

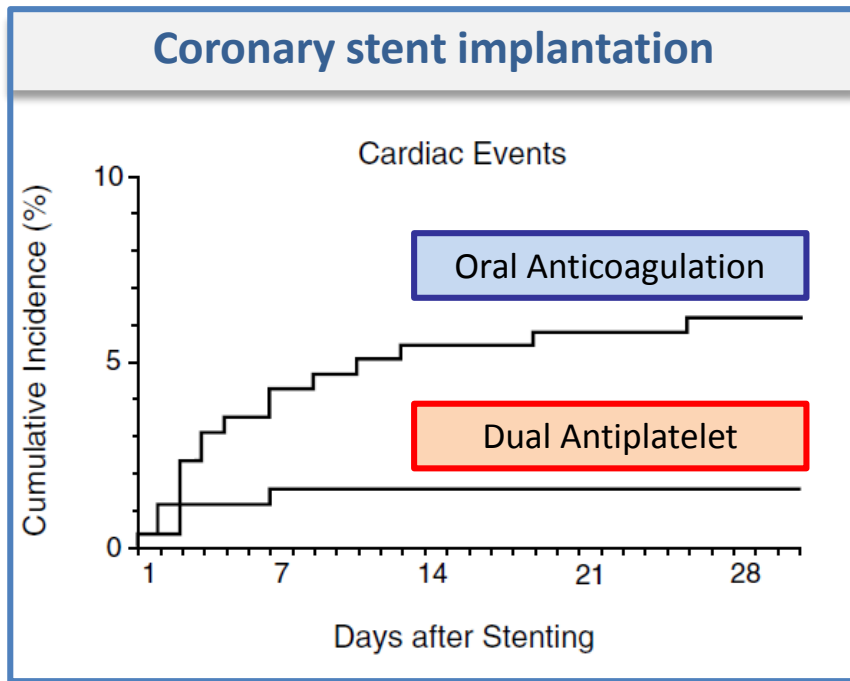
Duration of triple therapy in patients requiring oral anticoagulation after drug-eluting stent implantation (ISAR-TRIPLE Trial)

Katrin A. Fiedler, Michael Maeng, Julinda Mehilli, Stefanie Schulz, Robert A. Byrne, Dirk Sibbing, Petra Hoppmann, Simon Schneider, Massimiliano Fusaro, Ilka Ott, Steen D. Kristensen, Tareq Ibrahim, Steffen Massberg, Heribert Schunkert, Karl-Ludwig Laugwitz, Adnan Kastrati and Nikolaus Sarafoff

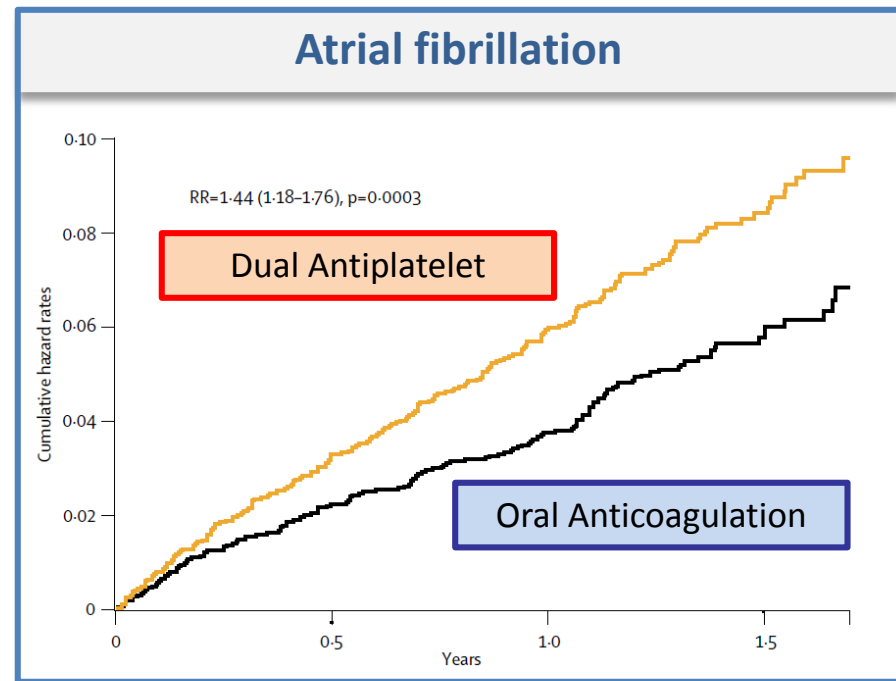
Deutsches Herzzentrum, Technische Universität, Munich, Germany; Aarhus University Hospital, Aarhus, Denmark; Klinikum der Ludwig Maximilians Universität, Munich, Germany; Klinikum rechts der Isar, Technische Universität, Munich, Germany

