EXCEL

Abbott Vascular

PROTOCOL 10-389
EXCEL Clinical Trial

Evaluation of XIENCE PRIME™ or XIENCE V® versus Coronary Artery Bypass Surgery for Effectiveness of Left Main Revascularization

Abbott
A Promise for Life

PCI (1st gen DES) vs. CABG for Left Main Ds. Meta-analysis of 4 RCTs, 1,611 Patients

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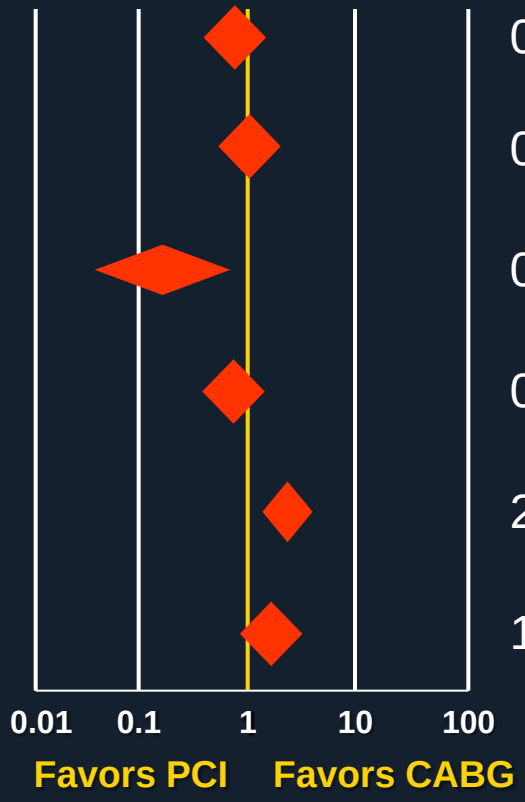
Trial	LEMANS	SYNTAX LM	Boudriot et al.	PRECOMBAT
Year	2008	2009	2010	2011
N total	105	705	201	600
Age, mean years	61	65	68	62
Male	67%	74%	75%	77%
Diabetes	18%	25%	36%	32%
Distal LM involved	58%	61%	71%	65%
+0/1/2/3 VD, %	0/9/23/68	13/20/31/36	29/31/27/14	10/17/32/41
Syntax Score, mean	25	30	24	25
Log Euroscore, mean	3.4	3.9	2.5	2.7
LIMA-LAD	81%	97%	99%	94%

Capodanno D et al. JACC 2011;58:1426-32

PCI (1st gen DES) vs. CABG for Left Main Ds.
Meta-analysis of 4 RCTs, 1,611 Patients

