Clinical, Angiographic, and IVUS Results from the Pivotal U.S. Randomized SPIRIT III Trial of the XIENCE™ V Everolimus-eluting Coronary Stent System

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for the SPIRIT III Investigators

Background

The XIENCE™ V DES elutes everolimus from a thin (7.8 um), robust, durable biocompatible fluoropolymer, incorporating thin cobalt chromium stent struts (0.0032”) for enhanced flexibility and deliverability.

The 300 pt randomized SPIRIT II trial found that the XIENCE™ V stent compared to the TAXUS stent reduced angiographic late loss at 6 months (0.11 ± 0.27 mm vs. 0.36 ± 0.39 mm, P<0.0001).

The SPIRIT III trial was thus designed as the U.S. pivotal approval study for the XIENCE™ V stent.

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Study Algorithm

1002 pts enrolled at 65 U.S sites

RVD ≥2.5 mm - ≤3.75 mm; Lesion length ≤28 mm

Max. 2 lesions each in a different epicardial vessel

Pre-rand: ASA ≥ 300 mg, clopidogrel ≥300 mg load unless on chronic Rx

Randomized 2:1 XIENCE V:TAXUS

Stratified by diabetes and intent for 1 vs. 2 lesion treatment

Pre-dilatation mandatory

Everolimus-eluting

XIENCE V

Paclitaxel-eluting

TAXUS

Aspirin ≥ 80 mg QD for 5 years; Clopidogrel 75mg QD for ≥6 months

Clinical f/u: 1, 6, 9 months and yearly for 1-5 years

Angio f/u (N=564) @ 8 mos; IVUS f/u (N=240) @ 8 mos

SPIRIT III Endpoints

- **Primary Endpoint:** In-segment late loss (LL) at 8 months
  - Assume LL = 0.24 ± 0.47 mm in both arms
  - Non-inferiority margin = 0.195 mm, one-sided α = 0.025
  - 564 total pts ⇒ 99% power (assuming 10% dropout)
  - Pre-specified sequential non-inferiority and superiority tests
  - In pts with 2 lesions, primary endpoint analysis based on a randomly assigned "analysis lesion"
- **Major Secondary Endpoint:** Ischemia-driven target vessel failure (TVF) at 9 months
  - Assume TVF rate = 9.4% in both arms
  - Non-inferiority margin = 5.5%, one-sided α = 0.05
  - 1,002 total pts ⇒ 89% power (assuming 1% dropout)
- **Both 1° and major 2° endpoints must be met for success**

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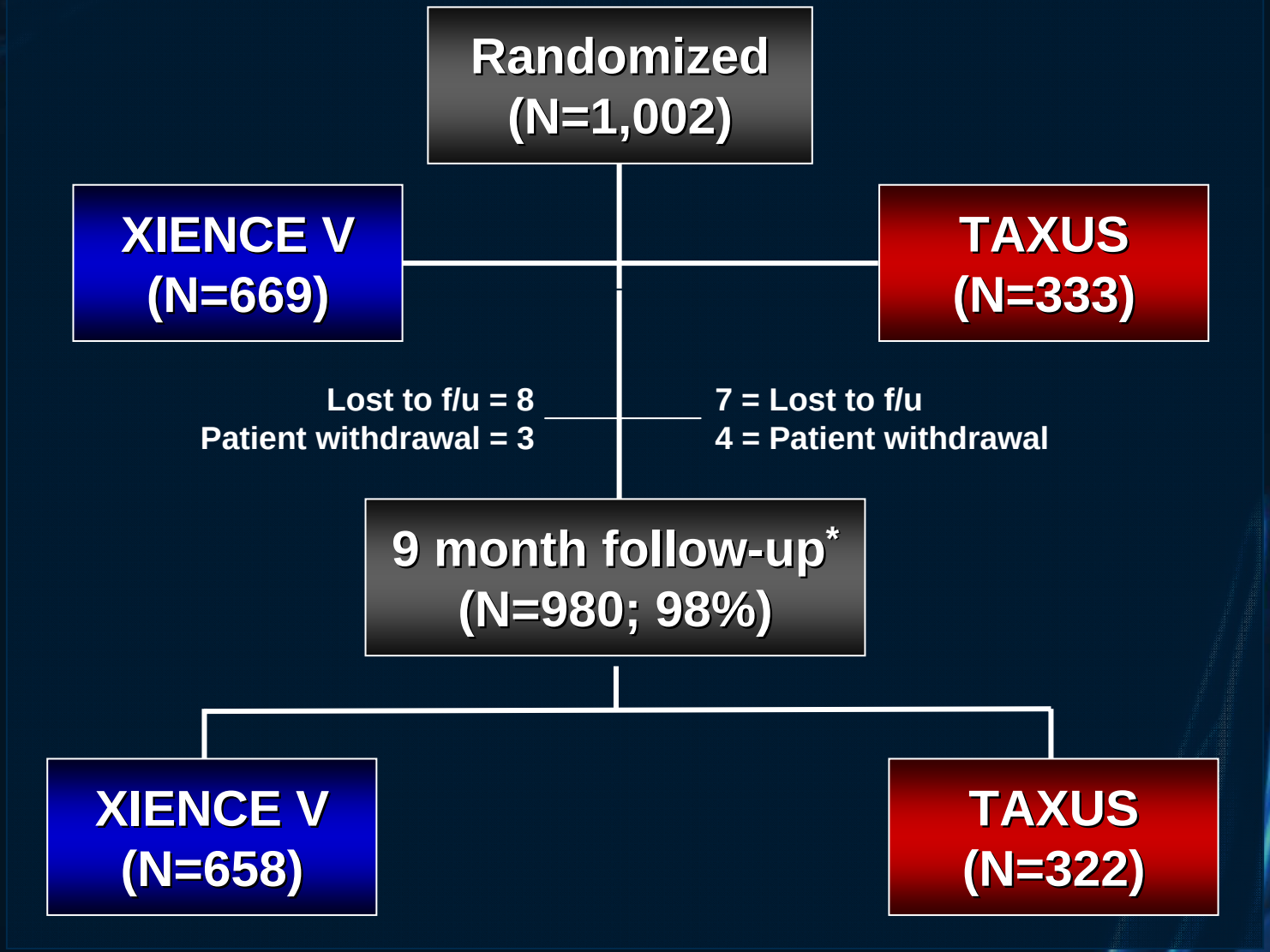
Patient Flow - Clinical



