



# **Two-year Clinical and Angiographic Outcomes from a Randomized Trial of Polymer-Free Dual Drug-Eluting Stents versus Polymer-Based Cypher and Endeavor Drug-Eluting Stents**

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Technische Universität Munich Germany**



*Lecture fees from Medtronic*

# Background



- First generation DES systems deliver high antirestenotic efficacy in comparison with BMS but do so at the cost of a delay in structural and functional healing of stented segment

# Delayed Arterial Healing

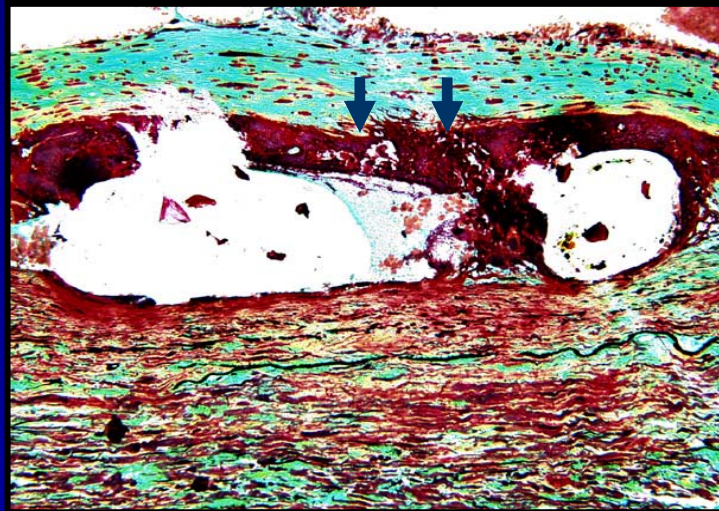
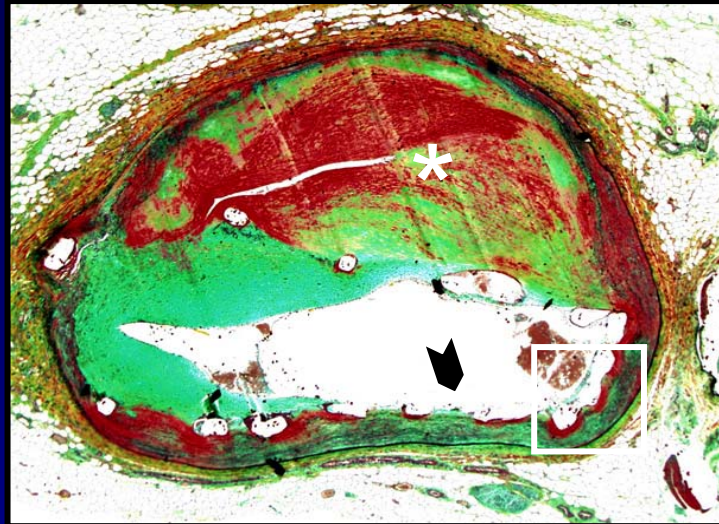


Incomplete  
Endothelialisation

Late Fibrin  
Deposition

Chronic  
Inflammation

Platelet Activation



# Delayed Arterial Healing

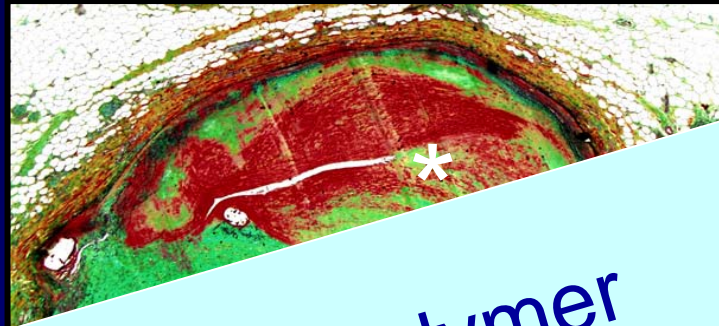


Incomplete  
Endothelialisation

Late Fibrin  
Deposition

Platelet Activation

Inflammatory Response to Polymer  
Residue May Play a Central Role



# Background



- Avoidance of polymer imposes efficacy limitations related to suboptimal drug release kinetics
- The incorporation of a second active agent targeted at a different element of the restenotic response cascade is a potential option to enhance anti-restenotic performance
- Probucol is a potent antioxidant which is also highly lipophilic and enhances the release kinetics of sirolimus

# Aim of ISAR-TEST-2 Study



to compare the anti-restenotic efficacy of:

polymer-free sirolimus+probucol-eluting stent  
**(Dual-DES)**

with

permanent polymer sirolimus-eluting stent  
**(Cypher)**

and

permanent polymer zotarolimus-eluting stent  
**(Endeavor)**

in patients with coronary artery disease



## Inclusion Criteria

- “De novo” lesions in native coronary arteries
- Written informed consent

## Exclusion Criteria

- Left main lesion
- Cardiogenic shock
- Comorbidities with a life expectancy  $< 12$  months
- Contraindication to aspirin, limus agents, probucol, stainless steel, thienopyridines



