

LM stenting or surgery?

Insights from Syntax Trial

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On behalf of the SYNTAX investigators
17:00–18:20, September 27, 2008
EBC meeting

Conflicts of Interest: None



Background: II



- At the time of the trial design (in 2003–2004), a retrospective website survey of 104 medical centers over a period of 3 months showed that 12,072 patients (1 / 3 LM, 2 / 3 3VD) were revascularized by surgery (2 / 3) or by PCI (1 / 3).
- The SYNTAX randomized trial is an attempt to provide an evidence–base to determine whether this approach, which is already currently practiced, is valid.

SYNTAX: *Intended All-Comers* Design with Nested Registries



- Intended all-comers study design *instead of* a highly selected patient population
- Consensus physician agreement (surgeon & cardiologist) *instead of* inclusion & exclusion criteria
- And, nested registries for CABG only and PCI only to define patient characteristics and outcomes of these two unique treatment options

SYNTAX Eligible Patients



De novo disease

Limited Exclusion Criteria

- Previous interventions
- Acute MI with CPK > 2x
- Concomitant cardiac surgery

Left Main Disease
(isolated, +1, +2 or +3 vessels)

3 Vessel Disease
(revasc all 3 vascular territories)

Patient Profiling

Local Heart team (surgeon & interventional cardiologist) assessed each patient in regards to :

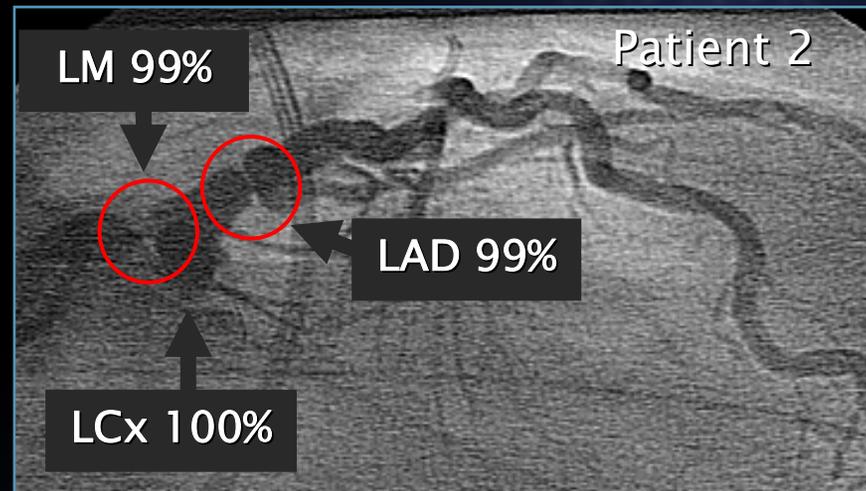
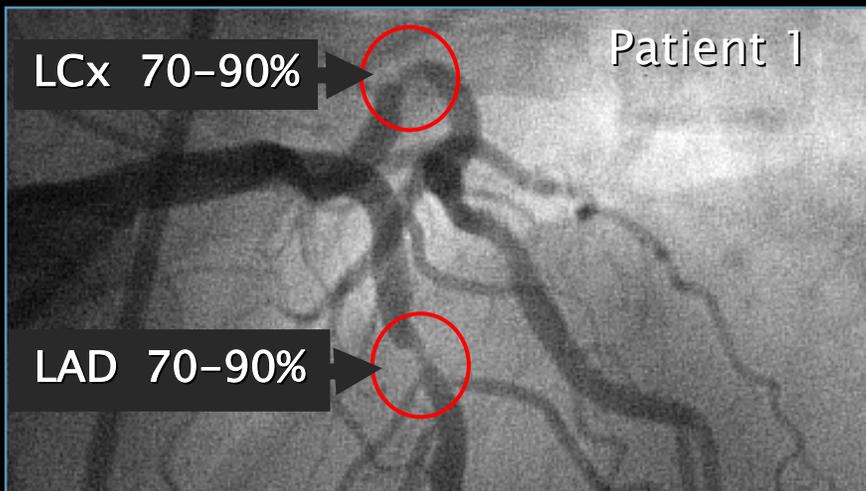
- Patient's operative risk (EuroSCORE & Parsonnet score)
- Coronary lesion complexity (Newly developed SYNTAX score)
- Goal: SYNTAX score to provide guidance on optimal revascularization strategies for patients with high risk lesions



Sianos et al, EuroIntervention 2005;1:219-227
Valgimigli et al, Am J Cardiol 2007;99:1072-1081
Serruys et al, EuroIntervention 2007;3:450-459

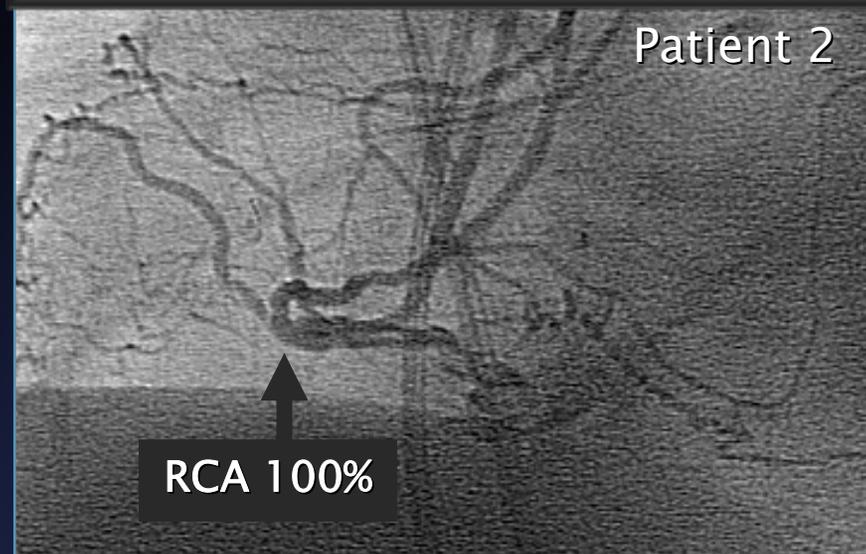
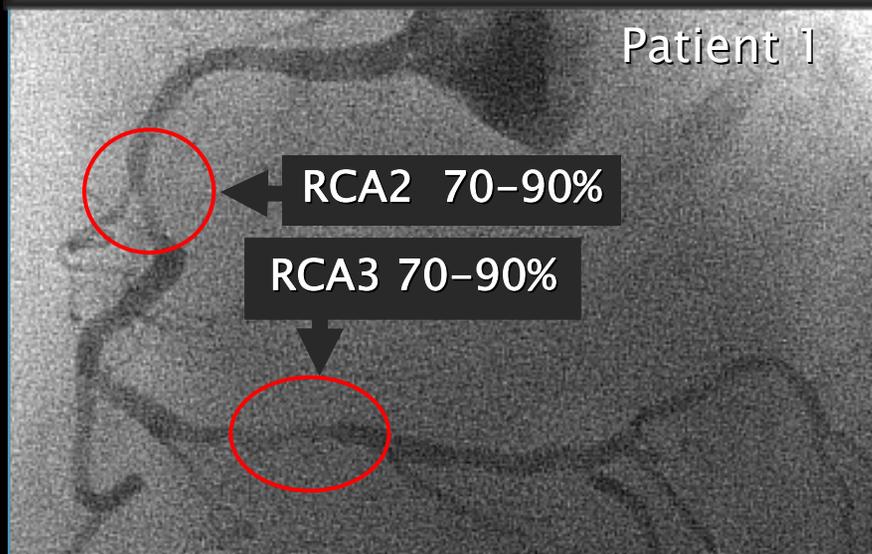
BARI classification of coronary segments
Leaman score, Circ 1981;63:285-299
Lesions classification ACC/AHA, Circ 2001;103:3019-3041
Bifurcation classification, CCI 2000;49:274-283
CTO classification, J Am Coll Cardiol 1997;30:649-656

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



SYNTAX SCORE 21

SYNTAX SCORE 52



SYNTAX Trial Design



 62 EU Sites +  23 US Sites

Heart Team (surgeon & interventionalist)

Amenable for both treatment options

Amenable for only one treatment approach

Stratification:
LM and Diabetes

Randomized Arms
N=1800

Two Registry Arms
N=1275

CABG
N=897

vs

TAXUS*
N=903

CABG
N=1077

PCI
N=198

DM 28.5% Non DM 71.5%

DM 28.2% NonDM 71.8%

*TAXUS Express

SYNTAX Primary Endpoint

Randomized trial



*The primary clinical endpoint is the 12 Month major Cardiovascular or Cerebrovascular event rate (MACCE *)*

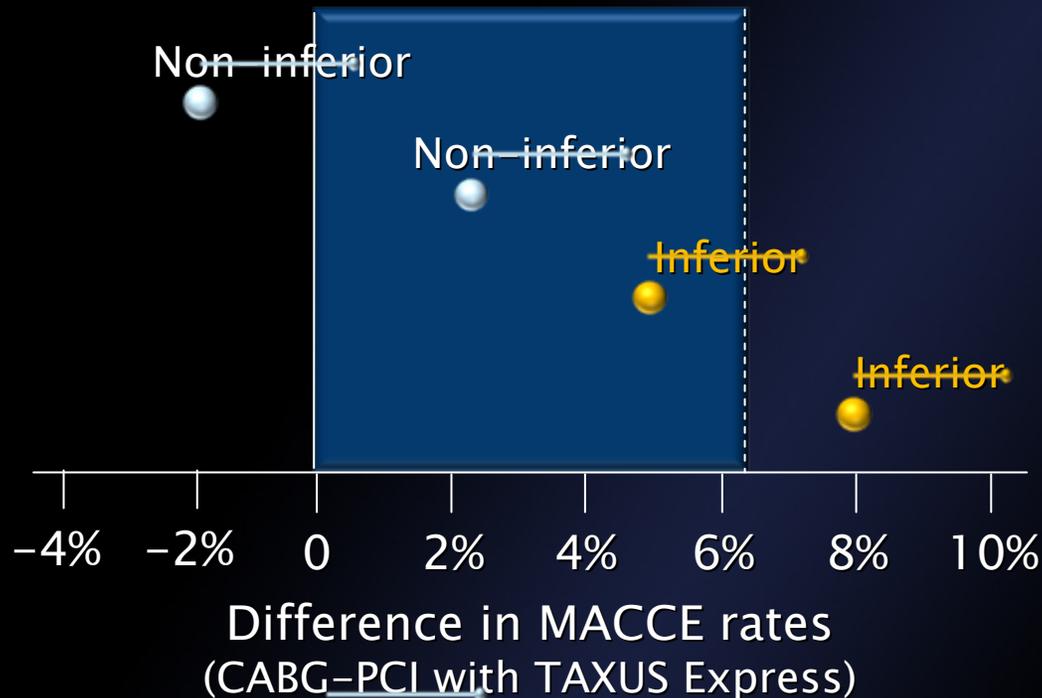
- MACCE is defined as:
 - All cause Death
 - Cerebrovascular Accident (CVA/Stroke)
 - Documented Myocardial Infarction (ARC definition)
 - Any Repeat Revascularization (PCI and/or CABG)
- All events CEC Adjudicated

* ARC MACCE definition Circ 2007; 115:2344-2351

Primary Endpoint (12 Month MACCE) *Non-inferiority to CABG*



Zone of Non-inferiority
Pre-specified Margin = 6.6%



● Difference in MACCE rates

Upper 1-sided 95% confidence intervals

Patient Characteristics (I)

Randomized Cohort

	CABG N=897	TAXUS N=903	P value
Age, mean \pm SD (y)	65.0 \pm 9.8	65.2 \pm 9.7	0.55
Male, %	78.9	76.4	0.20
BMI, mean \pm SD	27.9 \pm 4.5	28.1 \pm 4.8	0.37
Diabetes, %	28.5	28.2	0.89
Hypertension, %	77.0	74.0	0.14
Hyperlipidemia, %	77.2	78.7	0.44
Current smoker, %	22.0	18.5	0.06
Prior MI, %	33.8	31.9	0.39
Unstable angina, %	28.0	28.9	0.67
Additive EuroSCORE, mean \pm SD	3.8 \pm 2.7	3.8 \pm 2.6	0.78
Total Parsonnet score , mean \pm SD	8.4 \pm 6.8	8.5 \pm 7.0	0.76