*F/U window ±14 days

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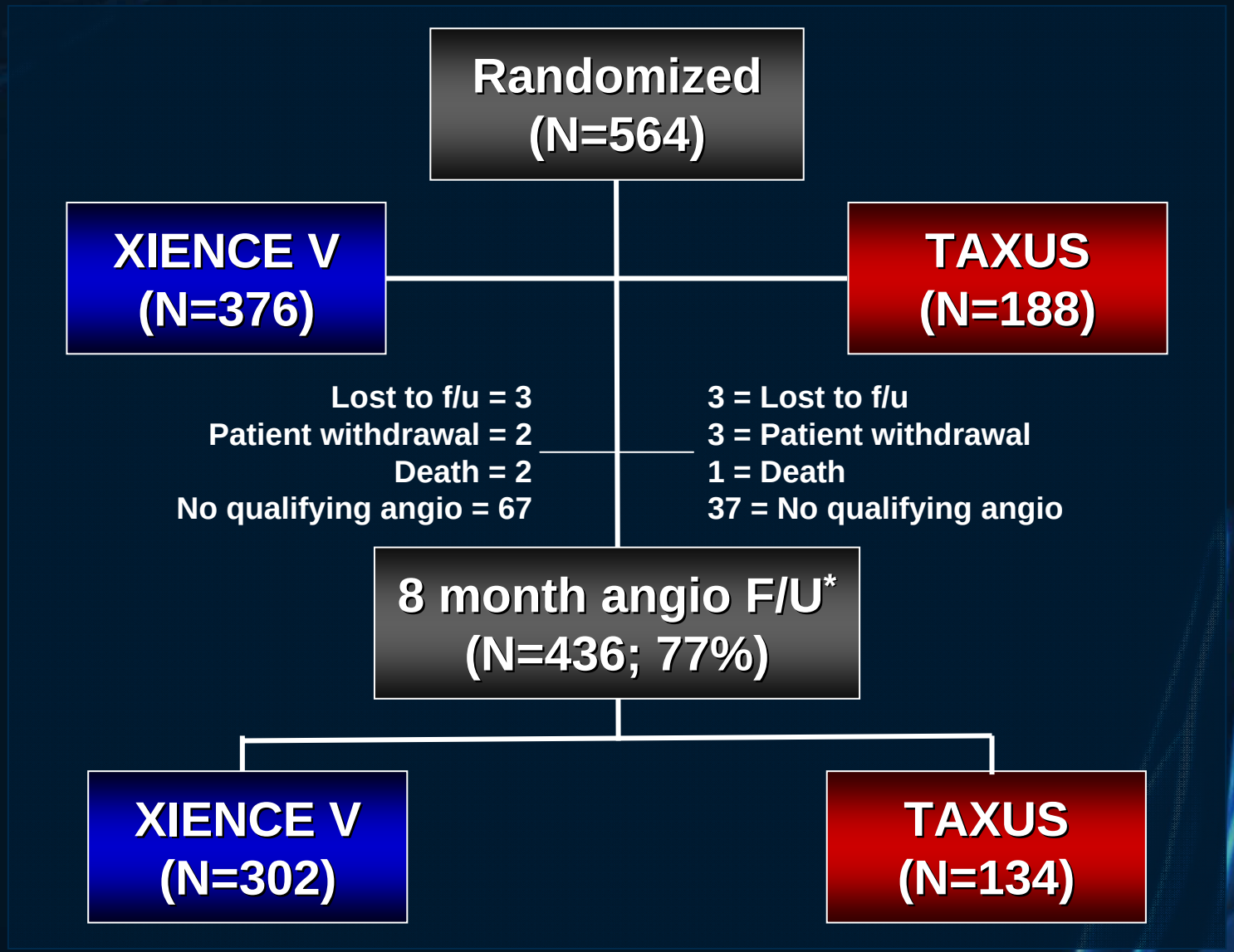
Patient Flow - Angiographic



*F/U window: ± 28 days

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Baseline Demographics

	XIENCE V 669 pts	TAXUS 333 pts	P value
Age (in years)	63.2 ± 10.5	62.8 ± 10.2	0.54
Male (%)	70.1	65.7	0.17
Hypertension (%)	76.2	74.0	0.48
Hypercholesterolemia (%)	74.2	71.5	0.36
Diabetes mellitus (%)	29.6	27.9	0.60
Insulin requiring (%)	7.8	5.5	0.19
Current smoker (%)	23.4	22.5	0.81
Prior MI (%)	19.9	18.0	0.49
Unstable angina (%)	18.7	25.1	0.02

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Baseline Angiography

	XIENCE V 767 lesions	TAXUS 382 lesions	P value
Lesion location			
LAD	41.3%	42.9%	0.61
LCX	27.6%	28.3%	0.83
RCA	31.0%	28.5%	0.41
LMCA	0.1%	0.3%	0.55
QCA			
RVD (mm)	2.77 ± 0.45	2.76 ± 0.46	0.87
MLD (mm)	0.82 ± 0.41	0.83 ± 0.40	0.79
% DS	70.0 ±13.3	69.4 ±13.6	0.54
Lsn length (mm)	14.7 ± 5.6	14.7 ± 5.7	0.92

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Procedural Results

	XIENCE V 669 pts 768 lesions	TAXUS 332 pts 382 lesions	P value
# lesions/pt*	1.2 ± 0.4	1.2 ± 0.4	1.0
2 lesion pts*	15.4%	15.4%	1.0
# stents/pt†	1.3 ± 0.6	1.3 ± 0.5	0.27
# stents/lesion†	1.2 ± 0.4	1.1 ± 0.3	0.07
Max. stent diameter/lesion (mm)	3.0 ± 0.4	3.0 ± 0.4	1.0
Max. stent diameter/RVD	1.1 ± 0.1	1.1 ± 0.1	0.56
Total stent length/lesion	22.8 ± 8.4	21.6 ± 7.8	0.02
Total stent length/lesion length	1.6 ± 0.5	1.5 ± 0.5	0.01
Maximum pressure (atm.)	14.8 ± 2.9	15.1 ± 2.6	<0.05

* All vessels had a single lesion except 5 pts in whom a single vessel had two lesions
† Of 1,322 total stents implanted, 8 were non study stents

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Post Procedure QCA

	XIENCE V 766 lesions	TAXUS 379 lesions	P value
RVD (mm)	2.84 ± 0.45	2.84 ± 0.46	0.74
Acute gain (mm)			
In-segment	1.54 ± 0.51	1.53 ± 0.50	0.62
In-stent	1.89 ± 0.48	1.91 ± 0.47	0.56
MLD (mm)			
In-segment	2.37 ± 0.45	2.36 ± 0.45	0.73
In-stent	2.71 ± 0.43	2.74 ± 0.41	0.38
% DS			
In-segment	13.5 ±7.6	14.4 ± 7.1	0.06
In-stent	0.3 ± 8.9	-0.2 ± 9.9	0.37

