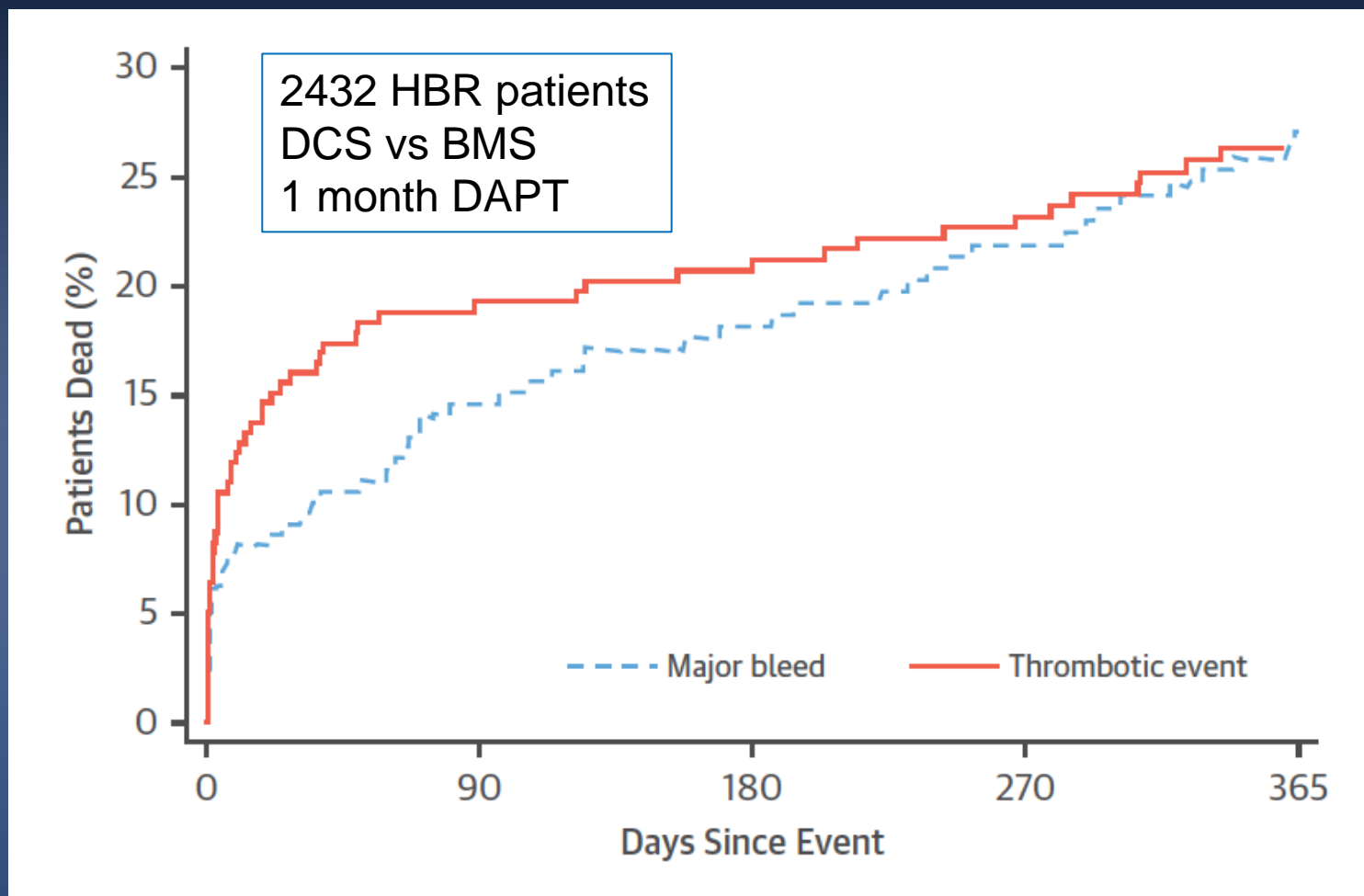


# Bleeding Risk after PCI: stents, drugs and others choices

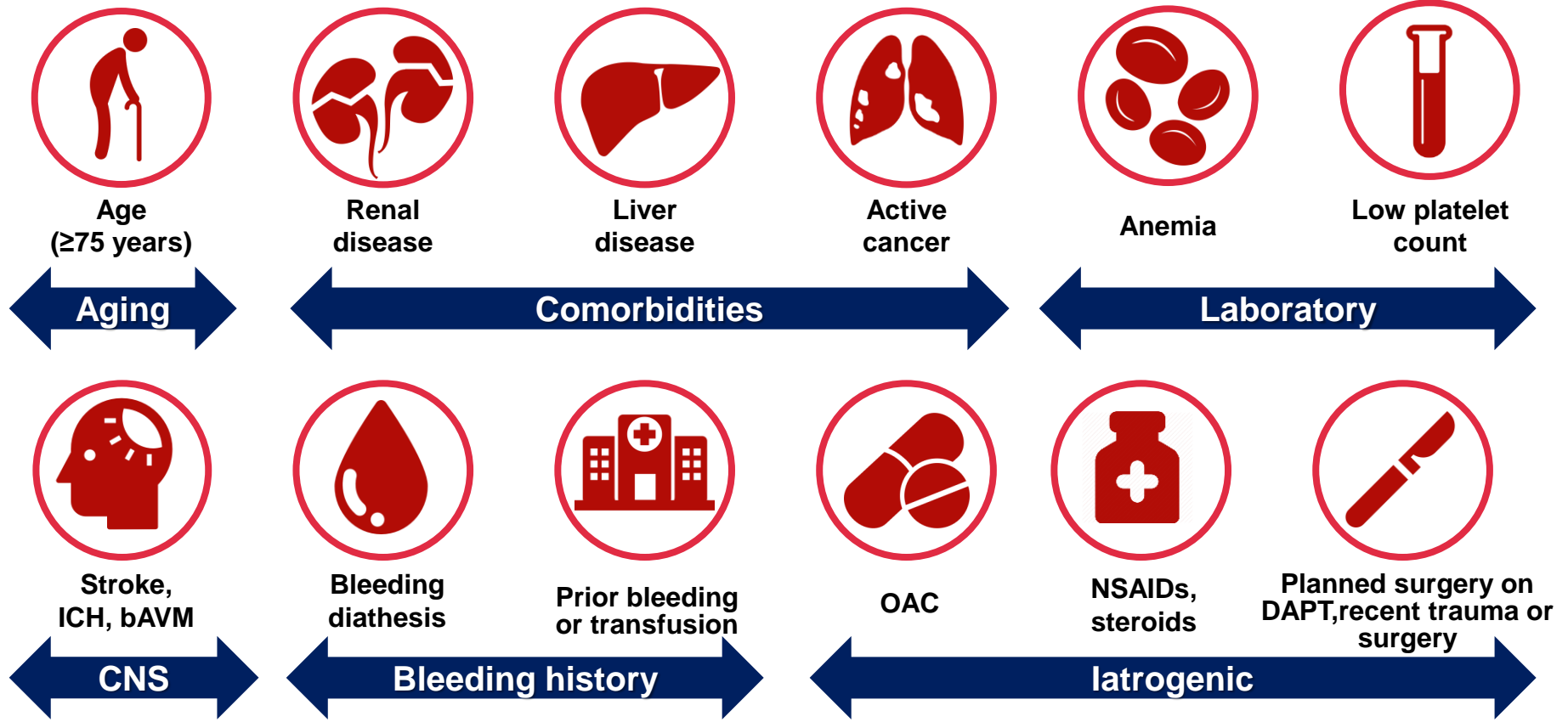
Philip Urban, La Tour Hospital,  
Geneva, Switzerland

# Does bleeding matter?

## 1-Year Mortality Following a Major Bleed or a Coronary Thrombotic Event



# Who is at risk?



# The ARC Focus Group on HBR



- Compliant with the ARC Charter, organized by CERC Europe
- Non-profit initiative, sponsored by 22 pharma and device companies
- 31 experts from Europe, USA, Japan and South Korea
- Two meetings in 2018 - Washington (US), April 13-14 and Paris (FR), October 19-20

ARC HBR definition to be presented at Euro-PCR, Paris, May 22

# Bleeding Risk after PCI: stents, drugs and others choices

- **Stents**
- Drugs
- Other options

# DES: 12 completed trials of short DAPT ( $\leq 3$ months)

trial	stent	type	limus kinetics	patients	experimental arm DAPT	control arm	primary endpoint
RESET (1)	Endeavor ZES	1 <sup>st</sup> G permanent polymer	fast	2117 low/med risk	3 months	Other DES & 12 months DAPT	Non-inferiority for NACCE
OPTIMIZE (2)	Endeavor ZES	1 <sup>st</sup> G permanent polymer	fast	3119 low/med risk	3 months	E-ZES & 12 months DAPT	Non-inferiority for NACCE
ZEUS (3)	Endeavor ZES	1 <sup>st</sup> G permanent polymer	fast	1606 doubtful DES candidates	30-180 days (IQR) median 32 days	BMS & same DAPT	Superiority for MACE
