TIDES-ACS Trial

Comparison of TItanium-nitride-oxide coated bioactive stent to the Drug (everolimus)-Eluting Stent in Acute Coronary Syndrome

on behalf of the Investigators

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ESC CONGRESS
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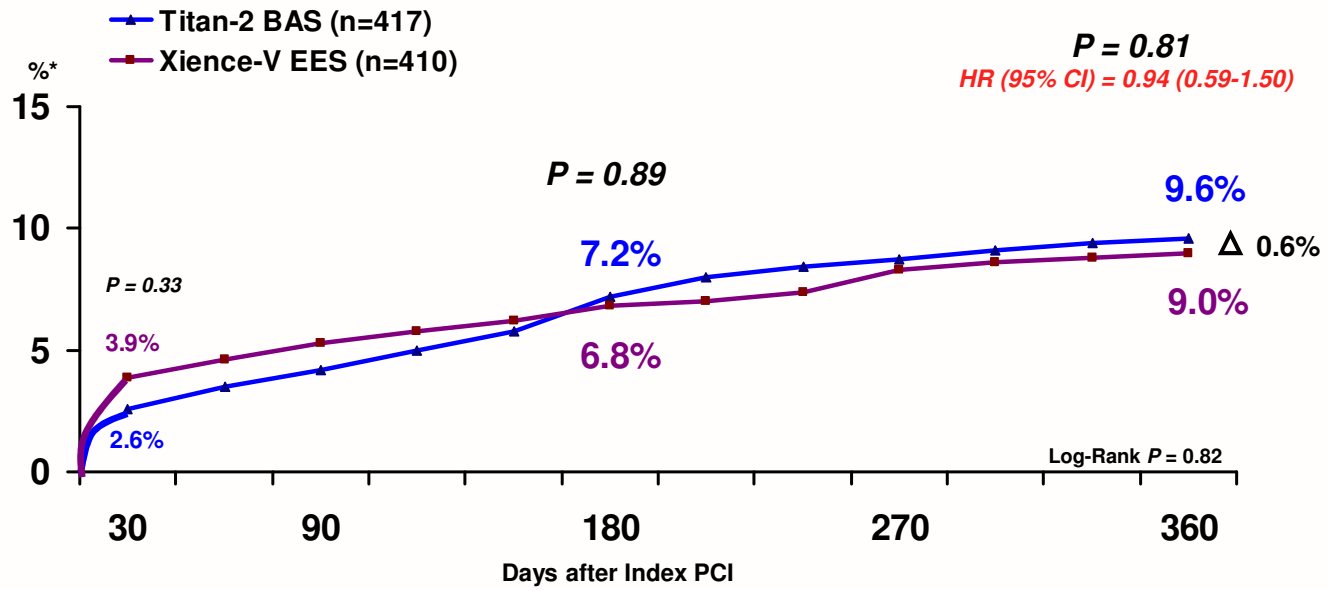
TIDES-ACS Background

- Titanium-nitride-oxide (TNO)-coated bioactive stents based on 316L stainless-steel platform showed non-inferiority to everolimus-eluting stents (EES), for the composite of MACE in patients presenting with ACS.

BASE-ACS

MACE at 12 months



Karjalainen, EuroIntervention, 2012

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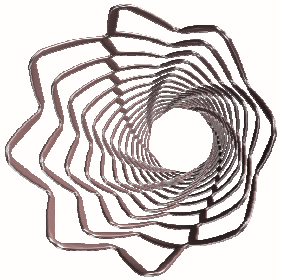
- Titanium-nitride-oxide (TNO)-coated bioactive stents based on 316L stainless-steel platform showed non-inferiority to everolimus-eluting stents (EES), for the composite of MACE in patients presenting with ACS.

