

Titanium-Nitride-Oxide Stents

Pim A.L. Tonino, MD, PhD

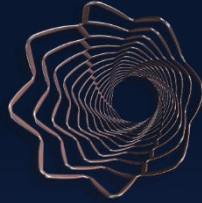
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Disclosure Statement of Financial Interest

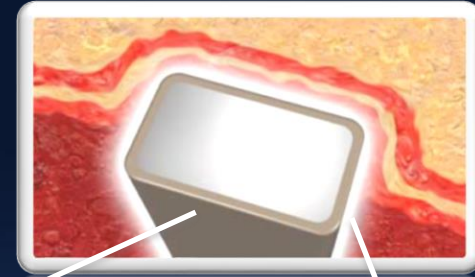
I, Pim A.L. Tonino DO NOT have a financial interest/arrangement or affiliation with one or more organizations that could be perceived as a real or apparent conflict of interest in the context of the subject of this presentation.

Titanium-Nitride-Oxide coated BAS

TITAN OPTiMAX



Hexacath, France



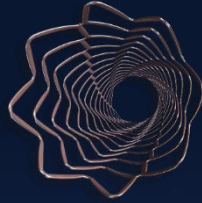
Active
Coating

Biological
Effect

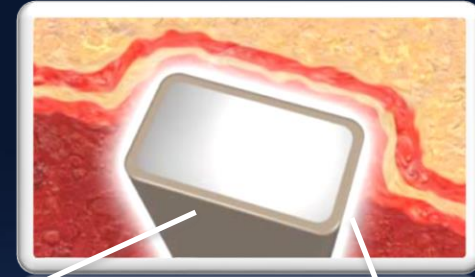
- Thin-strut (81um) balloon-expandable stent
- Cobalt chromium platform, twin helicoidal design
- Coated with TNO by plasma-enhanced vapour deposition of titanium in a gas mixture of NO and O₂, in a vacuum chamber
- No polymer, no antiproliferative drug

Ideal stent for ACS?

TITAN OPTiMAX



Hexacath, France



Active
Coating

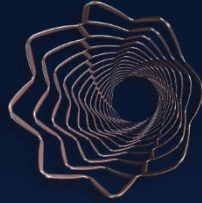
Biological
Effect

- Inhibits Platelet Aggregation
- Minimizes Fibrin Growth
- Less neo-intimal hyperplasia compared to BMS
- Less uncovered struts, less malapposed struts, more intimal hyperplasia compared to DES

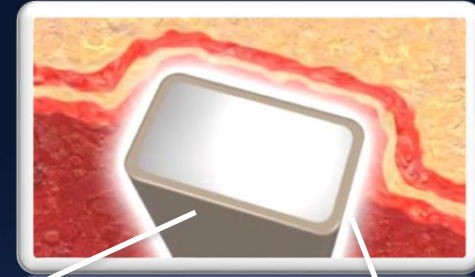
Lehtinen *Int J Cardiovasc Imaging* 2012
Karjalainen *Int J Cardiovasc Imaging* 2013
Windecker *Circulation* 2001
Zhang *Journal of Biomedical Material* 1998

Ideal stent for ACS?

TITAN OPTiMAX



Hexacath, France



Active
Coating

Biological
Effect

■ PCI in STEMI (EXAMINATION* and COMFORTABLE-AMI**) shows comparable cardiac death and infarction rates in DES vs BMS