Patient Characteristics (II)

Randomized Cohort



Patient-based

	CABG N=897	TAXUS N=903	P value
Total SYNTAX Score	29.1 ±11.4	28.4 ±11.5	0.19
Diffuse disease or small vessels, %	10.7	11.3	0.69
No. lesions, mean ± SD	4.4 ±1.8	4.3 ±1.8	0.44
3VD only, %	66.3	65.4	0.70
Left main, any, %	33.7	34.6	0.70
Left Main only	3.1	3.8	0.46
Left Main + 1 vessel	5.1	5.4	0.78
Left Main + 2 vessel	12.0	11.5	0.72
Left Main + 3 vessel	13.5	13.9	0.78
Total occlusion, %	22.2	24.2	0.33
Bifurcation, %	73.3	72.4	0.67
Trifurcation, %	10.6	10.7	0.92

Procedural Characteristics

PCI Randomized Cohort

SYNTAX

<i>Patient-based</i>	TAXUS N=903
Staged procedure, %	14.1
Lesions treated/pt, mean \pm SD	3.6 \pm 1.6
No. stents implanted, mean \pm SD	4.6 \pm 2.3
Total length implanted, mm \pm SD	86.1 \pm 47.9
Range, mm	8 - 324
Long stenting (>100 mm), %	33.2

Procedural Characteristics

CABG Randomized Cohort



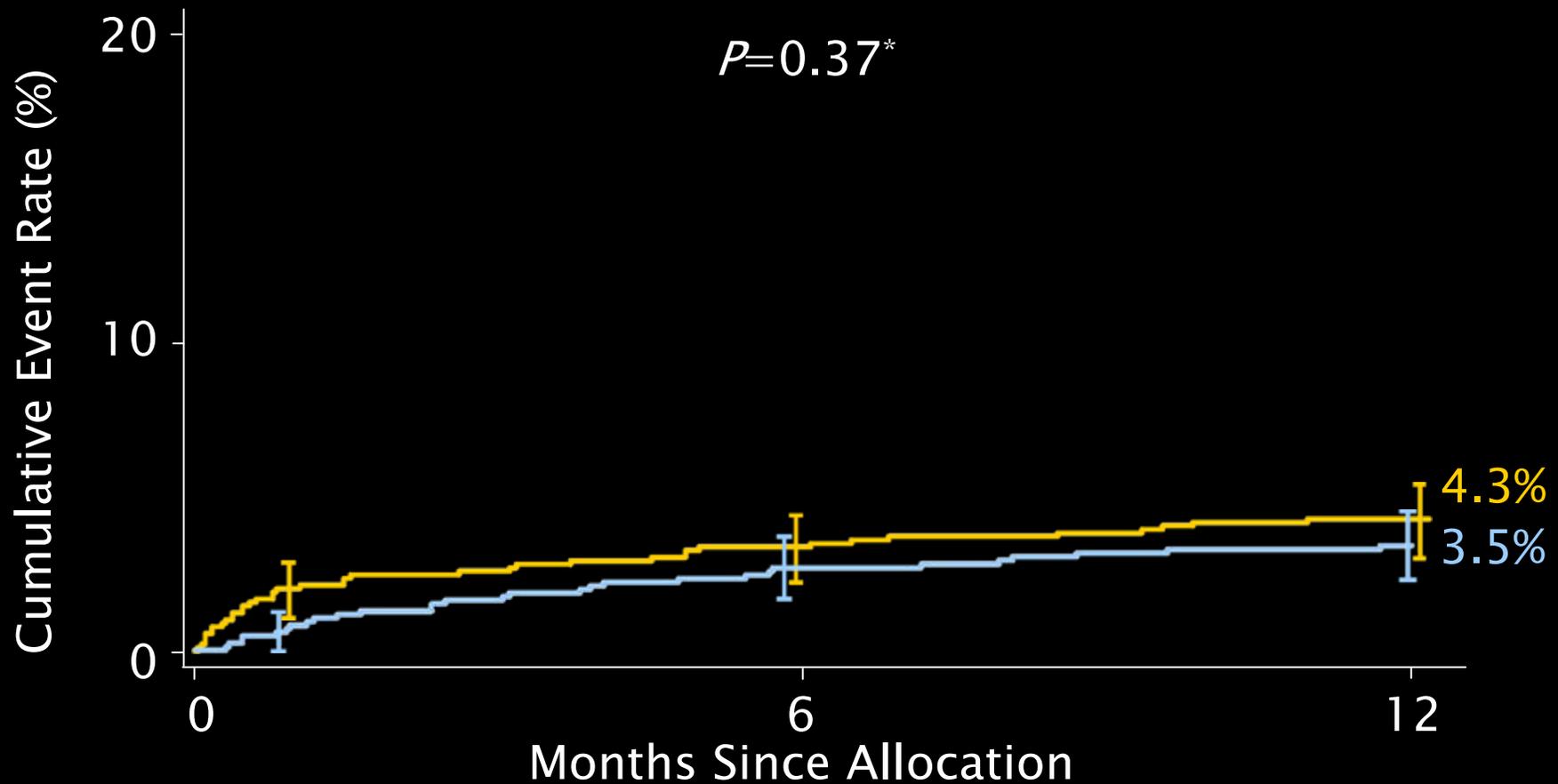
	CABG N=897
Off-pump surgery, %	15.0
Graft revascularization, %	
At least one arterial graft	97.3
Arterial graft to LAD	95.6
LIMA+venous	78.1
Double LIMA/RIMA	27.6
Complete arterial revascularization	18.9
Radial artery	14.1
Venous graft only	2.6
Grafts per patient, mean \pm SD	2.8 \pm 0.7
Distal anastomosis/pt, mean \pm SD	3.2 \pm 0.9

All-Cause Death to 12 Months



■ CABG (N=897)

■ TAXUS (N=903)



Event Rate \pm 1.5 SE. *Fisher's Exact Test

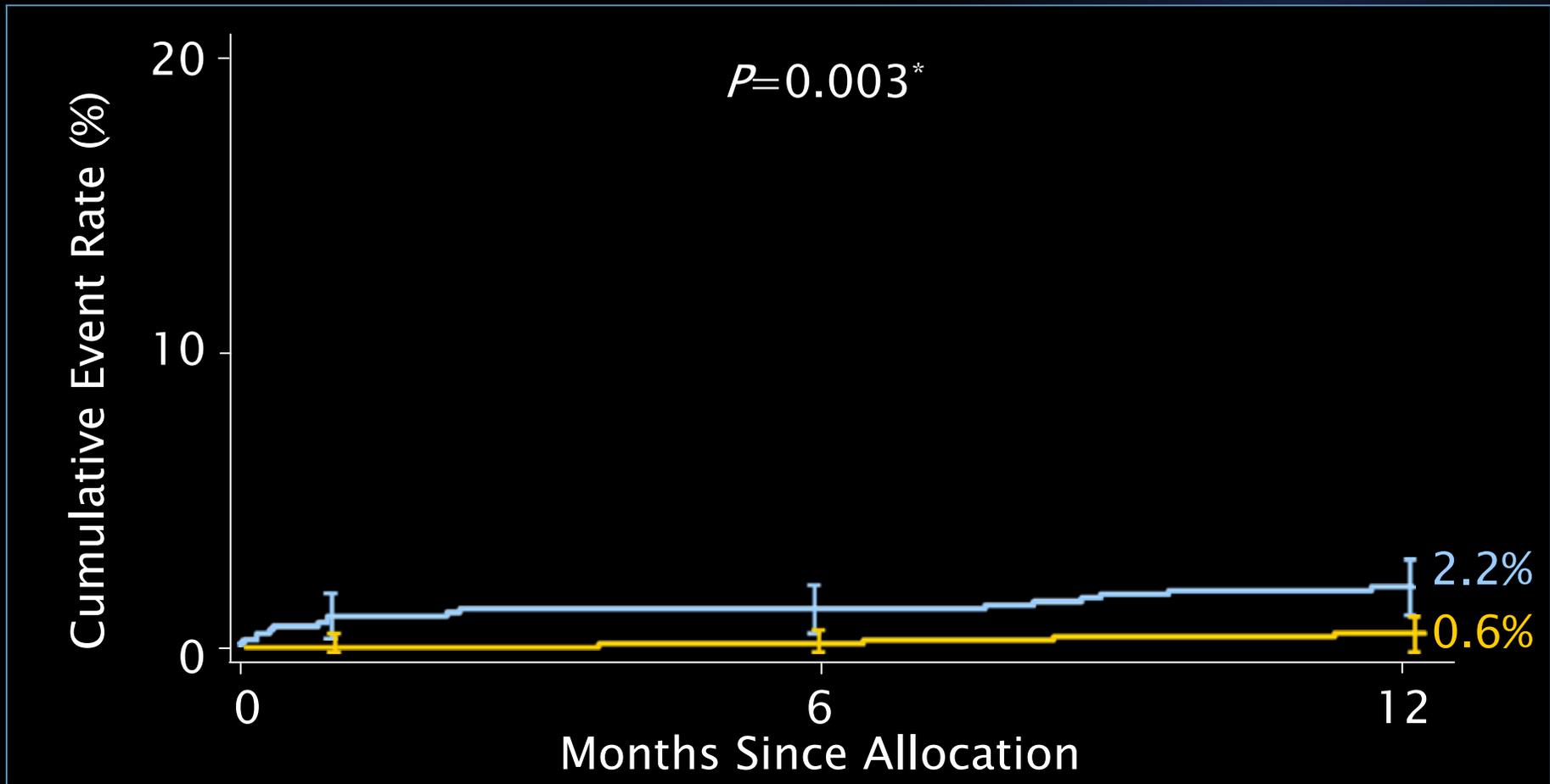
ITT population

CVA to 12 Months



■ CABG (N=897)

■ TAXUS (N=903)



Event Rate \pm 1.5 SE. *Fisher's Exact Test

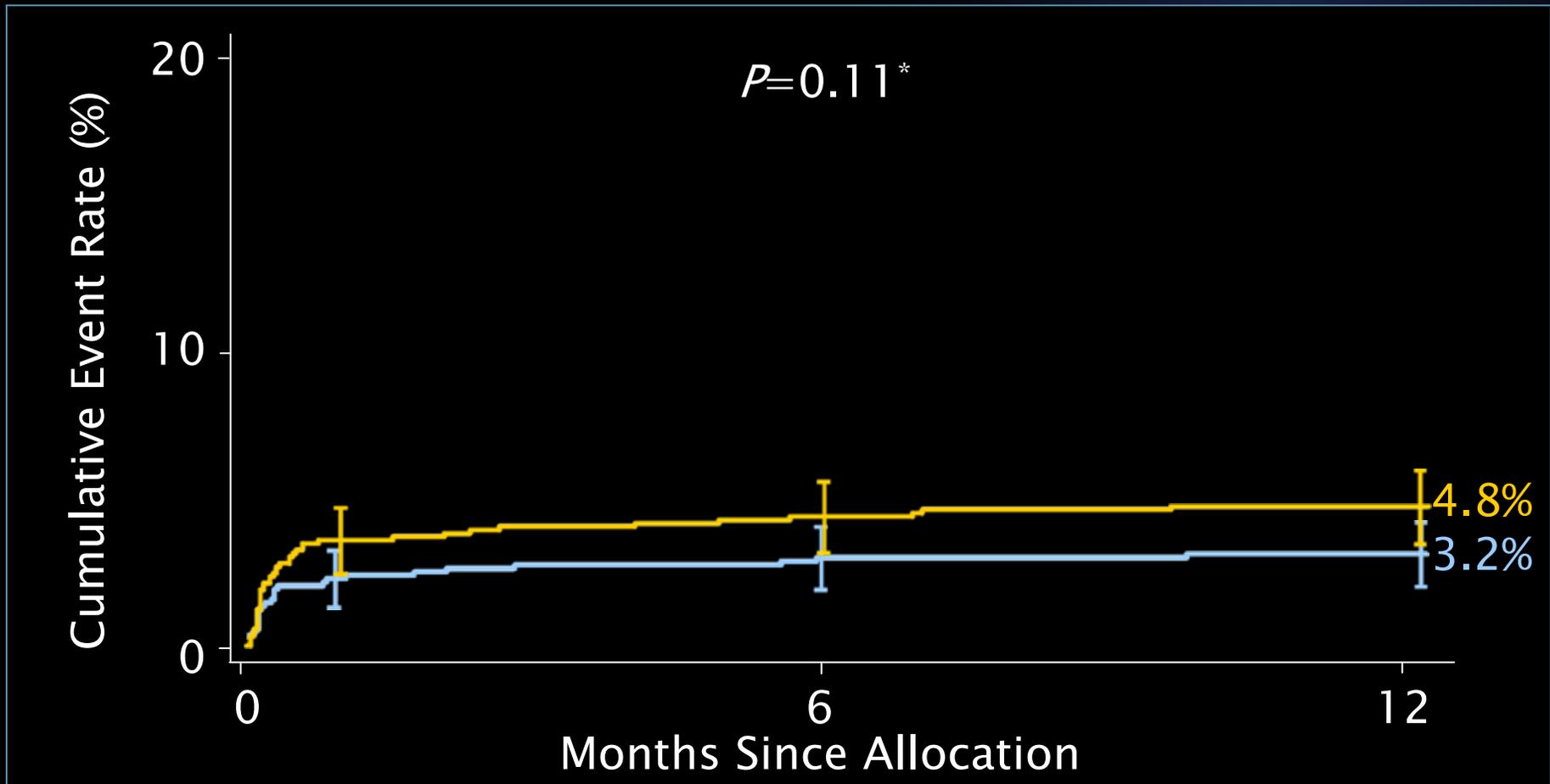
ITT population

Myocardial Infarction to 12 Months



■ CABG (N=897)