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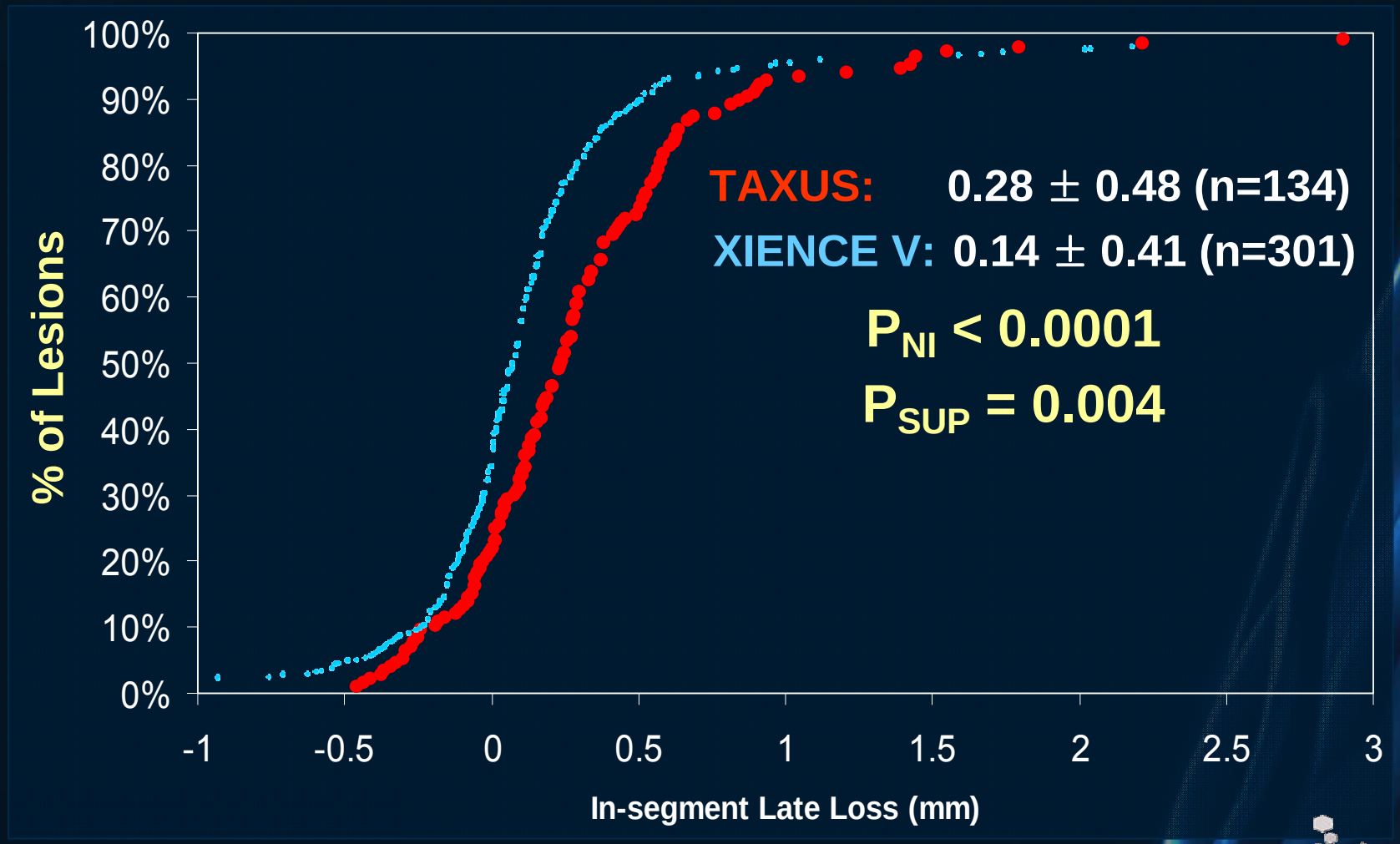
Primary Endpoint: In-segment LL at 8 Months*

(Analysis Lesion)



*F/U window ±28 days.

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Late Loss at 8 Months*

	XIENCE V 301 patients	TAXUS 134 patients	P value
Analysis lesion	301 lesions	134 lesions	
In-segment	0.14 ± 0.41	0.28 ± 0.48	0.004
In-stent	0.16 ± 0.41	0.31 ± 0.55	0.006
All lesions	343 lesions	158 lesions	
In-segment	0.14 ± 0.39	0.26 ± 0.46	0.003
In-stent	0.16 ± 0.41	0.30 ± 0.53	0.002

*F/U window ±28 days.

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QCA at 8 Months*
(All Lesions)

	XIENCE V 344 lesions	TAXUS 158 lesions	P value
RVD (mm)	2.77 ± 0.43	2.78 ± 0.42	0.84
MLD (mm)			
In-segment	2.22 ± 0.53	2.12 ± 0.60	0.08
In-stent	2.56 ± 0.53	2.45 ± 0.65	0.07
% DS			
In-segment	18.8 ± 14.4	22.8 ± 16.4	0.008
In-stent	5.9 ± 16.4	10.3 ± 21.4	0.02

*F/U window ±28 days.

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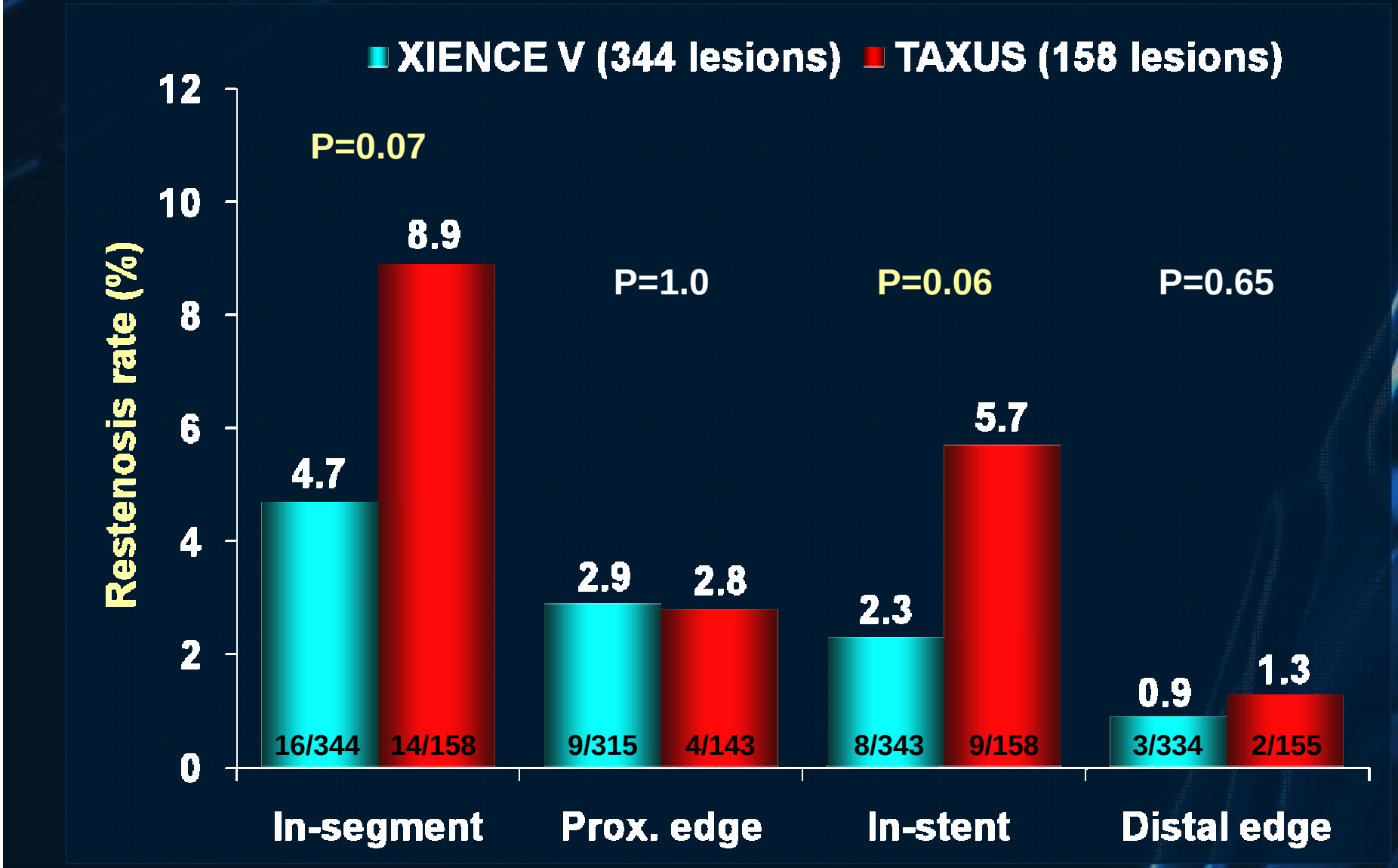
Binary Restenosis at 8 Months*