REDUCE (4)	Combo	DES + CD34 AB	slow	1500 ACS	3 months	12 months DAPT	Non-inferiority for NACCE
STOPDAPT-2 (9)	Xience EES	2 <sup>nd</sup> G permanent polymer	slow	3000 low/med risk successful PCI	1 month	1 year DAPT	Superiority for NACE (driven by lower bleeding rate)
SMART CHOICE (10)	2ndG DES (EES, SES)	any	na	3000 all-comers successful PCI	3 months (then P2Y12 SAPT)	1 year DAPT	Non-inferiority for MACE (superior for BARC2-5)
GLOBAL LEADERS (11)	BioMatrix BES	BD polymer	slow	16000 all-comers	1 mth ASA + tica. Then 23 mths <u>tica</u> . <u>SAPT</u>	Same stent, 1 year DAPT then SAPT	Not superior to guideline-based DAPT (Lancet 2018)
ReCre8 (12)	Cre8 Amphilimus-SES	polymer-free	slow	1532 all-comers	SCAD 1 month ACS 12 months	R-ZES same DAPT	Non-inferior (not powered for DAPT)
LEADERS FREE (5)	BioFreedom BA9 DCS	polymer-free	fast	2400 HBR	1 month	<b>BMS &amp; 1 month DAPT</b>	Superiority for safety Superiority for efficacy
ZEUS HBR (6)	Endeavor ZES	1 <sup>st</sup> G permanent polymer	fast	828 HBR	30 days	<b>BMS &amp; same DAPT</b>	Superiority for MACE
SENIOR (7)	Synergy EES	2 <sup>nd</sup> G biodeg. polymer	slow	1200 age $\geq 75$	1 month (SCAD) or 6 months (ACS)	<b>BMS &amp; same DAPT</b>	Superiority for MACE
LEADERS FREE II (8)	BioFreedom BA9 DCS	polymer-free	fast	1200 HBR	1 month	<b>BMS arm of LEADERS FREE</b>	Superiority for safety Superiority for efficacy