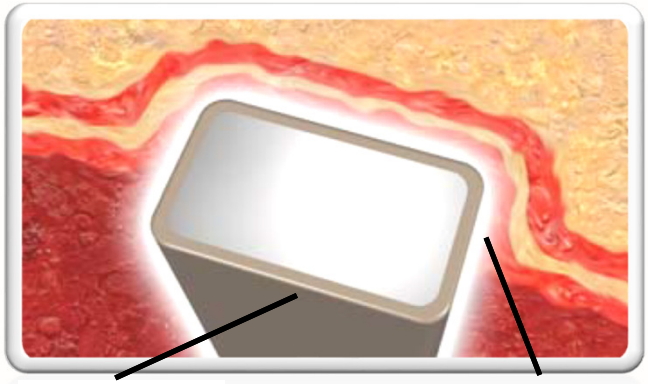
- Cobalt-chromium alloy has superior radial strength, compared with 316L stainless-steel, which allows development of stents with ultrathin struts; yet, preserved radial force and radio-opacity.

Titanium-Nitride-Oxide coated BAS
Ideal stent for ACS?

TITAN OPTiMAX



Hexacath, France



- **Inhibits Platelet Aggregation**
- **Minimizes Fibrin Growth**
- **Minimizes Thrombus Formation**
- **Reduce Inflammation**
- **Promotes Endothelial Healing**

Windecker et al. Circualtion 2001
Zhang et al. Journal of Biomedical Material 1998

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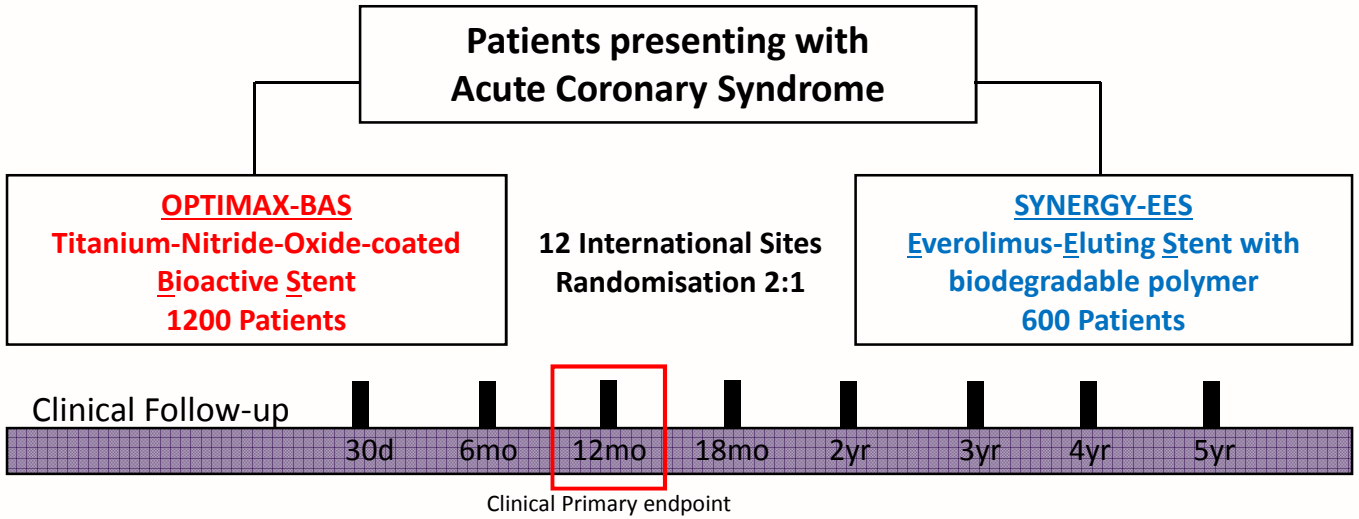
- Cobalt-chromium alloy has superior radial strength, compared with 316L stainless-steel, which allows development of stents with ultrathin struts; yet, preserved radial force and radio-opacity.

- We conducted a randomized non-inferiority trial to compare the safety and efficacy of cobalt-chromium-based TNO-coated stents versus platinum-chromium-based biodegradable-polymer EES in ACS patients.

