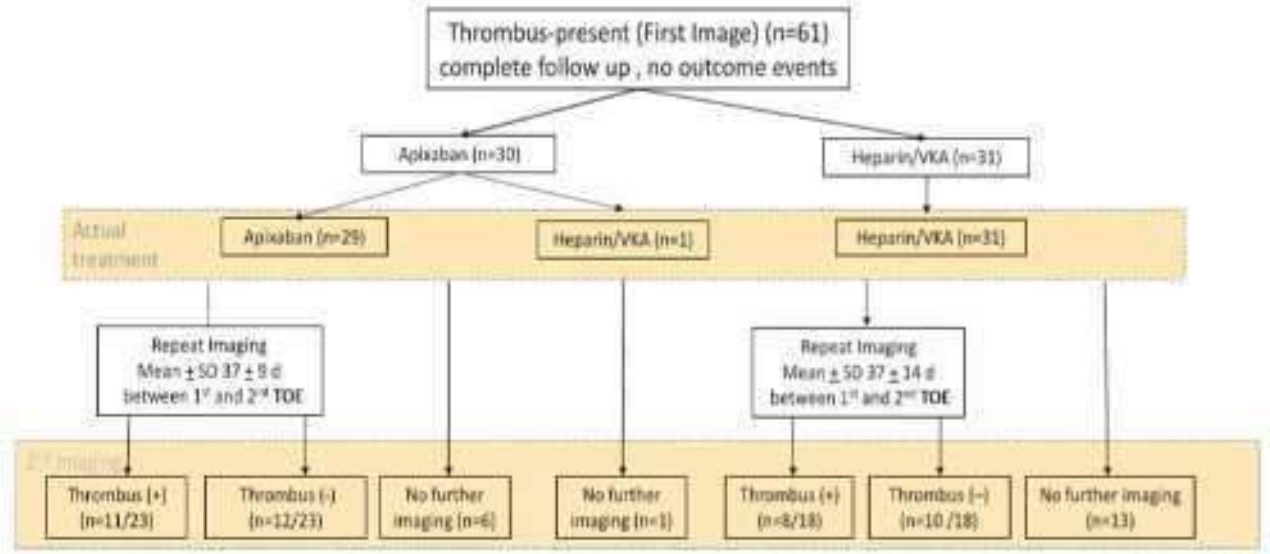
LAA-Thrombus bei 61 Patienten

Keine Ischämien

Nach 37 ± 11 Tagen kein Thrombus:

52% in der Apixaban-Gruppe

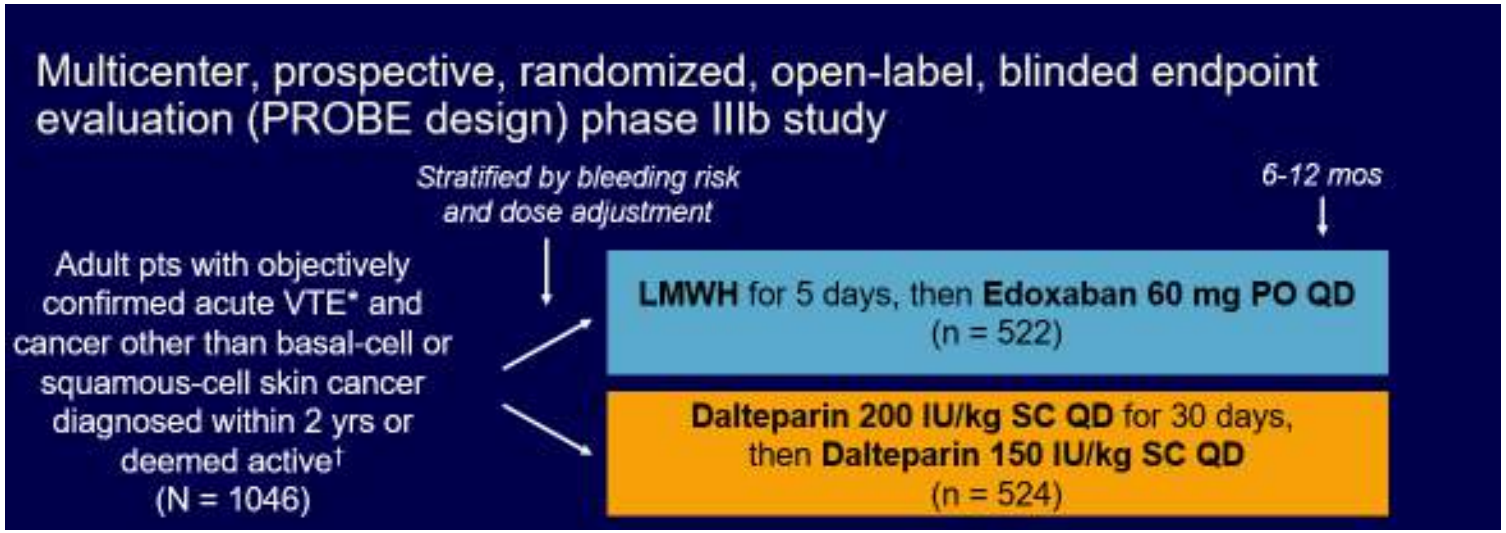
56% in der Heparin/VKA-Gruppe



Ezekowitz MD et al. EHJ 2018

Patienten mit aktiver Tumorerkrankung

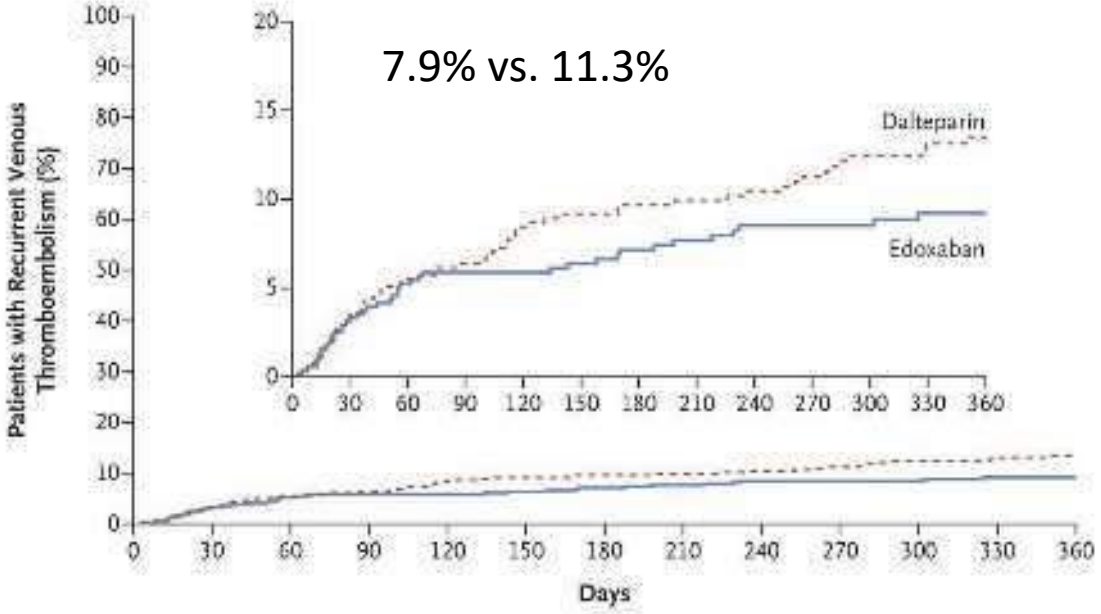
HOKUSAI VTE CANCER

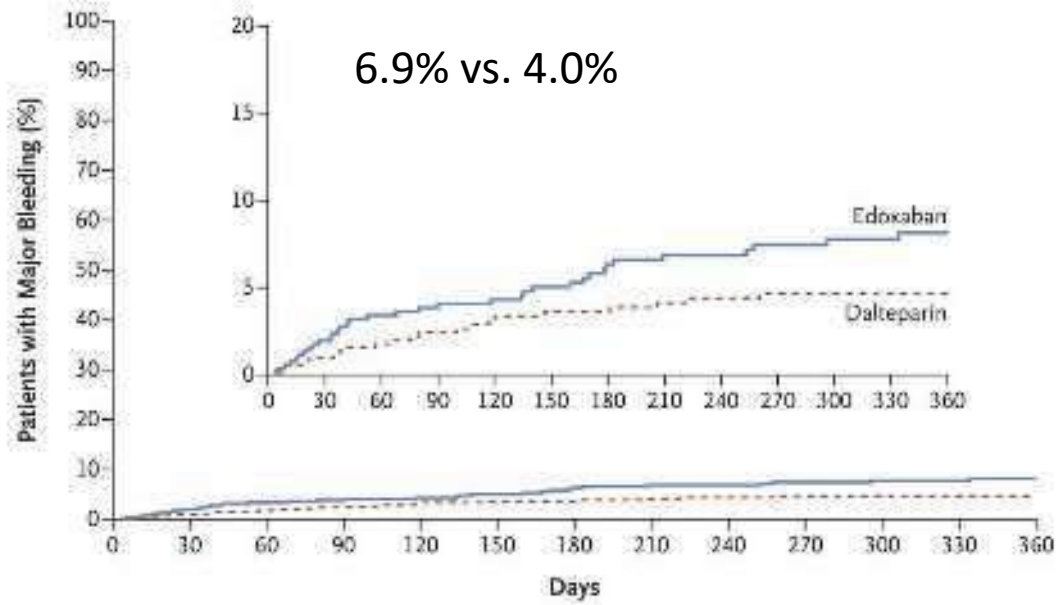


Characteristic	Edoxaban (n = 522)	Dalteparin (n = 524)
Mean age (SD)	64 (11)	64 (12)
Male, n (%)	277 (53)	263 (50)
PE ± DVT, n (%)	328 (63)	329 (63)
Symptomatic VTE, n (%)	355 (68)	351 (67)
Active cancer, n (%)	513 (98)	511 (98)
Metastatic disease, n (%)	274 (53)	280 (53)
Median treatment duration, days	211	184

Raskob GE et al. NEJM 2017

HOKUSAI VTE CANCER





12.8% (67/522) vs. 13.5% (71/524); p = 0.006 für Nicht-Unterlegenheit

p = 0.87 für Überlegenheit

Raskob GE et al. NEJM 2017

Hirnblutung: Wie hätten Sie entschieden?