1-Year Outcomes

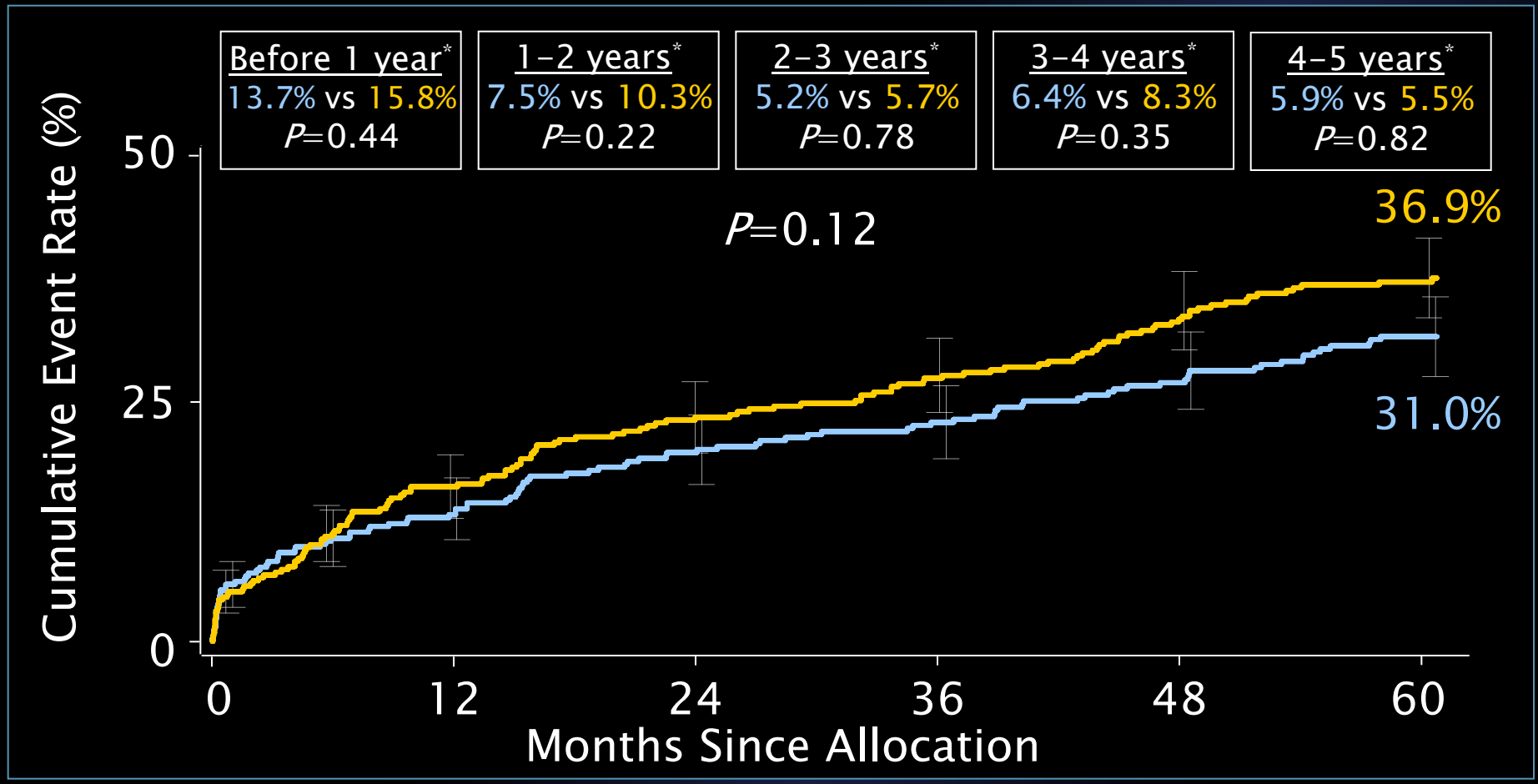
	PCI	CABG	OR (95%CI)	*p*-Value
Death	3.0% (24/807)	4.1% (32/790)	0.74 (0.43-1.28)	0.29
MI	2.8% (23/807)	2.9% (23/790)	0.98 (0.54-1.78)	0.95
Stroke	0.1% (1/707)	1.7% (12/689)	0.15 (0.03-0.67)	0.01
