TAXUS 'On-Label' Clinical Outcomes & 'Off-Label' Experiences in the Real World

Keith Dawkins MD FRCP FACC FSCAI
Associate Chief Medical Officer
Senior Vice President
Boston Scientific Corporation

Boston Scientific

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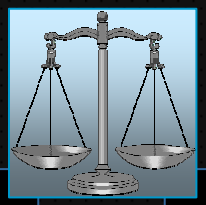
3rd APSIC Fellowship Convocation

Conflicts of Interest

- Employee & Stockholder:
  Boston Scientific Corporation
- I intend to reference unlabeled/unapproved uses of products in my presentation

Expectations of Stent Technology



Efficacy

- Deliverable
- Low TLR
- Low Restenosis
- Low Late Lumen Loss
- Cost-Effective

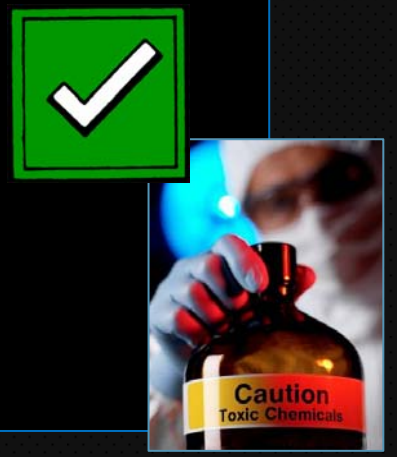
Safety

- No Device Malfunction
- No Early MACE
  - Q AMI
  - Non-Q AMI
- No Stent Thrombosis

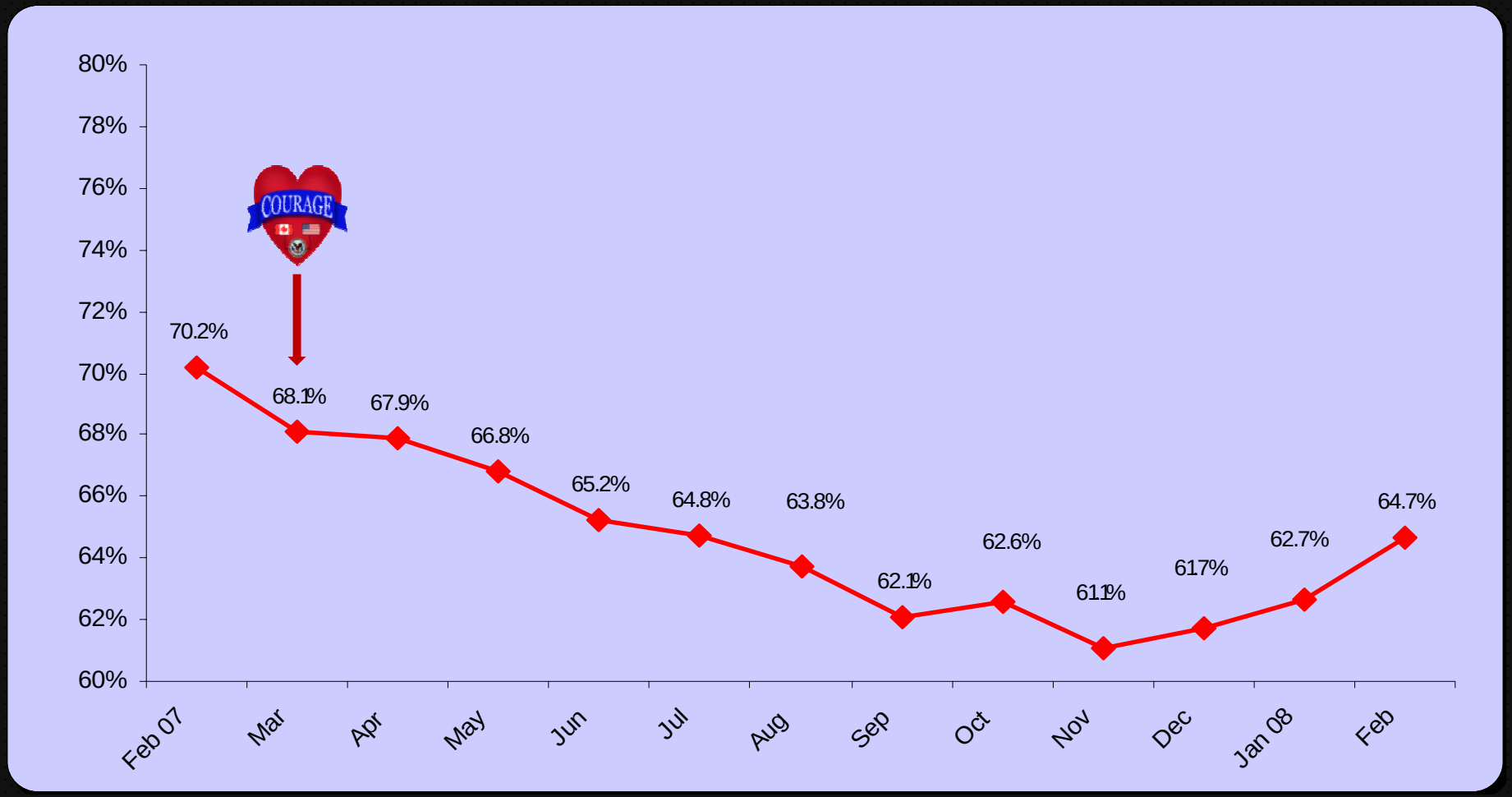
DES: Safety

The data supporting DES Safety are now *compelling* including…

- Western Denmark
- Ontario
- Mauri (Massachusetts)
- 'New' SCAAR
- TAXUS (CRF) meta
- CYPHER (CRF) meta
- Wake Forest
- NHLBI
- GHOST
- DEScover
- NY State
- MASS
- STENT Registry etc.,

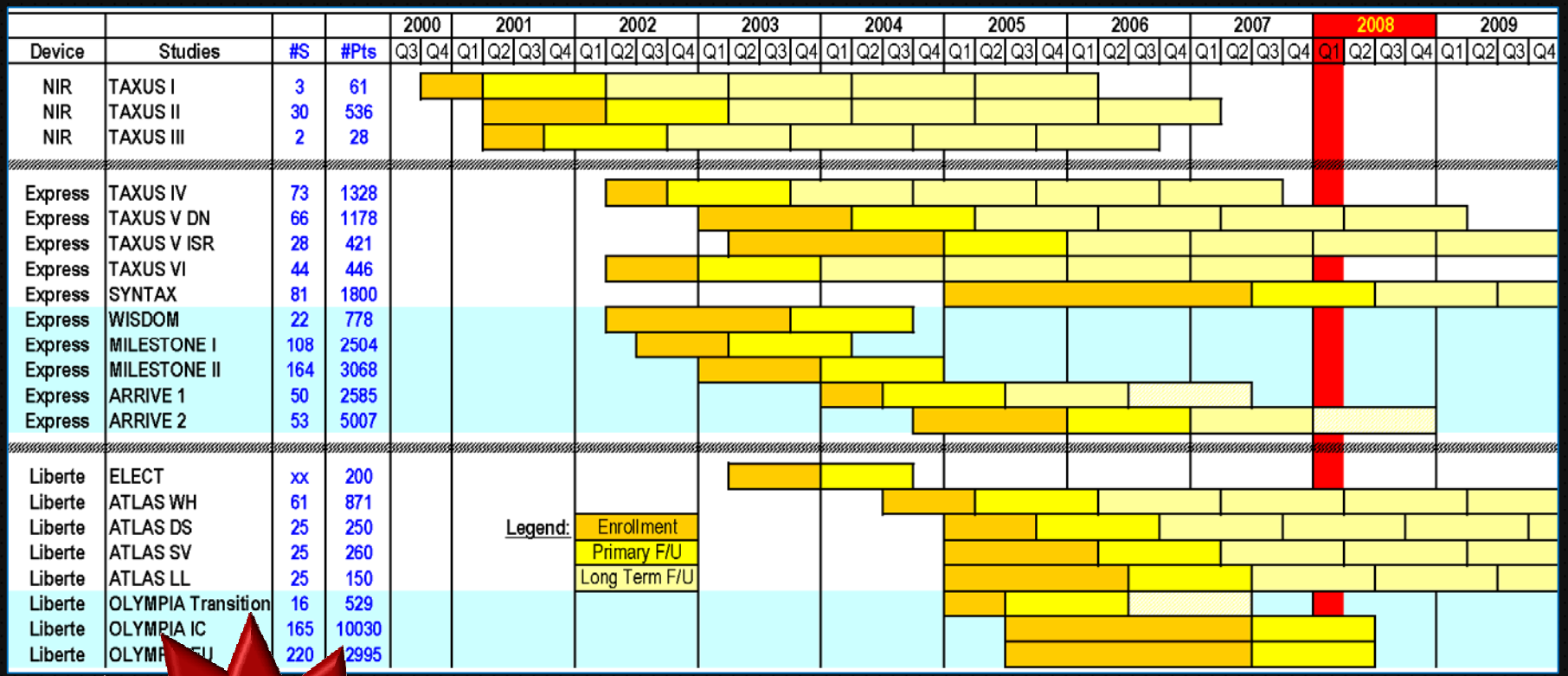


DES Penetration (USA) Source: MRG



Third consecutive month of increased DES penetration

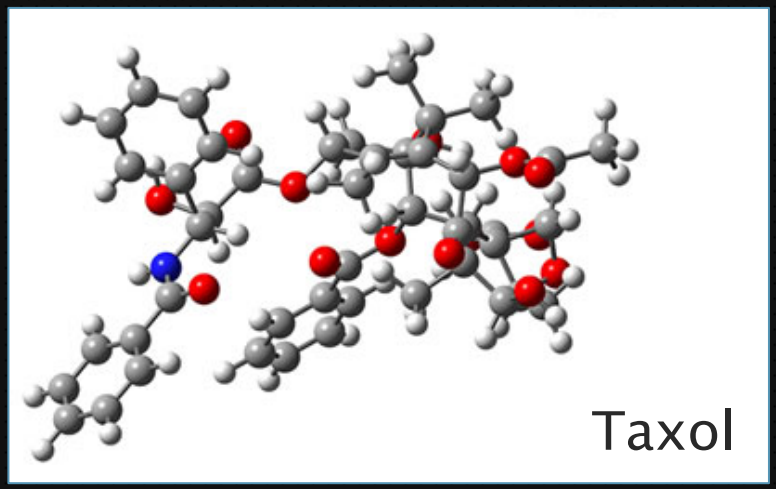
The TAXUS Program...



