

**A Large-Scale Randomized Comparison of
Everolimus-Eluting and Paclitaxel-Eluting Stents:
Two-Year Clinical Outcomes
from the SPIRIT IV Trial**

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Spirit IV

Disclosures

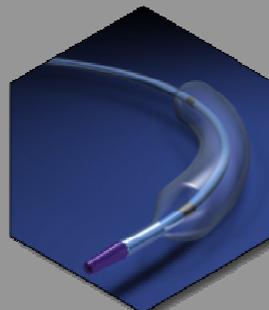
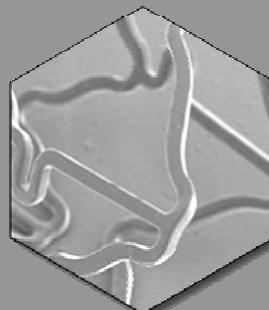
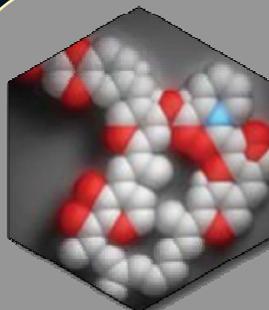
- **Gregg W. Stone, MD**
 - **Scientific advisory boards for and honoraria from Abbott Vascular and Boston Scientific**
 - **Consultant to Medtronic**



XIENCE V / PROMUS Everolimus-eluting Stent

Everolimus

**ML VISION®
Stent Platform**



**Durable
Fluorinated
Copolymer**

**ML VISION
Stent Delivery
System**

**EES vs. PES
SPIRIT
Clinical Trials**

Study Algorithm

3690 pts enrolled at 66 U.S. sites

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

Max. 3 lesions with a maximum of 2 per epicardial vessel

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

Randomized 2:1 XIENCE V:TAXUS Express²

Stratified by diabetes and presence of complex lesions

Pre-dilatation mandatory

Everolimus-eluting

XIENCE V

Paclitaxel-eluting

TAXUS

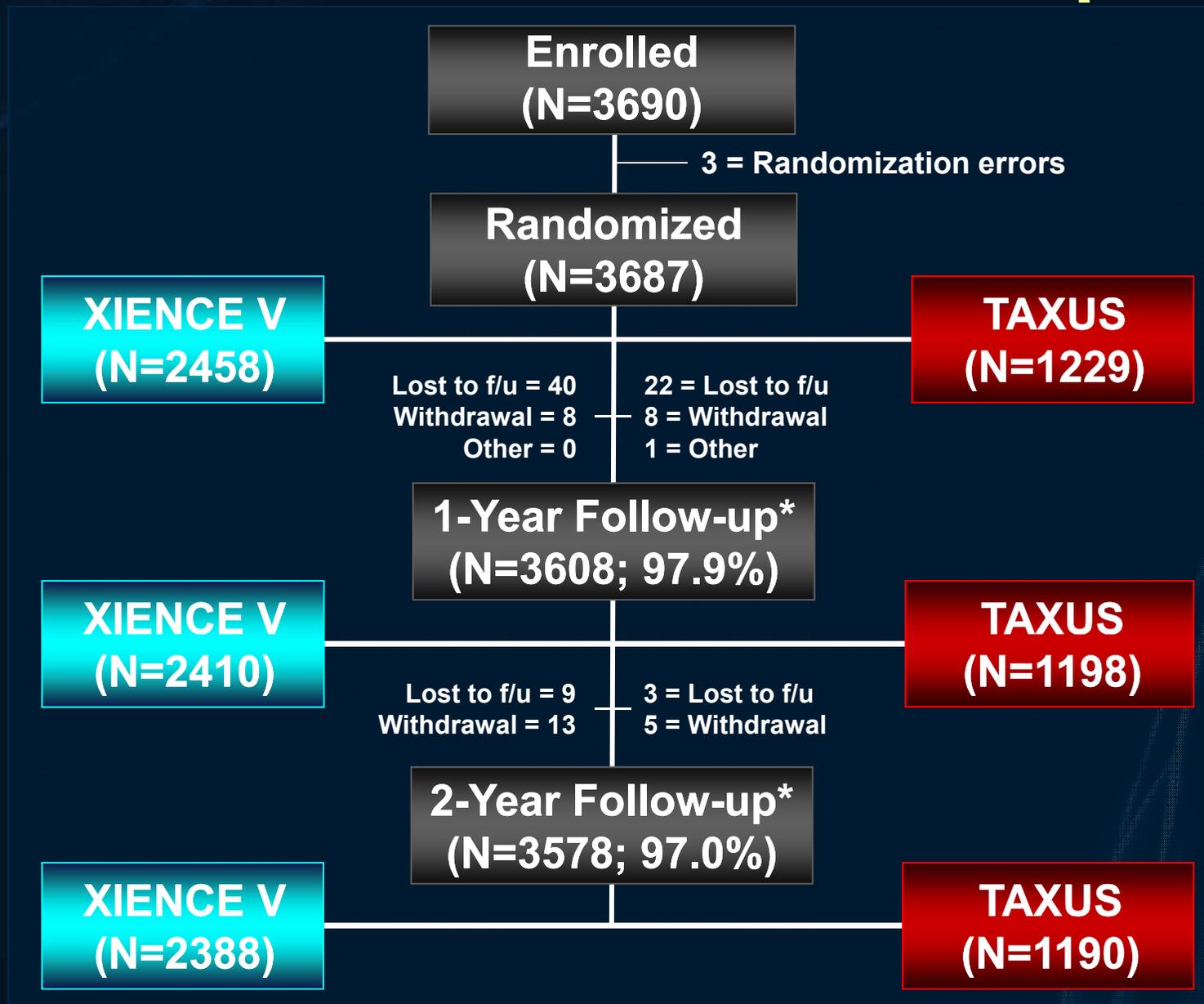
Aspirin ≥ 80 mg QD for 5 years; clopidogrel 75 mg QD for at least 12 mos (if not at high risk for bleeding)

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

Major Exclusion Criteria

- Any target lesion or vessel meets any of the following:
 - Left main or ostial LAD/LCX
 - In or distal to a bypass graft conduit
 - Bifurcation with sidebranch diameter ≥ 2 mm AND ostial DS $>50\%$ OR requiring pre-dilatation
 - Total occlusion, thrombus, restenotic, excessive tortuosity, angulation or heavy calcification
- Prior coronary brachytherapy
- High probability of additional PCI within 9 months

Patient Flow and Follow-up



*F/U window: \pm 28 days

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Baseline Demographics

	XIENCE V 2458 pts	TAXUS 1229 pts	P value
Age (in years)	63.3 ± 10.5	63.3 ± 10.2	0.80
Male (%)	67.7	67.8	1.00
Hypertension (%)	77.4	76.1	0.41
Hypercholesterolemia (%)	76.1	75.5	0.74
Diabetes mellitus (%)	32.0	32.5	0.79
- Insulin requiring (%)	8.5	9.7	0.24
Current smoker (%)	21.9	22.4	0.70
Prior MI (%)	21.1	19.9	0.41
Unstable angina (%)	27.7	28.9	0.46