* Sabate Lancet 2012

** Raber JAMA 2012

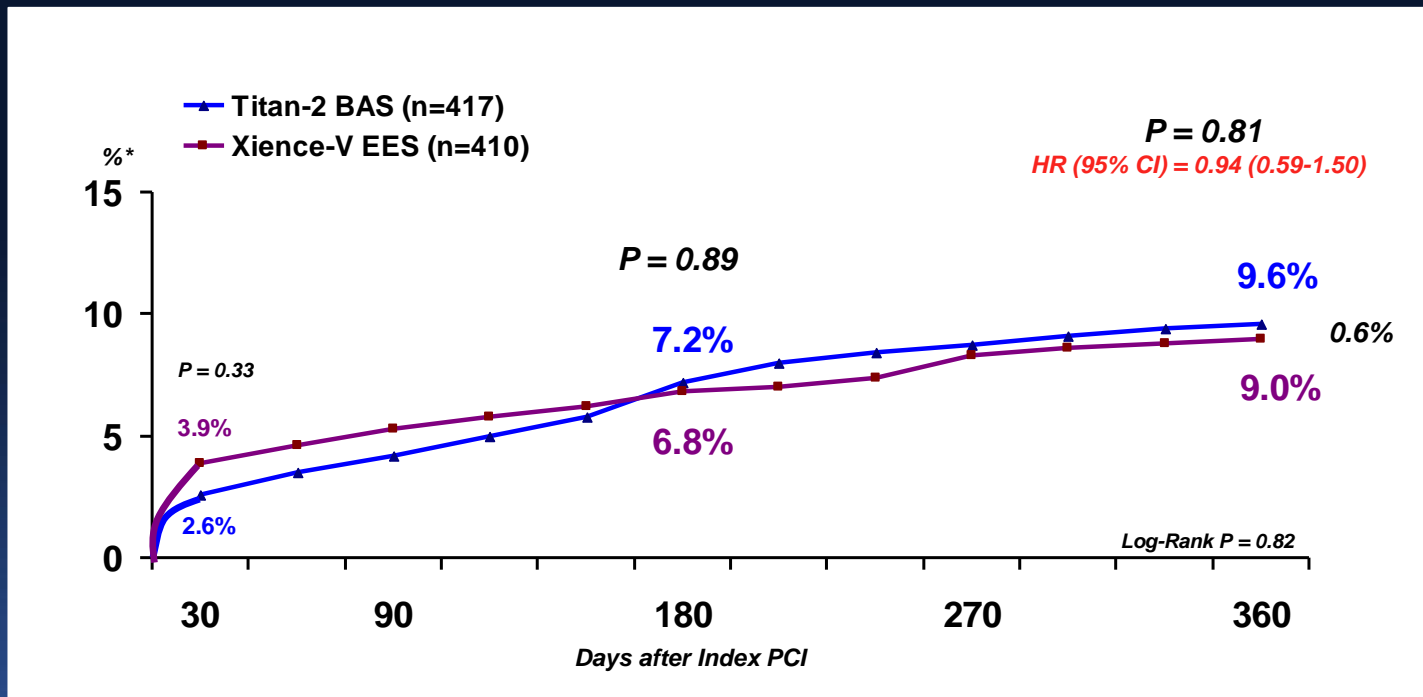
■ Potentially the 'bioactive' effects of OPTiMAX can improve these outcome measures in PCI for ACS compared to DES

BASE-ACS study

- 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

Development in TNO-coated stent

- 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.