N=45,025

Paclitaxel

- Multi-functional activities with cell
  - Dose dependent effects
  - Anti-proliferative
  - Anti-inflammatory
  - Prevents SMC migration
  - Promotes apoptosis at low doses
  - Cytostatic within the therapeutic range

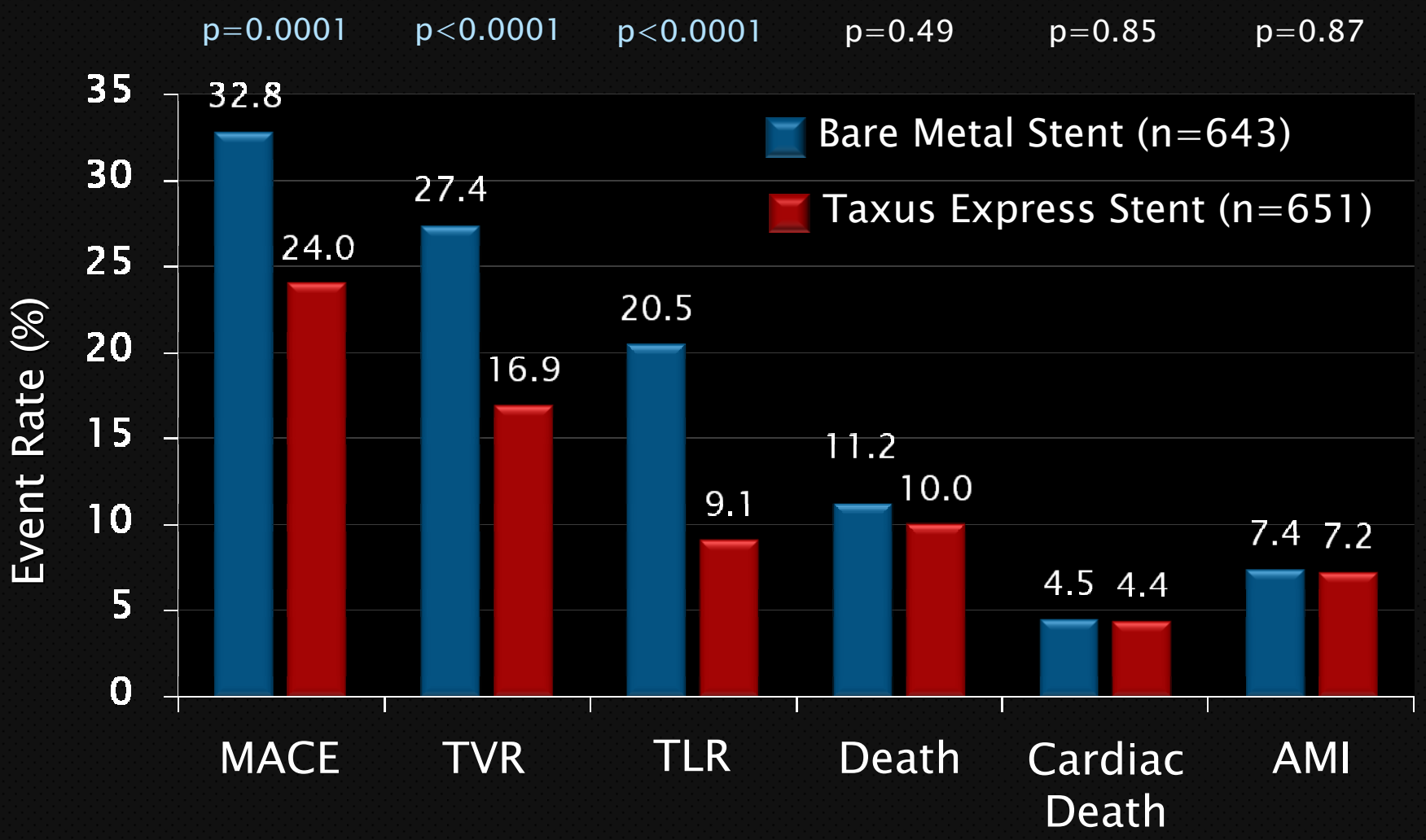


TAXUS IV: 5 Year Final Data

Study Design:	Prospective, randomized, double-blind trial
Primary Endpoint:	Ischemia-driven TLR
Follow-up:	Final 5-year outcomes
Patients Enrolled:	Taxus Express Stent = 662 Bare Metal Stent = 652
Number of Sites	73 US Sites

Ellis SG TCT 2007

TAXUS IV: 5 Year Clinical Results



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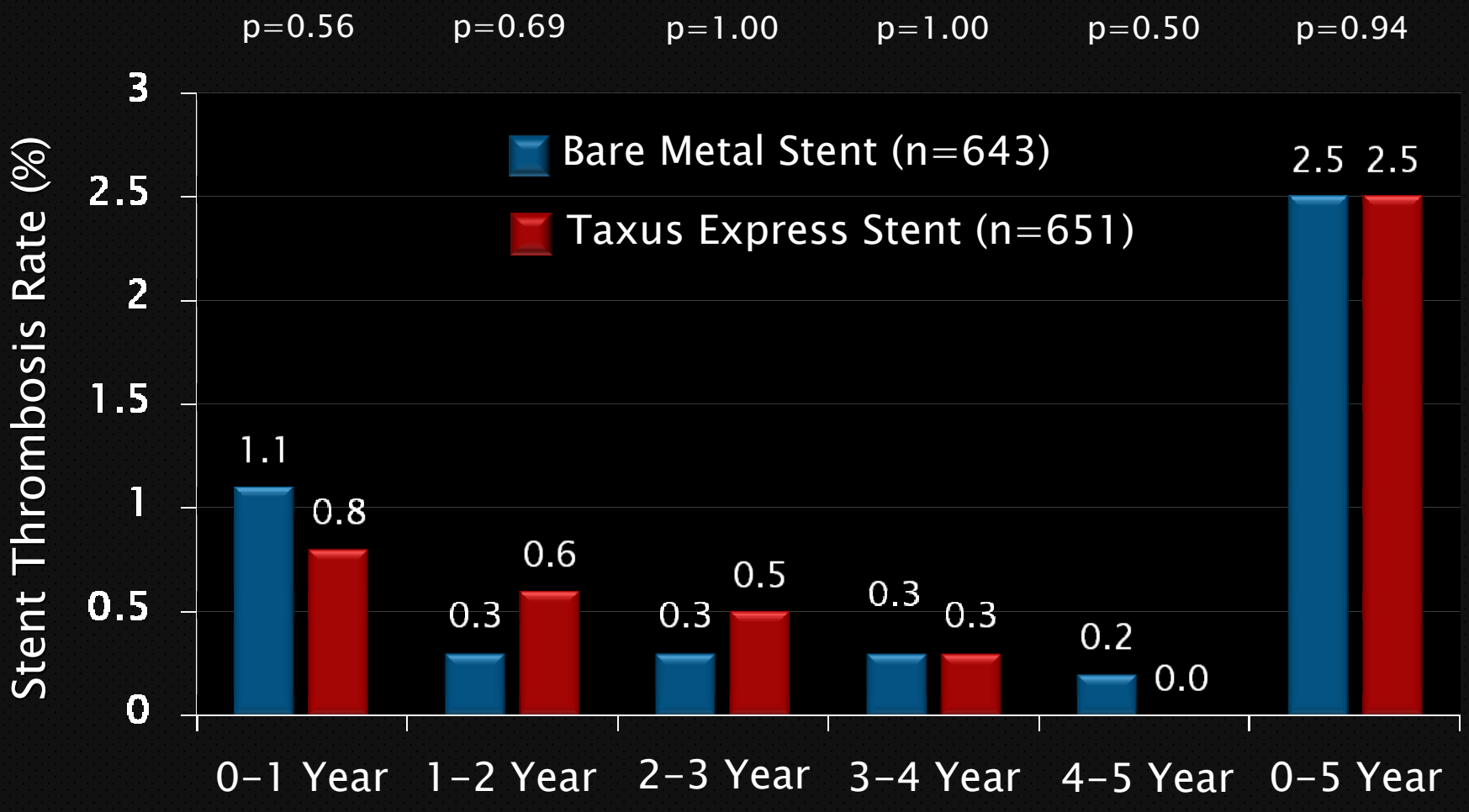
TAXUS IV: Stent Thrombosis (ARC)*