TIDES-ACS Devices

	Cobalt-chromium-based BAS (OPTIMAX™)	Platinum-chromium-based biodegradable-polymer EES (SYNERGY™)
Stent Platform	Cobalt-chromium platform Helicoidal Design Strut thickness 75 µm	Platinum-chromium platform Slotted Tube Strut thickness (74-81) µm
Drug	---	Everolimus
Drug Density	---	100 µg/cm^2
Coating	Titanium-Nitride-Oxide	---
Polymer	---	Abluminal poly (D,L-lactide-co-glycolide) (4 µm)
Manufacturer	Hexacath, Paris, France	Boston Scientific Corp. MA. USA

TIDES-ACS



Primary Endpoint: **MACE (Cardiac death, MI, and TLR) at 12 months**

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Co-PI *K Kervinen (FIN), J van Der Heyden (NED), H Romppanen (FIN), P Tonino (NED)*

CEC: J Marco (FRA), A de Belder (UK), R Wiseth (NOR), J Gomez-Hospital (SPA), D Formigli (ITA)

ClinicalTrials.gov: NCT02049229
Minerva Cardioangiol. 2015;63:21-9.

TIDES-ACS

Patient Eligibility

Inclusion Criteria:

- Written informed consent
- Age > 18 years
- Patient with acute coronary syndrome (ACS) requiring PCI
- ACS:
  - Unstable angina
  - Non-ST-elevation myocardial infarction
  - ST-elevation myocardial infarction

Exclusion Criteria:

- Prior PCI on target vessel (ISR)
- Unprotected LM disease
- Aorto-ostial lesion
- Contraindication to:
  - aspirin, heparin, clopidogrel
- Life expectancy < 12 months
- Stent length needed > 28 mm

TIDES-ACS

Study Endpoints

Primary Endpoint (non-inferiority)

Composite event rate at 12 months

- Cardiac death
- Myocardial Infarction (MI)
- Ischemia-driven Target Lesion Revascularization (TLR)

Co-Primary Endpoint (superiority)

Composite event rate at 18 months

- Cardiac death
- Myocardial Infarction (MI)
- Major bleeding

TIDES-ACS

Stent Thrombosis

Academic Research Consortium (ARC) definition:

(Circulation 2007;115:2344-51)

Definite:

- Acute coronary syndrome and angiographic (or autopsy) confirmation of stent thrombosis

Probable:

- Any unexplained death within the first 30 days
- Target vessel related acute MI

Possible:

- Any unexplained death from 30 days after PCI

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Statistical considerations

Primary Endpoint: MACE at 12 months

- **Expected MACE rate in SYNERGY EES (control) arm = 8.5%**
- **Non-inferiority margin (Δ) = 3.5% percentage points**
- **2-sided type I error (α) = 0.05** - **type II error (β) = 10%**

- **Enrollment of 1800 patients (2:1 randomization; 1200 in the OPTIMAX arm, and 600 in the SYNERGY arm) would yield 90% power to detect non-inferiority.**

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Statistical considerations

Co-Primary Superiority Endpoint at 18 months including

* **Myocardial Infarction (MI)**
* **Cardiac Death**
* **Major Bleeding**

- Expected event rate in SYNERGY vs. OPTIMAX; 6.5% vs. 3.5%

* **Sample size needed (α=5%; β=80%), N = 1500**

TIDES-ACS Clinical Sites

Investigators	Hospital	n
J Lalmand	C.H.U. de Charleroi, Charleroi, Belgium	50
P Tonino	Heartcenter Catharina Hospital, Eindhoven, Netherlands	391
M Laine, M Pentikäinen	Helsinki University Hospital, Helsinki, Finland	27
J Sia, T Pinola	Kokkola Central Hospital, Kokkola, Finland	82
H Romppanen, A Perälä	Kuopio University Hospital, Kuopio, Finland	220
P Frambach	INCCI Luxembourg Hospital, Luxembourg	86
J van der Heyden	St Antonius Hospital, Nieuwegein, Netherlands	236
K Kervinen, M Niemelä	Oulu University Hospital, Oulu, Finland	128
P Karjalainen, W Nammas, J Mikkelsson	Satakunta Central Hospital, Pori, Finland	174
A Serra	Hospital Sant Pau, Barcelona, Spain	30
Dr. Vaquerino, M Fuertes	Hospital del Mar, Barcelona, Spain	17
M Pietilä, J Airaksinen	Turku University Hospital,Turku, Finland	50