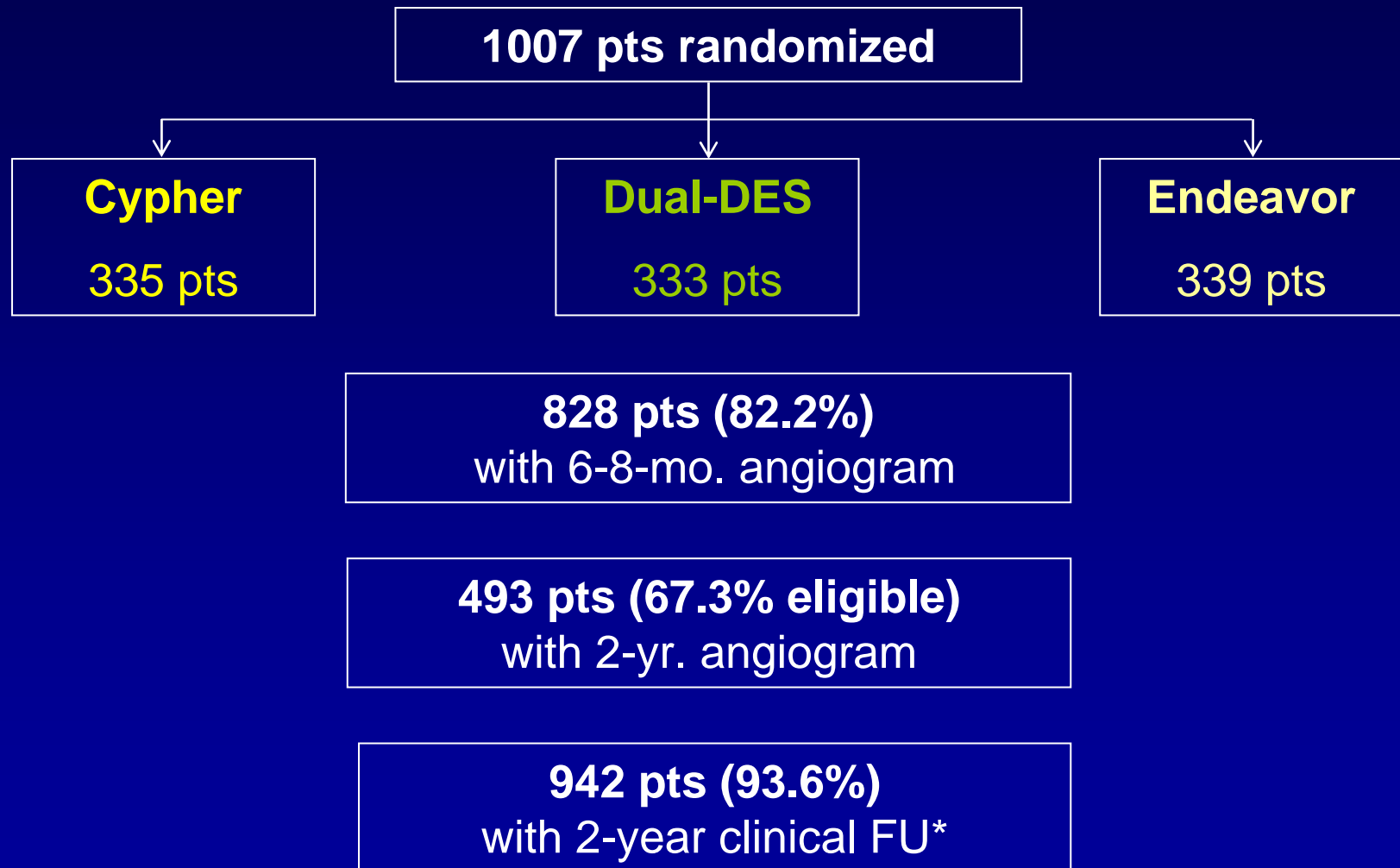
## Two-year **Safety** Endpoints:

- Composite of **death and myocardial infarction**
- **Stent thrombosis** according to ARC criteria

## Two-year **Efficacy** Endpoints:

- **Target lesion revascularization (TLR)** due to restenosis in the presence of symptoms or signs of ischemia
- *Composite binary restenosis* at 2 years based on latest available angiogram (whether at 6-8 months or 2 years)

# ISAR-TEST-2 Study Flow



\*Among n=65 patients without 2-yr FU, median FU was 21 [20-22] months

# Baseline Clinical Characteristics



	Cypher n=335	Dual-DES n=333	Endeavor n=339
Age, years	67 ± 11	67 ± 11	67 ± 11
Women	23	23	25
Arterial hypertension	64	65	68
Diabetes	27	29	26
Current smoker	17	20	18
Hypercholesterolemia	69	63	66
History of MI	30	25	26

*Data are percentage or mean ± standard deviation; Percentages may not total 100 due to rounding*



# Baseline Clinical Characteristics

	Cypher n=335	Dual-DES n=333	Endeavor n=339
Acute MI	13	12	15
Unstable angina	25	30	30
Stable angina	61	58	56
LV ejection fraction (%)	52±12	53±12	55±10

*Data are percentage or mean ± standard deviation; Percentages may not total 100 due to rounding*

# Angiographic Characteristics



	Cypher n=419	Dual-DES n=427	Endeavor n=420
Target vessel			
LAD	49	44	41
LCx	25	25	31
RCA	26	31	29
Multivessel disease	86	81	83
Complex lesions	73	70	75
Total occlusions	12	12	12

*Data are percentage; percentages may not total 100 due to rounding*



	Cypher n=419	Dual-DES n=427	Endeavor n=420
Vessel size, mm	2.75 ± .46	2.69 ± .52	2.71 ± .49
Lesion length, mm	14.8 ± 8.3	14.0 ± 8.2	14.7 ± 8.0
MLD after PCI, mm	2.55 ± .43	2.49 ± .48	2.51 ± .47
DS after PCI, %	10.8 ± 5.7	11.6 ± 5.0	10.7 ± 7.0