*ARC definite or probable thrombosis

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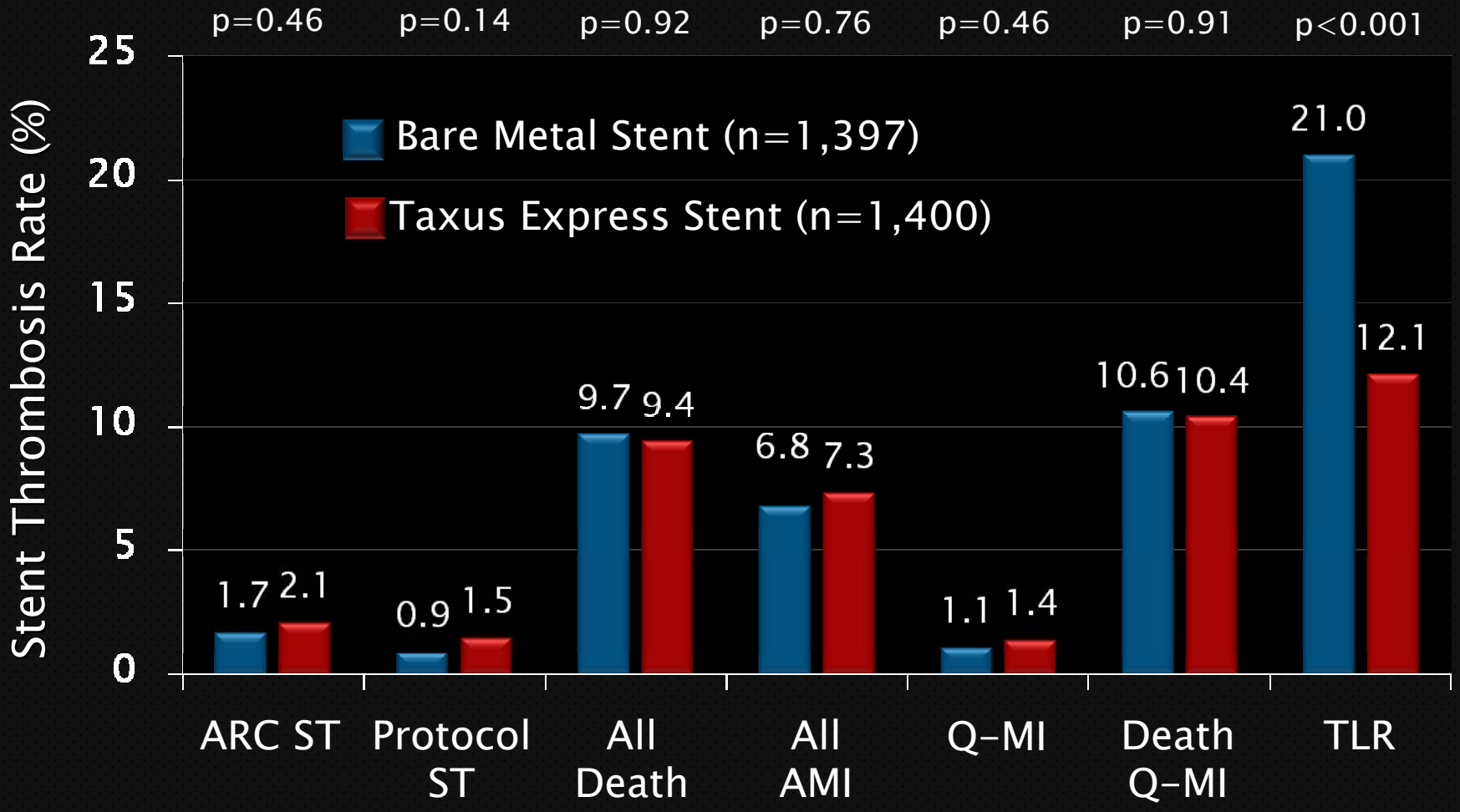
TAXUS SR Stent Patient Level Meta-analysis: 5 Year Results (TAXUS 1, II, IV, V)



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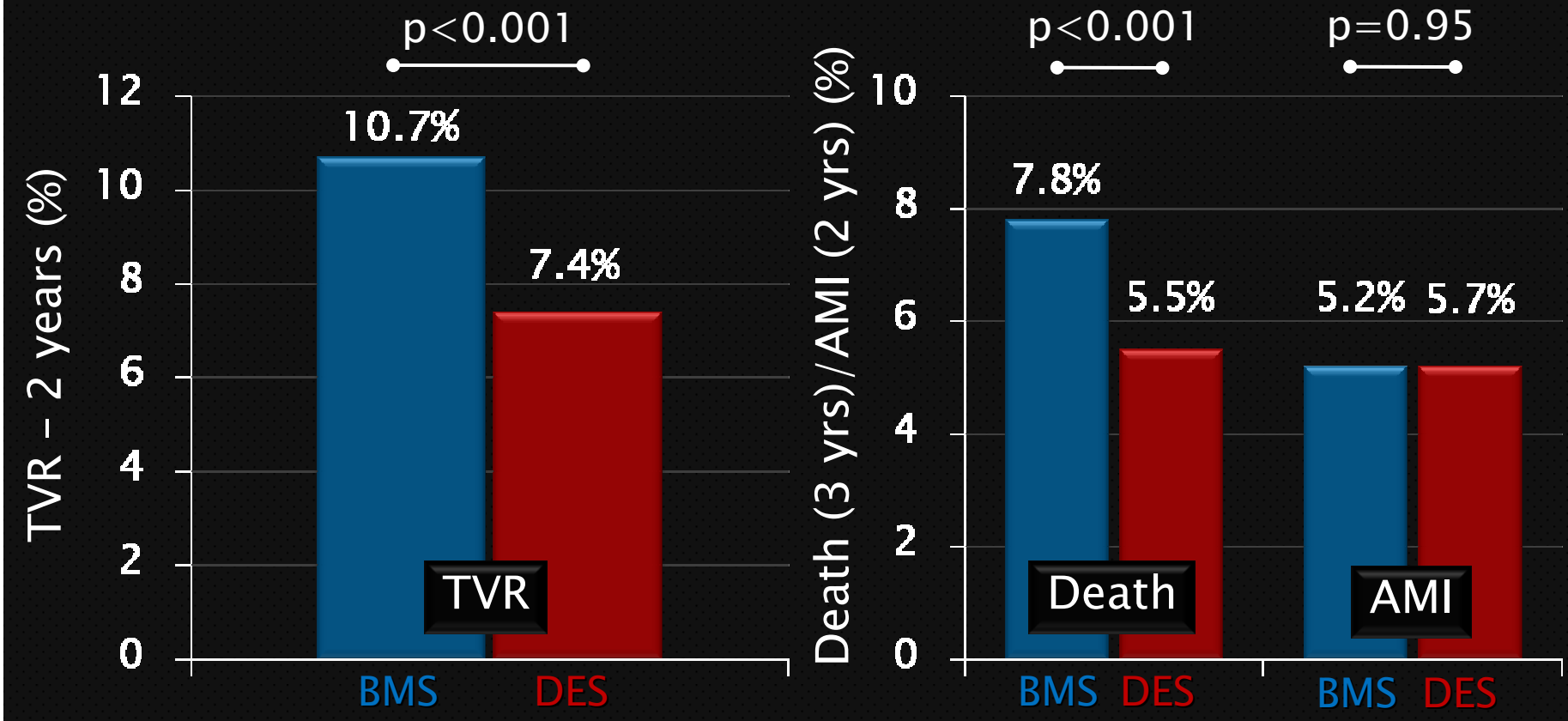
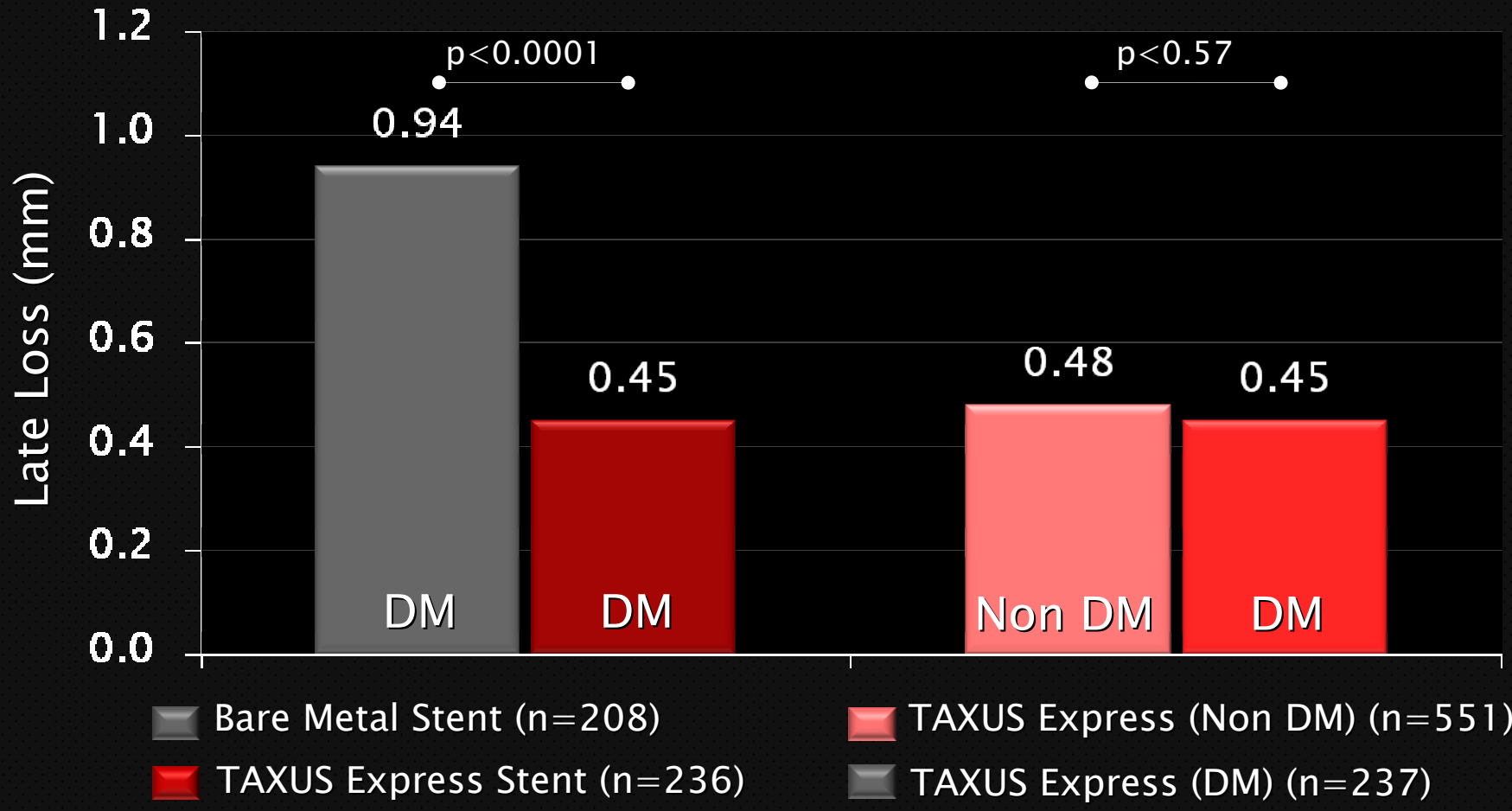
Effectiveness and Safety of Drug Eluting Stents in Ontario