1) Kim B-K et al. JACC 2012; 60: 1340-8  
 2) Feres F et al. JAMA 2013; 310: 2510-22  
 3) Valgimigli M et al. JACC 2015;65:805-15  
 4) Suryanapranata H et al, presented TCT 2017  
 5) Urban P et al. NEJM 2015; 373: 2038-47  
 6) Ariotti S et al. JACC interv 2016; 9: 426-36  
 7) Varenne O et al. Lancet 2017; 391: 41-50  
 8) Krucoff M. et al TCT 2018  
 9) Watanabe H et al. ACC 2019  
 10) Hahn JH et al. ACC2019  
 11) Vranckx P et al, Lancet 2018  
 12) ReCre8, Stella P et al,

# 10 ongoing trials of $\leq 3$ months DAPT for HBR patients

	Trial	stent	type	limus kinetics	patients	experimental arm DAPT	control arm	Status September 2018
randomized	ONYX ONE	Resolute Onyx DES vs. BioFreedom DCS	Permanent polymer vs. polymer-free	slow vs. fast	2000 HBR	1 month	1 month	follow-up
	COBRA-REDUCE	Cobra PzF	Polyzene-F nanocoating	na	840 on AVK or NOAC	2 weeks	EES or R-ZES & 6 months DAPT	enrolling
	MASTER DAPT	Ultimaster SES	2 <sup>nd</sup> G BD polymer	slow	4300 HBR	1 month	guidelines	enrolling
	TARGET SAFE	Firehawk	Biodegradable polymer	slow	1700 HBR	1 months DAPT	6 months DAPT	planned
single arm	EVOLVE SHORT DAPT	Synergy EES	2 <sup>nd</sup> G BD polymer	slow	2000 HBR	3 months	single arm trial	follow-up
	POEM	Synergy EES	2 <sup>nd</sup> G BD polymer	slow	1023 HBR	1 month	single arm trial	enrolling
	XIENCE 90 (Xience Short DAPT)	Xience EES	Permanent polymer	slow	2000 HBR	3 months	single arm trial	enrolling
	XIENCE Global 28	Xience EES	Permanent polymer	slow	800 HBR	1 month	single arm trial	enrolling
	ONYX ONE CLEAR	Resolute Onyx DES	Permanent polymer	slow	800 HBR	1 month	Single arm trial	enrolling
	LEADERS FREE III	CoCr BioFreedom	Polymer-free	fast	1200 HBR	1 month	DCS arm of LEADERS FREE	enrolling

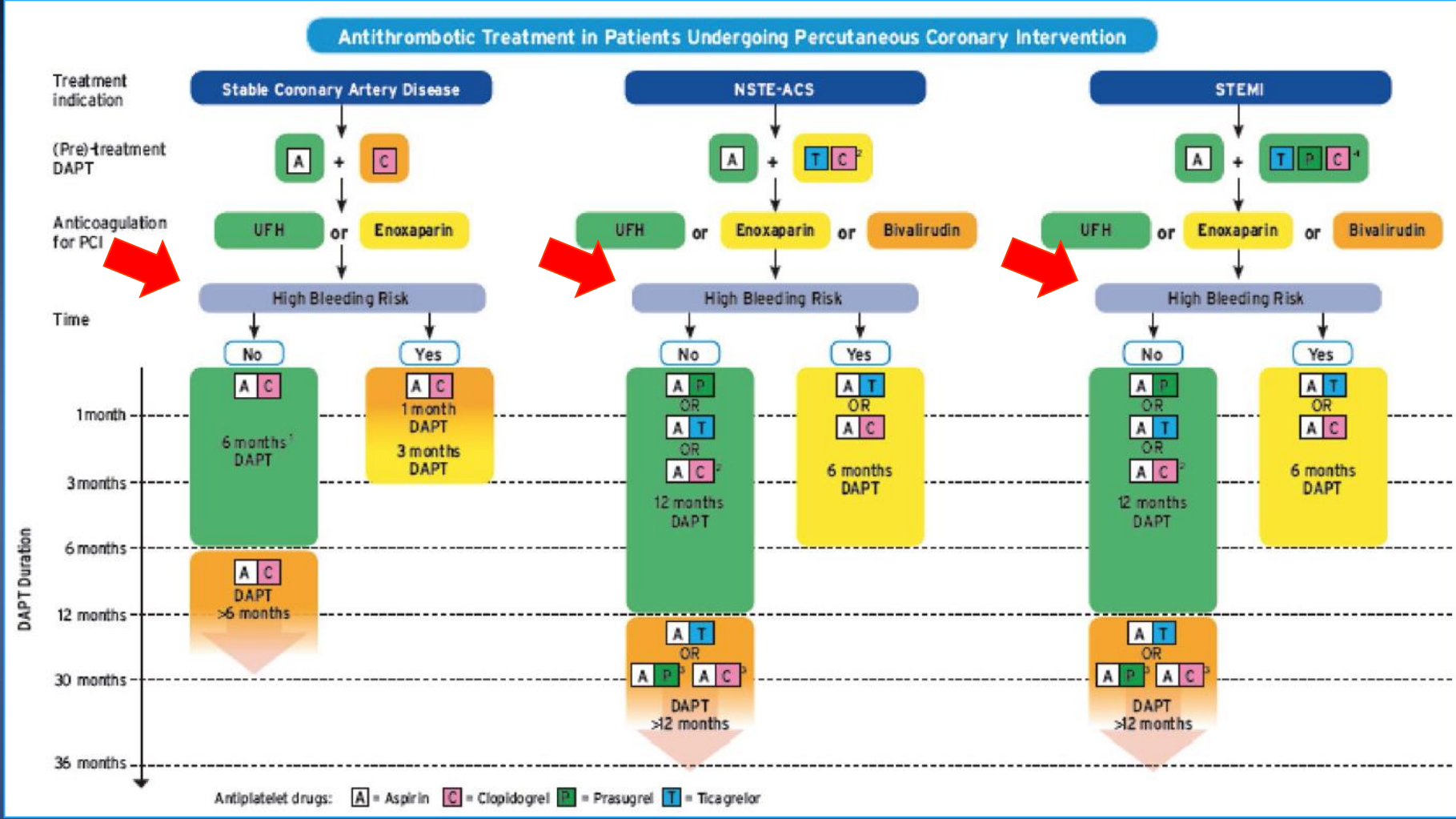
# Bleeding Risk after PCI: stents, drugs and others choices

