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Axxess Plus: The First DES for the Treatment of bifurcation Lesions

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Jeffrey W. Moses has no relationships to disclose

Randomized Study of Bifurcation Lesions with Sirolimus-eluting Stent

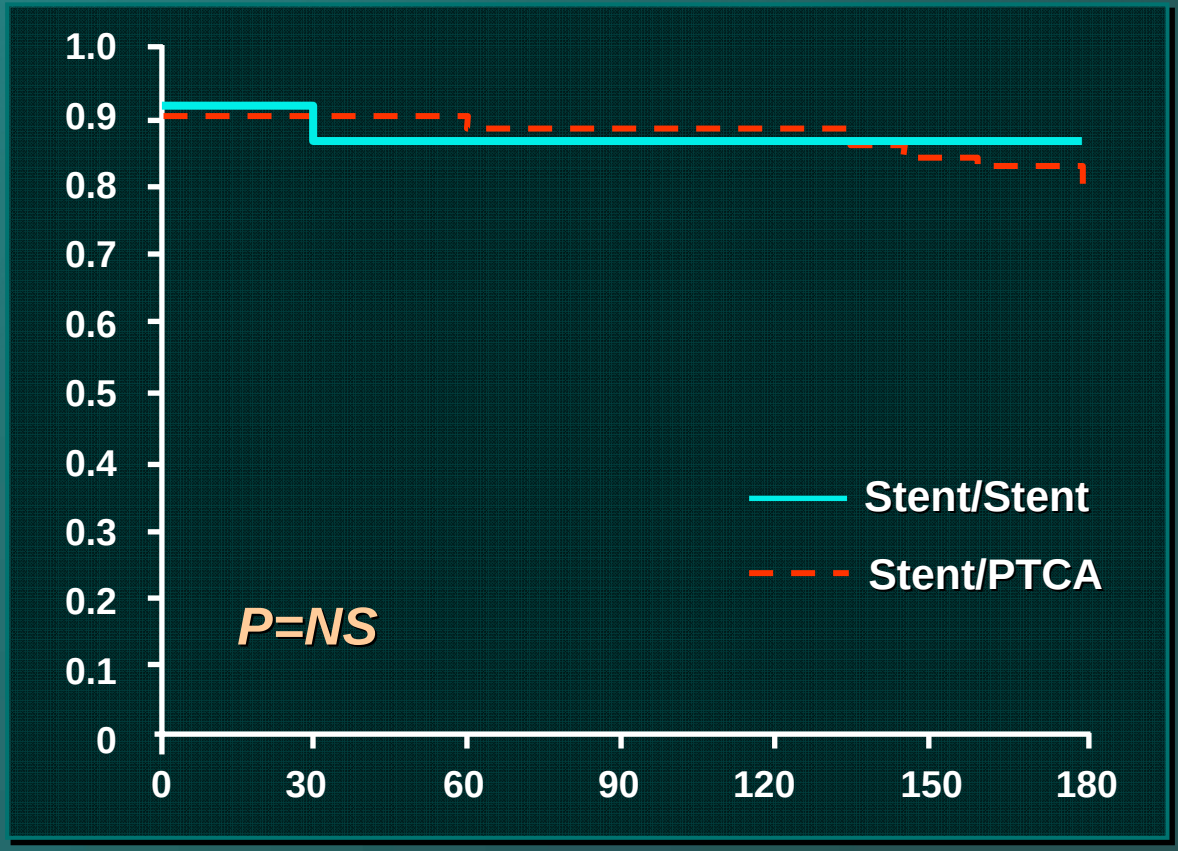
Restenosis and Major Adverse Cardiac Events at 6-month

P=NS for all comparisons	Stent/Stent n=63	Stent/PTCA n=22
Death	1 (1.6)	0
MI	7 (11.1)	2 (9.1)
TLR	6 (9.5)	1 (4.5)
TVR	7 (11.1)	2 (9.0)
MACE	12 (19.0)	3 (13.6)
MB restenosis	3/53 (5.7)	1/21 (4.8)
SB restenosis	12/55 (21.8)	3/21 (14.2)

Colombo A, et al. *Circulation.* 2004; 109: 1244-1249.

Randomized Study of Bifurcation Lesions with Sirolimus-eluting Stent

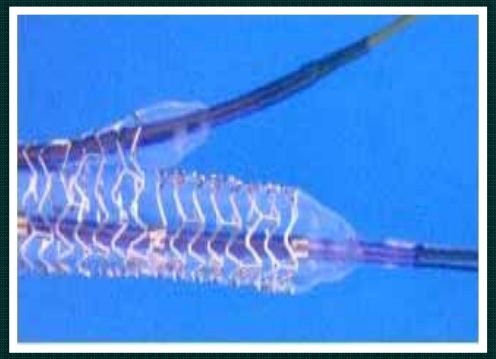
Treatment of Bifurcational Lesions



Kaplan-Meier survival estimates free of MACE at 6-month

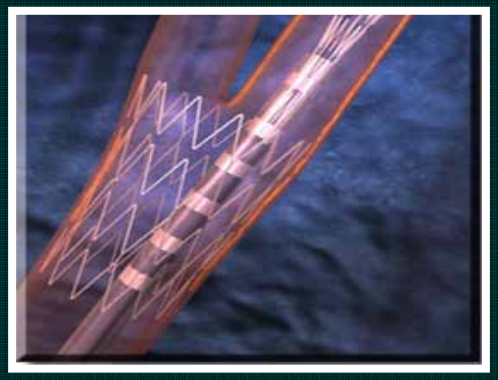
Dedicated Bifurcation Stents

BSC\AST petal

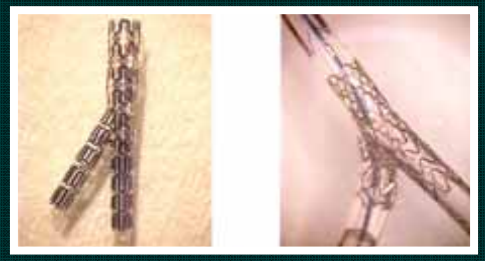


Guidant frontier

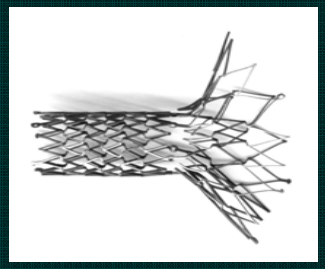
YMed sidekick



Devax (+ BA9)

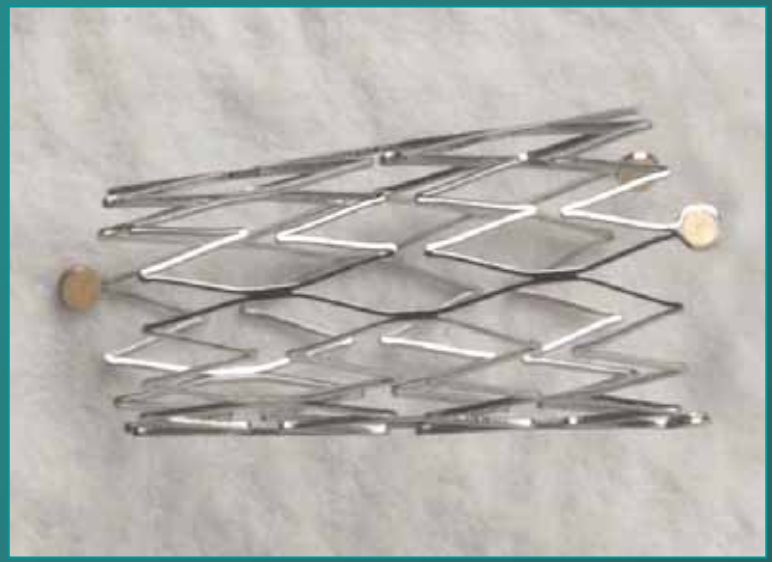


"True" Bifurcation Designs



Sidebranch Designs

AXXESS PLUS System



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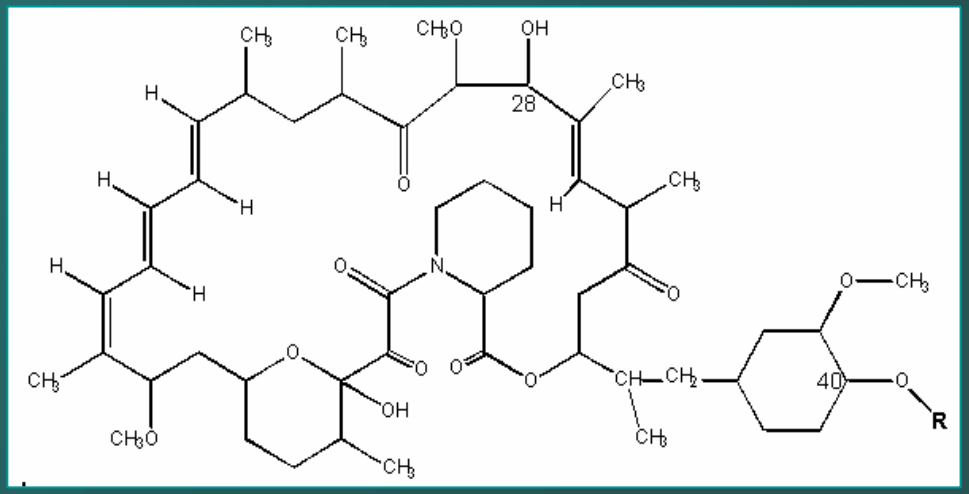
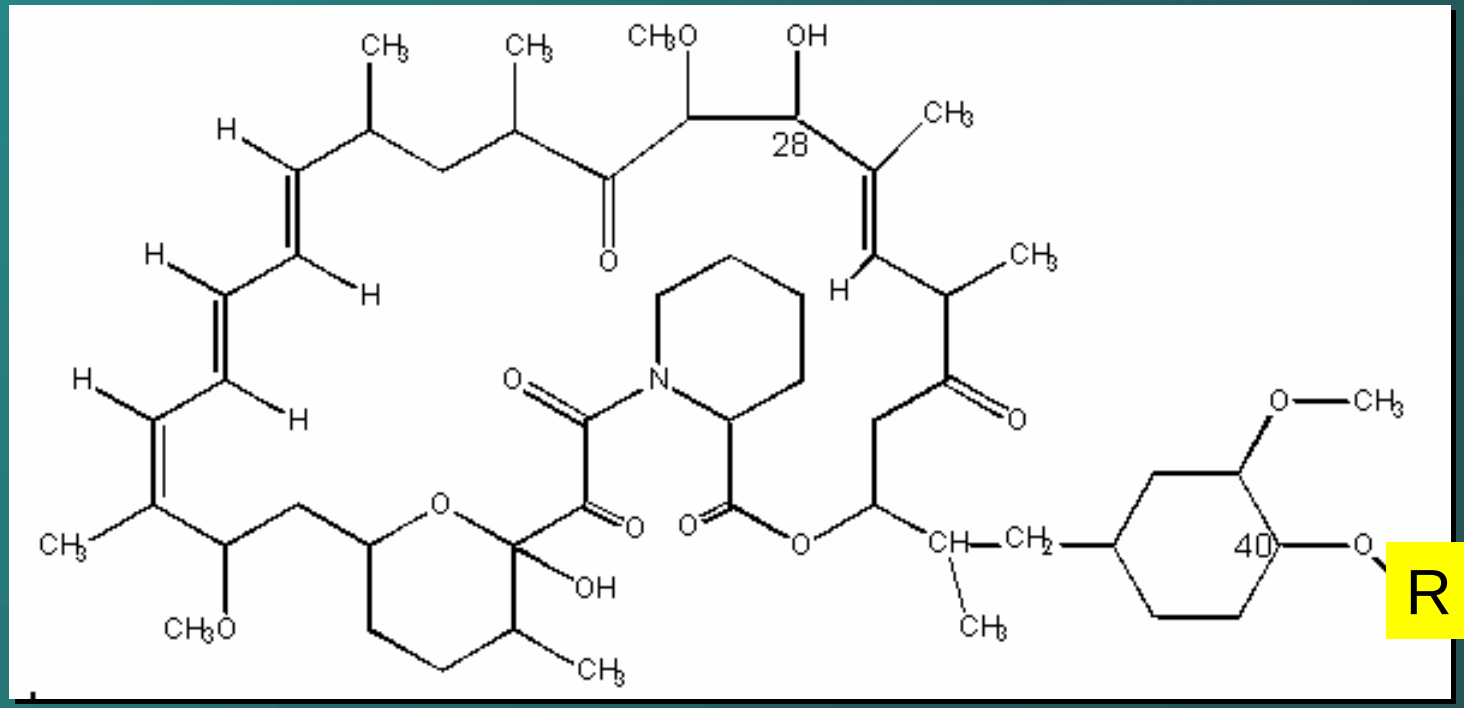


