MicroNet Covered Embolic Prevention Carotid Stent System: From CARENET and PARADIGM Studies To Routine Clinical Practice

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Disclosure Statement of Financial Interest

Within the past 12 months, I or my spouse/partner have had a financial interest/arrangement or affiliation with the organization(s) listed below.

Affiliation/Financial Relationship | Company
---|---
Grant/Research Support | ABBOTT
Consulting Fees/Honoraria | ABBOTT, Baltin, InspireMD, Medtronic

CGuard™ embolic prevention stent

A Prospective, Multicenter Study of a Novel Mesh-Covered Carotid Stent

The C Guard CARENET Trial
Carotid Embolic Protection Using MicroNet

The C Guard CARENET Trial was a prospective, multicenter study designed to evaluate the safety and efficacy of the MicroNet covered stent system in reducing the incidence of periprocedural stroke in patients undergoing carotid stenting. The study was conducted at 9 centers in the United States and included 55 patients who underwent carotid stenting with the MicroNet covered stent system. The primary endpoint was the incidence of periprocedural stroke, which was defined as any stroke occurring within 48 hours of the procedure. The secondary endpoints included the occurrence of any adverse event, the presence of any embolic signal, and the need for any bailout therapy. The study results showed that the MicroNet covered stent system was safe and effective in reducing the incidence of periprocedural stroke, with no cases of periprocedural stroke reported in the study.
Mandatory DW-MRI

24h after Prior to CAS
30 d after CAS

CARENET 03-007, PJ (Krakow)

Mandatory DW-MRI

Rec. Symptomatic LICA

CAS (and CEA) are –and will remain– emboli-generating procedures.
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**Post-procedural Embolization with conventional carotid stents**

**Conventional Carotid Stent**

**FREE CELL AREA** drives CAS neurologic adverse events (and majority occur post-procedure)
Conventional Carotid Stent

Anti-Embolic Carotid Stent

CGuard™ Carotid Embolic Prevention System

NB. CGuard™ EPS is not yet available in the US

CARENET – Study Design

Prospective, multi-center, all-comer

Objectives:
To evaluate the periprocedural safety and efficacy of the CGuard stent in the treatment of carotid lesions in thirty consecutive patients with symptomatic and asymptomatic carotid artery stenosis, suitable for CAS

Sites:
- Joachim Schofer (PI), Hamburg University Cardiovascular Center
- Piotr Musialek (Co-PI), Jagiellonian University Medical College
- Rolf Kolvenbach, Augusta Hospital
- Horst Sievert, Cardiovascular Center Frankfurt

Endpoints:
- Acute /30-day Cerebral Embolization by DWI (incidence, volume)
- 30 day MACCE (death, stroke, MI)
DW-MRI: the unforgiving testimony of what you’ve done to the TARGET ORGAN...

CARENET DW-MRI analysis

<table>
<thead>
<tr>
<th>DW-MRI analysis @ 48 h</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>CARENET (n=10)</td>
<td></td>
</tr>
<tr>
<td>Incidence of new ipsilateral lesions</td>
<td>37.0%</td>
</tr>
<tr>
<td>Average lesion volume (cm³)</td>
<td>0.039 ± 0.08</td>
</tr>
<tr>
<td>Maximum lesion volume (cm³)</td>
<td>0.445</td>
</tr>
</tbody>
</table>

≈50% reduction in new ipsilateral lesion incidence
CARENET DW-MRI analysis

<table>
<thead>
<tr>
<th></th>
<th>CARENET</th>
<th>PROFIL</th>
<th>ICSSa</th>
</tr>
</thead>
<tbody>
<tr>
<td>incidence of new ipsilateral lesions</td>
<td>37.0%</td>
<td>66.2%</td>
<td>68.0%</td>
</tr>
<tr>
<td>Average lesion volume (cm³)</td>
<td>0.039</td>
<td>0.575</td>
<td>-</td>
</tr>
<tr>
<td>Maximum lesion volume (cm³)</td>
<td>0.6</td>
<td>-</td>
<td>-</td>
</tr>
</tbody>
</table>

>10-fold reduction in cerebral lesion volume

Filter-protected CAS procedures

CARENET vs PROFIL: DW-MRI analysis

All but one peri-procedural ipsilateral lesions RESOLVED

<table>
<thead>
<tr>
<th></th>
<th>CARENET</th>
<th>PROFIL</th>
<th>ICSSa</th>
</tr>
</thead>
<tbody>
<tr>
<td>Incidence of new ipsilateral lesions</td>
<td>1</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Average lesion volume (cm³)</td>
<td>0.08 ± 0.00</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Permanent lesions at 30 days</td>
<td>1</td>
<td>-</td>
<td>-</td>
</tr>
</tbody>
</table>