TIDES-ACS Baseline Characteristics

	OPTIMAX BAS (n=989)	SYNERGY EES (n=502)	P value
Age (years)	62.7 ± 11.0	62.6 ± 10.5	0.85
Male	75.3%	76.3%	0.70
Diabetes	14.2%	12.5%	0.43
- Insulin treated	2.3%	3.8%	0.14
Hyperlipidemia	41.5%	40.2%	0.66
Hypertension	46.8%	43.6%	0.25
Current smoker	31.2%	35.9%	0.08
Prior myocardial infarction	7.6%	9.0%	0.37
Prior PCI	7.0%	6.6%	0.83
Prior CABG	0.6%	1.2%	0.23
NSTEMI	46.3%	45.0%	0.66
STEMI	44.9%	47.6%	0.32

TIDES-ACS Lesion Characteristics

	OPTIMAX BAS (n=989)	SYNERGY EES (n=502)	*P value*
No. of lesions treated/patient	1.17 ± 0.44	1.18 ± 0.49	0.83
2 or 3 vessels treated	36.0%	36.7%	0.75
RVD[a] (mm)	3.20 ± 0.45	3.21 ± 0.45	0.67
Lesion length (mm)	14.9 ± 6.5	14.8 ± 5.9	0.81
Culprit lesion location			
- Left anterior descendens	45.7%	45.8%	0.86
- Left circumflex	21.2%	20.0%	0.65
- Right coronary artery	33.0%	34.1%	0.56
B2/C type complex lesion	22.5%	21.7%	0.67
Thrombus in culprit lesion	33.1%	36.7%	0.18

[a] Reference vessel diameter

TIDES-ACS Procedural Data

	OPTIMAX BAS (n=989)	SYNERGY EES (n=502)	P value
Radial access	75.8%	76.9%	0.65
No. of stents/culprit lesion	1.13 ± 0.38	1.14 ± 0.37	0.80
- Stent diameter (mm)	3.22 ± 1.14	3.19 ± 0.43	0.51
- Stent length (mm)	18.6 ± 4.7	19.0 ± 4.9	0.13
- Total stent length/lesion (mm)	20.5 ± 7.8	20.6 ± 7.2	0.86
Post-Dilatation	33.0%	38.0%	0.06
Stent failure	0.3%	1.0%	0.13

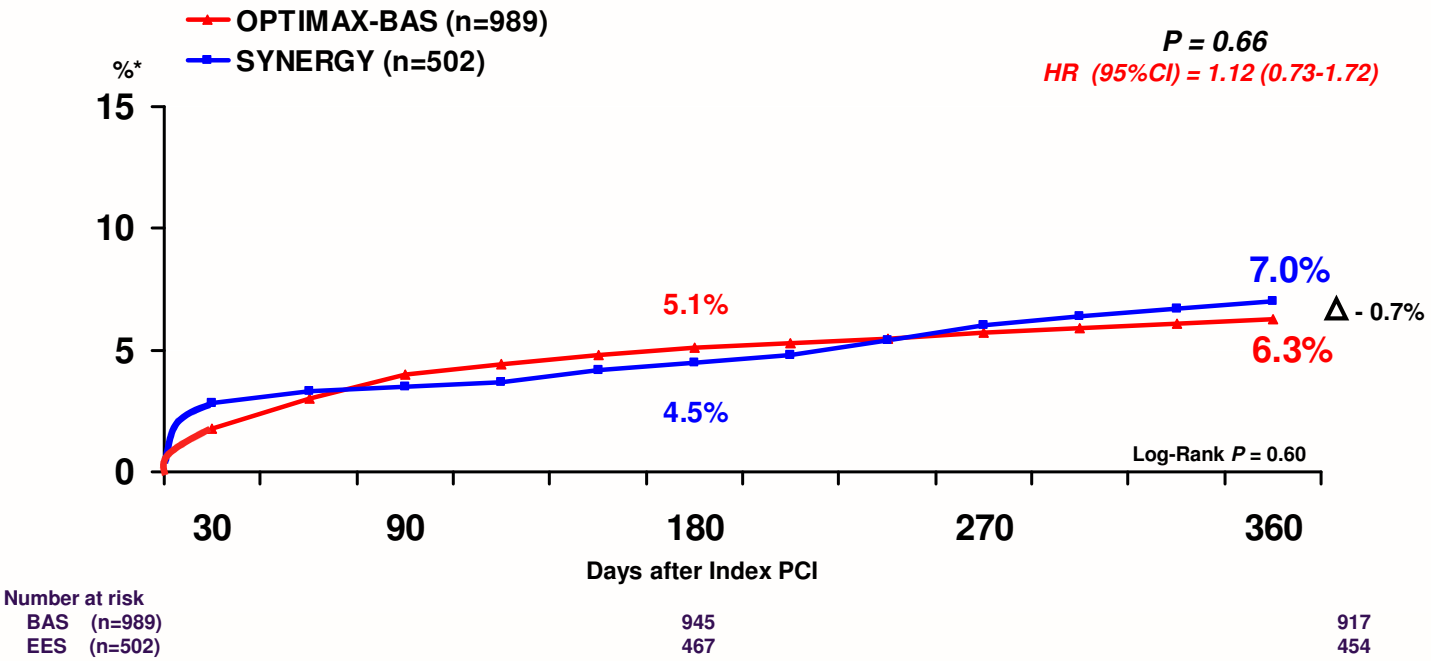
TIDES-ACS Antiplatelet Agent Utilization

