30-Day Results of the C-GUARDIANS Pivotal Trial of the C-Guard Carotid Stent System

The C-GUARDIANS Trial

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VIVA 23

Disclosure Statement of Financial Interest

Symposia Honoraria & Proctor Fees:

- Abbott, Endologix

Symposia Honoraria:

- Boston Scientific, Medtronic, Penumbra, Shockwave

VIVA Board Member

National PI/Co-PI:

- C-GUARDIANS, CONFIDENCE, SAPPHIRE WW, CANOPY, PERFORMANCE 3

Stock Options: INSPIREMD

Research Grants, Stocks, Equity: None

Background

- Goal is carotid artery stenting (CAS) performed at *low* risk of peri-procedural stroke
- More recent CAS trials have shown significant improvement in results, with 30-day stroke and death rates of ~2-3.5%*
- US : CMS requires use of embolic protection devices, which decrease but do not completely obviate procedural and peri-procedural embolic events
- Stents with additional “neuro-protective properties” may further decrease peri-procedural stroke events

*PROTECT, ARMOUR, EMBOLDEN , CREST 2 Registry (Matsumura, J et al JVS 2012; White, C. et al JACC 2022)

POST-CAS Strokes: Advantage for a Micro-Mesh Stent Design?

Approximately 2/3 of Events Occur AFTER the CAS Procedure

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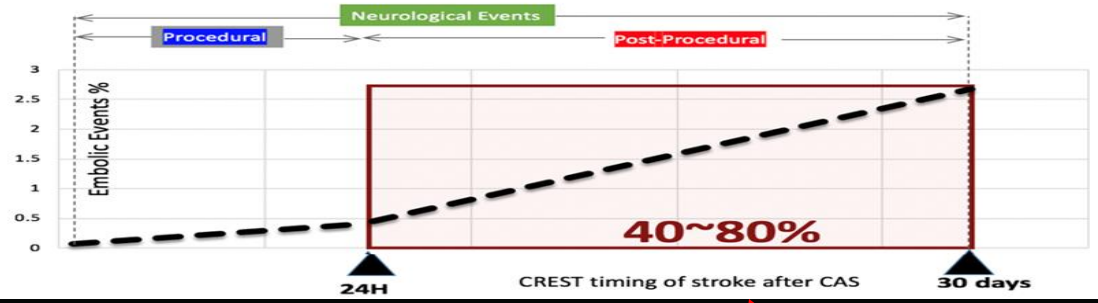
Table 6. Overview of event rates related to the different free cell area

	Total population			Symptomatic population			Asymptomatic population		
	Patients	All events	Post-procedural events	Patients	All events	Post-procedural events	Patients	All events	Post-procedural events
Free cell area									
<2,5 mm²	2107	48	26	882	20	11	1225	28	15
2,5–5 mm²	135	3	3	52	1	1	83	2	2
5–7,5 mm²	327	16	11	155	10	8	172	6	3
>7,5 mm²	610	23	21	228	17	16	382	6	5
Total	3179	90	61	1317	48	36	1862	42	25
Free cell area									
<2,5 mm²		2.3%	1.2%		2.3%	1.2%		2.3%	1.2%
2,5–5 mm²		2.2%	2.2%		1.9%	1.9%		2.4%	2.4%
5–7,5 mm²		4.9%	3.4%		6.5%	5.2%		3.5%	1.7%
>7,5 mm²		3.8%	3.4%		7.5%	7.0%		1.6%	1.3%
Total	3179	2.83%	1.9%	1317	3.6%	2.73%	1862	2.25%	1.3%

40-80% of CAS embolic events are post-procedural



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Does Free Cell Area Influence the Outcome in Carotid Artery Stenting?

