The EXAMINATION (a clinical Evaluation of Xience-V stent in Acute Myocardial INfArcTION) trial:

Manel Sabaté
Hospital Clínic, Barcelona
(On behalf of the Examination Investigators)

Background and Rationale (I)

- Acute coronary syndromes repeatedly appear as independent predictor of stent thrombosis in most of Clinical Registries. Although these registries reflect real world population, they may be subject to clinical bias.
- First generation drug-eluting stent (DES) have been evaluated in RCT in the setting of STEMI with (overall) positive results. However, most of these RCT lack of good generalizability of real world due to highly selected inclusion/exclusion criteria.
- Currently, no data exists regarding new generation DES in terms of safety and efficacy in this high risk group of patients with STEMI.

Background and Rationale (II)

- Recently, RCT with an "all-comers" design apply wide inclusion and few exclusion criteria that may result in a more representative sample of the target population.
- However, even in such design it is not expected that every consecutive patient will be enrolled. In a recent analysis from 2 all-comers RCT (Leaders and Resolute) only 48% of the total number of patients were actually included[1].
- We conducted a RCT with an "all-comers" design with the aim to evaluate the performance of 2nd generation DES in the complex setting of STEMI and to provide data that may be generalizable to the real world population.

[1] De Boer SPM. Eur Heart J 2011; May 2011, ahead of print

EXAMINATION TRIAL design

Multicentre, multinational, prospective, randomized, two-arm, single-blind, controlled trial

OBJECTIVE

To assess the safety and performance of the XIENCE™ V Everolimus Eluting Coronary Stent System vs. the cobalt chromium MULTI-LINK VISION® balloon expandable stent in the setting of primary percutaneous coronary intervention for treatment of patients presenting with ST-segment elevation myocardial infarction.

EXAMINATION trial

(A Clinical Evaluation of Xience-V stent in Acute Myocardial INfArctTION)

12 centres - 3 countries

Participants (I)

PI: M Sabaté; Clinic Hospital, Barcelona, SP

Co-PI: PW Serruys; Erasmus MC; R'dam, NL

Steering Committee:

M Sabaté; PW Serruys; A Cequier; A Iñiguez; M Valgimigli; R Hdez-Antolín, GA van Es.

Promotor: Spanish Society of Cardiology

CRO: Cardialysis, R'dam, NL

Monitoring: J Toro (SP) S Cellini (I), C Morelli (I), R Schneijdenber (NL)

DSMB: I Ferreira (SP); B Garcia del Blanco (SP)

CEC: P Vrancks (B); E McFadden (UK); B Rensing (NL)

Statistics: Cardialysis, R'dam, NL

Participants (II)

Centres:

- Spain:
  - H Prínceps d'Espanya, Barcelona; Dr. A Cequier
  - H Sant Pau, Barcelona; Dr. A Serra
  - H Clínic, Barcelona; Dr. M Sabaté
  - H do Meixoeiro, Vigo; Dr. A Iñiguez
  - H San Carlos, Madrid; Dr. R Hernández-Antolín
  - H Univ Alicante; Alicante; Dr. V Mainar
  - H Juan Canalejo; A Coruña; Dr. N Vázquez
  - H Son Dureta; Palma de Mallorca; Dr. A Bethencourt
- Italy
  - Univ H Ferrara- Dr. M Valgimigli
  - Univ H Bolognini Seriate- Dr. M Tespili
- The Netherlands
  - Erasmus MC, Rotterdam- Dr. PW Serruys
  - Amphia Ziekenhuis, Breda- Dr. den Heijer

Disclosures

Investigator Initiated Trial: NCT00828087.

Unrestricted grant from Abbott to the Spanish Heart Foundation.

EXAMINATION TRIAL design

PRIMARY ENDPOINT

- *Patient-oriented (ARC) primary endpoint at 1 year*

Composite endpoint of all-cause death, any myocardial infarction and any revascularization.

SECONDARY ENDPOINTS

- All-cause and cardiac mortality at 1 year and yearly up to 5 years.
- Recurrent MI at 1 year and yearly up to 5 years.
- TLR and TVR at 1 year and yearly up to 5 years.
- Stent thrombosis (ARC) at 1 year and yearly up to 5 years.
- Clinical device and procedure success.
- Major and minor bleeding at 1 year and yearly up to 5 years.

Inclusion criteria ("all-comer"):

√ Patients presenting with STEMI within 48 h requiring emergent PCI:

- STEMI < 12h ("primary PCI")
- Rescue PCI
- After successful thrombolysis
- Latecomers (>12h-48h)

√ Vessel size between 2.25-4.0 mm to allow the implantation of currently available stents.

√ Informed consent.

Exclusion criteria:

√ Age < 18y

√ Pregnancy

√ Intolerance to aspirin, clopidogrel, everolimus, cobalt chromium, heparin.

√ Need of chronic treatment with anti vitamin K agents.

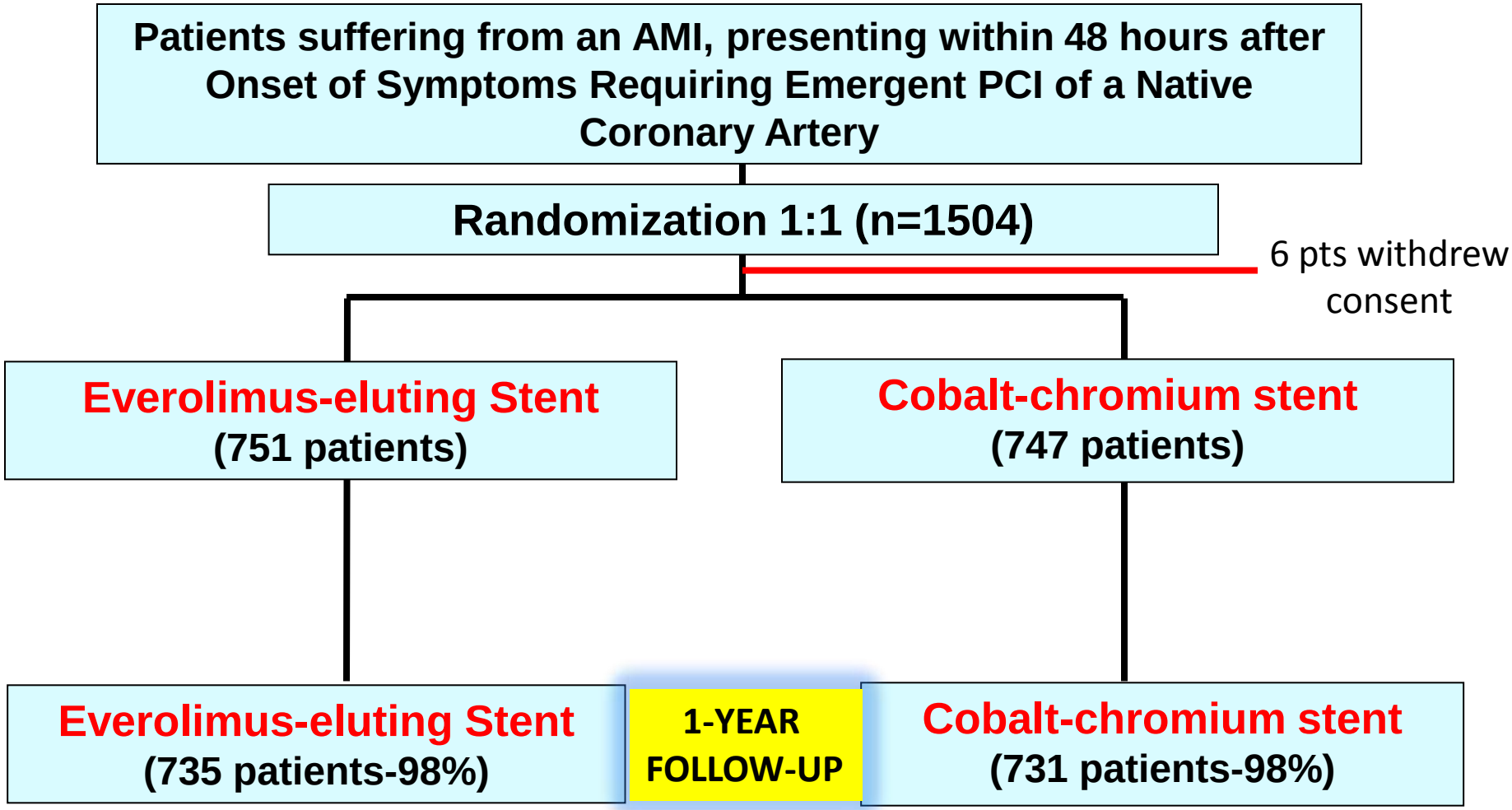
√ STEMI secondary to stent thrombosis.

√ Impossibility to obtain clinical follow-up.