# ISAR-TEST-2

## Primary Results



European Heart Journal (2009) 30, 923–931  
doi:10.1093/eurheartj/ehp044

**CLINICAL RESEARCH**

*Interventional cardiology and angiology*

## A polymer-free dual drug-eluting stent in patients with coronary artery disease: a randomized trial vs. polymer-based drug-eluting stents

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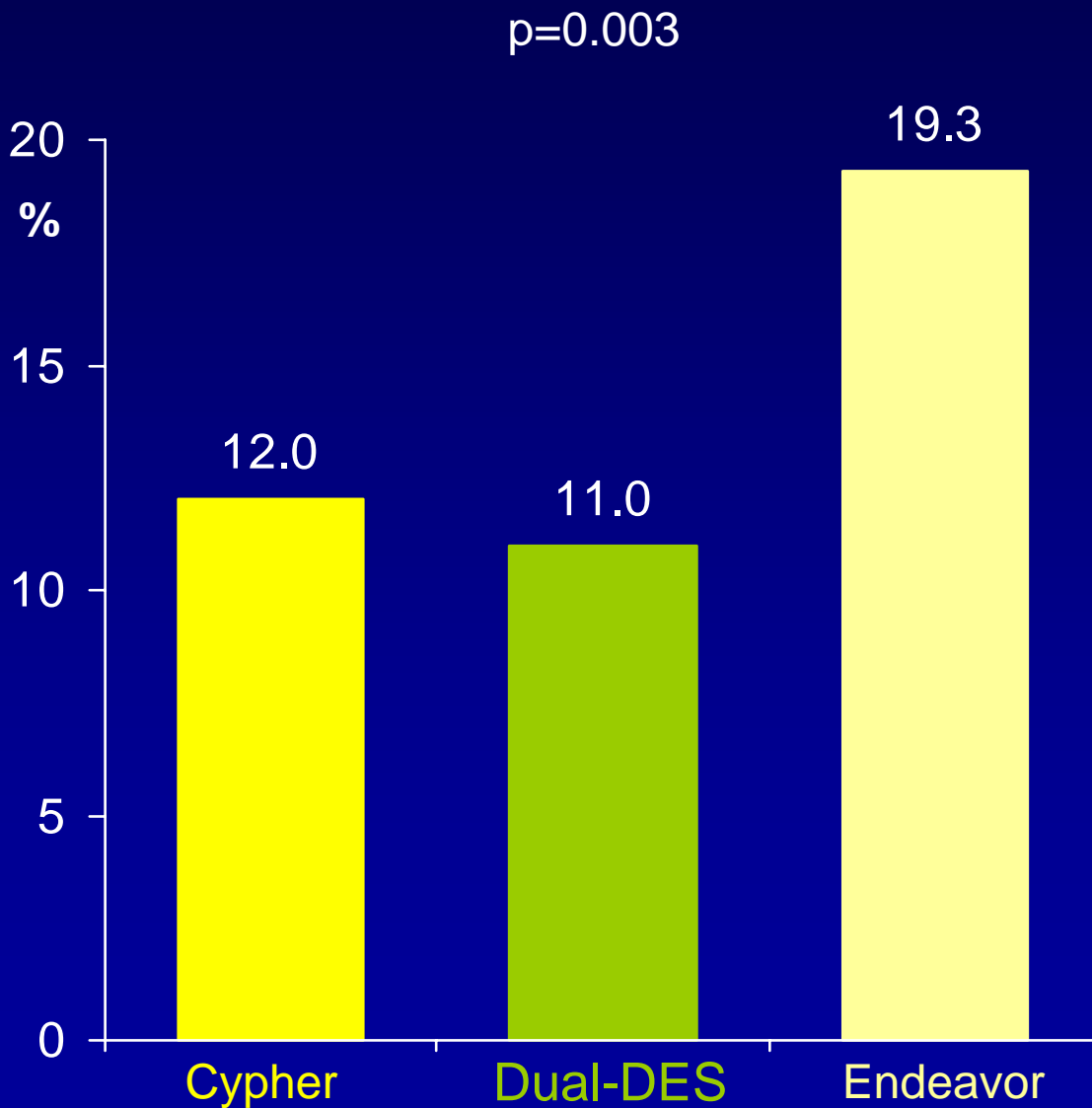