Patientin 77 Jahre, permanentes Vorhofflimmern

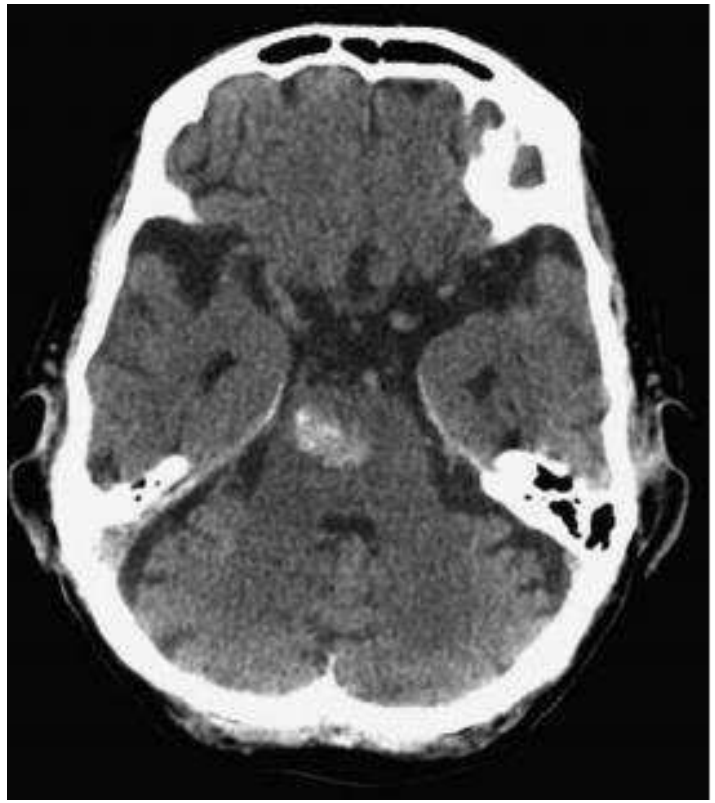
Vor 2 und 6 Jahren PRIND/TIA

Mäßiggradige Mitralinsuffizienz

Rivaroxaban 20 mg 1x/Tag

Hemiparese links und Dysathrie

cCT: Ponsblutung



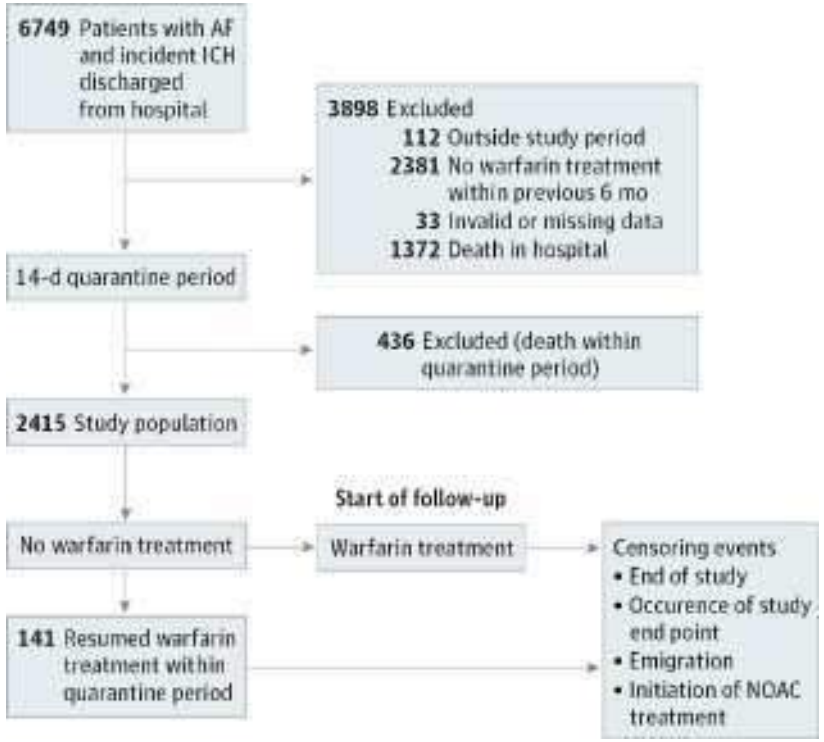


Table 2. Studied Outcomes During 1 Year of Follow-up

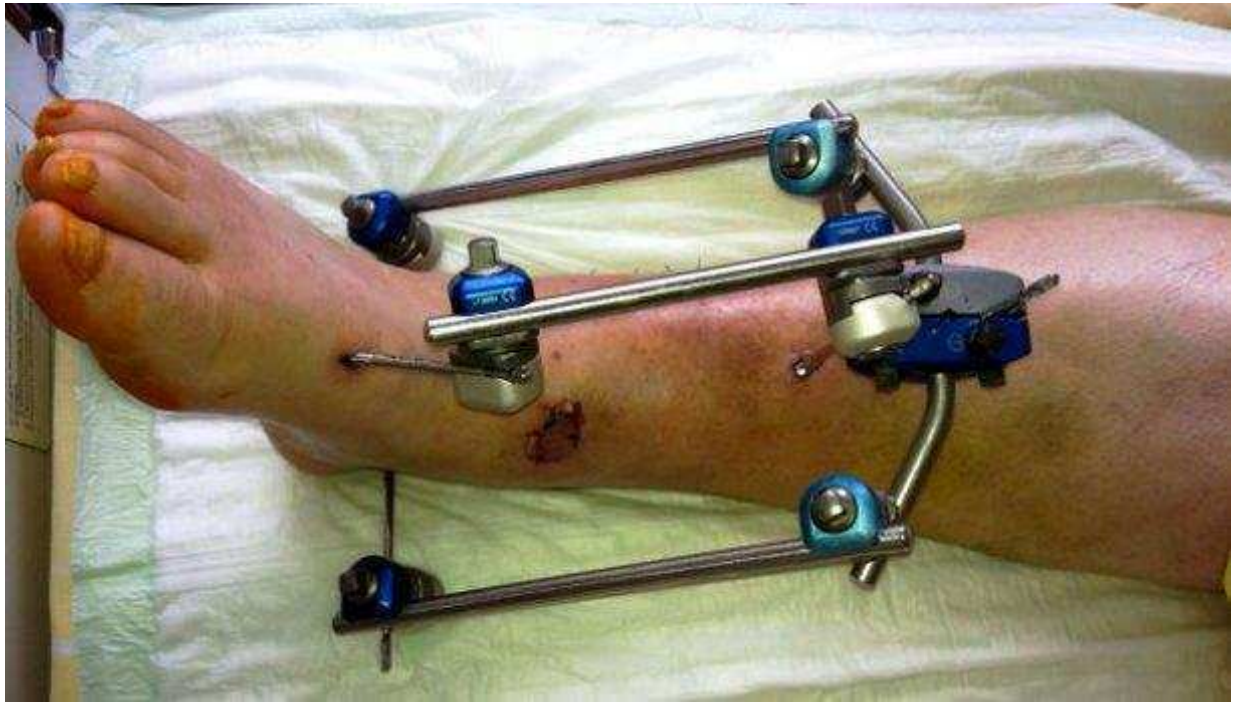
Outcome	Index ICH Event			
	Hemorrhagic Stroke		Traumatic ICH	
	No Warfarin Treatment Group	Warfarin Treatment Group	No Warfarin Treatment Group	Warfarin Treatment Group
Ischemic stroke/SE				
No. of events	60	9	20	7
Event rate per 100 person-years	8.9	3.3	4.1	2.2
Recurrent ICH				
No. of events	35	15	66	23
Event rate per 100 person-years	5.3	5.8	16.4	8.3
All stroke				
No. of events	78	19	31	10
Event rate per 100 person-years	12.1	7.3	6.6	3.1
All-cause mortality				
No. of events	250	55	169	41
Event rate per 100 person-years	35.5	19.6	34.0	12.1

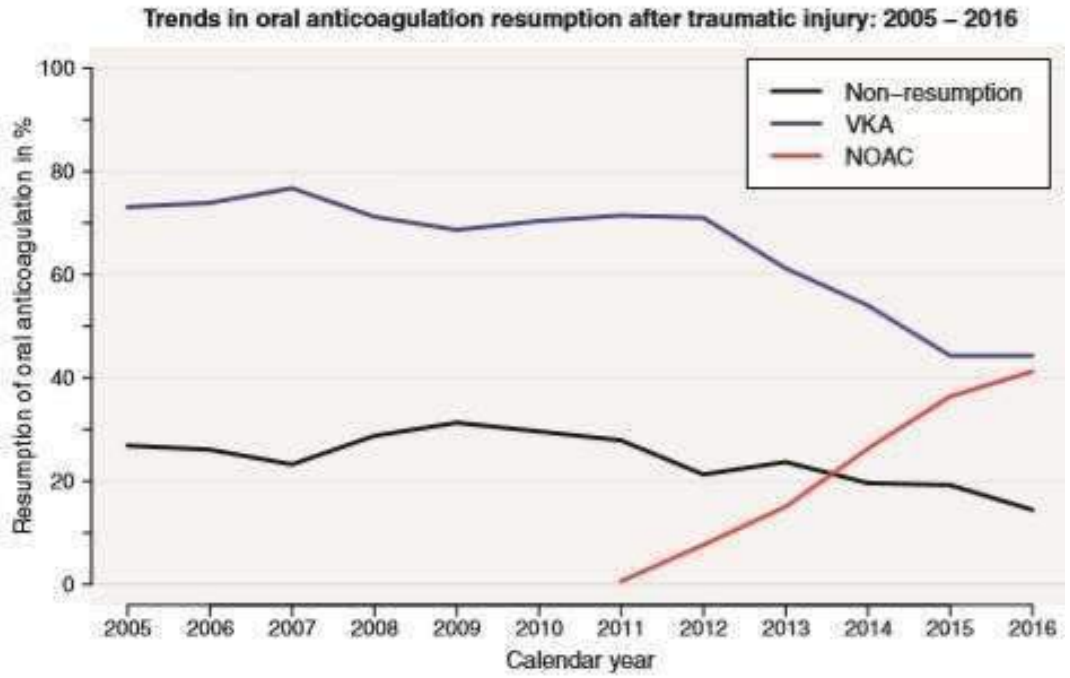
1325 spontane ICB: 23% 1-Jahres-Mortalität

1090 traumatische ICB: 19.3% 1-Jahres-Mortalität

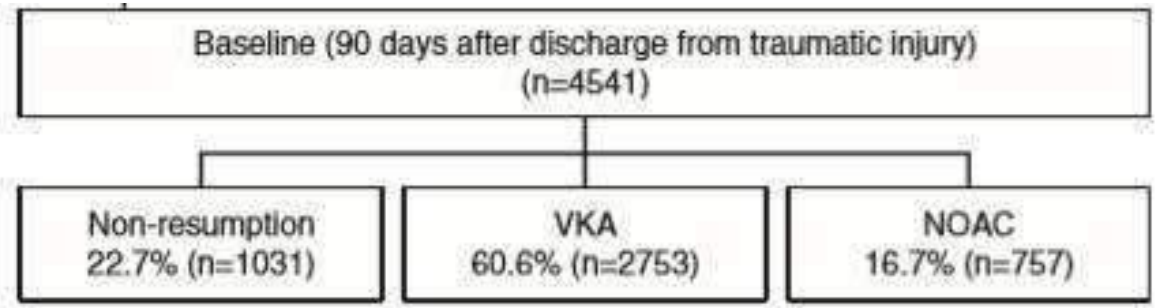
Nielson PB et al. JAMA Internal Medicine 2017

