Novel Bio-Active Stent (BAS) coated with titanium-nitride-oxide (NO-particles) in Patients with Acute Coronary Syndrome

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Head Doctor of Institut Coeur Paris Centre (ICPC), Paris, France
Are DES the answer to Acute Coronary Syndrome?

- Late stent thrombosis
- Polymer issue and re-endothelialisation
- Negative late loss
- Prolonged antiplatelet therapy
- Evidence for life prolongation?
TiNOX is an ACTIVE chemical compound (Titanium Oxide) with unique properties whose molecular structure is made of Titanium, Nitrogen and Oxygen.

- Inhibits Platelet aggregation
- Minimizes Fibrin growth
- Minimizes Thrombus formation
- Reduce Inflammation
- Promotes Endothelial Healing
Titanium-nitride-oxide (TiNOX) coating is associated with NO-particles on the stent surface.
Basic research has shown stent coating with titanium-nitride-oxide (TiNOX) is associated with NO particles on stent surface.

The Titan stent shows a large NO-peak on its surface which is not present on the BMS surface.

S. Windecker and al. EuroIntervention, Vol 2, Number 2, 2006
TiNOX stent is the only stent with NO-particles. TiNOX stent is not a BMS!

“The presence of NO on the stent surface might be beneficial with respect to platelet aggregation and neointimal proliferation.”
(Eurointervention 2006:2:146-148)

S. Windecker and al. EuroIntervention, Vol 2, Number 2, 2006
Randomized Comparison of a Titanium-Nitride-Oxide–Coated Stent With Stainless Steel Stent for Coronary Revascularization: The TiNOX Trial

Stephan Windecker, Rüdiger Simon, Markus Lins, Volker Klauss, Franz R. Eberhard, Marco Roffi, Giovanni Pedrazzini, Tiziano Moccetti, Peter Wenaweser, Mario Tobler, David Tüller, Rainer Zbinden, Christian Seiler, Julinda Mehilli, Adnan Kastrati, Bernhard Meier and Otto M. Hess

Circulation 2005;111;2617-2622; originally published online May 9, 2005;

Conclusions—Revascularization with titanium-nitride-oxide–coated stents is safe and effective in patients with de novo native coronary artery lesions. Titanium-nitride-oxide–coated stents reduce restenosis and major adverse cardiac events compared with stainless steel stents of otherwise identical design. (Circulation. 2005;111;2617-2622.)

« Titanium-nitride-oxide coated stents reduce restenosis and MACE compared with stainless steel stents of otherwise identical design. »

Late Loss Titanium Nitride Oxide : 0.55mm
Titanium-Nitride-Oxide (TiNOX) Randomized Control Trial

“Randomized multicenter control trial demonstrated that stent coating with titanium-nitride-oxide reduced late loss (and angiographic and ultrasonic measures of restenosis) significantly as compared with stainless steel control stents (BMS) of otherwise identical design.” (Circulation 2005; 111-116).

This « stuff » Works!
Reminder: No late catch up with TiNOX stent

**BAS: TINOX 5-YEAR FOLLOW UP**
- BAS: has shown No Late Catch Up
- No Late/Very Late stent thrombosis
- No long term dual antiplatelet treatment

**SES: RAVEL 5-YEAR FOLLOW UP**
- SES has shown Late Catch Up
- Issue with Late & Very Late stent thrombosis
- Long term dual antiplatelet treatment required

Windecker et al. EuroIntervention In Press
De Bruyne, WCC/ESC 2006
Patients presenting with Acute Coronary Syndrome (ACS) 

N = 827
14 International Sites
Randomisation 1:1

Clinical Follow-up
30d 6mo 12mo 18mo 2yr 3yr 4yr 5yr

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

Investigators: P Karjalainen (Finland), Principal Investigator (PI)
A Ylitalo (Finland), co-PI
O Hess† (Switzerland), co-PI
KEJ Airaksinen (Finland), co-PI
M Niemelä (Finland), co-PI

