The Tryton Bifurcation Trial:

A randomized comparison of a provisional one-stent vs. a dedicated two-stent strategy for true bifurcation coronary lesions

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for the Tryton Bifurcation Trial Investigators

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Disclosure Statement of Financial Interest
TCT 25: San Francisco, CA; Oct 27 - Nov 1, 2013

Martin B. Leon, MD

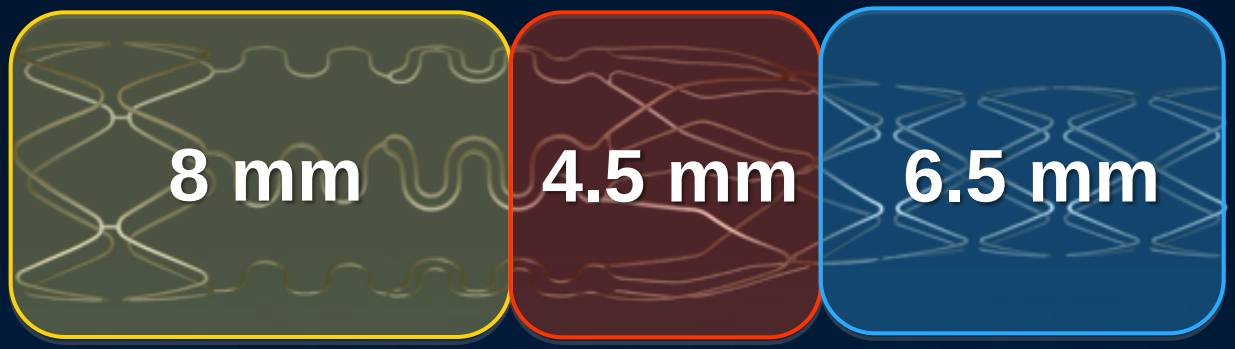
Within the past 12 months, I or my spouse/partner have had a financial interest/arrangement or affiliation with the organization(s) listed below.

Affiliation/Financial Relationship	Company
• Research Support (CUMC)	• Abbott, Boston Scientific, Medtronic
• Consulting Fees/Honoraria	• None
• Major Stock Shareholder/Equity	• None

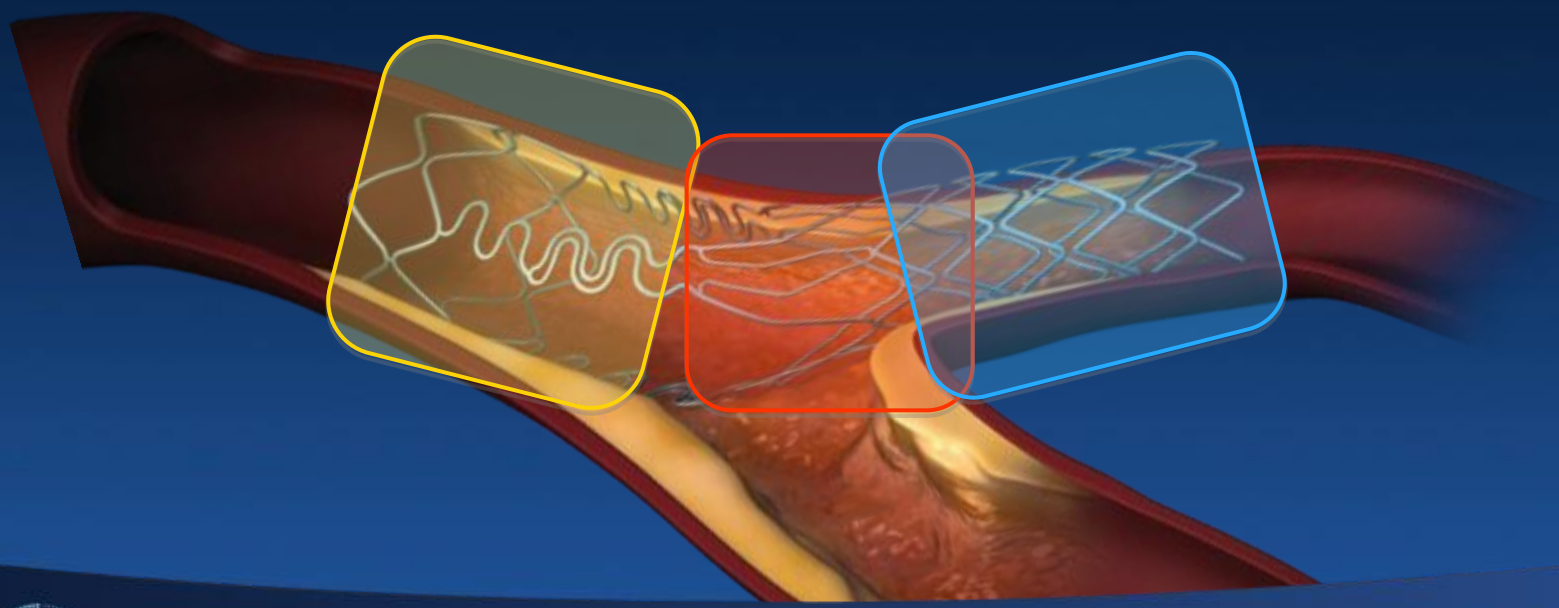
Purpose of the Study

- To compare the clinical outcomes and angiographic results of the accepted provisional one-stent strategy vs. the Tryton bifurcation two-stent approach in a randomized controlled trial of true coronary bifurcation lesions.

Tryton Side Branch Stent

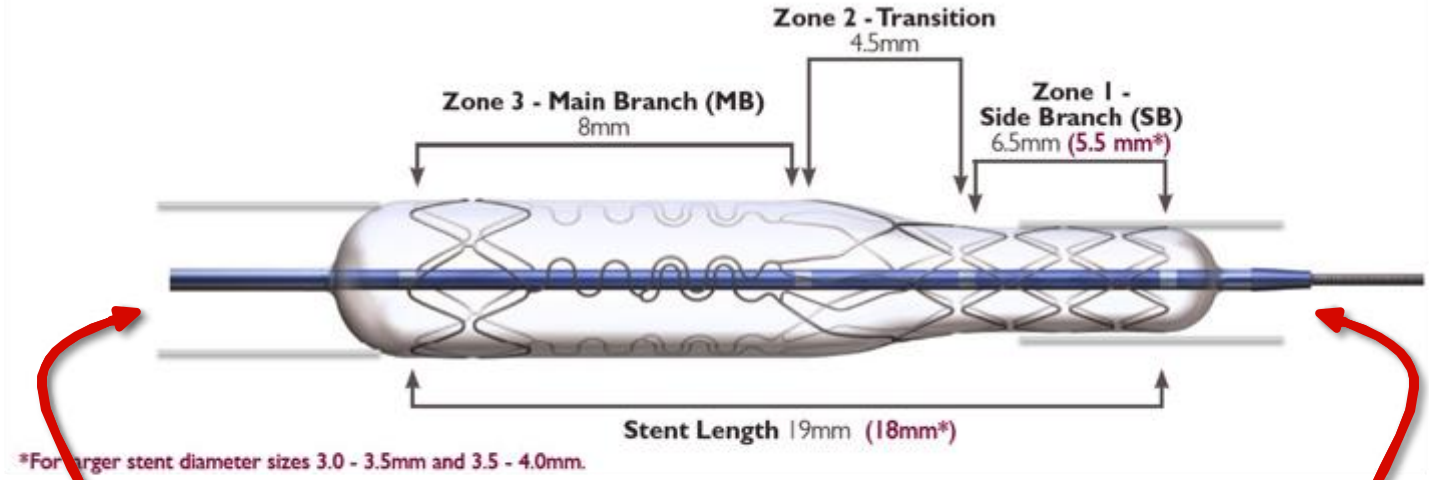


Main Branch Zone | Transition Zone | Side Branch Zone



Tryton is a Cobalt alloy bare metal stent

Tryton Side Branch Stent Sizes

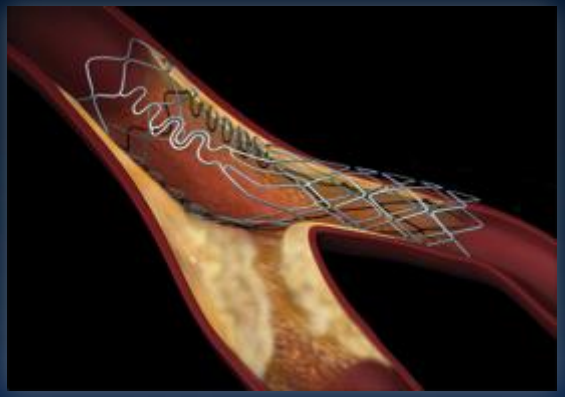


*For larger stent diameter sizes 3.0 - 3.5mm and 3.5 - 4.0mm.

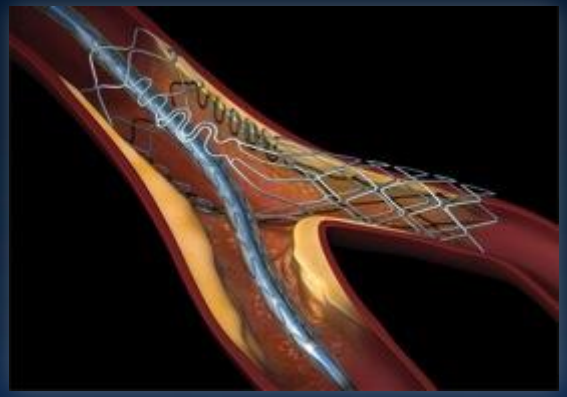
Main Branch Diameter (mm)	Side Branch Diameter (mm)
2.5	2.5
3.0	2.5
3.5	2.5
3.5	3.0
4.0	3.5