TAXUS Stents 83%

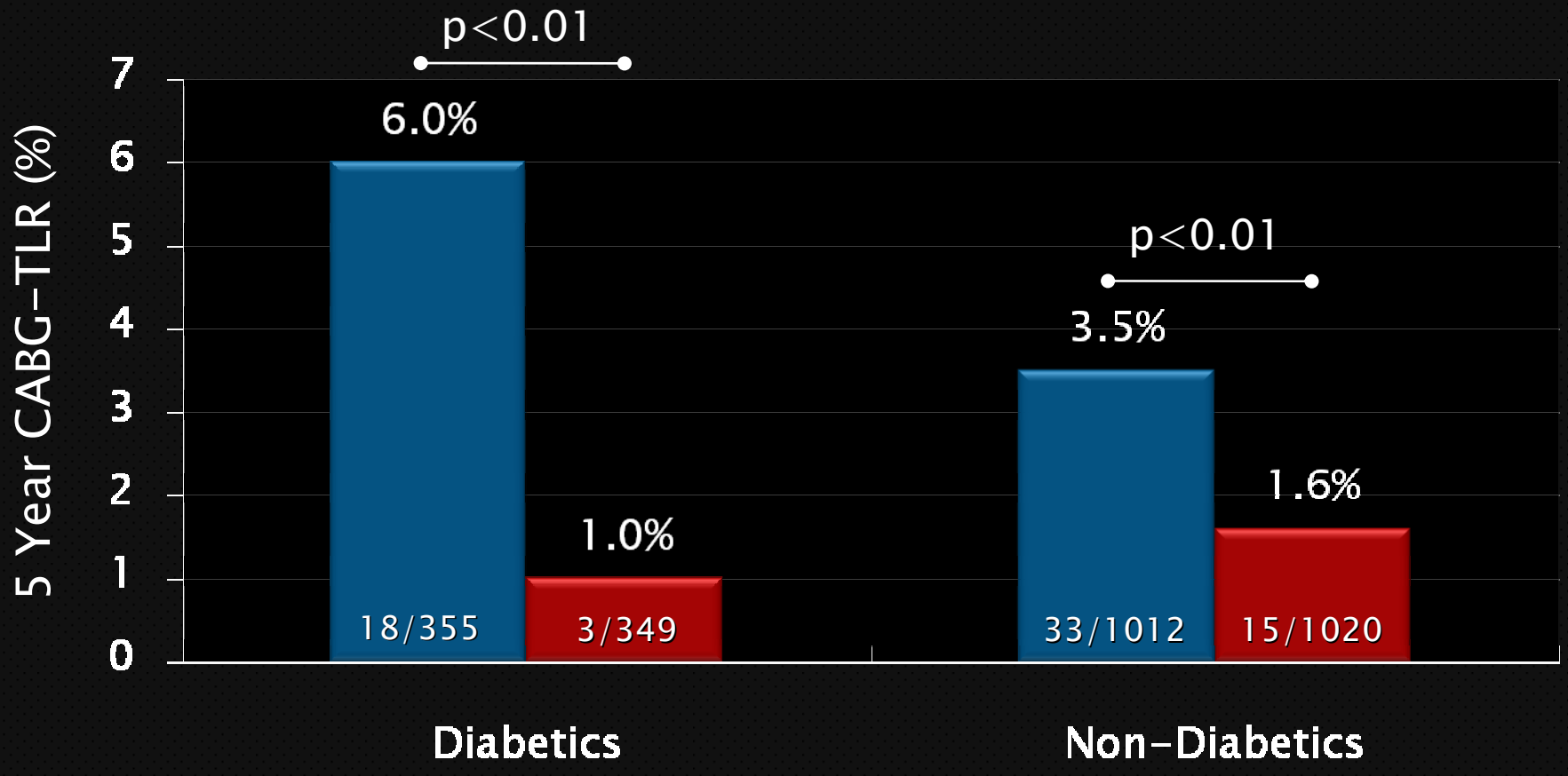
N Engl J Med 2007;357:1393-1402

TAXUS IV and V Diabetic Subset 8-Month Angiographic Results



ACC 2008

Surgical Revascularisation (CABG) in Diabetics following treatment with the Taxus SR* Stent *vs.* BMS Control (5 Years)



*TAXUS SR II, IV, V Trials (n=2,736)

TAXUS Stent Diabetic CE Mark

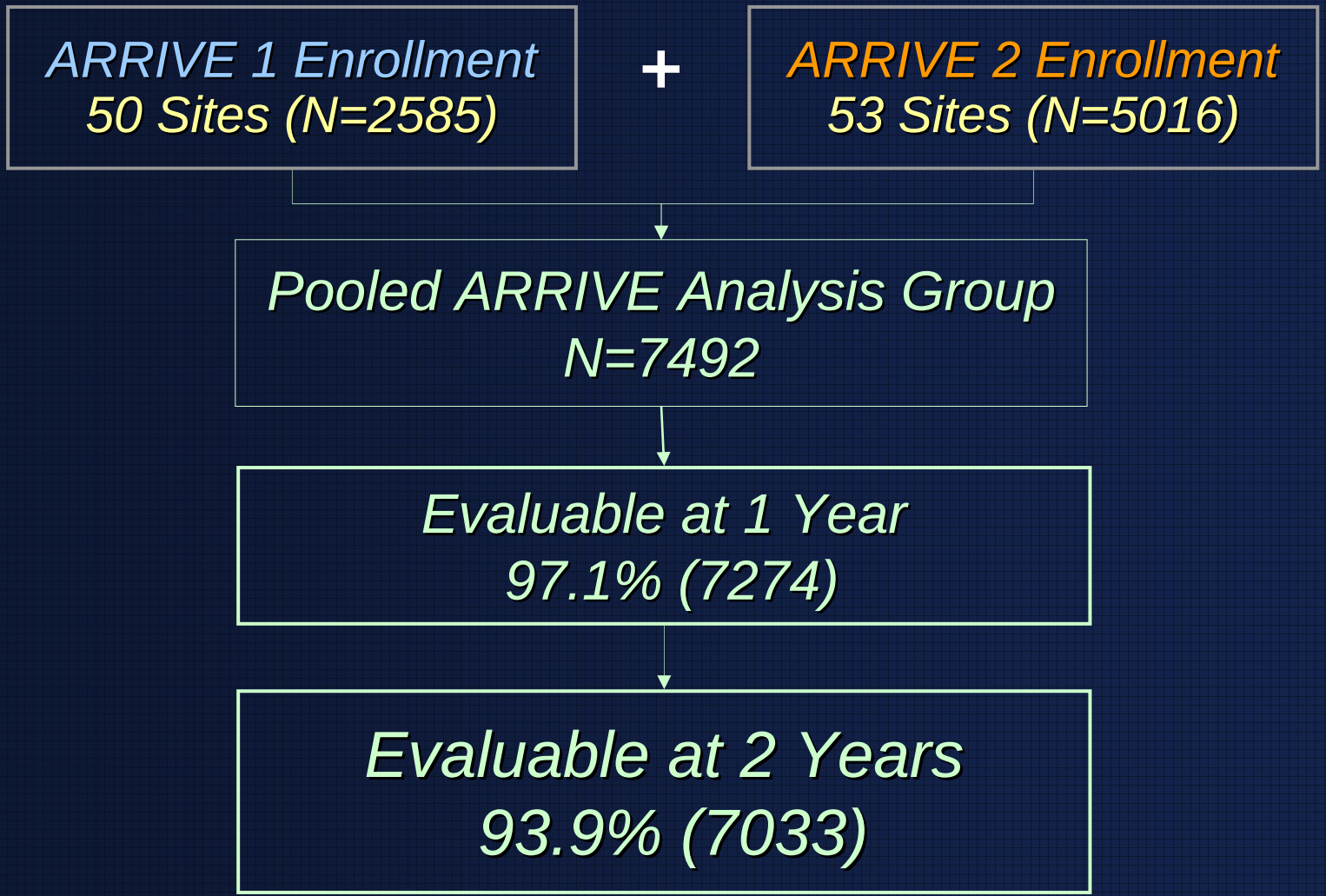
Diabetic Evidence Base

Study	TAXUS (n)	Control (n)
TAXUS IV	155	163
TAXUS V de novo	183	173
TAXUS V ISR	78	61
ATLAS WH, DS, SV, LL	413	517
ARRIVE I	756	–
ARRIVE 2	1549	–
OLYMPIA IC Transitional	264	–
Total Diabetic Patients (n)*	3398	914