Death, MI, or stroke	5.3% (35/655)	6.8% (43/636)	0.77 (0.48-1.22)	0.26
Repeat Revasc	11.4% (92/807)	5.4% (43/790)	2.25 (1.54-3.28)	<0.001
MACCE	14.5% (117/807)	11.8% (93/790)	1.28 (0.95-1.72)	0.11



MACCE to 5 Years
Left Main Subset

SYNTAX

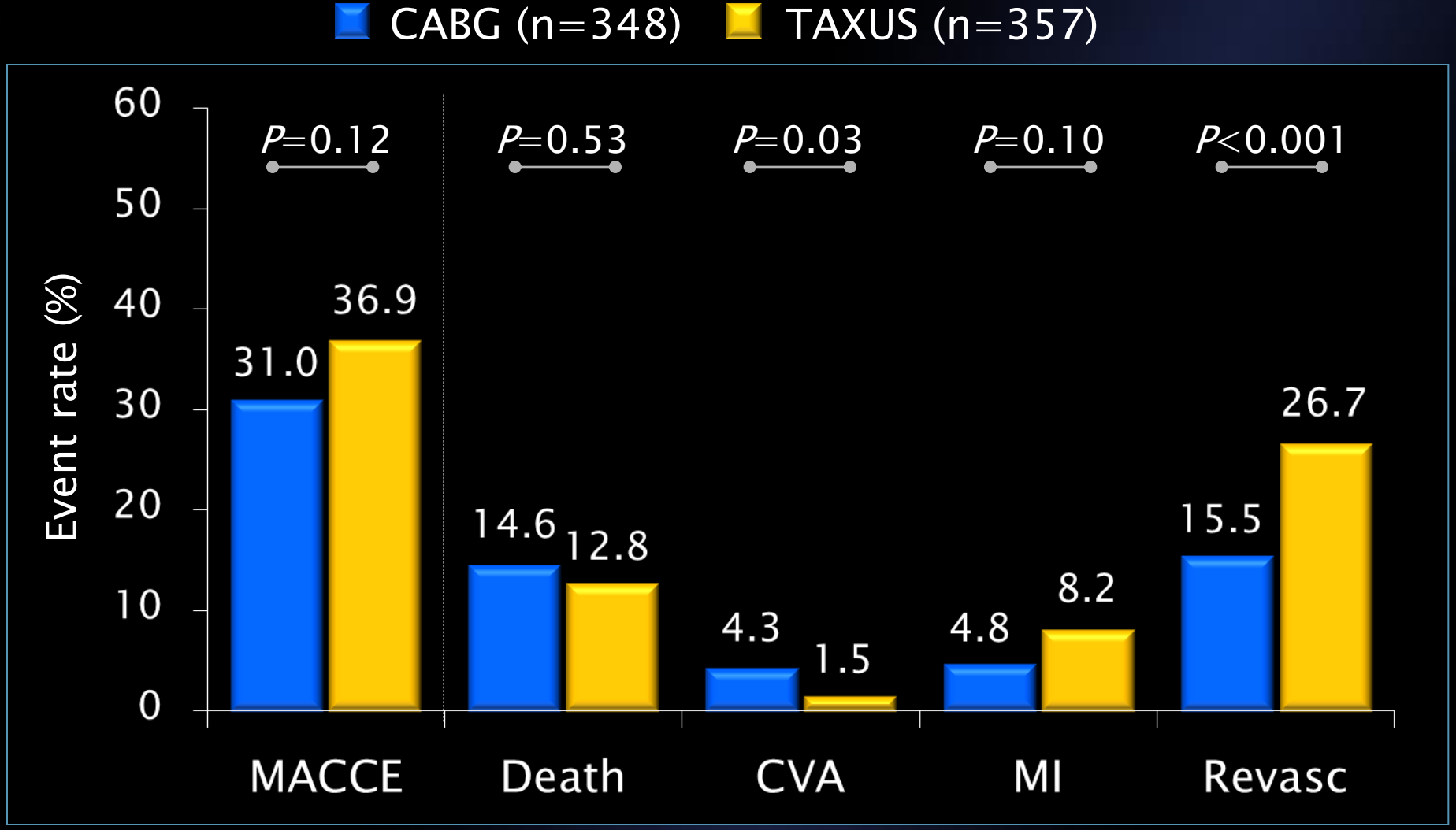
CABG (N=348) TAXUS (N=357)