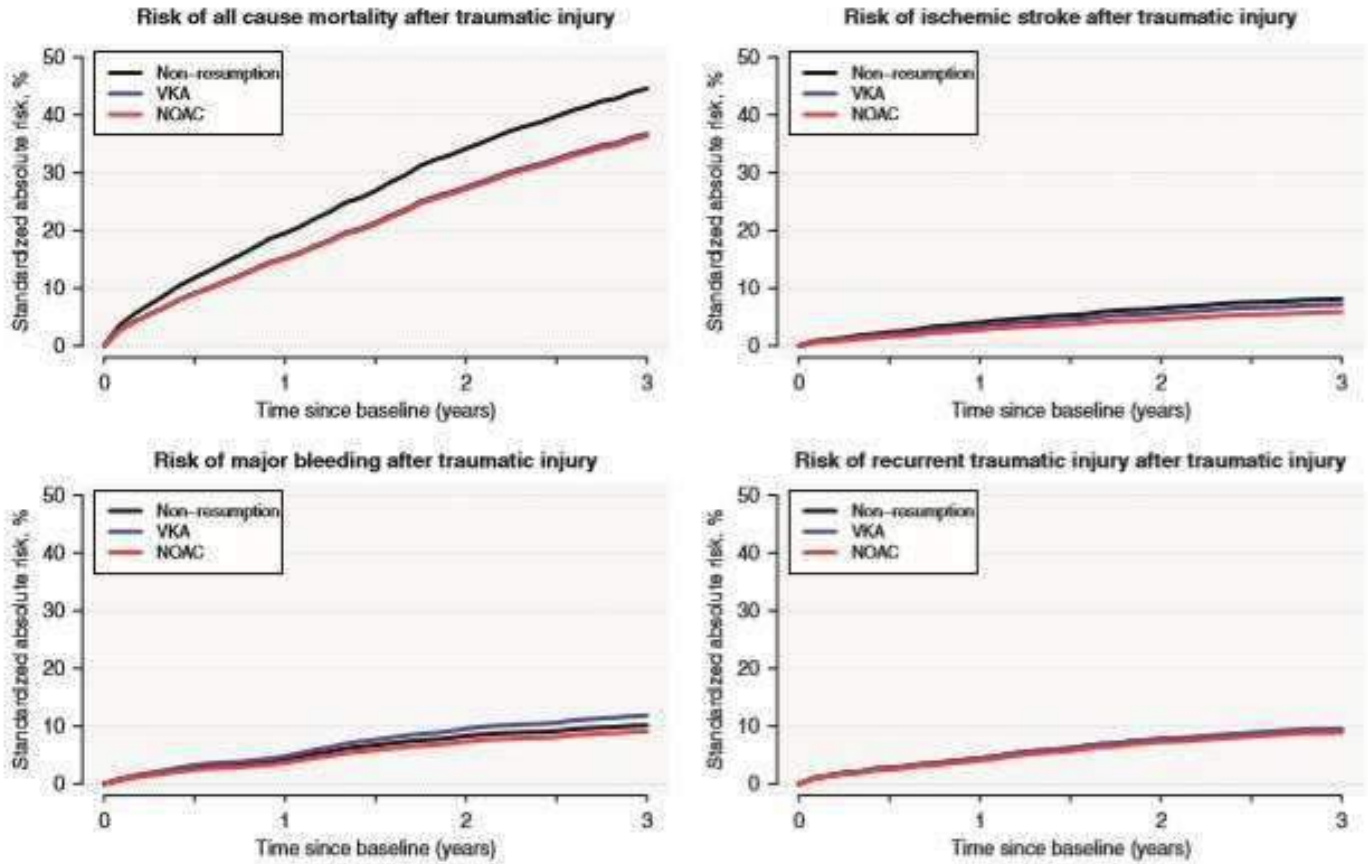
Trauma unter Antikoagulation

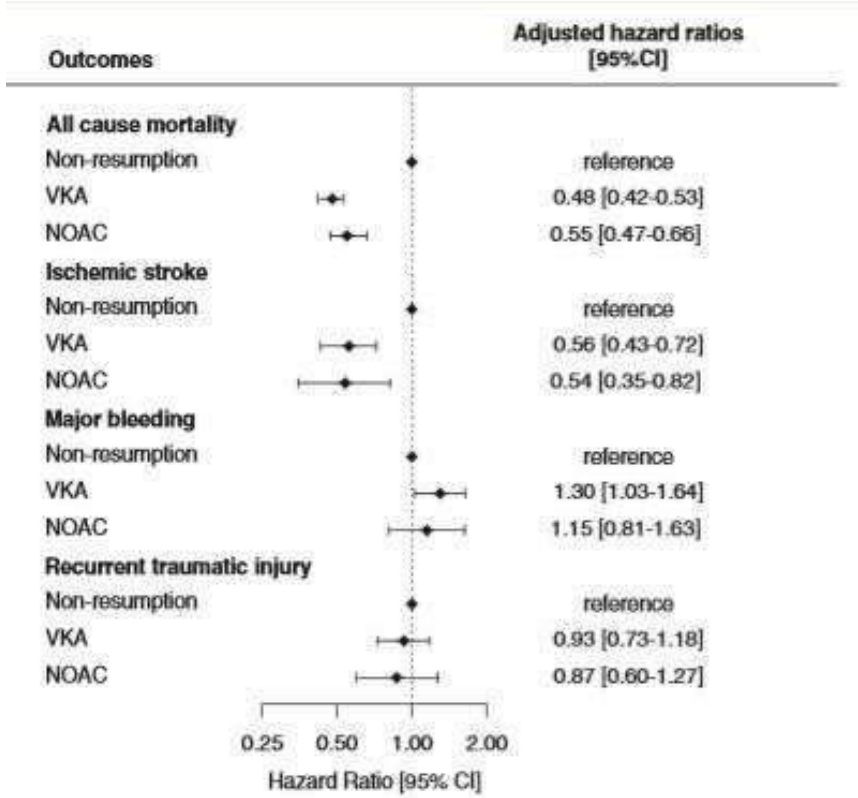




Resumption of oral anticoagulation following traumatic injury and risk of stroke and bleeding in patients with atrial fibrillation: a nationwide cohort study