- Stents
- **Drugs**
- Other options

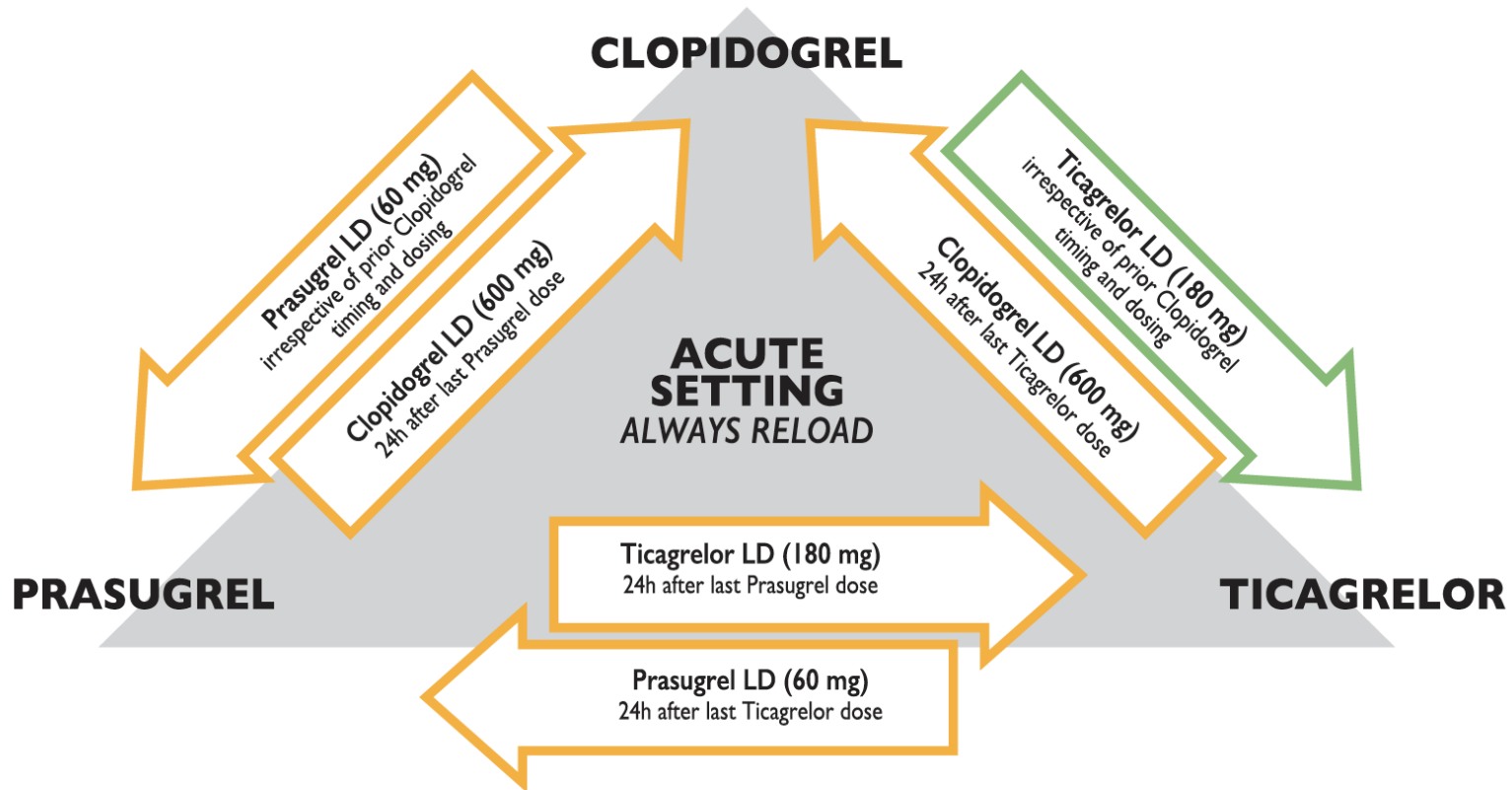


# 2018 ESC/EACTS Guidelines on myocardial revascularization

(Neuman F–J et al. European Heart Journal 2018 doi:10.1093/eurheartj/ehy394)