AXXESS Stent

PLUS

Biolimus-A9 Anti-proliferative & Bioerodable Polymer

Sirolimus, Everolimus, and Biolimus

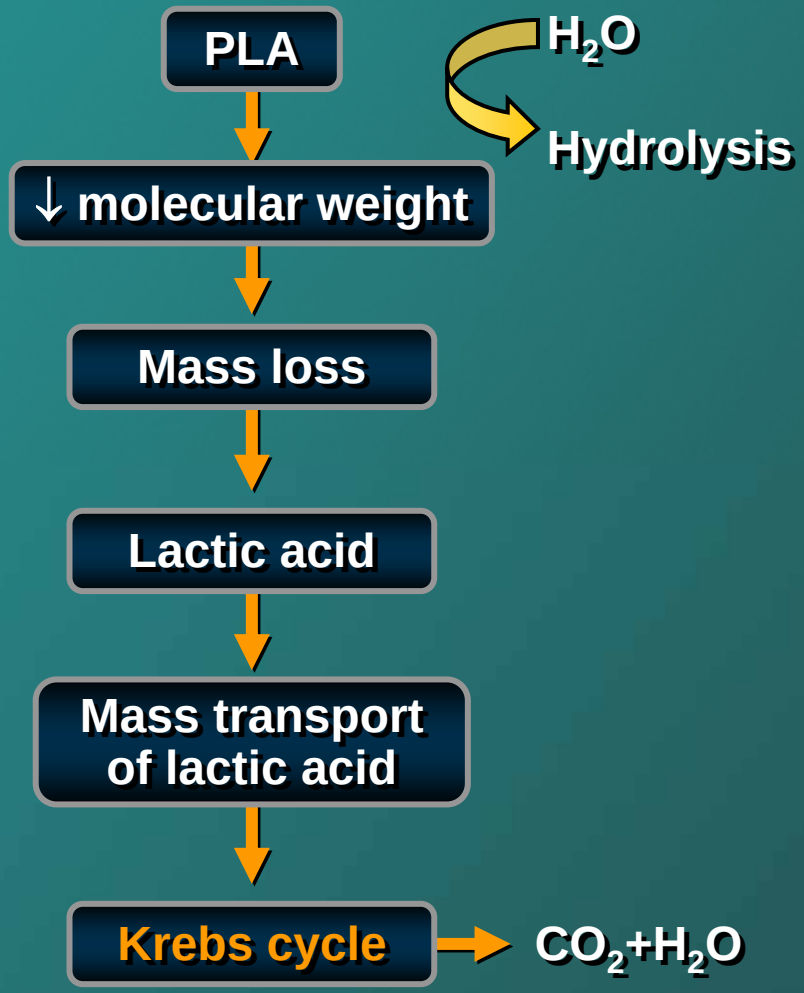


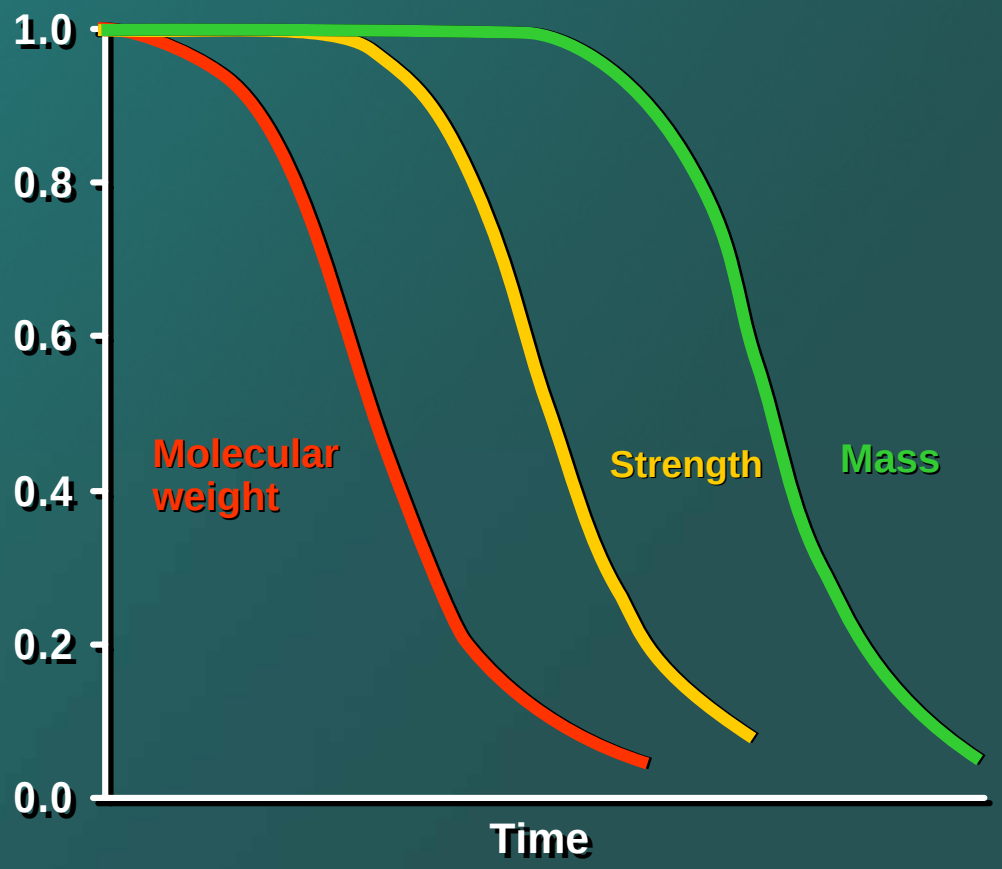
Sirolimus: R =H

Everolimus: R = CH_2CH_2OH

Biolimus: R =CH_2 CH_2 R'