Cumulative KM Event Rate ± 1.5 SE
log-rank *P* value; *Binary rates

Serruys PW et al. Lancet 2013;381:629–38

MACCE to 5 Years
Left Main Subset

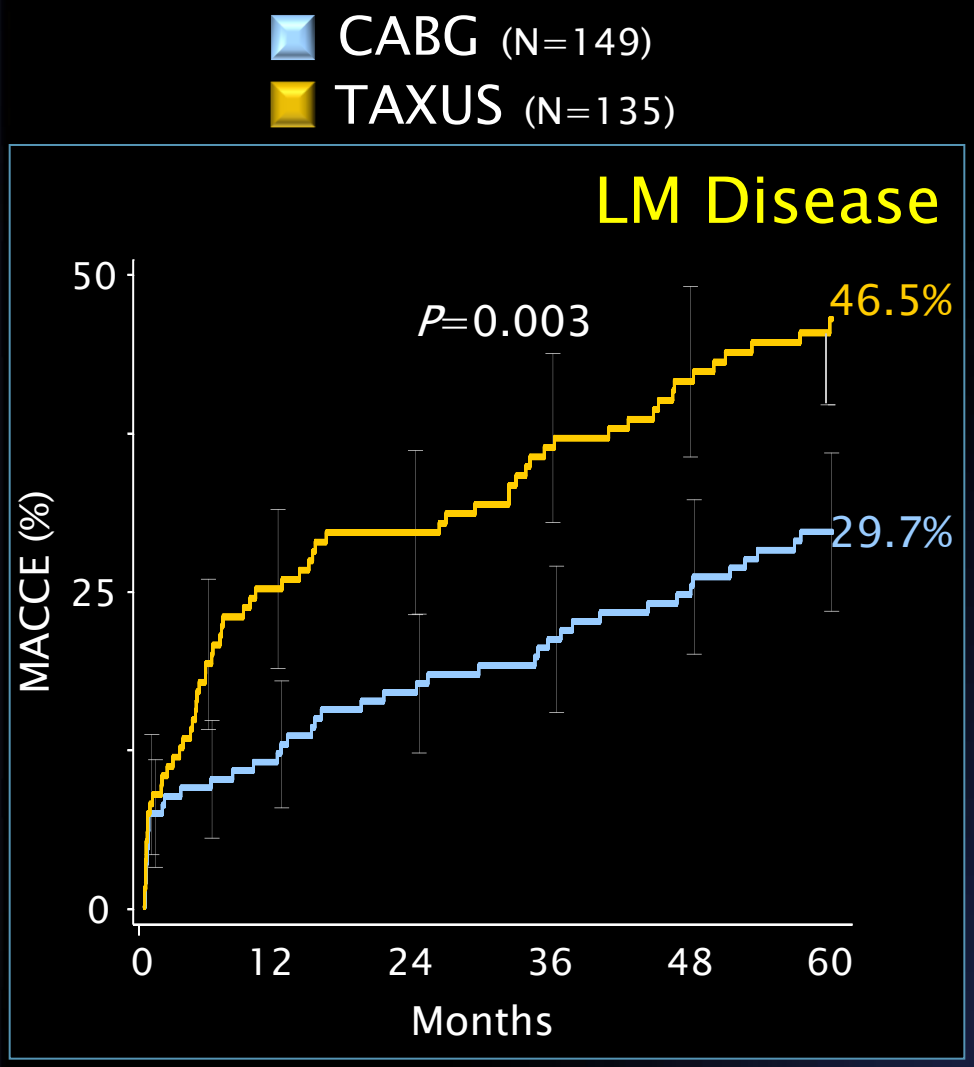


Cumulative KM Event Rate
Log-rank *P* value

Serruys PW et al. Lancet 2013;381:629-38

MACCE to 5 Years by SYNTAX Score Tercile

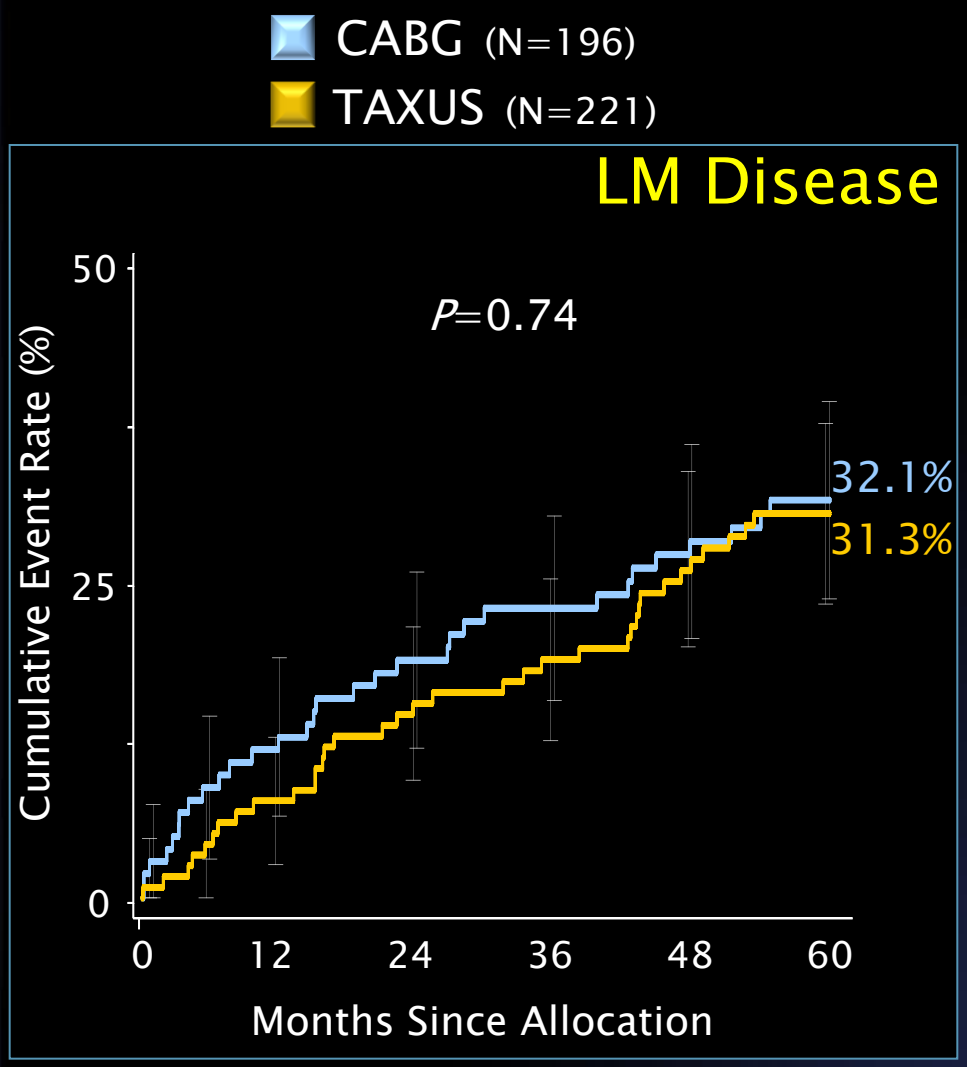
LM Subset High Scores ≥33



	CABG	PCI	*P* value
Death	14.1%	20.9%	0.11
CVA	4.9%	1.6%	0.13
MI	6.1%	11.7%	0.13
Death, CVA or MI	22.1%	26.1%	0.40
Revasc.	11.6%	34.1%	<0.001