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Objectives. To identify if carotid stent design, especially free cell area, impacts on the 30-day rates for stroke, death and TIA after carotid artery stenting (CAS).
Material and methods. A CAS database of 3179 consecutive CAS patients was retrospectively assessed. The distribution of neurological complications were analysed for association with the different stent types and designs. Events where subdivided into procedural and postprocedural events.
Results. The overall combined rate of TIA, stroke and death was 2.8% at 30 days (late events 1.9%). The post-procedural event rate analyzed for differences stents varied from 1.2% using BSCI Carotid Wallstent to 5.9% using Medtronic Exponent. The late event rates varied from 1.2% to 3.4% for free cell areas <2.5 mm² and >7.5 mm² respectively ($p < 0.05$). Post-procedural event rate was 1.3% for closed cells and 3.4% for open cells. All these differences were highly pronounced among symptomatic patients ($p < 0.0001$).
Conclusions. After carotid stenting, complication rates vary according to stent type, free cell area and cell design. In the symptomatic population (and also in the total population), post-procedural complication rates are highest for the open cell types and increase with larger free cell area.

Keywords: Carotid artery stenting; Carotid stenosis; Neurological complications; Cell design; Free cell area; Late embolic events.

Introduction

Carotid angioplasty and stenting (CAS) is increasingly used in the treatment of severely stenotic carotid disease.[1–4] With growing experience and the introduction of dedicated CAS materials, recent research showed that in high volume centers, there has been a shift from intra- to post-procedural complications.[5] Approximately 2/3 all events occurred after the procedure, which are probably caused by late emboli through the struts of the stent. During carotid endarterectomy (CEA) the complete plaque is removed. With carotid stenting the plaque remains contained in between the stent and the vessel wall. The stent needs to offer sufficient scaffolding in order to prevent post-procedural plaque embolization through the stent struts. Logically stents with a smaller free cell area and hence a greater percentage of wall coverage may better contain the fractured and dilated plaque after CAS resulting in a lower number of post-procedural events.

To investigate this hypothesis we reviewed the 30 day outcome after CAS in four centers with high volume experience, excluding the bias of the learning curve.

Materials and Methods

Patients

3281 patients were scheduled to undergo percutaneous carotid revascularization of the internal carotid artery in the Department of Vascular Surgery of the AZ St-Blasius in Dendermonde, Belgium, in the Department of Cardiovascular and Thoracic Surgery of the Imelda Hospital in Bonheiden, Belgium, in the Department of Vascular and Endovascular Surgery, University of Siena, Italy, and in the Interventional

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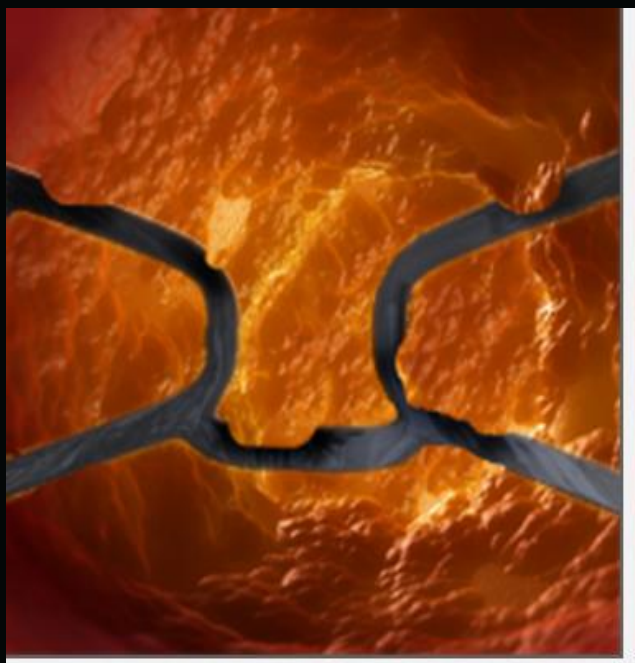
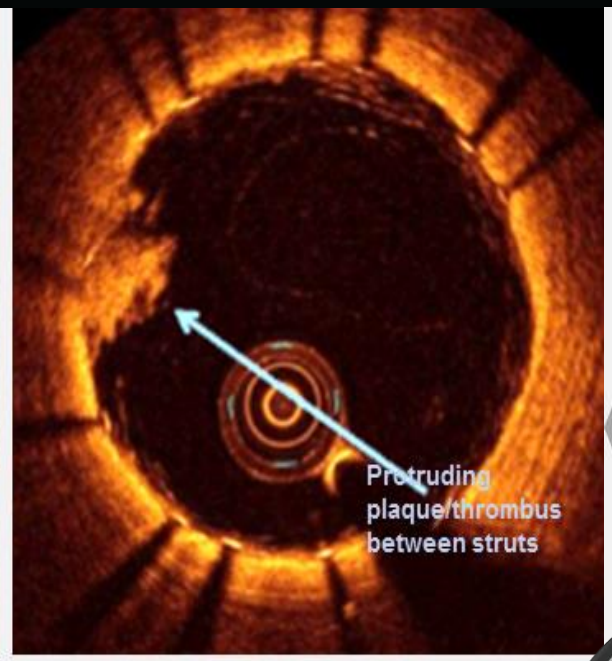
Stroke Prevention Strategy: MicroNet Technology