Recently Added

Tryton Deployment Sequence



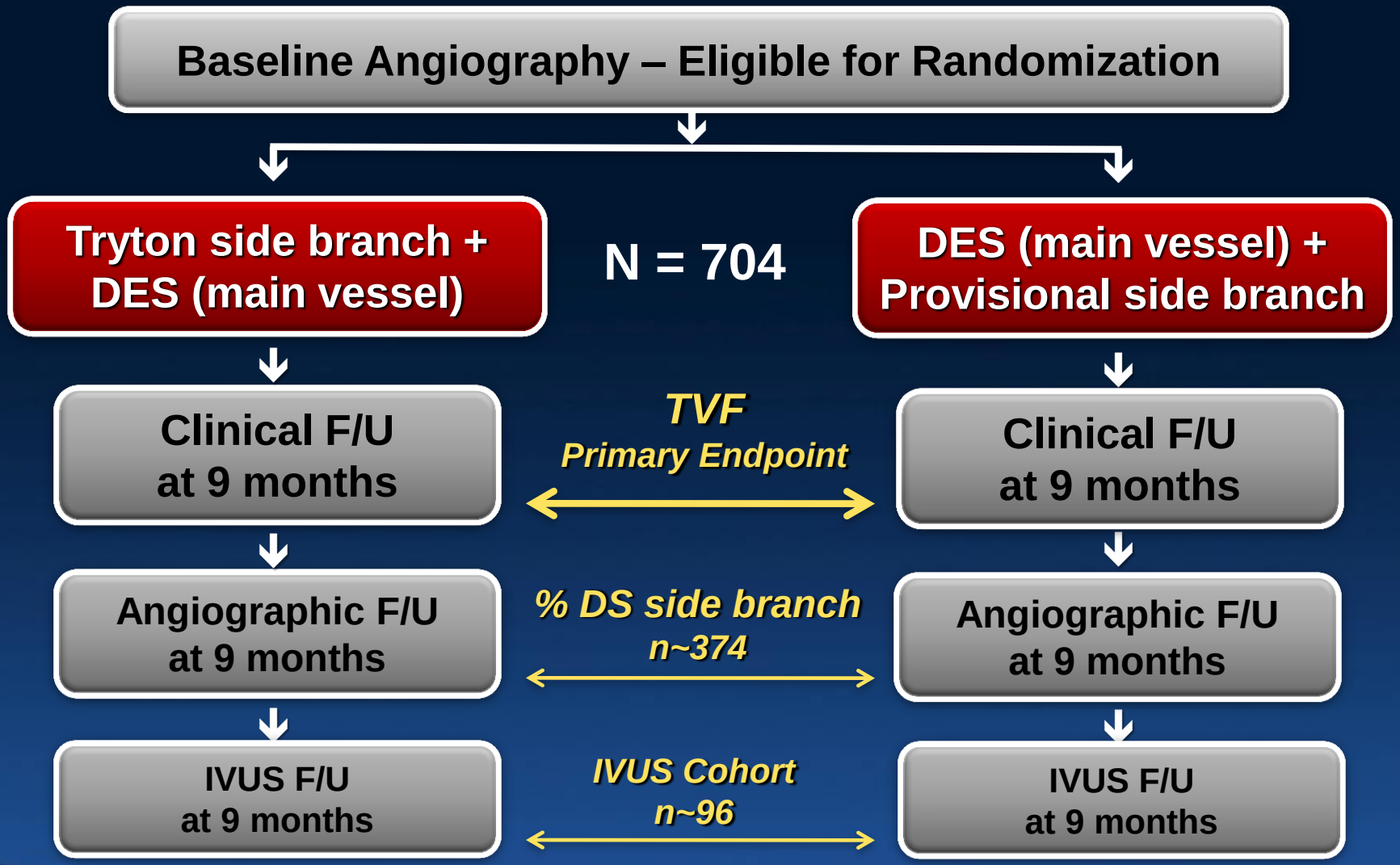
Tryton positioned and deployed after pre-dilatation (secures and protects side branch)



Main vessel treated with approved DES through main vessel portion of Tryton

Kissing balloon post-dilatation to insure complete lesion & ostium coverage

Tryton Study Design



Inclusion Criteria

- **Single de novo *"true"* bifurcation lesion** in a native coronary artery involving both the main vessel and the side branch (Medina classification 1.1.1, 1.0.1, or 0.1.1 by visual assessment)
- **Symptoms or objective evidence of ischemia**
- **Vessel diameter:** main vessel ≥ 2.5 mm and ≤ 4.0 mm; side branch ≥ 2.5 mm and ≤ 3.5 mm
- **Lesion length:** main vessel ≤ 28 mm; side branch ≤ 5 mm
- Limited treatment of **multi-vessel disease and staging,** per protocol (after successful treatment of ≤ 2 non-complex, non-target lesions)

Key Exclusion Criteria

Clinical…

- STEMI < 72 hours or STEMI/non-STEMI > 72 hours and increased CK-MB
- Hemodynamic instability
- Creatinine > 2.5 mg/dL or dialysis
- Bleeding diathesis or hypersensitivity to anticoagulant meds
- LVEF < 30%

Anatomic…

- Left main disease (unprotected or protected)
- Trifurcation lesion
- Complex morphology: severe Ca++, thrombus, TIMI 0/1 flow, severe tortuosity

Primary and Secondary Endpoints

- **Study design:** Intention-to-treat (ITT) is primary analysis cohort, 1:1 randomization
- **Primary Endpoint:** Target vessel failure @ 9 months follow-up (all patients): non-inferiority
  - cardiac death
  - target vessel MI (peri-procedural > 3X CK-MB)
  - target vessel revascularization (ischemia-driven, main vessel or side branch)
- **Secondary Endpoint:** % diameter stenosis (in-segment) of side branch at 9 months follow-up (angiographic cohort only): superiority

Operator Technique Recommendations

Tryton

- Pre-dilation (optimal lesion preparation)
- Tryton placement followed by POT (at ostium)
- DES placement followed by final kissing balloon dilation (with NC balloons)

Provisional

- Standard operator technique for pre-dilation and DES placement
- Side branch intervention (balloons or stents) only if… *< TIMI 3 flow, ≥ type B dissection, or > 80% stenosis*
- Final kissing balloon dilation (with NC balloons)

Trial Administration

Principal Investigator
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Columbia University Medical Center

Study Chairman
Patrick W. Serruys MD, PhD
Erasmus MC, Rotterdam
Imperial College, London

Executive Committee
Antonio Bartorelli MD, Thierry Lefèvre MD
Pieter Stella MD PhD, William Fearon MD
James Hermiller MD, Dean Kereiakes MD
David Williams MD

Data Management and Biostatistics
Donald E. Cutlip MD
Harvard Clinical Research Institute

Data Safety Monitoring Board
Chairman: Robert S. Safian MD
Beaumont Health System

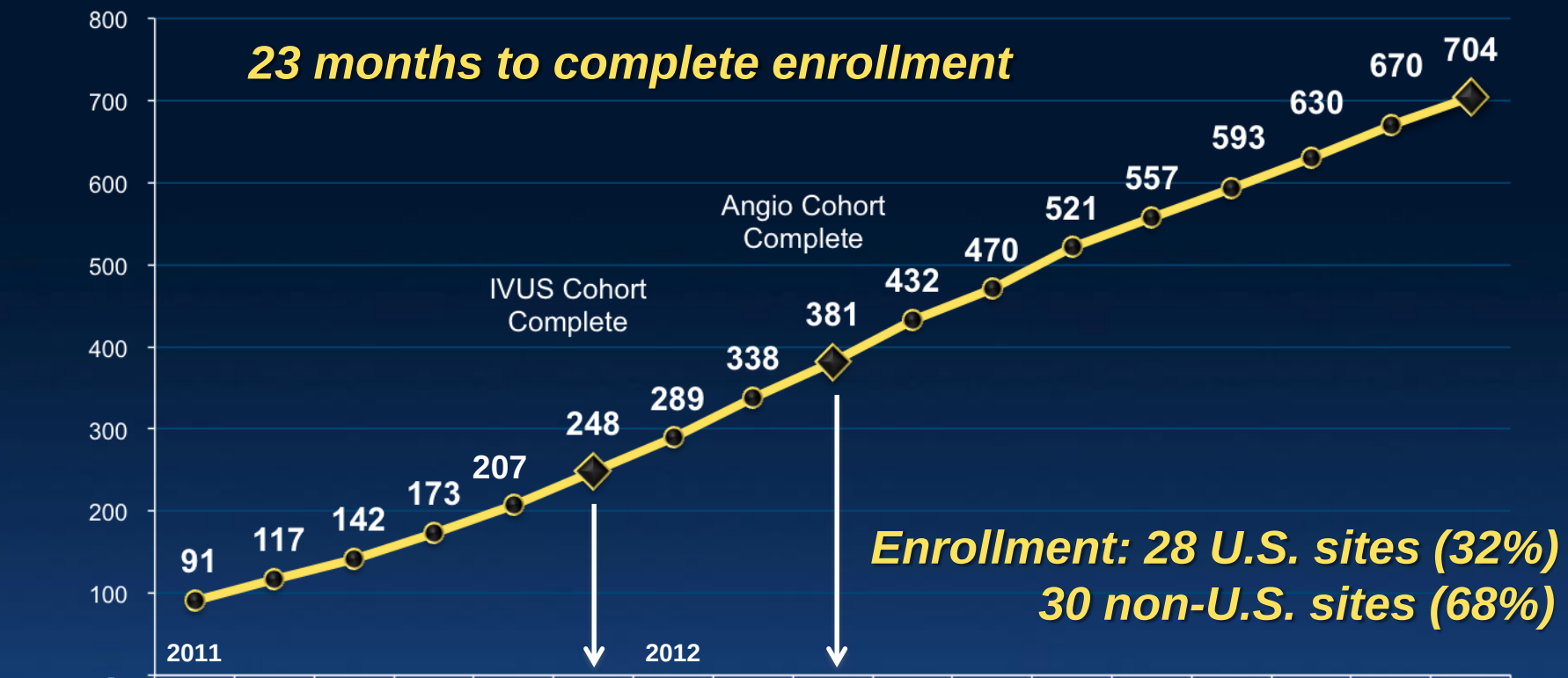
Clinical Events Committee
Donald E. Cutlip MD
Harvard Clinical Research Institute

Angiographic Core Lab
Philippe Généreux MD
Cardiovascular Research Foundation

IVUS & 3D Angiographic Core Lab
Hector Garcia-Garcia MD, PhD
Cardialysis, Rotterdam,
The Netherlands

Sponsor
Aaron V. Kaplan MD,
Linn Laak
Tryton Medical, Inc.

Enrollment Cadence



	JUL	AUG	SEP	OCT	NOV	DEC	JAN	FEB	MAR	APR	MAY	JUN	JUL	AUG	SEP	OCT	NOV
Actual	91	117	142	173	207	248	289	338	381	432	470	521	557	593	630	670	704

Enrollment by Site

Paula Stradins Clinical University Riga, Latvia I. Kumsars	54
Mount Sinai Medical Center New York, NY S. Sharma	44
OLVG Amsterdam, The Netherlands T. Slagboom	41
Karol Marcinkowski University Hospital Ponzan,Poland M. Lesiak	37
AMC Department of Cardiology Amsterdam, The Netherlands J. Wykrzykowska	26
Szegedi Tudományegyetem Szeged, Hungary I. Ungi	25
Gottsegaen Gyorgy Orszagos Kardiologai Budapest, Hungary G. Fontos	25
Wellmont CVA Heart Institute Kingsport, TN C. Metzger	24
UMCU Heidelberglaan Utrecht, The Netherlands P. Stella	22
Ziekenhuis Oost-Limburg Genk, Belgium J. Dens	20
MediQuest Research Group Ocala, FL R. Feldman	18
CHU Leige Domaine Univer du Sart Tilman Liege, Belgium V. Legrand	18
Hopital Rangueil Toulouse,France D. Carrié	17
ZNA Antwerpen, Belgium G. Van Langenhove	16

Enrollment by Site

Erasmus MC Thoraxcenter Rotterdam,The Netherlands R. van Geuns	16
Castle Hill Hospital Cottingham,United Kingdom A. Hoye	15
UZ Brussel Brussel, Belgium P. Kayaert	14
AZ Sint-Jan Cardiology Brugge,Belgium L. Muyldermans	14
Stanford University Medical Center and VA Palo Alto, CA W. Fearon	13
St. Antonius Ziekenhuis Nieuwegein, The Netherlands M. J. Suttorp	13
Rabin MC Belinson Campus Petach Tivka Israel A. Assali	12
Amphia Ziekenhuis Breda, The Netherlands P. den Heijer	12
Monzino Hosptail Centro Cardiologico Milan, Italy A. Bartorelli	12
Golden Jubilee Hospital Glasgo, United Kingdom A. Oldroyd	12
Tallahassee Research Institute, Inc. Tallahassee, FL W. Batchelor	11
St. Vincent Medical Group, Inc. Indianapolis, IN J. Hermiller	11
Scottsdale Healthcare Scottsdale, AZ D. Rizik	11
Padova University Hospital Padova, Italy G. Tarantini	11