Baseline Angiography

	XIENCE V 3142 lesions	TAXUS 1585 lesions	P value
Lesion location			
LAD	40.5%	39.8%	0.68
LCX	24.2%	25.4%	0.35
RCA	35.4%	34.8%	0.68
LMCA	0.0%	0.0%	-
QCA			
RVD (mm)	2.75 ± 0.48	2.75 ± 0.46	0.59
MLD (mm)	0.75 ± 0.38	0.76 ± 0.39	0.36
% DS	72.3 ± 12.6	72.0 ± 12.8	0.44
Lsn length (mm)	14.8 ± 6.7	14.5 ± 6.6	0.24

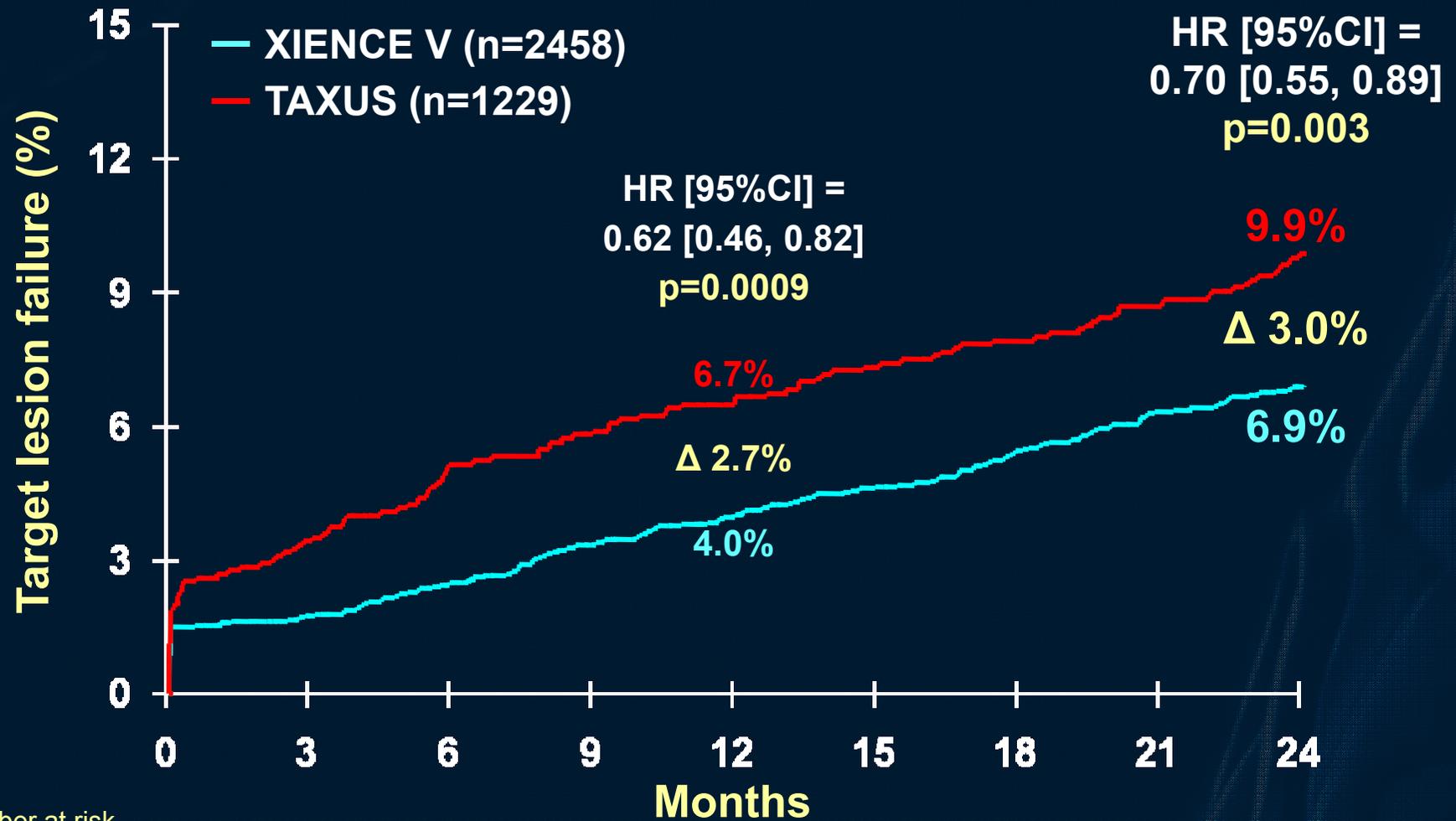
Procedural Results

	XIENCE V 2458 pts 3142 lsns	TAXUS 1229 pts 1585 lsns	P value
# lesions/patient	1.3 ± 0.5	1.3 ± 0.5	0.53
1 lesion	75.2%	74.7%	0.75
2 lesion	21.7%	21.6%	0.97
3 lesion	3.1%	3.7%	0.33
# stents/patient	1.5 ± 0.8	1.5 ± 0.8	0.35
# stents/lesion	1.17 ± 0.44	1.14 ± 0.41	0.01
Max. stent diameter/lesion (mm)	3.01 ± 0.39	3.01 ± 0.38	0.70
Max. stent diameter/RVD/lesion	1.11 ± 0.15	1.11 ± 0.14	0.85
Total stent length/lesion (mm)	22.4 ± 8.9	20.9 ± 8.9	<0.0001
Total stent length/lesion length	1.65 ± 0.72	1.55 ± 0.71	<0.0001

Antiplatelet Agent Utilization

	XIENCE V 2458 pts	TAXUS 1229 pts	P value
Aspirin			
- At 180 days	98.8%	98.5 %	0.54
- At 365 days	96.8%	96.9%	0.84
- At 540 days	96.5%	96.4%	0.92
- At 730 days	95.8%	96.3%	0.58
Thienopyridine			
- At 180 days	98.7%	99.1%	0.41
- At 365 days	93.9%	94.2%	0.76
- At 540 days	78.9%	77.8%	0.46
- At 730 days	71.9%	71.1%	0.63

TLF* Through 2 Years



Number at risk

XIENCE V	2458	2389	2361	2319	2287	2260	2235	2210	2188
TAXUS	1229	1166	1138	1119	1103	1091	1083	1072	1051

*TLF (primary endpoint at 1 year) = cardiac death, target vessel MI, or ischemia-driven TLR