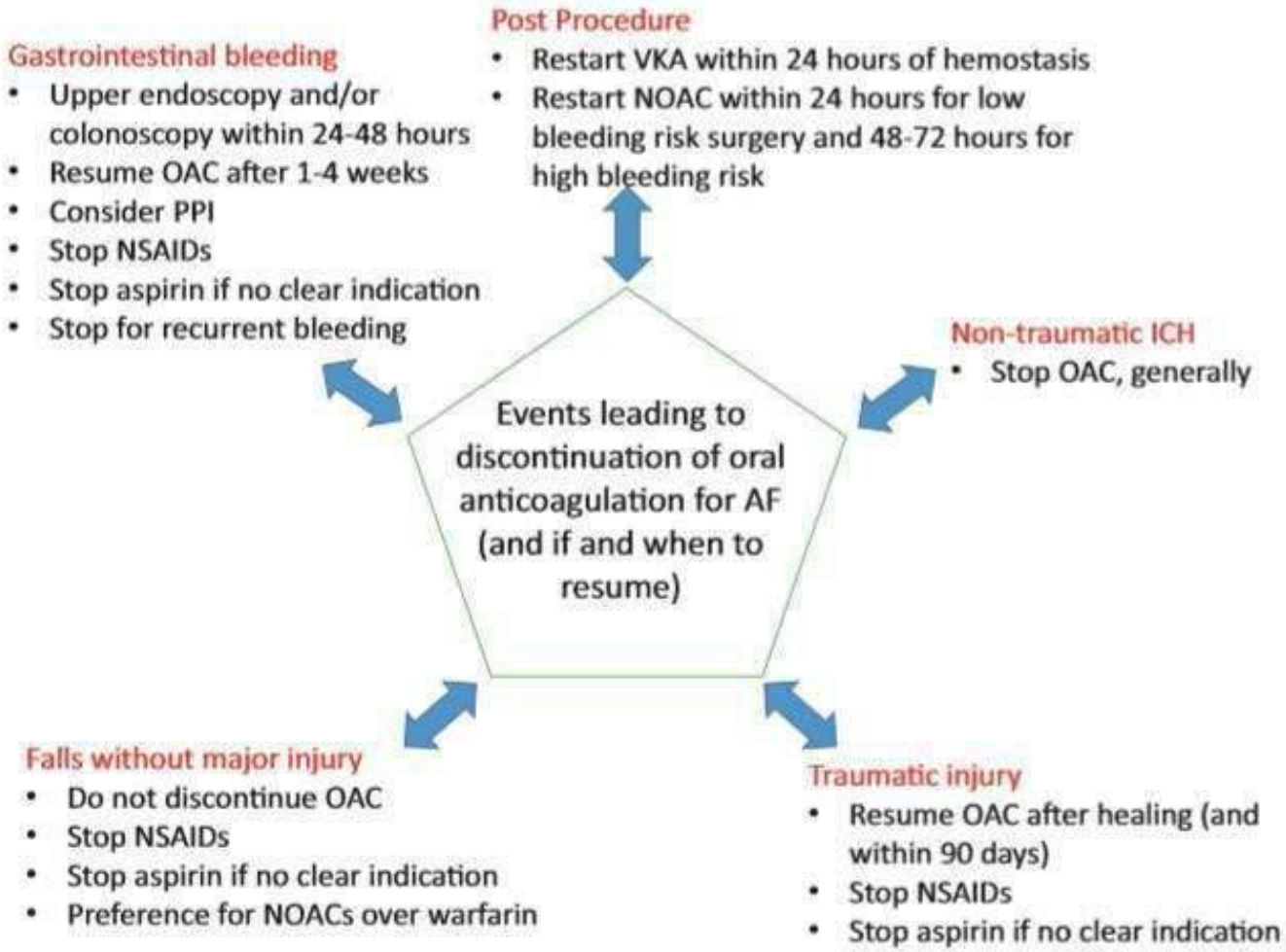




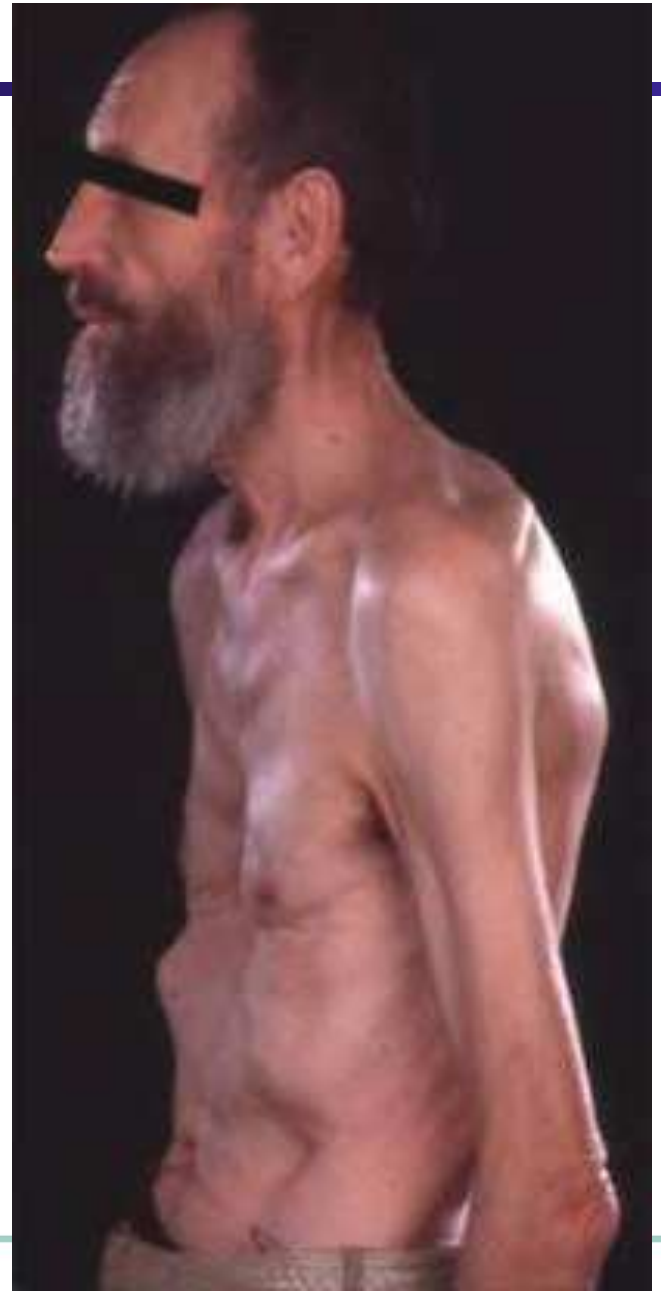


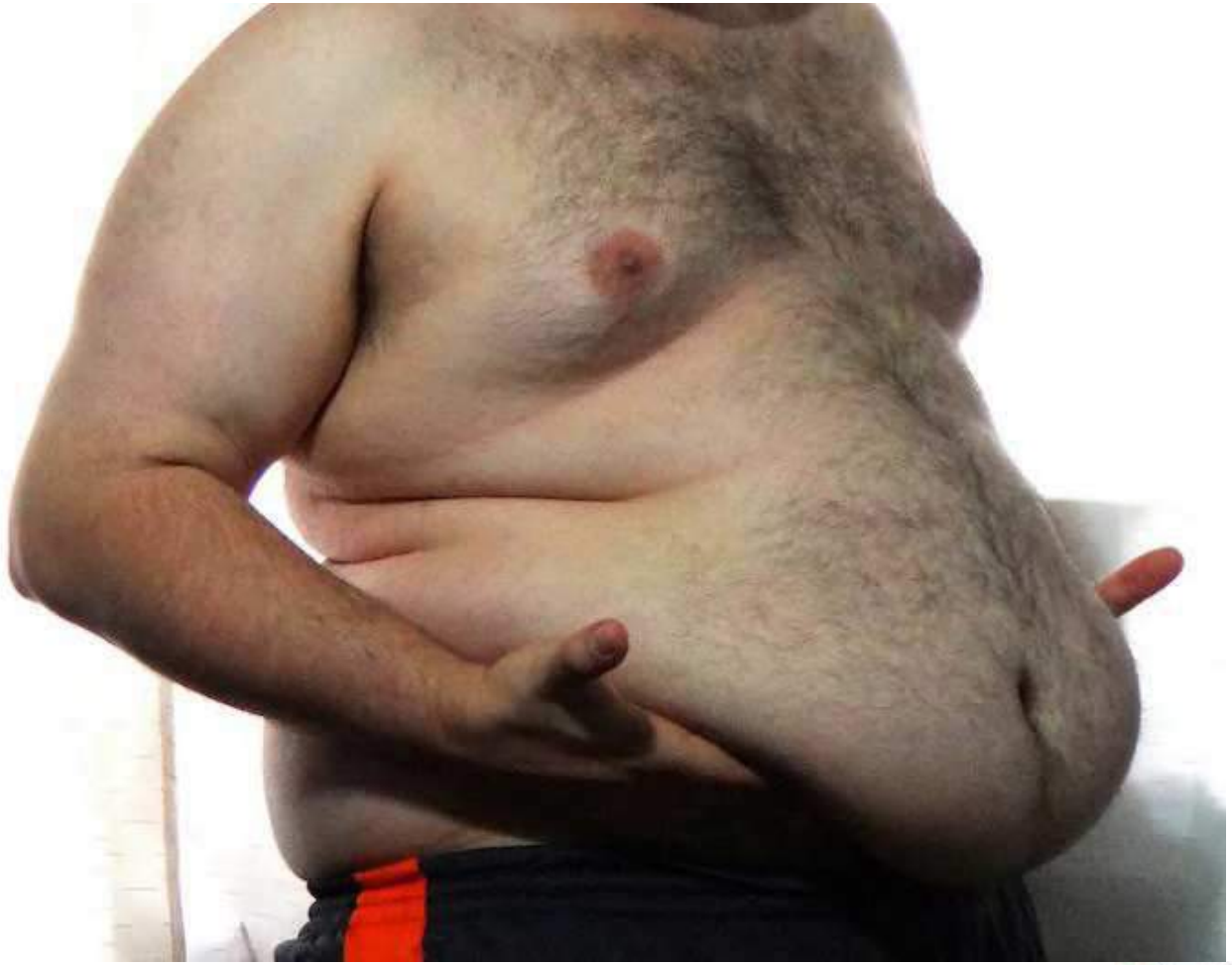
Staerk L et al. EHJ 2018

Traumatic injury: another unjustified reason to stop oral anticoagulation for atrial fibrillation



Pokorney SD and Granger CB. EHJ 2018

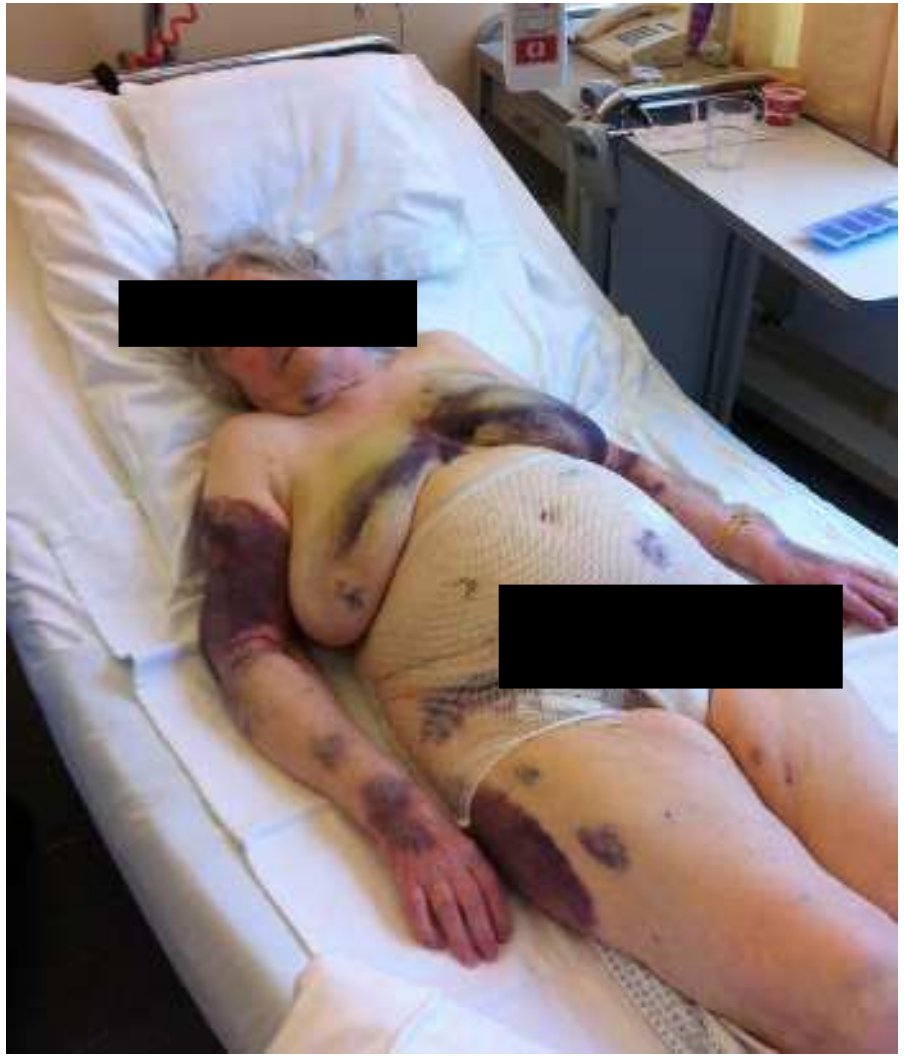


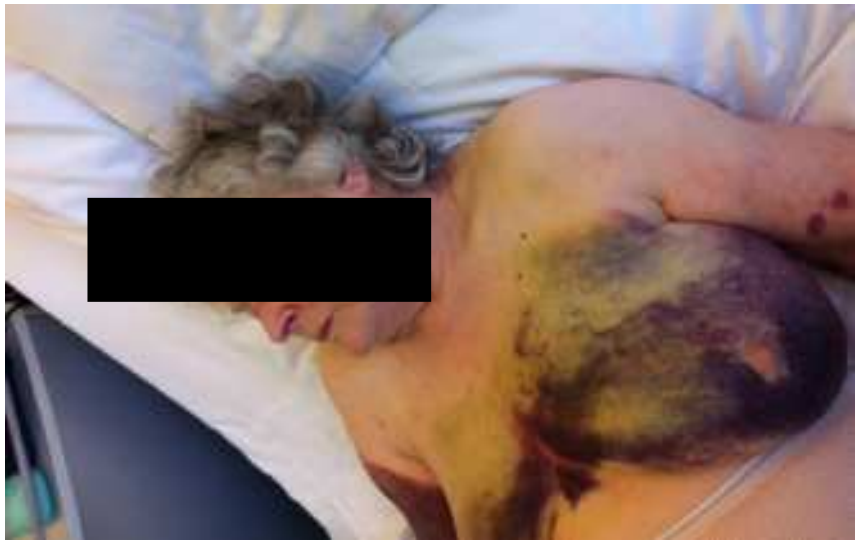


Antithrombotic therapy and body mass: an expert position paper of the ESC Working Group on Thrombosis

	< 60 kg	BMI > 40 kg/m²
Apixaban	2 x 2.5 mg/Tag (+ Krea > 1.5 od. > 80 J.)	nur unter FXa-Aktivität
Edoxaban	1 x 30 mg/Tag	nur unter FXa-Aktivität
Dabigatran	< 50 kg keine Daten („enge Überwachung“)	nur unter Thrombinzeit
Rivaroxaban	1 x 20 mg/Tag	nur unter FXa-Aktivität

Rocca B et al. EHJ 2018





Trop. 3.45 ng/ml, Ck 1245 U/l

OAK plus Hep. 5000 IE i.v.
plus ASS 500 mg i.v.
plus Clopidogrel 300 mg p.o.

Vorhofflimmern

Mechanischen Klappen

bei Ventrikel-Thrombus

größeres Aneurysma

schwerst eingeschränkte LV-Funktion (Echo-Kontrast)

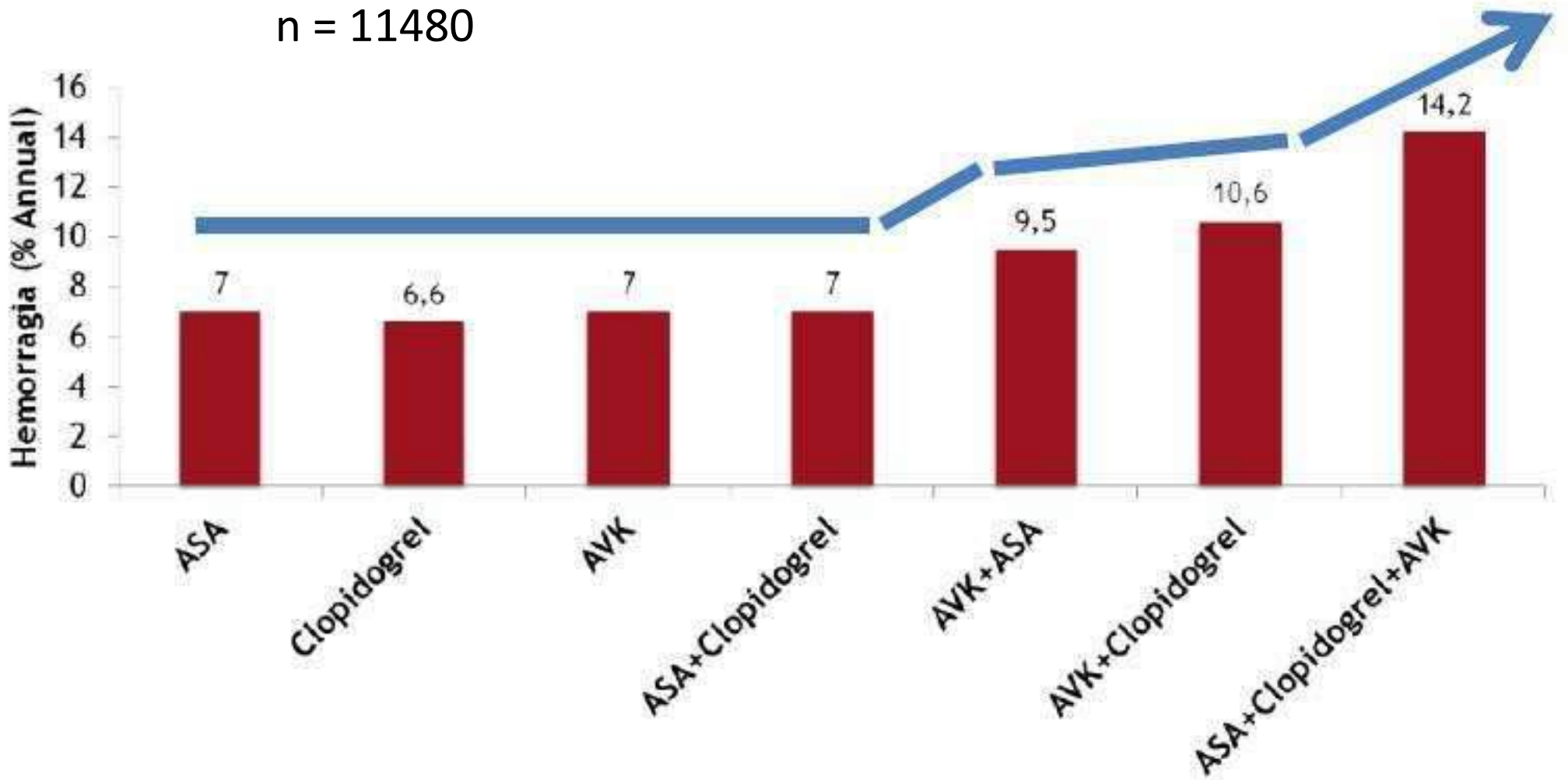
ektatische KHK

6 – 8% aller PCI-Patienten haben Indikation zur OAK

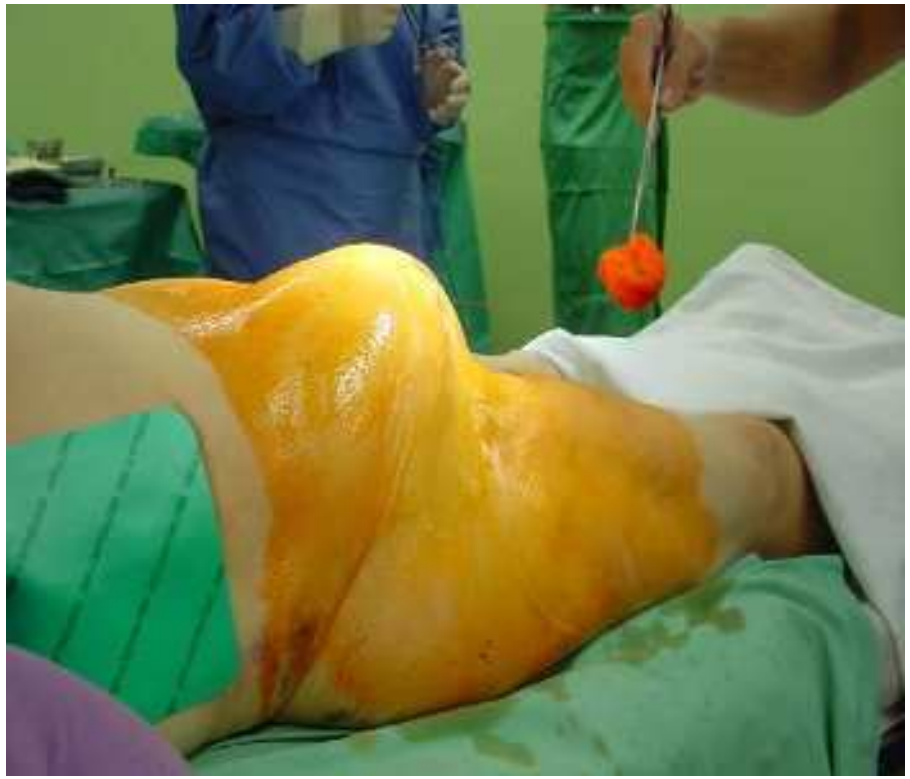
21% der ACS-Patienten haben Vorhofflimmern