Patient Flow

Randomized
N=704

Tryton + DES
N=355

Provisional + DES
N=349

Tryton
4= Lost to F/U
2= Patient withdrawal
4= Death

9 Month Follow-up
N=681
Tryton = 345
Provisional = 336

Provisional
6= Lost to F/U
5= Patient withdrawal
4= Death

Angiographic
N=326
Tryton= 158
Provisional= 168

IVUS
N=94
Tryton= 59
Provisional= 35

- **Clinical FU at 9 months = 97%**
- **Angiographic FU at 9 months = 87%**

Patient Demographics

Characteristic (%)	Provisional (N=349 Patients)	Tryton (N=355 Patients)
Age (years)	64.6±9.4	64.5±10.6
Male	73.4	71.8
MI	37.8	30.0
PCI	41.8	38.0
CABG	2.0	2.5
TIA / CVA	5.2	6.1
CHF	0.9	1.7
Diabetes Mellitus	28.1	23.9
Hypertension	73.6	73.2
Hypercholesterolemia	77.3	74.1
Current Smoking	15.2	17.5
Atrial Fibrillation	6.9	10.7

Patient Demographics

Characteristic (%)	Provisional (N=349 Patients)	Tryton (N=355 Patients)
Recent MI	9.7	10.7
Angina Type		
Stable	74.8	73.8
Unstable	19.8	20.0
CCS Class		
I	16.7	13.6
II	55.1	57.6
III	22.9	25.2
IV	5.3	3.6
Functional test (+ ischemia)	63.2	62.7
LVEF	57.5±9.8	57.7±9.6

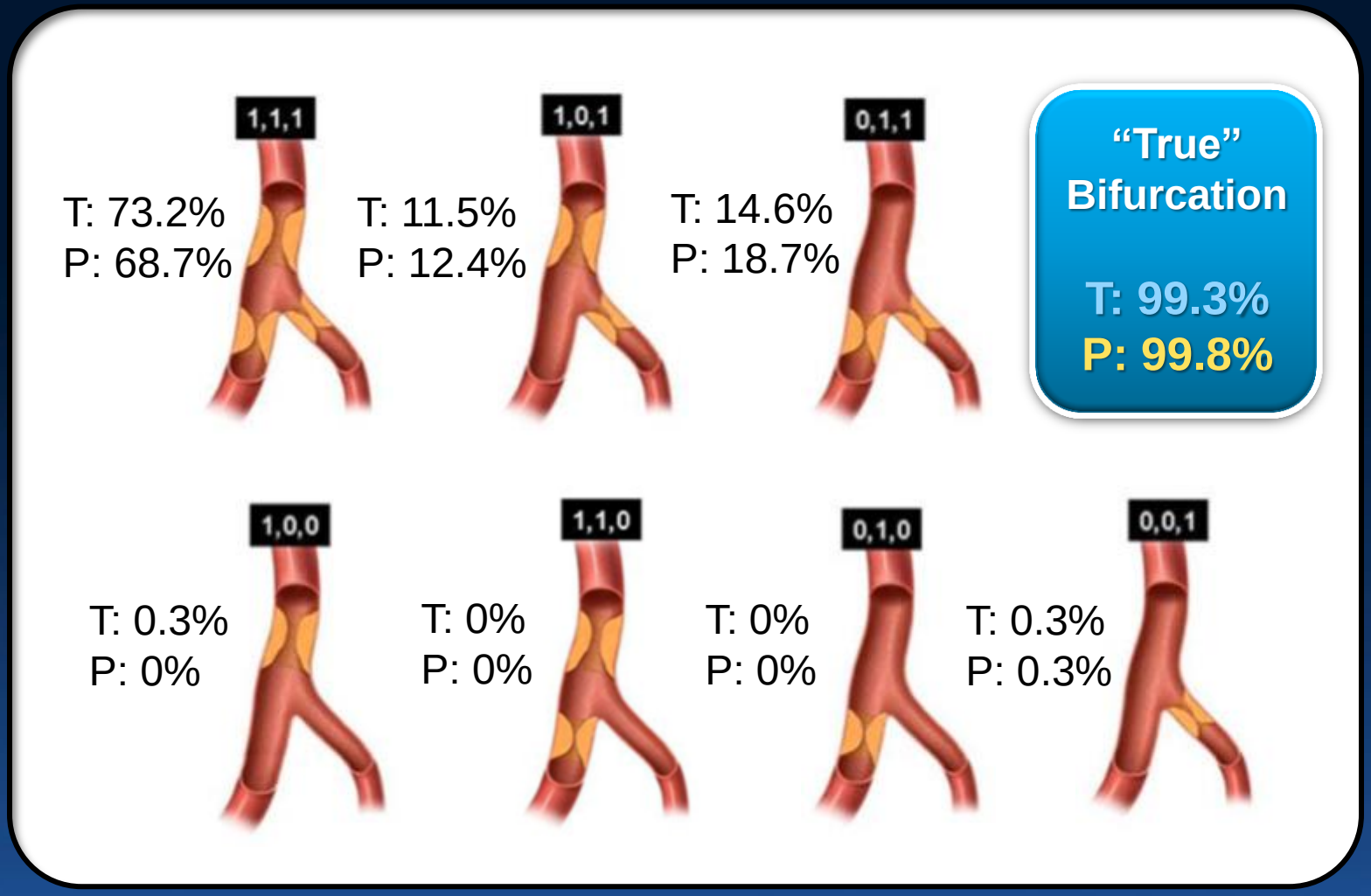
Main Vessel Characteristics

Characteristic (%)	Provisional (N=349 Patients)	Tryton (N=355 Patients)
Vessel Location		
LAD	75.1	76.6
LCX	18.6	17.8
RCA	6.3	5.6
Lesion Location		
Ostial	4.3	7.3
Proximal	49.0	44.4
Mid	19.8	24.3
Distal	26.9	24.0
Reference Vessel Diameter (mm)	2.91±0.35	2.91±0.36
Lesion Length (mm)	15.96±6.83	16.81±7.25
Morphology		
angulation ≥45°	8.9	10.2
thrombus	1.1	0.8
calcification – mod/severe	22.3	16.4
TIMI Flow (baseline) < 3	8.9	7.9

Side Branch Characteristics

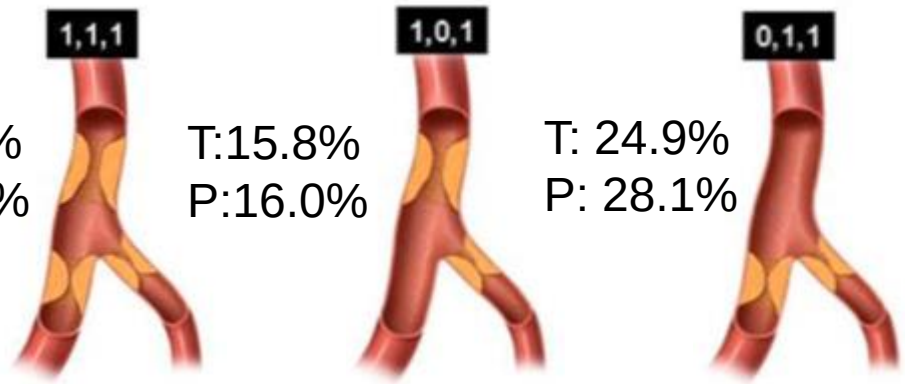
Characteristic (%)	Provisional (N=349 Patients)	Tryton (N=355 Patients)
Vessel Location		
LAD	74.8	77.1
LCX	18.9	17.2
RCA	6.3	5.6
Lesion Location		
Ostial	97.7	97.2
Proximal	1.4	1.7
Mid	0.0	0.3
Distal	0.9	0.8
Reference Vessel Diameter (mm)	2.21±0.33	2.25±0.30
Lesion Length (mm)	4.43±1.12	4.84±1.56
Morphology		
angulation ≥45°	25.9	17.2
thrombus	0.9	0.3
calcification – mod/severe	7.2	6.7
TIMI Flow (baseline) < 3	3.4	4.8

Medina Classification (Site Reported)



P = Provisional T = Tryton

Medina Classification (Core Lab)