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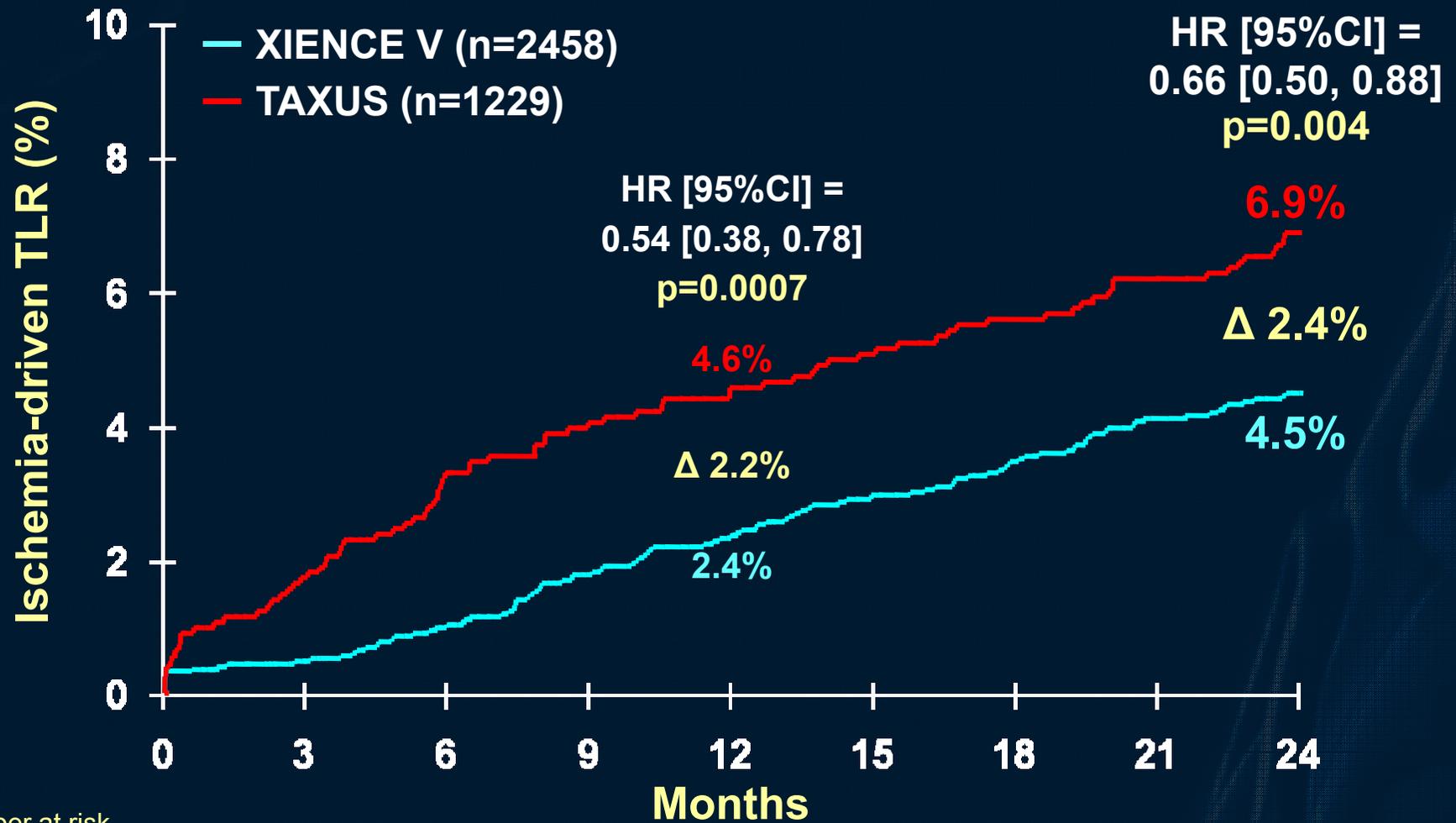
Multivariable Predictors of TLF at 2 Years

Variables	Odds Ratio [95% CI]	Odds Ratio [95% CI]	P Value
RVD (per 1 mm)		0.63 [0.47, 0.83]	0.001
Randomized to EES vs. PES		0.66 [0.51, 0.85]	0.001
Diabetes requiring treatment		1.45 [1.11, 1.88]	0.006
CCS III or IV		1.38 [1.02, 1.89]	0.04
Lesion length (per 10 mm)		1.37 [1.16, 1.62]	0.0002