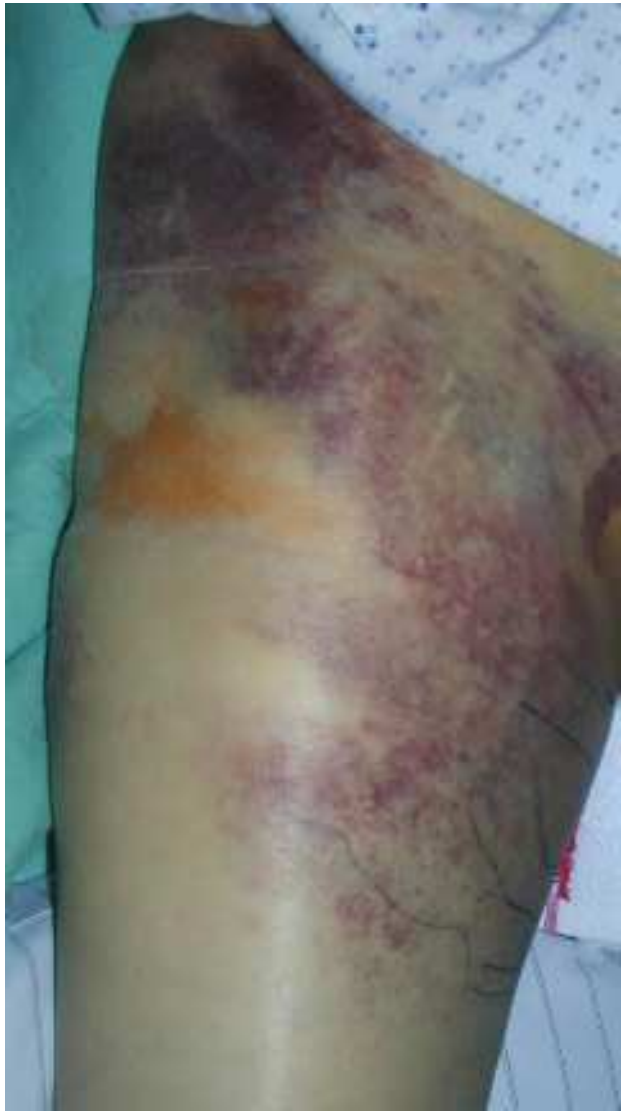
Schmitt et al EHJ 2009, Windecker et al. EHJ 2014

n = 11480



Lamberts et al. Circulation 2012





Hirnblutung

Volumenmangel

Hypotonie

Anämie

O2-Versorgung

O2-Bedarf

Pausieren der TAH

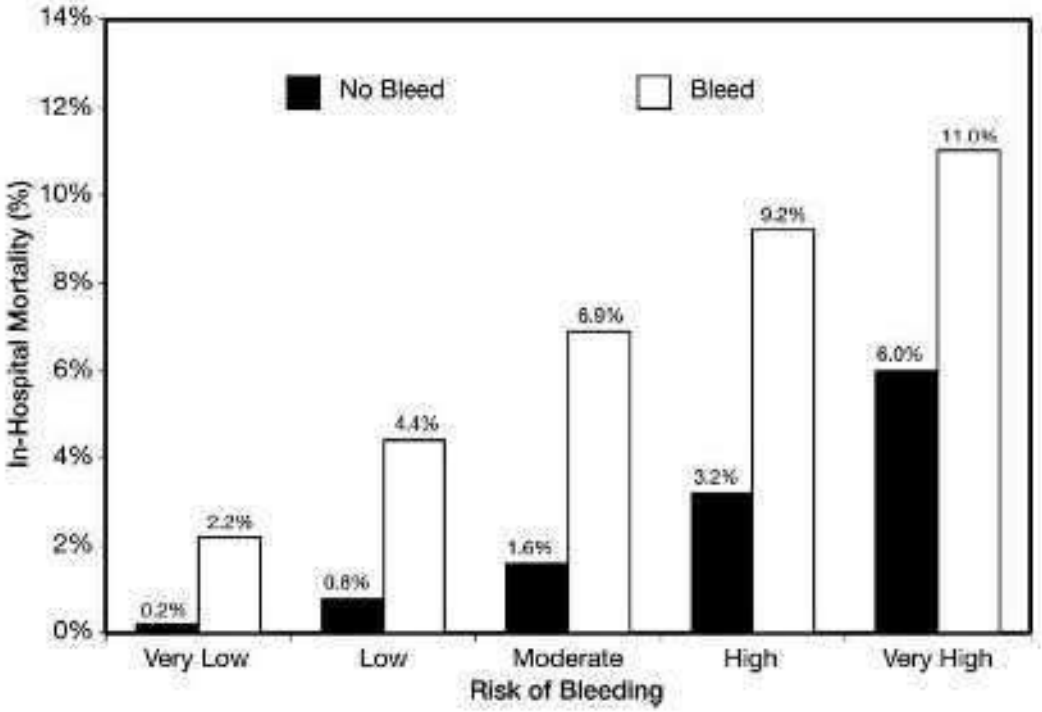
Stentthrombose

Bluttransfusion

pro-inflammatorisch

red. O2-Abgabe ins Gewebe

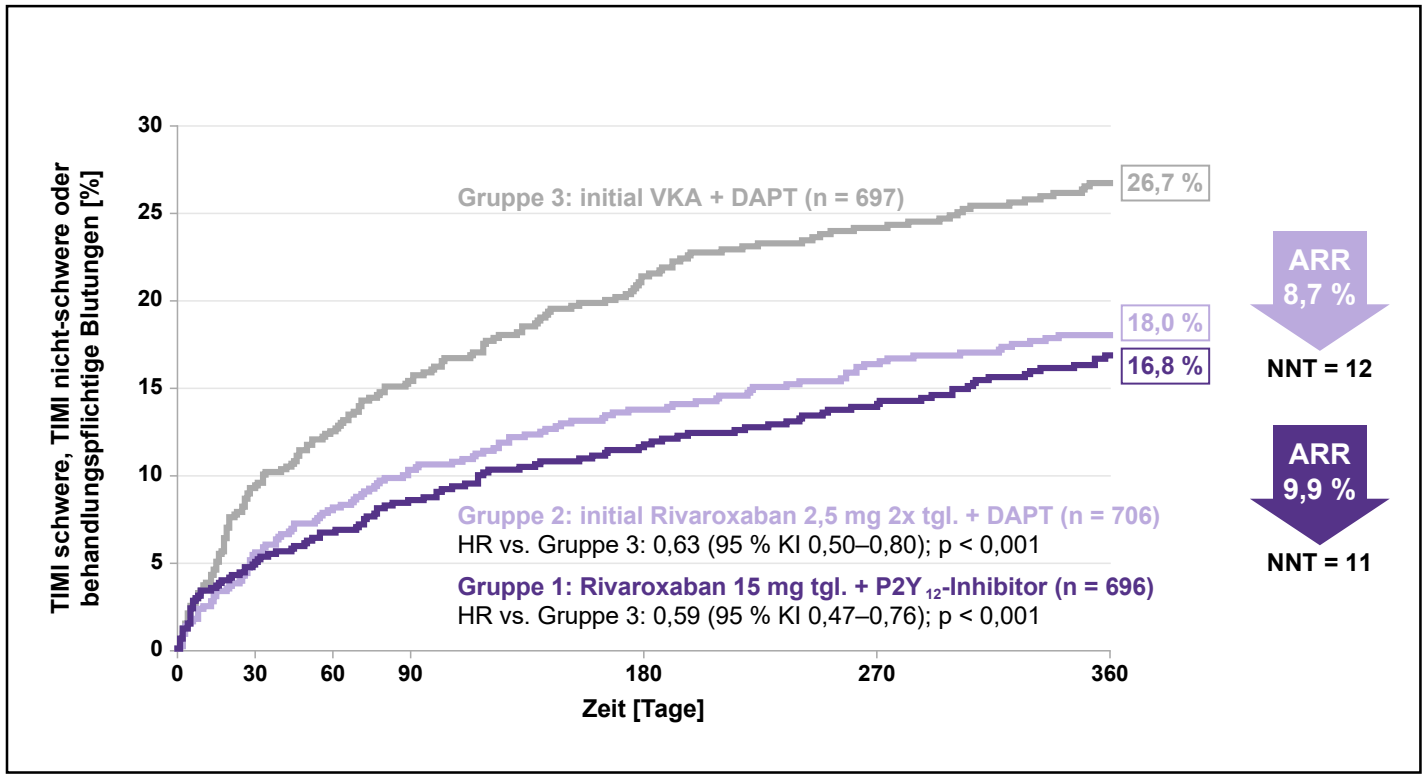
Mortalität
Morbidität

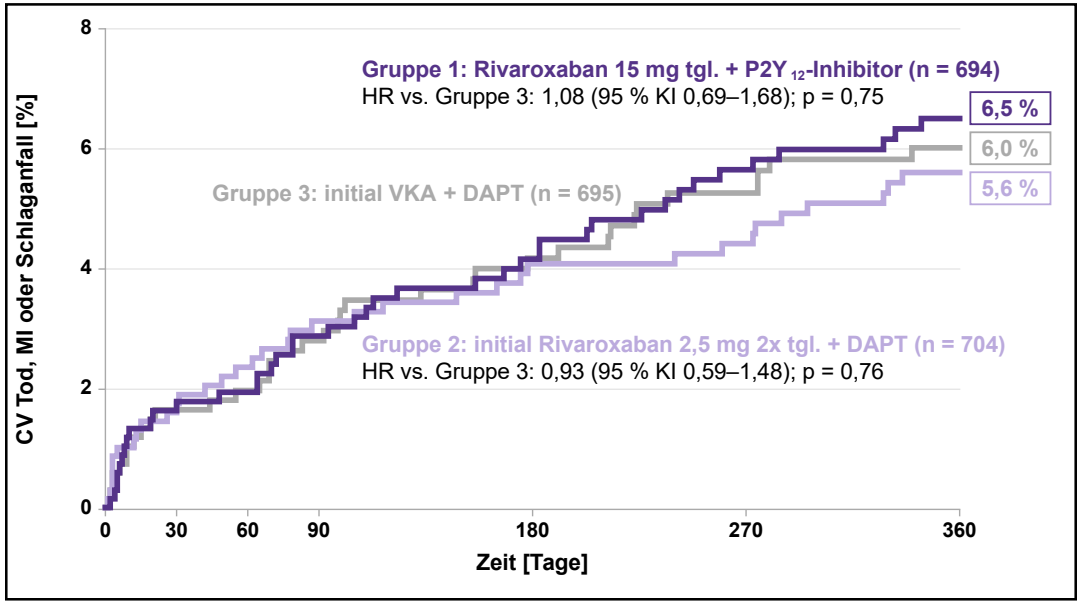


Ferreiro et al. Thromb Haemost 2010, Subherwal et al. Circulation 2009

Duale Therapie versus „Triple“-Therapie

WOEST	2013	n = 573	69% Vorhofflimmern	VKA + VKA
PIONEER	2016	n = 2124	100% Vorhofflimmern	Rivaroxaban 15 mg + $P2Y_{12}$-Ag. (> 90% Clopidogrel)