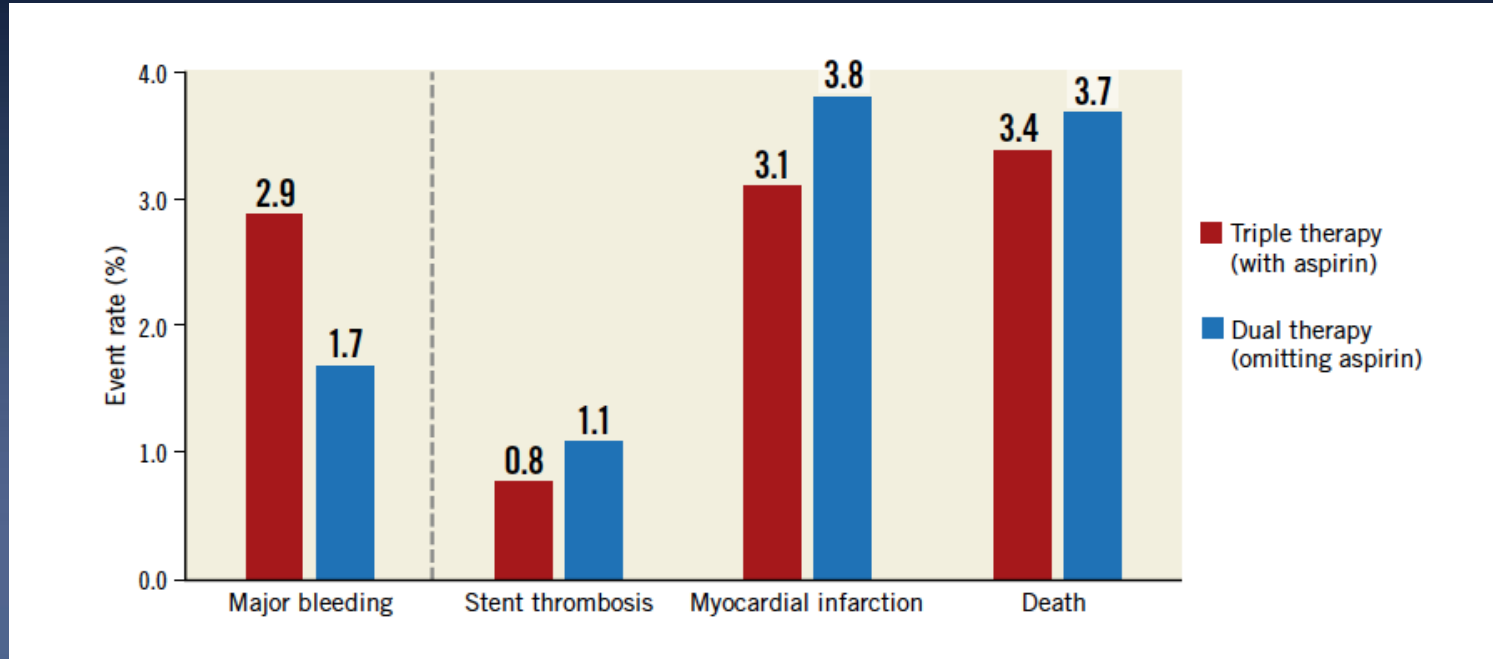
# P2Y12 SWITCHING



© ESC 2017

# Omission of aspirin after ACS or stenting in patients with OAC

Robert Byrne, EuroIntervention 2019;14:e1793–e1795



4 trials: WOEST, PIONEER–AF, REDUAL–AF, AUGUSTUS 9924 patients

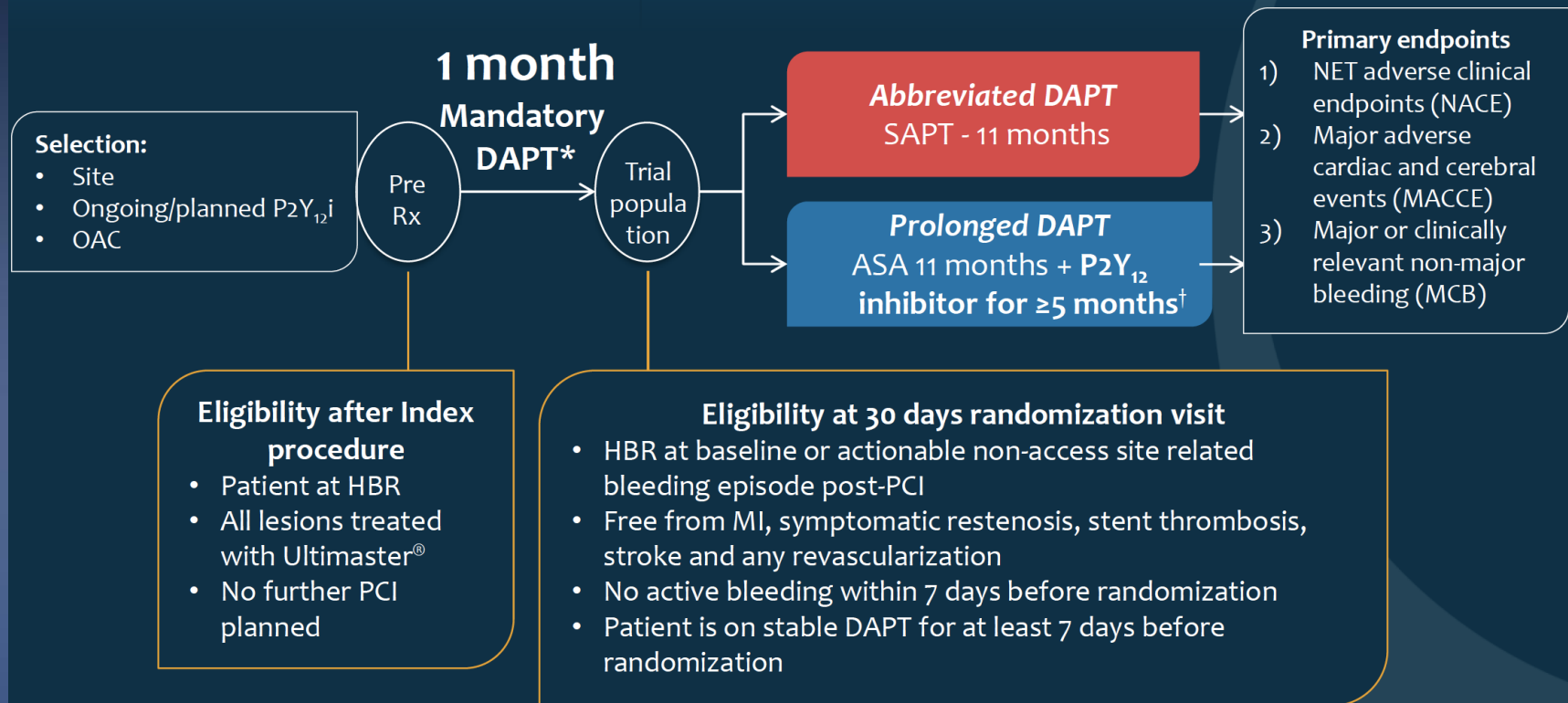
“systematic adoption of dual therapy for all patients receiving oral anticoagulation with ACS