0 1 2

TLF = cardiac death, target-vessel MI, or ischemia-driven TLR

Ischemia-Driven TLR* Through 2 Years



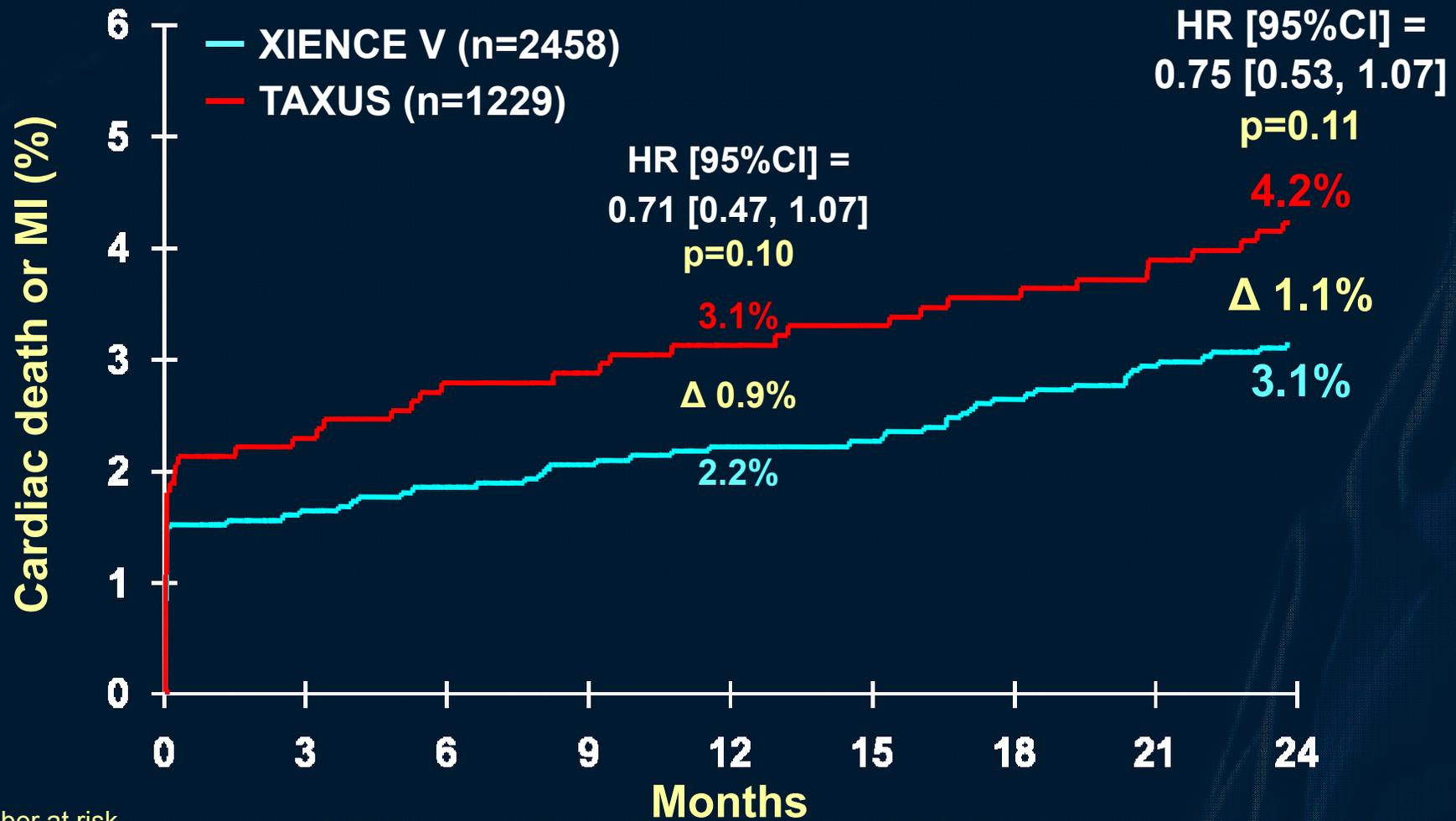
Number at risk

XIENCE V	2458	2419	2392	2350	2318	2291	2269	2246	2226
TAXUS	1229	1186	1159	1140	1124	1112	1104	1093	1073

*Major secondary endpoint at 1 year

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Cardiac Death or TV MI* Through 2 Years



Number at risk

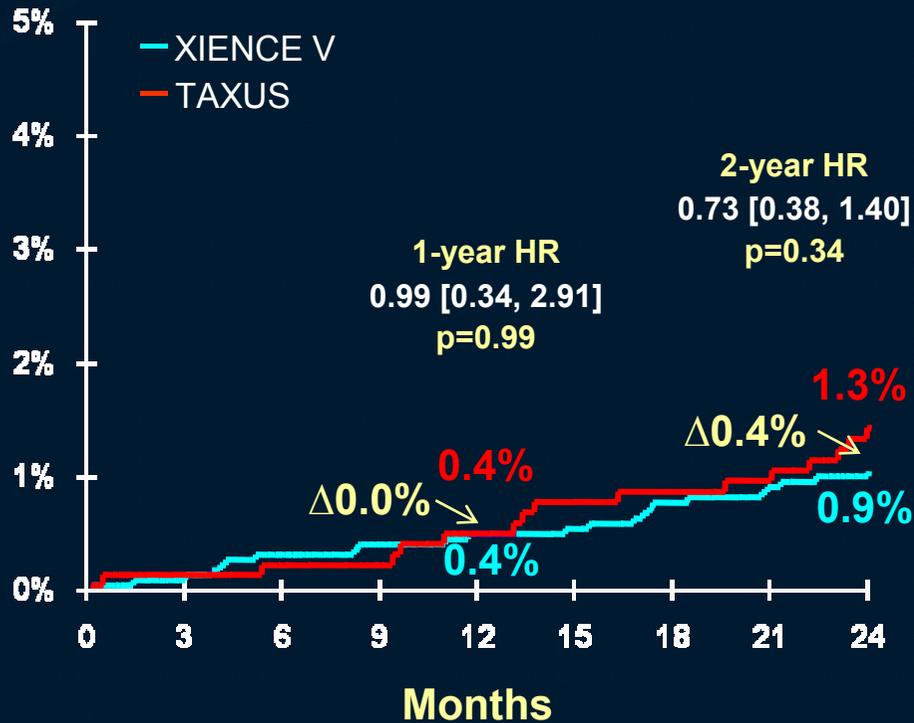
XIENCE V	2458	2392	2377	2350	2329	2316	2301	2290	2277
TAXUS	1229	1180	1167	1155	1146	1140	1136	1132	1118

*Major secondary endpoint at 1 year; TV MI = Target-Vessel MI

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Cardiac Death and TV MI Through 2 Years