	OPTIMAX BAS (n=989)	SYNERGY EES (n=502)	P value
Aspirin			
- At discharge	99.2%	99.2%	NS
- At 12 months	94.5%	95.3%	NS
Clopidogrel/Prasugrel/Ticagrelor			
- At discharge	99.4%	100%	0.56
- At 12 months	59.4%	76.7%	< 0.001
Mean duration of DAPT (months)	10.8 ± 2.7	11.1 ± 2.3	0.007

TIDES-ACS

MACE at 12 months

* Cumulative incidence of events (%)



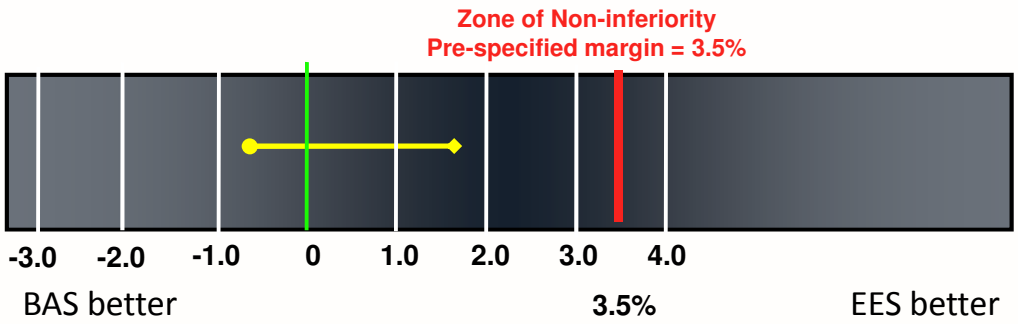
Number at risk			
BAS	(n=989)	945	917
EES	(n=502)	467	454