ISAR-TEST-2 *Eur Heart J* 2009



# Binary Angiographic Restenosis

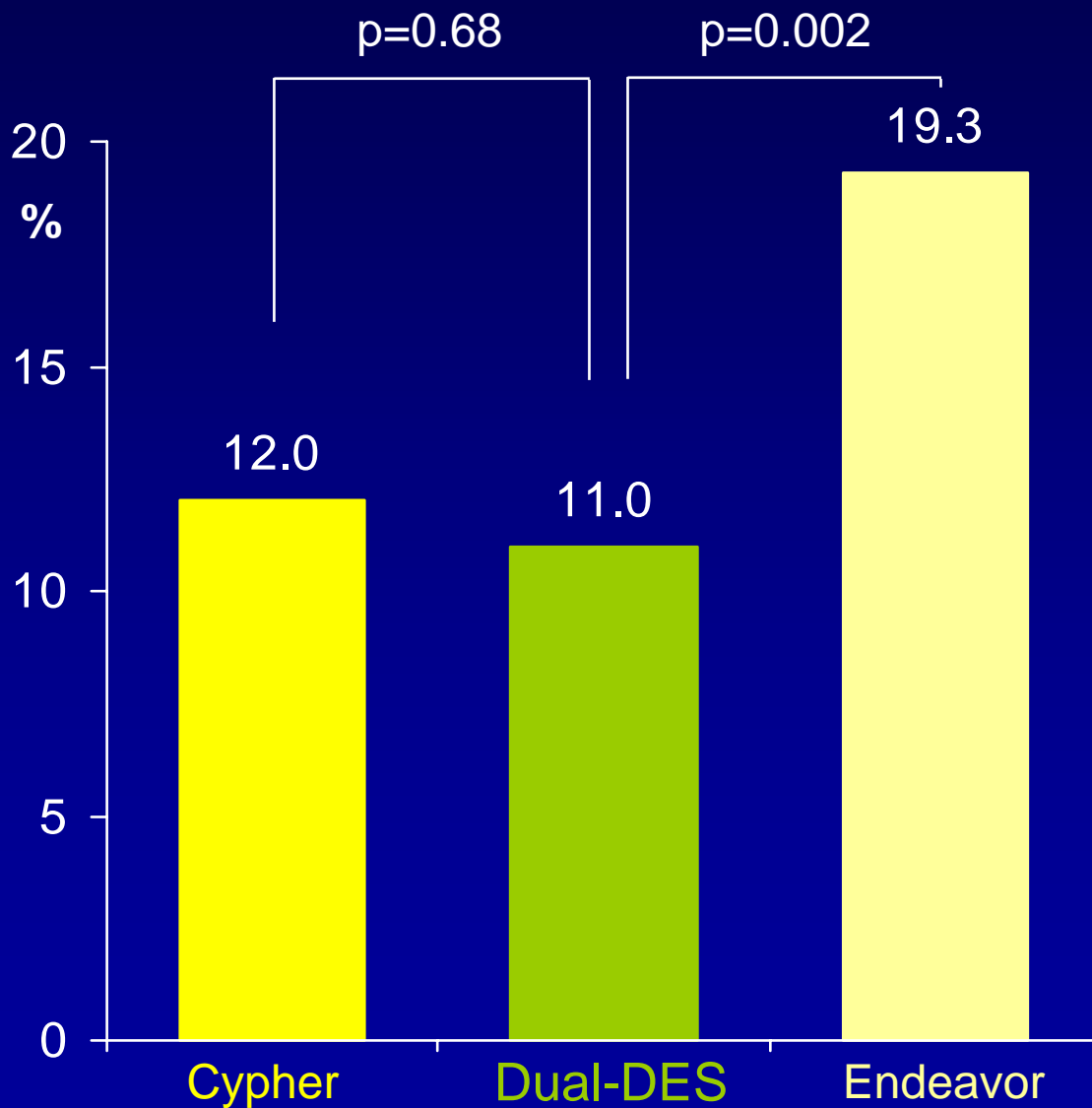
6-8 months





# Binary Angiographic Restenosis

6-8 months

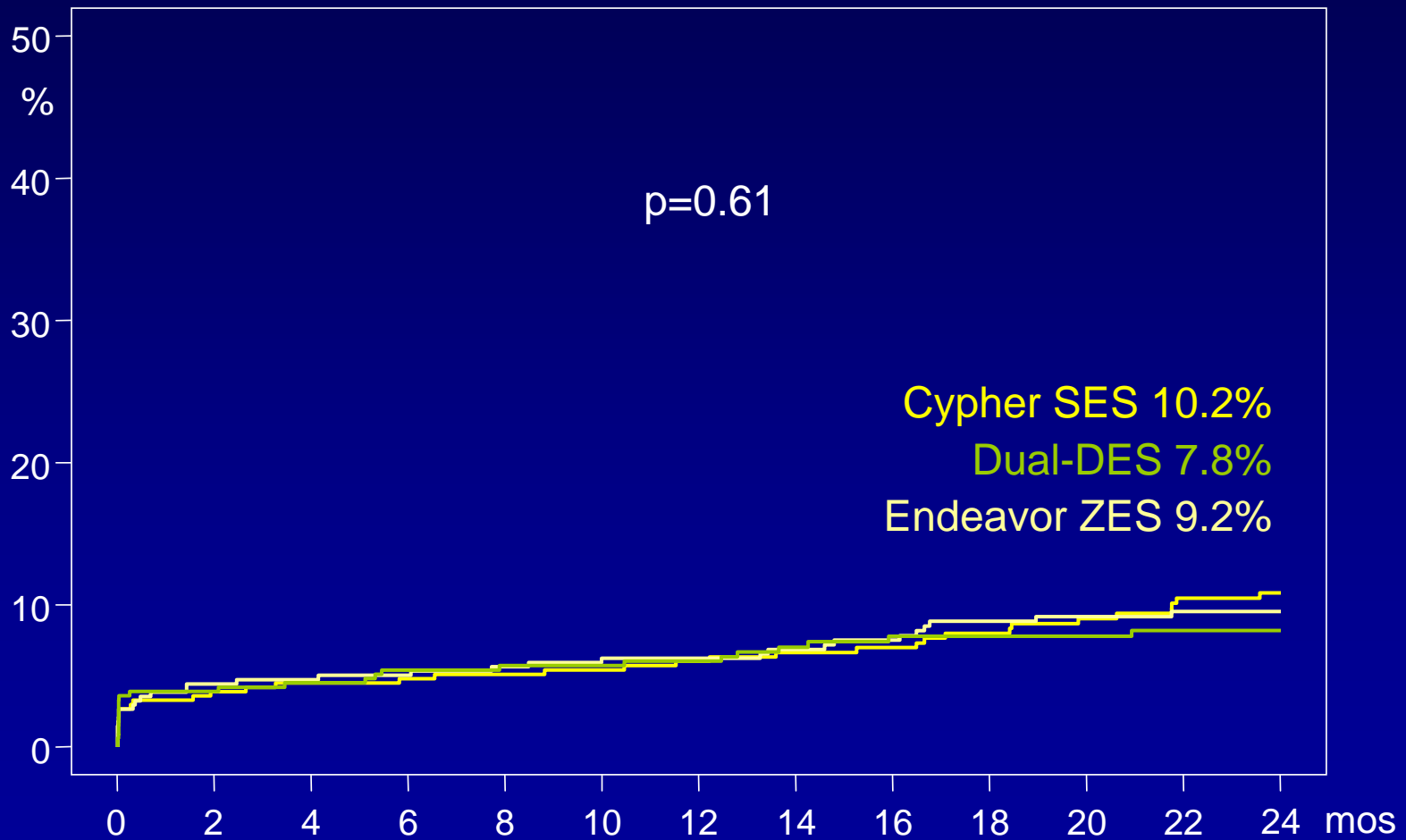