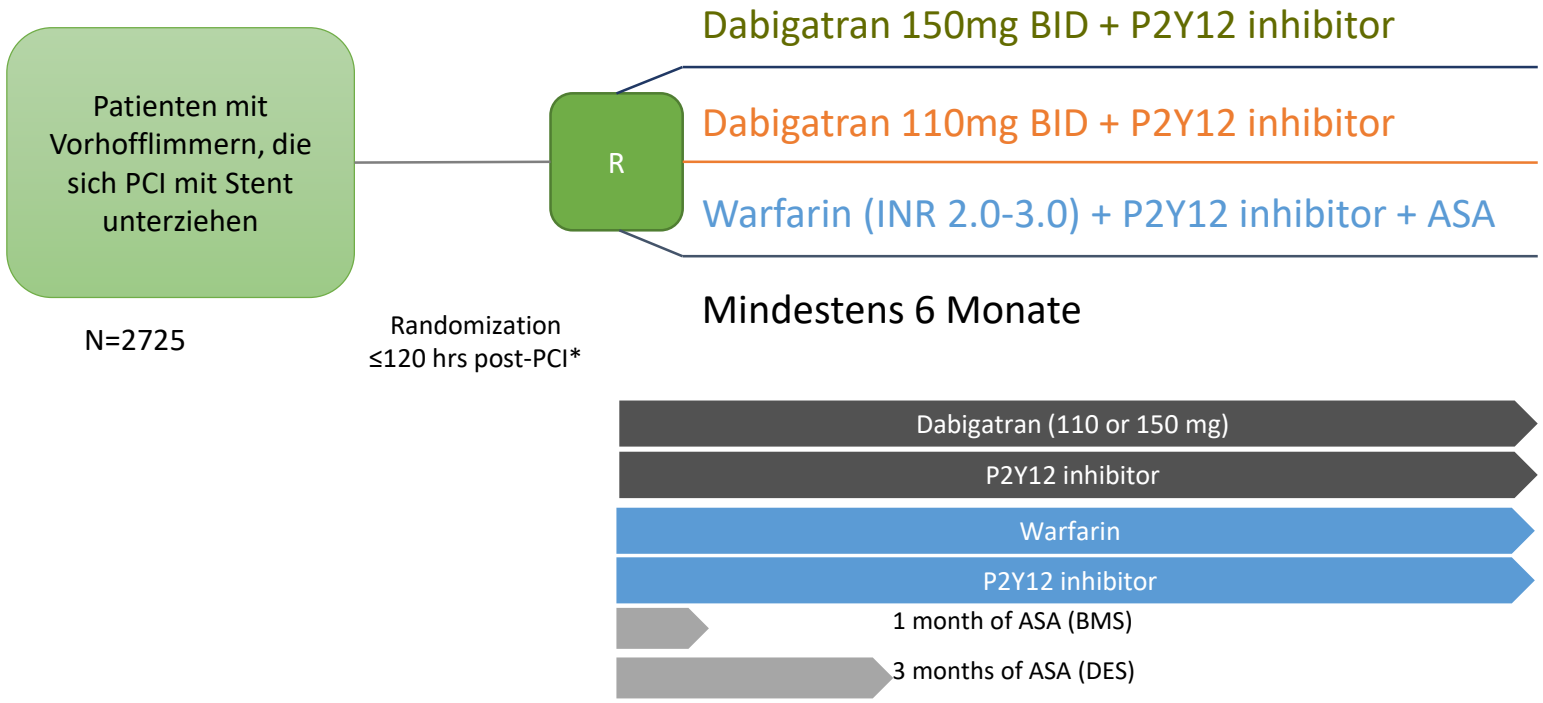
PIONEER AF-PCI

St. Theresien-Krankenhaus Nürnberg

Dewilde WJ et al. Lancet 2013, Gibson CM et al. NEJM 2016

Neue Daten: RE-DUAL PCI

Test der Sicherheit und der Effektivität / Blutungskomplikationen



Mean duration of follow-up:
≈14 months

RE-DUAL PCI™
Study in NVAF patients undergoing PCI

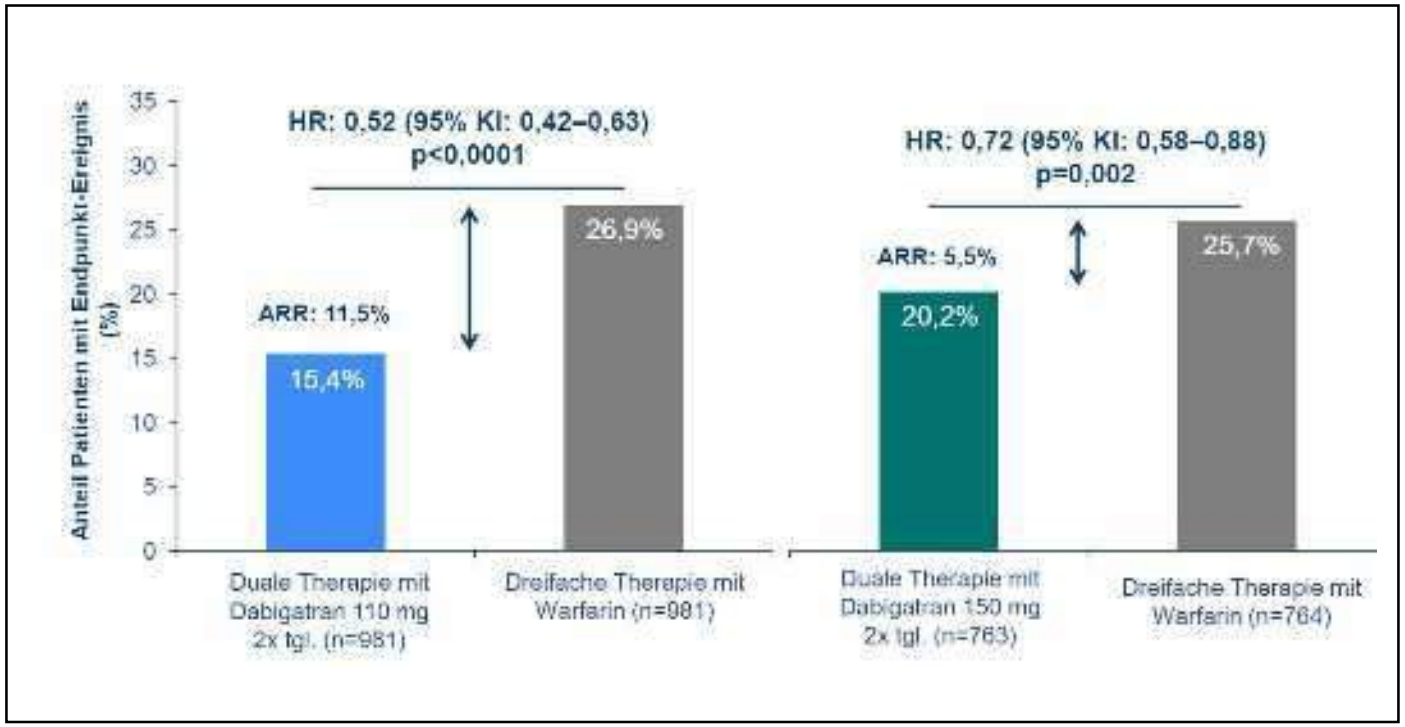
Cannon CP et al. NEJM 2017

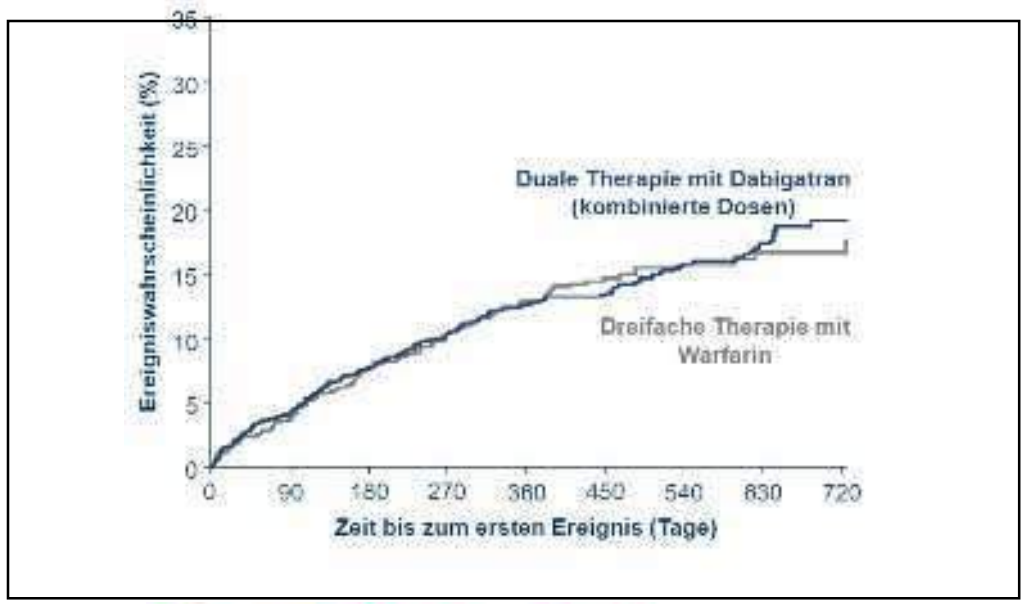
	Dabigatran 110mg dual therapy N=981	Warfarin triple therapy N=981	Dabigatran 150mg dual therapy N=763	Corresponding warfarin triple therapy N=764
CHA2DS2-VASc score (main)	3.7	3.8	3.3	3.6
ACS indication for PCI, %	51.9	48.4	51.2	48.3
DES only, %	82.0	84.2	81.4	83.5

St. Theresien-Krankenhaus Nürnberg

Duale Therapie versus „Triple“-Therapie

WOEST	2013	n = 573	69% Vorhofflimmern	VKA + VKA
PIONEER	2016	n = 2124	100% Vorhofflimmern	Rivaroxaban 15 mg + $P2Y_{12}$-Ag. (> 90% Clopidogrel)
RE-DUAL PCI	2017	n = 2725	100% Vorhofflimmern	Dabigatran 2 x 110/150 mg + $P2Y_{12}$-Ag. (> 90% Clopidogrel)