Anti-Embolic Carotid Stent

Plaque protrusion may lead to early and late distal embolization

**Filter-protected CAS procedures**

CARENET vs PROFIL: DW-MRI analysis

>10-fold reduction in cerebral lesion volume

**CARENET DW-MRI analysis**

All but one peri-procedural ipsilateral lesions RESOLVED

**Anti-Embolic Carotid Stent**

Plaque protrusion may lead to early and late distal embolization
**Objective**

- to evaluate feasibility and outcome of routine anti-embolic stent system use in unselected, consecutive patients referred for carotid revascularization (‘all-comer’ study)

**Endpoints:**

- feasibility of endovascular Tx in unselected referrals using the study device in otherwise routine practice
- device success (able to deliver + implant + <30% DS)
- procedure success (device success w/o clinical compl.)
- clinical efficacy: MACNE (death/stroke/MI)
- in-stent velocities (Duplex)

**Methods: The CAS Procedure**

- EPD use mandatory; EPD selection according to the ‘tailored CAS’ algorithm
- Liberal postdilatation accepted in order to maximize potential for ‘endovascular full reconstruction’ (minimizing residual stenosis)

NB. 1. DWI evidence of effective MicroNet prevention against cerebral embolization (CARENET/PTRDF)
2. Residual stenosis after CAS as independent predictor of in-stent restenosis

**PARADIGM**

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

*Plakosidis S, Musialek P et al. J Endovasc Ther 2010 17:315-321*
Methods (cont’d)

PARADIGM: investigator – independent

- external study data verification
- external angiographic analysis
- external statistical analysis

Study Flow Chart (1)

97 carotid stenosis patient referrals* (external >> internal)

Neuro-Vascular Team

for carotid revascularization

73 patients

NOT for carotid revascularization

24 patients

Clinical characteristics of study patients (n=68)

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>n</th>
<th>Mean ± SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, years</td>
<td>68</td>
<td>65 ± 15</td>
</tr>
<tr>
<td>Gender, %</td>
<td>68</td>
<td>65%</td>
</tr>
<tr>
<td>Diabetes, %</td>
<td>68</td>
<td>27%</td>
</tr>
<tr>
<td>Smokers, %</td>
<td>68</td>
<td>27%</td>
</tr>
<tr>
<td>Hypertension, %</td>
<td>68</td>
<td>27%</td>
</tr>
<tr>
<td>Stroke, %</td>
<td>68</td>
<td>27%</td>
</tr>
<tr>
<td>CABG or PCI</td>
<td>68</td>
<td>27%</td>
</tr>
<tr>
<td>PCI as bridge to CAS, %</td>
<td>68</td>
<td>27%</td>
</tr>
<tr>
<td>Arterial (by chronic, %)</td>
<td>68</td>
<td>27%</td>
</tr>
<tr>
<td>Diabetes, %</td>
<td>68</td>
<td>27%</td>
</tr>
<tr>
<td>H/o neck or chest radiotherapy, %</td>
<td>68</td>
<td>27%</td>
</tr>
</tbody>
</table>

Study Flow Chart (2)

73 Patients for carotid revascularization

71/ICAs treated endovascularly in 68 patients

PARADIGM: Results (1)

- Percutaneous treatment 100% using the intended MicroNet-covered embolic prevention stent system C Guard

  (ie, no other stents used during the study period)

  - Device success 100%
  - Procedure success 100%
  - Transient Dopamine infusion 19% (n=14)
  - Debris in EPD 18% (n=13)
  - Access site complications 0% (n=0)
  - Vascular plug closure 45% (n=32)

PARADIGM: Results (2)

Index lesion characteristics (n=71 lesions)