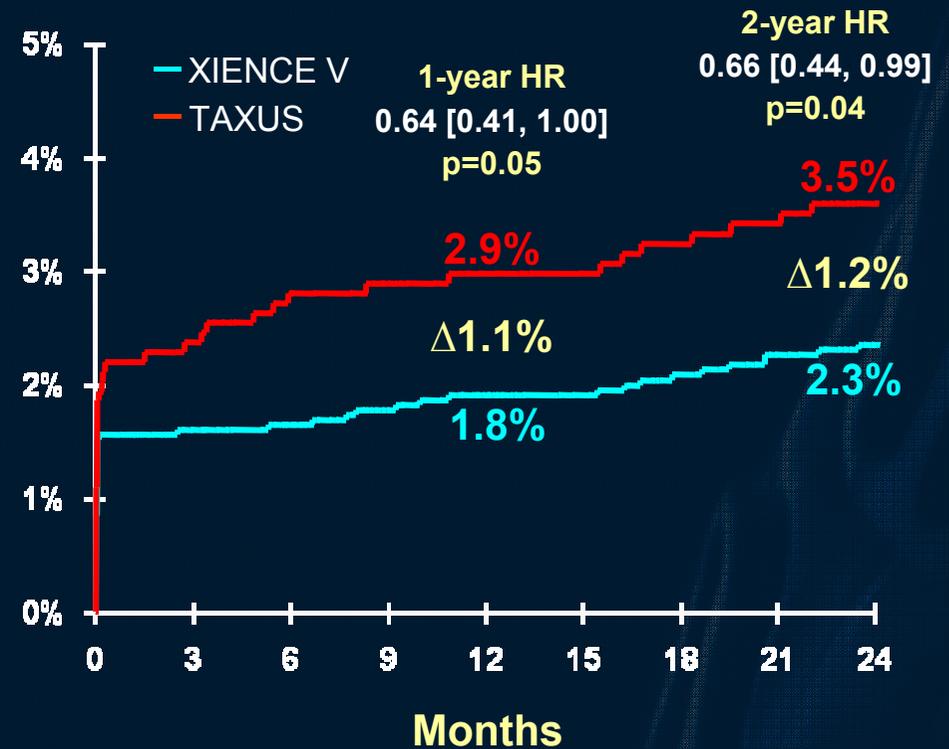
Cardiac Death



Number at Risk

	0	3	6	9	12	15	18	21	24
XV	2458	2430	2416	2391	2372	2359	2347	2339	2328
T	1229	1207	1199	1187	1178	1171	1169	1165	1152

Target Vessel MI



Number at Risk

	0	3	6	9	12	15	18	21	24
XV	2458	2392	2377	2350	2329	2316	2301	2290	2277
T	1229	1180	1167	1155	1146	1140	1136	1132	1118

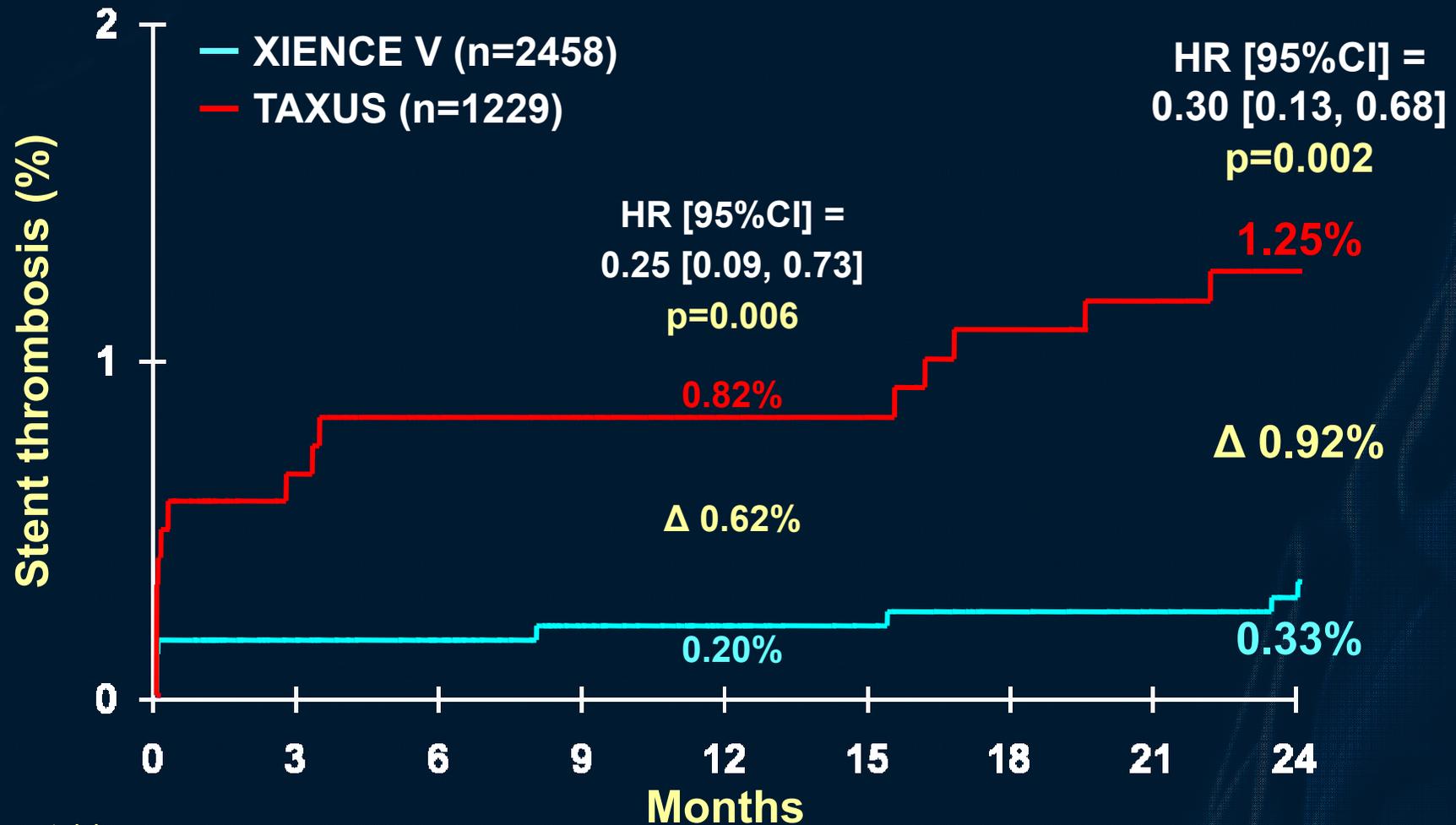
Clinical Outcomes at 2 Years

	XIENCE V (N=2458)	TAXUS (N=1229)	HR [95%CI]	Log- rank P value
Death, all	2.0%	2.7%	0.79 [0.51, 1.23]	0.30
- Cardiac	0.9%	1.3%	0.73 [0.38, 1.40]	0.34
- Non cardiac	1.2%	1.4%	0.85 [0.47, 1.54]	0.59
MI, target vessel	2.3%	3.5%	0.66 [0.44, 0.99]	0.04
MI, all	2.5%	3.9%	0.64 [0.44, 0.94]	0.02
- Q-wave	0.1%	0.8%	0.17 [0.04, 0.61]	0.002
- Non Q-wave	2.4%	3.3%	0.72 [0.48, 1.08]	0.11
ID-TLR	4.5%	6.9%	0.66 [0.50, 0.88]	0.004
PCI	4.1%	6.5%	0.64 [0.48, 0.86]	0.003
CABG	0.5%	0.7%	0.81 [0.33, 1.95]	0.63

Rates (%) are Kaplan-Meier estimates

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Stent Thrombosis (Protocol Definition)*