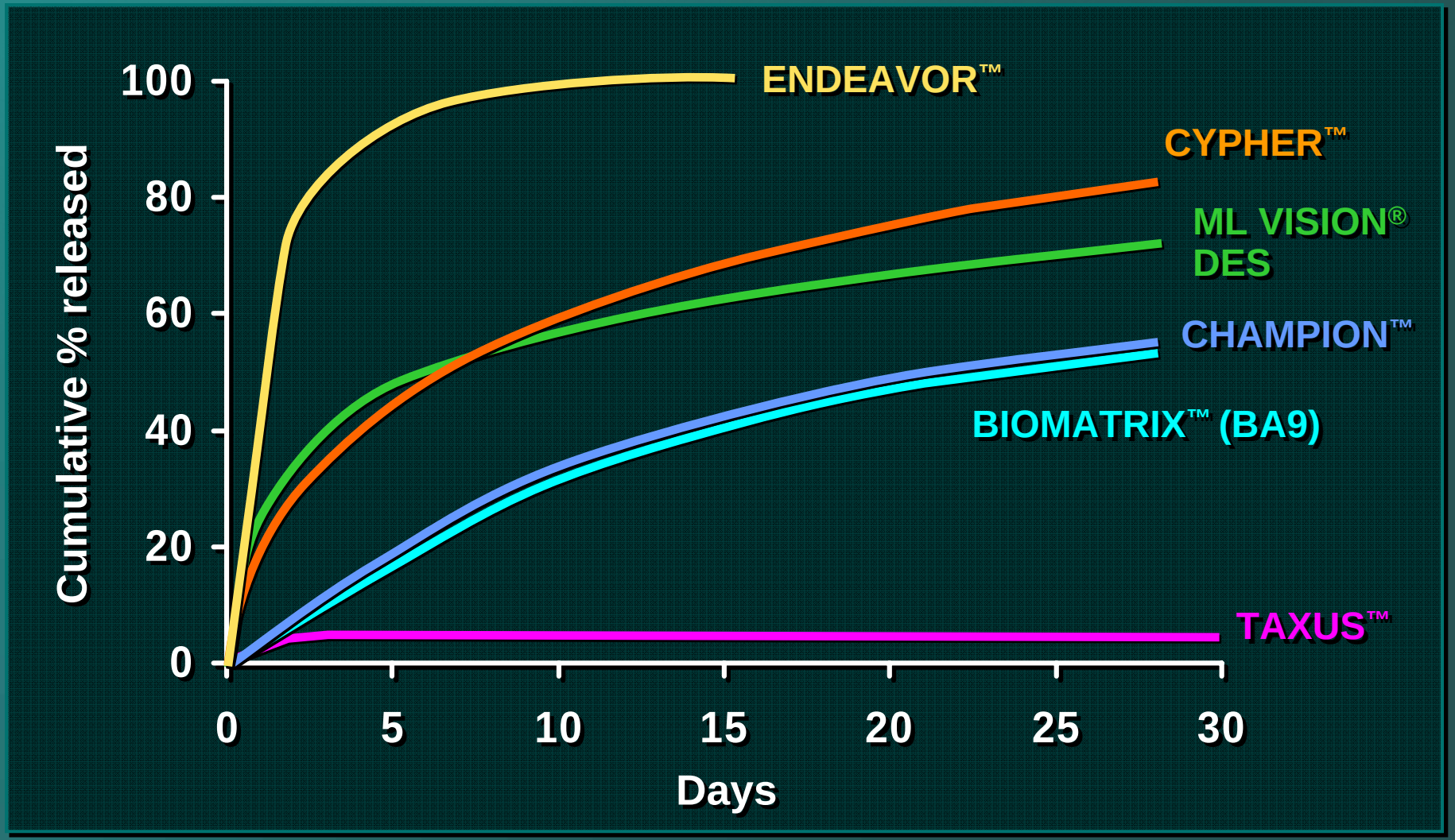
PLA Metabolic Pathway





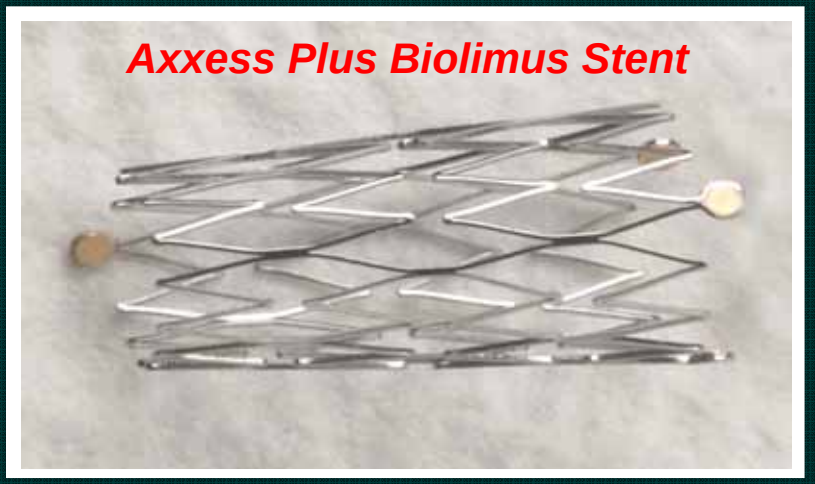
Generic curves showing the sequence of polymer-molecular weight, strength, and mass-reduction over time

Comparative Elution Profile of BioMatrix



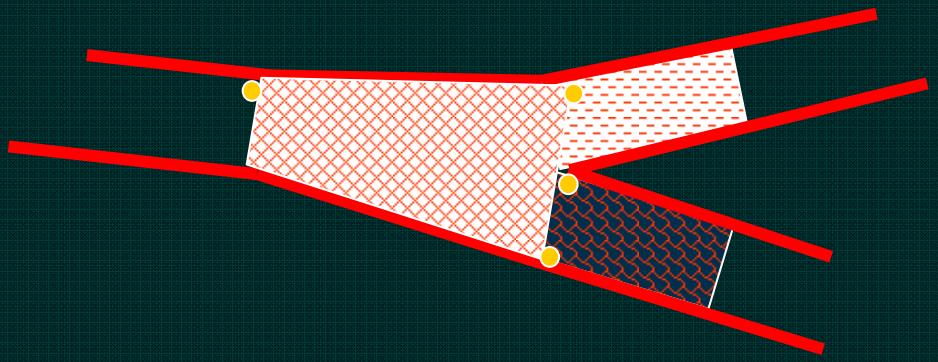
Axxess Plus Bifurcation Stent

- **Stent:** Self expanding nickel-titanium (Nitinol) alloy
  - 2.5, 3.0, or 3.5 diameter
  - 10, 14, or 20 mm length
- **Drug:** Biolimus A9, a sirolimus analog
- **Dose:** 22 ug/mm stent length
- **Drug carrier:** Bioabsorbable PLA polymer
- **Delivery:** covered sheath RX delivery catheter



AXXESS PLUS Concept

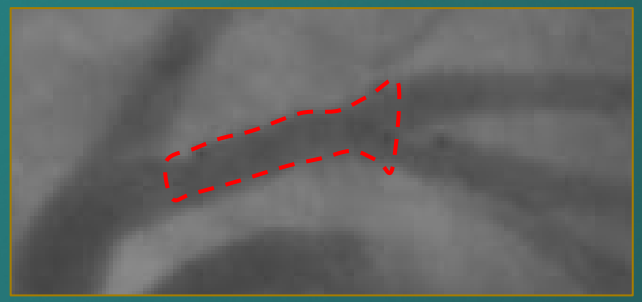
- The Axxess Plus stent is implanted at the level of the carina
- A successful implant will span the ostia of both branching vessels, indicated by the presence of one marker in each branch vessel



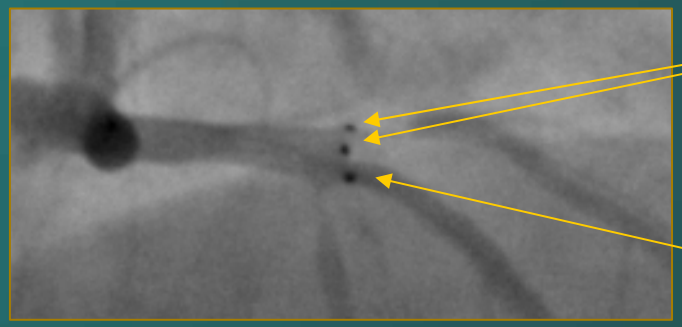
- Stents for the branch vessels are selected to match the length and diameter of the LAD and LCX

Why Self Expanding Stent?

The flared shape of the AXXESS PLUS stent matches the flared geometry of a bifurcation:

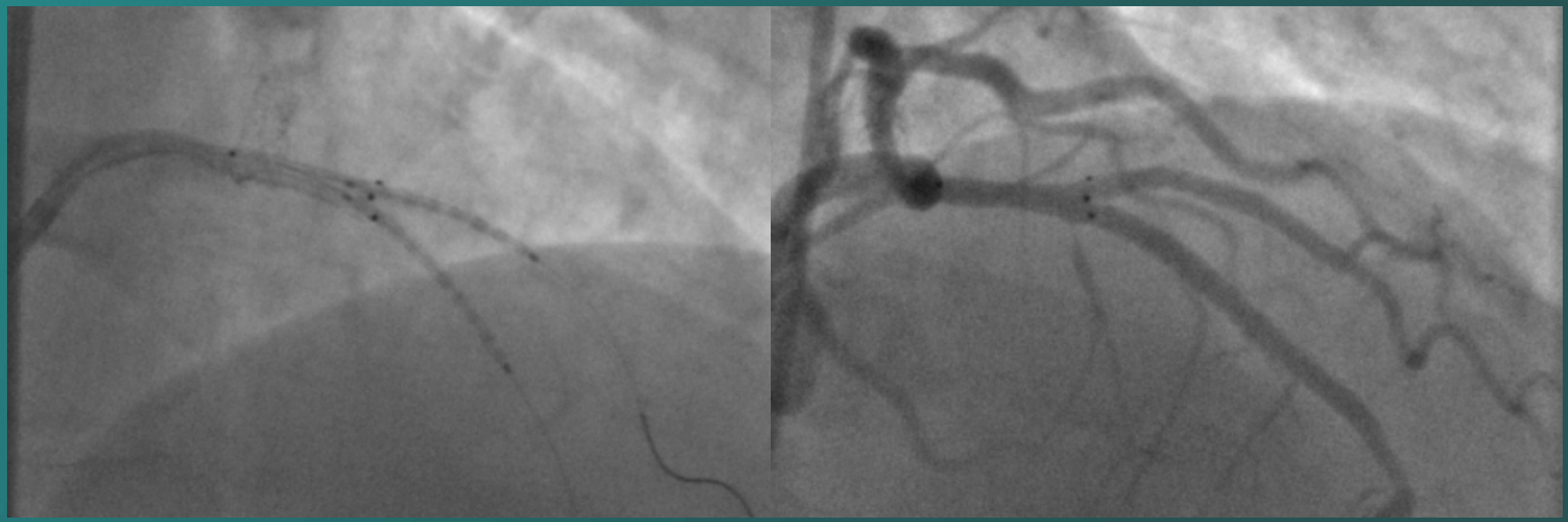


The Axxess Plus stent can expand into both the MB and SB, providing complete vessel coverage at the level of the carina:



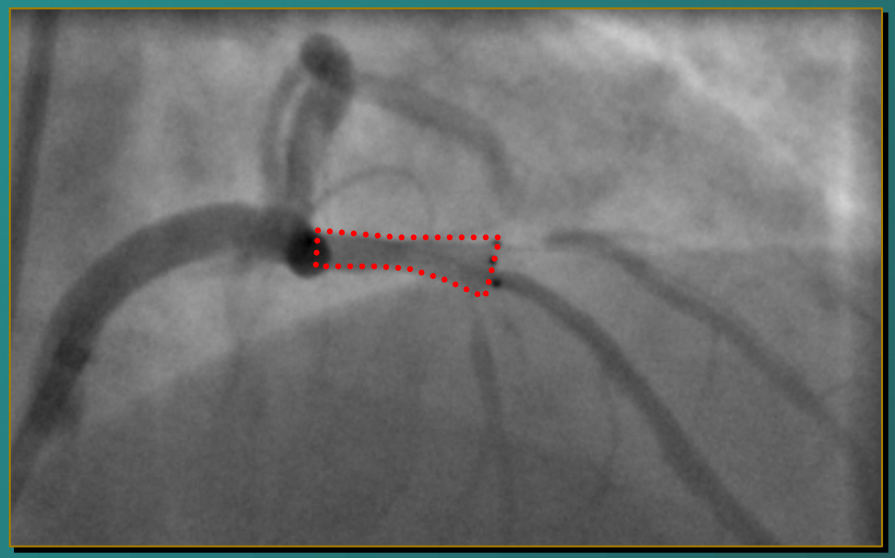
Why Self Expanding Stent?