Serruys PW et al. Lancet 2013;381:629–38

MACCE to 5 Years by SYNTAX Score Tercile *Low to Intermediate Scores (0–32)*



	CABG	PCI	*P* value
Death	15.1%	7.9%	**0.02**
CVA	3.9%	1.4%	0.11
MI	3.8%	6.1%	0.33
Death, CVA or MI	19.8%	14.8%	0.16
Revasc.	18.6%	22.6%	0.36

Serruys PW et al. Lancet 2013;381:629–38

ACC/AHA Guidelines

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IIa

B

Left main PCI for NSTEMI/unstable angina:

- If not a CABG candidate (otherwise CABG)

IIa

C

Left main PCI for STEMI:

- When distal coronary flow is TIMI flow grade <3 and PCI can be performed more rapidly and safely than CABG

2011 ACCF/AHA/SCAI Guidelines for PCI
JACC 2011;58;e44-e122;

ACC/AHA Guidelines

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IIa

B

Left main PCI for SIHD - Both must be present:

- Anatomic conditions associated with a low risk of PCI procedural complications and a high likelihood of good long-term outcome (e.g., a low SYNTAX score of ≤22, ostial or trunk left main CAD)
- Clinical characteristics that predict a significantly increased risk of adverse surgical outcomes (e.g. STS-predicted risk of operative mortality ≥5%)

2011 ACCF/AHA/SCAI Guidelines for PCI
JACC 2011;58;e44-e122;

ACC/AHA Guidelines

EXCEL

IIb

B

Left main PCI for SIHD - Both must be present:

- Anatomic conditions associated with a low to intermediate risk of PCI procedural complications and an intermediate to high likelihood of good long-term outcome (e.g., low-intermediate SYNTAX score of <33, bifurcation left main CAD)
- Clinical characteristics that predict an increased risk of adverse surgical outcomes (e.g., moderate-severe COPD, disability from prior stroke, or prior cardiac surgery; STS-predicted risk of operative mortality >2%)

2011 ACCF/AHA/SCAI Guidelines for PCI
JACC 2011;58;e44-e122;

ACC/AHA Guidelines

Left main PCI for SIHD: HARM

- In patients with unfavorable anatomy for PCI (e.g. Syntax score ≥33) and who are good candidates for CABG (vs. performing CABG)

2011 ACCF/AHA/SCAI Guidelines for PCI
JACC 2011;58;e44-e122;

ESC/EACTS Guidelines on Myocardial Revascularization

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IIa

- Left main PCI: Isolated or 1-vessel ds. with LM ostium/shaft involvement

IIb

- Left main PCI: Isolated or 1-vessel ds. with LM distal bifurcation involvement
- Left main PCI: 2- or 3-vessel disease, SYNTAX score ≤32

III

- Left main PCI: 2- or 3-vessel disease, SYNTAX score ≥33

Eur Heart J 2010;31:2501-2555

EXCEL Trial

EXCEL

3600 pts with unprotected left main disease

@ 150 international sites

SYNTAX score ≤32

Consensus agreement by heart team

No (N=1000)

Enrollment registry

Yes (N=2600)

R

PCI (Xience Prime) (N=1300)

CABG (N=1300)

Clinical follow-up:
1 mo, 6 mo and yearly through 5 years

Inclusion Criteria

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- Clinical and anatomic eligibility for both PCI and CABG by heart team consensus
- Silent ischemia, stable angina, unstable angina or recent MI
- Significant LM ds. by heart team consensus
  - Angiographic DS ≥70%, or
  - Angiographic DS ≥50% to <70% with
    - a markedly positive noninvasive study, and/or
    - IVUS MLA <6.0 mm^2, and/or
    - FFR <0.80

Principal Exclusion Criteria

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- Prior PCI within 1 year, or prior LM PCI anytime
- Prior CABG anytime
- Need for any cardiac surgery other than CABG
- Additional surgery required within 1 year
- Unable to tolerate, obtain or comply with dual antiplatelet therapy for 1 year
- Non cardiac co-morbidities with life expectancy <3 years
- Left main RVD <2.25 mm or >4.5 mm

Principal Exclusion Criteria

EXCEL

- The presence of any condition(s) which leads the participating cardiac surgeon to believe that clinical equipoise is not present (i.e. the subject should not be treated by CABG, but rather should be managed with PCI or medical therapy
- The presence of any condition(s) which leads the participating Interventionalist to believe that clinical equipoise is not present (i.e. the subject should not be treated by PCI, but rather should be managed with CABG or medical therapy
- Reasons will be documented