**Medically treated Diabetics*

Predictors for Stent Thrombosis and Revascularization in Real-World Use of the TAXUS Express^2 Paclitaxel-eluting Stent: Insights from the 7500-Patient ARRIVE Program

Patient Flow in TAXUS ARRIVE
Pooled evaluable patients at 2 years = 93.9%



Baseline/Procedural Characteristics
7492 pts; 10,668 lesions; 8795 vessels; 11,885 stents

Pooled ARRIVE

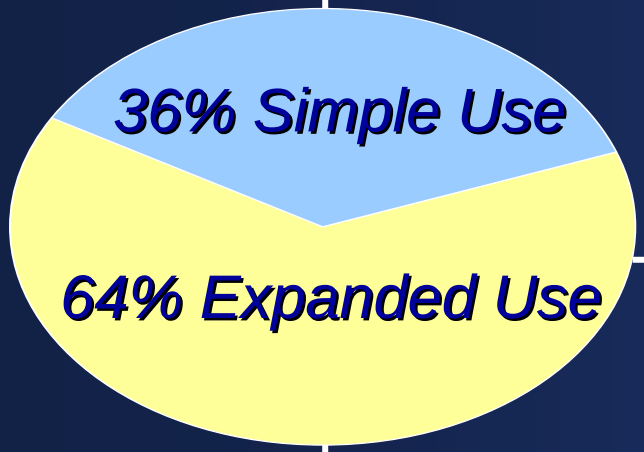
Patient		Lesion/Procedure	
Male	67.3%	Lesion RVD (mm)*	3.0±0.4
Age (yr)*	64.2±11.7	Lesion length (mm)*	15.6±9.2
Diabetes	31.6%	Stent length per pt*	29.5±19.2
Insulin	10.2%	Type B2/C (per lesion)	50.3%
Multivessel Dis.	36.9%	>1 Lesion treated	32.0%
Prior MI	36.3%	>1 Vessel treated	16.1%
Prior PCI	36.8%	Left main (per lesion)	1.6%
Prior CABG	20.1%	Graft (per lesion)	5.4%

*mean±SD; angiographic variables are site visual estimates; CABG=coronary artery bypass surgery; MI=myocardial infarction; PCI-percutaneous coronary intervention; RVD=reference vessel diameter

Analyzed Patient Distribution (N=7492)
Complex patients/lesions predominate in ARRIVE

Single Vessel, Single Stent

- With or without diabetes



*Complex Patients**

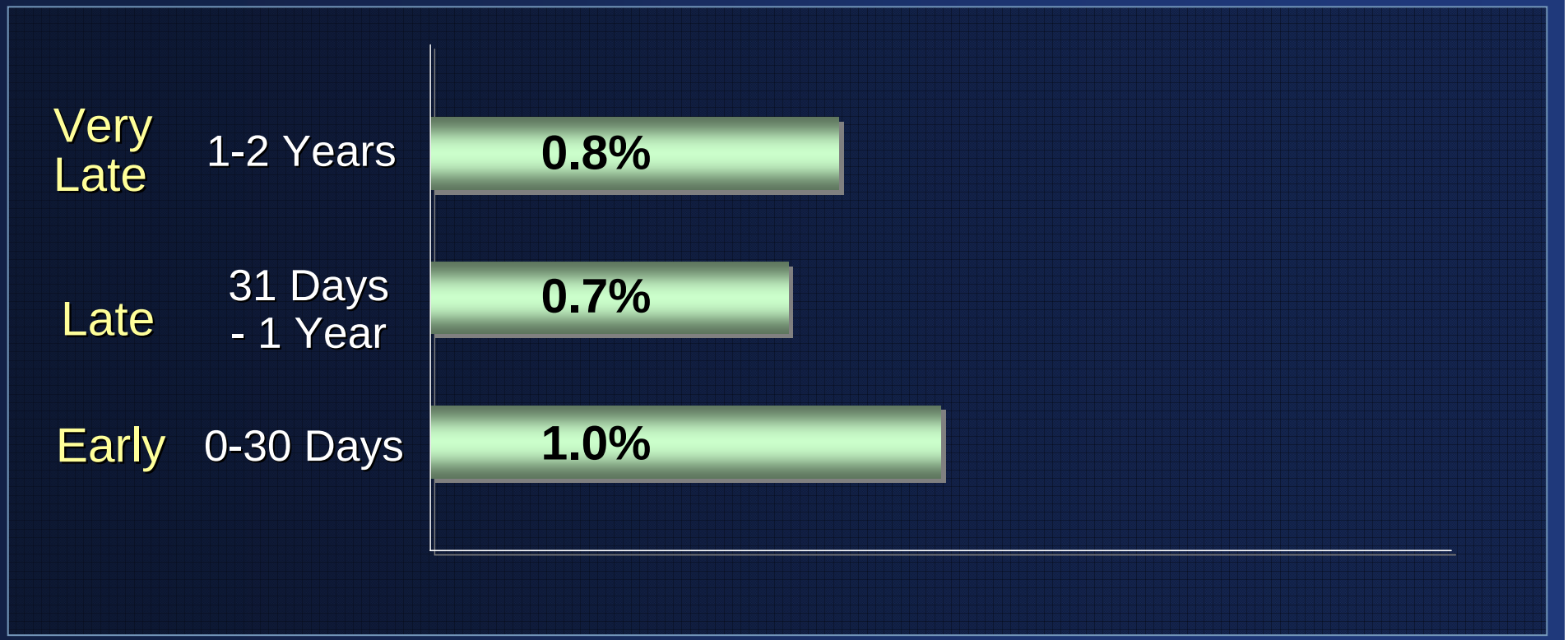
- Acute MI (12.7%)
- Congestive heart (6.8%)
- Left main disease (4.8%)
- Renal dysfunction (2.5%)
- Cardiogenic shock (0.4%)

*Patients with Complex Lesions**

- Calcification (mod./severe) (18.1%)
- Multivessel stenting (15.7%)
- Long lesion (>28mm) (10.0%)
- Ostial lesion (8.5%)
- Bifurcated lesion (7.7%)
- In-stent restenosis (6.5%)
- Graft stenting (6.3%)
- Severe tortuosity (3.4%)
- Small vessel (RVD<2.5mm) (3.4%)
- Chronic total occlusion (2.1%)
- Left main stenting (2.2%)
- Failed brachytherapy (0.4%)

* A patient may belong to >1 of the expanded-use groups

ARC Stent Thrombosis in ARRIVE
Rates aligned with population risks



Definite ST: • Angiographically confirmed*

Probable ST: • Unexplained death ≤30 days; MI related to documented acute ischemia in area of implanted stent without any other obvious cause*

* Cutlip, et al. *Circulation* 2007;115:2344

Multivariate Predictors of ARC ST in ARRIVE
Strongest Year 1 predictor = Limited clopidogrel use

N=7492 patients	*0–1 year (n=128 ST)*	*1–2 years (n=56 ST)*	*0–2 year (n=184 ST)*
Predictor	*Hazard Ratio (P value)*		
Thienopyridine ≤6 Mon	3.95 (<0.0001)	NS	3.01 (<0.0001)
Multiple Stents	1.94 (0.0017)	2.37 (0.0016)	1.86 (0.0002)
Lesion Length >28 mm	1.77 (0.0113)	NS	1.60 (0.0130)
Calcification (Mod./Severe)	1.58 (0.0200)	NS	NS
Failed Brachytherapy	NS	9.42 (0.0019)	NS
Smoking at Baseline	2.61 (<0.0001)	1.79 (0.0404)	2.23 (<0.0001)
Congestive Heart Failure	2.23 (0.0006)	NS	2.06 (0.0010)
Diabetes-Insulin	2.02 (0.0022)	NS	1.66 (0.0115)
Renal Disease	NS	3.86 (0.0098)	NS
Prior Myocardial Infarction	NS	2.51 (0.0007)	1.61 (0.0014)
Expanded- vs. Simple-use	NS	NS	1.57 (0.0258)

→ *Factors differ in yr 2; thienopyridines no longer predictive*

Multivariate Predictors of TLR in ARRIVE
Lesion-based predictors predominate

N=7492 patients	*0–1 year (n=373 TLR)*	*1–2 years (n=171 TLR)*	*0–2 year (n=544 TLR)*
Predictor	*Hazard Ratio (P value)*		
ISR Stenting	1.75 (0.0007)	NS	1.54 (0.0028)
Bifurcation Lesion	1.61 (0.0018)	NS	1.40 (0.0130)
Lesion Length >28 mm	1.59 (0.0012)	1.53 (0.0468)	1.67 (<0.0001)
Multiple Stents	1.55 (0.0001)	1.58 (0.0172)	1.59 (<0.0001)
Target Vessel LAD	1.54 (0.0001)	NS	1.39 (0.0002)
Calcification (Mod./Severe)	1.30 (0.0319)	NS	NS
CTO Stenting	NS	2.63 (0.0023)	NS
Multivessel Stenting	NS	1.50 (0.0172)	NS
RVD ≤ 2.5 mm	NS	NS	1.25 (0.0145)
Male Gender	0.68 (0.0003)	NS	0.76 (0.0020)
Age ≥ 75 years	0.52 (<0.0001)	0.64 (0.0368)	0.55 (<0.0001)
Previous CABG	1.37 (0.0158)	NS	1.34 (0.0058)
Previous PCI	NS	1.81 (0.0001)	1.27 (0.0099)