*F/U window ±28 days.

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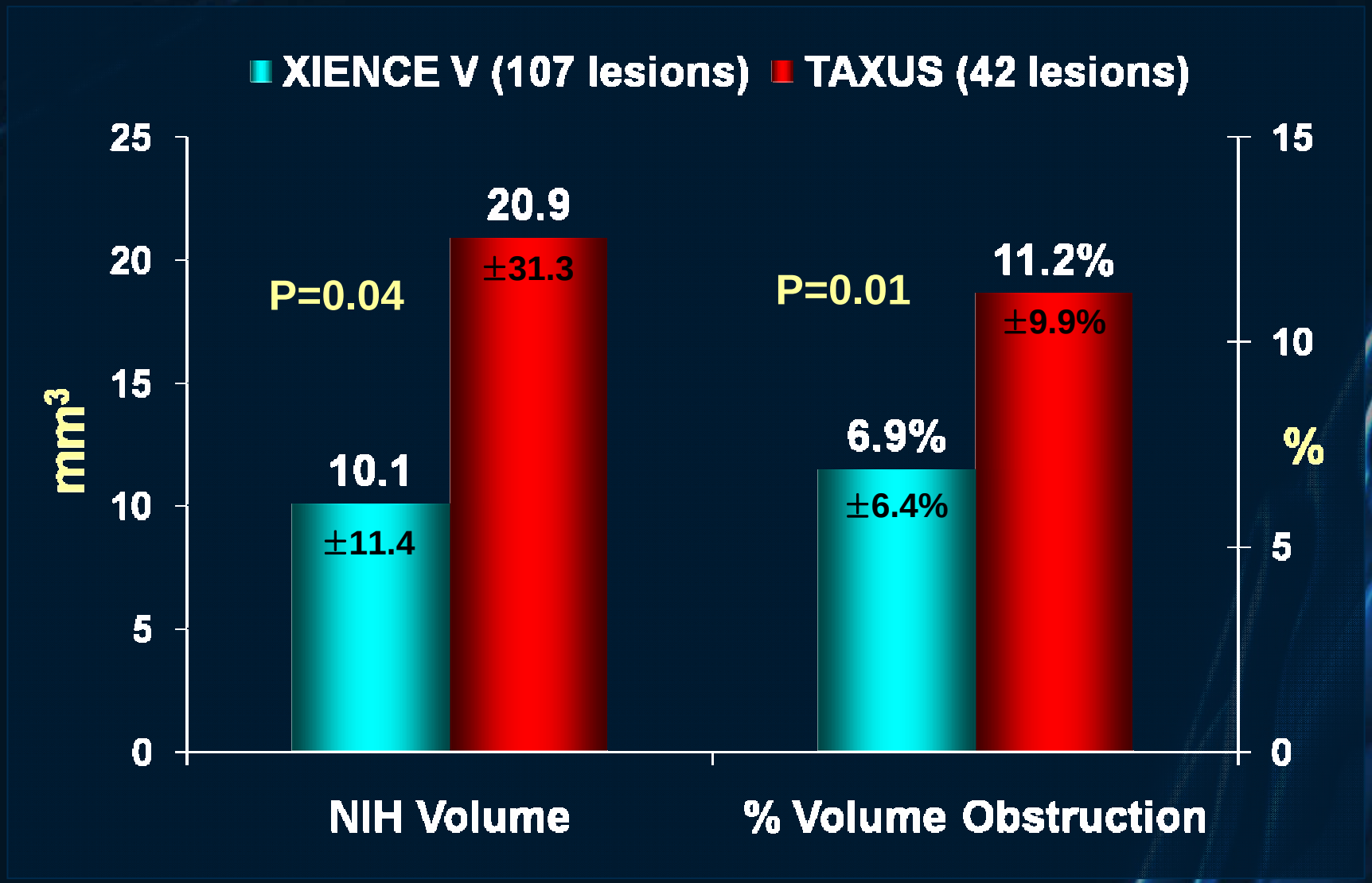
IVUS In-stent Measures at 8 Months*



*F/U window ±28 days.

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IVUS Incomplete Apposition
(Paired lesion serial analysis)

	XIENCE V 90 lesions	TAXUS 43 lesions	P value
Post procedure	34.4%	25.6%	0.33
8 months	25.6%	16.3%	0.27
Resolved	8.9%	9.3%	1.0
Persisting	24.4%	14.0%	0.18
Late acquired	1.1%	2.3%	0.54

IVUS performed in only 1 pt with stent thrombosis, showing no incomplete apposition either post procedure or at FU

