PARADIGM-Extend Prospective Academic Trial: Accruing long-term evidence for MicroNet-covered stent safety and stroke prevention efficacy


Jagiellonian University Dept. of Cardiac & Vascular Diseases
John Paul II Hospital, Kraków, Poland
& Collaborating Vascular Centres

Supported K/ZDS/007819 (Jagiellonian University Medical College)
Disclosures

Proctoring/Speaker Bureau/Advisory Boards - Abbott, InspireMD, Medtronic

Research Support - Abbott (IIS)

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Research work in this presentation is supported by the Jagiellonian University Medical College (K/ZDS/007819)
PARADIGM-Extend = Prospective evaluation of All-comer percutaneous carotid revascularization in symptomatic and increased-stroke-risk asymptomatic carotid artery stenosis using CGuard™ Micronet-covered embolic prevention stent system – clinical trial multi-centre extension
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Conventional Carotid Stents
Conventional Carotid Stents
Do Have A Problem

Human carotid artery treated using a conventional stent; OCT
Image courtesy Joan Rigla, MD PhD; Perceptual Imaging Lab, University of Barcelona
Conventional Carotid Stents Do Have A Problem

This translates into post-procedural minor strokes during the stent healing (≈30 days)

(CREST, CAPTURE)

≈40% 30d-strokes are post-procedural
FUNDAMENTAL
• CEA, by excluding the plaque, excludes the post-procedural problem of the plaque
CEA, by excluding the plaque, excludes the post-procedural problem of the plaque.

In CAS, the stent needs to exclude the plaque too.
CEA, by excluding the plaque, excludes the post-procedural problem of the plaque.

In CAS, the stent needs to exclude the plaque too.
# CGuard™– Carotid Embolic Prevention System

## System specifications

<table>
<thead>
<tr>
<th>Specification</th>
<th>Details</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stent type</td>
<td>Nitinol – self expanding</td>
</tr>
<tr>
<td>Micronet aperture size</td>
<td>150-180 μm</td>
</tr>
<tr>
<td>Guidewire</td>
<td>0.014”</td>
</tr>
<tr>
<td>Sizes</td>
<td></td>
</tr>
<tr>
<td>- Diameter</td>
<td>6-10mm</td>
</tr>
<tr>
<td>- Length</td>
<td>20-60mm</td>
</tr>
</tbody>
</table>

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**CE Mark – March 2014**

**Nitinol frame open-cell area ≈ 21 mm²**

**MicroNet closed-cell area ≈ 0.3 mm²**

- **LARGEST**
- **SMALLEST**
CGuard EPS  90 days/pig
**CGuard EPS**

30 & 90 days / pig

![Image of histomorphology parameters](image.png)

**Mean ± SD Standard Histomorphology Parameters (2 of 2)**

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Day 30</th>
<th>Day 90</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>BMS (n=3)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Injury (0-3)</td>
<td>0.00 ± 0.01</td>
<td>0.00 ± 0.01</td>
</tr>
<tr>
<td>Inflammation (0-3)</td>
<td>0.43 ± 0.23</td>
<td>0.41 ± 0.22</td>
</tr>
<tr>
<td>Neointimal Fibrin (0-3)</td>
<td>1.13 ± 0.23</td>
<td>0.82 ± 0.37</td>
</tr>
<tr>
<td>Adventitial Fibrosis (0-3)</td>
<td>0.00 ± 0.00</td>
<td>0.02 ± 0.07</td>
</tr>
<tr>
<td>Neointimal Maturation (0-3)</td>
<td>3.00 ± 0.00</td>
<td>3.00 ± 0.00</td>
</tr>
<tr>
<td>Endothelization (0-4)</td>
<td>3.67 ± 0.42</td>
<td>3.80 ± 0.35</td>
</tr>
<tr>
<td><strong>CGuard (n=9)</strong></td>
<td></td>
<td></td>
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<td>Injury (0-3)</td>
<td>0.00 ± 0.01</td>
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<td>0.51 ± 0.31</td>
<td>0.42 ± 0.22</td>
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<td>1.00 ± 0.00</td>
<td>0.81 ± 0.37</td>
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*InspireMD data / used with permission*
MicroNet mesh preventing prolapse

Tomyuki Umemoto et al.
*EuroIntervention* 2017

Musialek & Stabile
*EuroIntervention* 2017

ESC Congress Paris 2019
MicroNet mesh preventing prolapse

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Musialek & Stabile
*EuroIntervention* 2017
Objective

- to evaluate feasibility and outcome of routine anti-embolic stent system use in unselected, consecutive patients referred for carotid revascularization (‘all-comer’ study)
Prospective evaluation of All-comer percutaneous carotid revascularization in symptomatic and Increased-risk asymptomatic carotid artery stenosis using the CGuard™ Micronet-covered embolic prevention stent system

The PARADIGM Study
PARADIGM study: referrals flow chart
139 carotid stenosis patient referrals

- Neurologist
- Interventional angiologist
- Vascular surgeon
- Cardiologist

Neuro Vascular Team

for carotid revascularisation
108 patients

NOT for carotid revascularisation
31 patients

n=24: increased stroke risk and/or lesion severity criteria not met
n=2: ICA totally occluded on verification
n=2: ICA functional occluded + h/o prior ipsilateral large cerebral infarct with haemorrhagic transformation
n=1: major post-stroke disability, ICA functionally occluded
n=1: severe circulatory failure (ICA stenosis asymt.)
n=1: malignancy with limited life expectancy (ICA stenosis asymt.)