Primary Endpoint

MACE at 12 Months

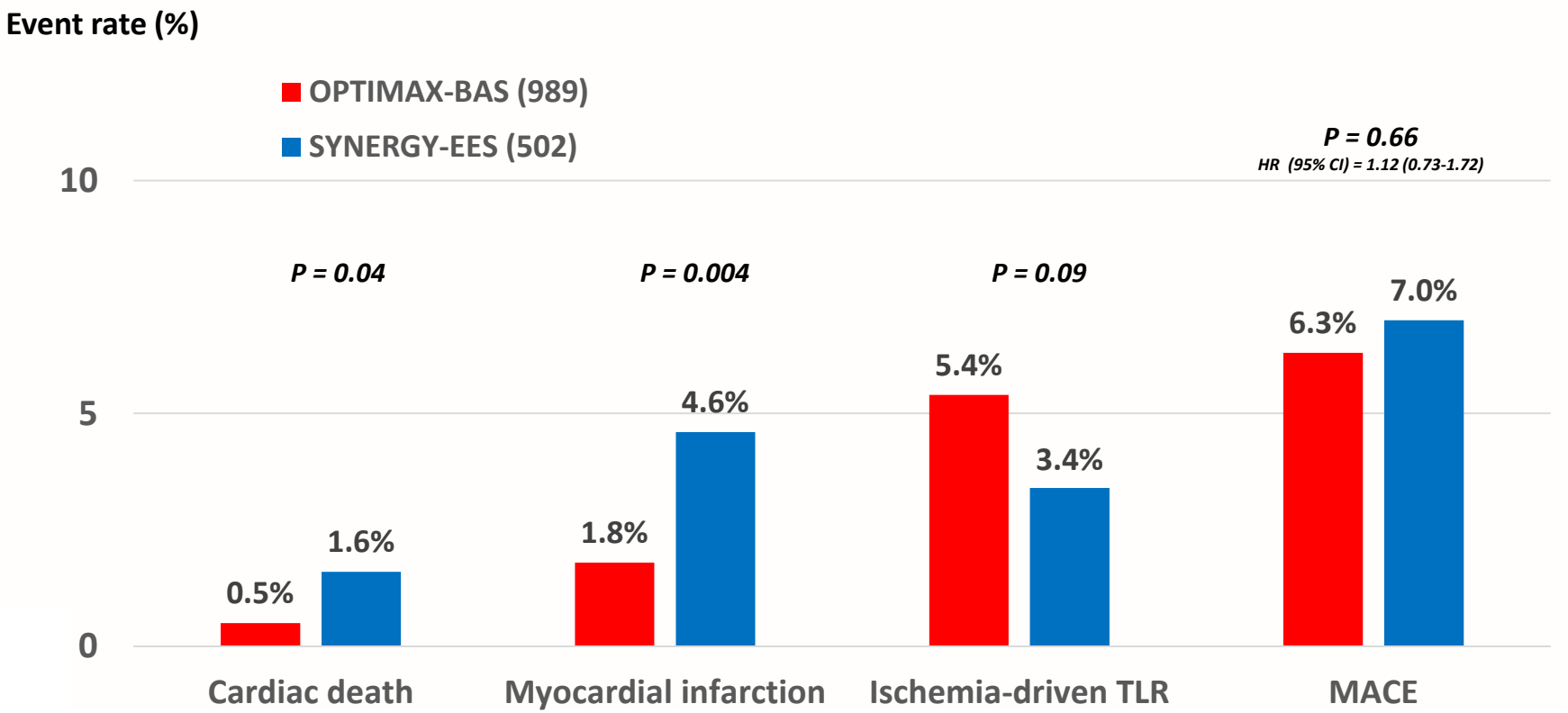
BAS (n=989)	EES (n=502)	Difference: - 0.7% (Upper boundary of 1-sided 95% CI)	*P* Value (Non-inferiority)
6.3%	7.0%	- 0.7% + 95% CI = 1.7%	< 0.001