RE-DUAL PCI

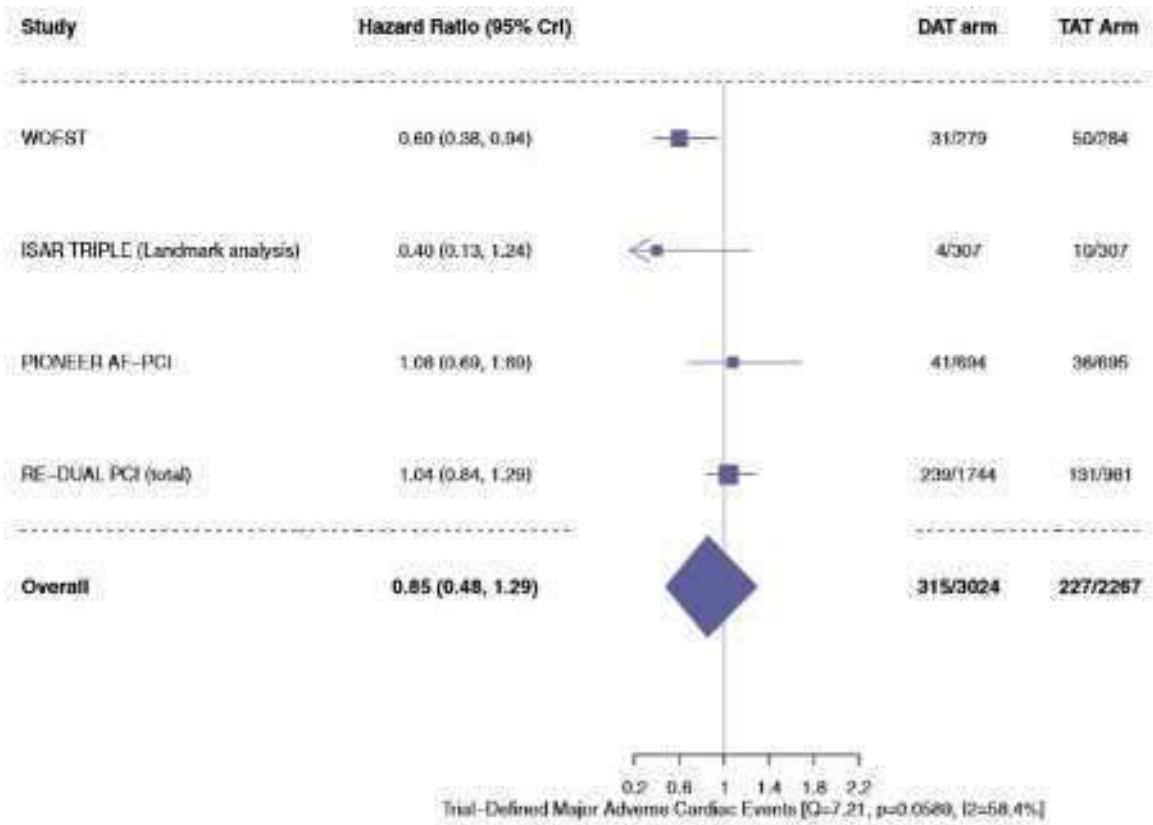
Study in NVAF patients undergoing PCI

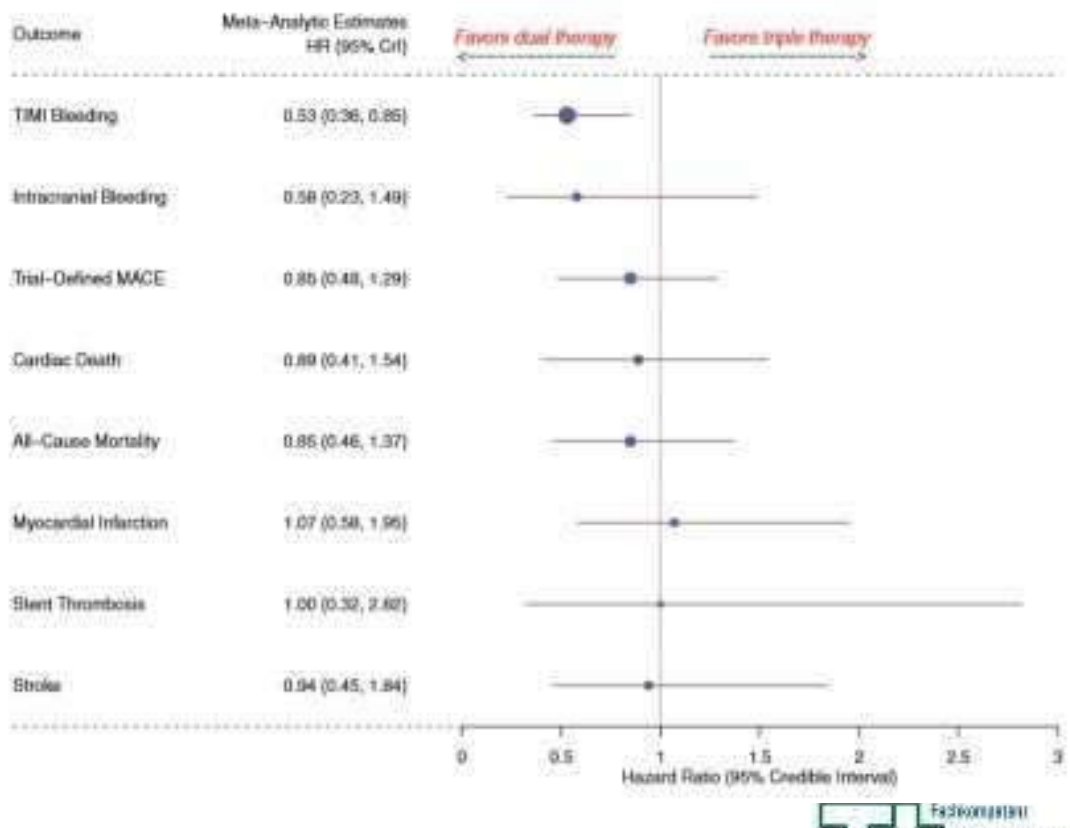
St. Theresien-Krankenhaus Nürnberg

Dewilde WJ et al. Lancet 2013, Gibson CM et al. NEJM 2016, Cannon CP et al. NEJM 2017

Safety and efficacy of dual vs. triple antithrombotic therapy in patients with atrial fibrillation following percutaneous coronary intervention: a systematic review and meta-analysis of randomized clinical trials

In summary, our systematic review and meta-analysis supports that DAT may be a better option than TAT in many patients with AF following PCI

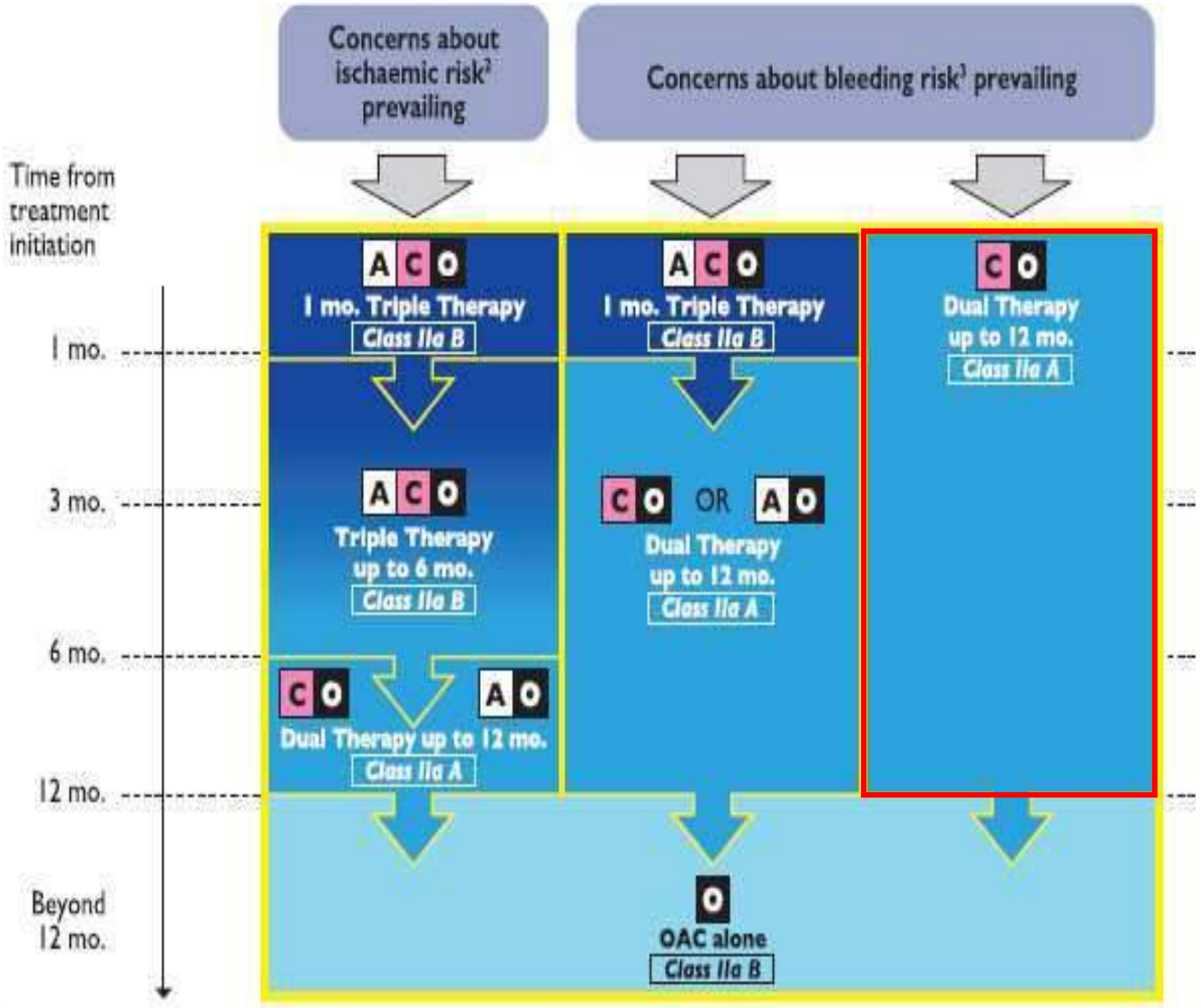




Golwala et al. EHJ 2018

N = 5317

„Triple“-Therapie: OAK plus DAPT



So kurz wie möglich

Nur Clopidogrel in der Kombination

Vorzugsweise NOAK

NOAK in der niedrigeren Dosis

Bei VKA niedriger INR (2.0 – 2.5)

Während Triple-Therapie PPI.

Vom Stent-Typ unabhängig

Ibanez et al. EHJ 2017

NAVIGATE ESUS

Rivaroxaban Trial in Patients With Embolic Stroke of Undetermined Source Stopped Early

Patienten mit kryptogenen Schlaganfall (Embolic Stroke of Undetermined Source, ESUS)

N = 7214; Rivoraoxaban 15 mg 1x/Tag vs. ASS 100 mg 1x/Tag, 11 Monate FU

Vergleichbare Effektivität (jeweils 4.7% erneuter Apoplex)

Höhere Blutungsrate (1.8% versus 0.7%),

Hart EG et al. NEJM 2018

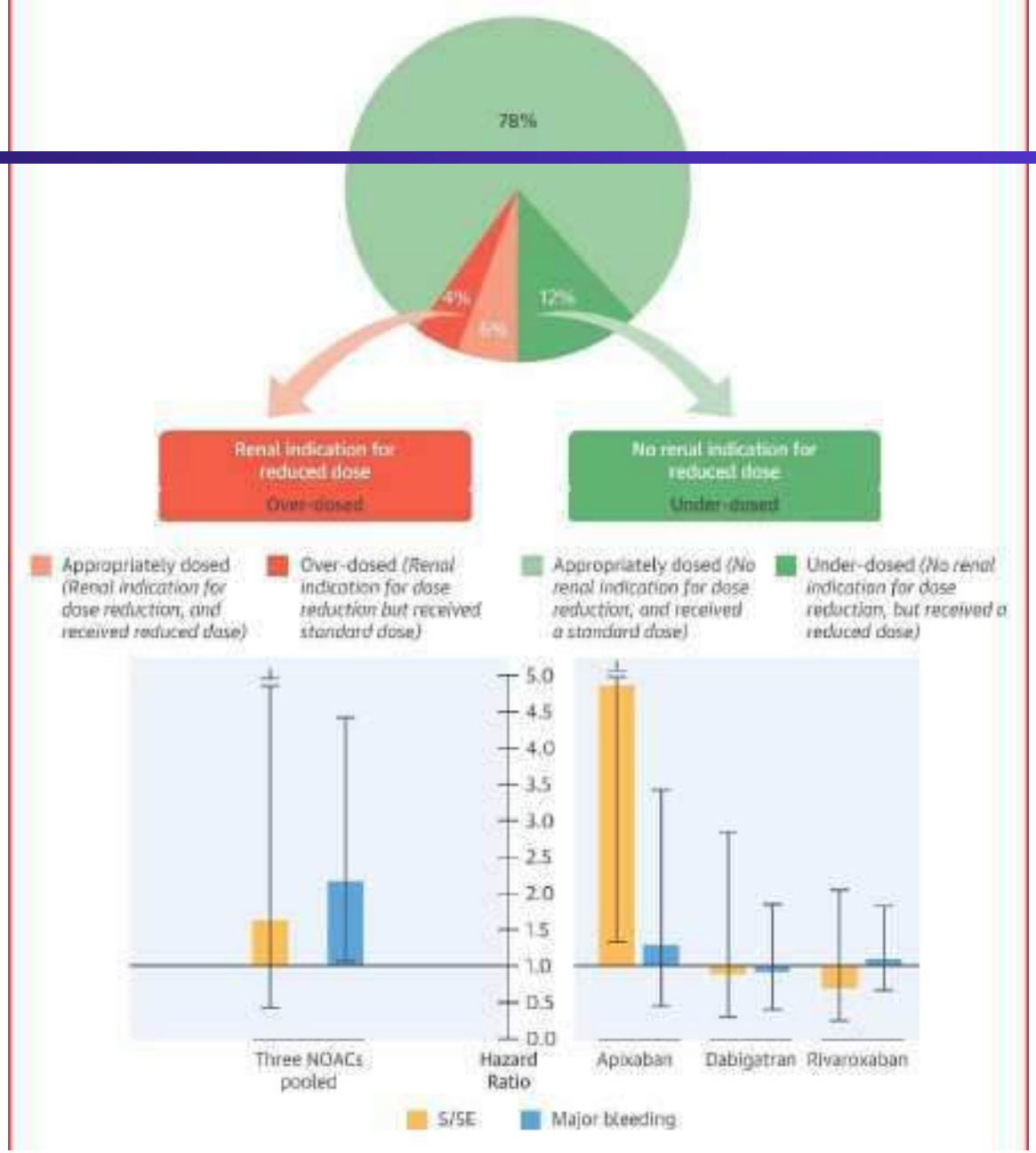
Richtig dosieren!!