■ TAXUS (N=903)



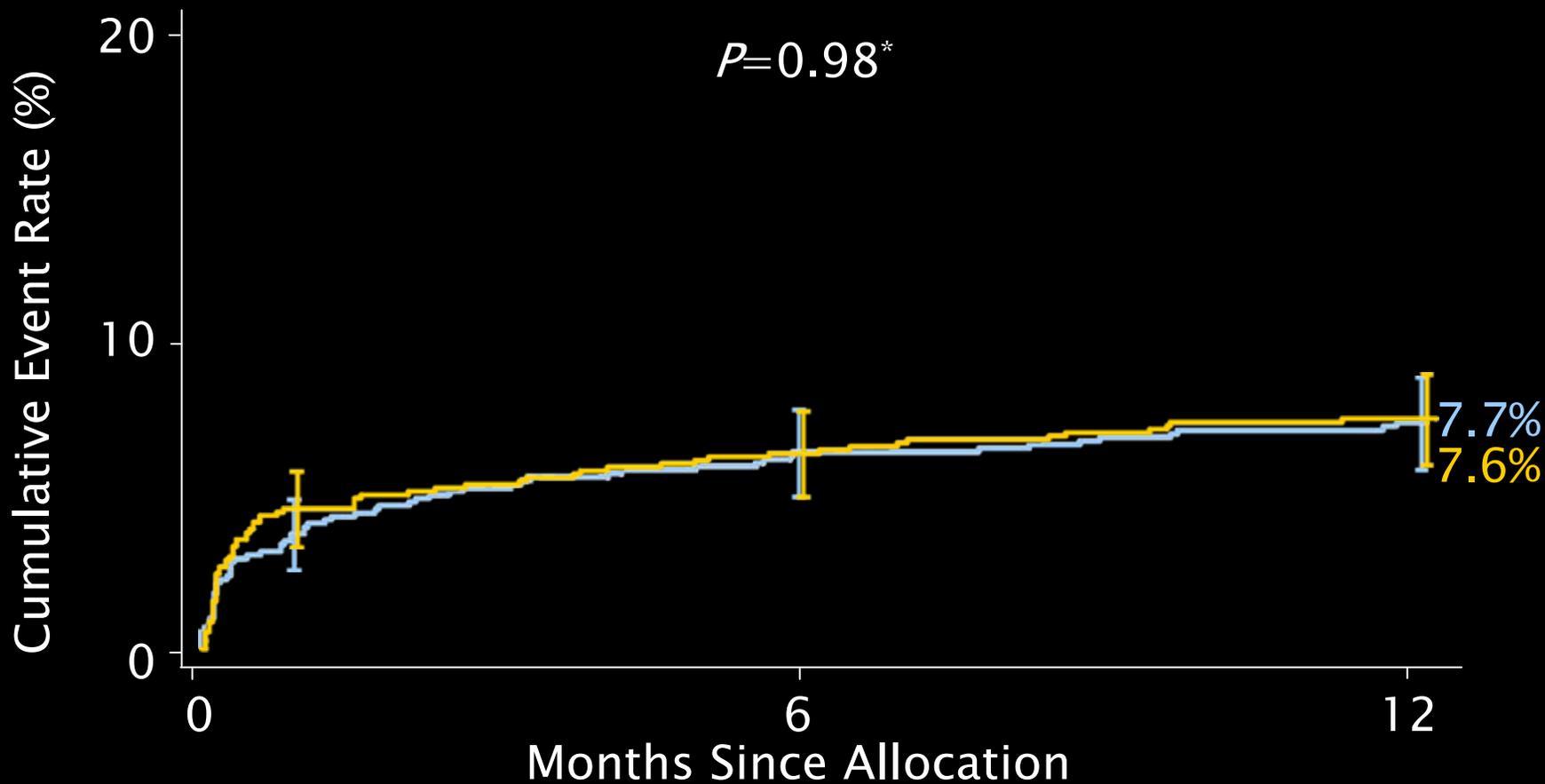
Event Rate \pm 1.5 SE. *Fisher's Exact Test

ITT population

All-Cause Death/CVA/MI to 12 Months SYNTAX

■ CABG (N=897)

■ TAXUS (N=903)



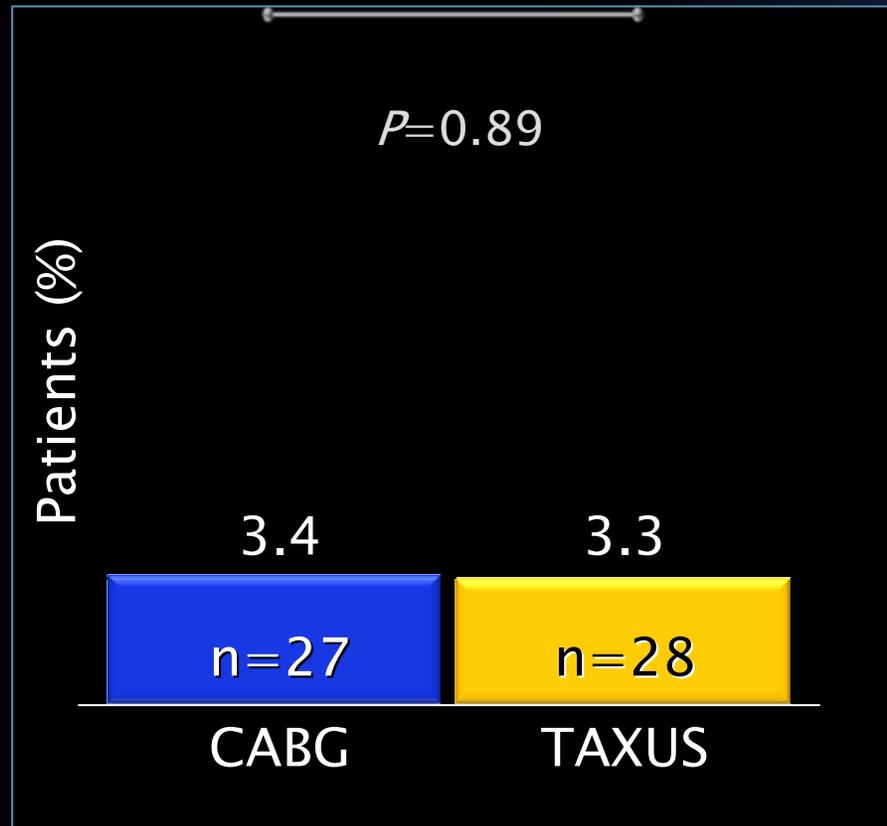
Event Rate \pm 1.5 SE. *Fisher's Exact Test

ITT population

Symptomatic Graft Occlusion & Stent Thrombosis to 12 Months



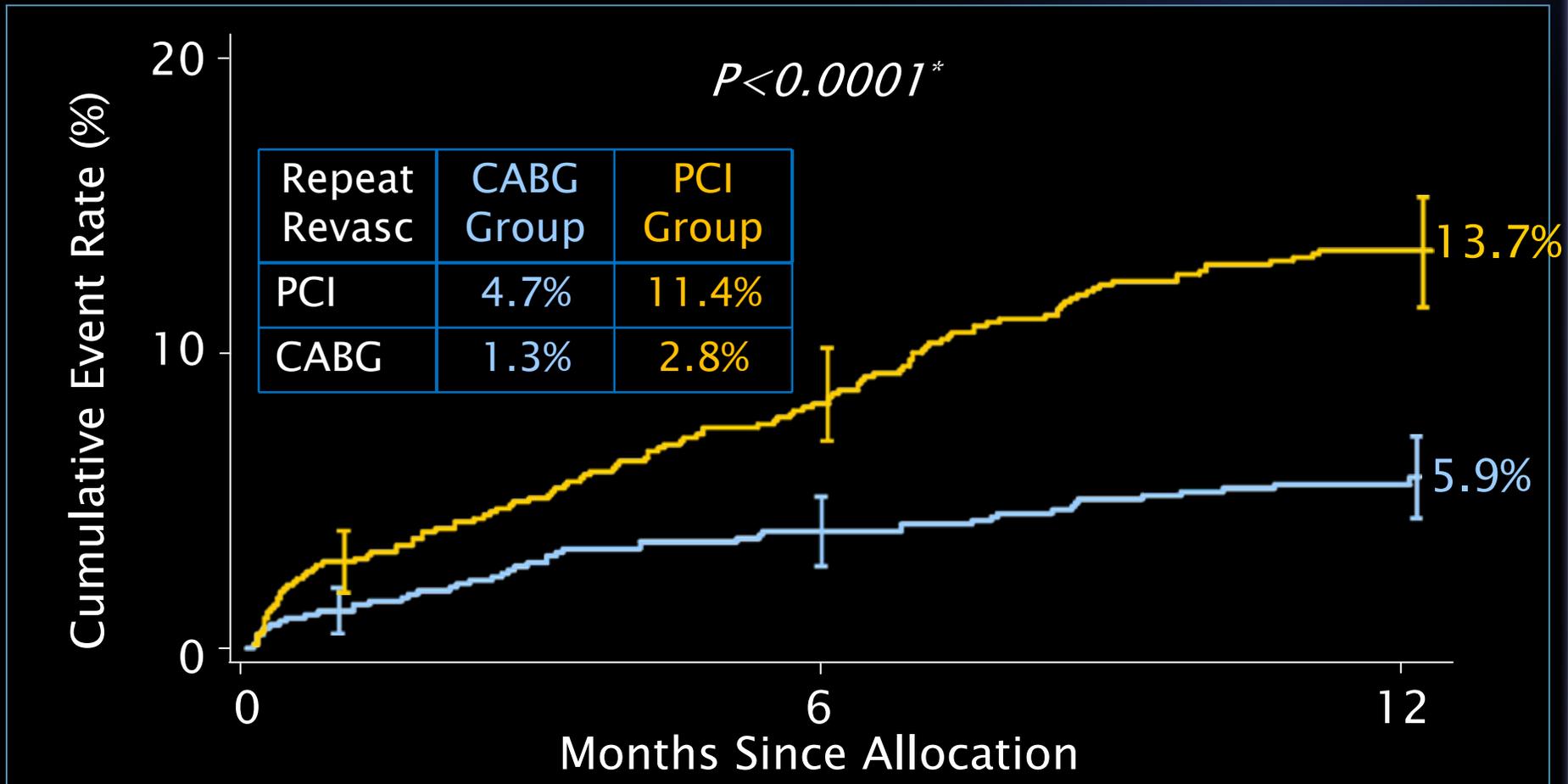
■ CABG (N=897) ■ TAXUS (N=903)