Primary Non-Inferiority Endpoint Met

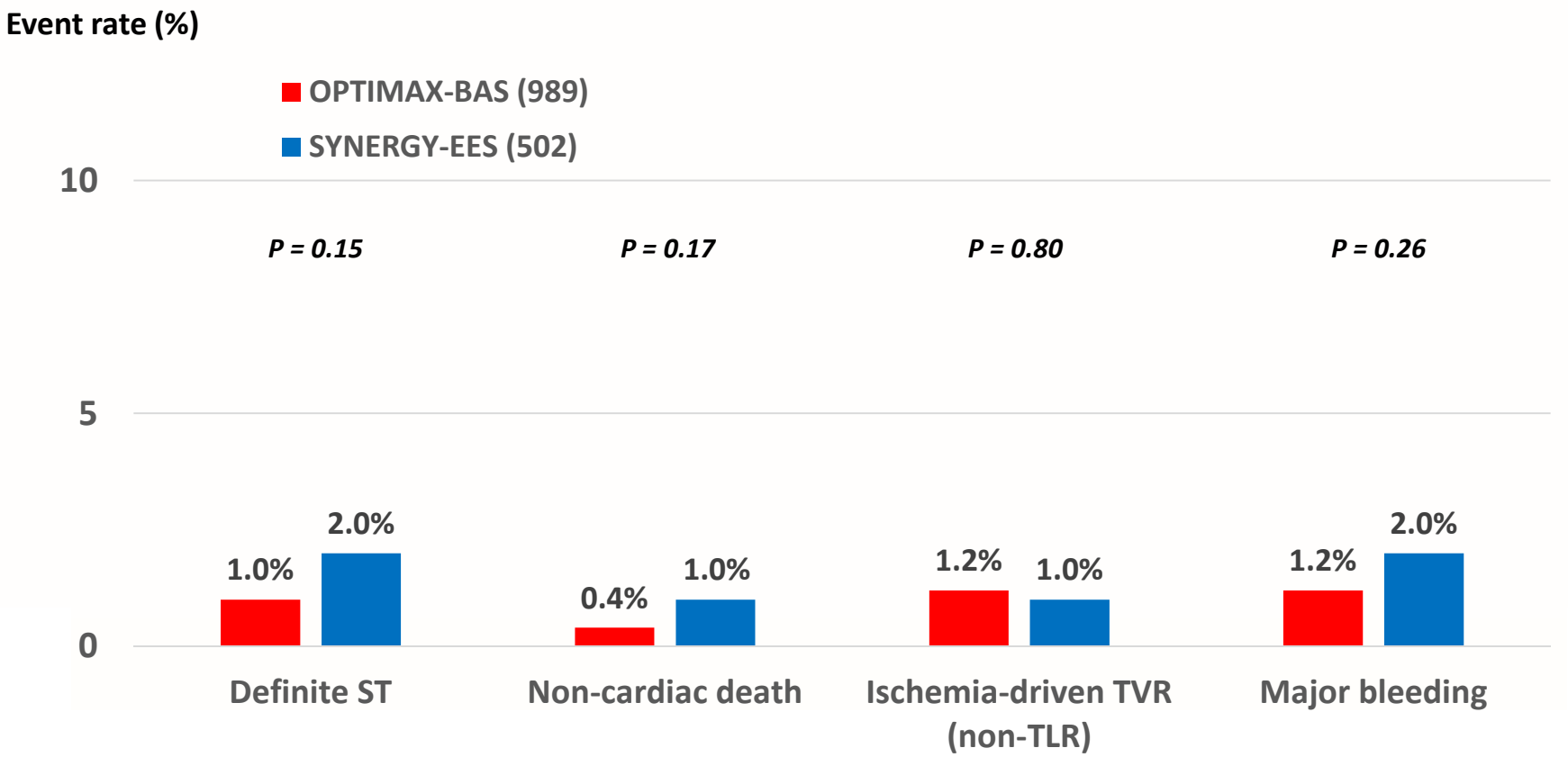


TIDES-ACS

TIDES-ACS MACE at 12 months



TIDES-ACS other events at 12 months



TIDES-ACS ARC Stent Thrombosis

	OPTIMAX BAS (n=989) n (%)	SYNERGY EES (n=502) n (%)	*P Value*
Definite ST	10 (1.0)	10 (2.0)	0.15
Probable ST	1 (0.1)	4 (0.8)	0.047
Definite or Probable ST	11 (1.1)	14 (2.8)	0.01

TIDES-ACS
Conclusions

- OPTIMAX-BAS was non-inferior to platinum-chromium-based biodegradable-polymer SYNERGY-EES for the primary composite of safety and efficacy outcome (MACE) at 12-month follow-up.

- Both cardiac death and MI were observed less frequent with OPTIMAX-BAS, whereas ischemia-driven TLR was undertaken more frequent in the OPTIMAX-BAS arm.

- Co-primary, “superiority” endpoint at 18 months (myocardial infarction, cardiac death and major bleeding) will be presented in spring 2018.