	Studien	Real World	EU label[5]
Rivaroxaban 15 mg 1x	20.7%	24.5%	
Apixaban 2.5 mg 2x	4.7%	35.5%	
Dabigatran 110 mg 2x	49.7%	53.7%	28.6%

Yao X et al. J Am Coll Cardiol 2017

St. Theresien-Krankenhaus Nürnberg

n = 14.865



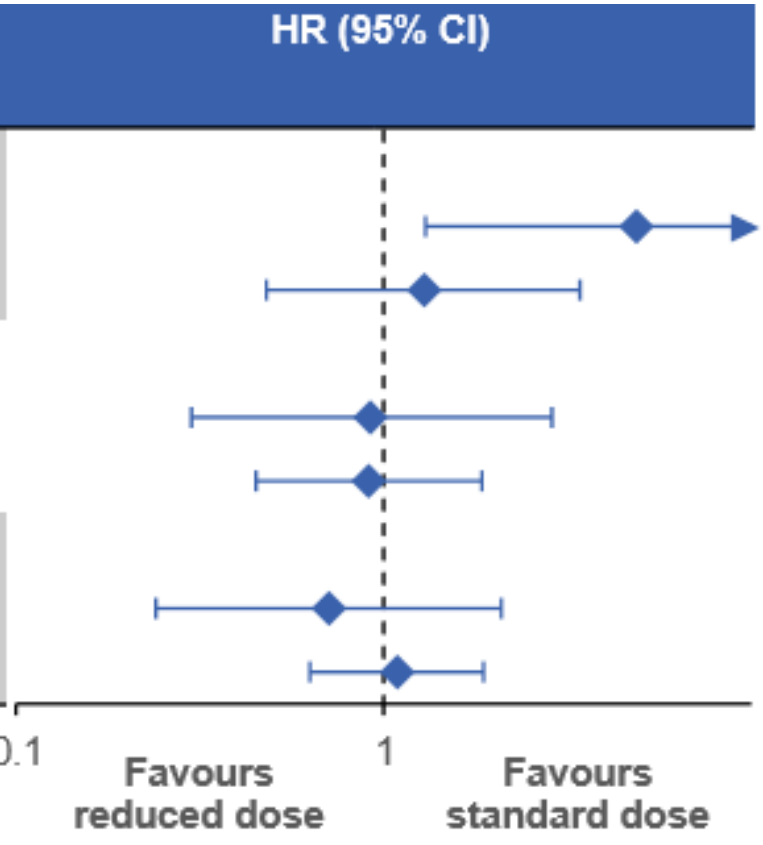
„When less is not more“

Pokorney et al.

Yao X et al. J Am Coll Cardiol 2017

St. Theresien-Krankenhaus Nürnberg

	Reduced dose	Standard dose	HR (95% CI)	*p*-value
	Event rate per 100 person-years			
Apixaban	N=550	N=550		
Stroke/SE	2.57	0.54	4.87 (1.30–18.26)	0.02
Major bleeding	6.01	4.64	1.29 (0.48–3.42)	0.61
Dabigatran	N=412	N=412		
Stroke/SE	1.64	1.75	0.92 (0.30–2.87)	0.89
Major bleeding	4.99	5.54	0.91 (0.45–1.85)	0.80
Rivaroxaban	N=815	N=815		
Stroke/SE	1.23	1.65	0.71 (0.24–2.09)	0.54
Major bleeding	5.42	4.90	1.09 (0.63–1.87)	0.76



- Median follow-up: 4.0 months (IQR 1.0–9.6 months)

Lip GYH et al, Thromb Haemost 2014

US Datenbasis (01/2015 – 06/2016): n = 120.051

NEWS | HRS 2018

NOACs Perform Worse Than Warfarin in Real-World Study, Especially When Adherence Is Low

NOAK: n = 67.686; 31% mit unzureichender Einnahme (40 – 80% d. Tage)

VKA: n = 52.365; 47% mit unzureichender Einnahme (40 – 80% d. Tage)

Schlaganfall: - 14% (zuverlässige NOAK-Einnahme; > 80% der Tage)
+ 48%(VKA)/+ 69%NOAK (p < 0.01;unzureichende Einnahme)

Lakkireddy DR et al. Heart Rhythm Society Sessions, Boston, 05/2018

St. Theresien-Krankenhaus Nürnberg

US Datenbasis (01/2015 – 06/2016): n = 120.051

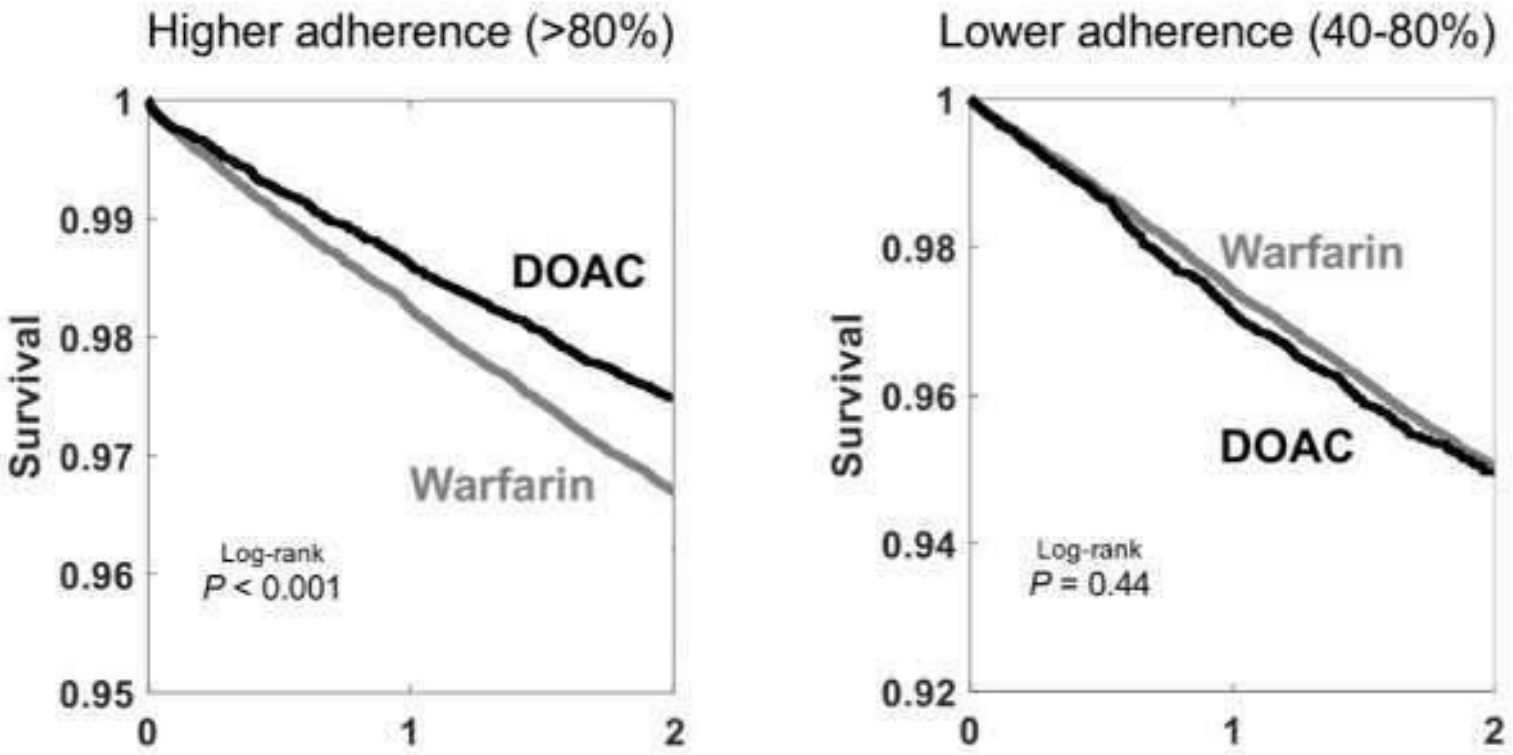


Figure: Freedom from thromboembolic events for patients prescribed warfarin or DOACs with higher and lower adherence.

Lakkireddy DR et al. Heart Rhythm Society Sessions, Boston, 05/2018

St. Theresien-Krankenhaus Nürnberg

Wechselwirkungen

The 2018 European Heart Rhythm Association Practical Guide on the use of non-vitamin K antagonist oral anticoagulants in patients with atrial fibrillation

	Via	Dabigatran etexilate	Apixaban	Edoxaban	Rivaroxaban
P-gp substrate		Yes	Yes	Yes	Yes
CYP3A4 substrate		No	Yes (≈25%)	No (<4%)	Yes (≈18%)
Antiarrhythmic drugs					
Amiodarone	moderate P-gp competition	↑12 to 60%	No PK data*	↑40%	Minor effect*
Digoxin	P-gp competition	No effect	No effect	No effect	No effect
Diltiazem	P-gp competition and weak CYP3A4 inhibition	No effect	↑40%	No data yet	No effect
Dronedarone	P-gp competition and CYP3A4 inhibition	↑70 to 100% (US: 2 × 75 mg if CrCl 30–50 mL/min)	No PK or PD data available	↑85%*	Moderate effect, should be avoided
Quinidine	P-gp competition	↑53%	No data yet	↑77% (no dose reduction required by label)	Extent of increase unknown
Verapamil	P-gp competition (and weak CYP3A4 inhibition)	↑12 to 180% (if taken simultaneously)	No PK data	↑53% (SR) (no dose reduction required by label)	No effect
Other cardiovascular drugs					
Atorvastatin	P-gp competition and CYP3A4 inhibition	No relevant interaction	No data yet	No effect	No effect
Ticagrelor	P-gp competition	↑25% (give loading dose 2h after dabigatran)*	No data	No data	No data
Antibiotics					
Clarithromycin; Erythromycin	Moderate P-gp competition and strong CYP3A4 inhibition	↑15 to 20%	↑60% AUC ↑30% C_{max}	↑90%	↑34% (Erythromycin)/ ↑54% (Clarithromycin)
Rifampicin	P-gp/BCRP and CYP3A4/ CYP2J2 inducers	Minus 66%	Minus 54%	Minus 35%, but with compensatory increase of active metabolites	Up to minus 50%

Steffel J et al. EHJ 2018

Zusammenfassung

Orale Antikoagulation im Verlauf verbessert

Signifikanter Anteil mit Unter- (und Über-) versorgung

Differenzierter Einsatz der NOAKs

Richtig dosieren