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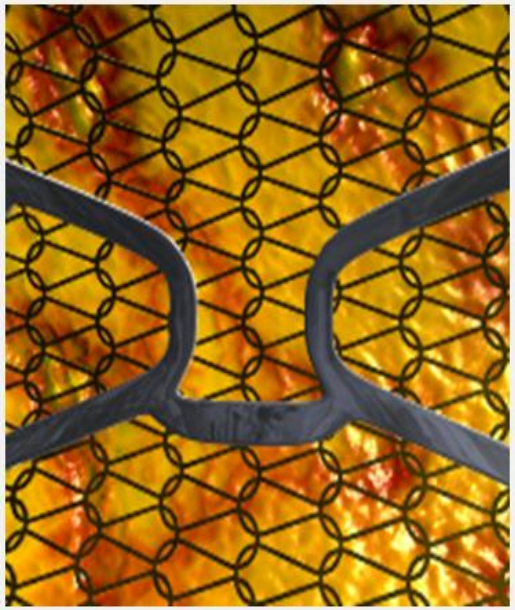
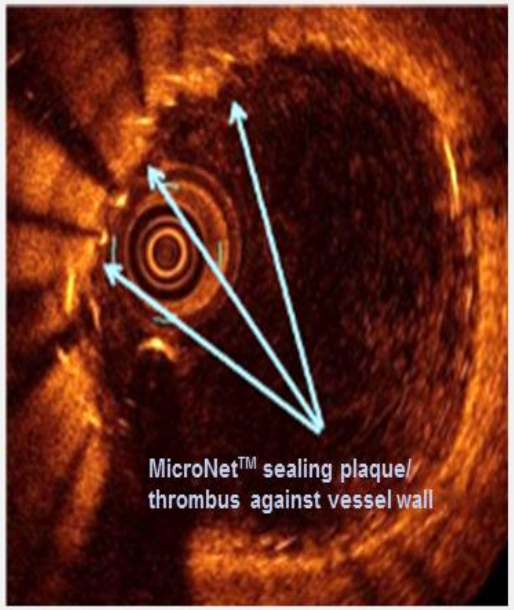




Conventional Open Cell Stent (1St GEN):