# ISAR-TEST-2

Two-year Results

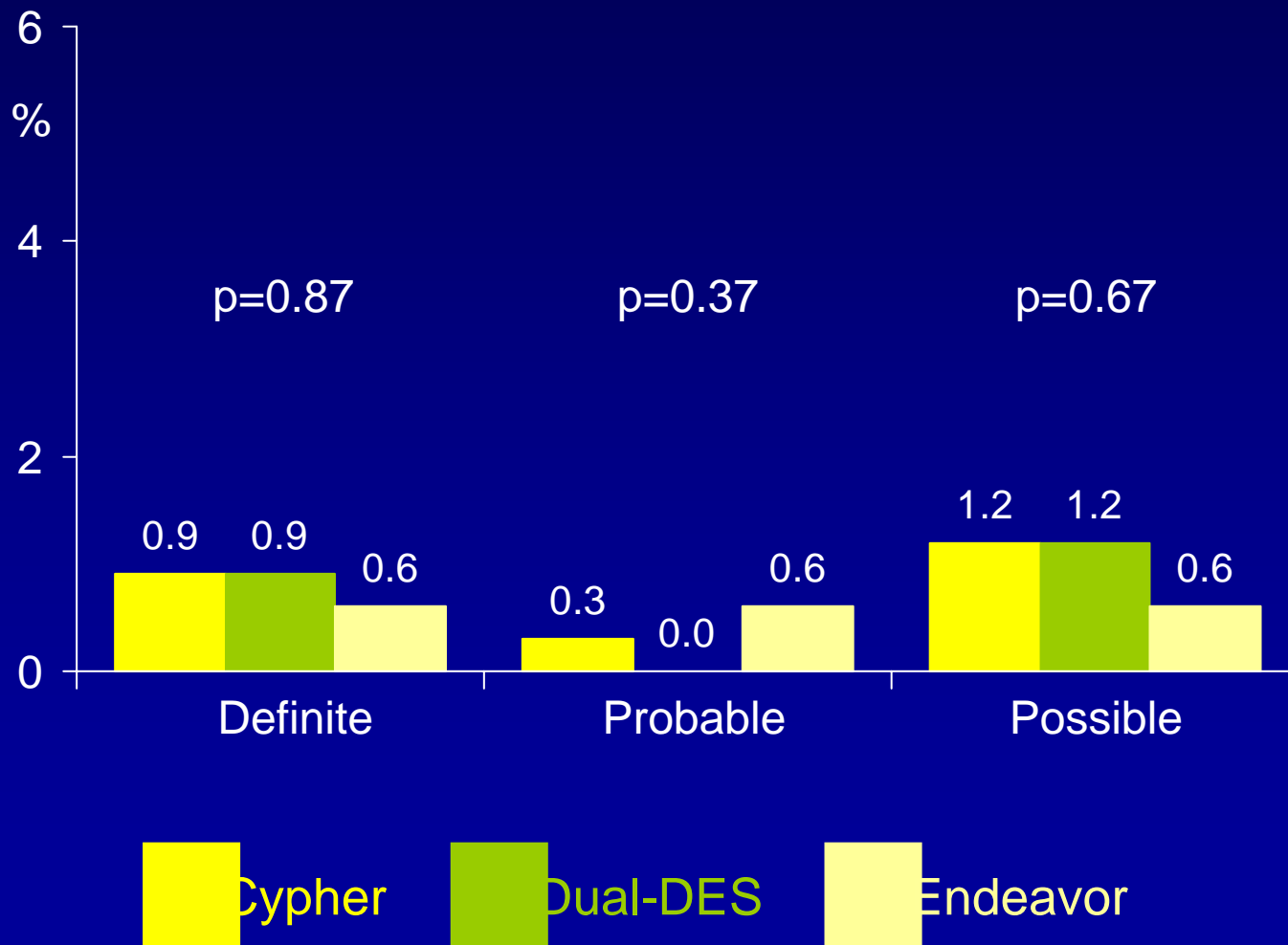
# Death or myocardial infarction



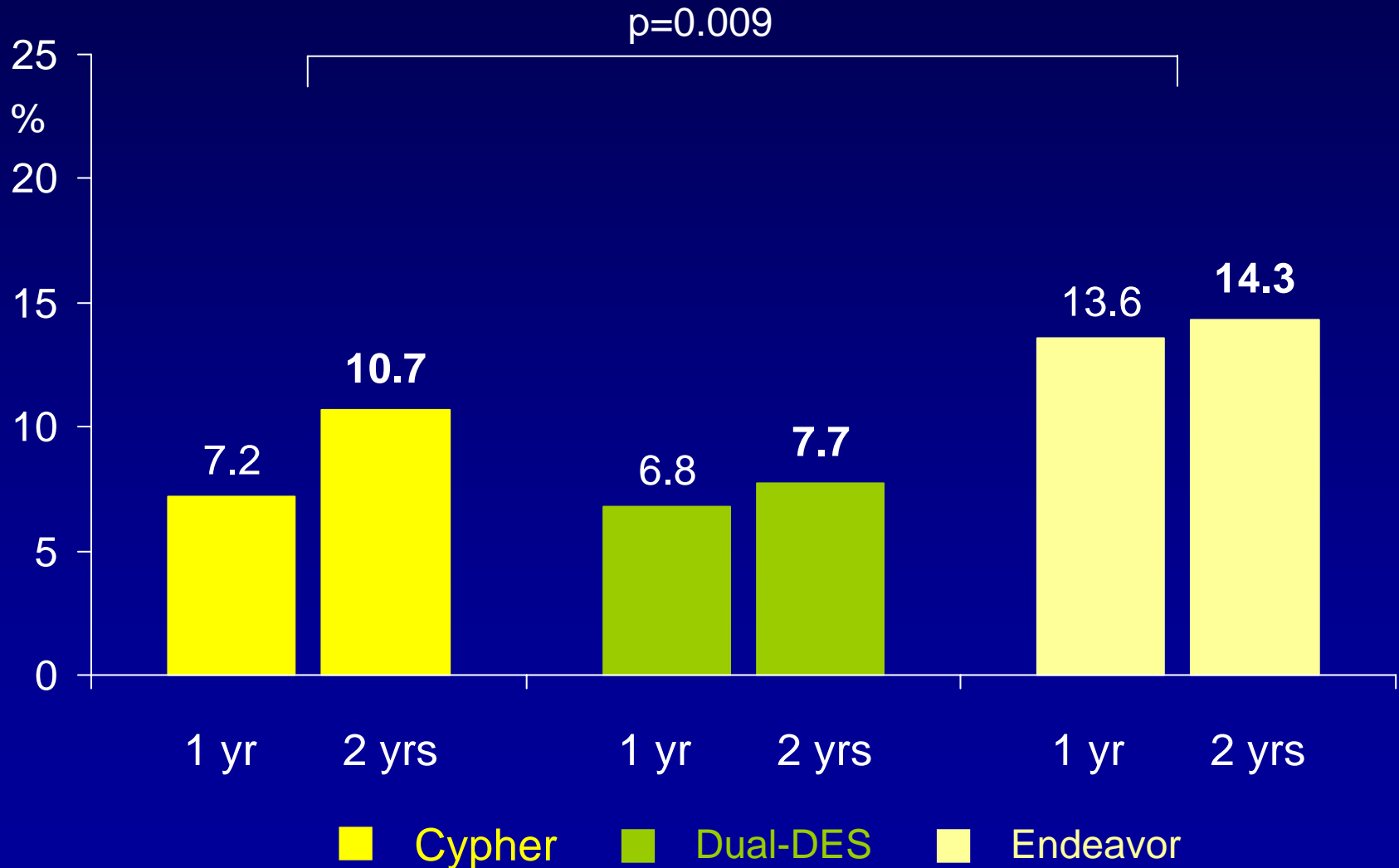
# Stent Thrombosis at 2 years



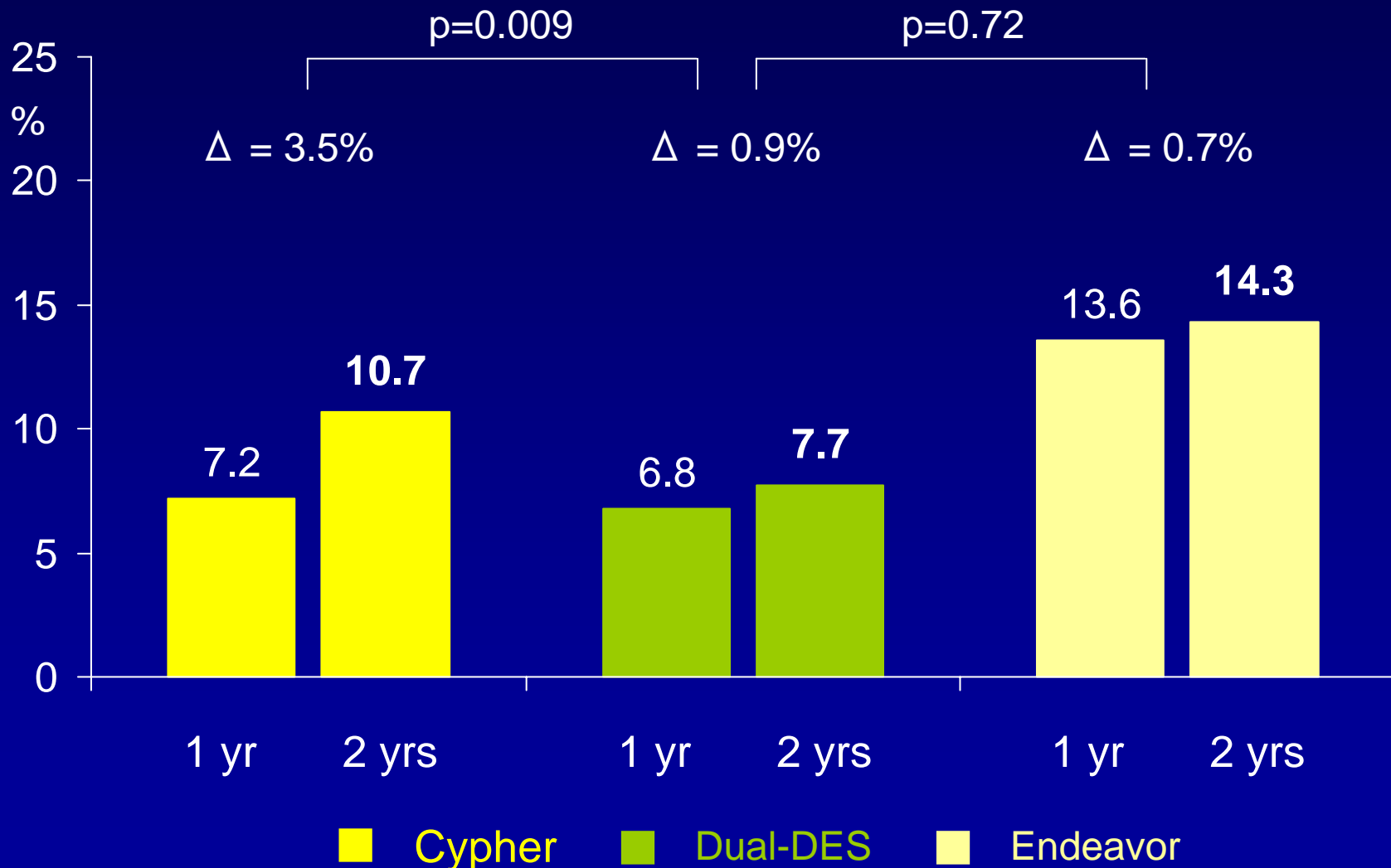
Incidence