Repeat Revascularization to 12 Months SYNTAX

■ CABG (N=897)

■ TAXUS (N=903)



Event Rate \pm 1.5 SE. *Fisher's Exact Test

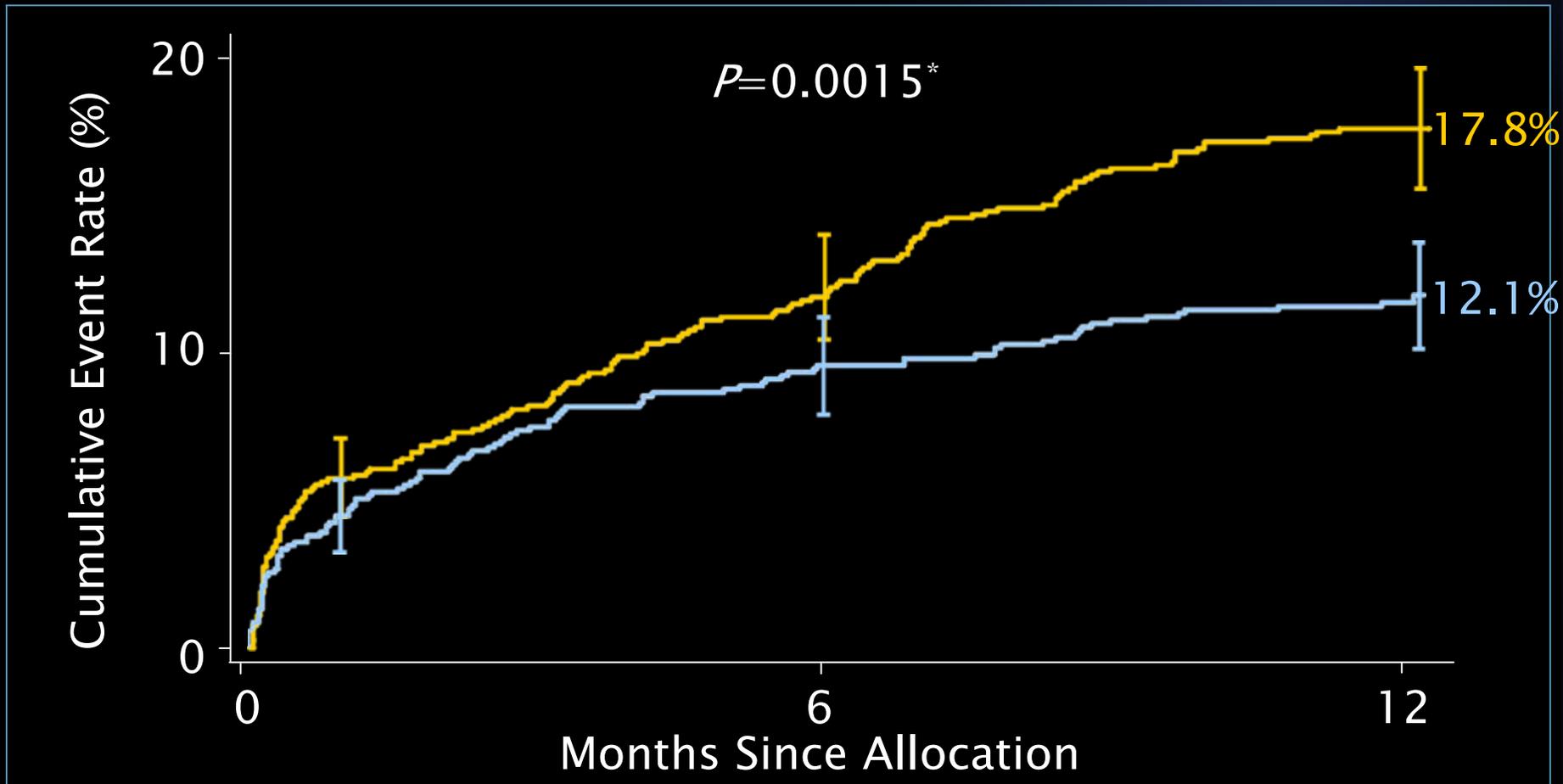
ITT population

MACCE to 12 Months



■ CABG (N=897)

■ TAXUS (N=903)