T:49.2%
P:42.1%

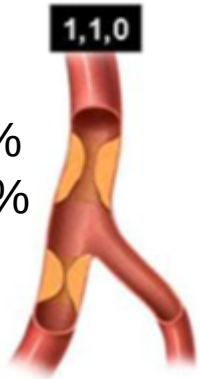
T:15.8%
P:16.0%

T: 24.9%
P: 28.1%

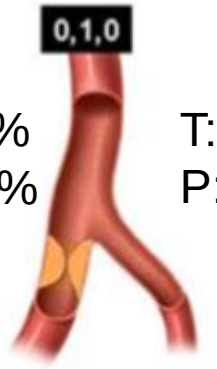
"True" Bifurcation

T: 89.9%
P: 86.2%

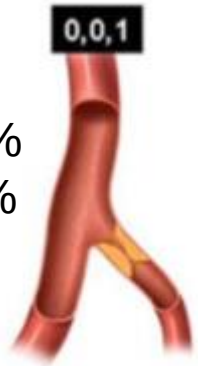
T: 1.4%
P: 2.6%



T: 2.3%
P: 4.9%



T: 2.8%
P: 4.0%



T: 3.4%
P:2.3%

P = Provisional T = Tryton

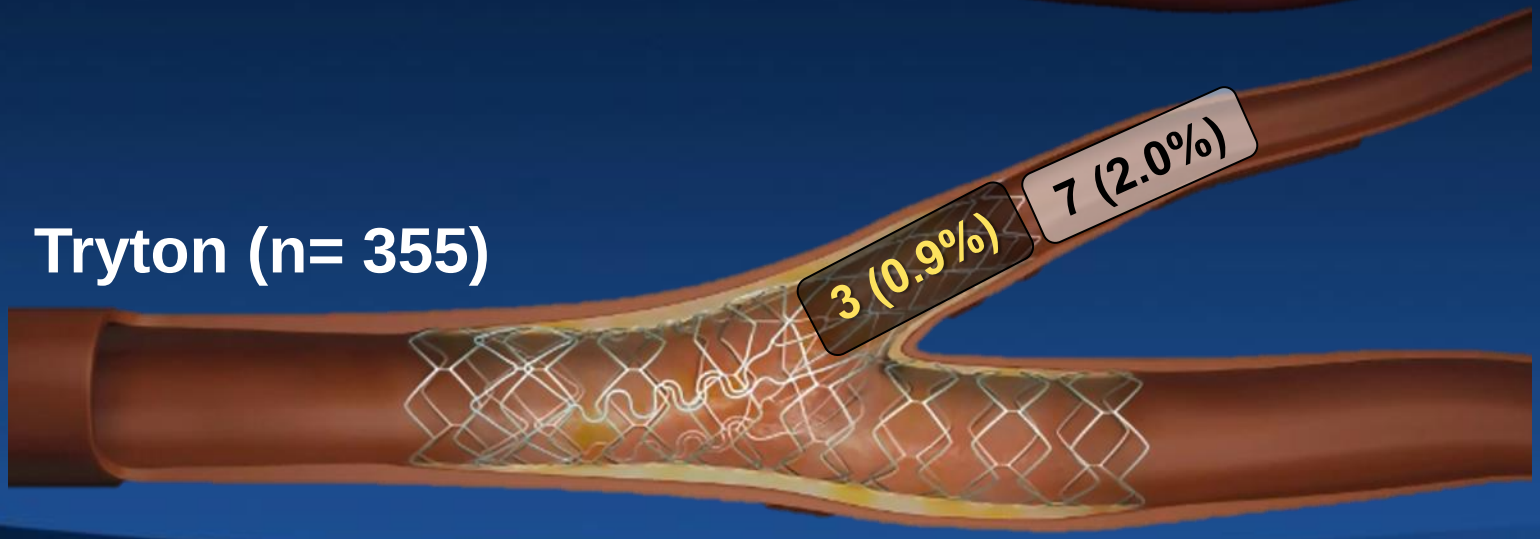
Procedural Details

	Provisional (N=349 Patients)	Tryton (N=355 Patients)
Non-target lesions treated (%)	16.9	12.1
Non-balloon lesion preparation (%)	1.4	1.7
Tryton stent implanted (%)	0.6	96.1
Side Branch		
Pre-dilation (%)	60.8	95.8
Maximum balloon diameter (mm)	2.4±0.39	2.6±0.37
Maximum balloon pressure (atm)	10.4±3.62	10.8±4.10
Main Vessel		
Pre-dilation (%)	79.8	89.2
Maximum balloon diameter (mm)	3.1±0.42	3.1±0.41
Maximum balloon pressure (atm)	11.3±3.90	11.2±4.20
Final “kissing balloon” dilation (%)	86.2	85.1

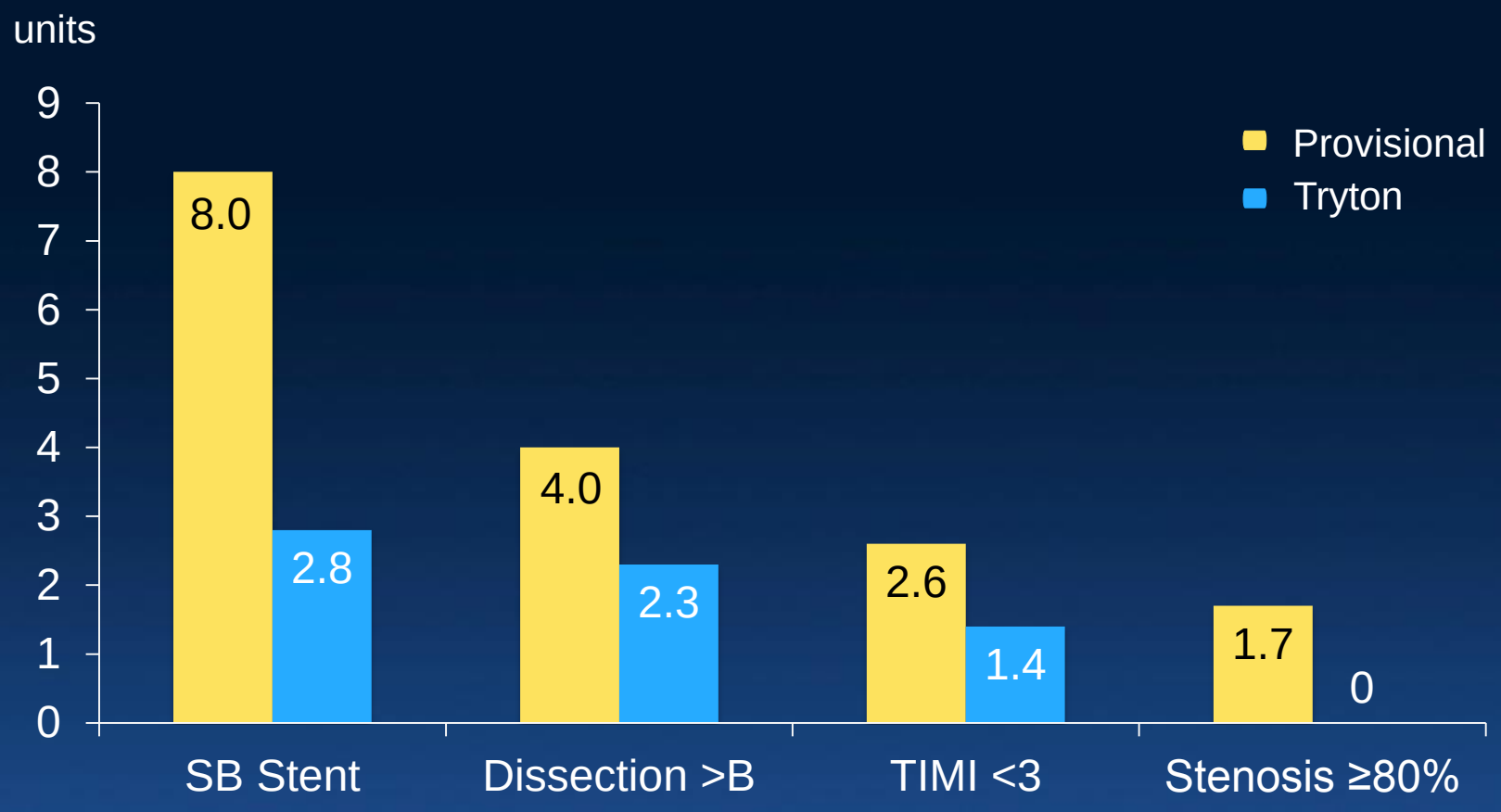
Additional Side Branch Stents
(Site Reported)

Provisional (n= 349)

Tryton (n= 355)



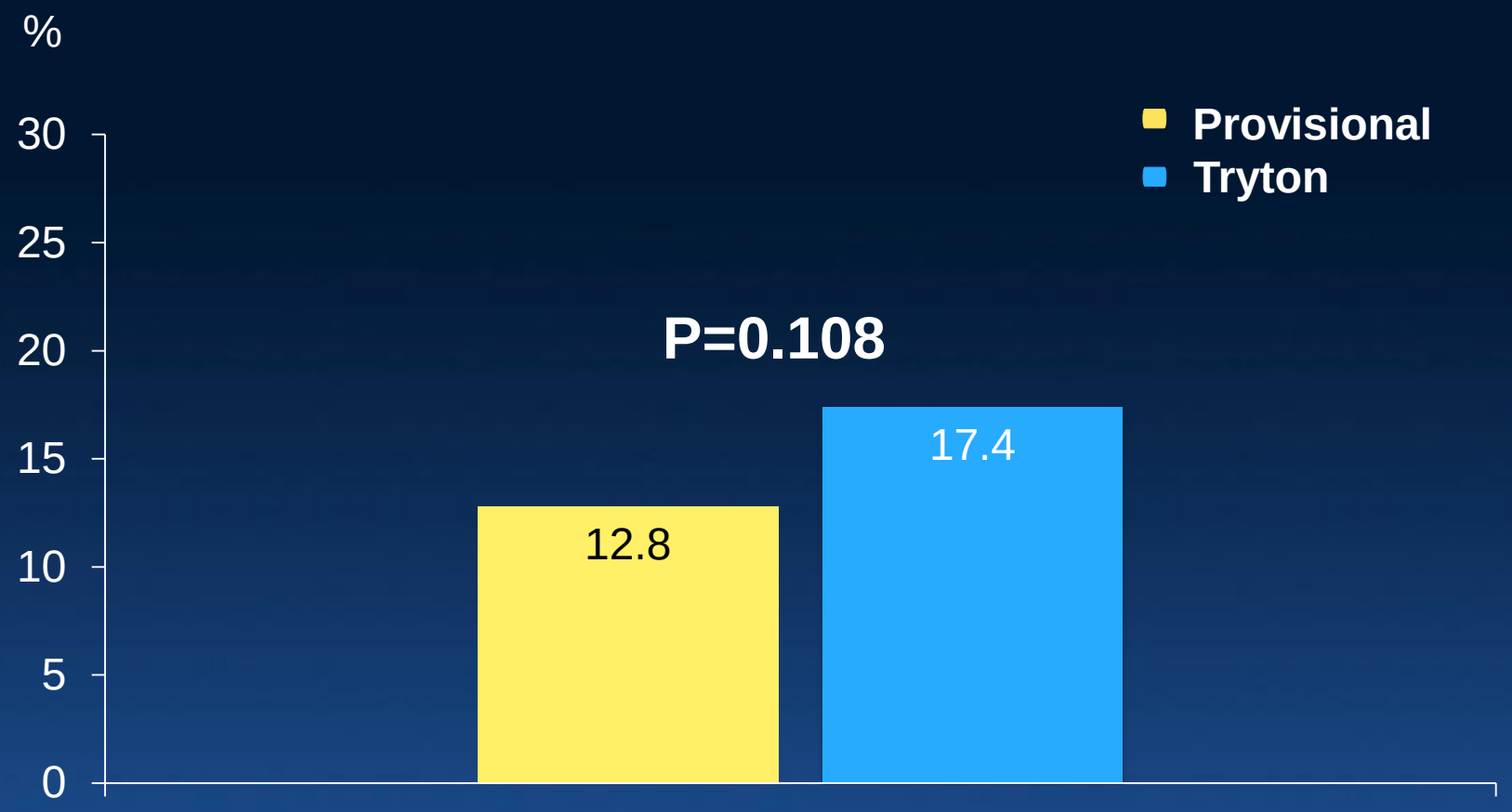
Additional Side Branch Stents
Indications (site-reported)