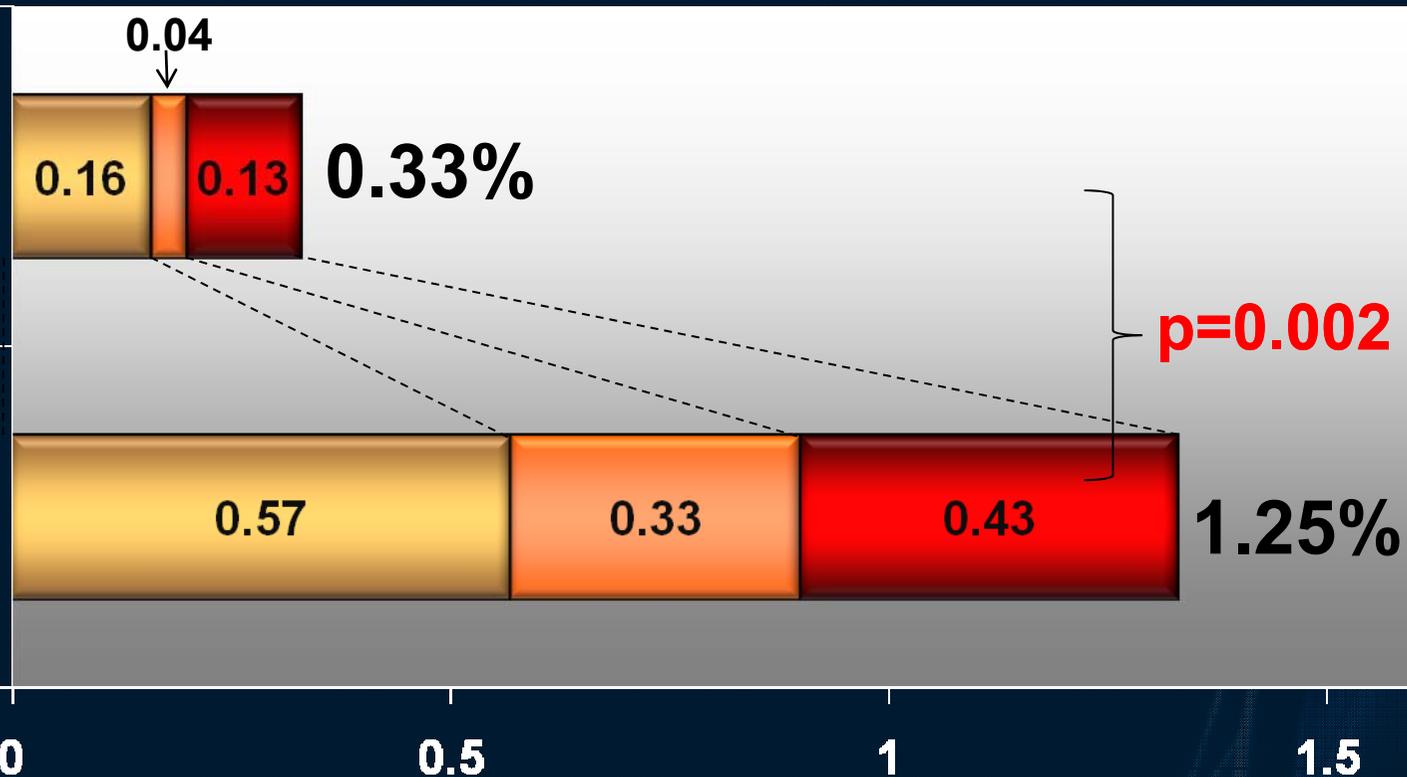


*ACS + angiographic thrombus, or unexplained death or STEMI/Q-wave MI in TL distribution within 30 days

Stent Thrombosis (Protocol Definition)*

■ Early (0 – 30 days) ■ Late (>30 days – 1 year) ■ Very Late (>1 year)

XIENCE V
N=2458



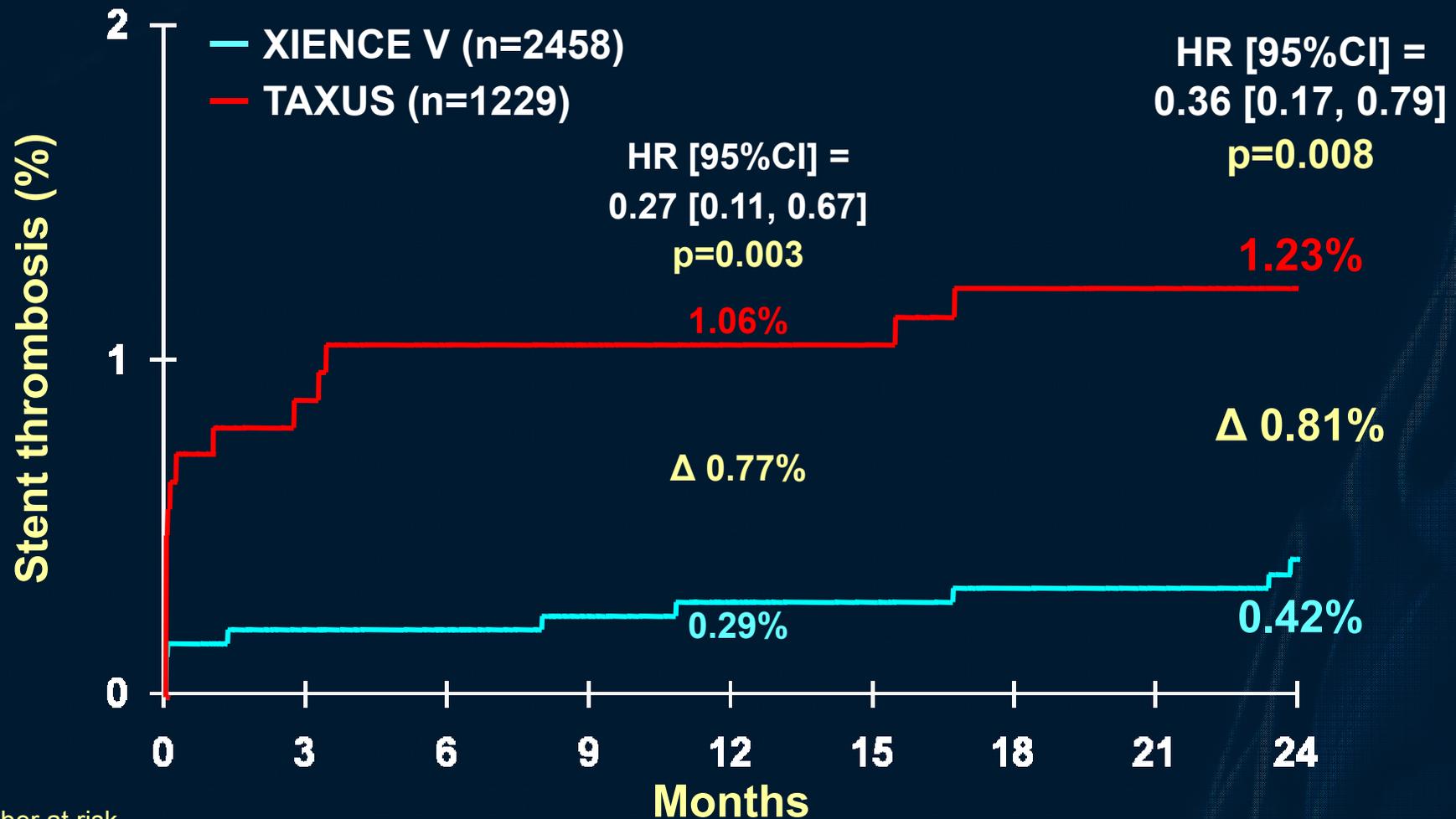
TAXUS
N=1229

Stent thrombosis (%)

*ACS + angiographic thrombus, or unexplained death or STEMI/Q-wave MI in TL distribution within 30 days
Rates (%) are Kaplan-Meier estimates.

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Stent Thrombosis (ARC Def or Prob)