All faculty disclosures are available on
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Background



ISAR, NEJM 1996



ACTIVE-W Lancet 2006



Dual Antiplatelet



Oral Anticoagulation

Background

- **Such triple therapy increases the risk of bleeding however.**
- **The optimal duration of triple therapy after drug-eluting stent (DES) implantation has not been defined. Two factors need to be considered in this regard:**
 1. The risk of stent thrombosis is highest in the early phase after PCI and declines over time
 2. The risk of bleeding is dependent on length and intensity of OAC therapy

Objective

To evaluate clinical outcomes of a therapy duration
of

6 weeks clopidogrel

versus

6 months clopidogrel

after DES implantation in patients receiving
concomitantly aspirin and oral anticoagulation

ISAR-TRIPLE: Study Organization

DESIGN:

Prospective, randomized open-label trial

INCLUSION CRITERIA:

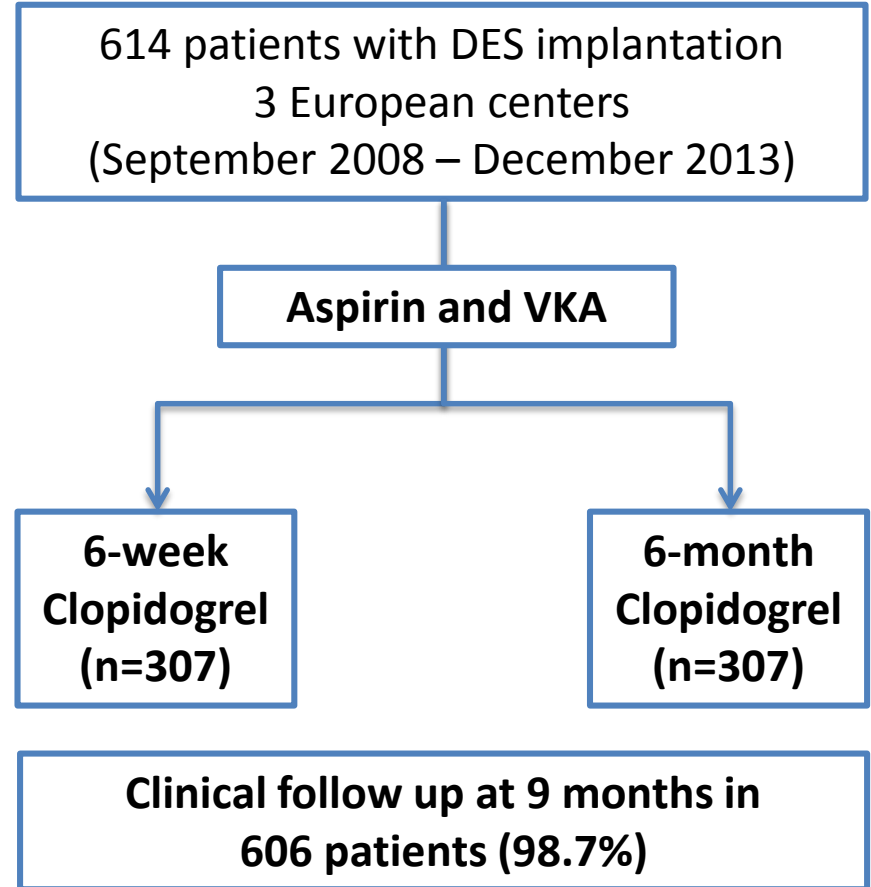
DES implantation and indication for oral anticoagulation

MAJOR EXCLUSION CRITERIA:

Previous stent thrombosis
DES in left main coronary artery

SPONSOR:

Deutsches Herzzentrum Munich,
(ClinicalTrials.gov # NCT00776633)