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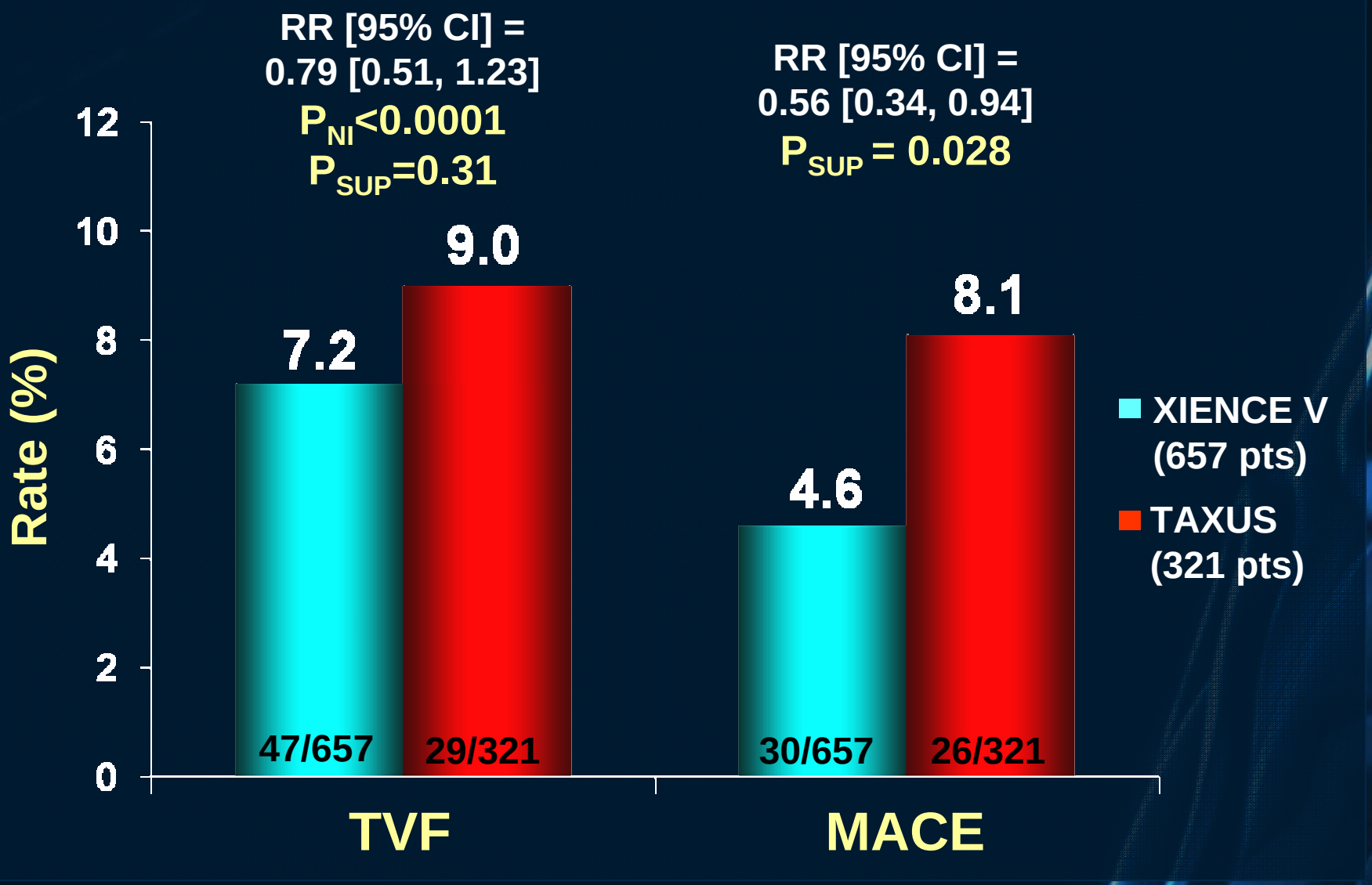
TVF and MACE Through 270 Days*



*F/U window ±14 days. TVF = Cardiac death, MI, ischemia-driven TVR.
MACE = Cardiac death, MI, ischemia-driven TLR.

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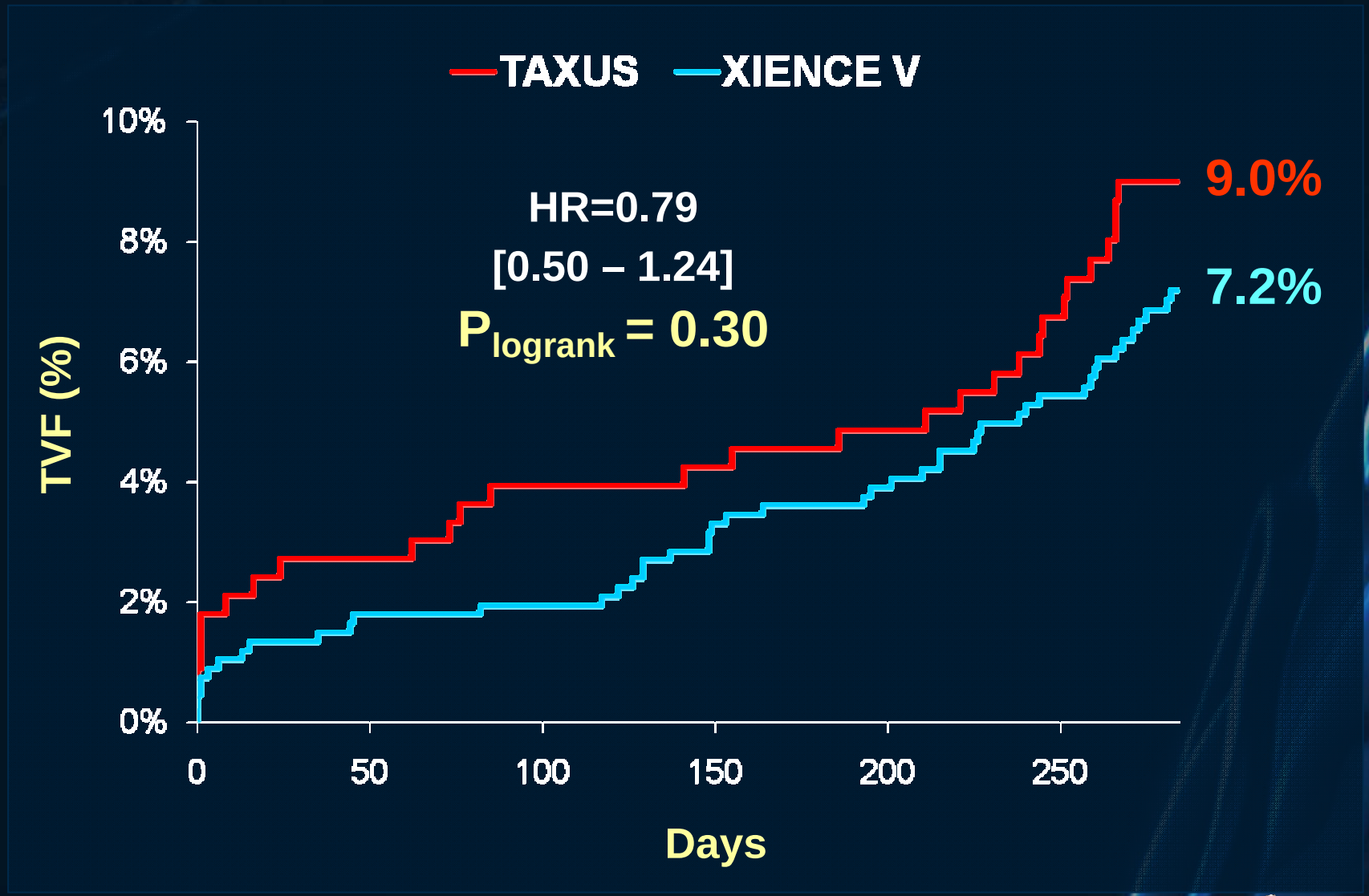
TVF Through 284 Days