Tryton Bifurcation Study

Main Study Results

Target Vessel Failure (TVF)*
Primary Endpoint

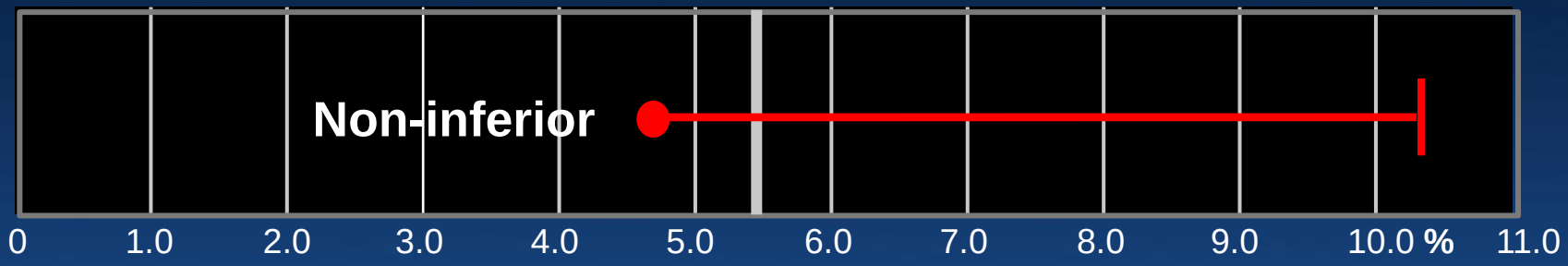


* TVF = Cardiac death, TV–MI and TVR

Primary Endpoint
Target Vessel Failure at 9 Months

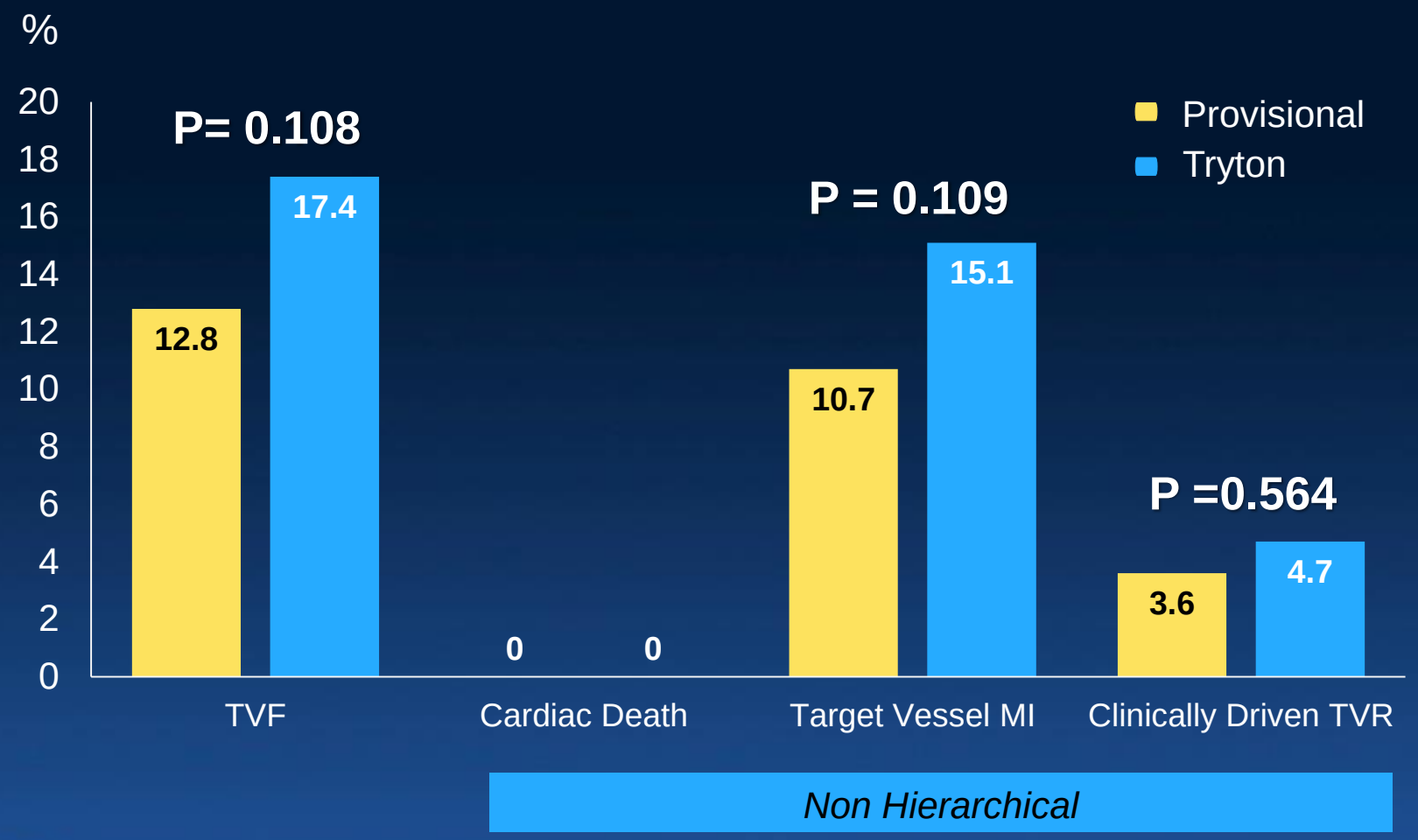
Tryton (N = 355)	Provisional (N = 349)	Difference	4.6%	Non-inferiority P value
17.4%	12.8%	Upper 1-sided 95% CI	10.3%	= 0.4167

Zone of non-inferiority pre-specified margin = 5.5%



Primary Non-Inferiority Endpoint Not Met

Target Vessel Failure (TVF)
Primary Endpoint



Stent Thrombosis (ARC)
9-month Follow-up

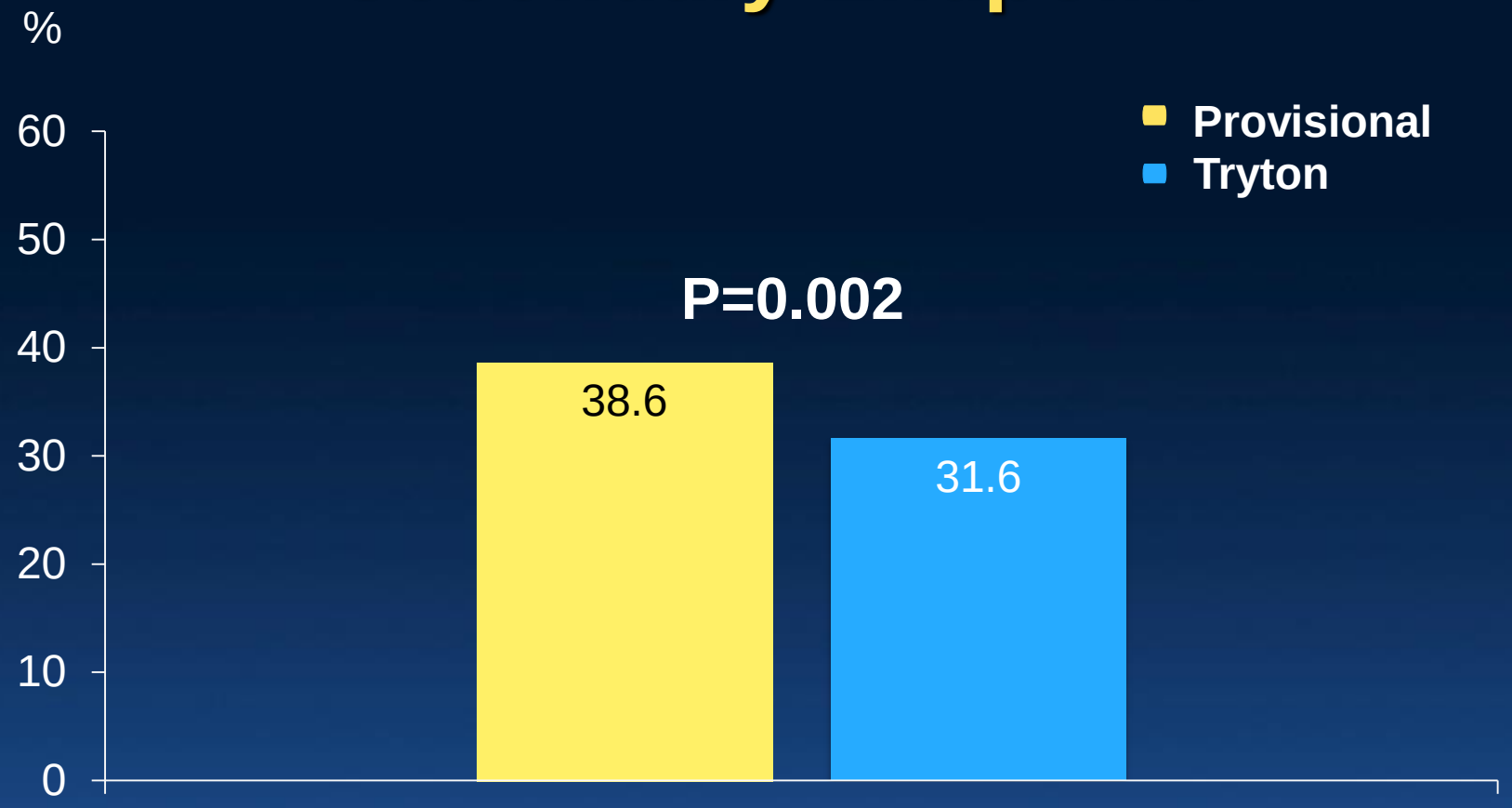
Event - % (n)	Provisional (N=349)	Tryton (N=355)	P-Value
All – to 270 days			
definite	0.3 (1)	0.6 (2)	1.00
probable	0	0	na
def + prob	0.3 (1)	0.6 (2)	1.00
Early (0-30 days)			
definite	0.3 (1)	0.6 (2)	1.00
probable	0	0	na
def + prob	0.3 (1)	0.6 (2)	1.00
Late (30-270 days)			
definite	0	0	na
probable	0	0	na
def + prob	0	0	na

Overall = 0.4%

Angiographic Results (QCA)
Follow-up (9 months)