ISAR-TRIPLE: Study Organization

TEST HYPOTHESES:

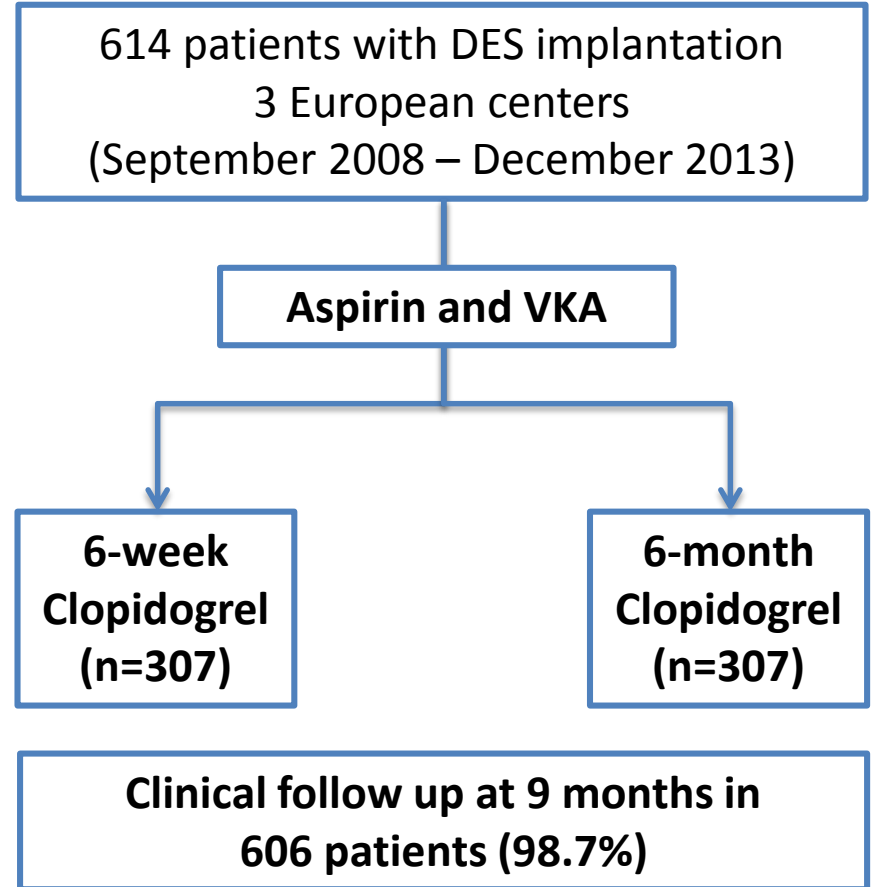
6-week superior to 6-month therapy;
Primary Endpoint 10%, Risk reduction
60% with 6-week therapy; Power = 80%,
alpha = 0.05; 283 patients per group

PRIMARY ENDPOINT:

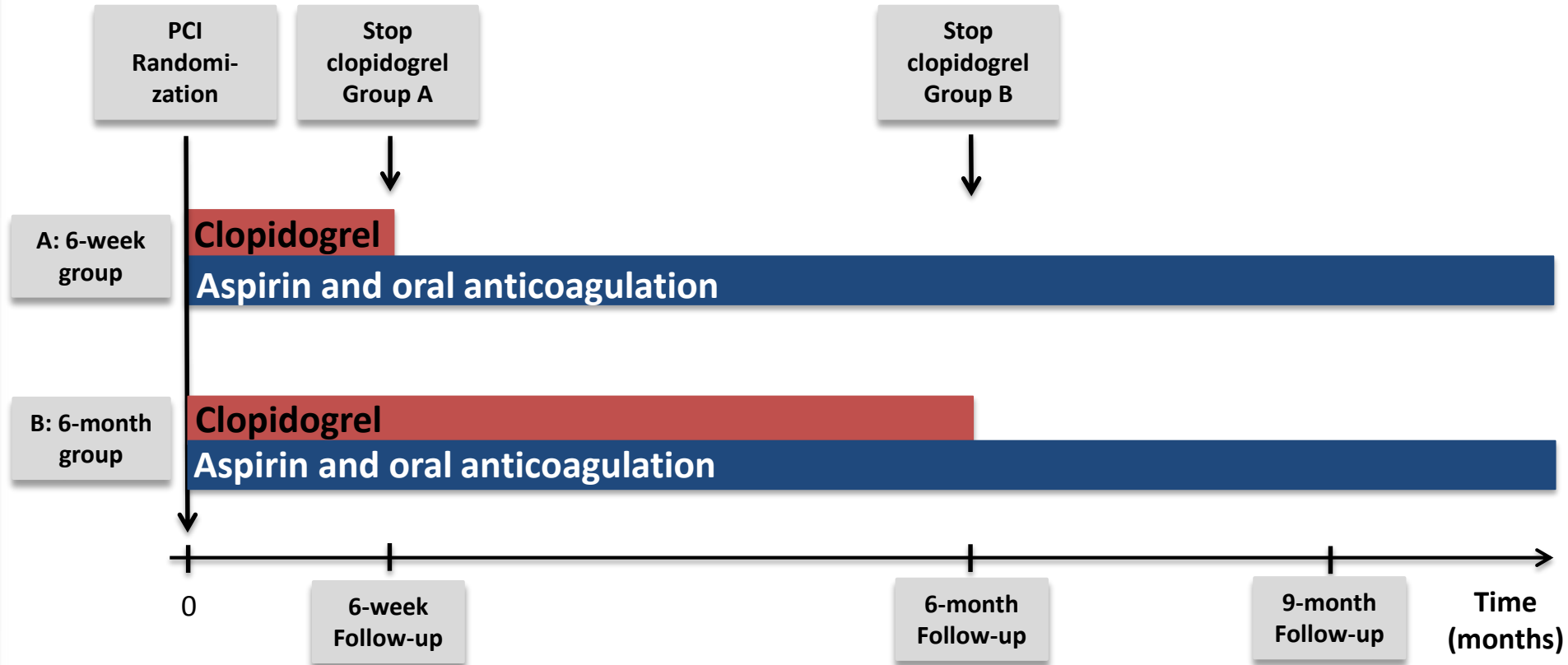
- Death, myocardial infarction, definite stent thrombosis, stroke or TIMI major bleeding at 9 months

SECONDARY ENDPOINTS:

- Ischemic complications: Cardiac death, myocardial infarction, definite stent thrombosis or ischemic stroke
- Bleeding complications (TIMI major)



Randomization



ISAR-TRIPLE Investigators

- **Deutsches Herzzentrum Munich, Germany:** Katrin A. Fiedler, Stefanie Schulz, Robert A. Byrne, Massimiliano Fusaro, Ilka Ott, Heribert Schunkert, Adnan Kastrati
- **Aarhus University Hospital, Aarhus, Denmark:** Michael Maeng, Steen D. Kristensen
- **Klinikum rechts der Isar, Munich, Germany:** Petra Hoppmann, Simon Schneider, Tareq Ibrahim, Karl-Ludwig Laugwitz
- **Klinikum der Ludwig Maximilians Universität, Munich, Germany:** Julinda Mehilli, Dirk Sibbing, Steffen Massberg, Nikolaus Sarafoff

Baseline Characteristics

		6-week group (n=307)	6-month group (n=307)
Age (years)		74 ± 8	73 ± 9
Female sex		25 %	21 %
Diabetes		28 %	23 %
History of myocardial infarction		29 %	25 %
Clinical presentation	ACS	33 %	31 %
	Stable Angina	67 %	69 %
Indication for OAC *	Atrial fibrillation	83 %	85 %
	Mechanical valve	5 %	9 %
	VTE	7 %	4 %
	other	4 %	2 %

*p=0.03; OAC= Oral Anticoagulation; VTE= Venous Thrombembolism

Antithrombotic therapy

ASPIRIN:

75-200 mg per day

CLOPIDOGREL:

75 mg per day

PHENPROCOUMON or WARFARIN:

Target INR 2.0 or 2.5 in patients with mechanical valves

Compliance	6-week FU	6-month FU	9-month FU
Aspirin*	97 %	95 %	96 %
OAC*	94 %	91 %	88 %
INR (median)*	2.2	2.3	2.3
Time in therapeutic range *	64 %	69 %	66 %
Clopidogrel 6-week group	97 %	26 %	23 %
Clopidogrel 6-month group	98 %	87 %	35 %