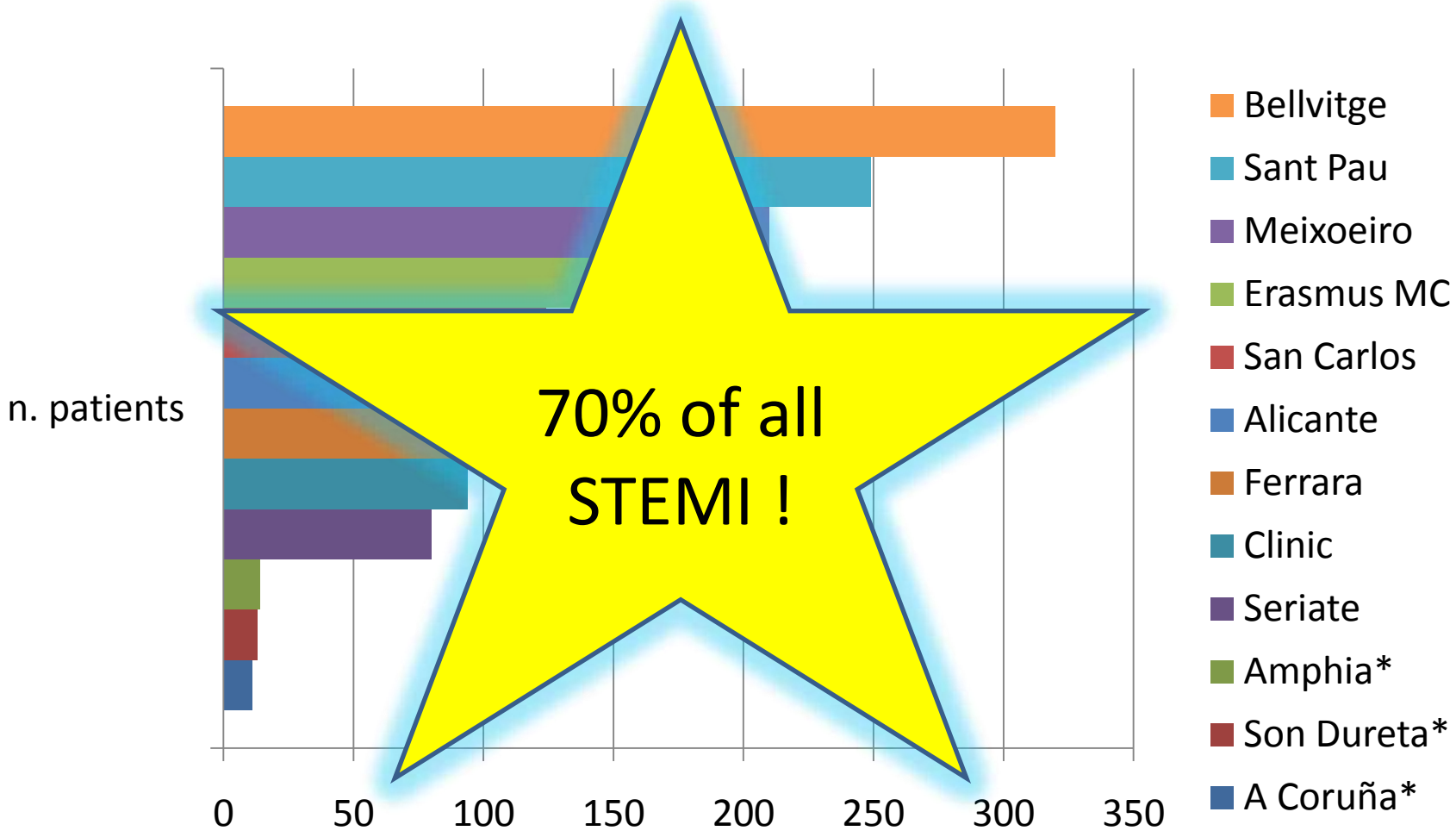
Statistical analysis:

- The overall sample size for the study of 1500 patients is based on the following assumptions:
  - A 2-sided type I error rate $\alpha = 0.05$
  - Randomization ratio is 1 (XIENCE V): 1 (Vision).
  - A statistical power of at least 86% to detect a (approximate 30%) reduction in the rate of the primary endpoint at 1 year by the Xience V stent as compared to the Vision stent
- The primary combined endpoint will be analyzed for the intent-to-treat population.
- Staged procedures that were indicated in the CRF at the time of the initial procedure, and are performed within one month of the initial procedure will not be counted as endpoints.