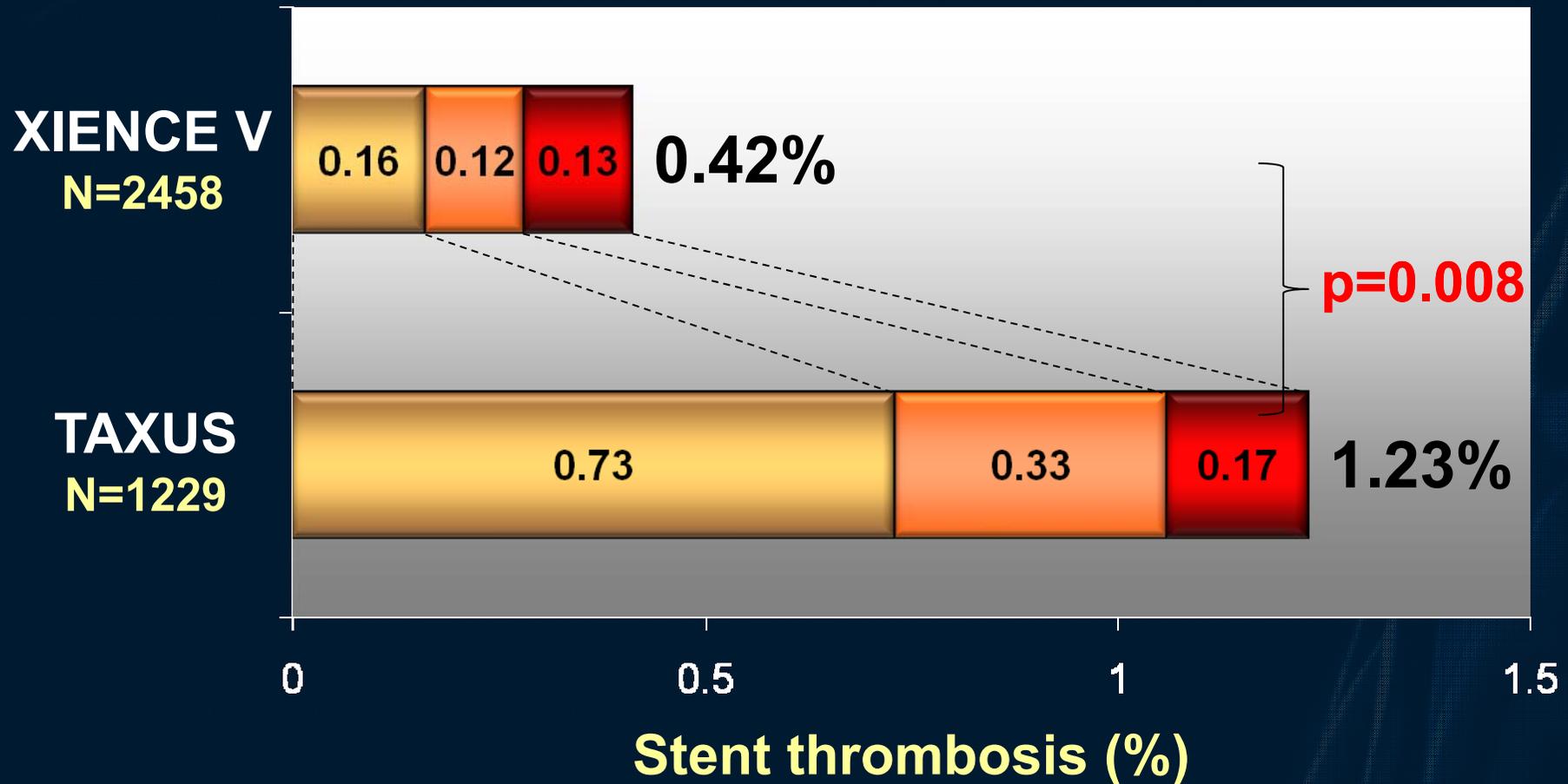


Number at risk

XIENCE V	2458	2426	2412	2386	2367	2354	2342	2334	2321
TAXUS	1229	1196	1186	1175	1166	1160	1156	1152	1139

Stent Thrombosis (ARC Def or Prob)

■ Early (0 – 30 days) ■ Late (>30 days – 1 year) ■ Very Late (>1 year)



Rates (%) are Kaplan-Meier estimates.

SPIRIT IV: 11 Subgroups Examined

Age \geq 65 (n=1600)

Age < 65 (n=1978)

Male (n=2433)

Female (n=1145)

Hypertension* (n=2754)

No hypertension* (n=819)

Hypercholesterolemia* (n=2679)

No hypercholesterolemia* (n=841)

BMI \geq 30 (n=1744)

BMI < 30 (n=1834)

Stable angina (n=2068)

No stable angina (n=1443)

Diabetes (n=1131)

No diabetes (n=2443)

Lesion number = Single (n=2686)

Lesion number = Multi (\geq 2) (n=892)

Lesion length > median (13.3 mm; n=1337)

Lesion length \leq median (13.3 mm; n=1335)

RVD > median (2.75 mm; n=1343)

RVD \leq median (2.75 mm; n=1336)

Bailout (n=312)

No bailout (n=3266)

RVD and lesion length from the single lesion treated subgroup.

* Requiring medication

SPIRIT IV Subgroup Analysis: TLF at 2 Years

Group	EES (%)	PES (%)	Relative Risk (95% CI)	Relative Risk (95% CI)	P interaction
All randomized (n=3687)	7.2	10.0		0.72 [0.57, 0.90]	—
Age ≥ 65 yrs (n=1600)	7.0	8.2		0.85 [0.60, 1.22]	0.20
Age < 65 yrs (n=1978)	7.3	11.5		0.64 [0.48, 0.85]	
Male (n=2433)	7.3	9.6		0.75 [0.57, 0.99]	0.52
Female (n=1145)	6.9	10.8		0.64 [0.44, 0.95]	
Hypertension* (n=2754)	7.5	10.5		0.72 [0.56, 0.92]	0.99
No hypertension* (n=819)	6.1	8.6		0.71 [0.43, 1.18]	
Hypercholesterolemia* (n=2679)	6.8	10.0		0.68 [0.52, 0.88]	0.48
No hypercholesterolemia* (n=841)	8.4	10.2		0.82 [0.53, 1.28]	
BMI ≥ 30 (n=1744)	7.8	10.1		0.77 [0.57, 1.05]	0.52
BMI < 30 (n=1834)	6.6	9.9		0.66 [0.48, 0.91]	
Stable angina (n=2068)	7.1	11.1		0.65 [0.49, 0.86]	0.32
No stable angina (n=1443)	7.3	8.9		0.82 [0.57, 1.17]	



TLF = cardiac death, target vessel MI, or ischemia-driven TLR; 2 Years = 730 ± 28 days; *Requiring medication