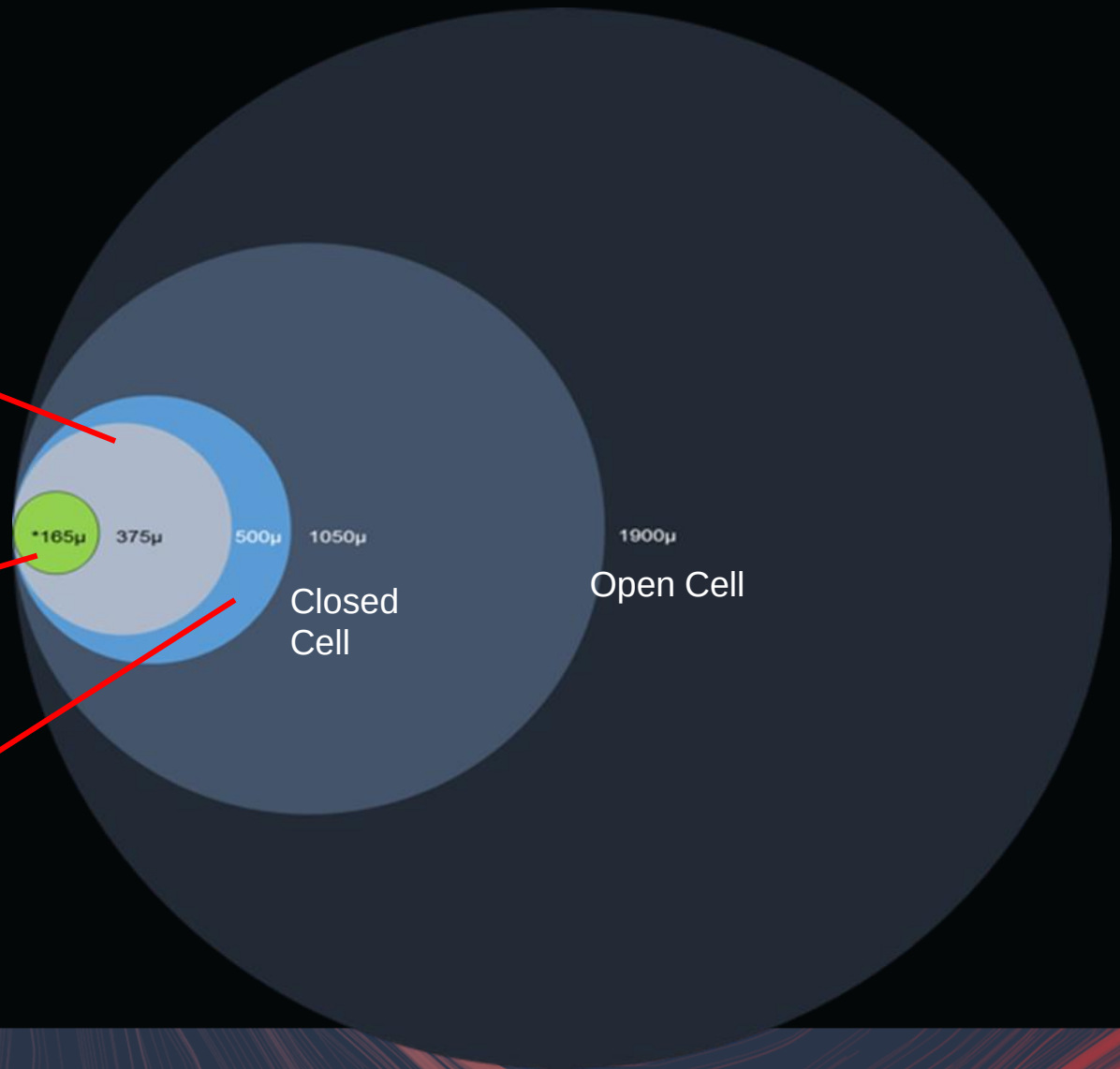
Bare or dual layer approach, with plaque protrusion risk

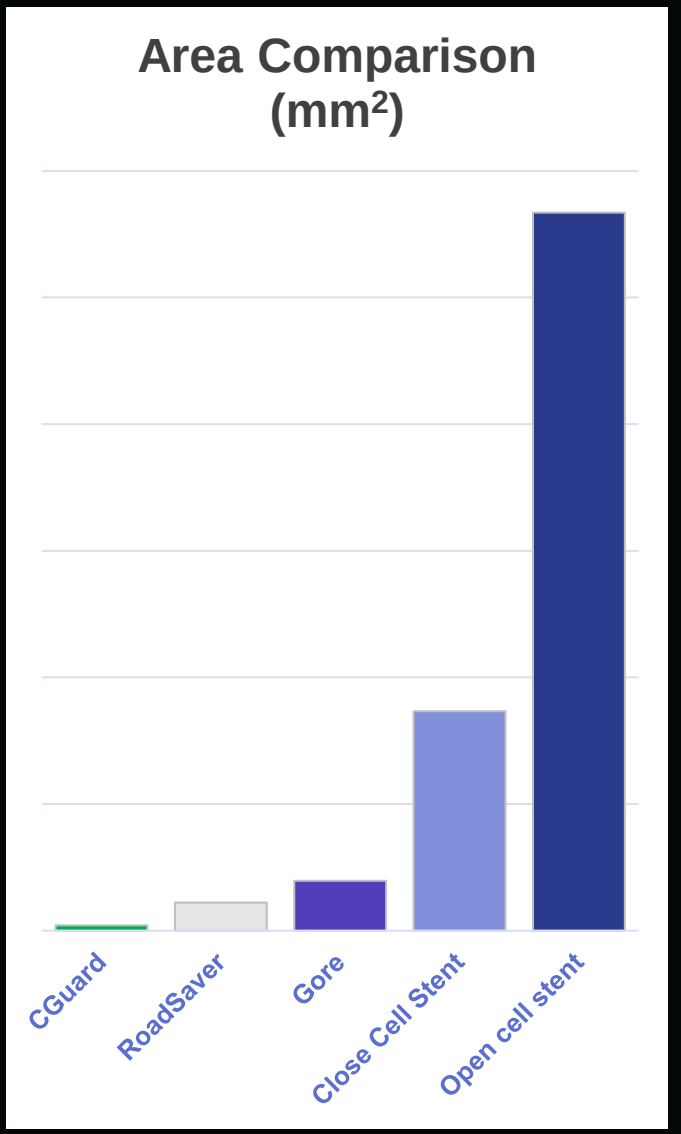
CGuard Stent System (3rd GEN):