or undergoing coronary intervention would seem ill–advised, as we cannot be sure that omitting aspirin does not cause harm. At a minimum, it would seem pertinent that the period of highest risk for stent thrombosis should be covered by DAPT”

# DAPT: how long & how short?



# Study Design and Key Features

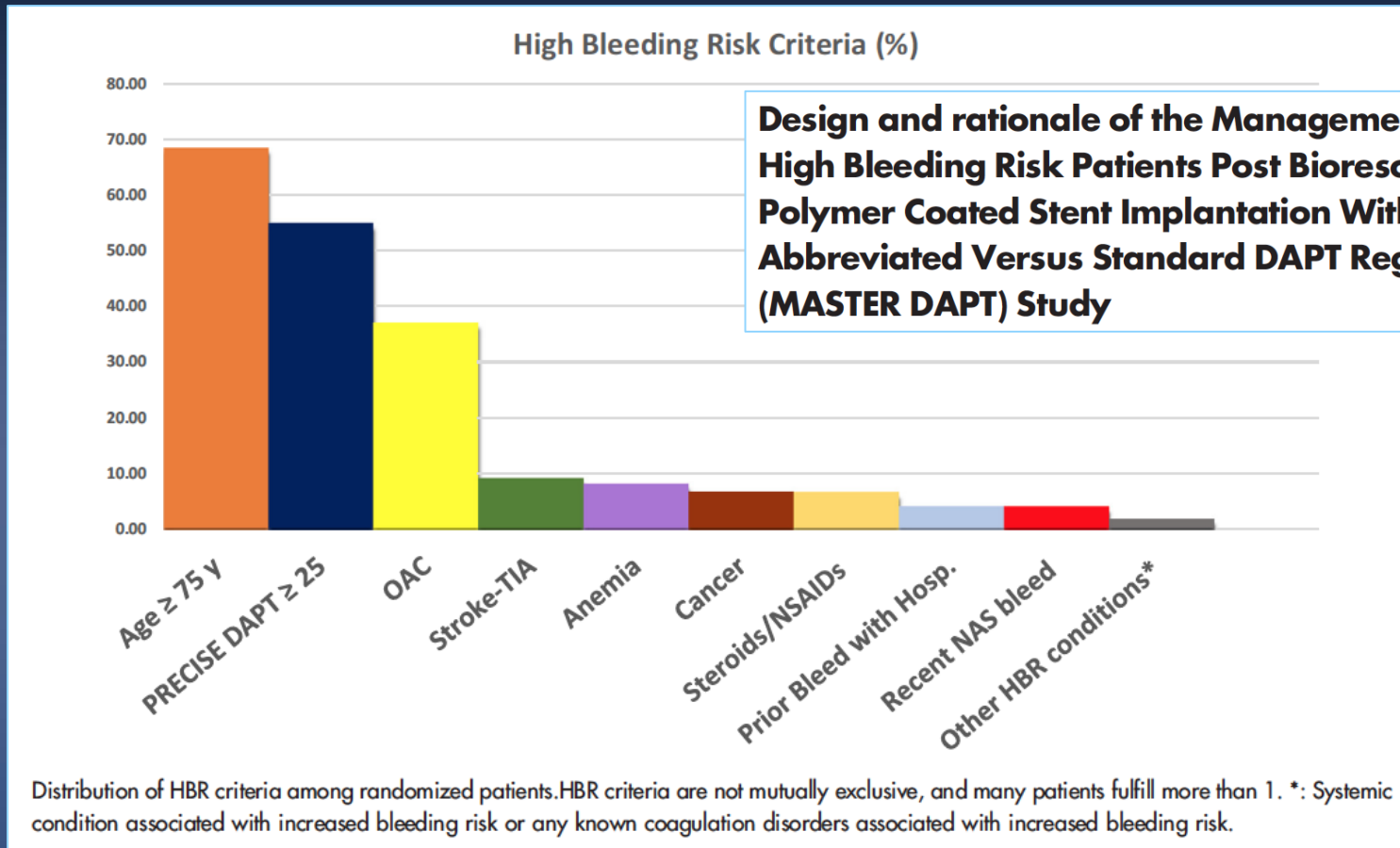
4300 patients - >100 international sites



