Absorbable Metal Stent, Clinical Update and DREAMS: Concept and preclinical Data

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Complete occlusion of the left pulmonary artery after de-banding and closure of the arterial duct with a clip (the device with three markers is for calibration purposes)
Crossing the stenosis with a guide wire angiography revealed reperfusion
Implantation procedure of Mg Stent 3.0/10mm with a contrast filled balloon catheter

Peter Zartner, M. D., Pediatric Cardiology University of Erlangen-Nuremberg, Germany
At one week follow up after Mg Stent the left lung was reperfused.
Why bio-absorbable stents?

Provides stent scaffolding and radial strength properties as long as needed to ensure an open lumen - same as a permanent stent

Different to permanent stents:
- Leaves no stent behind long-term (no chronic inflammation, no long-term impact on local vasomotion)
- No “Full metal jacket” makes later treatments of the same segment easier (e.g., surgical bypass)
- MRI / CT compatibility (allows non-invasive follow-ups)
- Potentially: no late stent thrombosis and no need for prolonged antiplatelet therapy
Absorbable Metal Stent

Biocompatibility – BIOTRONIK Magnesium Alloy

Magnesium and the human body
- Essential element for human body, involved in the synthesis of more than 300 enzymes
- Physiologically occurrence: 4th most common mineral
- Quantity in human body: ~ 20 g
- Daily need (adult): ~ 350 mg
- Quantity in the intracellular space: > 40%

BIOTRONIK AMS features
- Weight of a 3.0x10mm stent: ~ 3 mg
- Complete absorption: ≈ 12 weeks
First generation AMS device (AMS 1)

Available sizes
- Diameter: 3.0 and 3.5mm
- Length: 10mm and 15 mm

Magnesium alloy device
- Weight of a magnesium stent: ~3 mg
- Complete absorption: several months
- High collapse pressures
Analysis of degradation products by EDX analysis

Mg alloy before degradation

Conversion layer: soft shell of Ca(PO₄)₂

Mg alloy after 13 days in porcine blood
Compatibility of AMS in MRI and multi-slice CT

- No stent artefact
- Optimal vessel lumen imaging
CT compatibility of AMS

Bare Metal Stent

Absorbable Metal Stent

16-row MSCT
First in Man Coronary Study of AMS 1: PROGRESS 1

Clinical Performance and Angiographic Results of the Coronary Stenting with Absorbable Metal Stents

Principal Investigator: Prof. Raimund Erbel
PROGRESS AMS 1

- **Purpose**: To evaluate the clinical feasibility of the Absorbable Metal Stent in the treatment of a single de novo lesion in a native coronary artery

- **Design**: Prospective, multi-center, consecutive, non-randomized FIM (First In Man – coronary) study

- **Patients**: The study included 63 patients at 8 international clinical sites
## PROGRESS: Clinical Results

<table>
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<th>In Hospital</th>
<th>4 Months</th>
<th>4-12 Months</th>
<th>12 Months</th>
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<tr>
<td></td>
<td>N</td>
<td>%</td>
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<td>%</td>
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<td>MACE</td>
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<td>0</td>
<td>15</td>
<td>23.8</td>
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<td>Death</td>
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<td>0</td>
<td>15</td>
<td>23.8</td>
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</table>
TLR occurrence in PROGRESS 1
AUS 004-001

Post Implantation

4 Months

16 Months
IVUS Analysis

- Stent Volume
- Lumen Volume
- Vessel Volume
- Stent CSA
- IH Volume

Index | 4month | FU | long term | FU

The graph shows changes in these parameters over time.
IVUS CSA

![Graph showing IVUS CSA over FU time (month)]
IVUS Intimal Hyperplasia Volume

![Graph showing IVUS Intimal Hyperplasia Volume over time for different patients.](image-url)
First evidence of vessel flexibility in AMS stented area by angio pre/post nitroglycerin

pre I.S.D.N.