Stents are covered in MicroNet

Important Note: The C-GUARD stent is an *investigational device ONLY* in the US

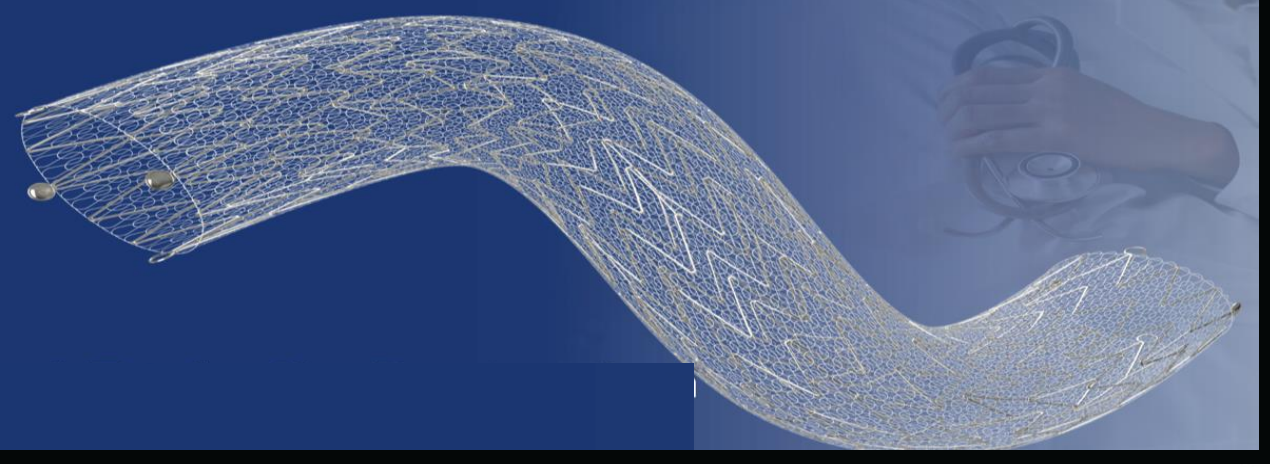
“Pore Size” Comparisons of Carotid Stents