\*DAPT duration is counted from the day of last implanted stent; staging has to be pre-specified at the time of screening and cannot be planned later than 2 months after index PCI; <sup>†</sup>Patients on OAC can stop DAPT 2 months after confirmed randomization

ASA, acetylsalicylic acid; MI, myocardial infarction; SAPT, single antiplatelet therapy

# HBR criteria applied (n=2196)



# Bleeding Risk after PCI: stents, drugs and others choices

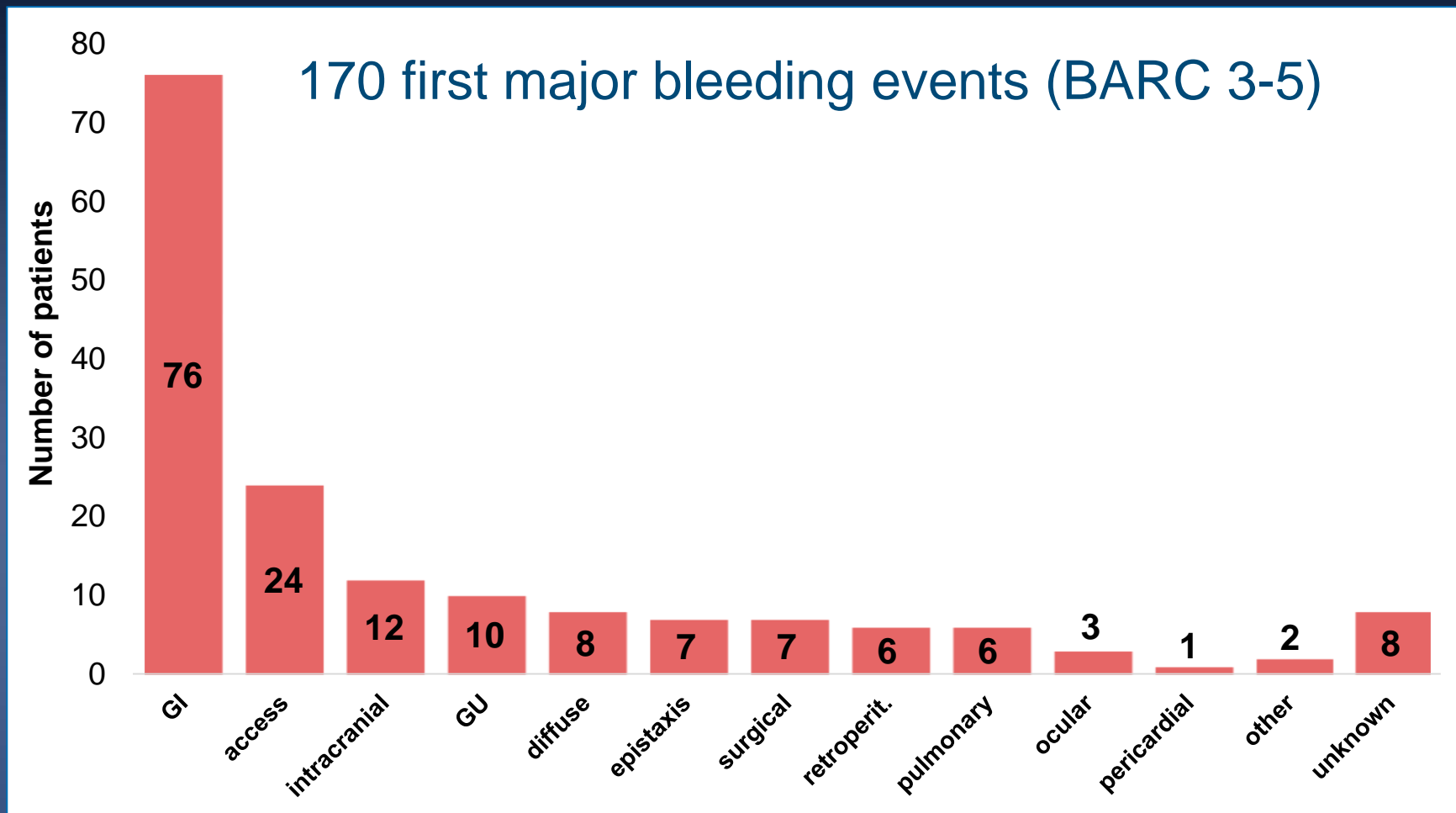
- Stents
- Drugs
- **Other options**

# Bleeding Risk after PCI: drugs, stents and others choices

- **Radial access** ✓
- **Liberal use of PPI**
- **Also assess thrombotic risk**



# Location of Major Bleeding



# Bleeding Risk after PCI: drugs, stents and others choices

- Radial access
- Liberal use of PPI
- Also assess thrombotic risk

# High-risk features of stent-driven recurrent ischaemic events

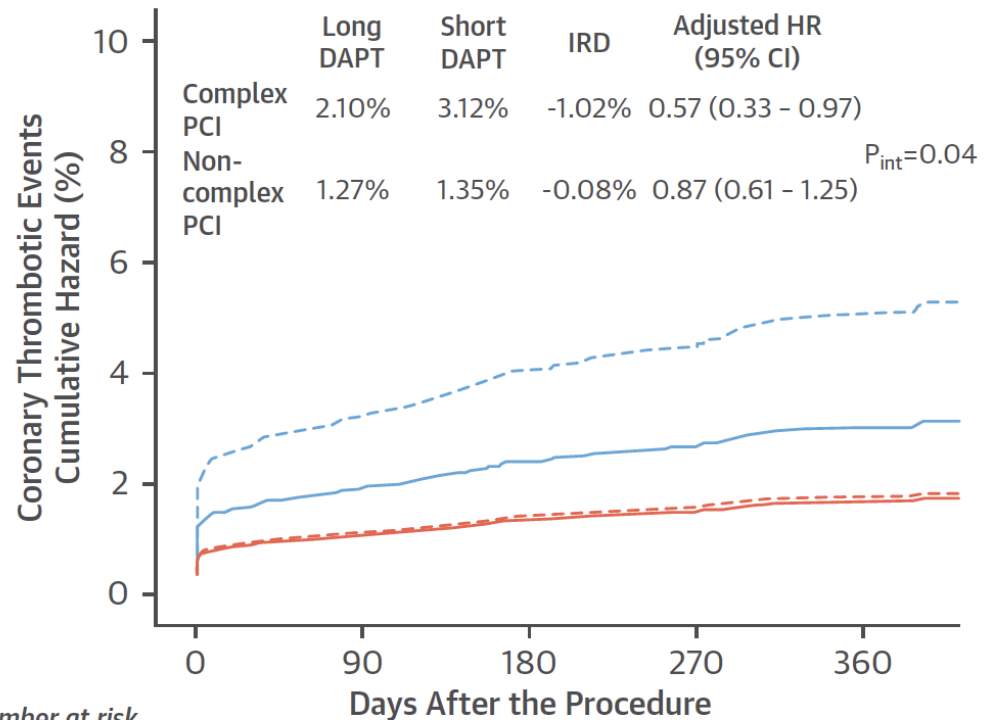
- Prior stent thrombosis on adequate antiplatelet therapy
- Stenting of the last remaining patent coronary artery
- Diffuse multivessel disease especially in diabetic patients
- Chronic kidney disease (i.e. creatinine clearance <60 mL/min)
- At least three stents implanted
- At least three lesions treated
- Bifurcation with two stents implanted