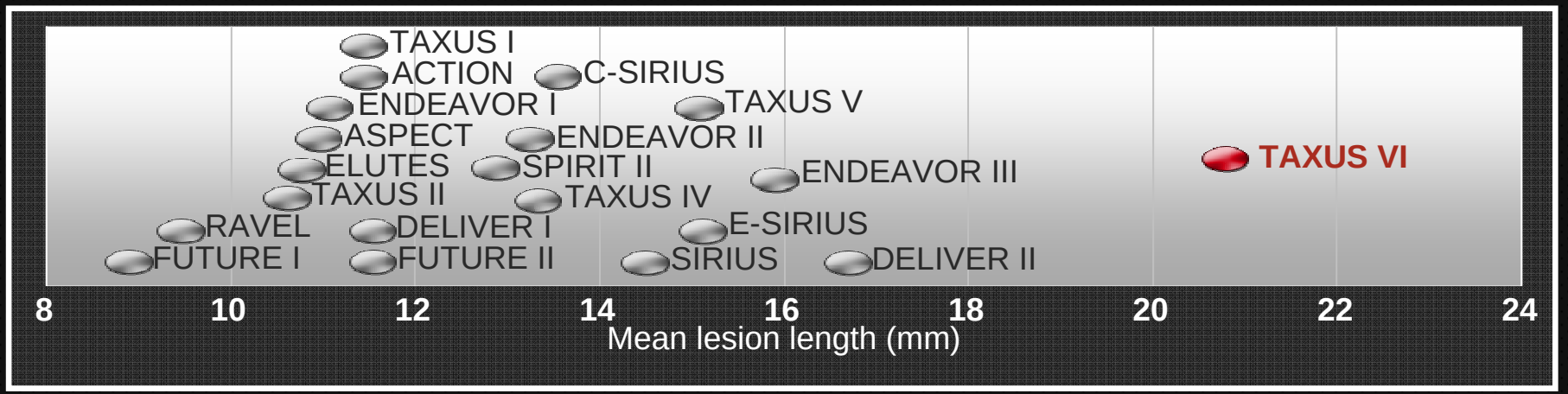
Summary & Conclusions
Insights on ST & TLR predictors from TAXUS ARRIVE

- This large (~7500 patient) real-world population identifies several predictors of definite/probable ST
  - Discontinuation of clopidogrel before 6 months is a significant predictor of ST in yr 1, and at 2 years (3-4 fold increased risk), but not in yr 2
  - Predictors of ST changed between 0-1 year (mostly lesion-based) and 1-2 years (more biologic)
  - Smoking at baseline and congestive heart failure double the risk
  - Expanded-use patients have 50-80% greater risk
- Lesion-based predictors predominate for TLR (yr 1 and yr 2)
  - Complex lesion characteristics increased TLR risk through 2 years by 25-65% per factor
  - Older age and male gender appear protective through 2 years
- Determination of DES baseline predictors may help identify patients at highest risk for ST and TLR

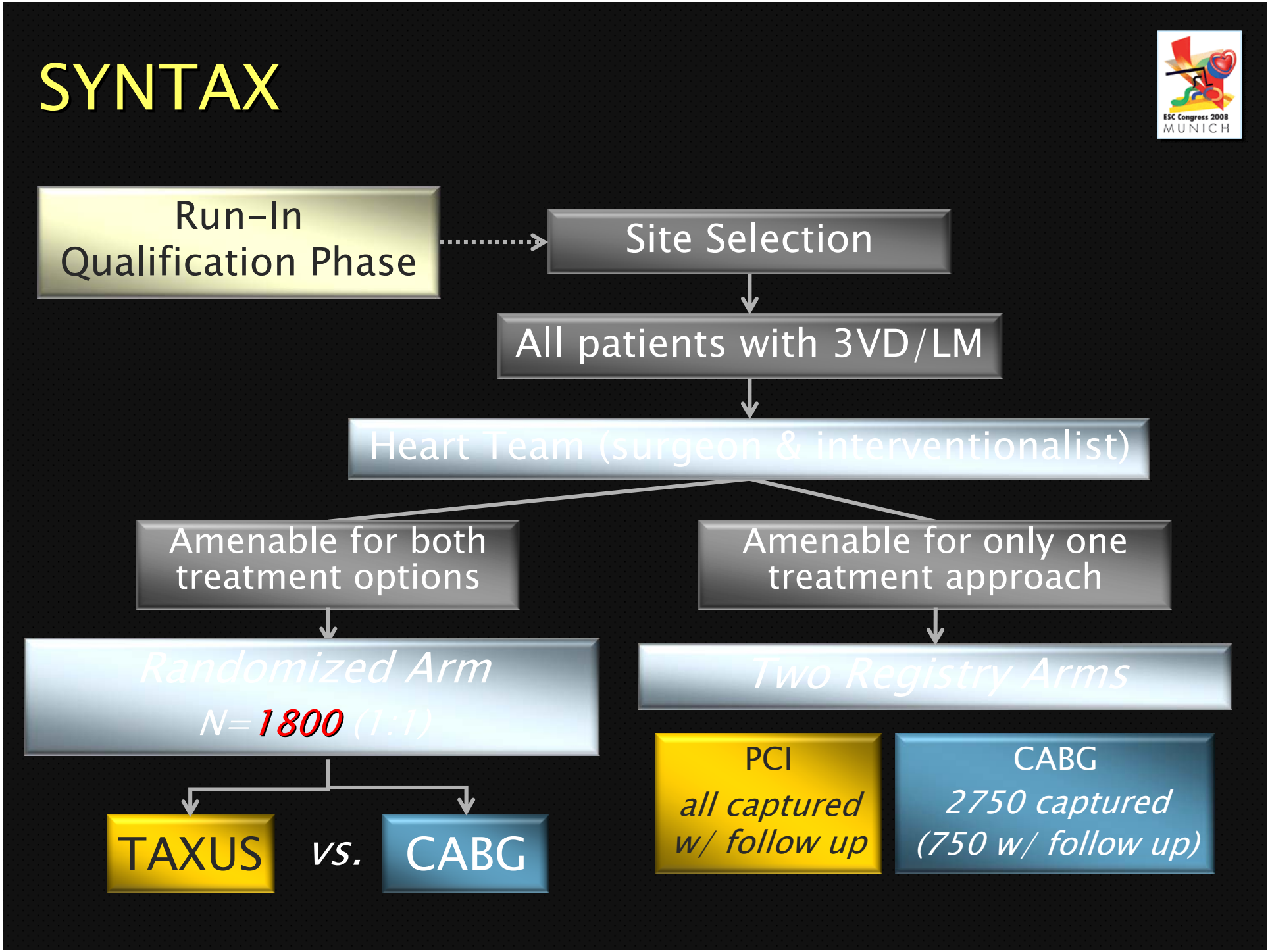
TAXUS VI

Long-term Outcomes in Complex Patients Treated with the TAXUS Express² Moderate Release (MR) Stent

Final 5-Year Results



SYNTAX

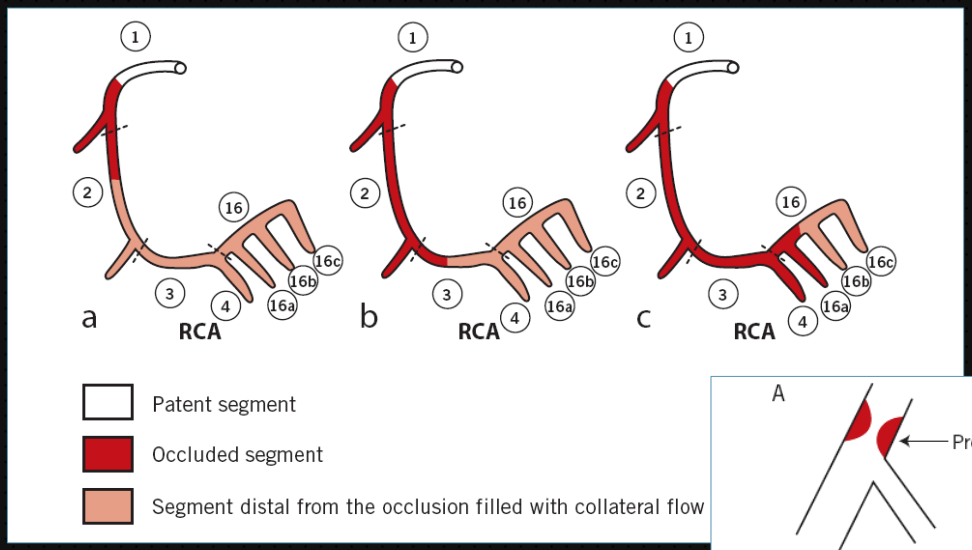

Run-In
Qualification Phase
Site Selection
All patients with 3VD/LM
Heart Team (surgeon & interventionalist)
Amenable for both treatment options
Amenable for only one treatment approach
Randomized Arm
N=1800 (1:1)
Two Registry Arms
TAXUS
vs.
CABG
PCI
all captured w/ follow up
CABG
2750 captured
(750 w/ follow up)