Study Design = All-comer RCT



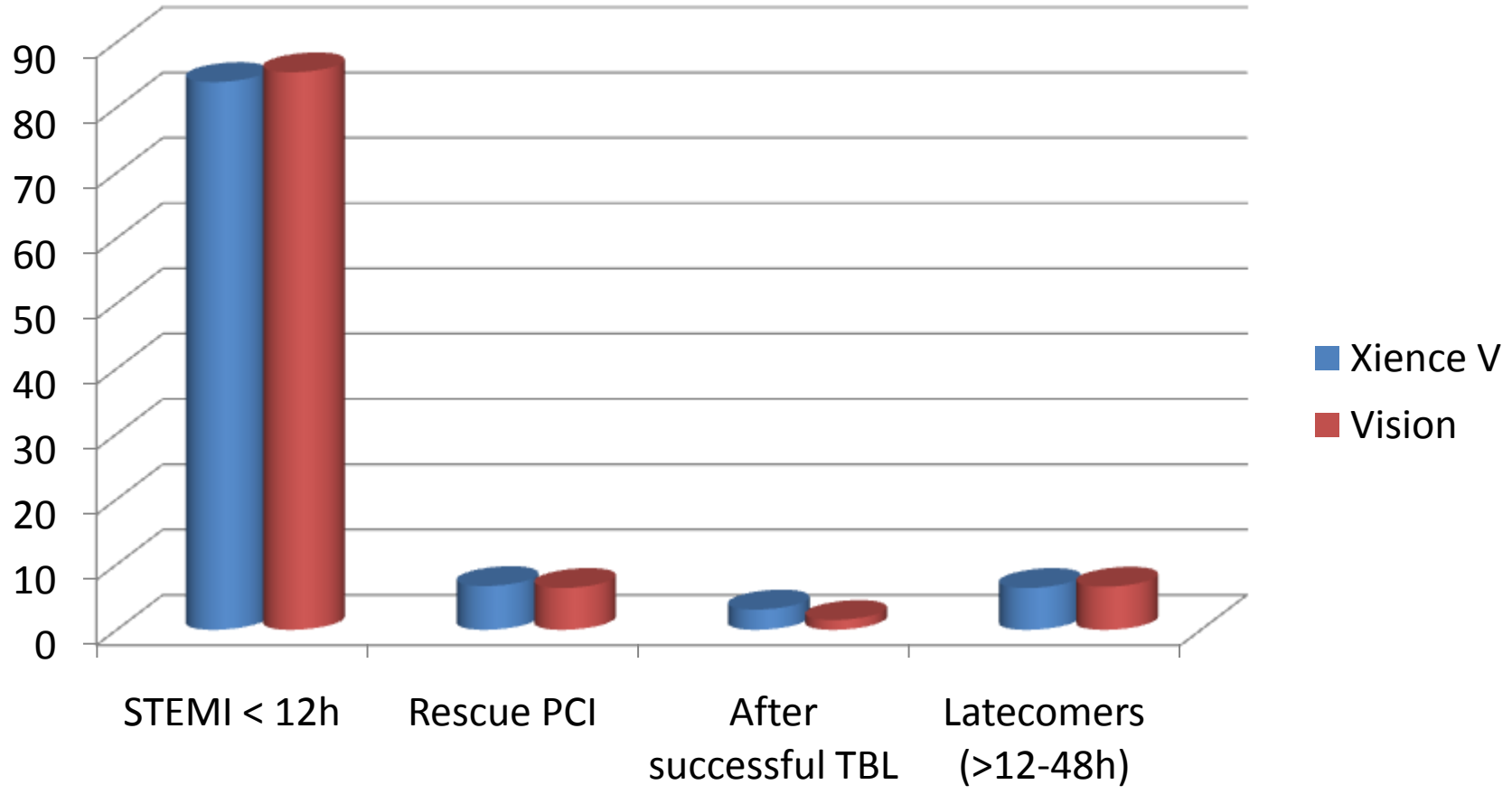
Number of patients included per centre



* Recruitment period < 3 mths

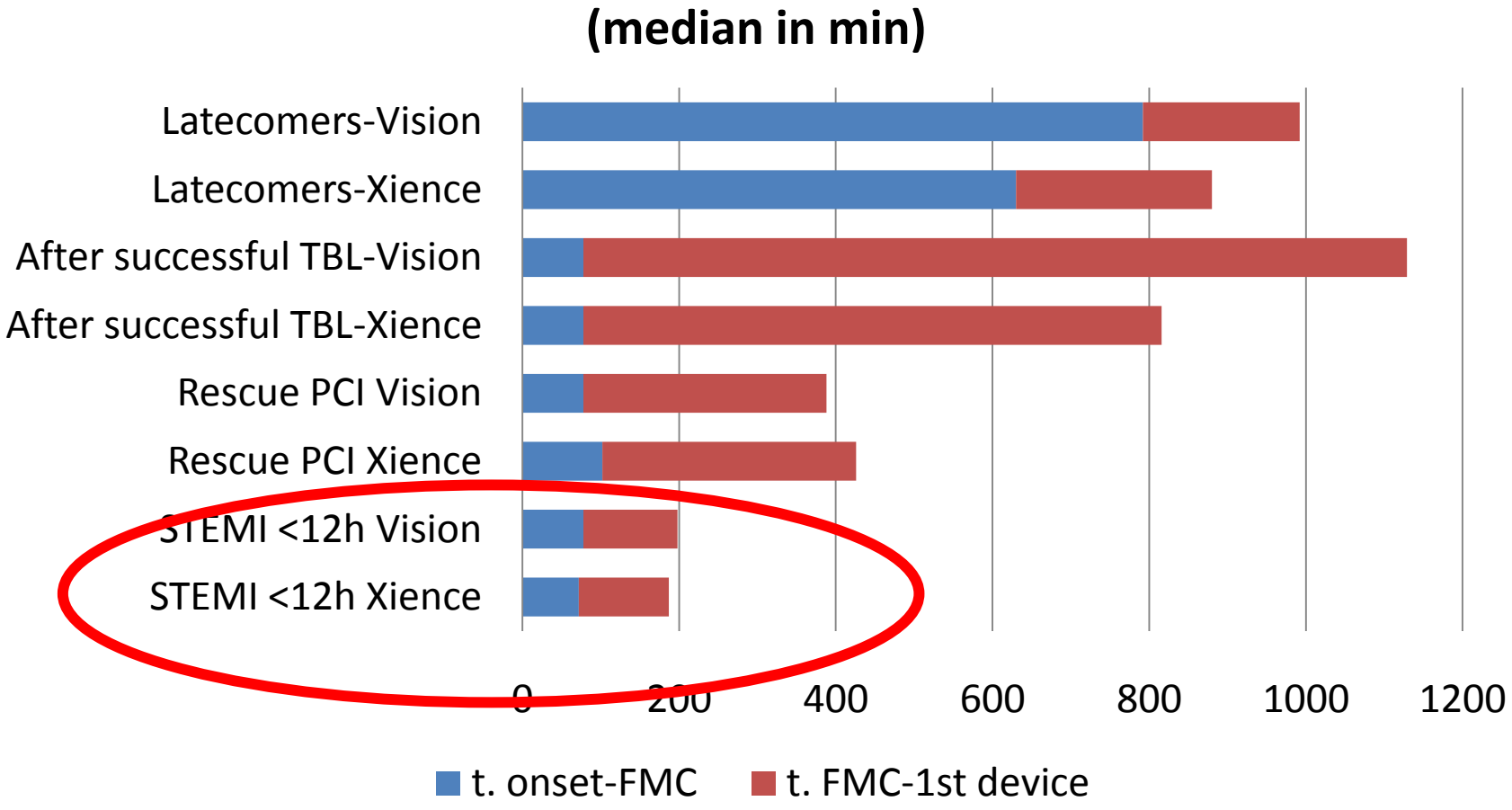
Baseline Characteristics	Xience V n=751	Vision n=747
Age, years	61 ± 12 (28-90)	62 ± 12 (27-95)
Male, %	84.4	81.7
Body mass index, Kg/m^2	27 ± 4	27 ± 4
Diabetes, %	18	16
Hypertension, %	46	50
Smoker, %	72	72
Dyslipidemia, %	47	40
Family History, %	18	16
Previous Myocardial Infarction, %	4.4	6.3
Previous PCI, %	3.9	4.3
Previous CABG, %	0.4	0.9
Previous stroke, %	1.6	2.5

Clinical presentation



Cardiogenic shock: 1.3 % Xience V vs. 1.1% Vision; p=NS

Ischemia time according to clinical presentation

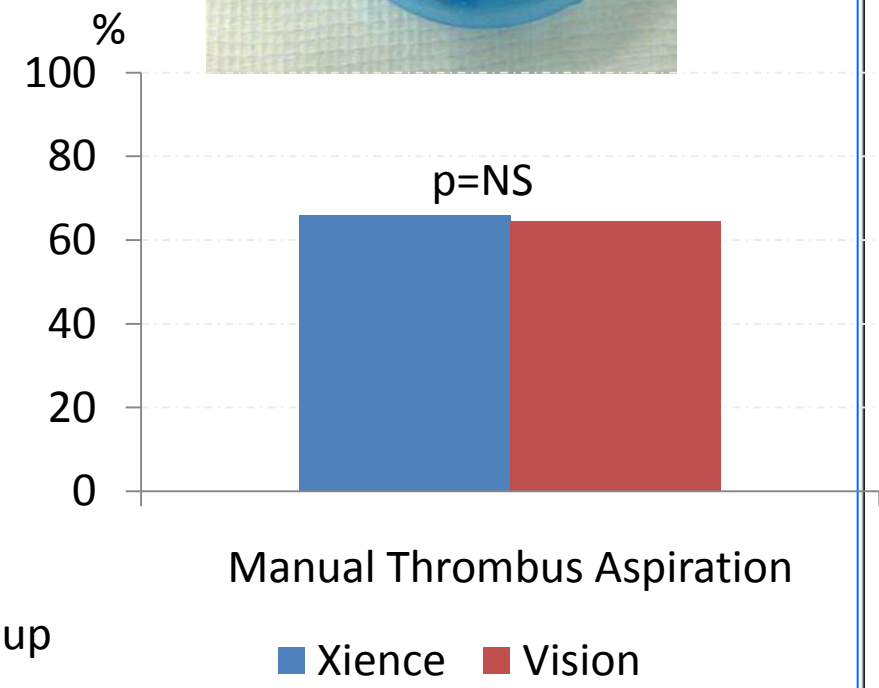


Anatomical Characteristics	Xience V n=751	Vision n=747
Infarct-related artery:		
LAD, n (%)	379 (42)	343 (39)
RCA, n (%)	380 (42)	396 (45)
LCx, n (%)	130 (15)	132 (15)
Left Main, n (%)	6 (0.7)	4 (0.5)
SVG, n (%)	4 (0.4)	4 (0.5)
N. diseased vessels:		
One, n (%)	645 (86)	654 (88)
Two, n (%)	76 (10)	63 (8.4)
Three, n (%)	24 (3.2)	25 (3.4)
Ejection fraction, %; median [IQR]	52 [45-58]	51.5 [45-58]

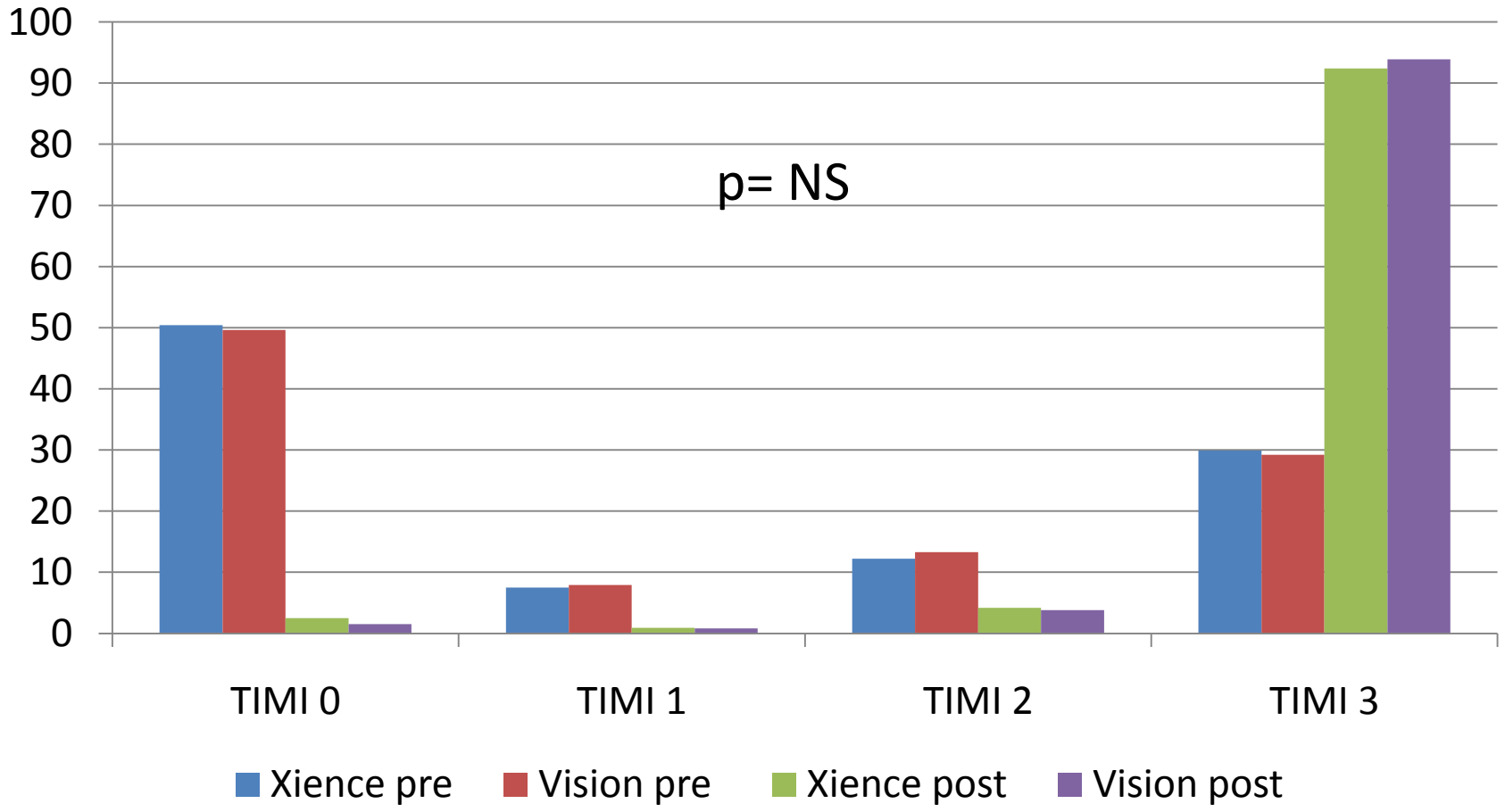
Procedural Aspects

Antithrombotic Therapy	Xience V n=751	Vision n=747
Unfractioned heparin, n (%)	597 (79.5)	587 (78.7)
LMWH, n (%)	62 (8.3)	71 (9.5)
Bivalirudin, n (%)	49 (6.5)	56 (7.5)
IIb/IIIa inh.* (99% reopro), n (%)	400 (53.3)	383 (51.2)
Aspirin, n (%)	692 (92.1)	691 (92.6)
Clopidogrel, n (%)	710 (94.5)	703 (94.2)