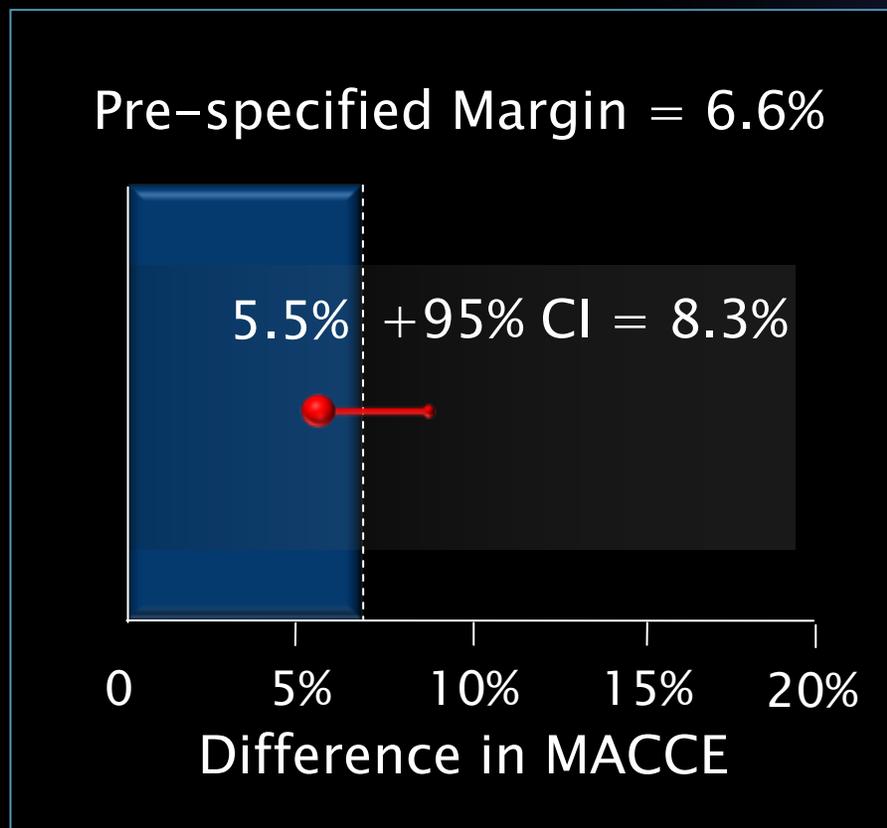


Event Rate \pm 1.5 SE. *Fisher's Exact Test

ITT population

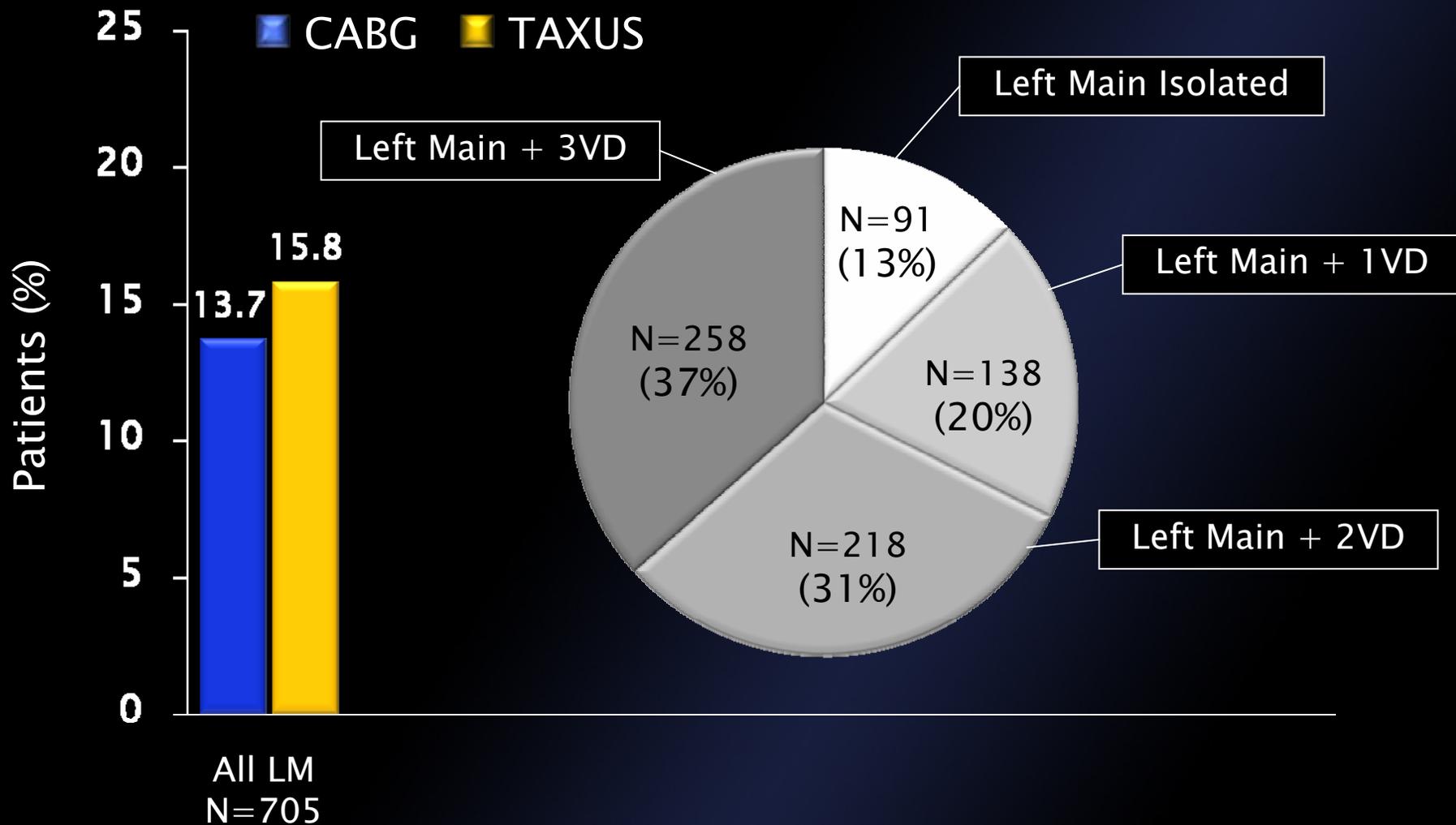
Primary Endpoint: 12 Month MACCE

Non-inferiority analysis

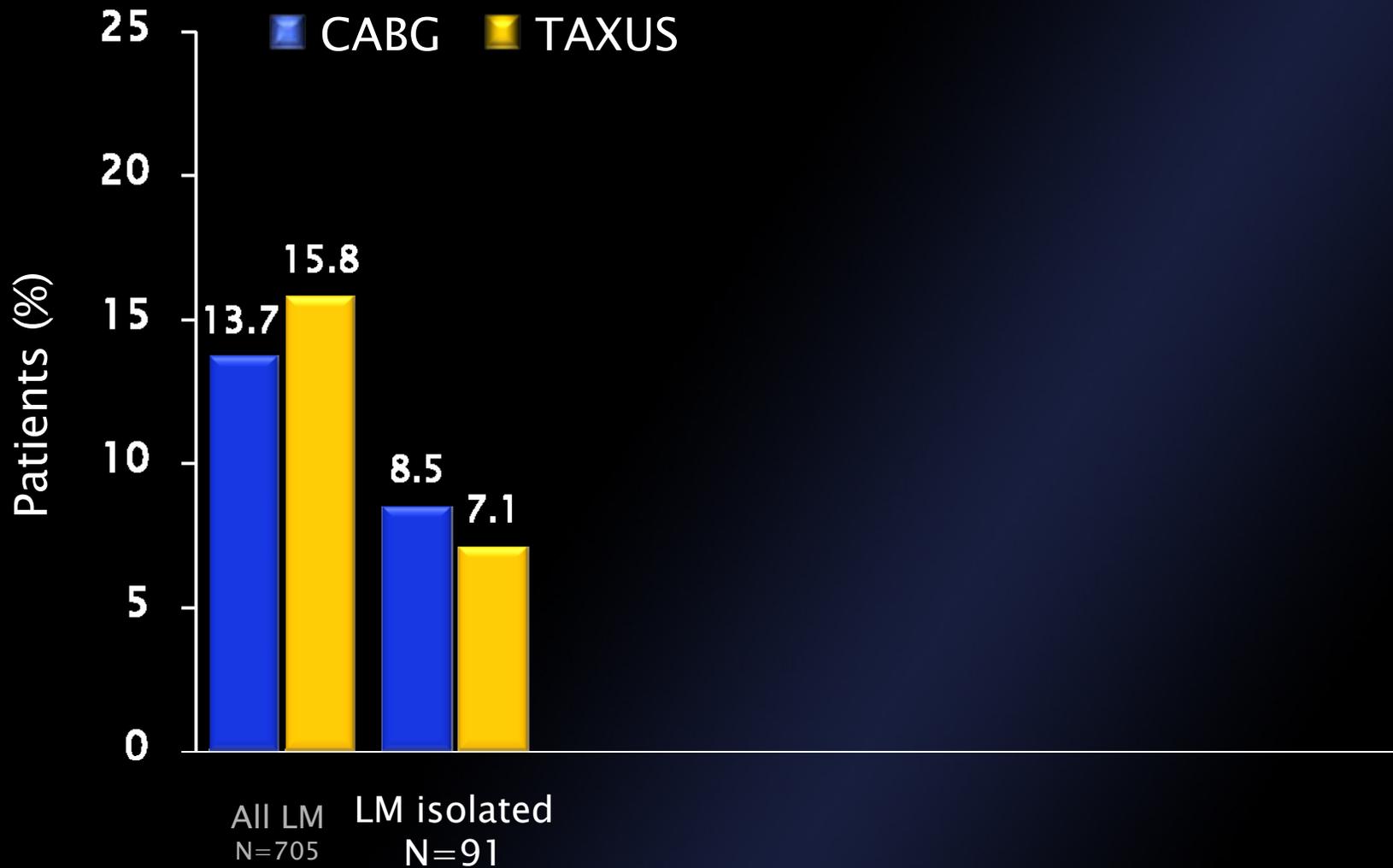


→ The criteria for non-inferiority comparison was not met for the primary endpoint, further comparisons for the LM and 3VD subgroups are observational only and hypothesis generating