PARADIGM

Methods (cont’d):

- **ASYMPTOMATIC** patients treated interventionally only if at stroke risk
- established lesion-level increased-risk criteria used:
  - thrombus-containing
  - documented progressive
  - irregular and/or ulcerated
  - contralateral ICA occlusion/stroke
  - asymptomatic ipsilateral brain infarct

PARADIGM study: revascularisation flow chart

108 patients for carotid revascularisation

- (93%) CAS in n=100 patients (bilateral in 5)
- (1%) CAS+CEA in n=1 patient (LICA-CEA and RICA-CAS) hybrid management
- (6%) CEA in n=7 patients
  - n=1 eGRF 14 → no contrast
  - n=2 hostile access
  - n=1 major ICA kink/loop
  - n=1 severe aortic valve disease + calcific LICA (AVR+CEA)
  - n=1 floating thrombus in CCA
  - n=1 ICA diameter <2.0 mm + contralateral ICA occlusion

106 ICAs treated endovascularly in 101 patients using exclusively the MicroNet-covered embolic prevention stent system

Symptomatic – 54.5%

n=106 arteries in 101 patients
PARADIGM – Extend continues as an ALL-Comer Multi-Centre Study

No exclusion criteria other than absence of carotid stenosis that requires revascularization by NVT recommendation
PARADIGM – Extend continues as an ALL-Comer Multi-Centre Study

31 July 2019

- 402 patients / 436 arteries
  
  NeuroVascular Team decision-making on endovascular revascularization
PARADIGM – Extend continues as an ALL-Comer Multi-Centre Study

31 July 2019

- 402 patients / 436 arteries
  NeuroVascular Team decision-making on endovascular revascularization
- Age 48-87 years, 56.4% symptomatic
- Crossed the trial first follow-up window (30d)
PARADIGM – Extend continues as an ALL-Comer Multi-Centre Study

31 July 2019

- 402 patients / 436 arteries
  *NeuroVascular Team decision-making on endovascular revascularization*
- Age 48-87 years, 56.4% symptomatic
- Crossed the trial first follow-up window (30d)
- 100% CGuardEPS use, Proximal/distal EPD ≈ 50% : 50%
PARADIGM – Extend continues as an ALL-Comer Multi-Centre Study

31 July 2019

- 402 patients / 436 arteries
  
  NeuroVascular Team decision-making on endovascular revascularization

- Age 48-87 years, 56.4% symptomatic

- Crossed the trial first follow-up window (30d)

- 100% CGuardEPS use, Proximal/distal EPD ≈ 50% : 50%

- Angiographic diameter stenosis was reduced from 84±8% to only 6.9±5% (p<0.001, ‘CEA-like’ effect of CAS)
PARADIGM – Extend

402 patients / 436 arteries

31 July 2019

- Peri-procedural outcome
  0 death/major stroke – 0%
  1 minor stroke – 0.25%
  1 MI (type2) – 0.25%
PARADIGM – Extend
402 patients / 436 arteries

31 July 2019

● **Peri-procedural outcome**

  0 death/major stroke – 0%
  1 minor stroke – 0.25%
  1 MI (type2) – 0.25%

● **By 30 days**

  1 haemorrhagic transformation of prior ischaemic cerebral infarct leading to death – 0.25%

  1 bleeding-related death – 0.25%
PARADIGM – Extend

402 patients / 436 arteries

31 July 2019

- **Total**
  30-day death/MI/any stroke – **0.995 %** (4/402)

- **no major stroke by 30 days** – **0.0 %** (0/402)
PARADIGM – Extend

402 patients / 436 arteries

31 July 2019

- **Total**
  
  30-day death/MI/any stroke – 0.995 % (4/402)

- **no major stroke by 30 days** – 0.0 % (0/402)