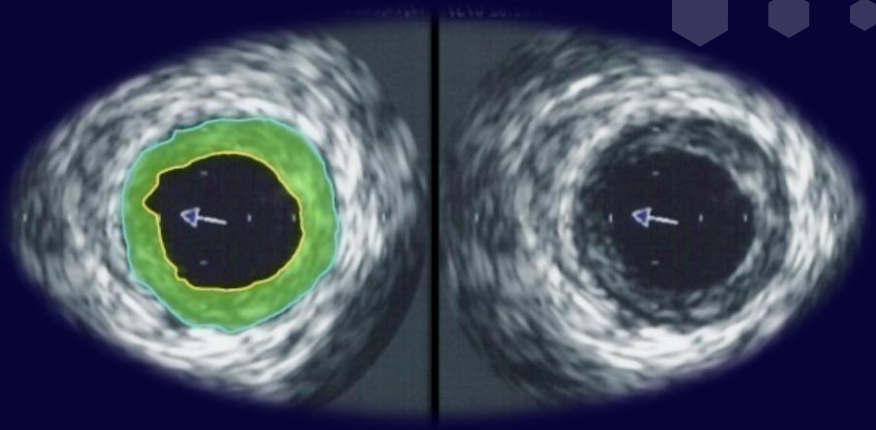
Principal Endpoints

- **Primary endpoint: Death, MI, or stroke at 3 year FU - Powered for sequential noninferiority and superiority testing**
- Major secondary endpoints (powered):
  1. Death, MI, or stroke at 30 days
  2. Stroke at 30 days
  3. Unplanned repeat revascularization for ischemia at 3 years
- Additional secondary endpoint (powered):
  1. Death, MI, stroke or unplanned revascularization for ischemia at 3 years
- Quality of life and cost-effectiveness assessments:
  At baseline, 1 month, 1 year, 3 years and 5 years

IVUS Sub-study

Purpose:

To explore whether procedural use of IVUS improves outcomes of left main stenting, as well as determine the IVUS parameters that most strongly correlate with left main stent thrombosis or restenosis



IVUS data captured will be used to show whether the utility of IVUS guidance improves the acute and late results of left main stenting with the XIENCE Prime™ or XIENCE V® stent

All patients who are randomized to the PCI arm and have IVUS performed during the procedure will be included in the IVUS substudy. All left main lesions in which IVUS was used will undergo rigorous central core laboratory evaluation.

EXCEL Sites locations

Active Global sites and RCT patients

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Argentina	8 RCT	1 site
Australia	7 RCT	2 sites
Belgium	42 RCT	3 sites
Brazil	17 RCT	3 sites
Canada	**102 RCT**	**10 sites**
France	**80 RCT**	**8 sites**
Germany	**62 RCT**	**8 sites**
Hungary	**130 RCT**	**3 sites**
Italy	**55 RCT**	**11 sites**
Latvia	11 RCT	1 site
Netherlands	**67 RCT**	**3 sites**
Poland	48 RCT	4 sites
S. Korea	13 RCT	1 site
Spain	**61 RCT**	**4 sites**
Switzerland	0 RCT	1 site
UK	**229 RCT**	**9 sites**
USA	**289 RCT**	**68 sites**

Abbott Vascular

EXCEL Top Enrollers (1 to 10)

Country	Site Name	PI Names	Total RCT Patients
United States	Piedmont Heart Institute	Lembo/Brown	88
United Kingdom	John Radcliffe Hospital	Banning/Taggart	79
Hungary	Semmelweis University	Merkely/Horkay	62
Hungary	Cardiology Center University of Szeged	Ungi/Bogáts	49
Netherlands	Medisch Centrum Leeuwarden	van Boven/Boonstra	49
Spain	Hospital Clinic,	Sabate/Pomar	37
United Kingdom	Glenfield Hospital, University Hospitals of Leicester NHS Trust	Gershlick/Hickey	36
Poland	Polsko-Amerykanskie Kliniki Serca,	Buszman/Bochenek	35
Canada	CHUM-Hotel-Dieu Hospital	Mansour/Noiseux	29
United Kingdom	Royal Sussex County Hospital	Hildick-Smith/Trivedi	28

EXCEL Top Enrollers (11 to 20)

Country	Site Name	PI Names	Total RCT Patients
United Kingdom	Liverpool Heart and Chest Hospital	Stables/Pullan(PI)	27
Germany	Ruhr-Universitaet Bochum - Herz-und Diabeteszentru	Scholtz/Börgermann (PI)	25
France	Clinique Saint Hilaire - CHU Rouen	Dr. Berland/Bessou (PI)	22
Belgium	Ziekenhuis Oost-Limburg	Vrolix/Dion (PI)	21
Canada	Hopital Sacre-Coeur de Montreal	Schampaert/Page (PI)	21
Belgium	OLV Ziekenhuis Aalst	Barbato/Vanermen (PI)	19
Hungary	Hungarian Institute of Cardiology	Fontos/Székely (PI)	19
France	Hopital Prive Franciscaines	Maupas/Durrleman (PI)	18
Canada	Montreal Heart Institute	Doucet/Pellerin (PI)	16
United Kingdom	St Thomas' hospital	Thomas/Young (PI)	16