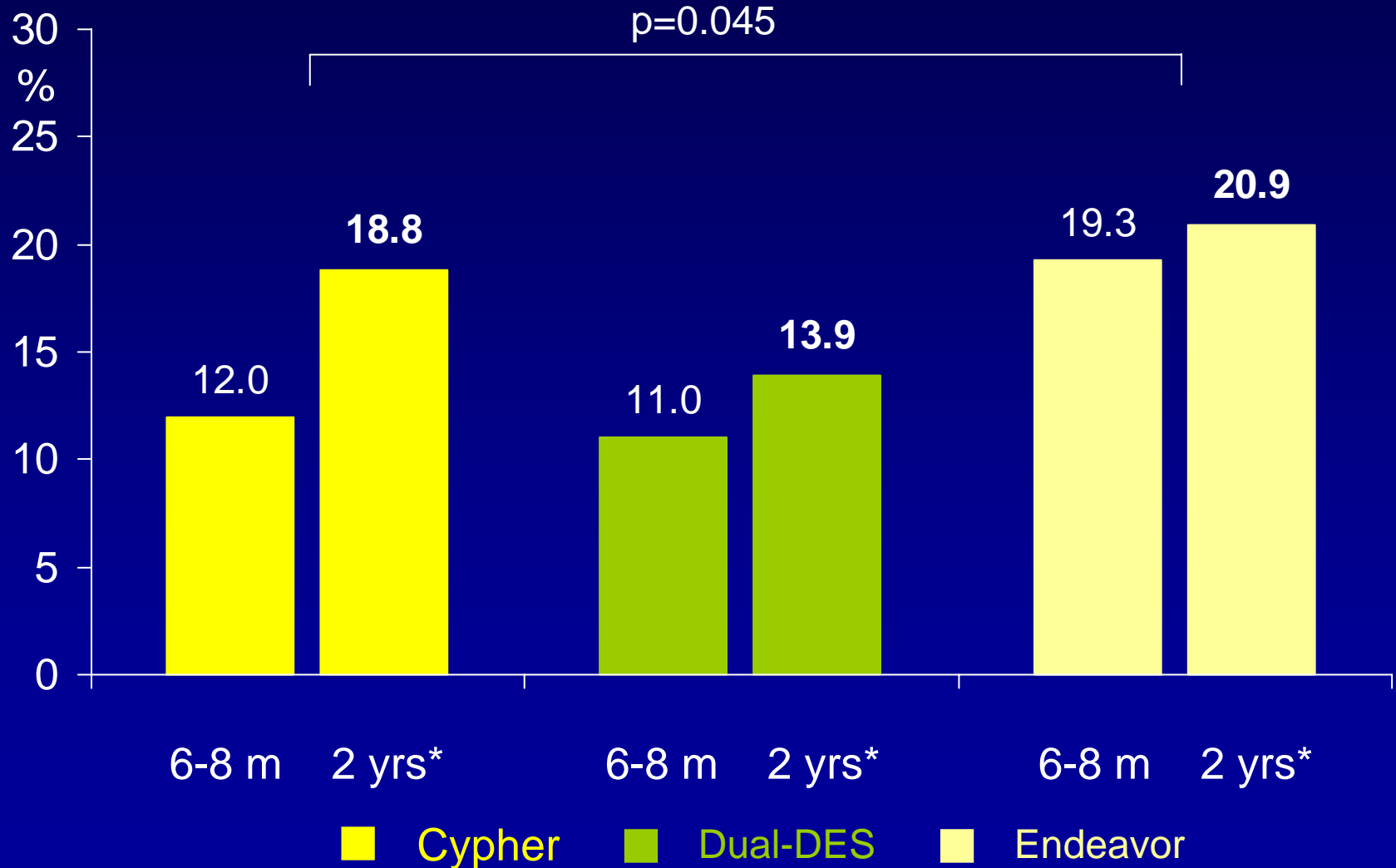
# Target Lesion Revascularization



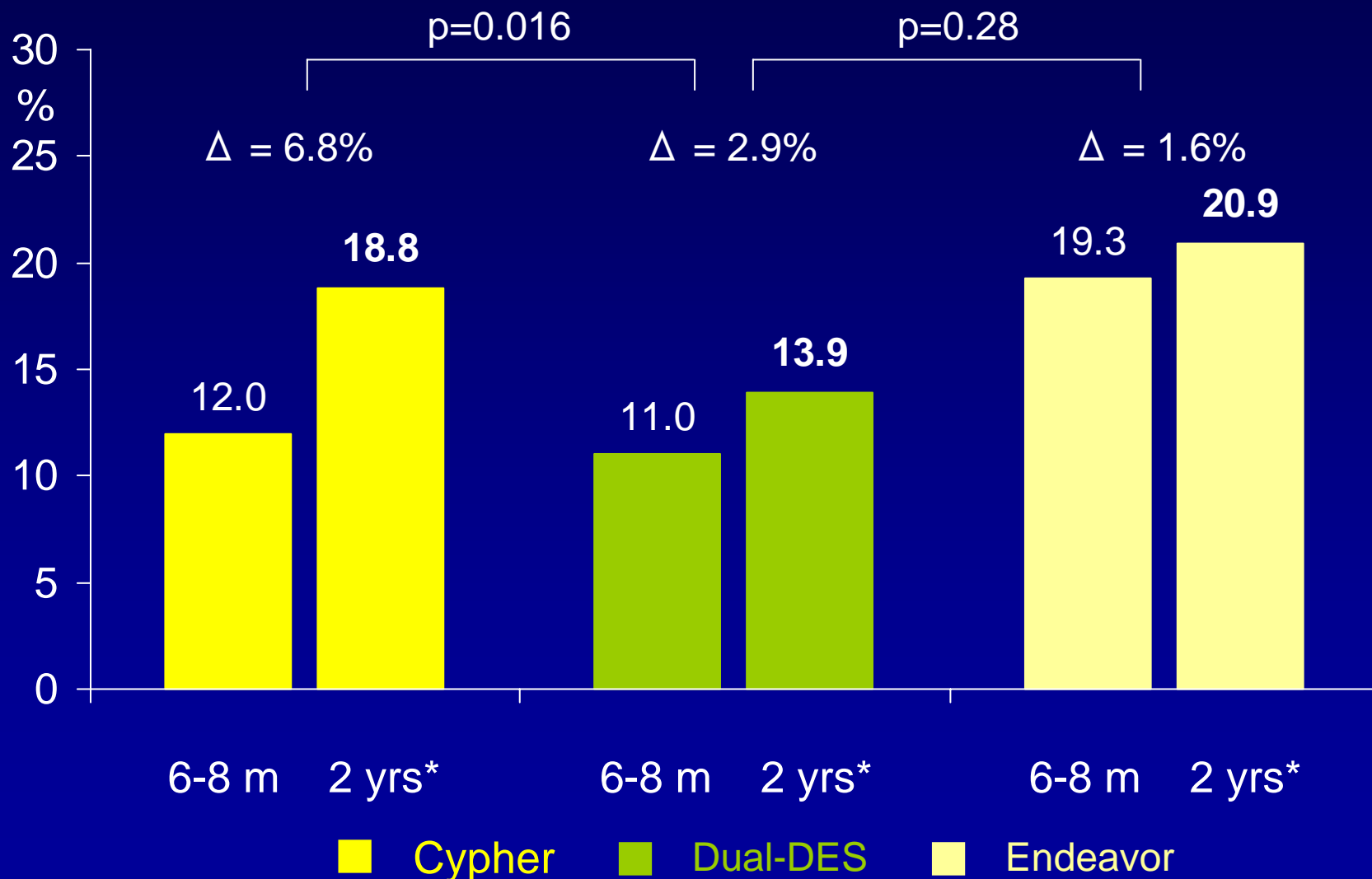
# Target Lesion Revascularization



# Binary restenosis



# Binary restenosis



# Conclusions



- The occurrence of safety events beyond 1 year was rare; there was no signal of a differential safety profile between the Dual-DES, Cypher and Endeavor out to 2 years
- The antirestenotic efficacy of both Dual-DES and Endeavor remained durable between 1 and 2 years with Dual-DES maintaining an edge
- There was evidence of a slight decrement in efficacy with Cypher from 1 to 2 years

# Thank You



## ISAR-TEST-2 Trial

Deutsches Herzzentrum, Munich. Germany