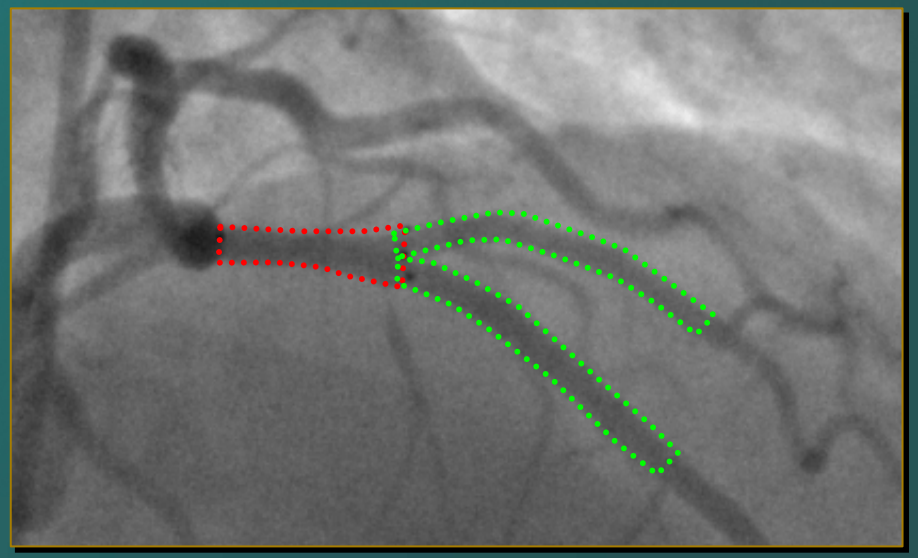
- With the Axxess Stent covering the ostia, branch vessel stents are placed just distal to the bifurcation



Distal stents are implanted in their natural shape, and do not need to be “remodeled” by PTCA to fit the anatomy of the bifurcation

Therapeutic Concept





The concept of the Axxess Plus system:

- **Implant a stent with the appropriate shape to treat the troublesome anatomy of the bifurcation, then**
- **Provisionally add subsequent stents to cover the lesion as needed stent “end to end”, rather than “through the side”**

The Axxess Plus Trial

- **Study Objectives**
  - Evaluate the safety and efficacy of the Axxess Plus stent in de-novo coronary bifurcation lesions of all types
  - Determine optimal treatment strategy using DES in branch vessels
- **Study Design**
  - Non-randomized multi-center registry with 125 patients
  - Control: Axxess bare metal stent (from prior study)
  - Plavix and aspirin prescribed for 6 months post procedure

The Axxess Plus Trial

- **Primary Endpoint**
  - In-stent late loss at 6 months in Axxess Plus stent
- **Secondary Endpoints**
  - MACE at 1, 6, and 12 months
  - Late Loss and Restenosis in parent vessel and side branch at 6 months
  - Tissue volume by IVUS in subgroup

Study Hypothesis & Sample Size

- **Control:** A bare metal Axxess stent was evaluated in 41 patients at 3 European centers from January to December 2003. In this study, 6 month angiographic late loss was 0.46 mm
- **Study Hypothesis:** Axxess Plus Biolimus will reduce late loss compared to the bare metal version
- **Sample Size:** 100 patients with 6 month follow up will detect a 50% reduction in LL with >90% power. To allow for loss to follow up, 125 patients should be enrolled

Principal Inclusion/Exclusion Criteria

Exclusion

- Known allergy to Plavix, aspirin, the stent/drug or polymer materials, or other required medications
- Major co-morbidity
- MI within 72 hours of the procedure
- LVEF < 30%
- Presence of thrombus in the TL or severe calcification.
- More than 1 lesion in the target vessel

Inclusion

- 18-80 years symptomatic patient with CCS $\geq$ 1 or positive functional study
- De novo bifurcation lesion in a native coronary artery
- 2.5-4.0 mm RVD in the parent vessel (PV)
- >2.25mm RVD in the side branch (SB)
- Lesion length up to 30 mm in PV, 15 mm in SB
- Concurrent treatment of second vessel allowed.

13 Participating Centers

Herzzentrum Siegburg	34 pts
▪ Eberhard Grube, MD (PI)	
Herzzentrum Bad Krozingen	24
▪ Prof FJ Neumann	
AZ Middelheim Hospital	18
▪ Stefan Verheye, MD, PhD	
Dante Pazzenese	15
▪ Alexandre Abizaid, MD	
Christchurch Hospital	11
▪ Dougal McClean, MD	
Herzzentrum Trier	9
▪ Karl Hauptmann, MD	
King's College Hospital	7
▪ Martyn Thomas, MD	
Southampton General Hospital	7
▪ Keith Dawkins, MD	
UZ Leuven	5
▪ Prof. Joseph Dens	
Munich Neuperlach	4
▪ Prof. Harald Mudra	
OLV Aalst	2
▪ Bernard De Bruyne, MD	
Amphia Hospital Breda	2
▪ Peter den Heijer, MD, PhD	
University Hospital Utrecht	1
▪ Prof. Pieter Stella	

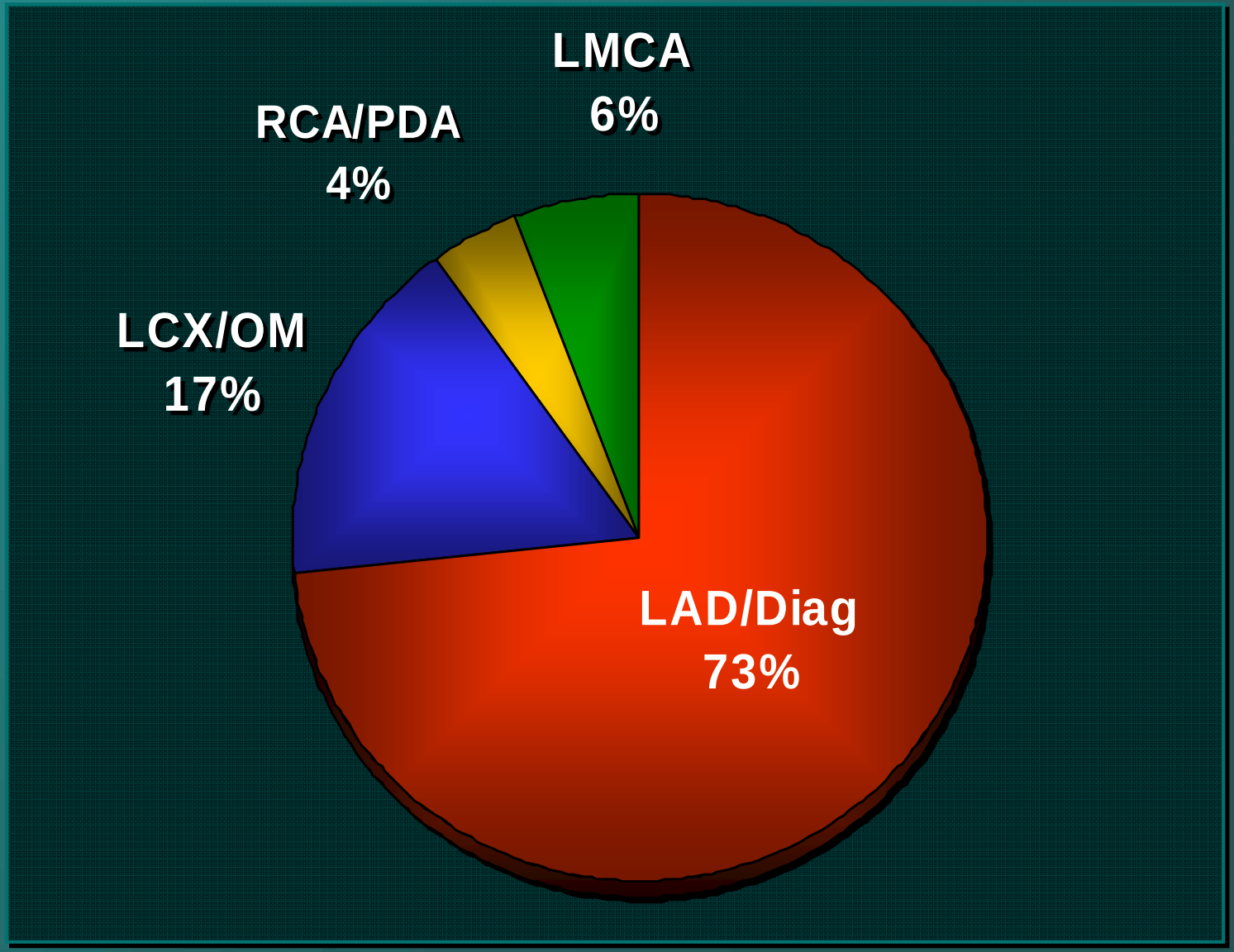
Trial Management

- **Data Collection Center**
  - Cardiovascular Research Foundation, New York, NY
  - Roxana Mehran, MD, Director
- **Angiographic Core Laboratory**
  - Cardiovascular Research Foundation, New York, NY
  - Alexander Lansky, MD, Director
- **IVUS Laboratory**
  - Cardiovascular Core Analysis Laboratory, Stanford, CA
  - Peter Fitzgerald, MD, PhD, Director
- **Clinical Events Committee**
  - George Dangas, MD, PhD, Chairman
- **Data Safety & Monitoring Committee**
  - John Ambrose, MD, Chairman

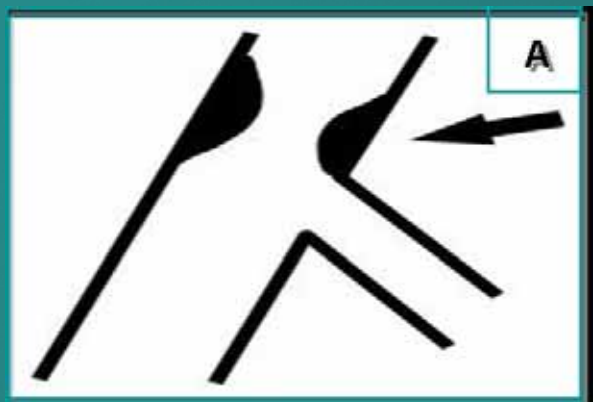
Patient Demographics

Number Enrolled	139
Age	64.4 ± 10.2
Male	73.4%
Diabetic	16.5%
Insulin Dependent	5.8%
Current Smoker	12.9%
w/ history	38.8%
Hypercholesterolemia	78.8%
Hypertension	73.4%
Previous MI	30.9%
Previous PCI	30.2%
CCS III or IV	36.7%