TIDES-ACS Trial

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

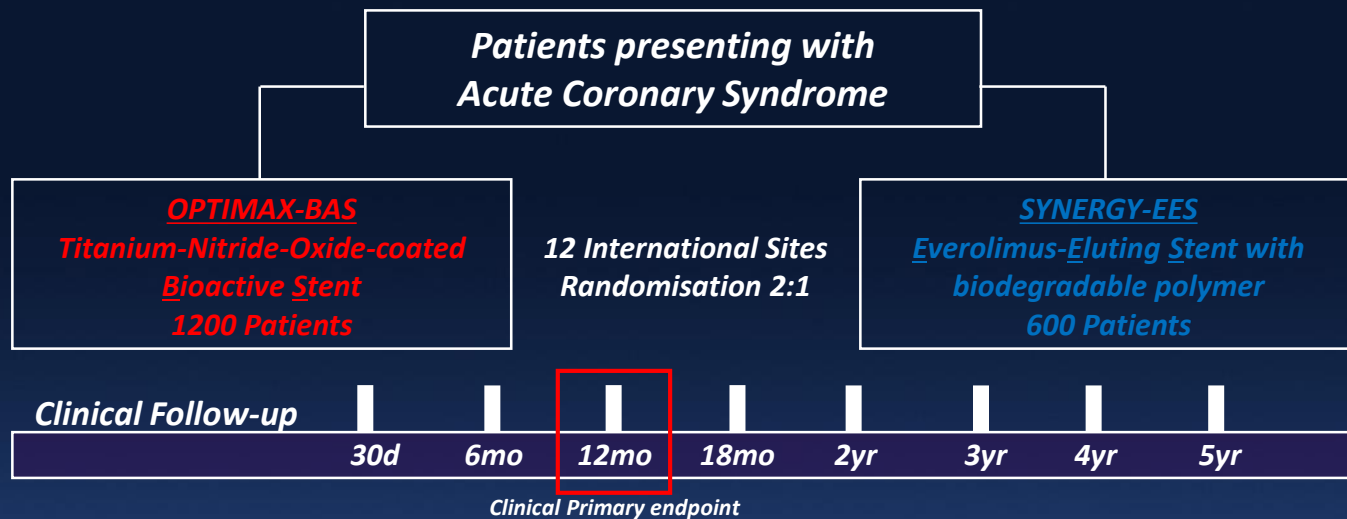
on behalf of the Investigators

Pim A.L.Tonino, MD, PhD

TIDES-ACS Devices

	Cobalt-chromium-based BAS (OPTIMAX™)	Platinum-chromium-based biodegradable-polymer EES (SYNERGY™)
Stent Platform	Cobalt-chromium platform Helicoidal Design Strut thickness 81 µm	Platinum-chromium platform Slotted Tube Strut thickness (74-81) µm
Drug	---	Everolimus
Drug Density	---	100 µg/cm²
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 Baseline Characteristics

	OPTIMAX BAS (n=989)	SYNERGY EES (n=502)	P value
Age (years)	62.7 ± 11.0	62.6 ± 10.5	0.84
Male	75.3%	76.3%	0.68
Diabetes	14.2%	12.5%	0.39
- Insulin treated	2.3%	3.8%	0.10
Hyperlipidemia	41.5%	40.2%	0.65
Hypertension	46.8%	43.6%	0.24
Current smoker	31.2%	35.9%	0.07
Prior myocardial infarction	7.6%	9.0%	0.35
Prior PCI	7.0%	6.6%	0.77
Prior CABG	0.6%	1.2%	0.23
NSTEMI	46.3%	45.0%	0.63
STEMI	44.9%	47.6%	0.32

TIDES-ACS Lesion Characteristics

	OPTIMAX BAS (n=989)	SYNERGY EES (n=502)	P <i>value</i>
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	0.80
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	34.0%	35.1%	0.67
Thrombus in culprit lesion	33.1%	36.7%	0.16