- *Then clinical (inc. Neurology exam) and Duplex follow-up every 12 months*
<table>
<thead>
<tr>
<th>Time Period</th>
<th>n</th>
<th>Ipsilateral Stroke</th>
</tr>
</thead>
<tbody>
<tr>
<td>1-12 mo</td>
<td>311</td>
<td>0</td>
</tr>
<tr>
<td>13-24 mo</td>
<td>205</td>
<td>0</td>
</tr>
<tr>
<td>25-36 mo</td>
<td>108</td>
<td>1</td>
</tr>
<tr>
<td>37-48 mo</td>
<td>61</td>
<td>1</td>
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NB. ALL-Comer, Unselected Population (eg. AFib 8.9%)
# PARADIGM – Extend

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<tr>
<td><strong>ipsilateral</strong></td>
<td>0</td>
<td>0</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td><strong>any stroke</strong></td>
<td>0</td>
<td>2</td>
<td>1</td>
<td>2</td>
</tr>
</tbody>
</table>

- **1 cerebellal**
- **1 contralat.**
- **1 brain stem**
- **(1 contralat.)**

**NB.** ALL – Comer, Unselected Population (eg. AFib 8.9%)

**ESC Congress Paris 2019**
## PARADIGM – Extend

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<th>Ipsilateral Stroke</th>
<th>Any Stroke</th>
<th>Stroke-Related Death</th>
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<tr>
<td>1-12 mo</td>
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<td>0</td>
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<tr>
<td>Ipsilateral stroke</td>
<td>0</td>
<td>0</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
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<td>0</td>
<td>2</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>Stroke-related death</td>
<td>0</td>
<td>1</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>MI or other non-cerebral VA</td>
<td>3</td>
<td>3</td>
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<td>0</td>
<td>2</td>
<td>1</td>
<td>2</td>
<td>4</td>
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</tbody>
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NB. ALL-Comer, Unselected Population (eg. AfiB 8.9%)

- CHF-4, Ca-3, PE-1, MI-2, COPD-1, urosepsis-1, surg-1
- CHF-3, Ca-2, MI-2, surg-2, intrac. bleed-1
- CHF-2, Ca-2, MI-1, urosepsis -1
- CHF-2, Ca-2, MI-2

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Paris 2019
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<td>0</td>
<td>1</td>
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<td>1</td>
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<td><strong>in-stent velocities</strong></td>
<td>PSV 0.79±0.41 m/s</td>
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<td>EDV 0.21±0.11 m/s</td>
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**PARADIGM – Extend**

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**NB. ALL-Comer Unselected Population (eg. AFib 8.9%)**

By 48 months:

- Normal healing
- No Stent Thrombosis
- No abnormal ISR signal

(Per-vessel ISR 0.92% - 4/436; DEB-PTA)

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PARADIGM–EXTEND

@ 48 months

Favourable Cerebral Outcome

- NO device-related adverse events
- NO procedure-related events
PARADIGM–EXTEND

@ 48 months
Favourable Cerebral Outcome

• NO device-related adverse events
• NO procedure-related events

sustained stroke prevention
Endovascular Solution for All-Comers

Endovascular Reconstruction of the Carotid Bifurcation

Prevention of embolism, High radial force, Conformability
Human 3D OCT, symptomatic lesion
systematic CEA-like effect of CAS
This concept has been desired.

And it works.
This concept has been desired.

And it works.

This is the future of Carotid Artery Stenting
Double-Layer Carotid Stents: From the Clinical Need, through a Stent-in-Stent Strategy, to Effective Plaque Isolation... the Journey Toward Safe Carotid Revascularization Using the Endovascular Route

Piotr Musiałek, MD, DPhil¹ and Gary S. Roubin, MD, PhD²

Keywords
carotid artery stenosis, carotid artery stenting, carotid endarterectomy, closed-cell stent, MicroNET, open-cell stent, plaque protrusion, stent-graft, restenosis, double-layer stent, unstable plaque

Both surgical and endovascular routes of carotid revascularization are associated with the risk of symptomatic and asymptomatic cerebral embolism.¹⁻⁴ Optimized pharmacotherapy, the mainstay of atherosclerosis management, can reduce or delay but not abolish the risk of stroke from atherosclerotic carotid artery stenosis.⁵⁻⁷ Interventional elimination or sequestration of the thromboembolic carotid plaque⁸⁻¹⁰ remains an important consideration in a significant proportion of patients if carotid stenosis-related strokes are to be prevented rather than experienced. This is the focus and the stent-free-cell area also affect the risk of embolism after stent placement. Thus, while optimized neuroprotection during CAS may minimize intraprocedural cerebral embolism, the problem of early or delayed postprocedural embolism remains.¹¹⁻¹³ With optimal patient selection technique and antiplatelet therapy, post-stent embolic phenomena are largely related to intrastent plaque prolapse, balloon trauma, and subsequent embolization. This may occur after the period of intraprocedural cerebral protection using flow reversal techniques and/or filters.
This concept has been desired.
And it works.

This is the future of Carotid Artery Stenting
This concept has been desired.

And it works.

This is the future of Carotid Artery Stenting.

revascularization!