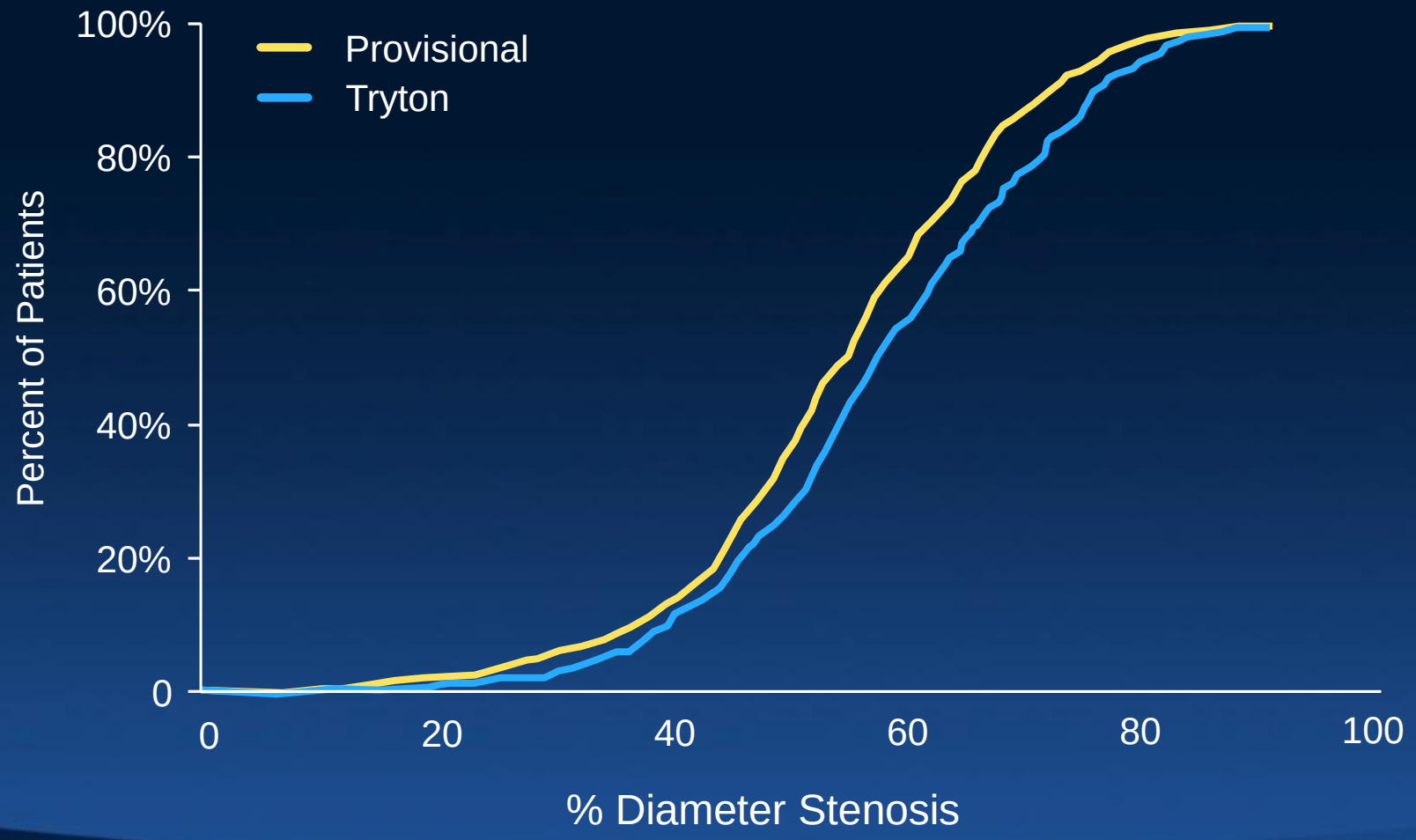
	Provisional (N=168)	Tryton (N=158)	P-Value
Main Vessel			
RVD (mm)	2.88±0.32	2.95±0.35	0.050
MLD (mm)			
In-stent	2.44±0.43	2.47±0.54	0.581
In-segment	2.13±0.48	2.14±0.56	0.851
% DS			
In-stent	14.94±12.75	16.47±14.28	0.308
In-segment	26.02±14.01	27.77±15.87	0.292
Side Branch			
RVD (mm)	2.24±0.31	2.29±0.29	0.103
MLD (mm)			
In-stent	na	1.67±0.62	na
In-segment	*1.36±0.38*	*1.56±0.56*	*<0.001*
% DS			
In-stent	na	26.72±25.44	na
In-segment	*38.63±16.16*	*31.57±22.91*	*0.002*