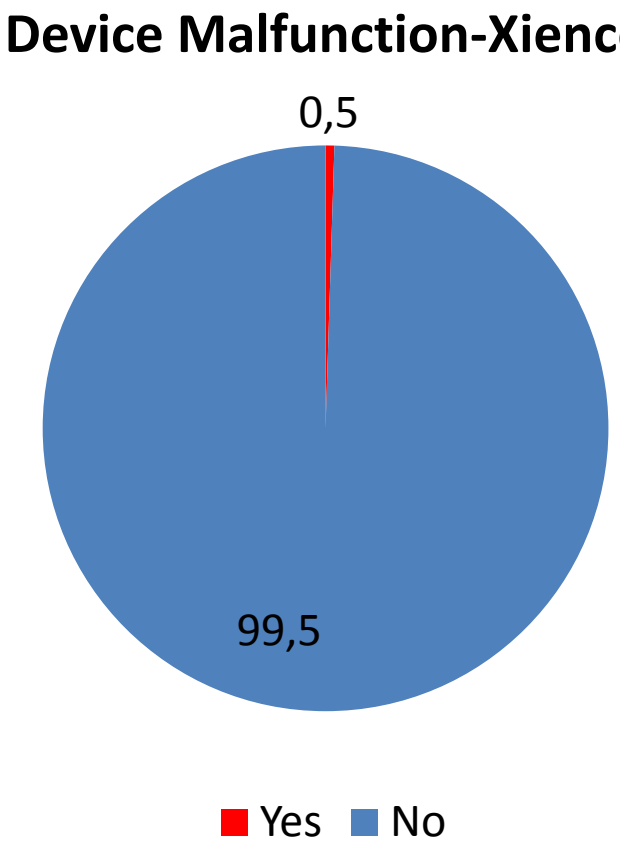
* 63% vs 60% when analysed within STEMI <12h group