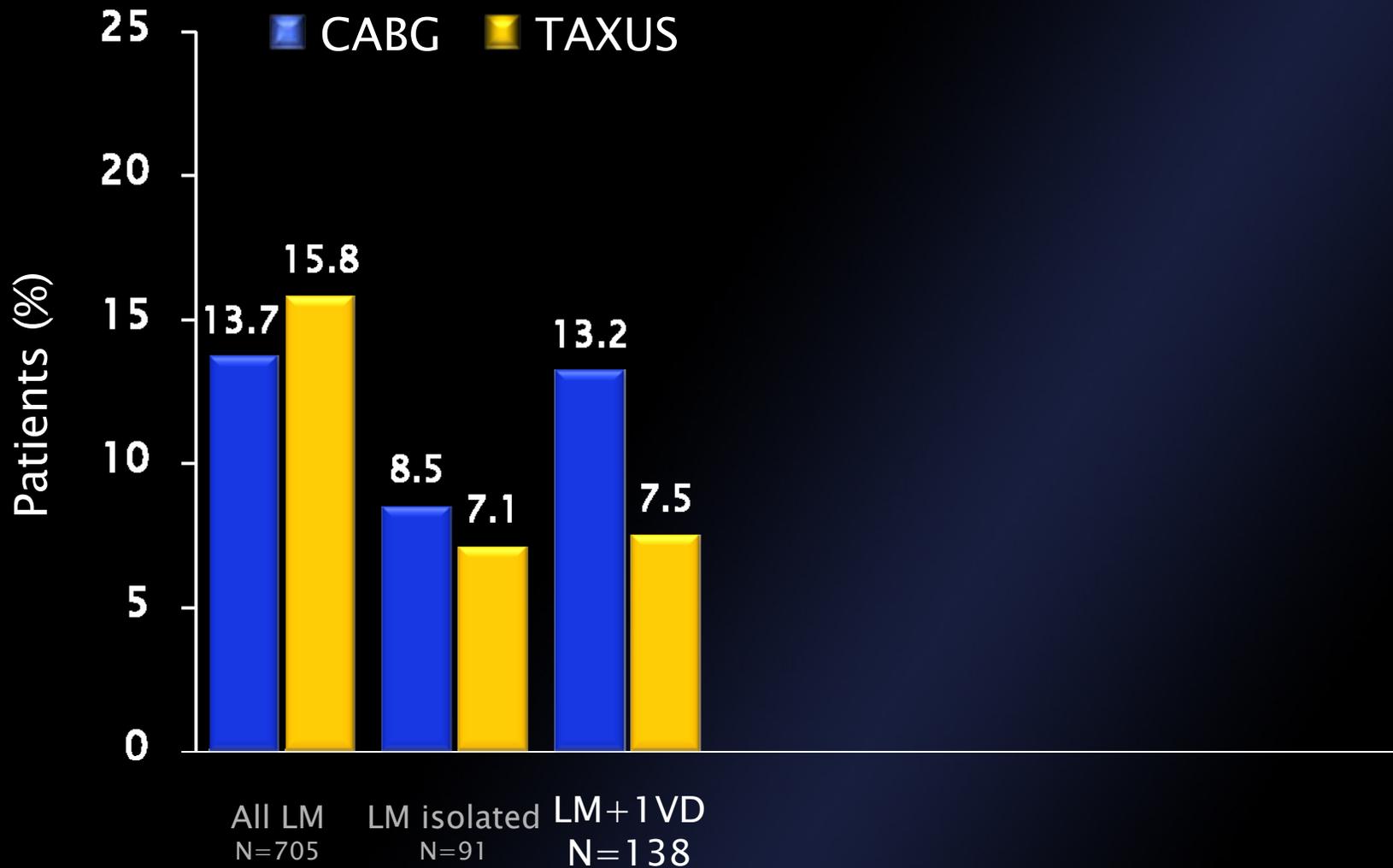
12 Month LM Subgroup MACCE Rates



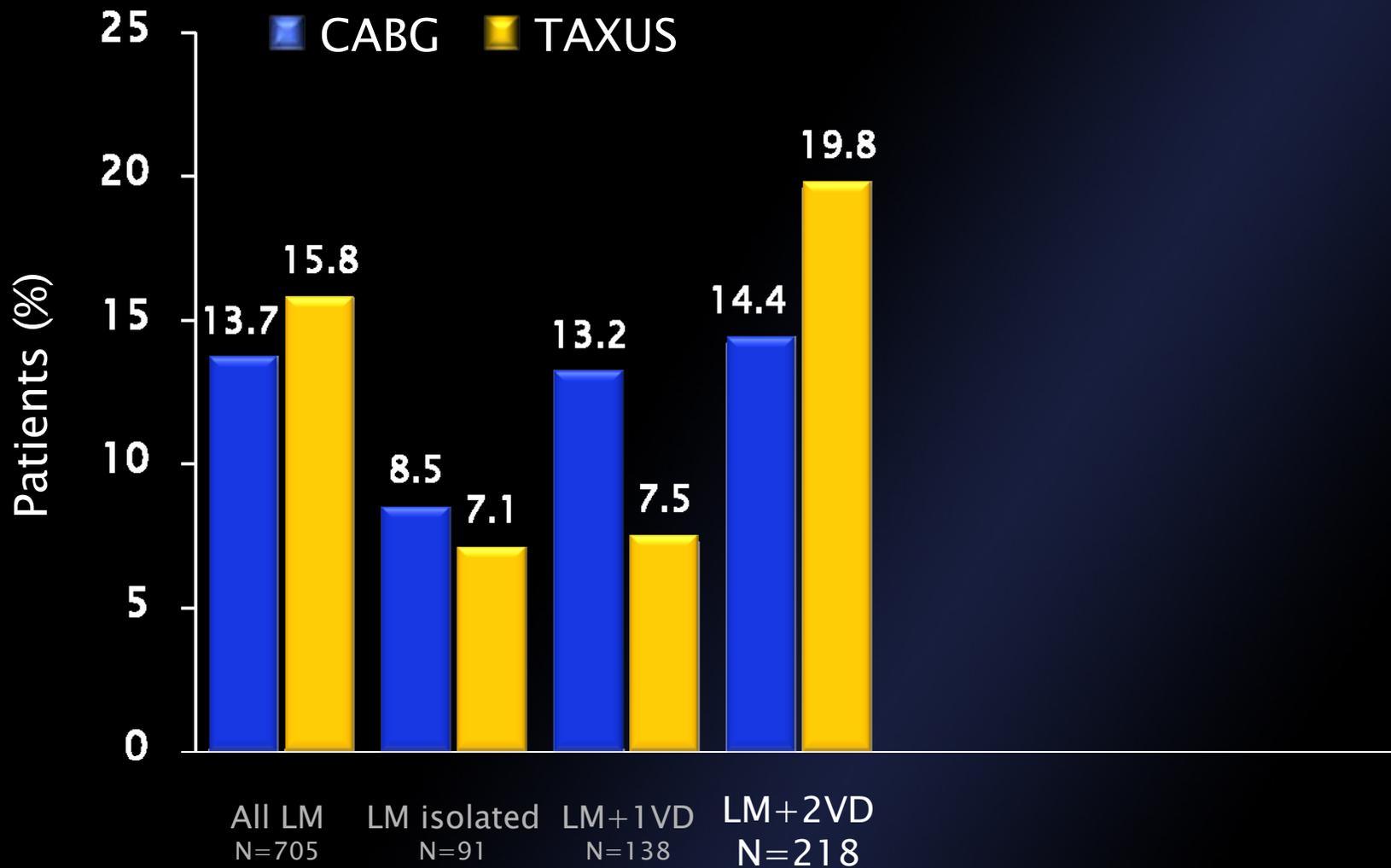
12 Month LM Subgroup MACCE Rates



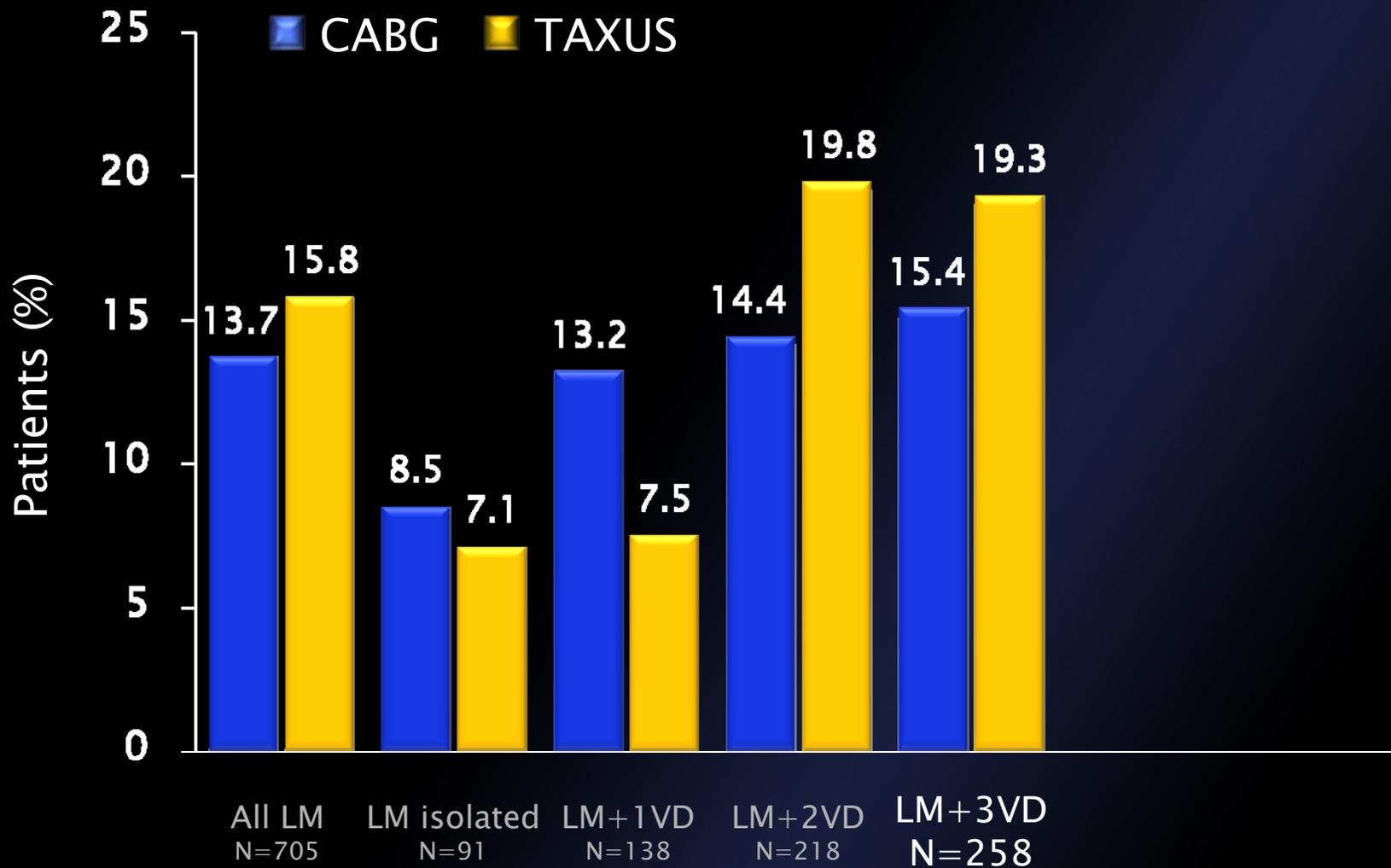
12 Month LM Subgroup MACCE Rates



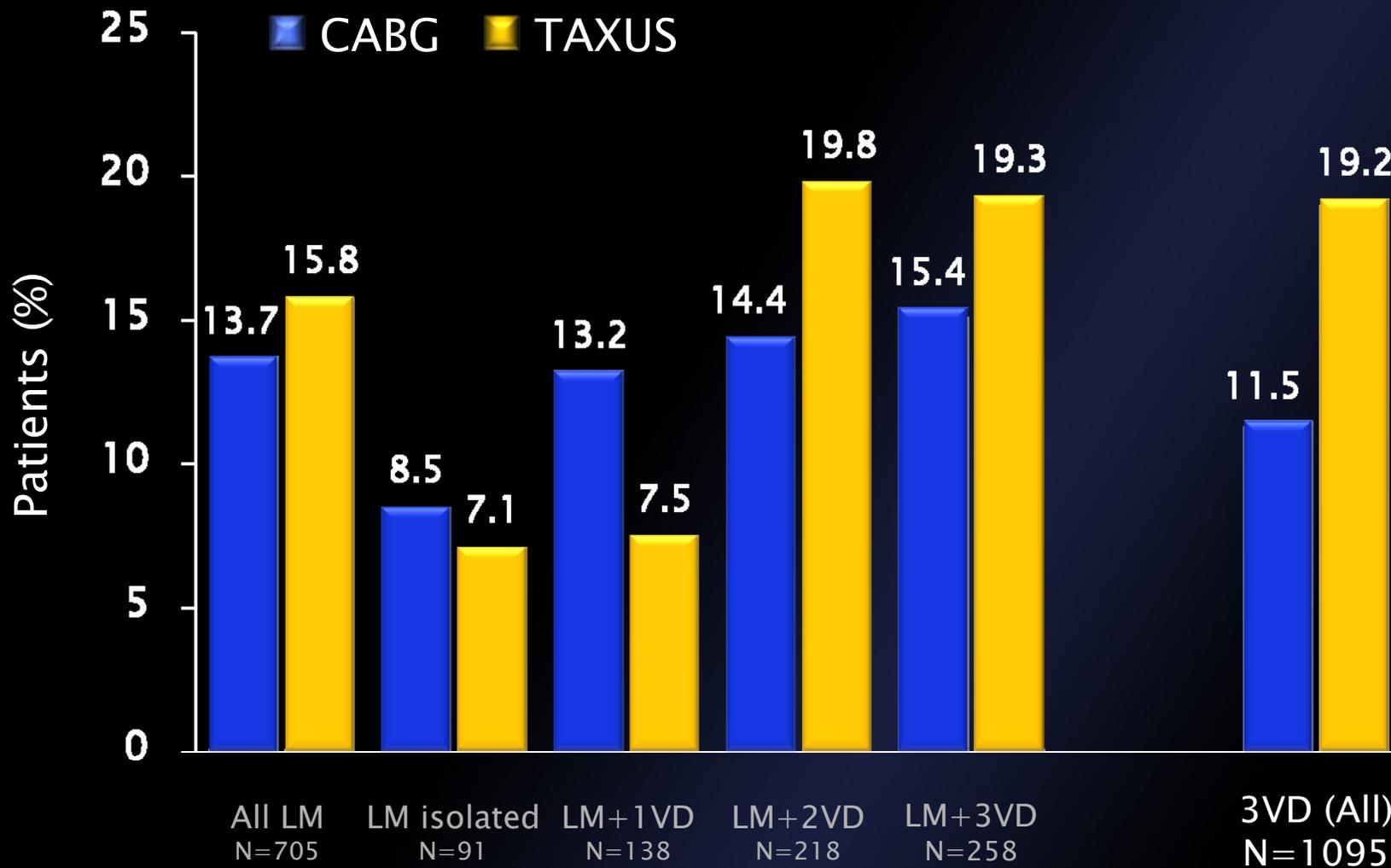
12 Month LM Subgroup MACCE Rates



12 Month LM Subgroup MACCE Rates



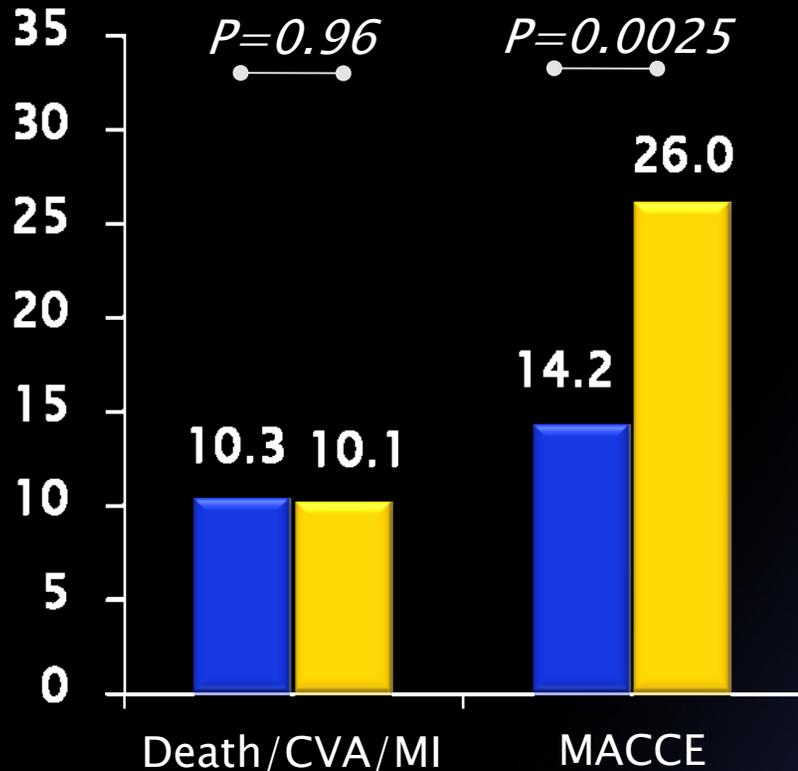
12 Month Subgroup MACCE Rates



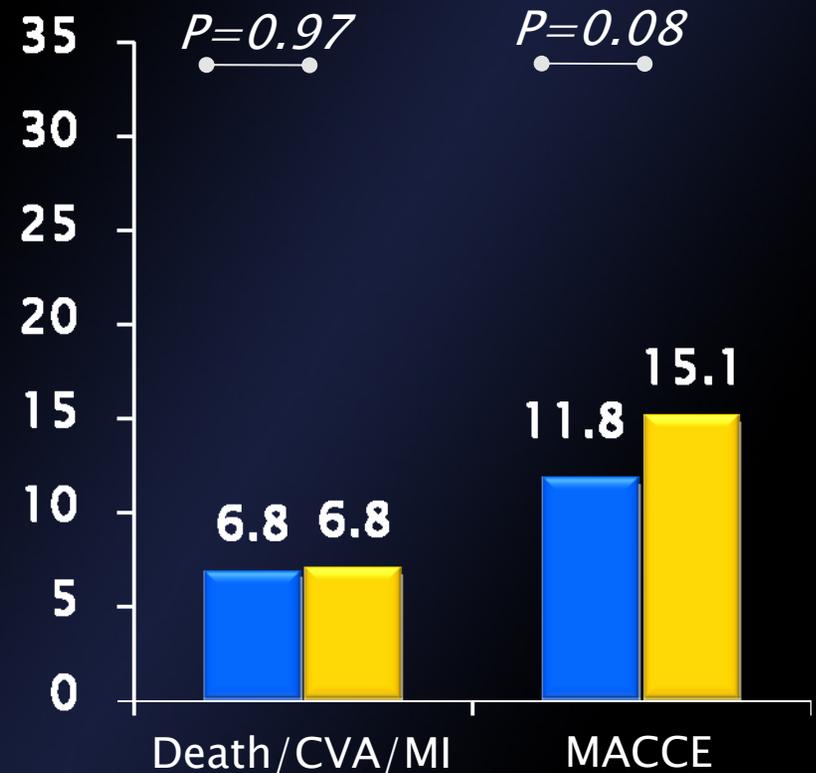
Outcome according to Diabetic Status



CABG TAXUS



Diabetic (Medical Treatment)
N=452



Non-Diabetic
N=1348

Predictors of 12 month MACCE: Pre-procedure



	Variable	Odds Ratio [95% CI]	<i>P</i> value [†]
CABG	COPD	2.45 [1.25, 4.80]	0.009
	Unstable Angina	1.88 [1.14, 3.09]	0.01
	Moderate or Poor LVEF	1.98 [1.13, 3.47]	0.02
	SYNTAX Score	0.97 [0.95, 1.00]	0.02
	Race	0.33 [0.14, 0.82]	0.02
	Emergent Revasc.	2.78 [1.08, 7.17]	0.03
	Prior MI	0.57 [0.33, 0.99]	0.045
	Age	1.03 [1.00, 1.05]	0.047
TAXUS	Medically Treated Diabetes	2.07 [1.40, 3.05]	<0.001
	SYNTAX Score	1.02 [1.00, 1.04]	0.02
	Age	1.02 [1.00, 1.04]	0.03