Bifurcation Lesion Location

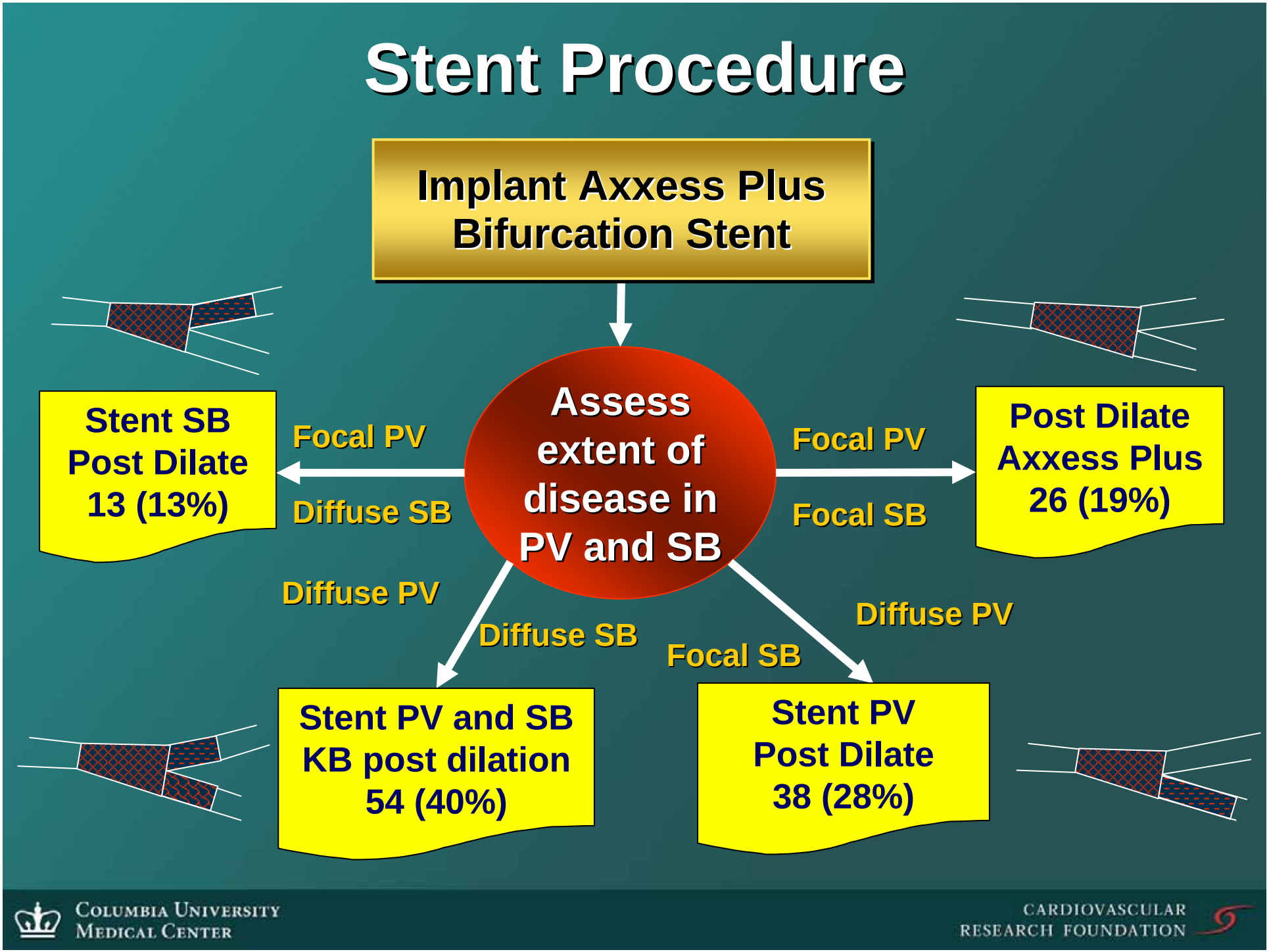


Bifurcation Type Treated

A	B	C
		
Prebranch	Postbranch	Parent Vessel Only
18 (13%)	4 (3%)	6 (4%)

D	E	F
		
Bifurcation	Ostial	Prebranch and Ostial
81 (60%)	1 (1%)	25 (18%)

Stent Procedure



Breakdown of 326 Stents Implanted

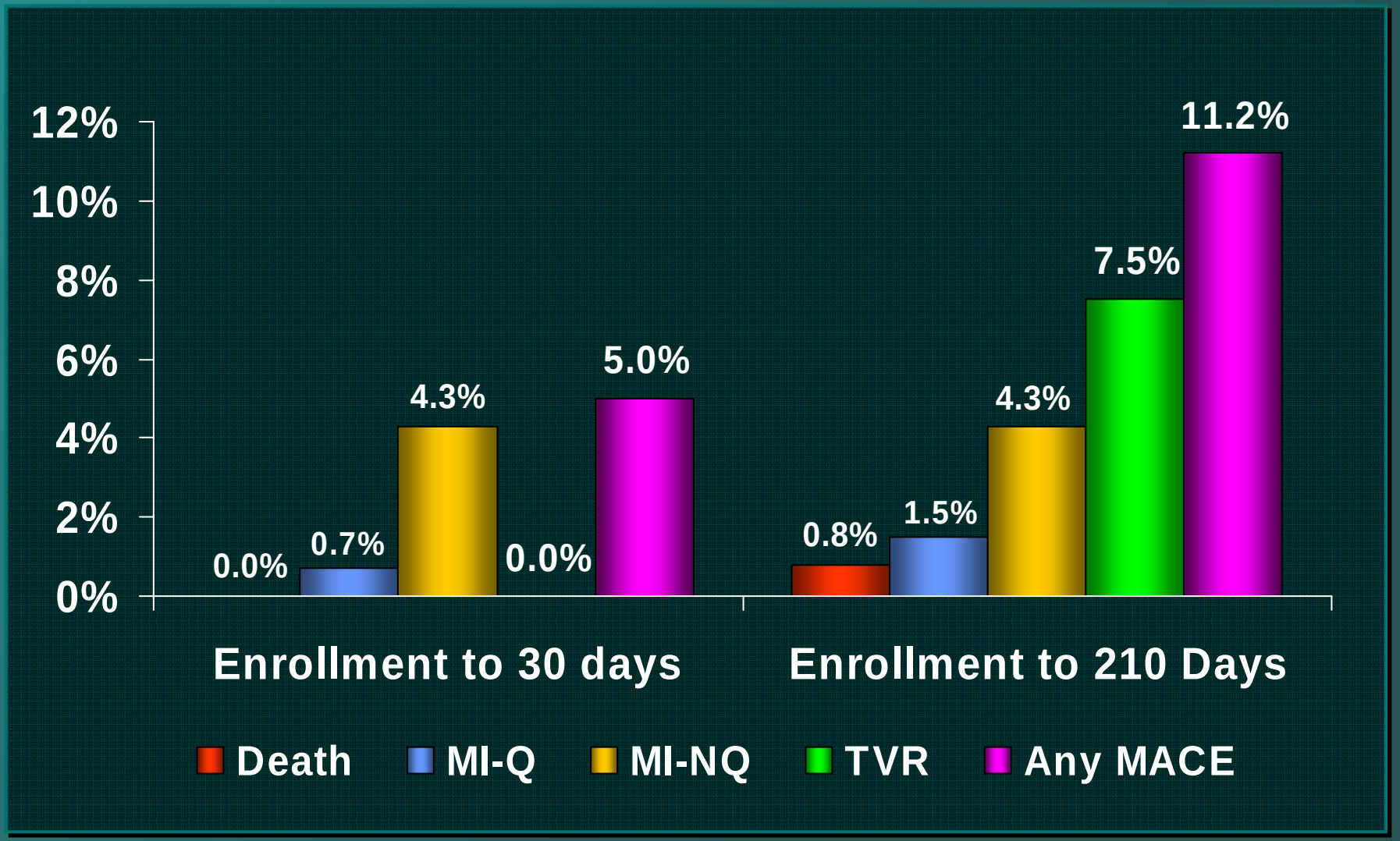
	Axxess Plus	Cypher	Taxus	Metal
Proximal PV	136	-	-	-
Distal PV	17	82	12	1
Side Branch	4	63	9	2
Total	157 (48%)	145 (44.5%)	21 (6.4%)	3* (0.9%)

** Placed in a single patient & omitted from QCA*

Procedure Results

	Parent Vessel	Side Branch
Baseline QCA		
Lesion Length mm	16.28 ± 7.44	7.43 ± 3.90
Reference Vessel	2.86 ± 0.35	2.34 ± 0.32
MLD, mm	0.78 ± 30	0.88 ± .39
Diameter Stenosis	73%	62%
Procedure Outcomes		
Avg. stents implanted	1.8 ± 0.7	0.58 ± 0.2
Angiographic success	100%	91.2%
Procedure success	94.9%	86.0%

Cumulative Clinical Events



Angiographic Outcomes by QCA: DES in the Parent Vessel

Angiographic FU	124/136 (91.2%)
Acute Gain	
Axxess Plus stent only	2.05 ± 0.48
All stents in PV	1.85 ± 0.49
Late Loss	
Axxess Plus	0.09 ± 0.56
All stents in PV	0.21 ± 0.44
In segment	0.26 ± 0.53
Binary Restenosis	
Axxess Plus only	4.0%
All stents (Axxess + distal DES)	5.6%
In segment	10.5%

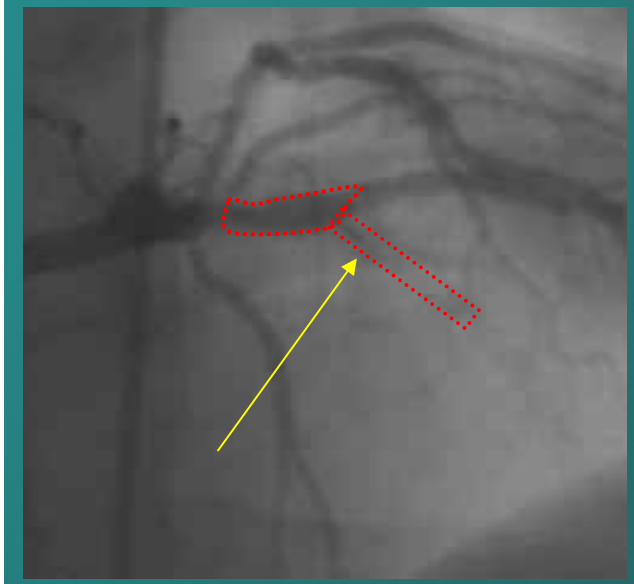
Angiographic Outcomes by QCA: Side Branch Analysis