Side Branch %DS (In-segment)
Secondary Endpoint

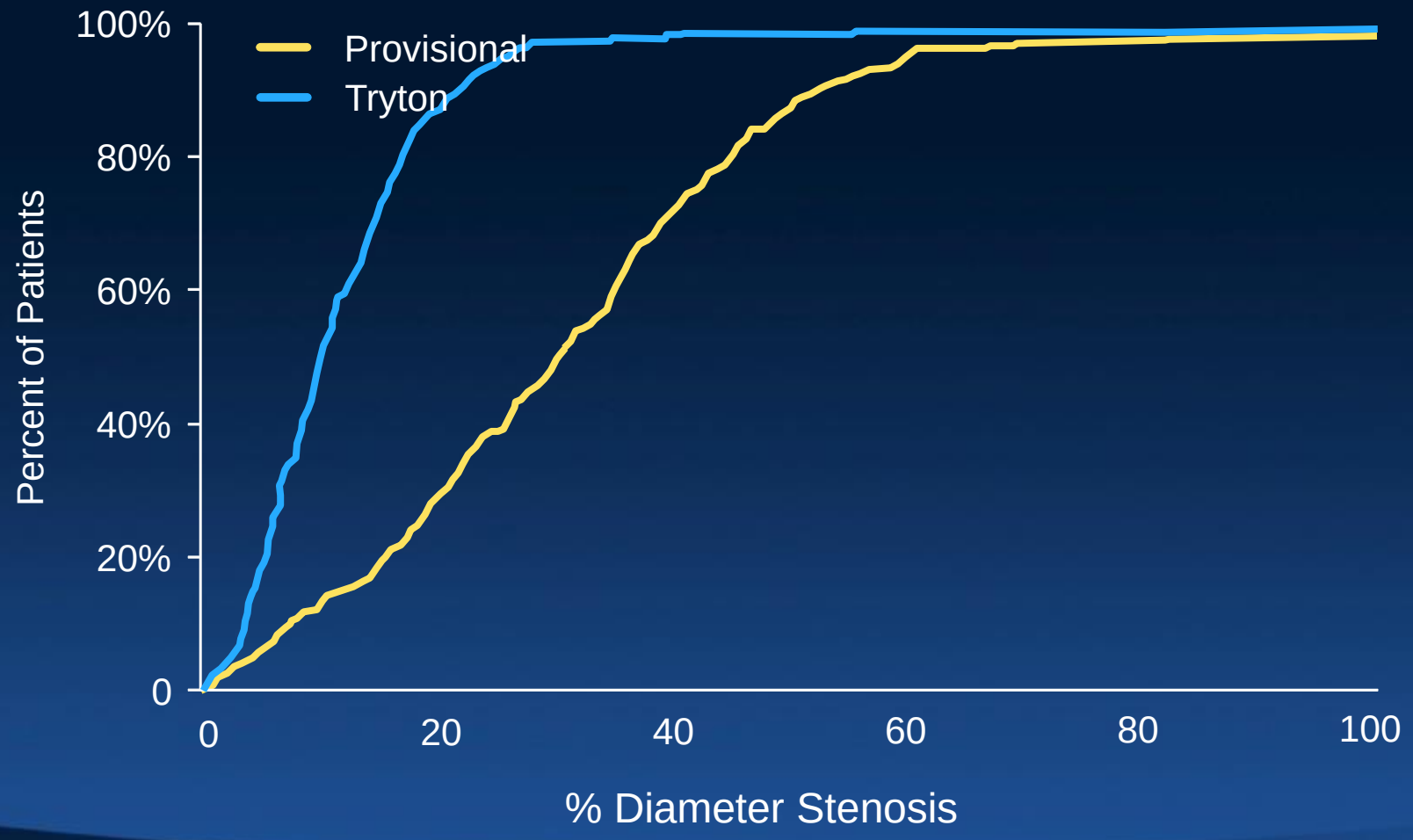


Secondary Superiority Endpoint Met

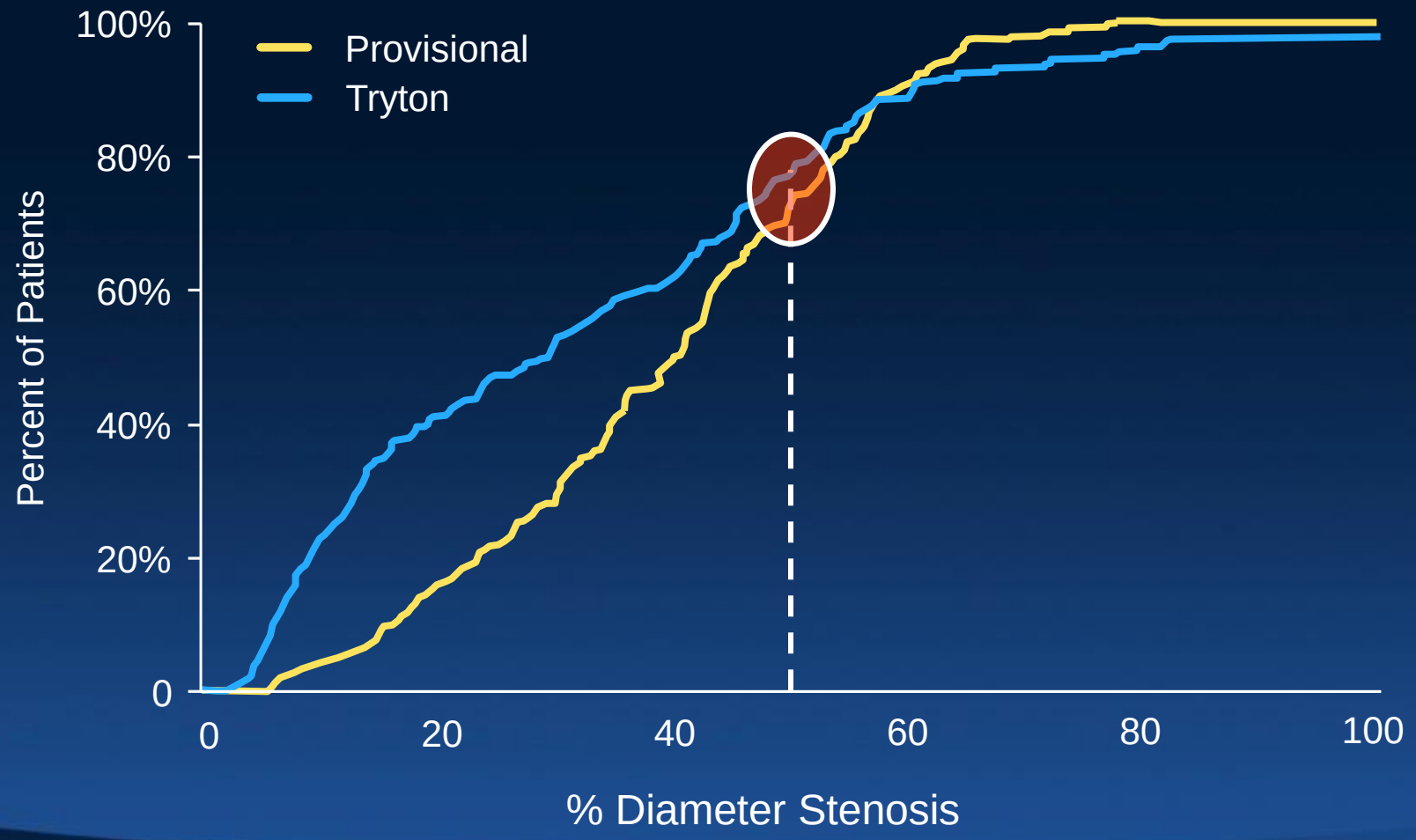
Side Branch % DS (In-segment)
Baseline



Side Branch % DS (In-segment)
Final



Side Branch % DS (In-segment)
9-Month FU

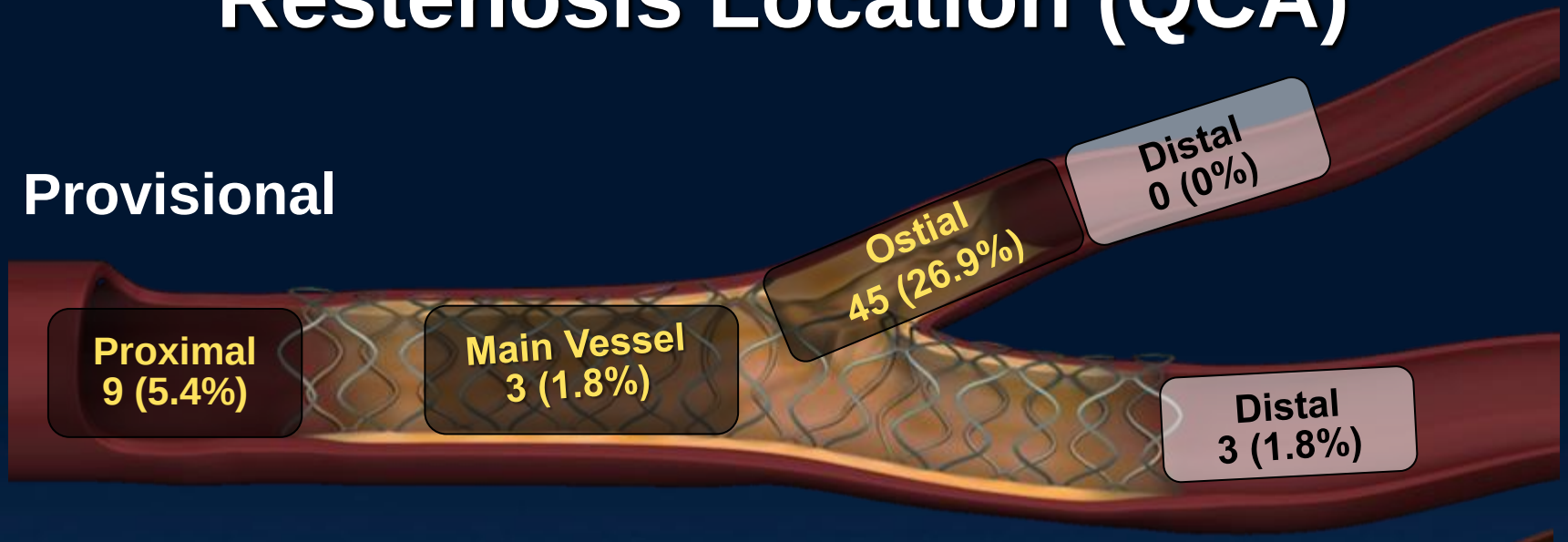


Angiographic Results
Binary Restenosis (9 months)

	Provisional (N=168)	Tryton (N=158)	P-Value
Main Vessel (%)			
In-stent	1.8	4.4	0.208
In-segment	8.9	10.1	0.851
Side Branch (%)			
In-stent	na	20.4	na
In-segment	26.8	22.6	0.439
MV or SB (Total, %)			
In-stent	na	21.6	na
In-segment	33.3	28.2	0.337

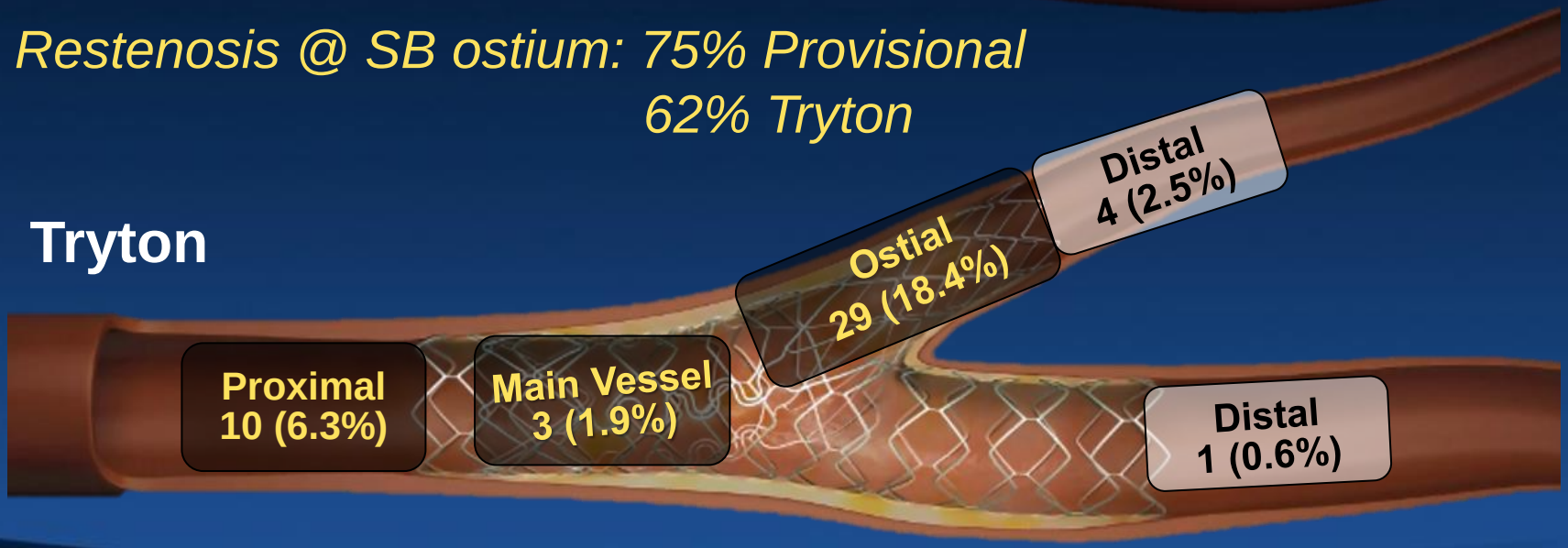
Restenosis Location (QCA)