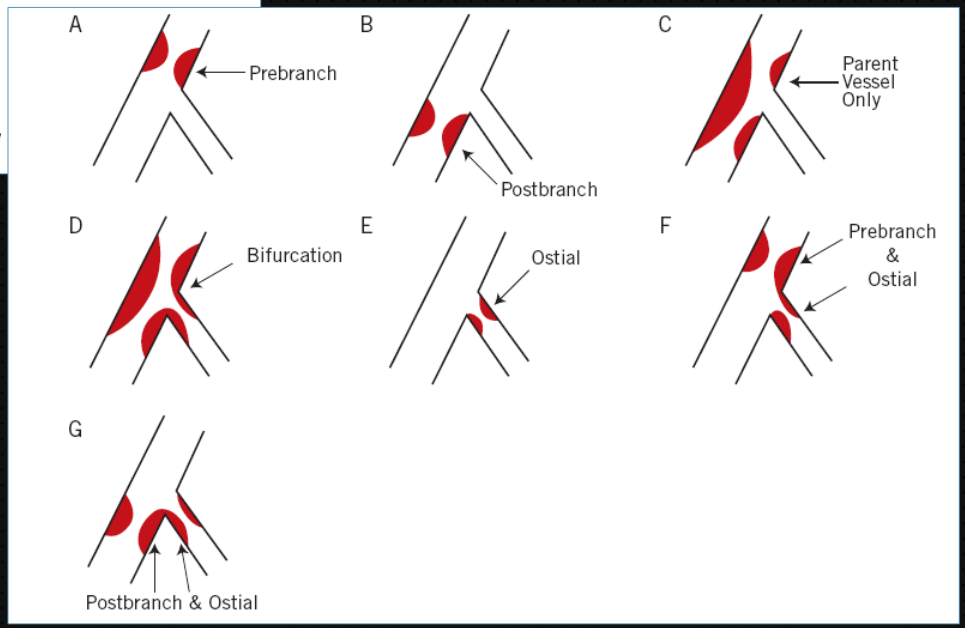
SYNTAX

Primary Endpoint: *Randomized trial*

- The primary clinical endpoint is the 12-Month binary MACCE rate. MACCE is defined as:
  - All cause Death
  - Cerebrovascular Event (Stroke)
  - Documented Myocardial Infarction
  - Repeat Revascularization (PCI and/or CABG)
- The primary endpoint (12-month MACCE) will be analyzed for all patients as well as the subgroups of patients with 3VD only and patients with LM disease.

SYNTAX Score



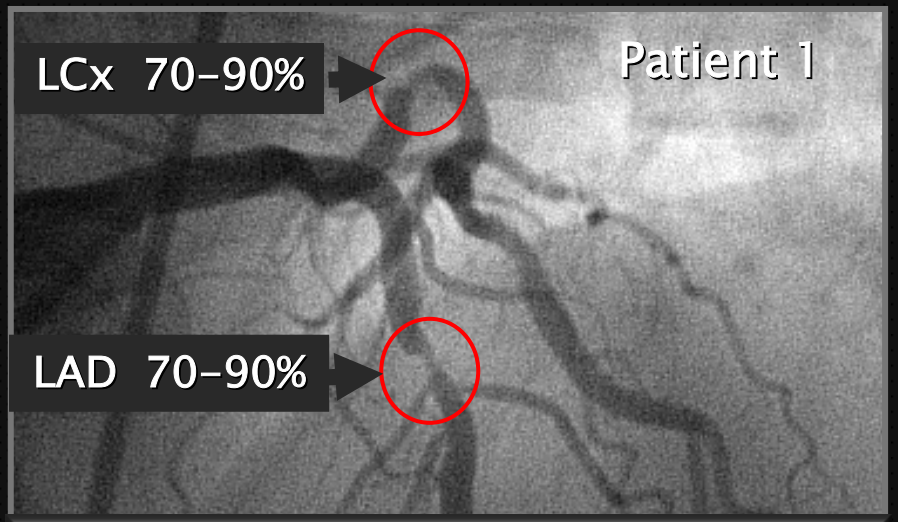


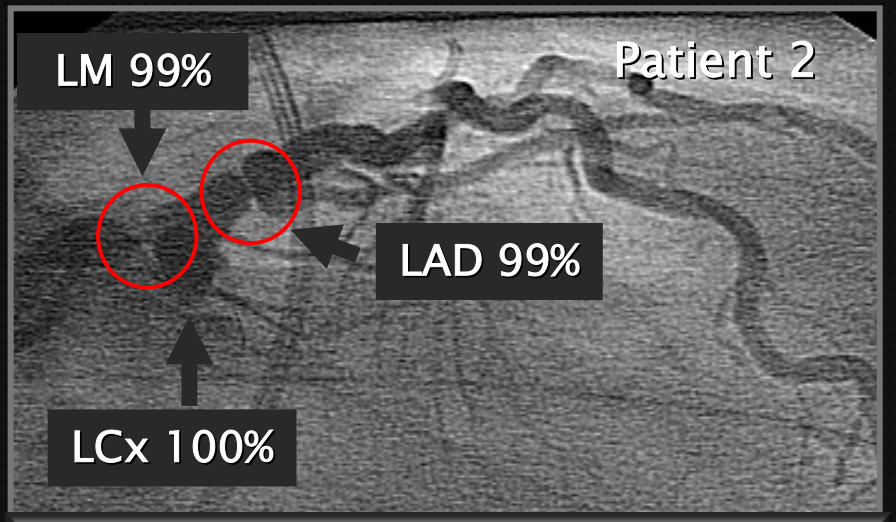
- Occlusion
- Ostial location
- Tortuosity
- Length >20mm
- Heavy calcification
- Thrombus
- Diffuse disease

Raw SYNTAX Score → *MACE (1 yr)* → *Weighted SYNTAX Score*

EuroInterv 2005;1:219-227

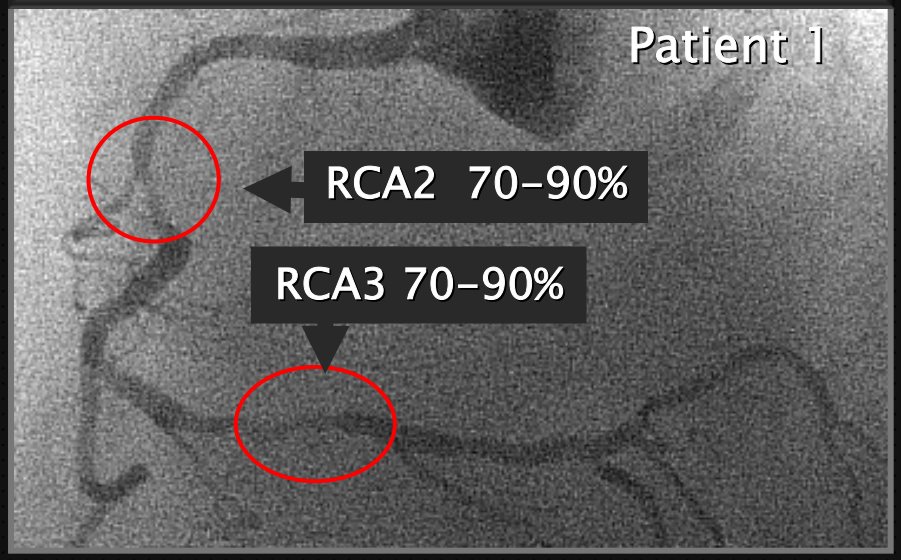
There is '3-vessel disease' and '3-vessel disease'