	No Treatment	PTCA	Stent
Angiographic FU	25/26 (96%)	36/40 (90%)	65/70 (93%)
Lesion Success (<50%)	96.2%	77.5%	97.1%
Late Loss - stent Late Loss - segment	- 0.24 ± 0.31 mm	- 0.19 ± 0.31 mm	0.29 ± 0.46 mm 0.21 ± 0.49 mm
Restenosis - stent - segment	- 12.0%	- 25.0%	7.9% 7.9%
Outcomes for patients with lesion success in the SB at time of procedure:			
Restenosis –segment	8.3%	13.8%	8.2%

Stent Thrombosis (3 cases)

Cypher

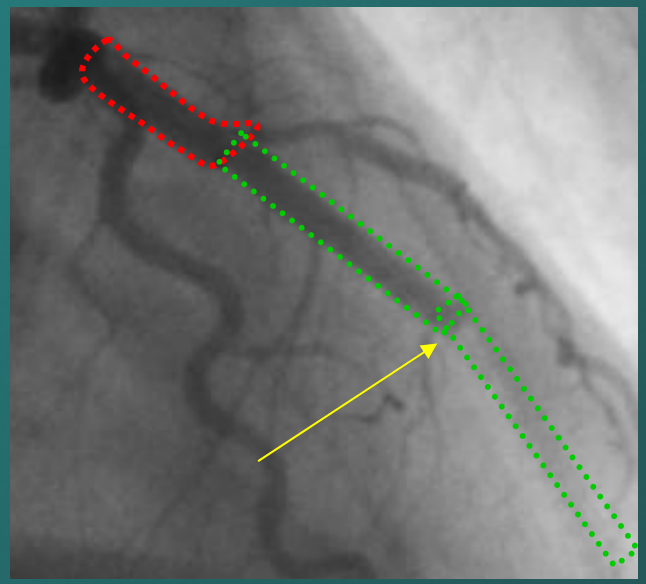
Axxess Plus



Pt 1-04: 61 days

Patient taken off Plavix post prostate surgery due to bleeding

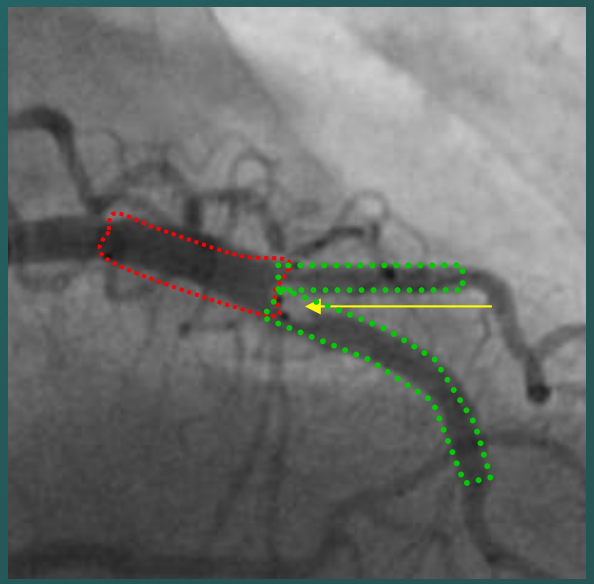
MI/TVR



Pt 15-11: 182 days

Total occlusion due to thrombosis in 2nd distal Cypher placed to cover spiral dissection.

Asymptomatic at FU.



Pt 15-18: 98 days

Patient not maintaining Plavix after 1 month. Partial occlusion due to throbosis distal to Axxess Plus stent.

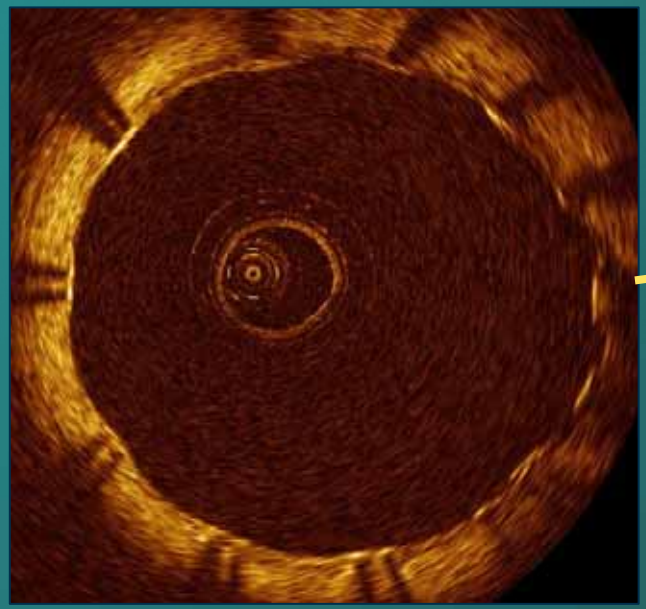
TVR. Returned for angio at 182 days with excellent outcome.

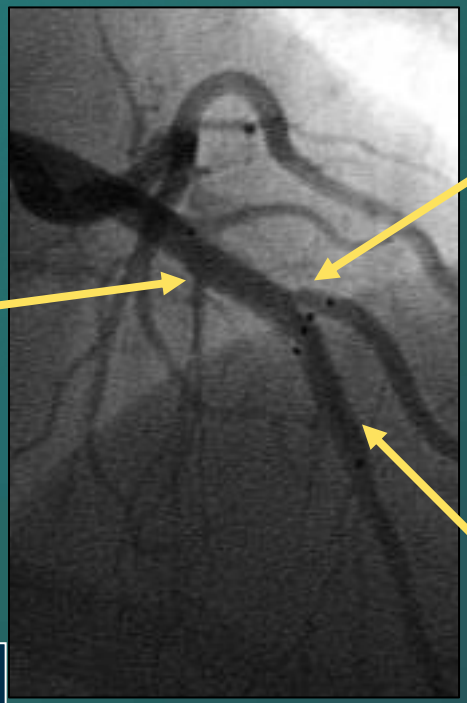
Primary Endpoint

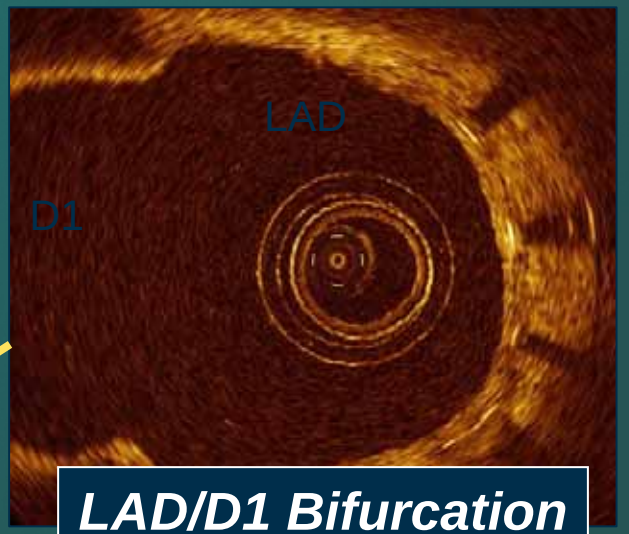
Primary endpoint: LL in Axxess Plus stent compared to bare metal

	Axxess Plus Biolimus Stent	Axxess Metal Stent	*p*
N with AFU (%)	126 (93%)	37 (90%)	
Angiographic Late Loss*- Devax Stent	0.11 ± 0.62 mm	0.46 ± 0.51 mm	0.002