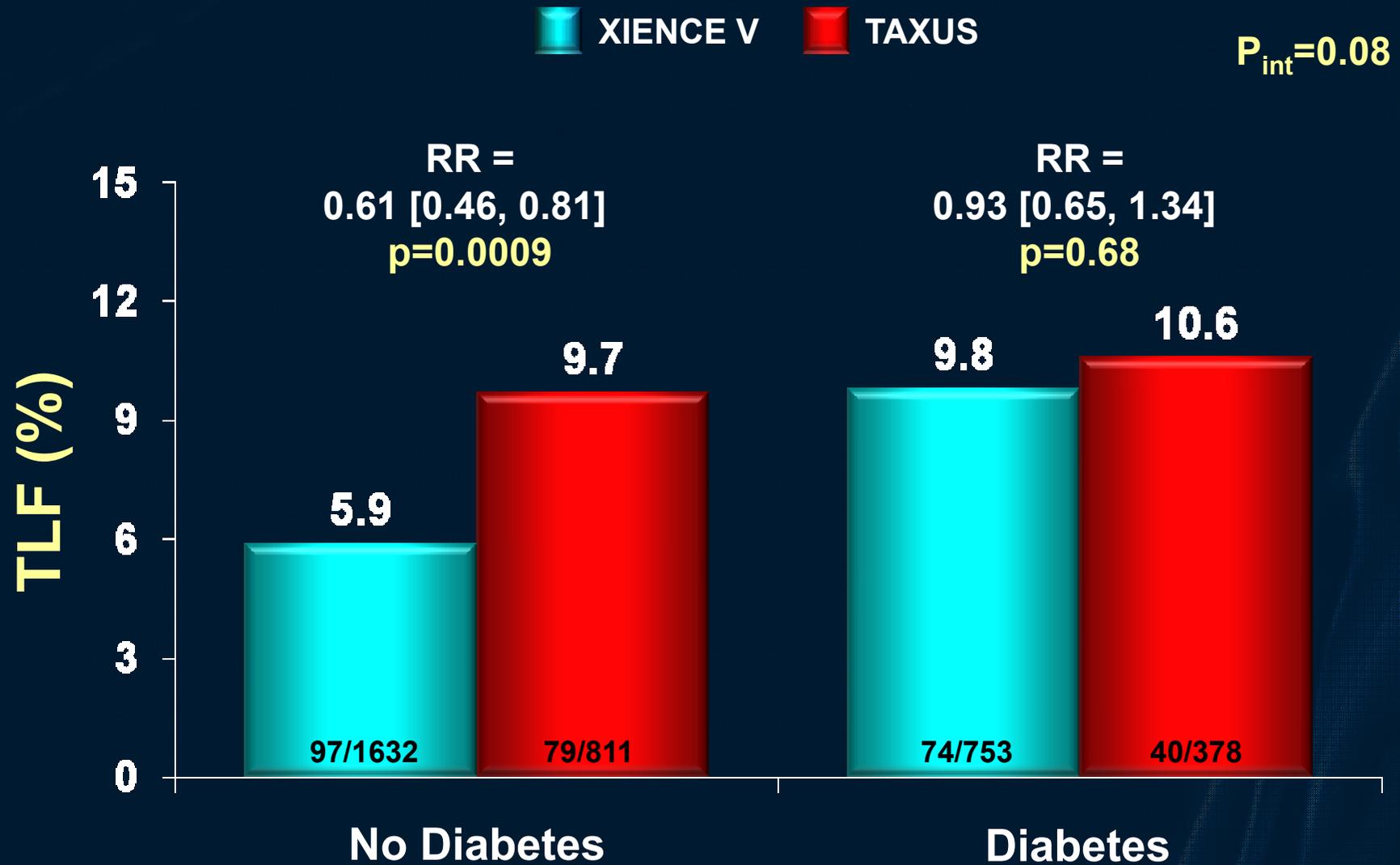
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SPIRIT IV Subgroup Analysis: TLF at 2 Years

Group	EES (%)	PES (%)	Relative Risk (95% CI)	Relative Risk (95% CI)	P interaction
All randomized (n=3687)	7.2	10.0		0.72 [0.57, 0.90]	—
Single lesion treated (n=2686)	6.4	9.1		0.70 [0.53, 0.92]	0.80
Multiple lesions (≥2) treated (n=892)	9.6	12.8		0.75 [0.51, 1.11]	
RVD > 2.75 mm (n=1343)	5.5	7.4		0.74 [0.49, 1.14]	0.68
RVD ≤ 2.75 mm (n=1336)	7.3	10.9		0.67 [0.47, 0.95]	
Lesion length > 13.3 mm (n=1337)	7.2	11.3		0.64 [0.44, 0.91]	0.50
Lesion length ≤ 13.3 mm (n=1335)	5.5	7.3		0.76 [0.50, 1.16]	
Bailout (n=312)	8.0	17.4		0.46 [0.24, 0.86]	0.14
No bailout (n=3266)	7.1	9.4		0.75 [0.59, 0.95]	
Diabetes (n=1131)	9.8	10.6		0.93 [0.65, 1.34]	0.08
No diabetes (n=2443)	5.9	9.7		0.61 [0.46, 0.81]	

TLF = cardiac death, target vessel MI, or ischemia-driven TLR; 2 Years = 730 ± 28 days
 Single lesion treated data are used for RVD & lesion length subgroup analyses

Impact of Diabetes on TLF at 2 years



TLF = cardiac death, target-vessel MI, or ischemia-driven TLR
Categorical (binary) event rates

Clinical Outcomes Through 2 Years

- No Diabetes Mellitus -

	XIENCE V 1669 pts	TAXUS 829 pts	P value
Cardiac death or TV-MI	2.5%	3.8%	0.08
Death, all	1.7%	2.7%	0.09
Cardiac death	0.6%	1.0%	0.32
MI, all	2.1%	3.5%	0.05
Target vessel MI	1.9%	3.2%	0.05
ID-TLR	3.8%	6.9%	0.001
TLF	5.9%	9.7%	0.0009
MACE	6.1%	9.7%	0.002
TVF	8.1%	11.0%	0.02
ST, protocol	0.06%	1.01%	0.0009
ST, ARC def/prob	0.12%	1.27%	0.0005

TLF = cardiac death, target-vessel MI, or ID-TLR; MACE = cardiac death, all MI, or ID-TLR;
TVF = cardiac death, all MI, or ID-TVR.

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Clinical Outcomes Through 2 Years

- Diabetes Mellitus -

	XIENCE V 786 pts	TAXUS 399 pts	P value
Cardiac death or TV-MI	4.8%	5.3%	0.77
Death, all	3.2%	2.6%	0.71
Cardiac death	1.6%	1.9%	0.81
MI, all	3.6%	5.0%	0.27
Target vessel MI	3.3%	4.2%	0.50
ID-TLR	6.5%	6.9%	0.80
TLF	9.8%	10.6%	0.68
MACE	10.1%	11.1%	0.61
TVF	13.0%	13.5%	0.85
ST, protocol	1.09%	1.88%	0.28
ST, ARC def/prob	1.23%	1.35%	1.00

TLF = cardiac death, target-vessel MI, or ID-TLR; MACE = cardiac death, all MI, or ID-TLR;
TVF = cardiac death, all MI, or ID-TVR.

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SPIRIT IV Conclusions

- In the large-scale, prospective, multicenter, randomized SPIRIT IV trial, the benefits of the everolimus-eluting XIENCE V stent compared to the paclitaxel-eluting TAXUS Express stent present at 1-year were sustained at 2-years
- At 2 year follow-up, treatment with XIENCE V rather than TAXUS resulted in:
 - A 30% relative (3.0% absolute) reduction in TLF
 - A 34% relative (2.4% absolute) reduction in ID-TLR
 - A 36% relative (1.4% absolute) reduction in MI
 - A 64% relative (0.8% absolute) reduction in stent thrombosis (ARC)
 - A 39% relative (3.8% absolute) reduction in TLF in pts without diabetes, and non significantly different rates of TLF in pts with diabetes
 - Consistent relative reductions in TLF in other complex subgroups (including multiple lesions, long lesions and small vessels)