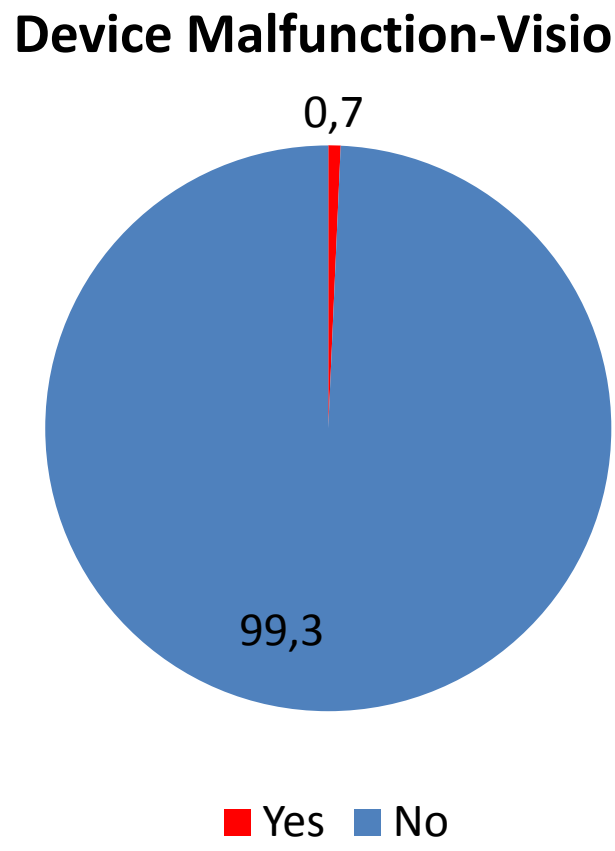
Acute Results



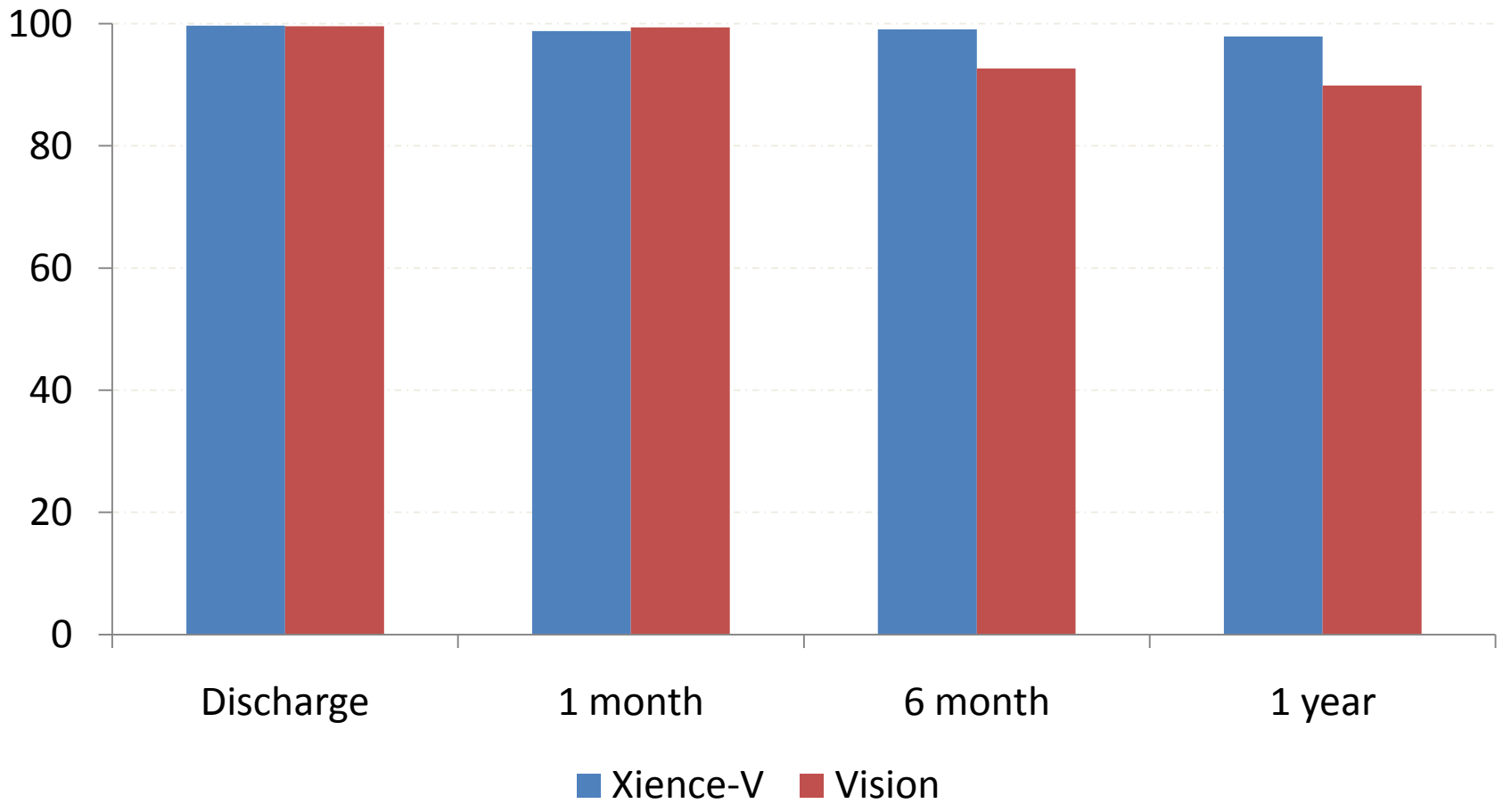
Acute performance



p = NS



Dual Antiplatelet Regimen

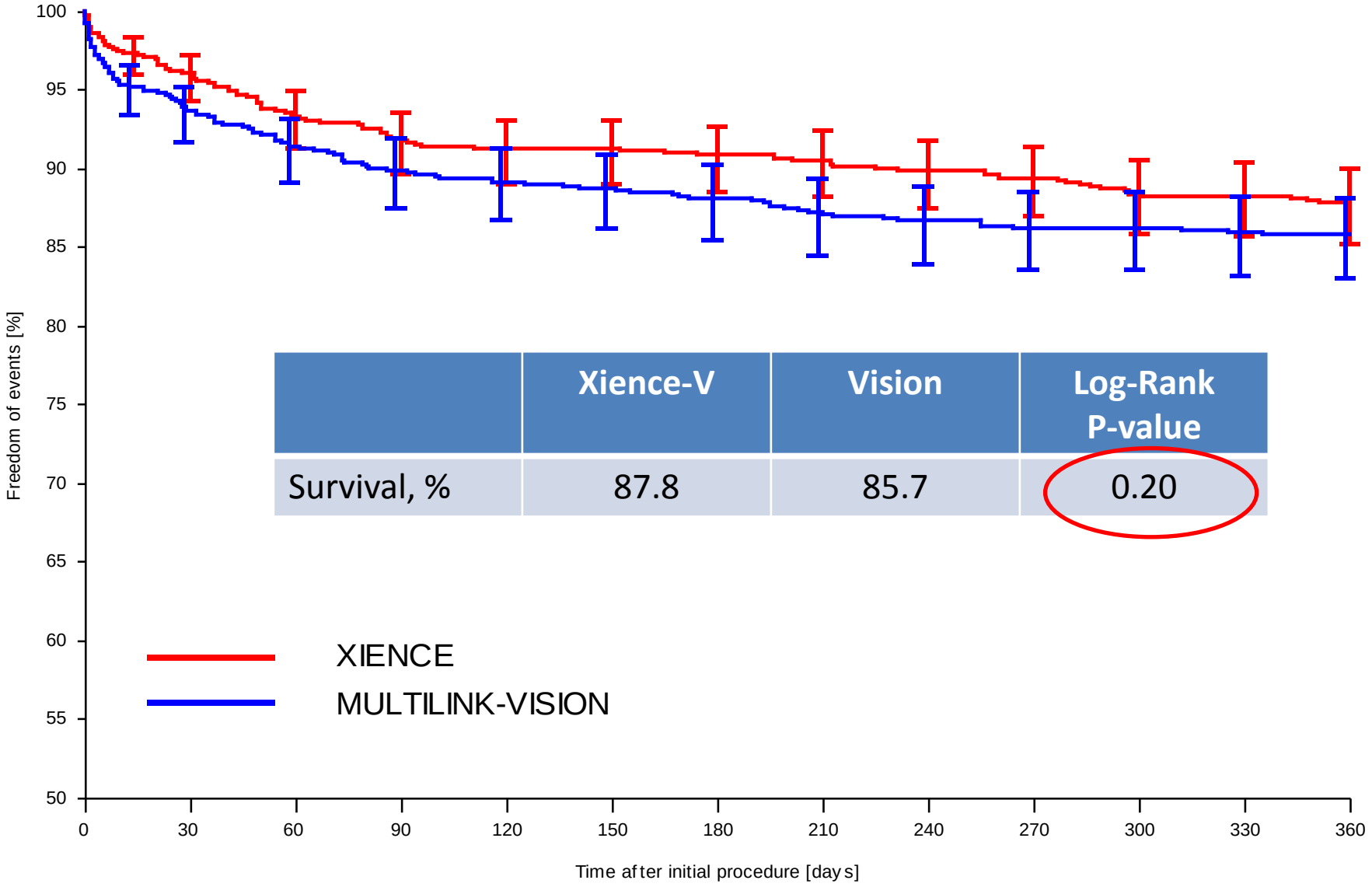


1-YEAR RESULTS

EXAMINATION trial

Primary Endpoint:

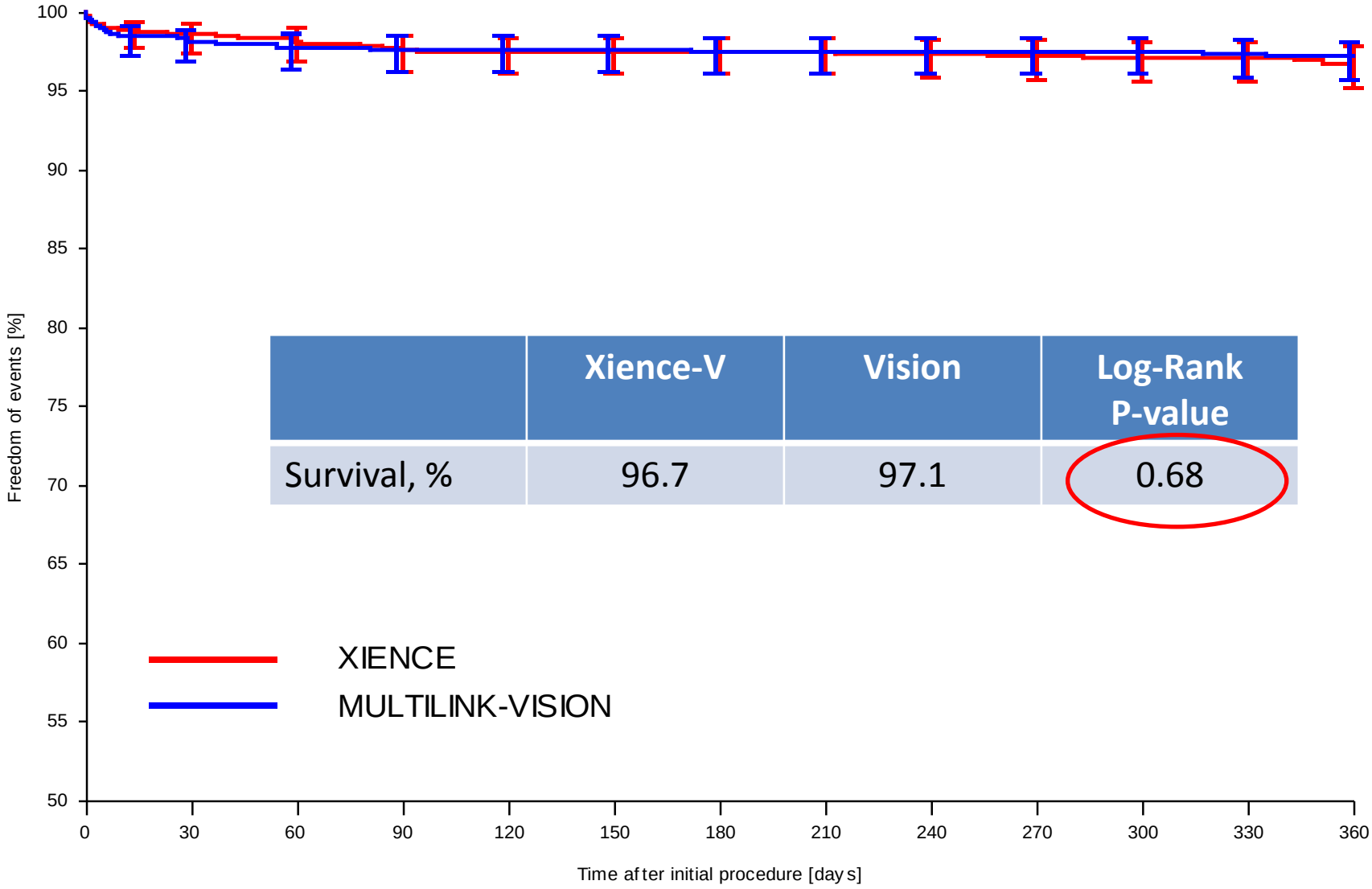
Composite of all-cause death, any MI or any revascularization



	Xience-V	Vision	Log-Rank P-value
Survival, %	87.8	85.7	0.20

Secondary Endpoints:

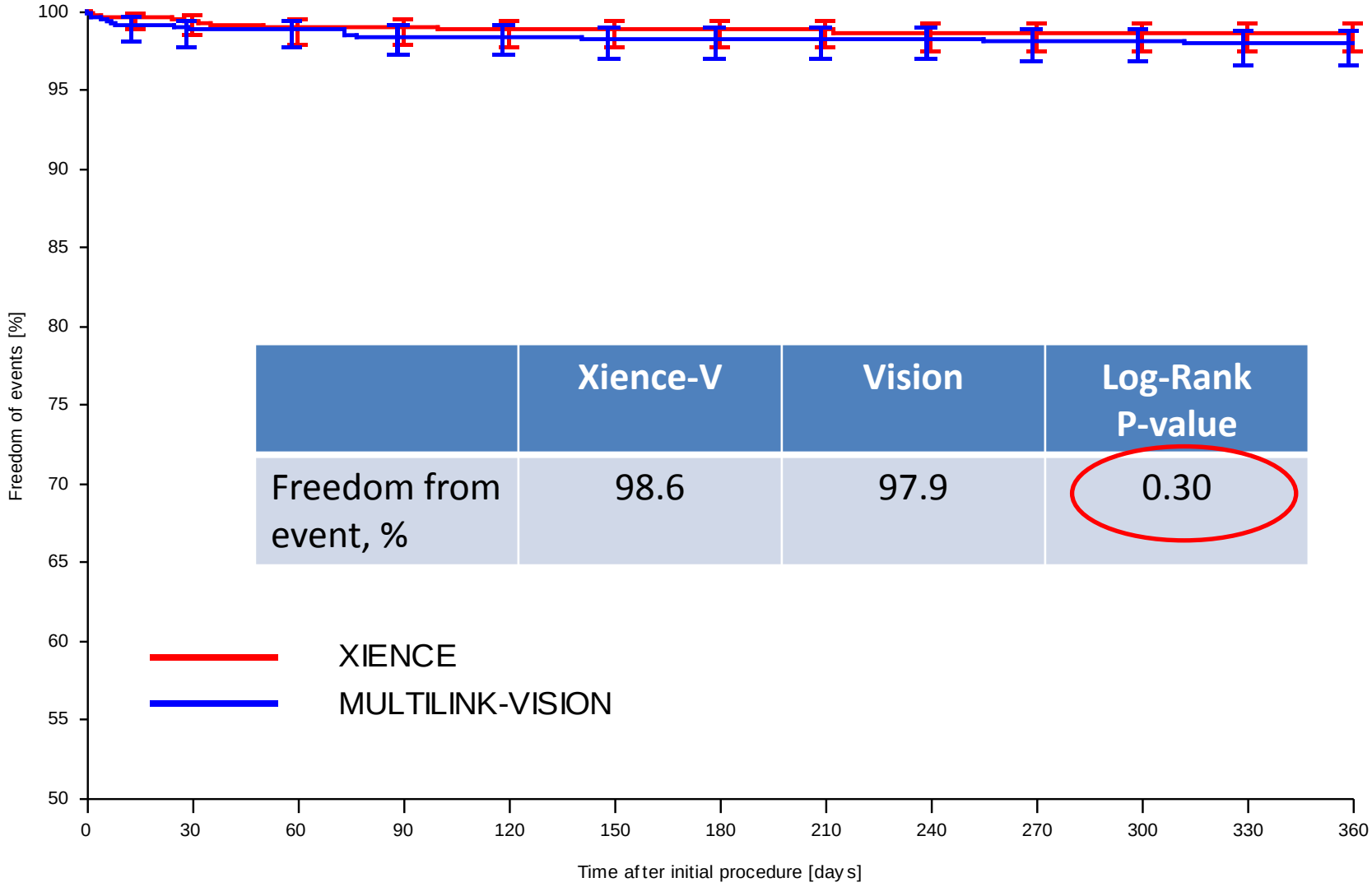
Cardiac Death



	Xience-V	Vision	Log-Rank P-value
Survival, %	96.7	97.1	0.68

Secondary Endpoints:

Recurrent Myocardial Infarction

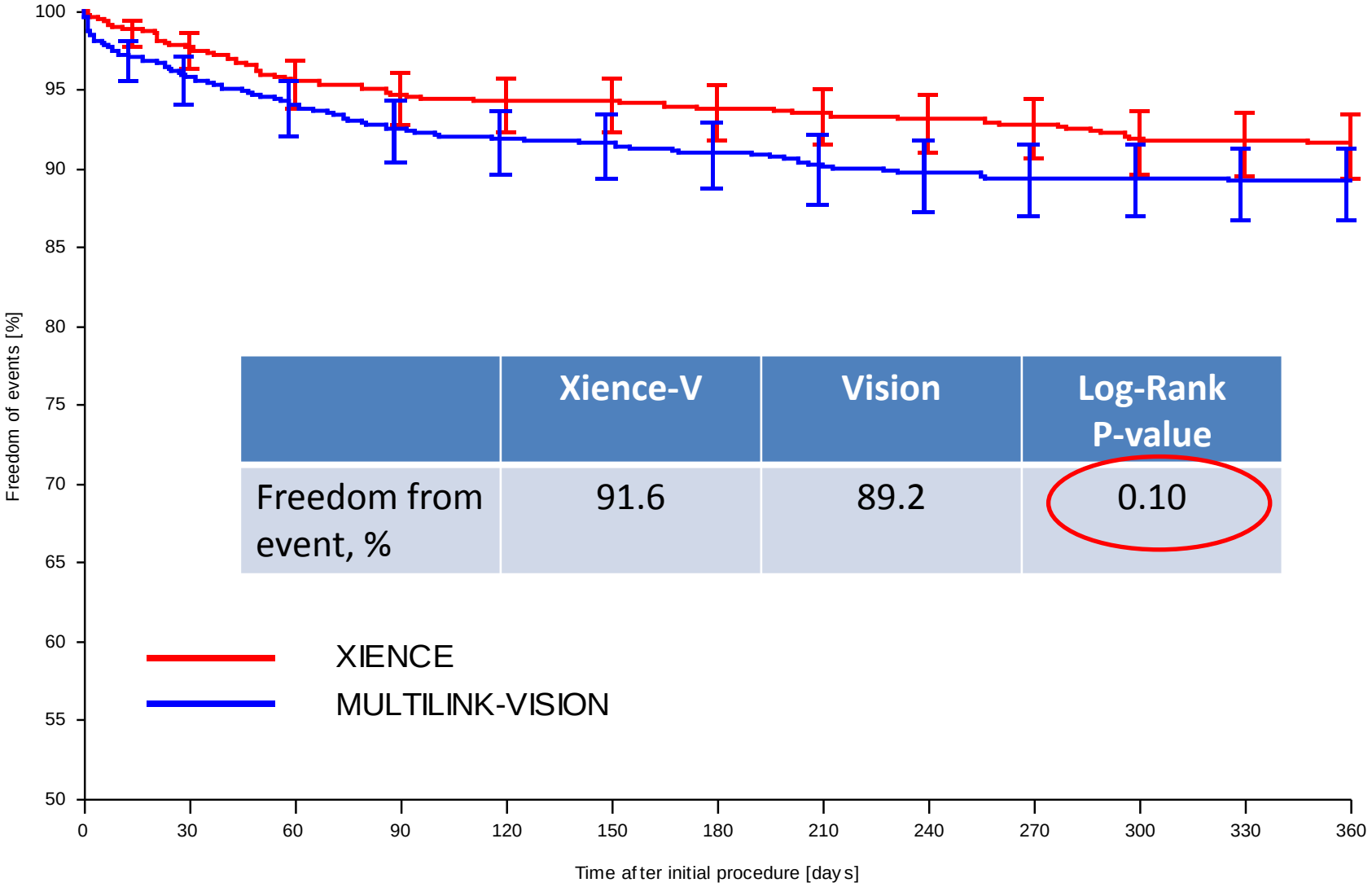


	Xience-V	Vision	Log-Rank P-value
Freedom from event, %	98.6	97.9	0.30

EXAMINATION trial

Secondary Endpoints:

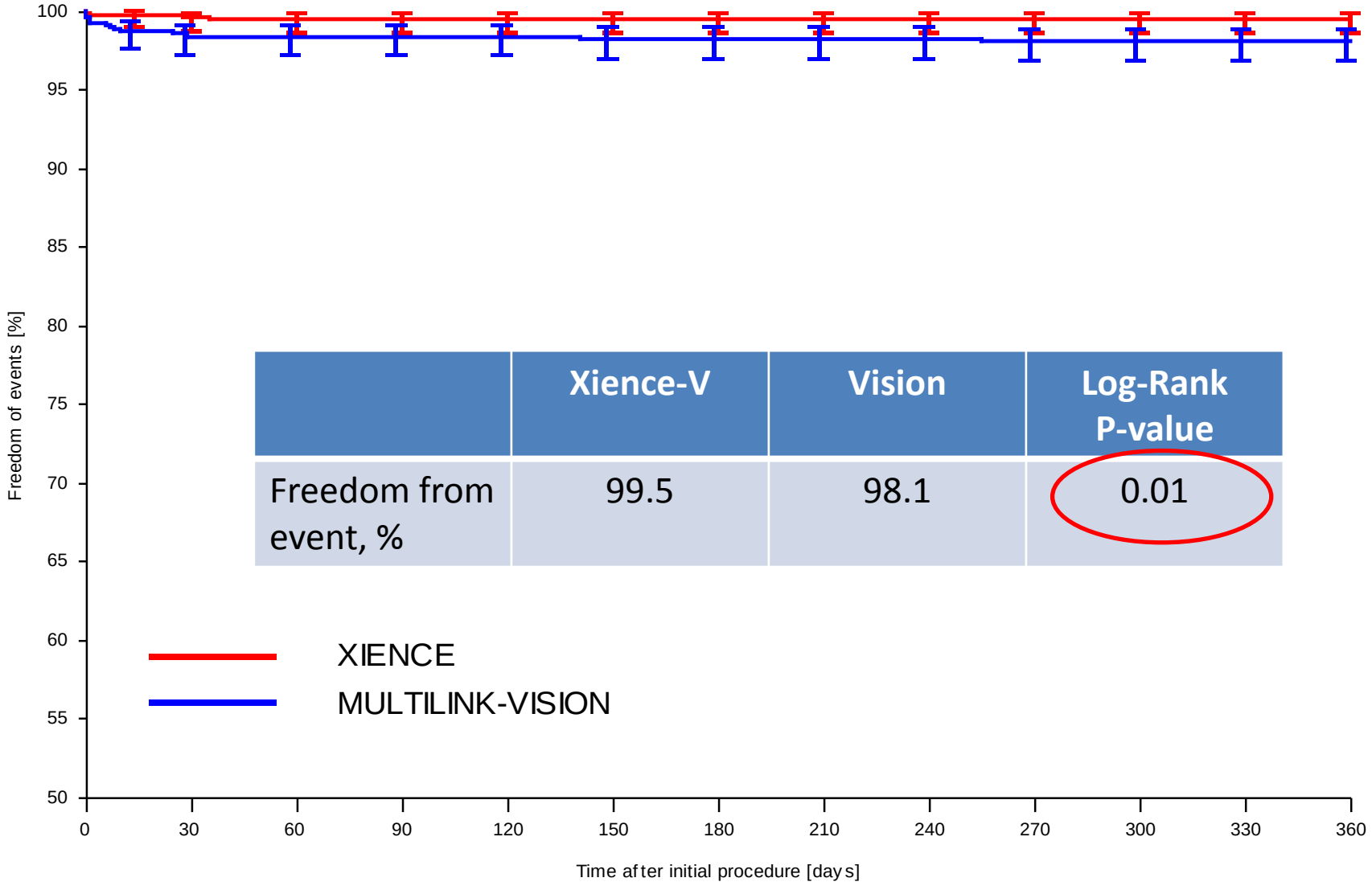
Repeat Revascularization



	Xience-V	Vision	Log-Rank P-value
Freedom from event, %	91.6	89.2	0.10

Secondary Endpoints:

Definite Stent Thrombosis

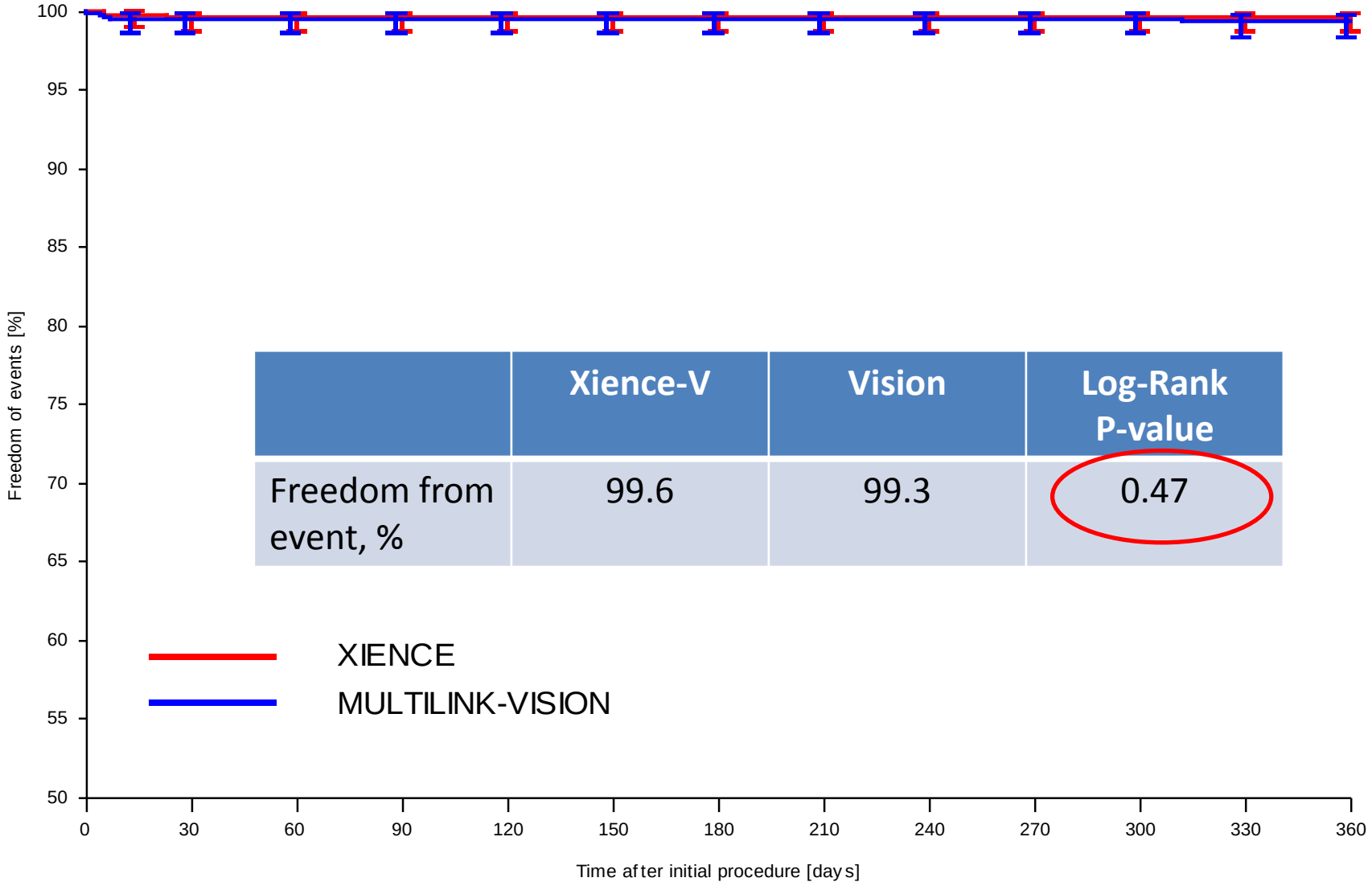


	Xience-V	Vision	Log-Rank P-value
Freedom from event, %	99.5	98.1	0.01

EXAMINATION trial

Secondary Endpoints:

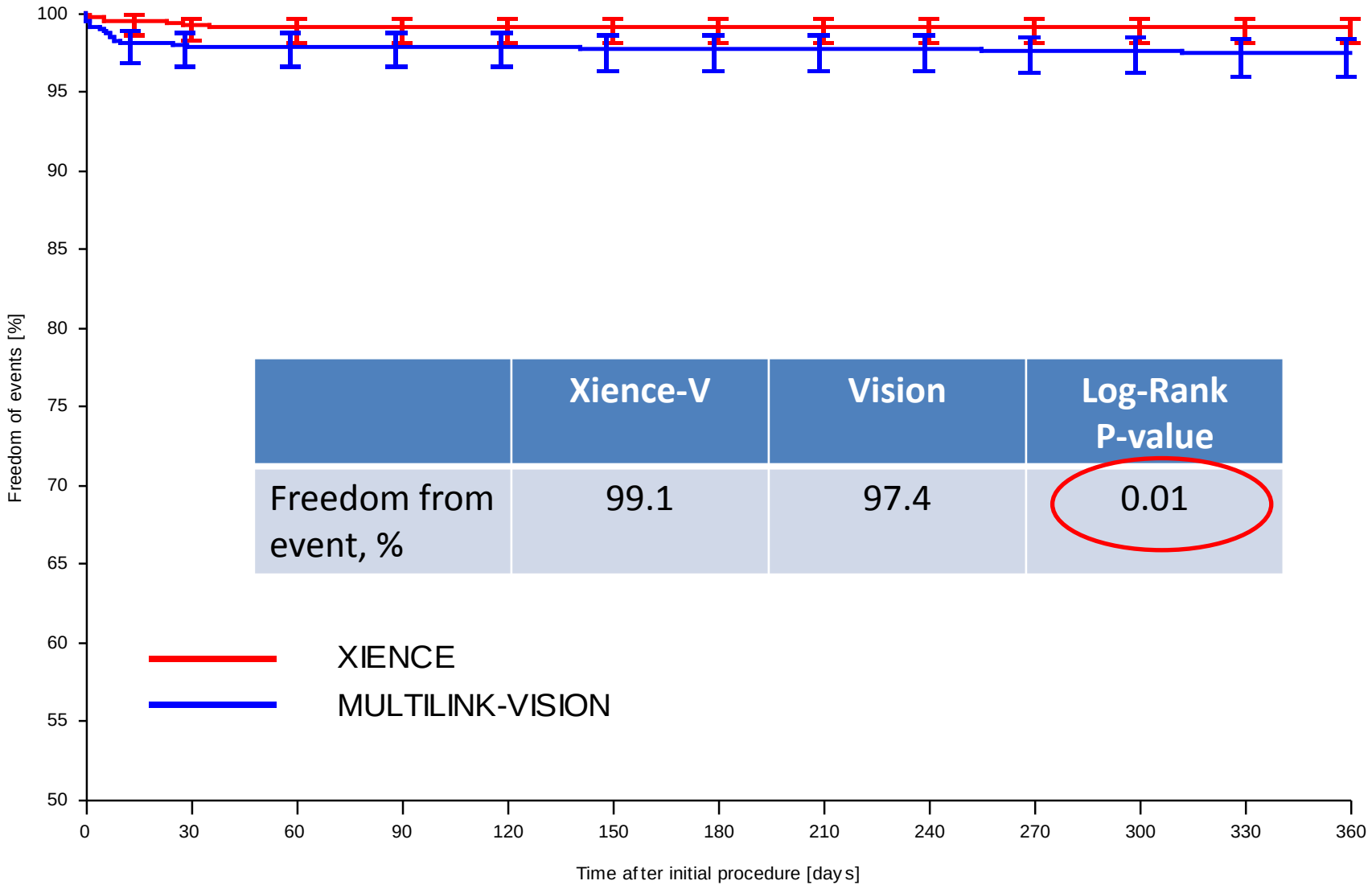
Probable Stent Thrombosis



	Xience-V	Vision	Log-Rank P-value
Freedom from event, %	99.6	99.3	0.47

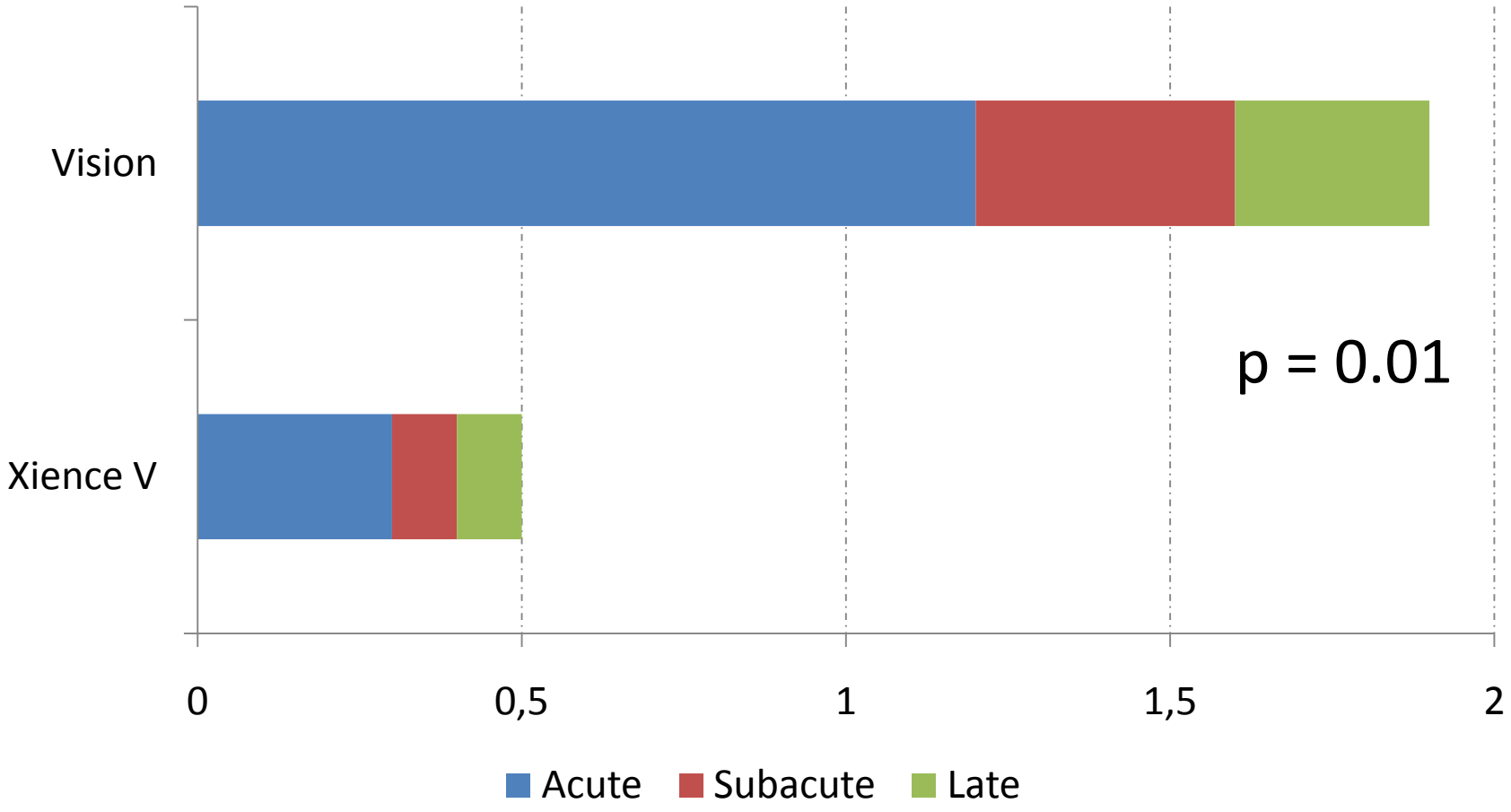
Secondary Endpoints:

Definite/Probable Stent Thrombosis

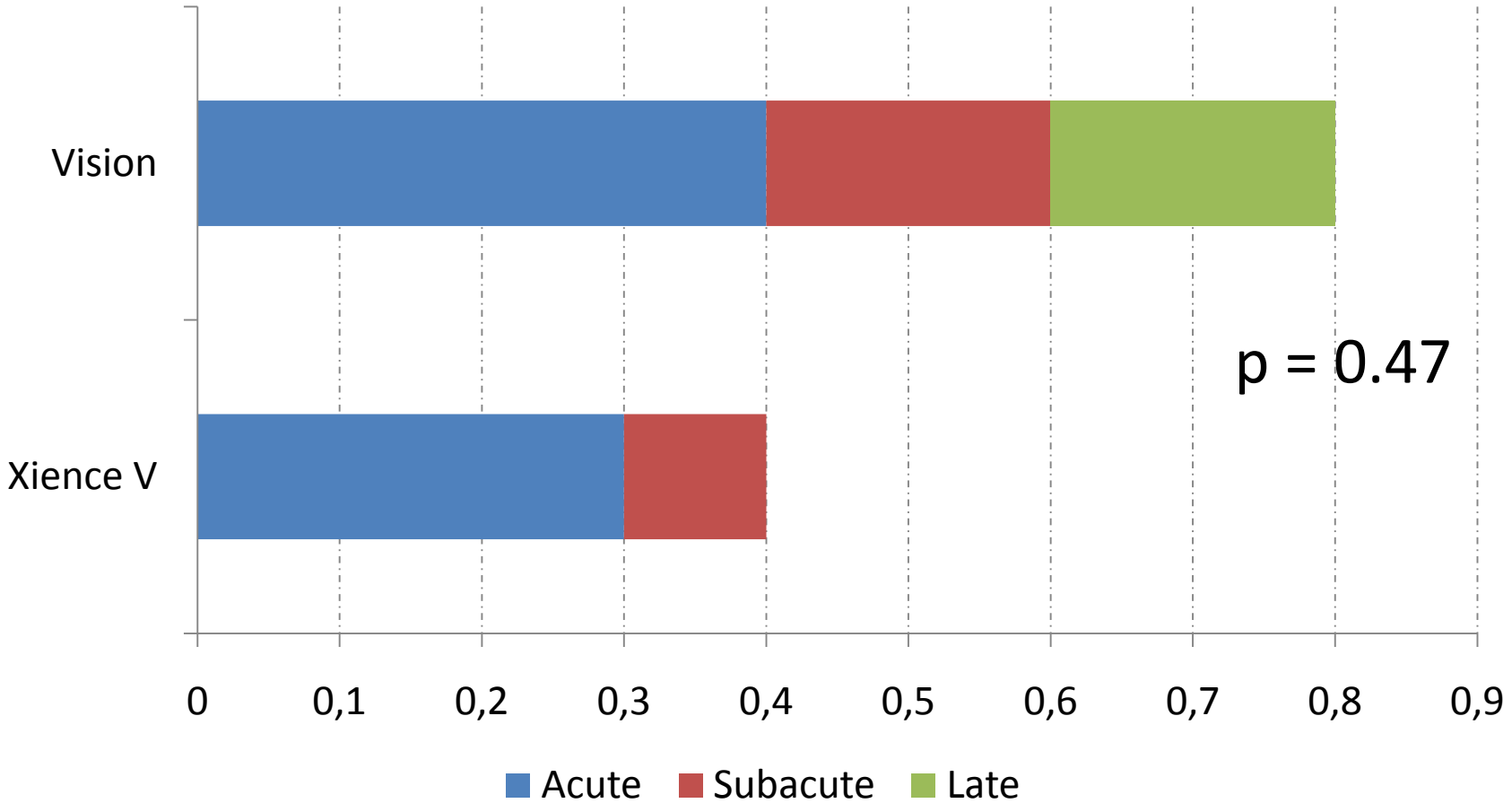


	Xience-V	Vision	Log-Rank P-value
Freedom from event, %	99.1	97.4	0.01

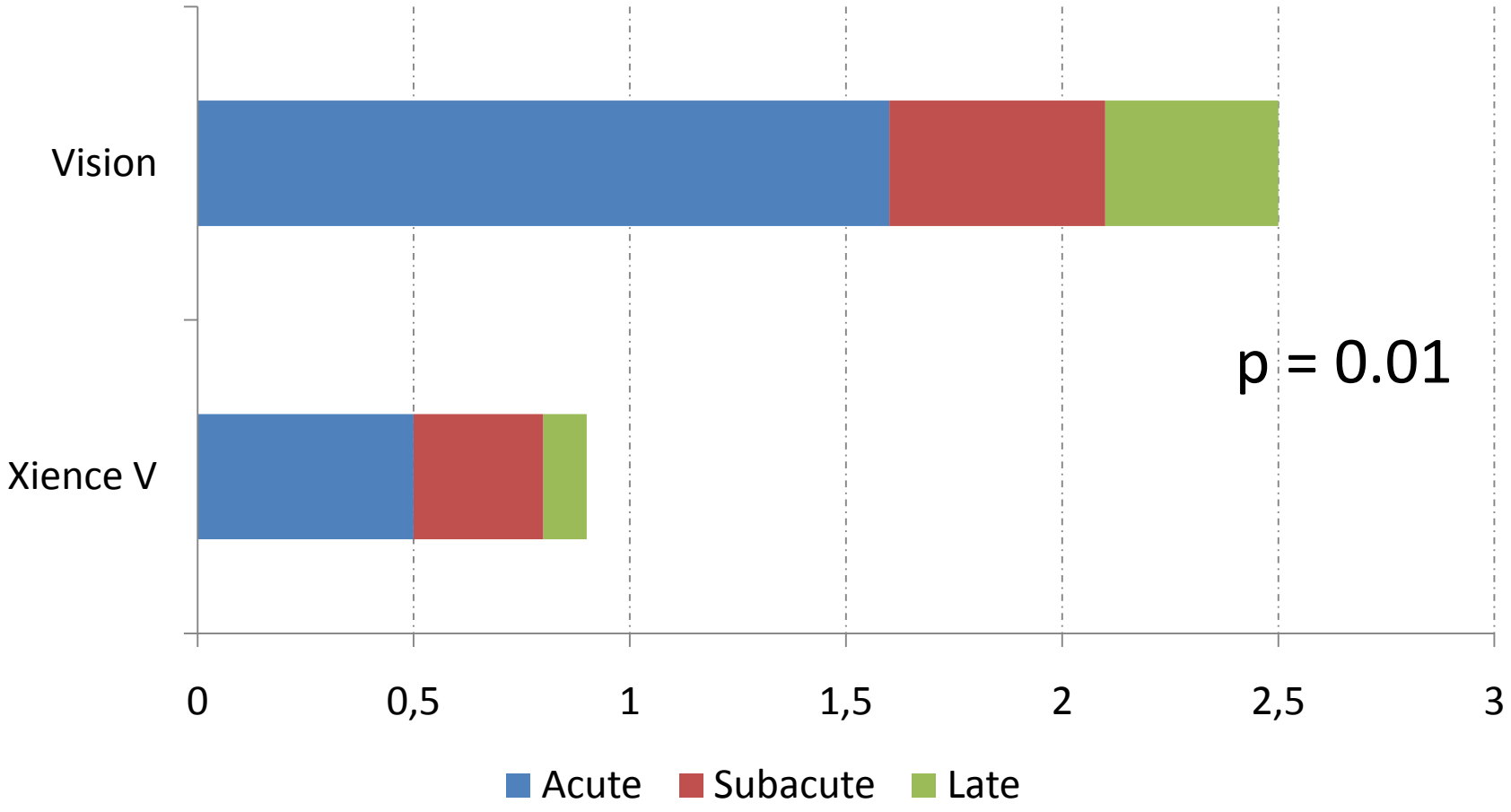
Definite Stent Thrombosis



Probable Stent Thrombosis



Definite/Probable Stent Thrombosis



Conclusions

- The use of Xience V stent in the setting of STEMI resulted in a numerically (not significantly) reduced primary endpoint at the expense of a trend in reduction the repeat revascularization rate.
- The significant reduction observed in the definite and definite/probable stent thrombosis rates suggest an excellent safety profile of the Xience V stent in this high risk patients presenting with STEMI.
- The results of this “all-comer” randomized controlled trial are highly representative of the real world population.