EXCEL Top Enrollers (20 to 30)

Country	Site Name	PI Names	Total RCT Patients
United States	UVA Medical Center	Ragosta/Kron (PI)	16
United Kingdom	Royal Brompton Hospital	Di Mario/De Souza (PI)	14
Italy	Ospedale Civile Maggiore	Ribichini/Faggian (PI)	13
Netherlands	Erasmus MC	Schultz/Kappetein (PI)	13
South Korea	Asan Medical Center	Park/Lee (PI)	13
United States	Wake Heart Research	Mann/Landvater (PI)	13
Canada	Hamilton Health Science General Site	Mehta/Cybulsky (PI)	12
France	CHU TOULOUSE RANGUEIL	Carrie/Glock (PI)	12
France	Hôpital Privé Jacques Cartier	Lefevre/Romano (PI)	12
Germany	University - Heart center Leipzig	Schuler/Borger (PI)	12

Site Activation

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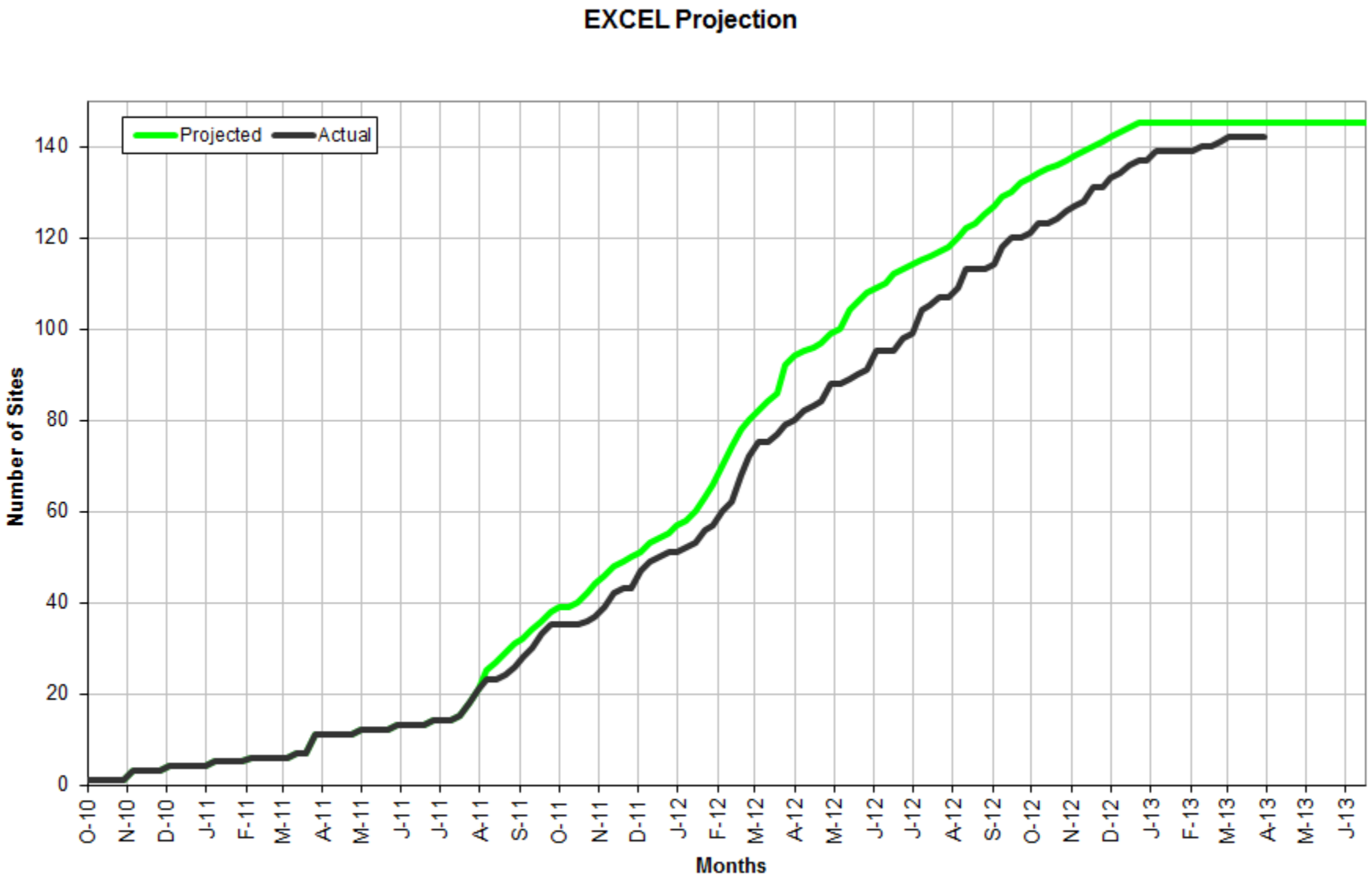