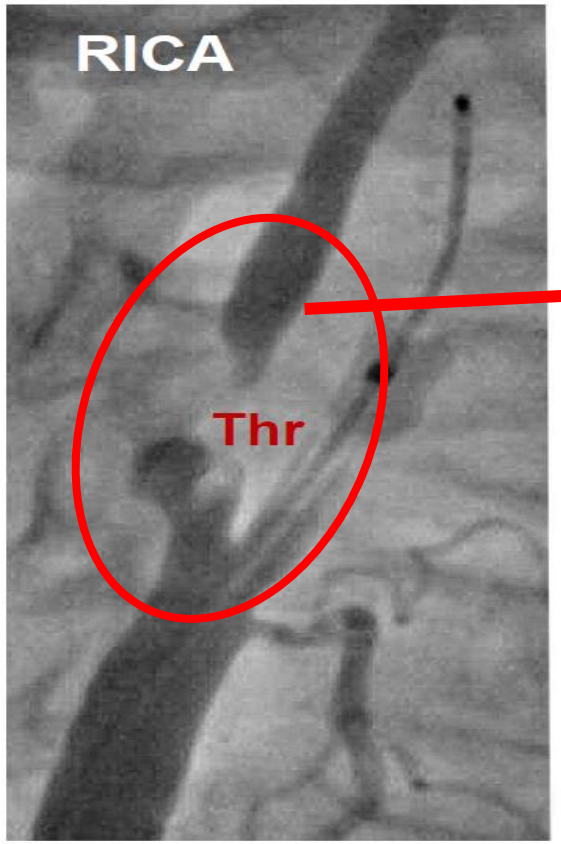


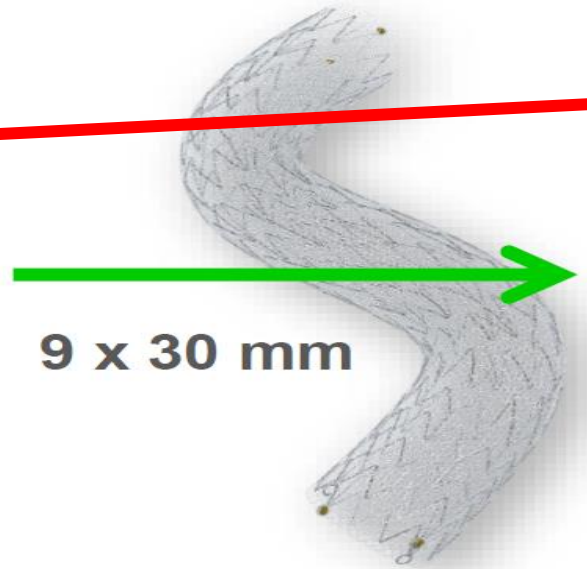
Theoretic Advantages of CGuard Stent

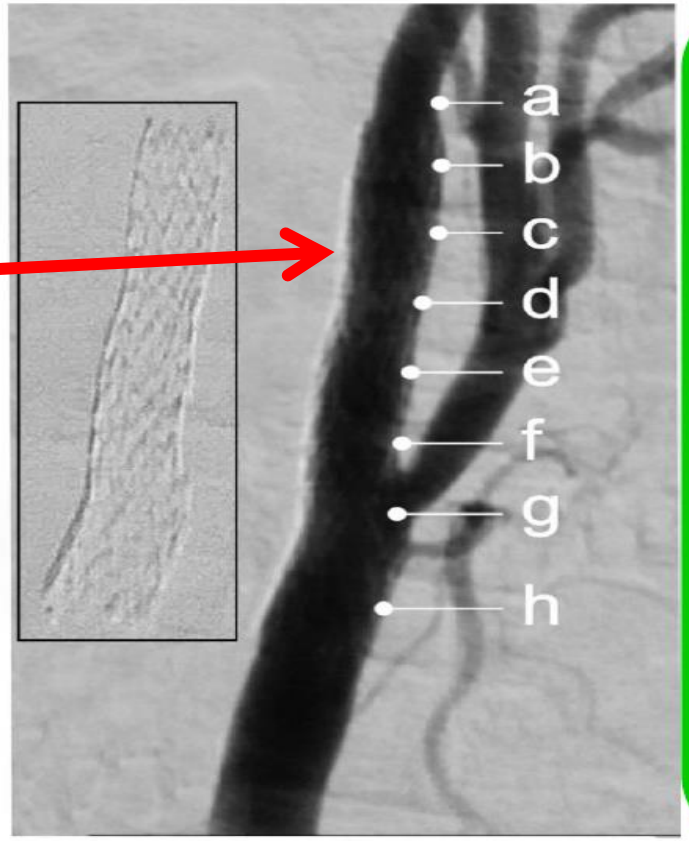
- Maximized *conformability* suitable for more carotid anatomies (“open –cell” stent with proprietary “Smart Fit” auto-taper technology)
- Coupled with maximized *scaffolding and plaque coverage* with smallest pore size and free cell area of available carotid stents
- Potential to minimize plaque protrusion/embolization *during* procedure at highest risk intervals (stent placement, post dilatation) *and* post - procedure