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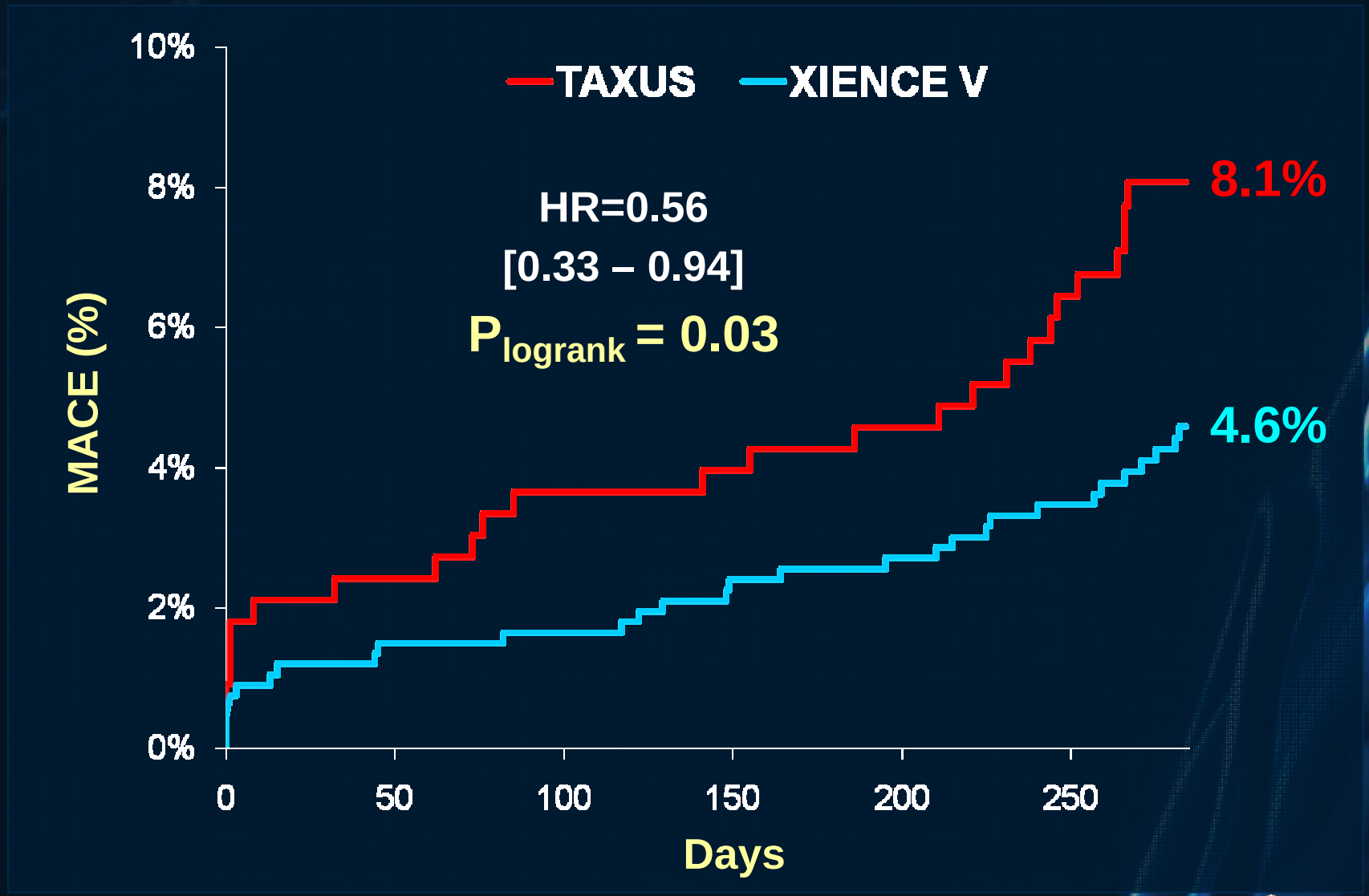
MACE Through 284 Days



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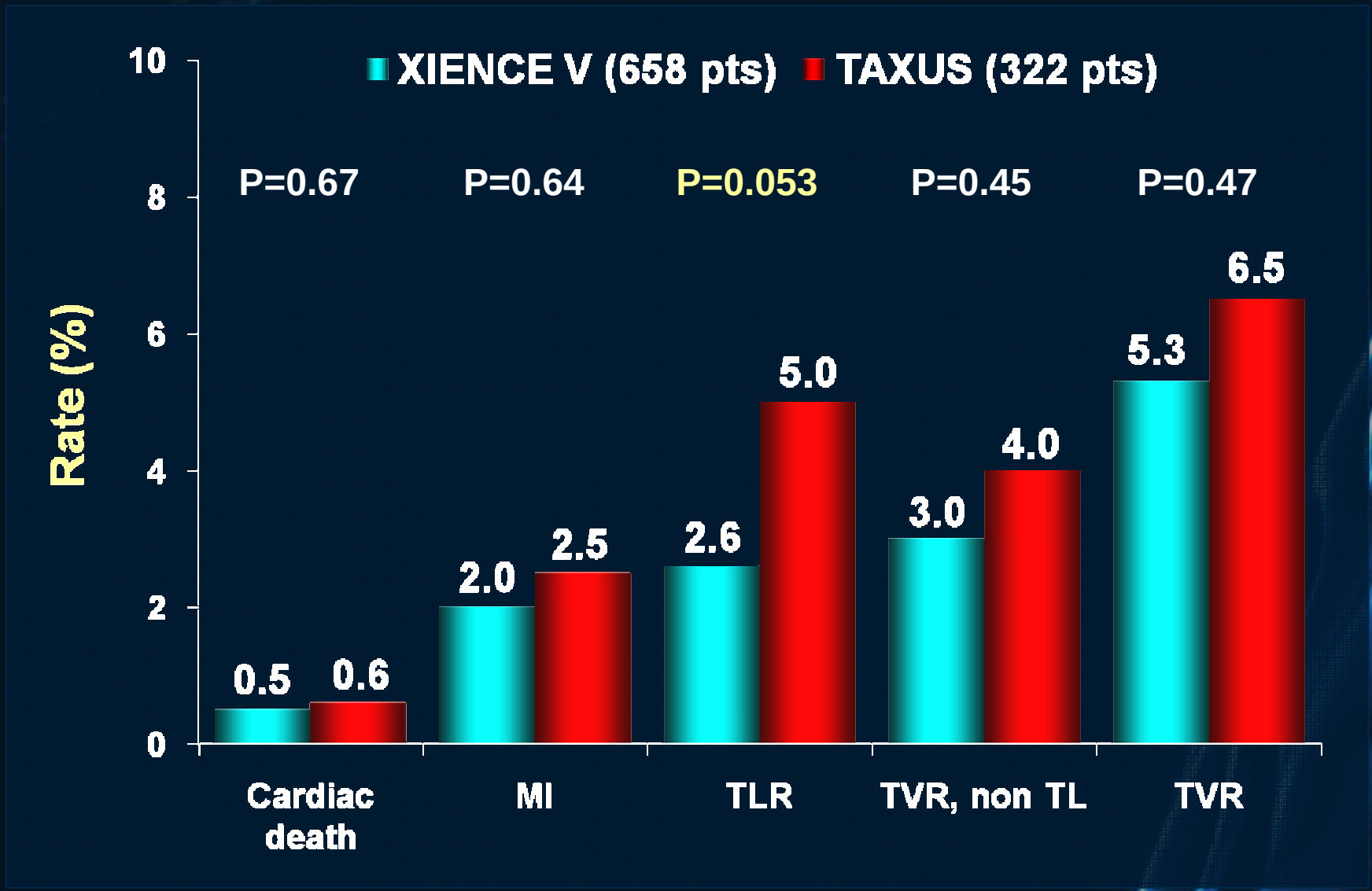
TVF Components Through 270 Days*



*F/U window ±14 days.