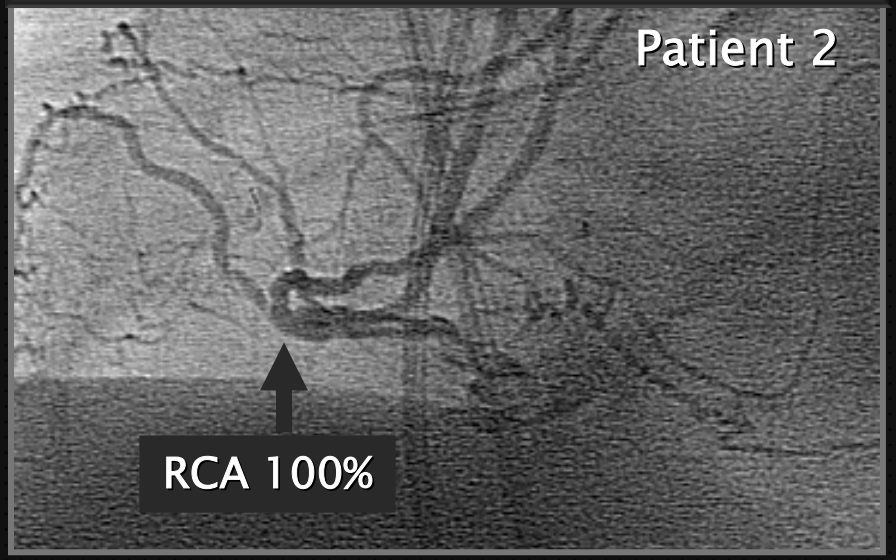




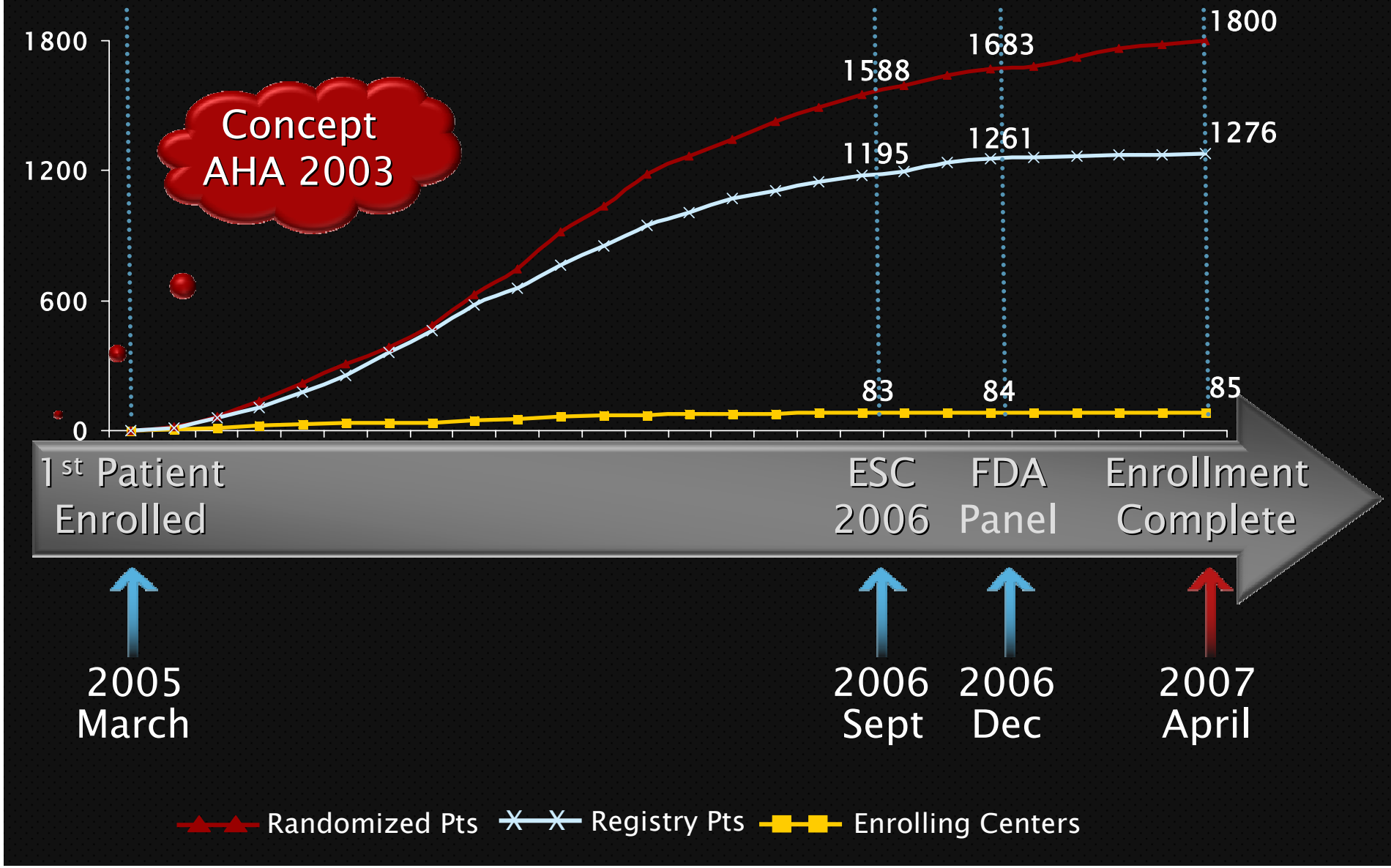
SYNTAX SCORE 21

SYNTAX SCORE 52





SYNTAX Enrolment



Final Enrollment Data

Enrollment Completed April 2007

Sites

N=62

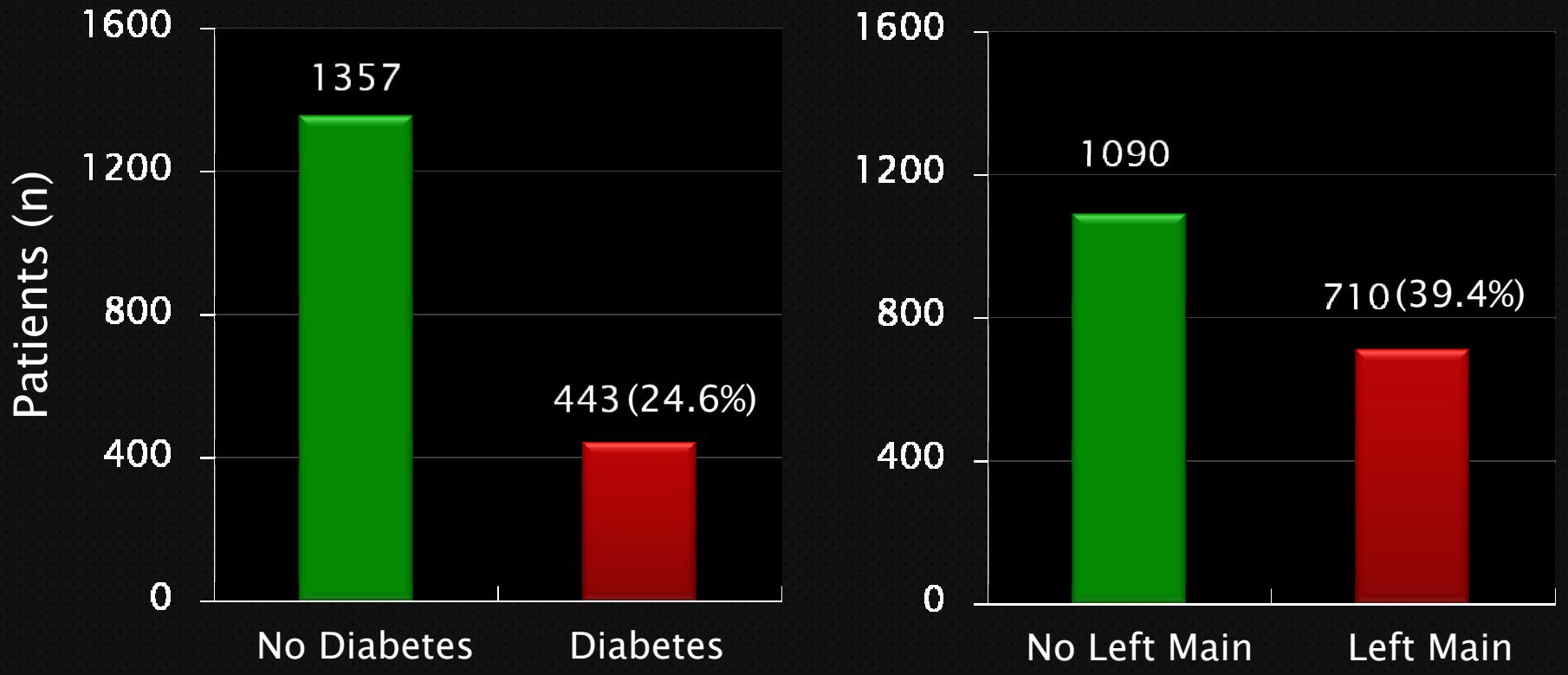
N=23

Total Enrolment N=3076

- PCI N=198
- Randomized N=1800
- CABG N=1078

SYNTAX

Randomized Enrollment Status: Left Main & Diabetes



Lesion and Patient Complexity

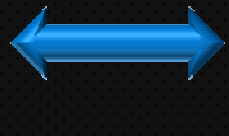
Randomized vs. Registry Cohorts

		Randomized N=1800	CABG Registry N=649	PCI Registry N=198
Patient	3 Vessel Disease (%)	60.6%	54.5%	65.2%
	LM (%)	39.4%	45.5%	34.8%
	Diabetics (%)	24.6%	29.4%	35.5%
PCI	Bifurcation (% pts)*	62.7%	–	58.6%
	Total Occlusion (% pts)	27.2%	–	39.6%
	Total stent length >100mm (% pts)	34.2%	–	11.2%
	Number of stents (per pt)	4.7	–	3.1
CABG	Arterial grafts (%)	94.9%	91.5%	–
	Complete arterial revascularization (%)	18.6%	12.5%	–
	Double IMA grafts (%)	26.7%	16.0%	–
	Conduits used to LAD (%)	94.8%	93.0%	–

Data are site reported *Based on baseline SYNTAX score

PCI

1, 2 Vessel Disease
Discrete 3VD
Ostial Left Main
Graft Disease
ACS
Stroke History
Pulmonary Disease
Renal Impairment
Premature CAD



CABG

Diffuse Disease
Distal Left Main
Previous PCI
Poor LV Function
± Valve Surgery
± Arrhythmia Surgery

HORIZONS AMI

TCT 2008
TRANSCATHETER CARDIOVASCULAR THERAPEUTICS

≥3400* pts with STEMI with symptom onset ≤12 hours

Aspirin, thienopyridine

R 1:1

- UFH + GP IIb/IIIa inhibitor (abciximab or eptifibatide)
- Bivalirudin monotherapy (± provisional GP IIb/IIIa)

Emergent angiography, followed by triage to…

CABG – Primary PCI – Medical Rx

3000 pts eligible for stent randomization

R 1:3

- Bare metal stent
- TAXUS Paclitaxel-eluting stent

Clinical FU at 30 days, 6 months, 1 year, and then yearly through 5 years

*To rand 3000 stent pts

Conclusions:

- The TAXUS program provides an unparalleled dataset in the DES field
- TAXUS safety and efficacy is beyond doubt
- Expanded use confirms the utility of the TAXUS stent
- Later this year results of TAXUS VI, SYNTAX and HORIZONS will become available