Patient Enrollment (1224 RCT)

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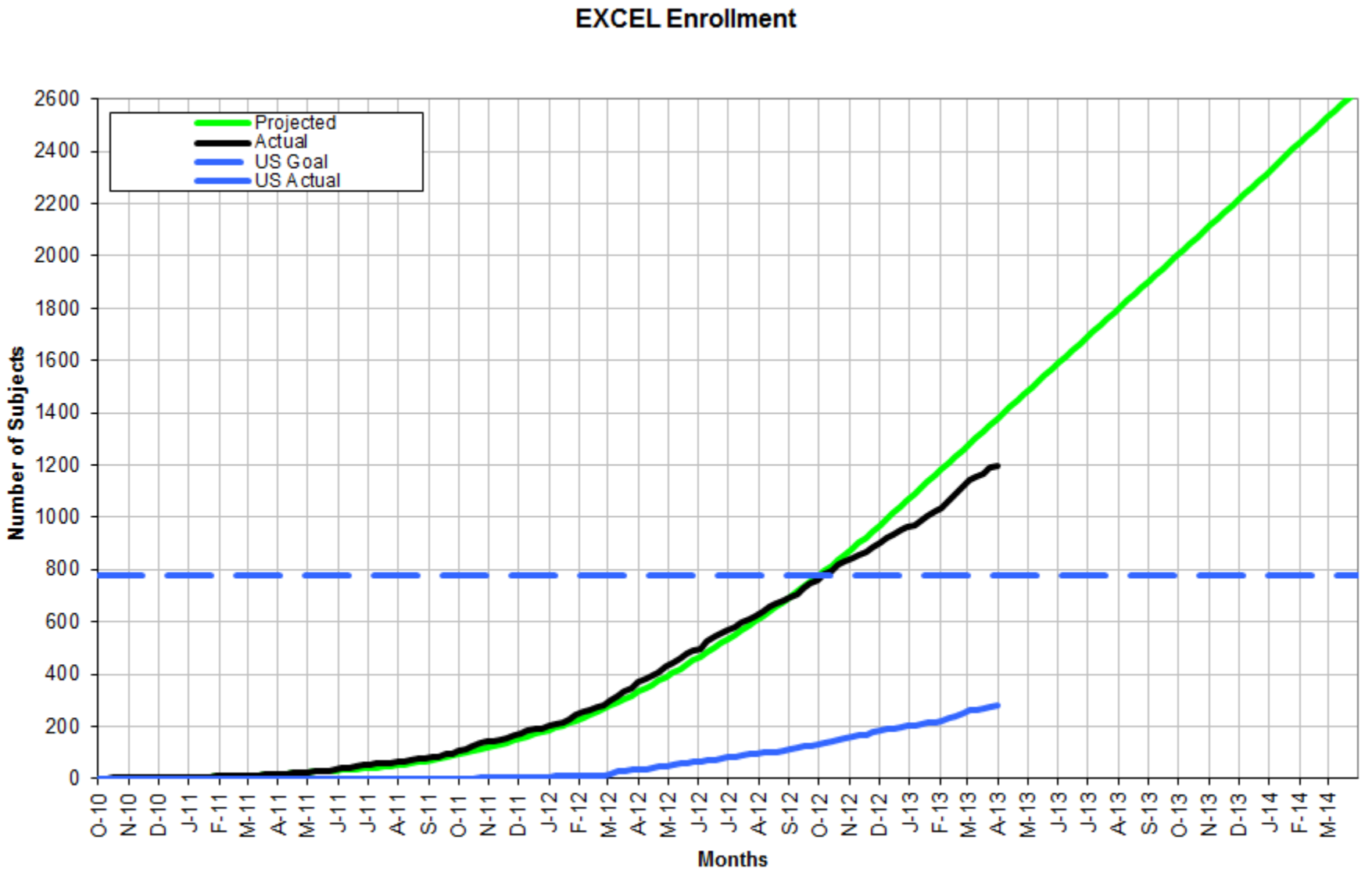

Conclusions

1. EXCEL is the largest and ONLY ongoing prospective multicenter randomized trial comparing CoCr EES (Xience) DES PCI to CABG for unprotected LM disease with or without MV disease in properly-selected patients with SYNTAX scores<33

2. EXCEL is now very close to ½ enrolled, with expectation to complete enrollment 04/2014

3. EXCEL will be *the final answer* for DES vs CABG in the era of metallic DES and will provide Class I evidence for the treatment of these patients