BASE-ACS Randomized Trial

TITAN-2® stent
Titanium-Nitride-Oxide Coated
Bio-Active Stent (BAS)
417 Patients

XIENCE-V™/PROMUS™ stent
Everolimus-Eluting Stent (EES)
410 Patients

TITAN vs 2nd gen DES in ACS patients
BASE-ACS: background
Primary Endpoint: MACE at 12 months
(late breaking clinical trial; EuroPCR2011
Eurointervention 2012)

Primary Non-Inferiority Endpoint Met

Titan-2 BAS (n=417)
Xience-V EES (n=410)

%*

P = 0.82
P = 0.81
HR (95% CI) = 0.94 (0.59-1.50)

P = 0.89

P = 0.33

Log-Rank P = 0.82

P = 0.81

Titan-2 BAS (n=417)
Xience-V EES (n=410)

3.9% 6.8% 7.2% 9.0%

0 5 10 15

30 90 180 270 360

Days after Index PCI

TiNOX vs EES
MACE Components
5 years cumulative events

- Myocardial Infarction: 4.8% (Titan-2 BAS) vs 8.5% (Xience-V EES)
- Cardiac Death: 2.6% (Titan-2 BAS) vs 2.9% (Xience-V EES)
- Ischemia-driven TLR: 7.9% (Titan-2 BAS) vs 9.0% (Xience-V EES)
- MACE: 13.9% (Titan-2 BAS) vs 16.6% (Xience-V EES)
- ST: 1.0% (Titan-2 BAS) vs 3.2% (Xience-V EES)

P-values:
- Myocardial Infarction: P = 0.02
- Cardiac Death: P = 0.80
- Ischemia-driven TLR: P = 0.57
- MACE: P = 0.29
- ST: P = 0.02
"Randomized clinical trial with clinical outcome as primary end point showed TiNOX stent is not inferior to EES in ACS patients including UA, STEMI & NSTEMI."

EuroIntervention 2012; 8:306-315

Level of evidence B (according to the rules of the ESC Guidelines)
Introducing Optimax
Titanium-nitride-oxide Technology
New Platform
(Co-Cr Alloy)

- **20%** THINNER STRUTS (75 microns)
  - Improved Radio-Opacity
  - Higher Radial Force

Stainless Steel Stent Platform

Cobalt Chromium Stent Platform

91 μm

75 μm & 60 μm
Enhanced Coating Process

- 100% INCREASED TiNOX COATING THICKNESS
  - Higher Titanium-Nitride-Oxide concentration
  - Lower Thrombogenicity
  - Fast Re-endothelialization

Stent Strut

**Ti**

**N**

**O**

**N**

**O**

Stent Strut

HEXACATH ICI 2015
OPTIMAX first-in-man study

PURPOSE OF THE STUDY

In a prospective first-in-man observational study design, we explored the 6-month clinical outcome of a Titanium-Nitride-Oxide coated OPTIMAX-stent based on cobalt-chromium platform, in *de novo* coronary lesions.

*Between January 2013 and October 2013, all consecutive patients scheduled for stent implantation were considered for this prospective registry.*
### OPTIMAX first-in-man study

<table>
<thead>
<tr>
<th>Category</th>
<th>Values</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>69 ± 9</td>
</tr>
<tr>
<td>Male, n (%)</td>
<td>129 (70)</td>
</tr>
<tr>
<td>Diabetes, n (%)</td>
<td>28 (15)</td>
</tr>
<tr>
<td>Current smoking, n (%)</td>
<td>35 (19)</td>
</tr>
<tr>
<td>Hypertension, n (%)</td>
<td>105 (57)</td>
</tr>
<tr>
<td>Hypercholesterolemia, n (%)</td>
<td>92 (50)</td>
</tr>
<tr>
<td>Previous MI, n (%)</td>
<td>17 (9)</td>
</tr>
<tr>
<td>Previous PCI, n (%)</td>
<td>20 (11)</td>
</tr>
<tr>
<td>Previous CABG, n (%)</td>
<td>5 (3)</td>
</tr>
<tr>
<td>STEMI, n (%)</td>
<td>26 (14)</td>
</tr>
<tr>
<td>NSTEMI, n (%)</td>
<td>82 (45)</td>
</tr>
</tbody>
</table>