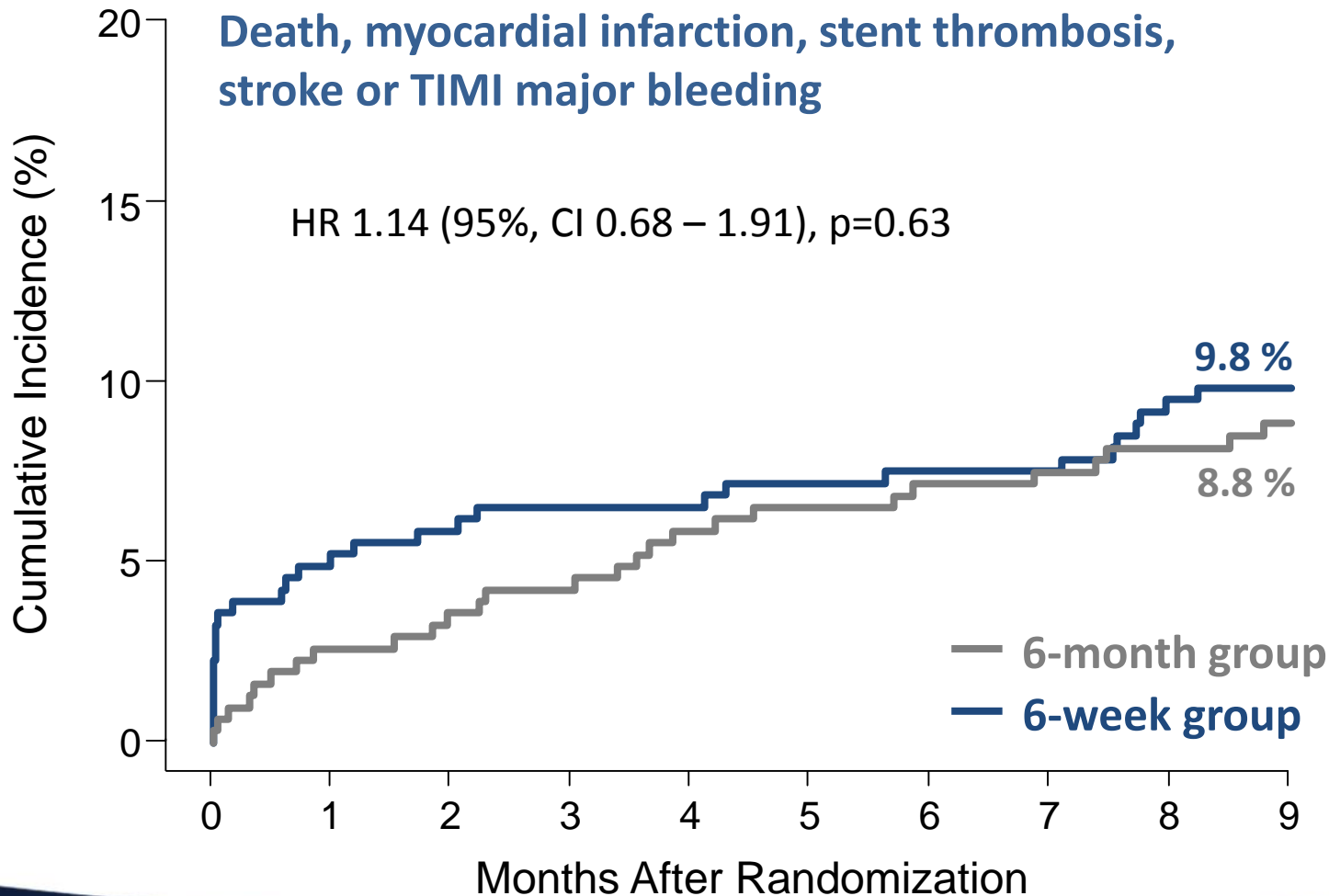
*No significant differences between groups; FU= Follow Up time point

Stent type

	6-week group (417 lesions)	6-month group (409 lesions)
2nd gen. permanent polymer DES	203 (48.7)	206 (50.4)
Biodegradable polymer DES	131 (31.4)	134 (32.8)
Polymer free DES	45 (10.8)	46 (11.2)
1st gen. permanent polymer DES	29 (6.9)	16 (3.9)
BVS	4 (1.0)	3 (0.7)
BMS*	2 (0.5)	0
DEB/PTCA**	3 (0.7)	4 (1.0)