GRB009-007
RCA, Ø3.0
asyptomatic TLR
at 4 months FU

post I.S.D.N.
Vessel Reactivity

Intracoronary ISDN induced vasodilatation in Permanent Metal Stent (PMS) control patients and Absorbable Metal Stent (AMS) patients within stent and in proximal reference segments at 4 months post implant.

% change in cross sectional area post IC ISDN

Reference segment
p = 0.3806

Stented segment
p = 0.0017

PMS  AMS  PMS  AMS

Courtesy of Dr Miles Dalby
Royal Brompton & Harefield
15 months after AMS implantation in human

- Very thin neointima
- Perfect ingrowth of AMS
- Completed healing of the stented vessel
Conclusions - PROGRESS 1

- The AMS technology is feasible (high technical and procedural success), absorption of the device as intended
- The AMS provided safety (no death, no MI, no stent thrombosis)
- The study met the primary endpoint (MACE <30%)
- Further improvement of the AMS 1 technology are needed to improve efficacy for coronary use
Results PROGRESS 1 - IVUS

Post implantation

Contribution to lumen loss

- Negative remodeling/recoil: 42%
- Thickening of extra-stent tissue: 13.5%
- In-stent neointima: 41%

4 months follow-up
Improvement of AMS 1

AMS 1 is currently improved by...

...prolonged mechanical stability

- Improved stent design
- Surface passivation
- Modified Alloy

...reduction of neointima hyperplasia

"DREAMS" = Drug elution
Selection trial - Stent structure after 4 weeks

AMS 1

AMS 1 design &
New alloy

AMS 1 alloy &
New design
Description of new AMS 2 device

- Bare stent (no coating)
- Special Magnesium alloy
- Refined stent design
- Stent range
  - Diameters: 3.0 and 3.5mm
  - Lengths: 10 and 15 mm
- 6F compatible system, RX catheter
Combination trial - Angiography

Late Lumen Loss (mm), median

2 weeks

4 weeks

AMS 1

AMS 2
Combination trial-
Representative histology 4 weeks

AMS 1

AMS 2

Source: R. Virmani, CVPath
Combination trial - Representative stent structure at 2 weeks

AMS 1

AMS 2
Combination trial - Representative stent structure at 4 weeks

AMS 1

AMS 2
Histology 4 weeks

Source: R. Virmani, CVPath
Stent structure at 3 month
Combination trial - Histomorphometry

2 weeks

4 weeks

Source: R. Virmani, CVPath
Status AMS 2 - Summary

• The optimization of both the Magnesium alloy and the stent design contribute to a longer stent integrity in animal

• The new AMS generation with increased integrity shows significantly improved efficacy in animal
DREAMS concept

- Degradable carrier from Magnesium alloy
- Effective anti-proliferative drug
- Specialized proprietary matrix to cope with degradation of Magnesium alloy
  - Non-permanent polymer
  - Optimized rate of drug elution
DREAMS DRUG-Eluting Stent System

**Stent:**
Bioabsorbable Magnesium Alloy
Discrete Drug Delivery Reservoirs

**Drug:**

**Carrier:**
Bioresorbable Matrix
Brachytherapy and AMS - Study design

- Domestic Pigs
  - Vision stent implantation
  - AMS 1 stent implantation
  - 24 Gy beta radiation
  - AMS 1 stent implantation
  - Sacrifice
Brachytherapy and AMS - Histopathology
Brachytherapy and AMS - representative images

Vision

AMS 1

AMS 1 + VBT
AMS program

AMS 1
First clinical experience: AMS is “safe”

AMS 2
Improved mechanical integrity by modified alloy and improved stent design

AMS 3
Drug-eluting AMS (DREAMS) incl. surface passivation and X-ray markers
Status of AMS 2007

- Safe in human coronaries
- Safe in peripheral arteries (tibial)
- Absorbed as intended < 90 days
- Fully compatible with CT or MRI angiography
- Restenosis mainly due to early recoil and neointima formation
- New Generations AMS under preclinical testing
- Resume Clinical testing to be announces

Thank You