**OPTIMAX stent**

(n=184)
# Procedural and Lesion Characteristics

<table>
<thead>
<tr>
<th>OPTIMAX stent (n=184)</th>
</tr>
</thead>
</table>
| **Thrombus, n (%)**    | 19 (10)  
| **Calcified lesion, n (%)** | 64 (35)  
| **Bifurcation involved, n (%)** | 33 (18)  
| **Reference vessel diameter (RVD), mm** | 3.03 ± 0.37  
| **Lesion length, mm** | 17.3 ± 6.4  
| **Stent diameter, mm** | 3.10 ± 0.38  
| **Stent length (Total stent length), mm** | 19.5 ± 5.5 (21.4 ± 8.4)  
| **Thrombus aspiration, n (%)** | 14 (8)  
| **Direct stenting, n (%)** | 50 (27)  
| **Post-dilatation, n (%)** | 140 (76)  
| **DURATION of DAPT*, months** | 4.6 ± 2.5  

*Aspirin 100mg + Clopidogrel in 95.1% of patients (Prasugrel in 2.7% and Ticagrelol in 2.2%)

ICI 2015
<table>
<thead>
<tr>
<th>Event</th>
<th>%</th>
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<tbody>
<tr>
<td>MI</td>
<td>3.1%</td>
</tr>
<tr>
<td>TLR</td>
<td>3.1%</td>
</tr>
<tr>
<td>Cardiac Death</td>
<td>1.3%</td>
</tr>
<tr>
<td>ST</td>
<td>0%</td>
</tr>
<tr>
<td>MACE</td>
<td>6.3%</td>
</tr>
<tr>
<td>All Cause Death</td>
<td>2.2%</td>
</tr>
</tbody>
</table>

*Follow-up 100%*
OPTIMAX vs TITAN*
12-Months* MACE Composition

Titan stent (n=201)
Optimax stent (n=224)

<table>
<thead>
<tr>
<th>Event</th>
<th>Titan Stent (%)</th>
<th>Optimax Stent (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>MI</td>
<td>3.1%</td>
<td>4.5%</td>
</tr>
<tr>
<td>TLR</td>
<td>3.1%</td>
<td>5.0%</td>
</tr>
<tr>
<td>Cardiac Death</td>
<td>1.3%</td>
<td>0.5%</td>
</tr>
<tr>
<td>ST</td>
<td>0%</td>
<td>0%</td>
</tr>
<tr>
<td>MACE</td>
<td>10.9%</td>
<td>6.3%</td>
</tr>
<tr>
<td>All Cause Death</td>
<td>2.2%</td>
<td>2.5%</td>
</tr>
</tbody>
</table>

OPTIMAX first-in-man Study

PURPOSE OF THE STUDY

Confirms the results are as good as Titan first generation TiNOX stent and most probably better in terms of clinical outcomes.

In addition the biomechanics of Optimax is far superior to the one of Titan2 making this new device one of the best biomechanical platform available today to reach and treat the most complex lesions.
TIDES-ACS – Trial Design

Prospective, multicenter, randomized non-inferiority trial

Patients presenting with Acute Coronary Syndrome (ACS)

2:1 Randomization

OPTIMAX
Titanium Nitride-Oxide Stent (BAS)
1200 Patients

SYNERGY
Everolimus-Eluting Stent (EES)
600 Patients

1800 Patients enrolled Clopidogrel, Prasugrel or Ticagrelor for 6 months minimum

Clinical endpoint assessment

Clinical f/u

30d  6mo  12mo  18mo  2yr  3yr  4yr  5yr

Primary Endpoint

• MACE (MI, TLR, and Cardiac Death) at 12 months
Thank You

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Laurent Sebagh, MD
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On behalf of AFICARDIO and the French Cardiological Community, I would like to thank our colleagues for their warm support after the tragedy which has shaken Paris few weeks ago.