ACCESS Plus Follow-up with Optical Coherence Tomography

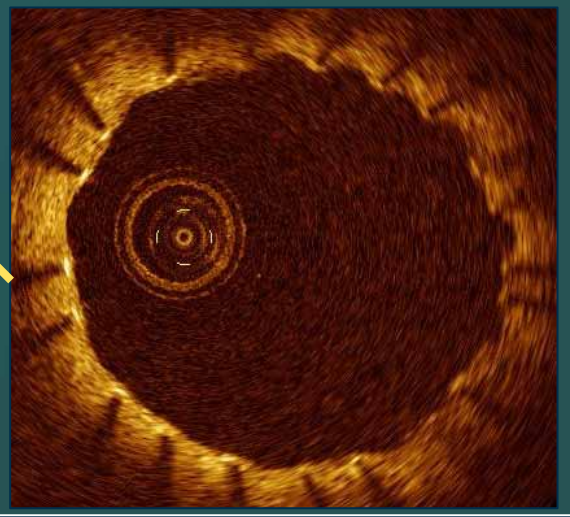






LAD/D1 Bifurcation

Bifurc Devax in prox LAD



'Straight' Devax in mid LAD

6 mths follow-up

Case Study

7-8F Guide
Double Wire

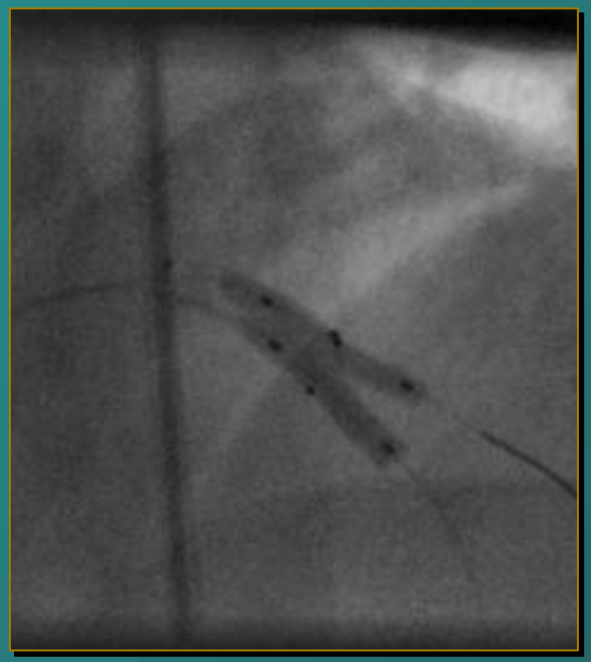
Pre dilate PV
& SB as req'd

Single or KB dilation

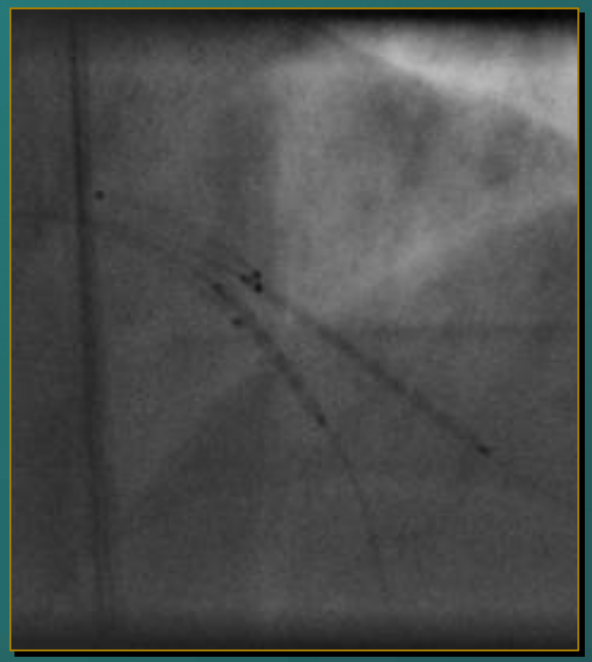
Axxess Plus
Stent @ carina

Markers in both branches

Case Study



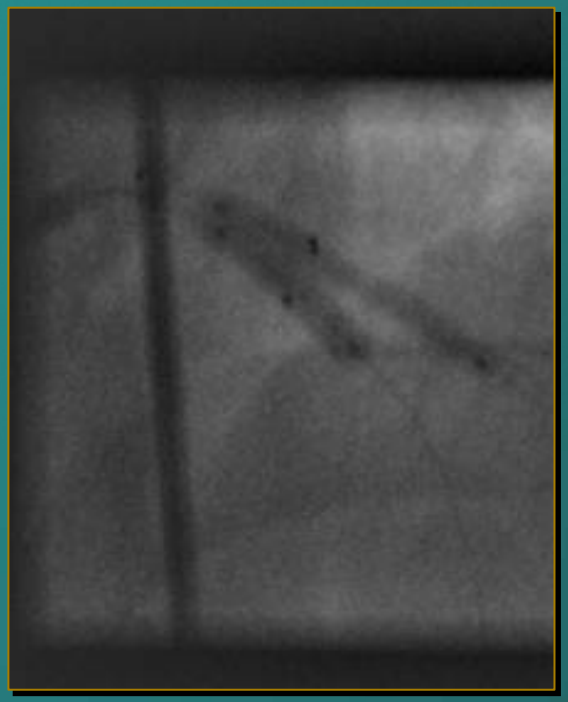
Dilation of
Distal Vessels



Cypher
Placement

Simultaneous
deployment

Case Study

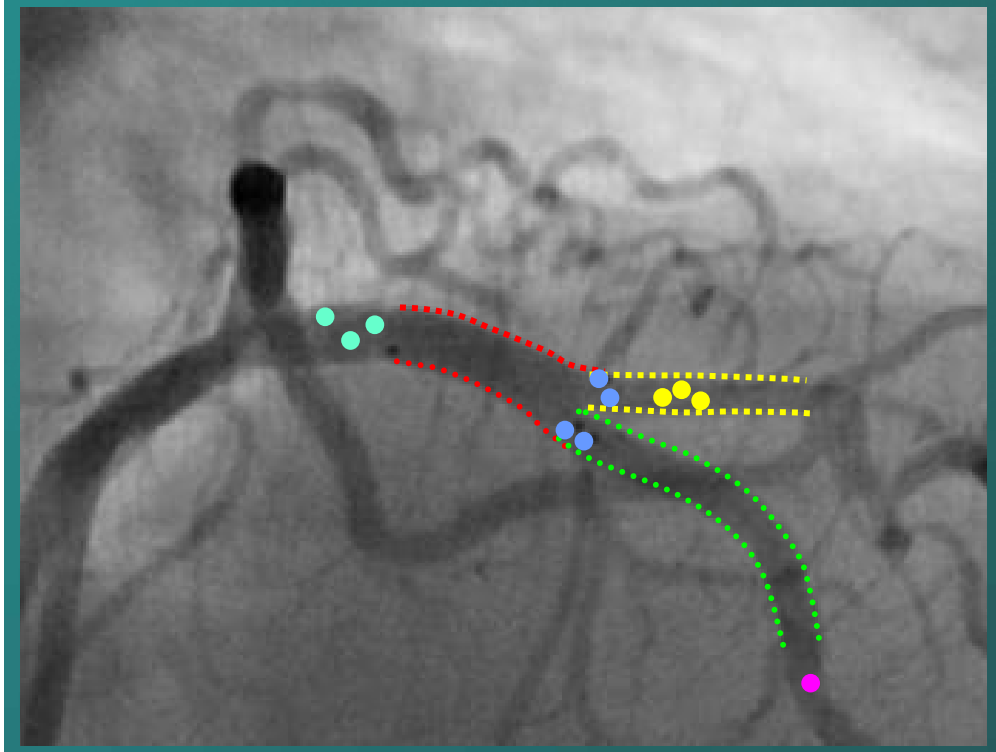


Final
Kiss

Final
Result

6 Month
Follow Up

Locations of Restenosis

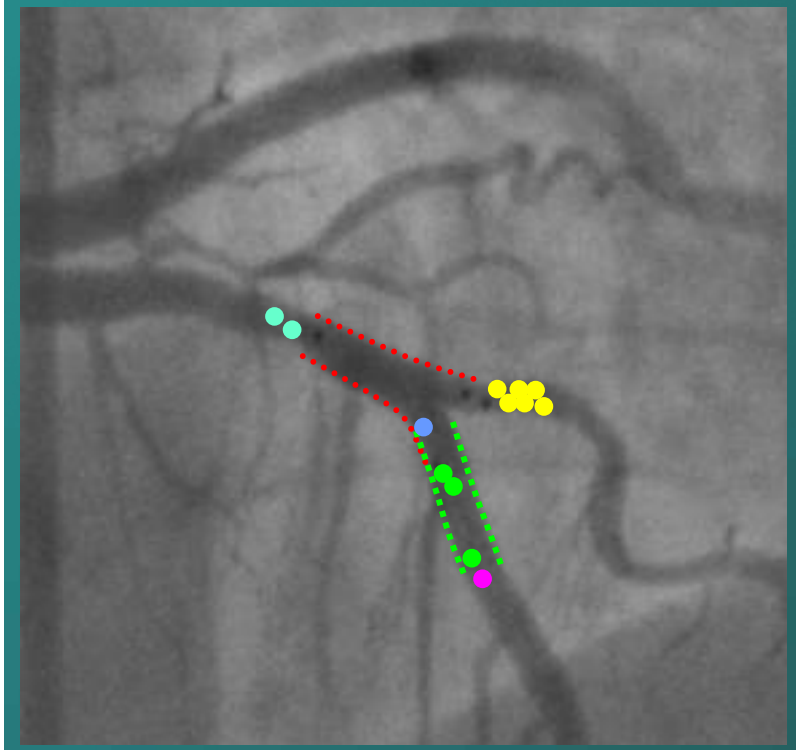


63 Patients with a SB stent:

- **Proximal Edge: 3 (4.9%)**
- **Axxess Plus stent: 0**
- **Ostium/overlap: 4 (6.6%)**
- **PV DES: 0**
- **Distal PV edge: 1 (1.6%)**
- **In SB DES: 3 (4.9%)**

In stent lesions were focal
Out of stent lesions were more diffuse.