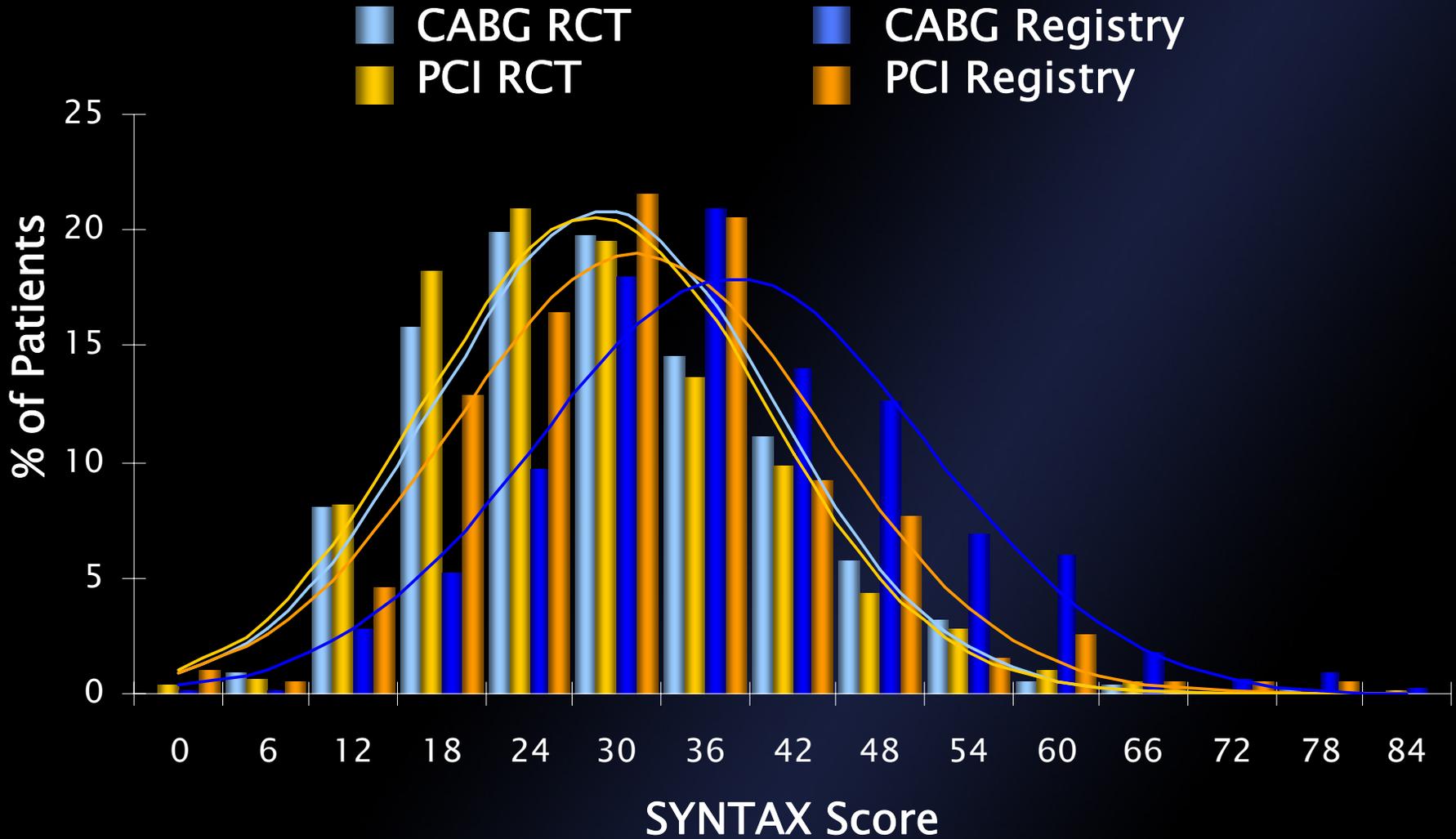
Multivariate Analysis: Procedure



	Variable	Odds Ratio [95% CI]	<i>P</i> value [†]
CABG	Blood Cardioplegia	0.38 [0.22, 0.67]	<0.001
	Procedure Time	1.38 [1.08, 1.76]	0.01
	Number of Distal Anastomosis	0.67 [0.48, 0.94]	0.02

TAXUS	Emergent Revasc.	0.54 [0.37, 0.78]	0.001
	Number of Vessels Treated	1.40 [1.04, 1.88]	0.03

SYNTAX Score Distribution by Cohort and Treatment Group



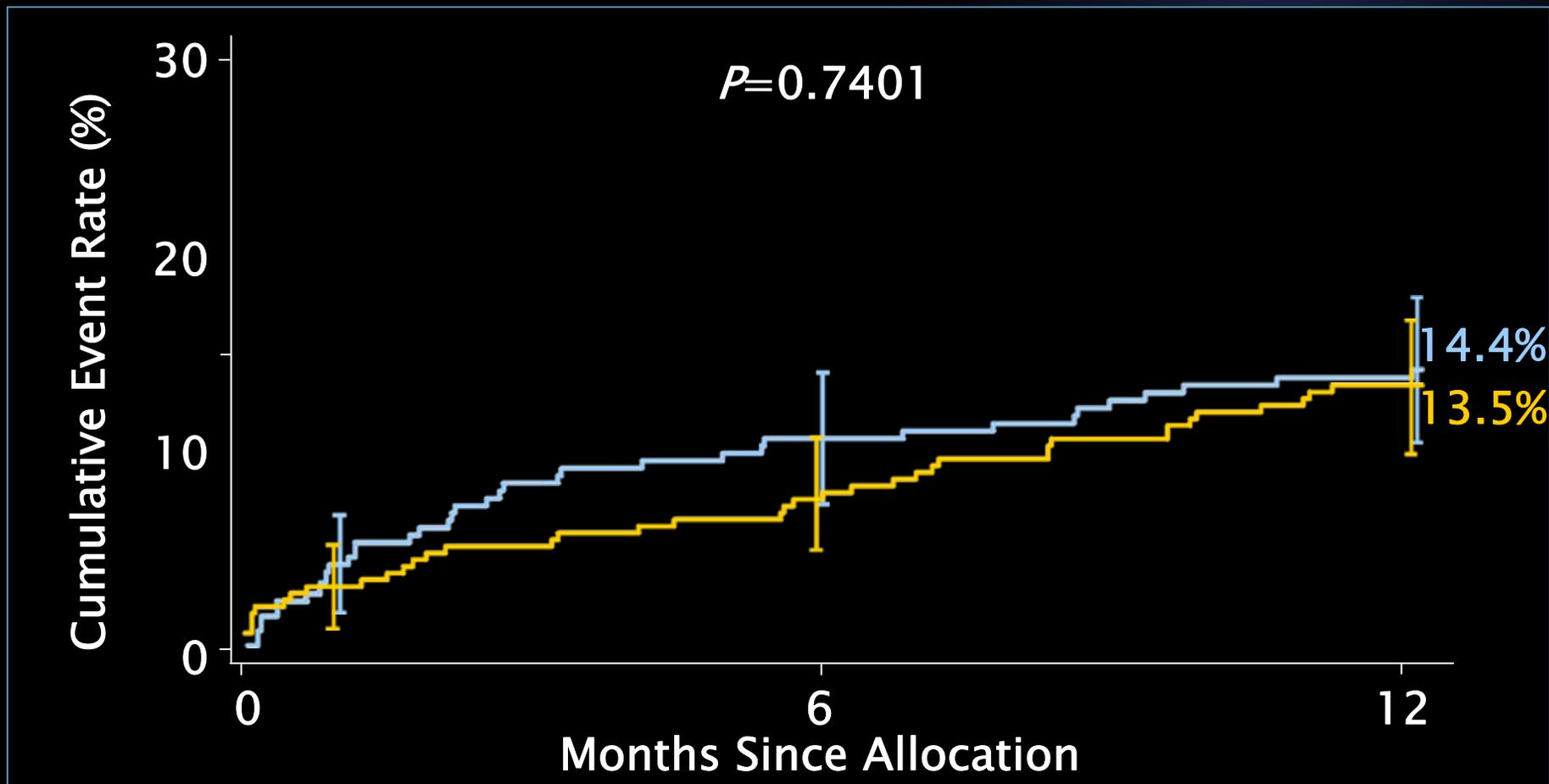
MACCE to 12 months *vs.* SYNTAX

Score: Low scores (0-22)



■ CABG (N=274)

■ TAXUS (N=299)



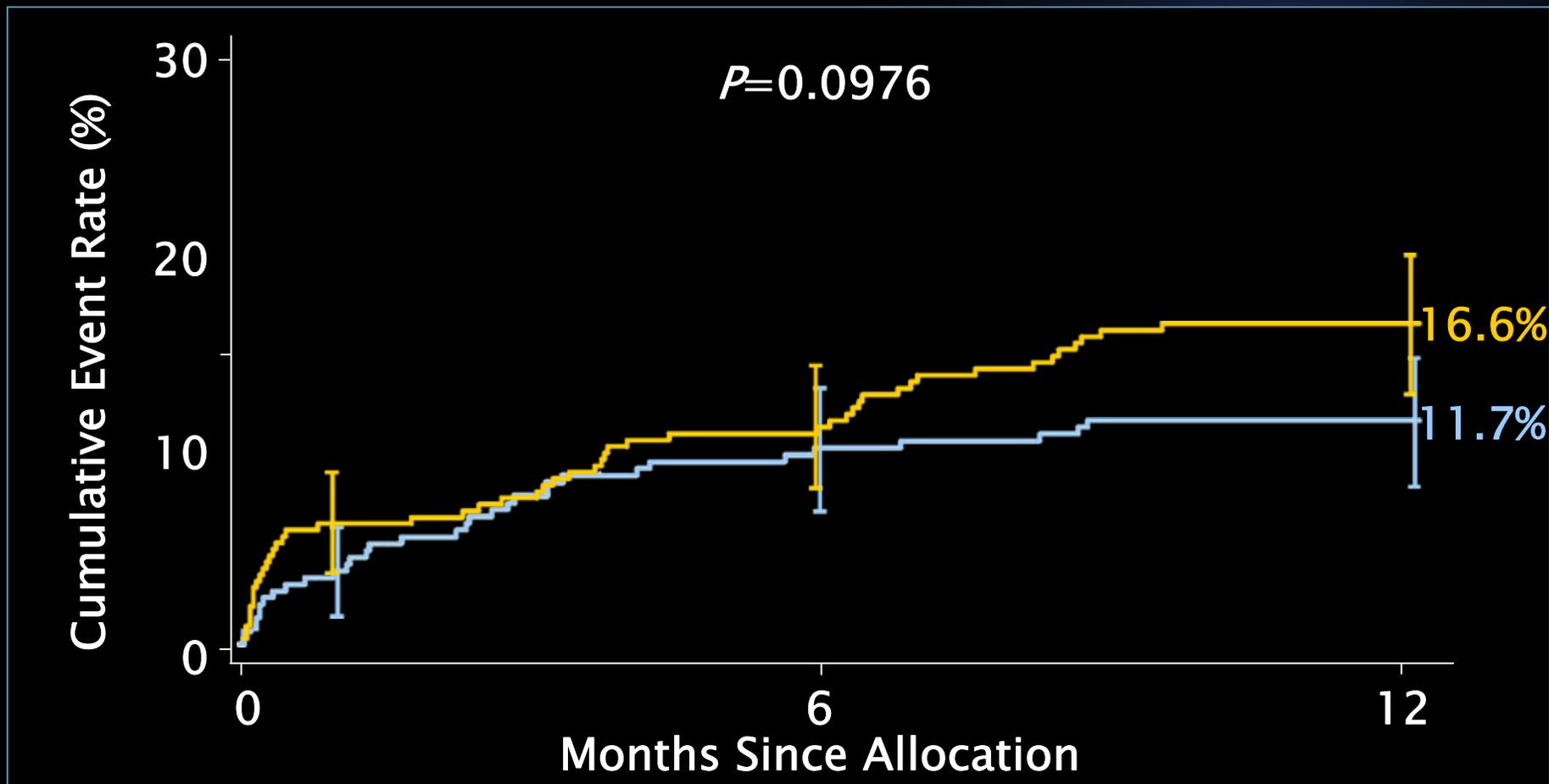
Event Rate \pm 1.5 SE; log-rank P value; raw SYNTAX score for illustrative purposes only

MACCE to 12 months *vs.* SYNTAX Score: Intermediate scores (23–32)



■ CABG (N=300)

■ TAXUS (N=310)



Event Rate \pm 1.5 SE; log-rank P value; raw SYNTAX score for illustrative purposes only