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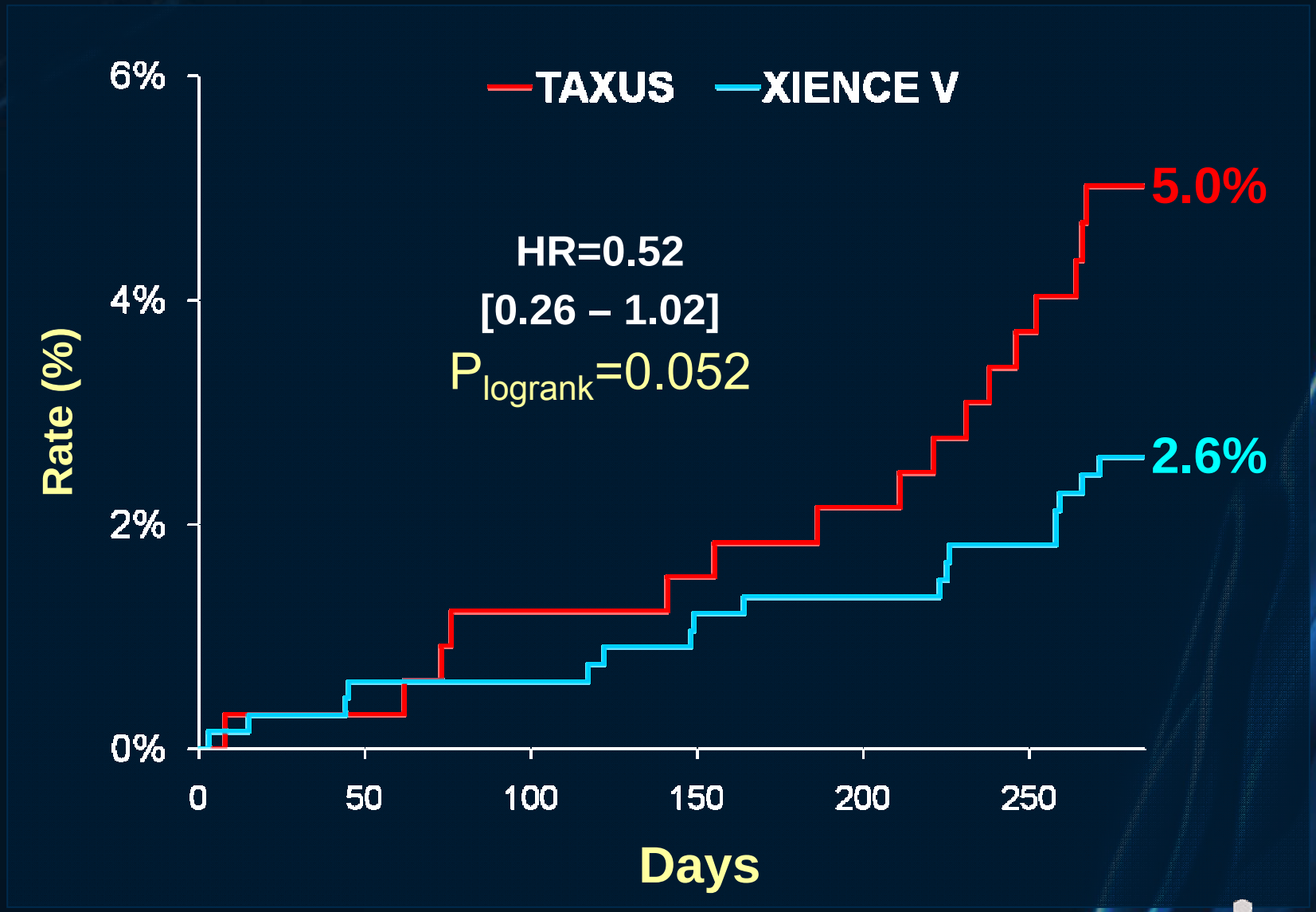
Ischemia-driven TLR Through 284 Days



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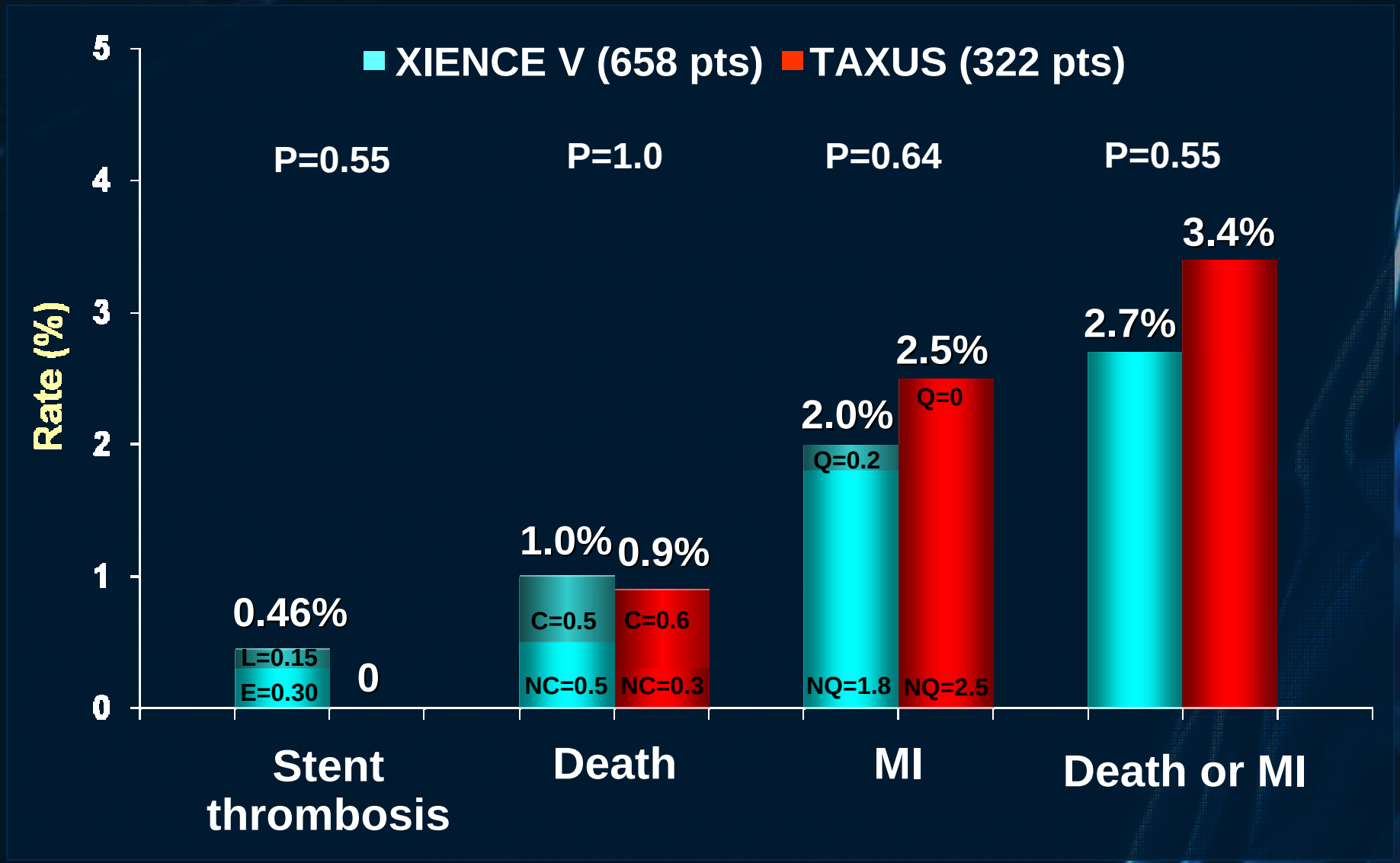
Safety Endpoints at 270 Days*