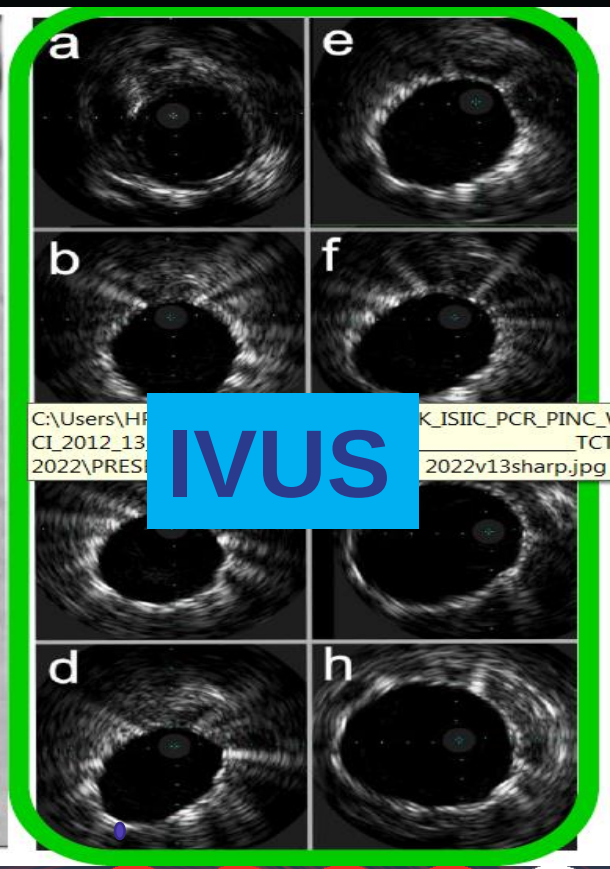


Images courtesy of Piotr Musialek, MD









C-GUARDIANS US Pivotal IDE Trial

Disclaimers:

- CE Mark Approved Europe 2015
- INVESTIGATIONAL Only in US
  - In C-GUARDIANS IDE Trial (enrollment completed), and allowed as part of ongoing CREST 2 trial
- *Results presented today are 30- day results, although the primary endpoint for the trial is a 1-year composite endpoint*
  - FDA approved this 30- day result presentation

C-GUARDIANS Study Design	Prospective, multicenter, single- armed IDE Pivotal trial
Sample size/ Sites	316 Patients; 25 US and European Sites
Primary Endpoint	***Composite of death, stroke, MI (DSMI) at 30 days*** or ipsilateral stroke at 1 year
Sponsor	INSPIRE MD
Principal Investigator **Co- Principal Investigator**	D. Chris Metzger, MD Piotr Musialek, MD
Study Enrollment Period	July, 2021 to June, 2023 (23 months)
Monitor/ CRO	Hart Clinical Consultants

Other Key Study Personnel

Clinical Trial Executive	**Christina Brennan, MD, MBA**
Angiographic and Duplex Core Lab	Syntropic; Raghu Kolluri, MD
DSMB	Chair: Gary Ansel, MD
CEC (adjudicated all cardiac & neuro events)	Chair: Mark Burket, MD
Senior Clinical Manager	Mena Shiano Lo Moriello
Screening Committee	Chair: Bruce Gray, DO
Hart Global Project Manager	Patricia Ayers

25 investigative sites in the US and Europe

- Ascension Seton Heart (UT Austin)
- Asklepios Hospital St Georg
- Avera Heart Hospital (NC Heart)
- Ballad Wellmont Holston Valley
- Baylor Plano
- Brookwood Baptist
- Cleveland Clinic
- Columbia Medical Center
- Imland Klinik Rendsburg
- John Paul II Hospital
- Mercy Heart & Vascular
- Miriam Hospital
- Novant Health/Forsyth MC
- Ochsner
- Prairie Research
- Prisma Health
- Silesian Medical University
- St. John's
- SUNY Stony Brook UMC
- Tennova Healthcare
- UNC Heart & Vascular
- University of Buffalo
- University of Florida
- University of Leipzig
- UPMC Pinnacle

CGuard Stent system is investigational only and not for sale in the USA.