^a Reference vessel diameter

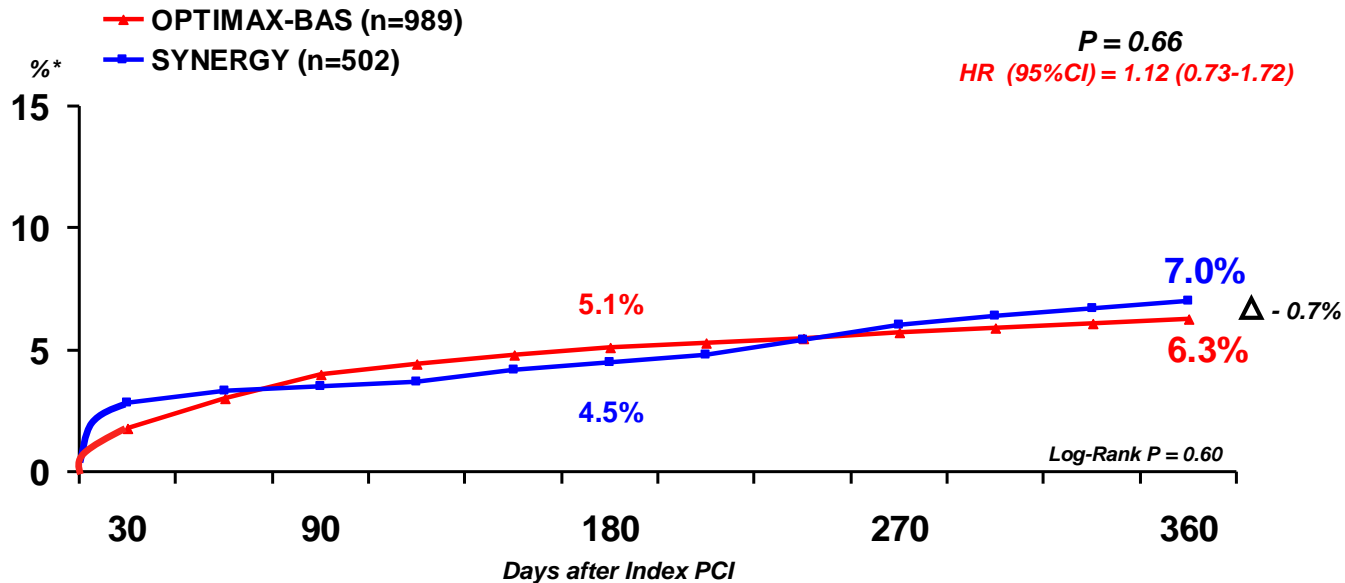
TIDES-ACS Procedural Data

	OPTIMAX BAS (n=989)	SYNERGY EES (n=502)	P value
Radial access	75.8%	77.0%	0.60
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	0.80
Post-Dilatation	33.0%	38.0%	0.05
Stent failure	0.3%	1.0%	0.12

TIDES-ACS

MACE at 12 months

* Cumulative incidence of events (%)

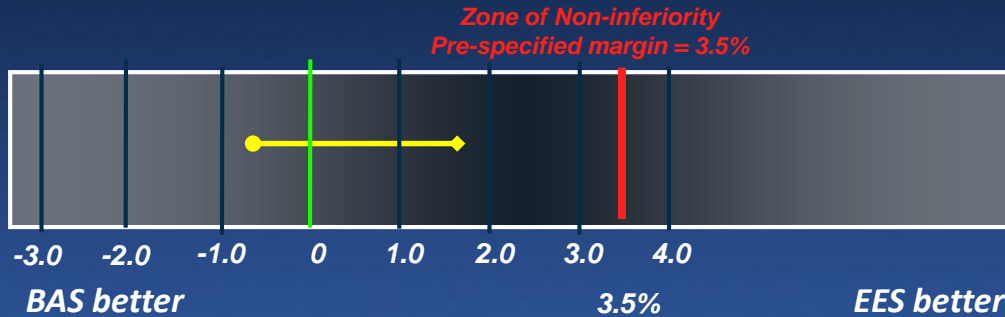


Primary Endpoint

MACE at 12 Months



Primary Non-Inferiority Endpoint Met



TIDES-ACS Antiplatelet Agent Utilization

	OPTIMAX BAS (n=989)	SYNERGY EES (n=502)	P value
<u>Aspirin</u>			
- At discharge	99.2%	99.2%	NS
- At 12 months	94.5%	95.3%	NS
<u>Clopidogrel/Prasugrel/Ticagrelor</u>			
- 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

15

Event rate (%)

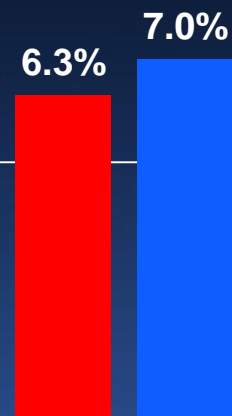
■ OPTIMAX-BAS (989)

■ SYNERGY-EES (502)

10

$P = 0.60$

5



Cardiac death

Myocardial infarction

Ischemia-driven TLR

MACE

TIDES-ACS MACE at 12 months

15

Event rate (%)

■ OPTIMAX-BAS (989)

■ SYNERGY-EES (502)

10

$P = 0.60$

$P = 0.03$

$P = 0.002$

$P = 0.10$

5

0.5%

1.6%

1.8%

4.6%

5.4%

3.4%

6.3%

7.0%

Cardiac death

Myocardial infarction

Ischemia-driven TLR

MACE



TIDES-ACS other events at 12 months

15

Event rate (%)

■ OPTIMAX-BAS (989)

■ SYNERGY-EES (502)

10

$P = 0.01$

$P = 0.17$

$P = 0.80$

$P = 0.23$

5

1.1%

2.8%

0.4%

1.0%

1.2%

1.0%

1.2%

2.0%

Def or Prob ST

Non-cardiac death

TVR (non-TLR)

Major bleeding



TIDES-ACS

Conclusions

- in patients with ACS undergoing PCI, the use of **cobalt-chromium-based TNO-coated stents** compared to platinum-chromium-based BP EES is:
 - *non-inferior with respect to 12 months MACE*
 - *associated with lower rates of cardiac death, non-fatal MI, and ST at 12 months*
 - *showing a trend towards higher TLR rate for TNO-coated stents*