*F/U window ±14 days. E = early (≤30d); L = late (>30d-9mo);
C = cardiac; NC = non cardiac; Q = Q-wave; NQ = non Q-wave

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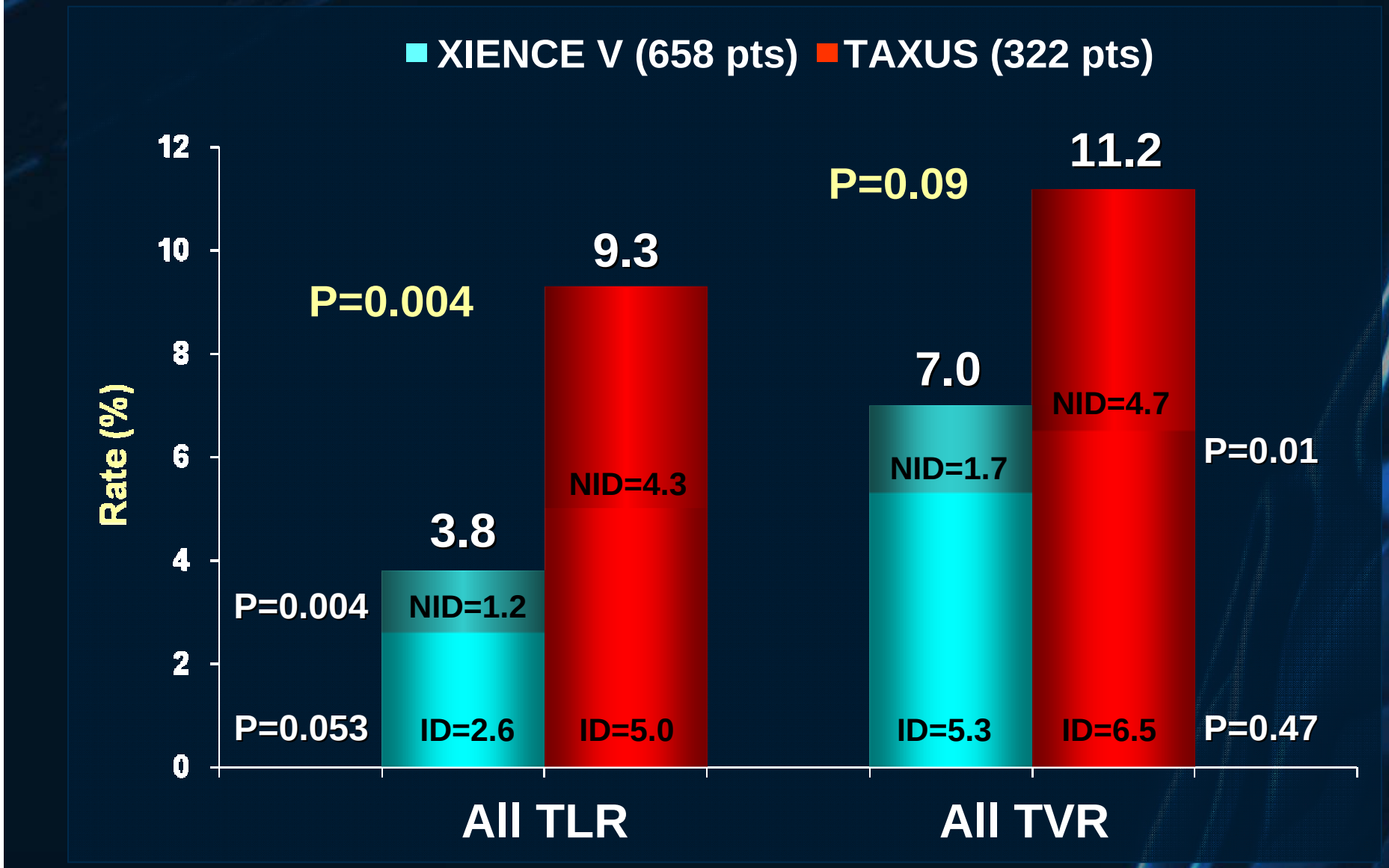
All Revascularization Through 270 Days*



*F/U window ±14 days. ID=ischemia-driven; NID=non ischemia-driven

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Conclusions I

- **In the large, multicenter, randomized SPIRIT III trial, the everolimus-eluting XIENCE V stent compared to the paclitaxel-eluting TAXUS stent:**
  - **Was both non-inferior and superior in reducing in-segment late loss, the primary endpoint of the trial**
  - **Significantly reduced in-stent late loss at 8 months**
  - **Reduced angiographic FU diameter stenosis with a strong trend toward lower binary restenosis**
  - **Resulted in a significant reduction in in-stent volume obstruction without excess late acquired malapposition**

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Conclusions II

- **In the large, multicenter, randomized SPIRIT III trial, the everolimus-eluting XIENCE V stent compared to the paclitaxel-eluting TAXUS stent:**
  - **Demonstrated non-inferior rates of TVF at 9 months, with a significant 44% reduction in MACE**
  - **Showed a strong trend toward reduced ischemia-driven TLR, with a significant reduction in any TLR**
  - **Had similar rates of death, MI and stent thrombosis**
- **The primary and major secondary endpoints of the SPIRIT III trial were met**

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