Study Patients

- Patients ≤ 80 years of age at high risk for carotid endarterectomy
- Asymptomatic ≥ 80%, symptomatic ≥ 50% stenosis
  - Pre-specified 25% of population symptomatic per FDA
- All patients had pre-CAS carotid duplex and CTA/MRA
- All patients were approved by screening committee (2 approvals)
- All patients required to have embolic protection with Abbott Emboshield NAV 6, MoMa proximal embolic protection, or both
- All neurologic and cardiac events adjudicated by CEC

Study Visits and Evaluations

Pre- Procedure	NIHSS, CDU, CTA
Post CAS, Discharge or 96 hours	NIHSS, Clinical events
30 Days Post CAS	NIHSS, CDU, Clinical exam and events
6 months post CAS	NIHSS, CDU, Clinical exam and events
1 year	NIHSS, CDU, Clinical exam and events
2 year	NIHSS, CDU, Clinical exam and events
3 year	NIHSS, CDU, Clinical exam and events

Patient Demographics

Characteristic	ITT (N = 316)
Age (mean ± SD)	69.0 ± 6.6
% Symptomatic	24.3%
% Male	63.9%
Diabetes Mellitus	41.8%
Hypertension	92.6%
Dyslipidemia	90%
CAD	52.1%
COPD	23.8%
Current Smoker	26.4%
PVD	28.6%

Embolic Protection Utilized

Emboshield NAV 6 Distal embolic protection	**261**
MoMA Proximal embolic protection	78
Both (Nav6 and MoMa)	24
None	1

C-GUARDIANS 30-day Results

ITT Analysis (N = 316)	Event rate in % (n)
Death, Stroke or MI*	0.95%(3)
Death#	0.32% (1)
Any stroke#	0.95% (3)
Major Stroke#	0.63% (2)
Minor Stroke#	0.32% (1)
MI	0.0% (0)
Death or any stroke*	0.95% (3)
Death or major stroke*	0.63% (2)

* Hierarchical: patient count (each patient first occurrence of the most serious event).

Non-hierarchical: event count (multiple events in each patient are counted individually).

C-Guardians: 30-day Major Adverse Events

The CEC independently adjudicated all neurological, cardiac events:

- 1 major fatal stroke on post procedural day 10 after all DAPT stopped contrary to per protocol requirements.
- 1 major stroke. (NIHSS 2, post procedure). NIHSS 1, CDU patent 30 days, NIHSS 0 at 6 and 12 months
- 1 retinal infarct in a patient presenting with amaurosis fugax, adjudicated as a minor stroke. (NIHSS 1). NIHSS 0, CDU patent 30 days

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C-Guardians: 30-day Major Adverse Events

Event rate in % (n)	ITT (N=316)	Per Protocol^
Death, Stroke or MI*	0.95% (3)	0.63% (2)
Death#	0.32% (1)	0.% (0)
Any stroke#	0.95% (3)	0.63% (2)
Major Stroke#	0.63% (2)	0.32% (1)
Minor Stroke#	0.32% (1)	0.32% (1)
MI#	0.0% (0)	0.0% (0)
Death or any stroke*	0.95% (3)	0.63% (2)
Death or major stroke*	0.63% (2)	0.32% (1)

* Hierarchical: patient count (each patient first occurrence of the most serious event).

Non-hierarchical: event count (multiple events in each patient are counted individually).

^ Per Protocol Analysis excludes 1 patient (did not take dual antiplatelet therapy; had a major stroke and died).

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Conclusions

- In the C-GUARDIANS IDE Pivotal trial of patients at high risk for carotid endarterectomy with obstructive carotid disease (25% symptomatic), treatment with carotid artery stenting with the CGuard carotid stent system with embolic protection had a low incidence of stroke, death, or MI post-procedure to 30 day follow up
- These results appear to confirm a potential “neuro-protective” effect of this stent
- We await the pre-specified 1- year primary composite endpoint results of this trial

Event Rate in % (n)	ITT	Per Protocol
Death/ Stroke/ MI	0.95%	0.63%
Death/ Stroke	0.95%	0.63%

Thank You for Your Attention!