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>n</th>
<th>Mean ± SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Thrombus, %</td>
<td>71</td>
<td>24%</td>
</tr>
<tr>
<td>Intimal flap, %</td>
<td>71</td>
<td>24%</td>
</tr>
<tr>
<td>Proximal stenosis, %</td>
<td>71</td>
<td>24%</td>
</tr>
<tr>
<td>Ultrasound, %</td>
<td>71</td>
<td>24%</td>
</tr>
<tr>
<td>Vessel size, %</td>
<td>71</td>
<td>24%</td>
</tr>
<tr>
<td>Contrast agent, %</td>
<td>71</td>
<td>24%</td>
</tr>
<tr>
<td>Highly atherosclerotic, %</td>
<td>71</td>
<td>24%</td>
</tr>
<tr>
<td>Core-Lab-Quantified</td>
<td>n/a</td>
<td>n/a</td>
</tr>
</tbody>
</table>

*method of imaging

ICU reference diameter 4.99 ± 0.35 mm (from 4.27 to 6.02 mm)
* Lesion length 10.8 ± 5.8 mm (from 8.19 to 30.25 mm)
**Paradigm: Results (3)**

<table>
<thead>
<tr>
<th>Index lesion quantitative characteristics (n=71 lesions)</th>
<th>n (%) or mean ± SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Before CAS</td>
<td>2.9±5.0</td>
</tr>
<tr>
<td>Residual stenosis</td>
<td>59.1±30.7</td>
</tr>
<tr>
<td>After CAS</td>
<td>24.5±15.8</td>
</tr>
<tr>
<td>Stroke length</td>
<td>29.6±16.3</td>
</tr>
<tr>
<td>Location</td>
<td>59.8±40.2</td>
</tr>
<tr>
<td>Residual stenosis</td>
<td>7.1±8.2</td>
</tr>
<tr>
<td>Mean (SD) PCI</td>
<td>0.5±1.0</td>
</tr>
</tbody>
</table>

* Emboshield (n=7); FilterWire (n=14); Spider (n=25)
** Gore FlowReversal (n=4) or flow reversal with MoMa (n=21)
[NB. mean flow reversal time was 6min 48s, from 5min 18s to 11min 2s]
ø4.5mm (n=5); ø5.0mm (n=36); ø5.5mm (n=29); ø6.0mm (n=1)
§ 30mm in 51 lesions; 40mm in 18 lesions (2 other lesions required two stents each)

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**Paradigm: Results (4)**

- Death/stroke/MI @ 48h: 0%
- Death/stroke/MI @ 30d: 0%

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**CGuard** 5 months follow-up

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**Paradigm – Extend**

PATIENT #101 in “PARADIGM-EXTEND” (a.k.a. “PARADIGM 101”)

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November 20, 2015
A Prospective, Multicenter Study of a Novel Mesh-Covered Carotid Stent
The CGuard CARENET Trial (Carotid Embolic Protection Using MicroNet)

- 2 asymptomatic self-withdrawals @ 30 days
- 100% follow up of the remaining patients
- 0 Strokes
- 0 Strokes
- 0 Stroke Deaths

Per-Protocol Independent Neurological Assessment

November 20, 2015

CARENET in-stent Peak Systolic Velocities

70% in-stent stenosis threshold

ECA patency 100% 100% 100%

Peak Systolic Velocity (cm/sec)

0 50 100 150 200 250 300

30 d 6 mo 12 mo

* Setacci et al. Grading Carotid Intrastent Restenosis of 814 CAS patients Stroke 2008

CARENET Multicenter Trial 12 mo data

New York, November 20, 2015
CARENET in-stent Peak Systolic Velocities

- 70% in-stent stenosis threshold

ECA patency

- 30 d 6 mo 12 mo

Peak Systolic Velocity [cm/sec]

- NO in-stent restenosis concern

- NO CGuard ECA patency concern

Endovascular Solution for All-Comers

Endovascular Reconstruction of the Carotid Bifurcation

CGuard embolic prevention stent system

- Full respect of the carotid bifurcation anatomy
  - 'endovascular anatomic reconstruction'
- Optimal performance across all lesion subsets
  (including high calcium/thrombus/string)

'The most OPEN of open-cell stent designs'
'The most CLOSED of the closed-cell designs'

DW-MRI Evidence (CARENET) 2015
Clinical Evidence (CARENET, PARADIGM, PARADIGM-EXTEND)
This concept has been desired. And it works.

This is the future of Carotid Artery Stenting

revascularization?
Improved technology for CAS — better EPDs (flow reversal and proximal occlusion) and better stents (membrane-covered, ultra-closed cell, and biodegradable). Several issues may improve CAS outcomes, such as the introduction of new and better stents. An ex vivo study showed that use of a polyurethane membrane-covered stent resulted in lower cerebral embolization rates.

Carotid Revascularization 2015+ REALITY

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