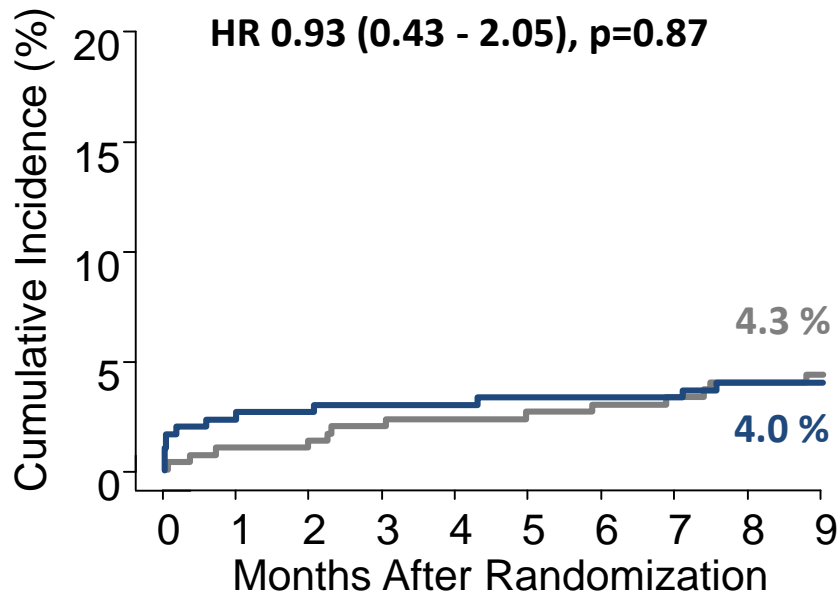
DES = Drug-eluting stent; BMS = Bare-metal stent; BVS = Bioresorbable vascular scaffold; DEB = Drug-eluting balloon; *One patient had 1 DES and 1 BMS and 1 patient had 1 BMS only. ** These patients were treated with drug eluting balloons (DEB) except for 1 patient in the 6-week group and 1 patient in the 6-month group.

Primary Endpoint

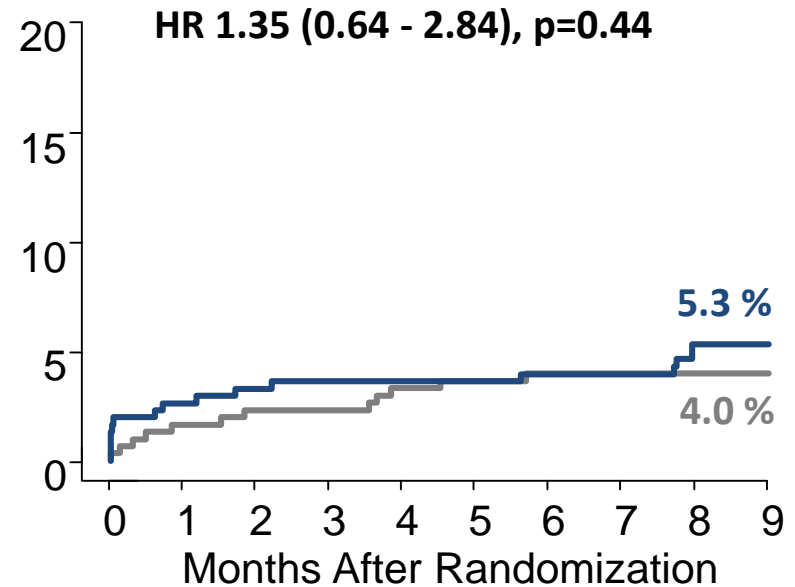


Secondary Endpoints

Cardiac death, myocardial infarction,
stent thrombosis or ischemic stroke



TIMI major bleeding



— 6-month group
— 6-week group

Results

	6-week group (n=307)	6-month group (n=307)	Hazard ratio (95% CI)	p value
Death	12 (4.0)	16 (5.2)	0.75 (0.35 - 1.59)	0.45
Cardiac death	5 (1.7)	9 (3.0)	0.56 (0.19 - 1.66)	0.29
Myocardial infarction	6 (2.0)	0	-	0.03
Definite stent thrombosis	2 (0.7)	0	-	0.50
Stroke	4 (1.3)	6 (2.0)	0.67 (0.14 - 2.78)	0.75
Ischemic stroke	3 (1.0)	4 (1.3)	0.75 (0.11 - 4.40)	0.99