Provisional



Restenosis @ SB ostium: 75% Provisional
62% Tryton

Tryton

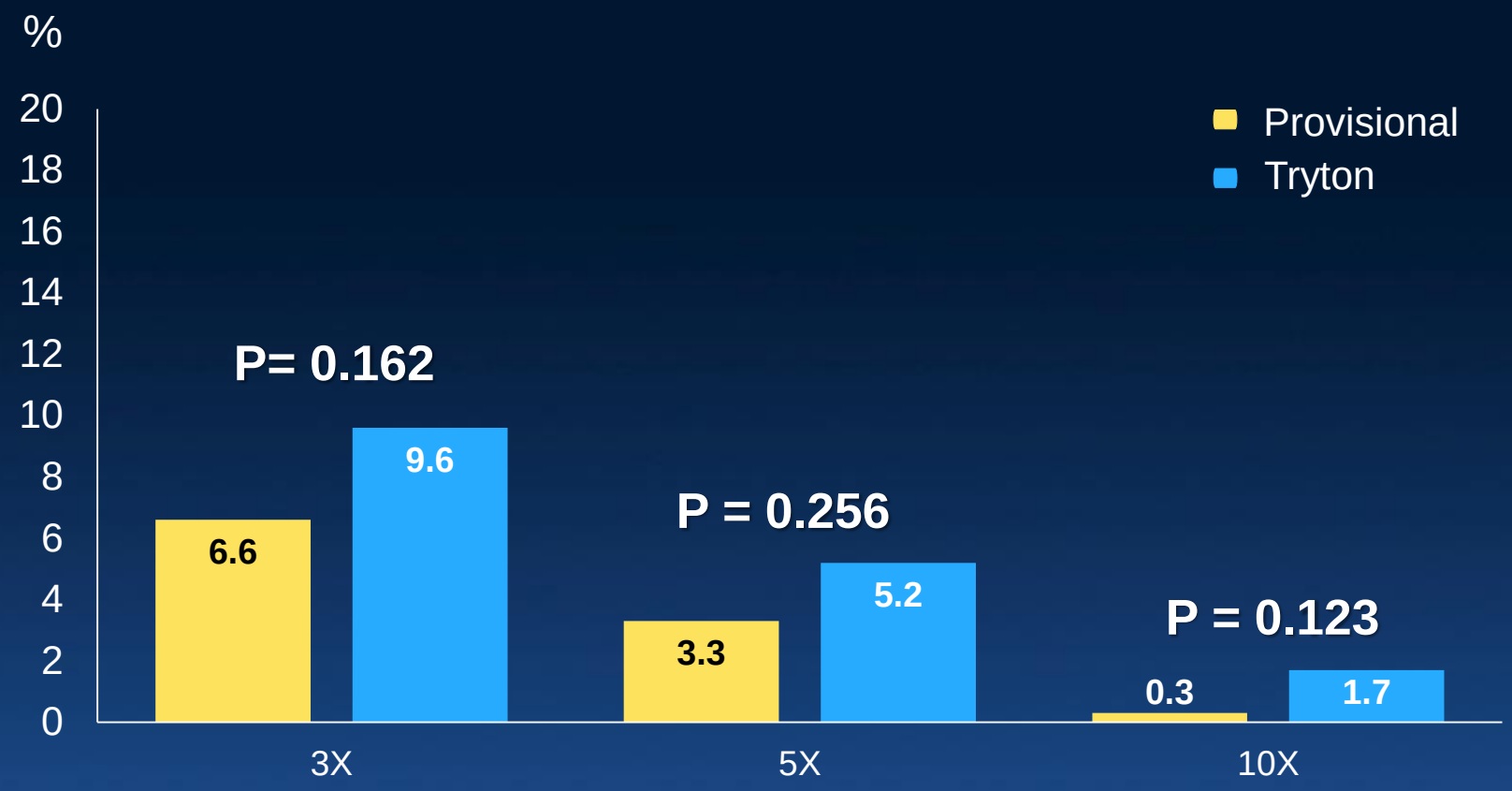


Tryton Bifurcation Study

Post-hoc Subset Analyses

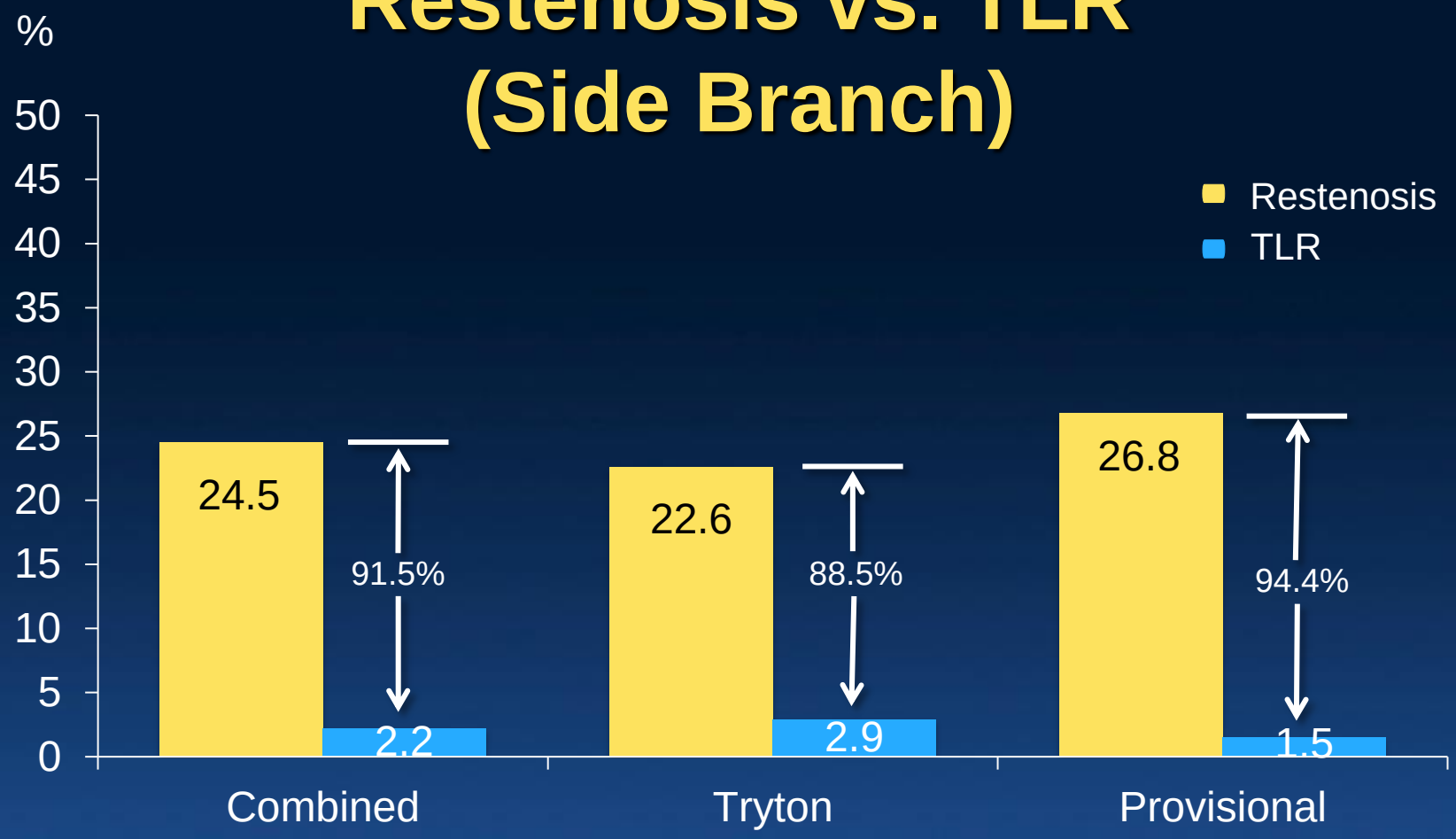
Target Vessel - MI

3X, 5X, 10X CK-MB Only Criteria



Occulostenotic Paradox

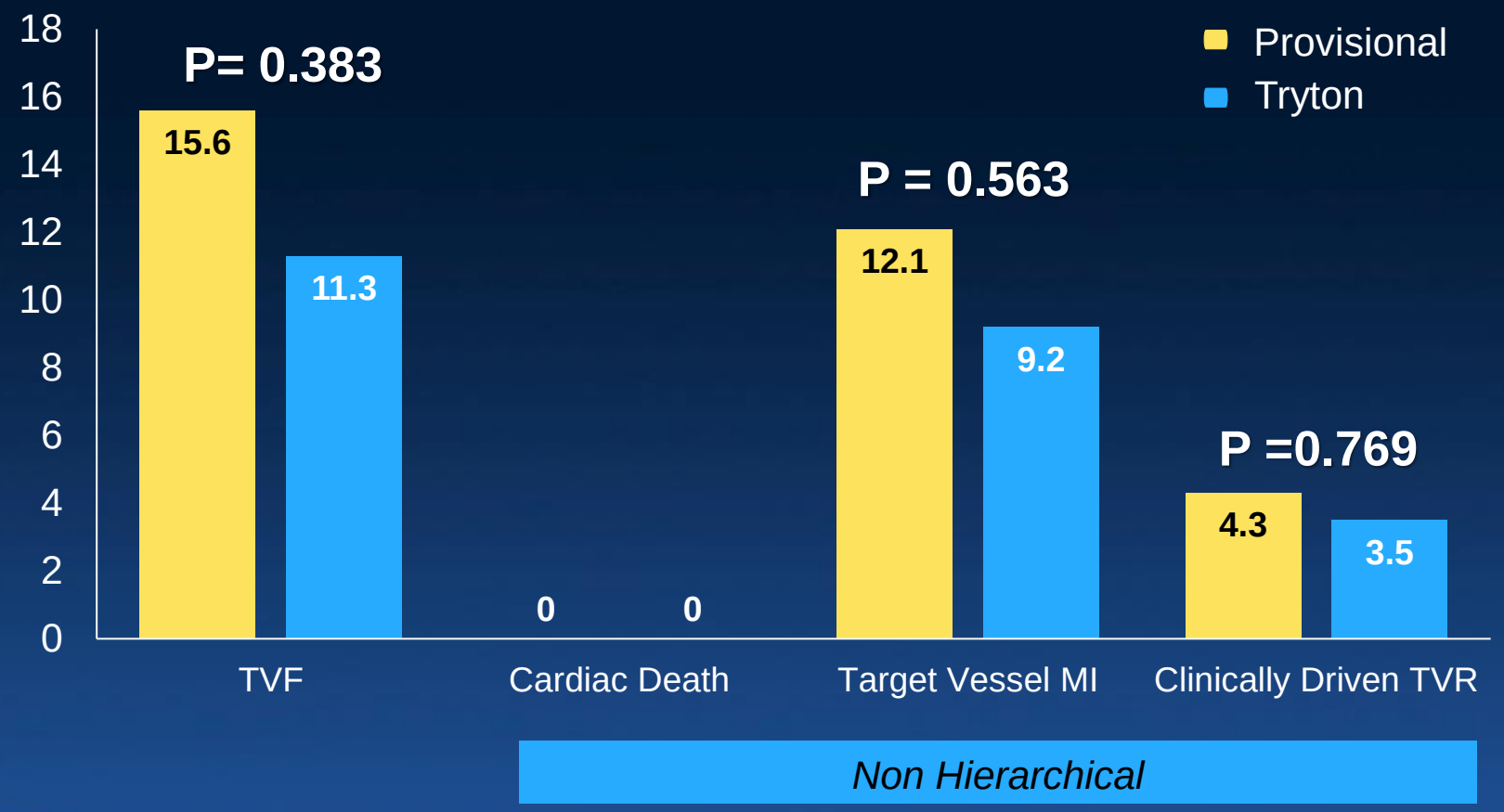
Restenosis vs. TLR (Side Branch)



Target Vessel Failure (TVF)

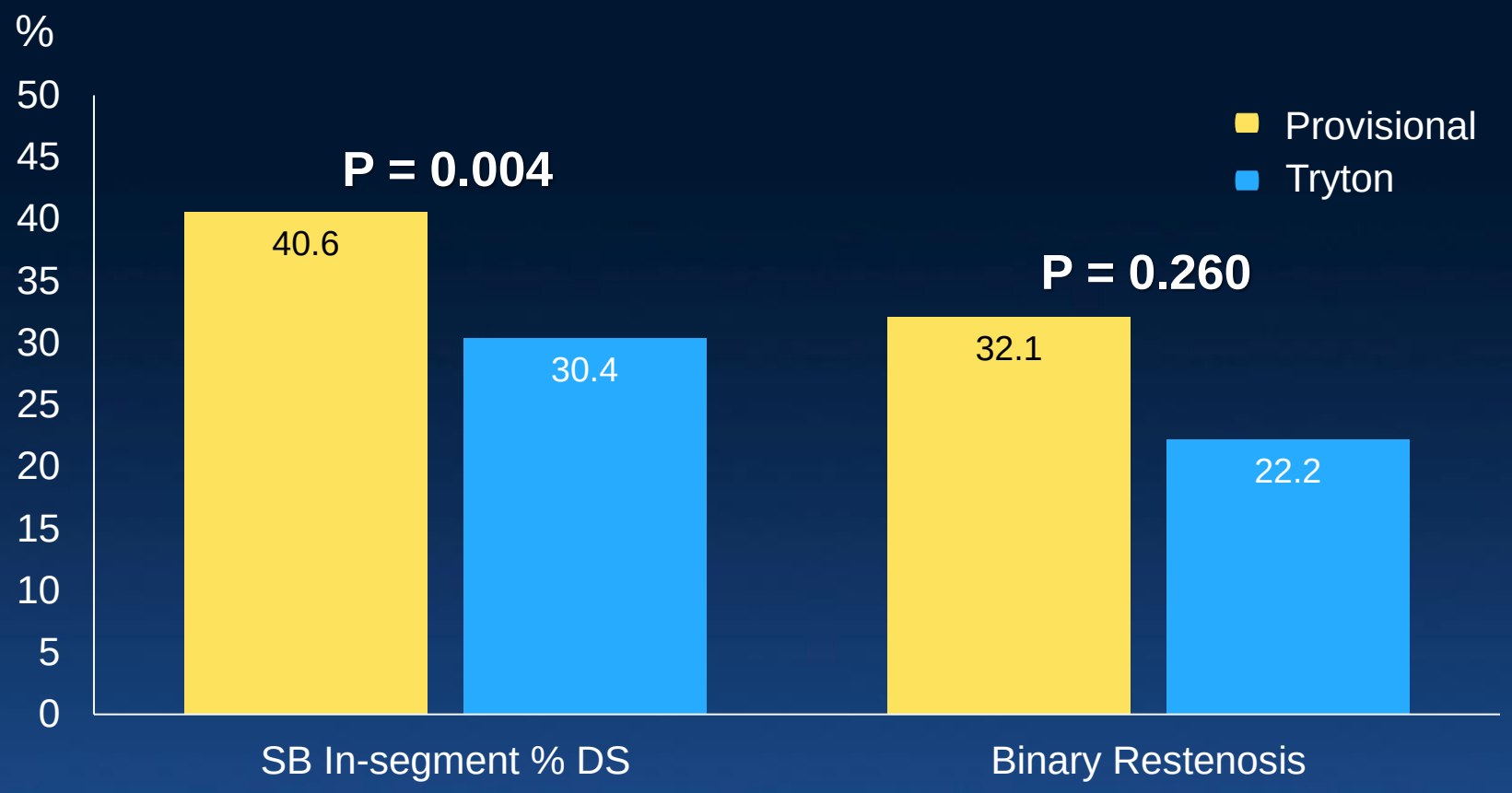
Side Branch ≥ 2.25 mm

Diff (95% CI) = -4.3% (-12.2, 3.7%)



Provisional (N=141) Tryton (N=141)

Angiographic Outcomes (QCA)
Side Branch ≥ 2.25 mm



Provisional (N=81) Tryton (N=63)

Conclusions

- The Tryton two-stent strategy in true bifurcations (88%) compared with the provisional strategy (8.0% side branch stents) did not meet the non-inferiority clinical endpoint (TVF), due to a relatively higher frequency of small peri-procedural CK-MB elevations.
- However, both strategies were safe (rare clinically significant MIs and stent thrombosis) and both had low 9-month clinically-driven TVR (P:3.6%,T:4.7%).
- DES in the main vessel performed well in both arms.
- Tryton improved side branch % diameter stenosis at FU (secondary endpoint; P=0.002)

Conclusions

- *Post-hoc subset analyses indicated:*
  - A striking disparity between binary restenosis and clinically-driven TVR for both arms, indicating that side branch angiographic restenosis is uncommonly expressed clinically.
  - Improved clinical and angiographic outcomes with Tryton in larger side branches (> 2.25 mm side branches = 41% of enrolled patients).

Clinical Implications

- It's difficult to enroll complex "high-risk" bifurcation lesions in clinical trials (only 41% had side branches ≥ 2.25 mm).
- Small peri-procedural CK-MB elevations occur more frequently with a two-stent strategy and dominate the clinical endpoint (TVF).
- Moderate stenoses in smaller side branches are not clinically active (occulostenotic paradox).
- In larger side branches (≥ 2.25 mm), a Tryton two-stent strategy improved side branch angiographic results and clinical outcomes.