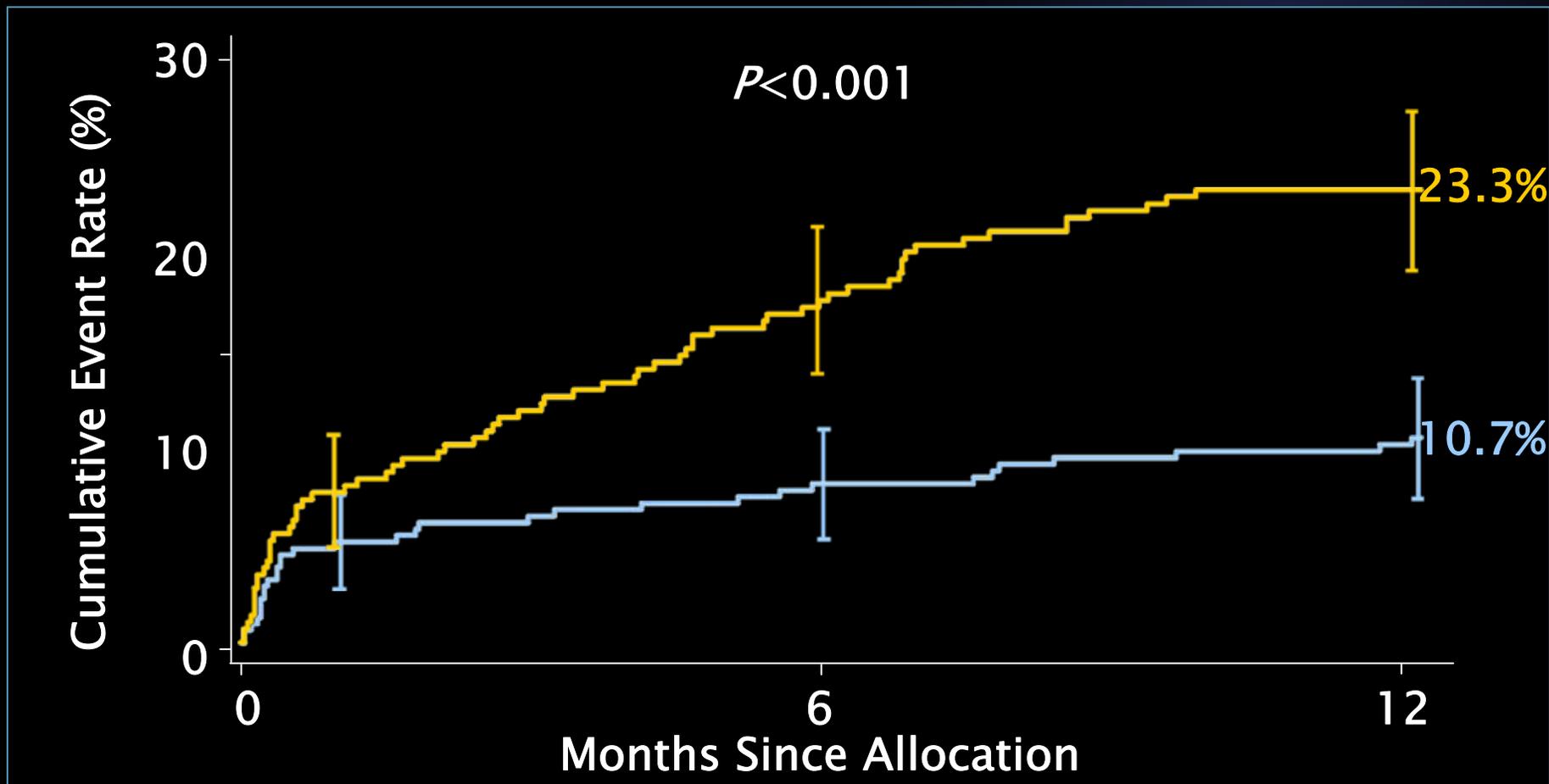
MACCE to 12 months vs. SYNTAX

Score: High scores (>33)



■ CABG (N=316)

■ TAXUS (N=290)

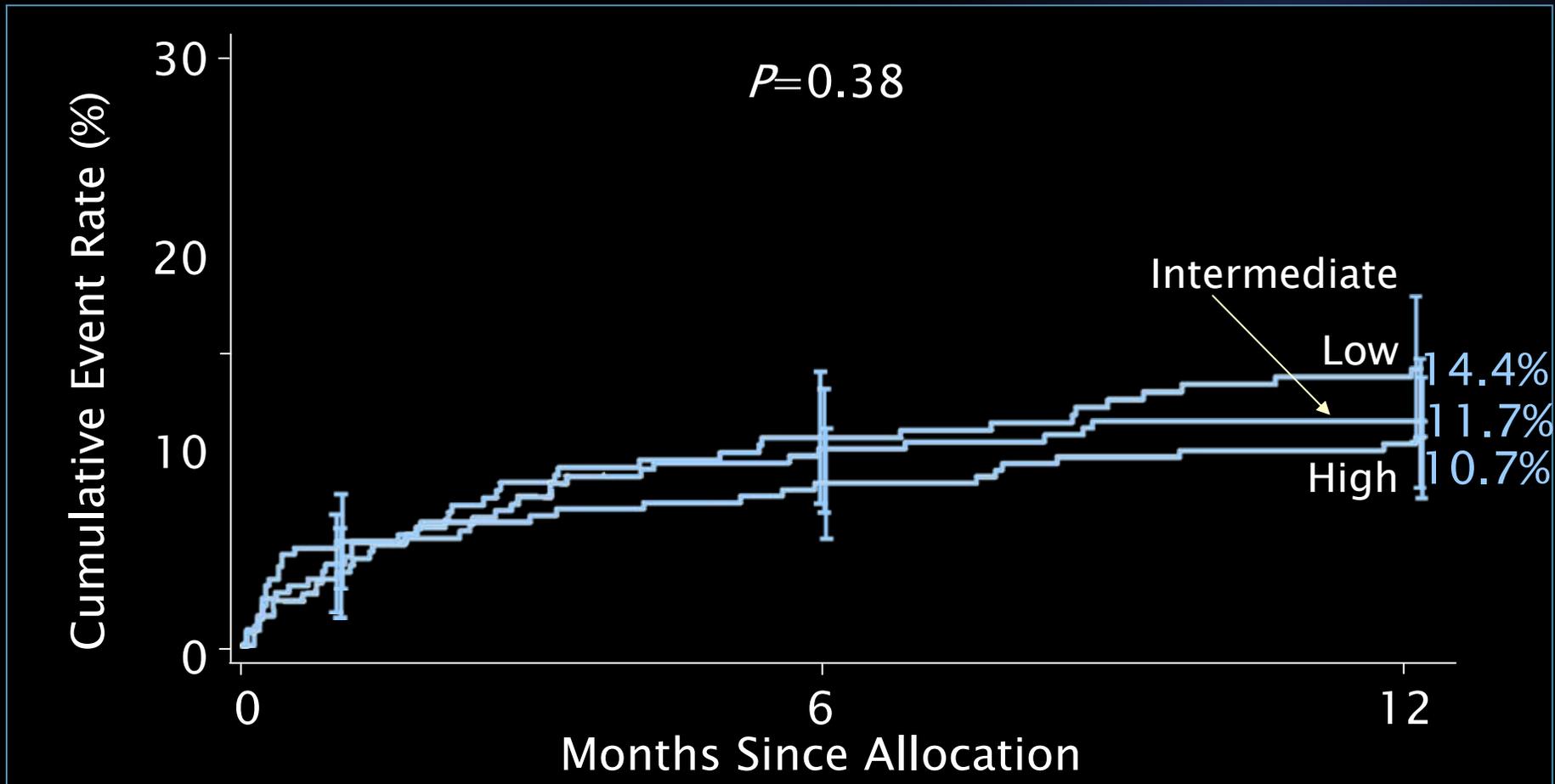


Event Rate \pm 1.5 SE; log-rank P value; raw SYNTAX score for illustrative purposes only

MACCE to 12 months vs. SYNTAX Score: CABG arm



Low: ≤ 22 (N=274) Intermediate: 23-32 (N=300) High: ≥ 33 (N=316)



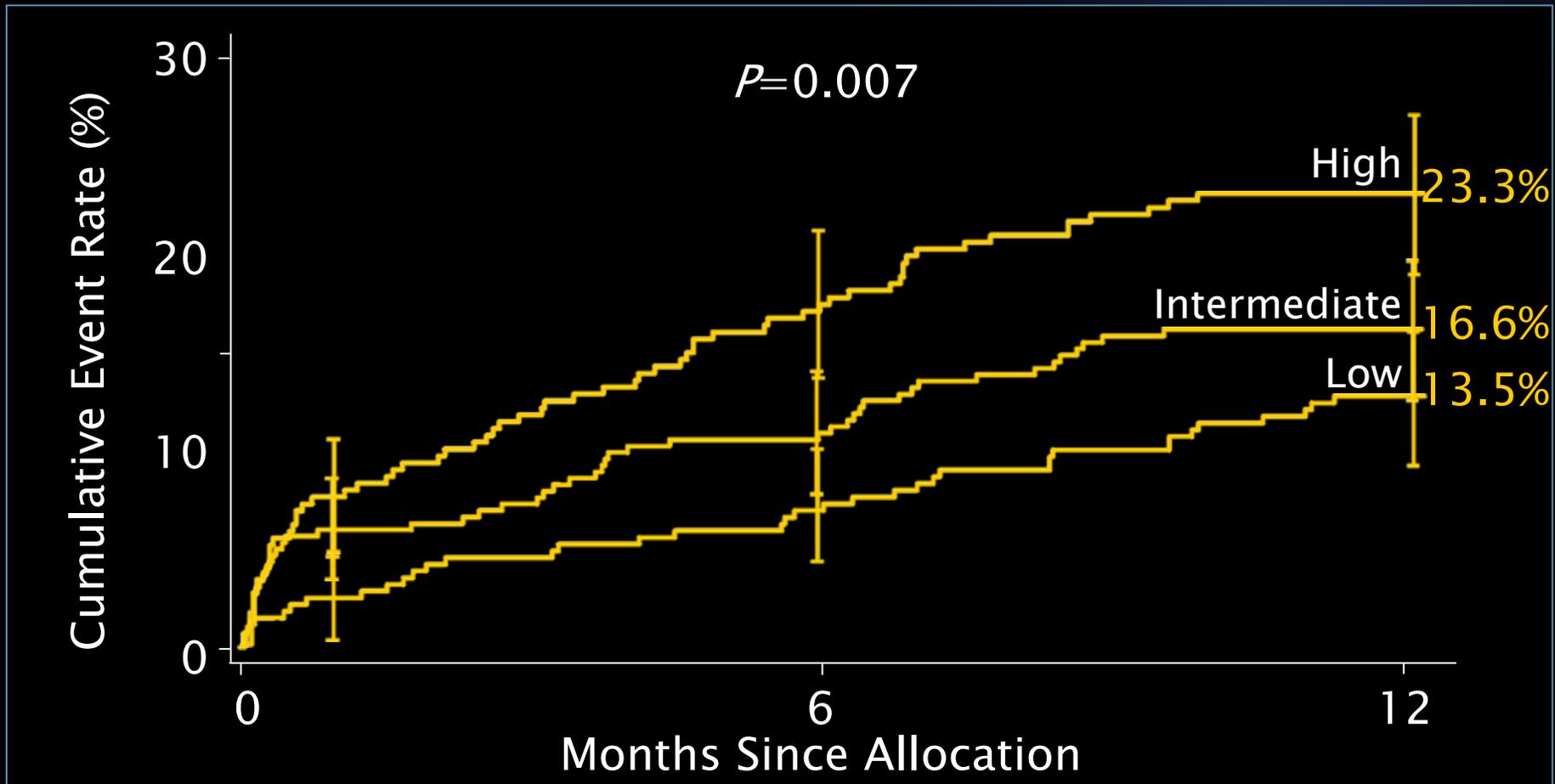
Event Rate ± 1.5 SE; log-rank P value; raw SYNTAX score for illustrative purposes only

RCT ITT pts; site-reported data

MACCE to 12 months vs. SYNTAX Score: TAXUS arm



Low: ≤ 22 (N=299) Intermediate: 23-32 (N=310) High: ≥ 33 (N=290)



Event Rate \pm 1.5 SE; log-rank P value; raw SYNTAX score for illustrative purposes only

RCT ITT pts; site-reported data

Conclusions:



- In the randomized SYNTAX cohort, there were comparable overall safety outcomes (Death, CVA, MI,) in CABG and PCI patients at 12 months (7.7 *vs.* 7.6 %).
- There was a significantly higher rate of revascularization in the PCI group (13.7 *vs.* 5.9 %), and a significantly higher rate of CVA in the CABG group (2.2 *vs.* 0.6 %).
- Overall MACCE in the PCI group was higher (17.8 *vs.* 12.1 %) due to an excess of redo revascularization compared with CABG.
- Per protocol rates of symptomatic graft occlusion and stent thrombosis were similar.
- The SYNTAX score will help stratify patients for the appropriate revascularization option.