Temporal distribution of MIs in 6-week group:

4 within 24h of PCI

1 at 2.5 weeks

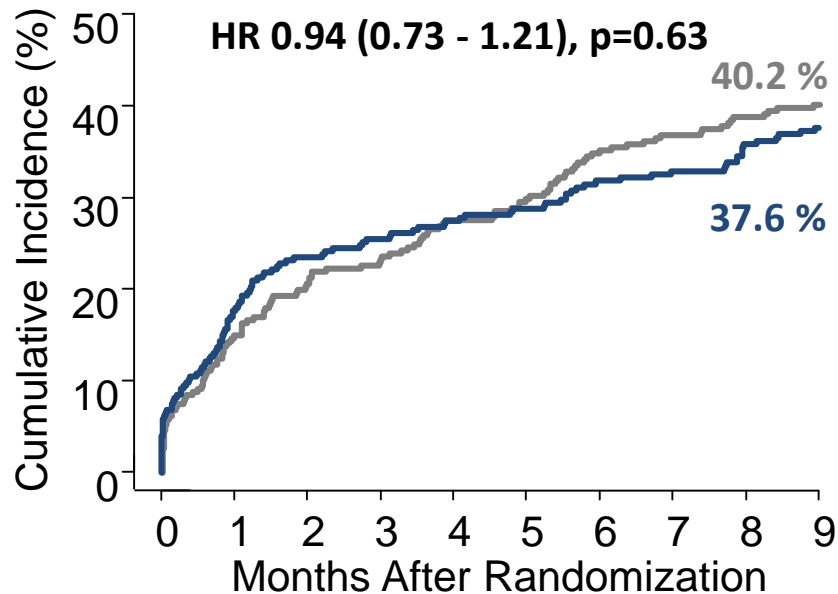
1 at 7 months

} Both groups on triple therapy

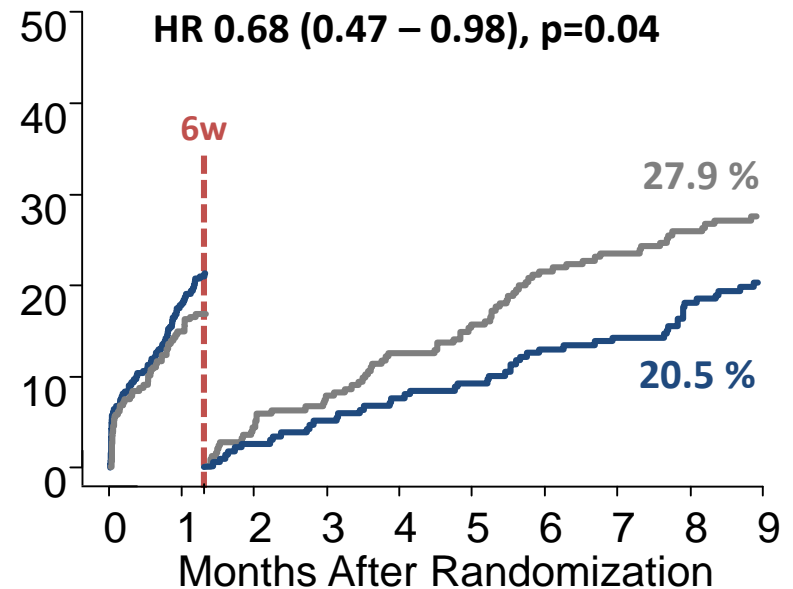
} Both groups on aspirin and OAC

Any BARC Bleeding (type 1-5)

Any BARC Bleeding



Post-hoc landmark analysis of any BARC Bleeding before and after 6 weeks (6w)



— 6-month group
— 6-week group

Conclusion

- **The main finding was that a 6-week triple therapy is not superior to a 6-month triple therapy with regard to net clinical outcomes**
- **Shortening the duration of triple therapy neither reduced the incidence of major bleeding nor increased the incidence of ischemic events**

Conclusion

- **ISAR TRIPLE is the largest randomized trial to date investigating triple therapy after stenting and the first trial evaluating duration of triple therapy**

Thank You For Your Attention