Locations of Restenosis

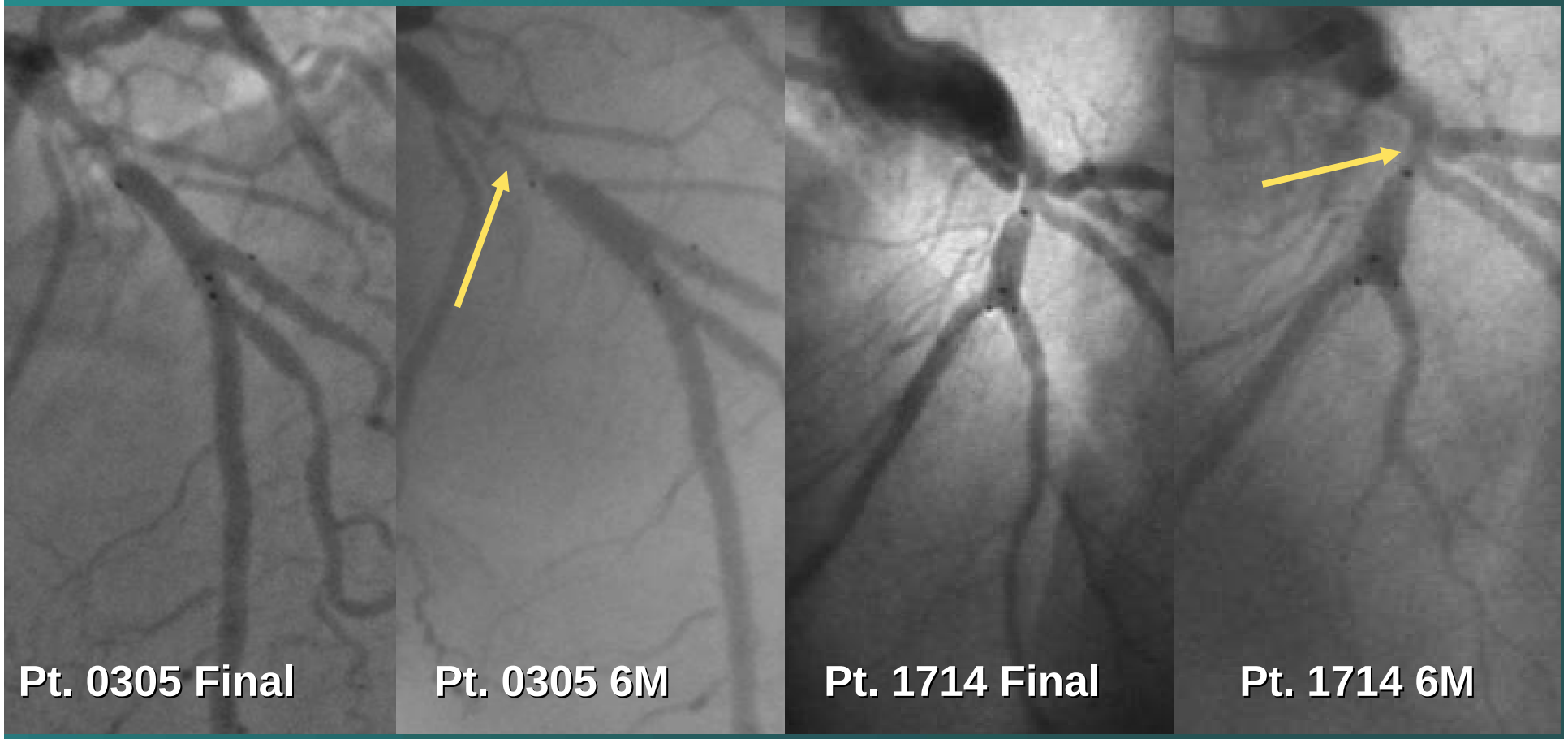


53 Patients with PTCA or no Tx in SB (excludes SB index failures):

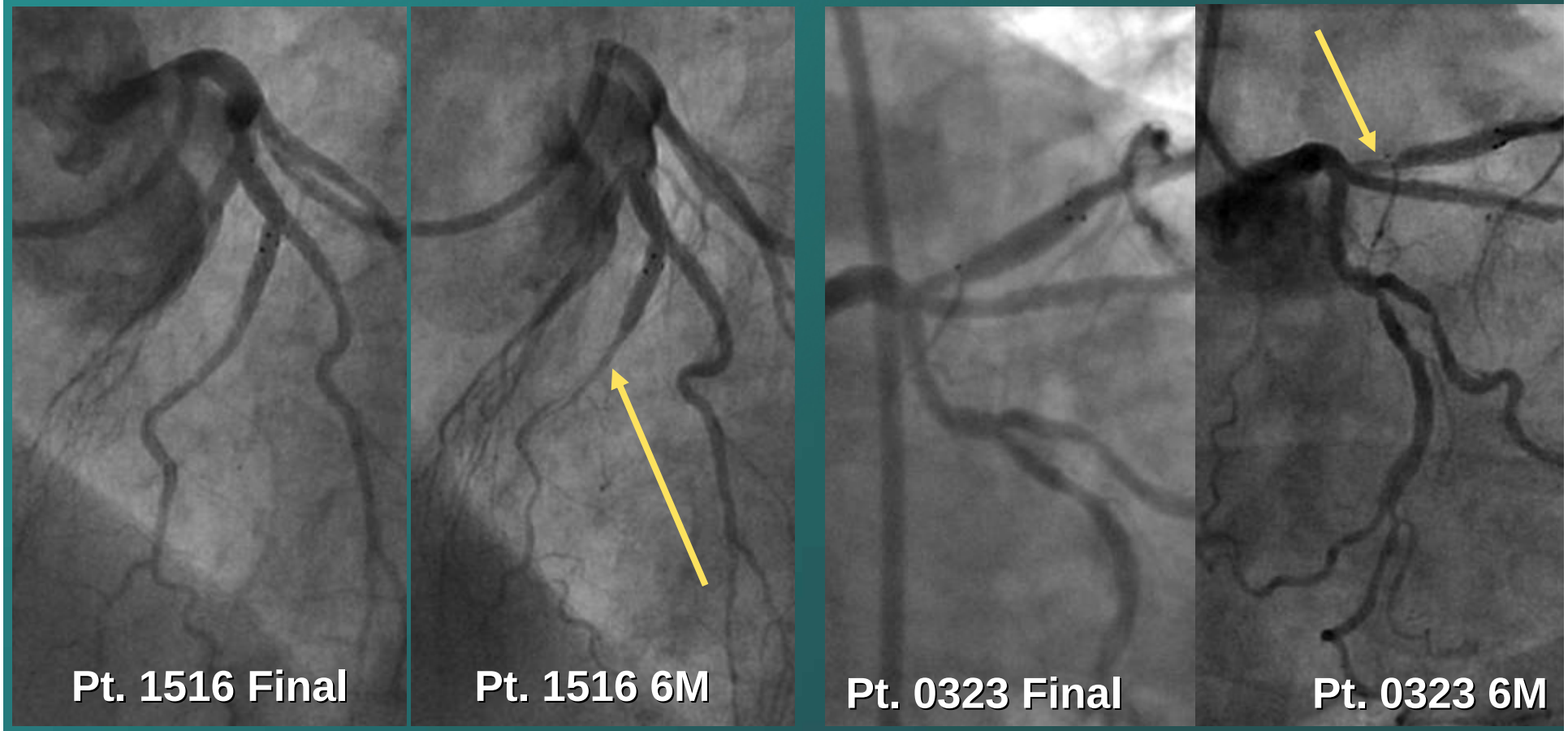
- **Proximal Edge: 2 (2.6%)**
- **In Axxess Plus stent: 0**
- **Ostium/overlap: 1 (1.3%)**
- **PV DES: 3 (5.6%)**
- **Distal PV edge: 1 (1.3%)**
- **SB ostium - 5mm : 6 (11.3%)**

In stent lesions were focal
Out of stent lesions were more diffuse.

Examples of Edge Restenosis



Examples of Edge Restenosis



DIVERGE: a Prospective, Single-arm, Multi-center Registry Drug Stent Intervention for Treating Side Branches Effectively

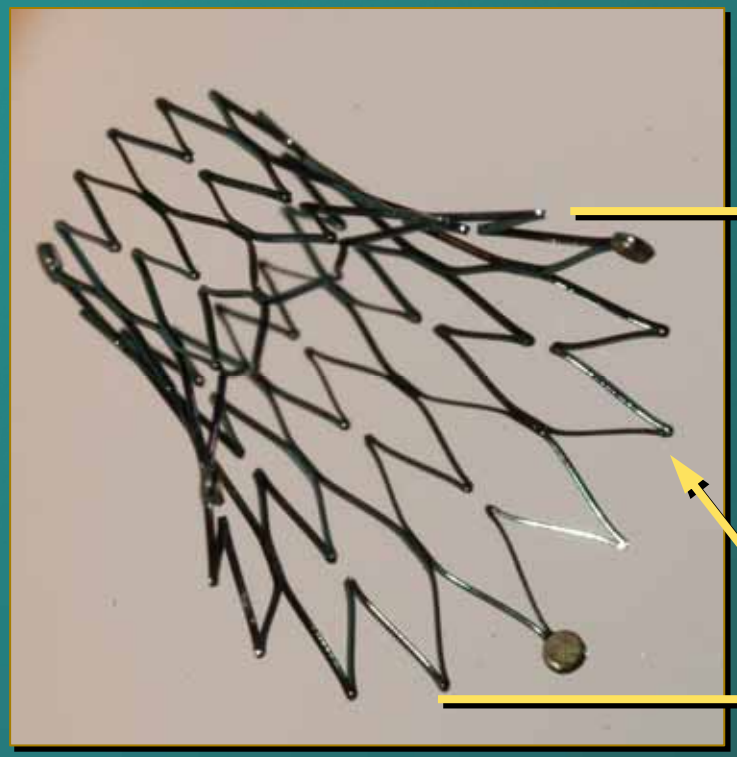
Patients with de novo bifurcated lesions in native coronary arteries N=600

PCI using Axxess™ stent System

Angio F/U at 9 mo in 300 pts
Annual clinical F/U for 5 years

PRIMARY Endpoint: 9-mo MACE: death, MI, TLR
SECONDARY Endpoints: device success, binary restenosis, late loss

AXXESS PLUS LM System

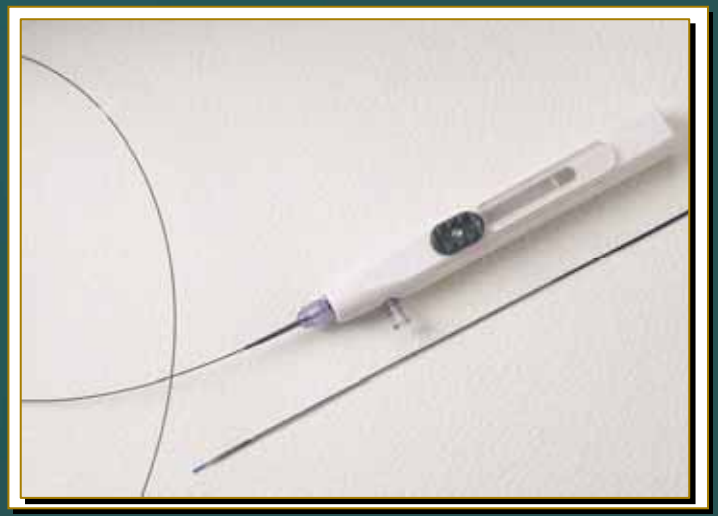


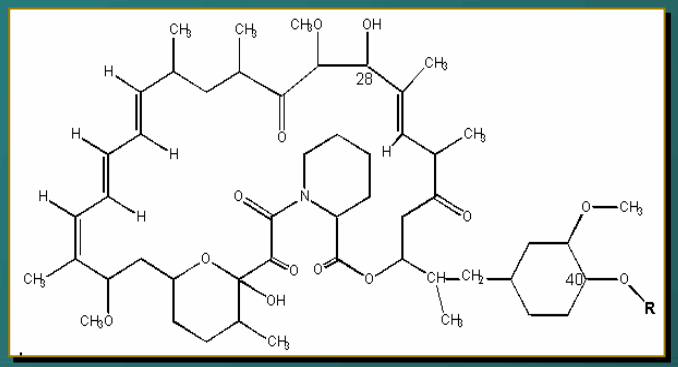
Flared Distal-End Stent Design

Self Expanding Nitinol Material

8, 10, or 12 mm flare diameter

4.8F Rx Delivery System





Biolimus A9 antiproliferative strut coating

The AXXENT Trial

- AXXENT
  - Axxess Plus Biolimus Stent in LMCA Bifurcations Trial
- Study Objective
  - Evaluate the safety and efficacy potential of the Axxess Plus stent in LMCA bifurcation lesions (protected or not)
- Study Design and Status
  - Multi-center registry, 40 patients enrolled in follow up.

Summary

- First experience with a dedicated Bifurcation DES
- The Biolimus drug effectively reduces late loss by 75% in the Axxess Plus stent
- In Stent Restenosis PV 5.6%, Late Loss 0.21mm
- This is the first multicenter study to report <10% restenosis rate in stented side branches
- Despite frequent stenting, stent thrombosis was rare when antiplatelet therapy was maintained

Summary

- This study did not prospectively assign a treatment method for all patients.
- Half of the restenosis in this study was either located outside the stent borders, or due to a residual stenosis in the SB at the end of the procedure
- These factors suggest the procedure may be further improved by:
  - Completely covering all disease in the PV
  - Stenting the SB if the residual stenosis after PTCA is >30%