- Total stent length >60 mm
- Treatment of a chronic total occlusion

**+ SVG**

# Complex PCI in DAPT trials after PCI

1680 patients of 9577 (17.5%)  
underwent complex PCI  
Data from PRODIGY, OPTIMIZE, RESET,  
EXCELLENT, SECURITY, ITALIC.

Complex PCI		Non-complex PCI	
Long DAPT	—	Long DAPT	—
Short DAPT	- - -	Short DAPT	- - -



	Number at risk				
	0	90	180	270	360
Non-complex PCI - Short DAPT	3938	3873	3817	3784	3515
Non-complex PCI - Long DAPT	3932	3875	3828	3797	3524
Complex PCI - Short DAPT	801	776	767	760	671
Complex PCI - Long DAPT	840	817	806	797	694

# Conclusions

- For HBR patients considered to require ultra-short (1 month) DAPT today, the BA-9 DCS (stable or ACS presentation) and the biodegradable polymer EES (stable presentation) are superior to BMS
- Clopidogrel is generally the preferred P2Y12 blocker for HBR patients, either immediately or following early de-escalation, and there is increasing (but not definitive) evidence that dual rather than triple therapy should often be preferred early after PCI for patients on oral anticoagulation
- The optimal duration and intensity of DAPT for HBR patients is currently not known. The MASTER-DAPT trial will help to better understand the trade-off between bleeding and thrombotic risks