TURIN, 20TH—21ST NOVEMBER 2008

GREAT INNOVATIONS IN CARDIOLOGY

4TH JOINT MEETING WITH MAYO CLINIC

4TH TURIN CARDIOVASCULAR NURSING CONVENTION

SESSION V:

NEW APPROACH TO CARDIOVASCULAR DISEASES

H. Benamer (Massy—France)

Spirit woman: rational and current status

XIENCE V SPIRIT WOMEN Program

Dr BENAMER Hakim
ICPS Massy

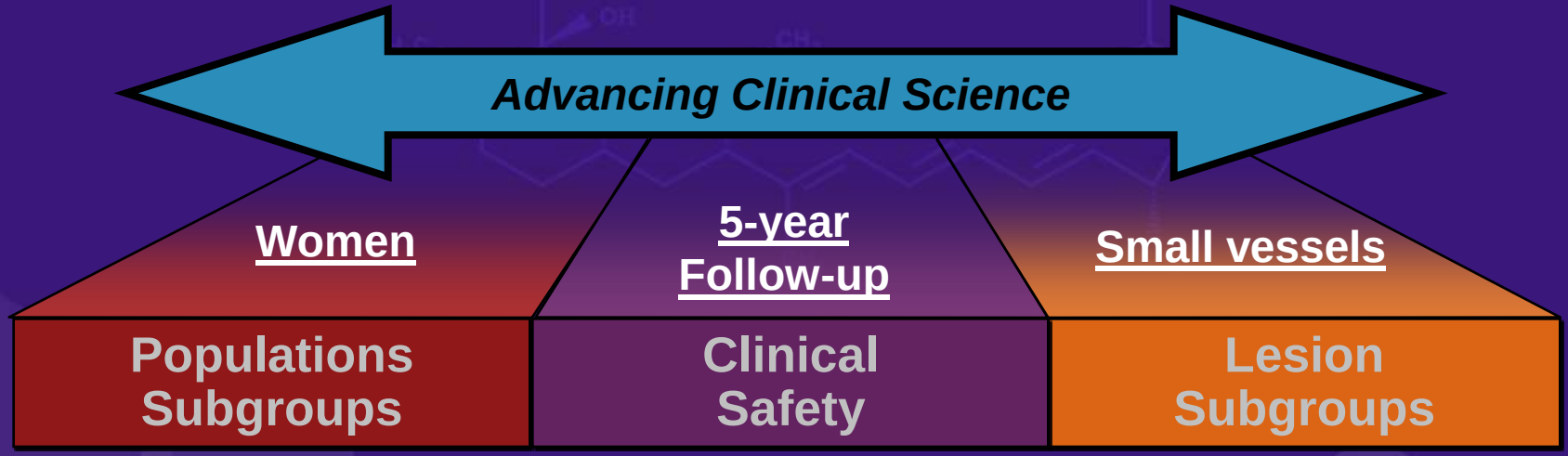
Xience V

ABBOTT VASCULAR - SPIRIT WOMEN STUDY

SPIRIT WOMEN Clinical Study

A Clinical Evaluation of the XIENCE V Everolimus Eluting Stent System in the Treatment of Women with *de novo* Coronary Artery Lesions

SPIRIT WOMEN is the Primary International Study for Abbott Vascular in 2008



Integrated Clinical Program (N > 16,000)

	Pre-approval Clinical Data
SPIRIT First	RCT 1:1 XIENCE V vs. VISION (n = 60) OUS
SPIRIT II	RCT 3:1 XIENCE V vs. TAXUS (n = 300) OUS
SPIRIT III	RCT 2:1 XIENCE V vs. TAXUS (n = 1,002) US
SPIRIT III 4.0	Registry 4.0 mm (n = 80) US

	Ongoing and Planned Clinical Data
SPIRIT III Japan	Registry (n = 88) Japan
SPIRIT IV	RCT XIENCE V vs. TAXUS 2:1 Continued Access (n = 3,690) US
SPIRIT V	Registry (n = 2,700), RCT Diabetics 2:1 vs. TAXUS (n = 300) OUS
XIENCE V SPIRIT Women	Registry (n = 1,550) RCT 2:1 vs. CYPHER (n = 450) OUS
XIENCE V USA	Post-approval Registry – real world (n ~ 5,000) US
XIENCE V India	Post-approval Registry – real world (n = 1,000) OUS

SPIRIT III - 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

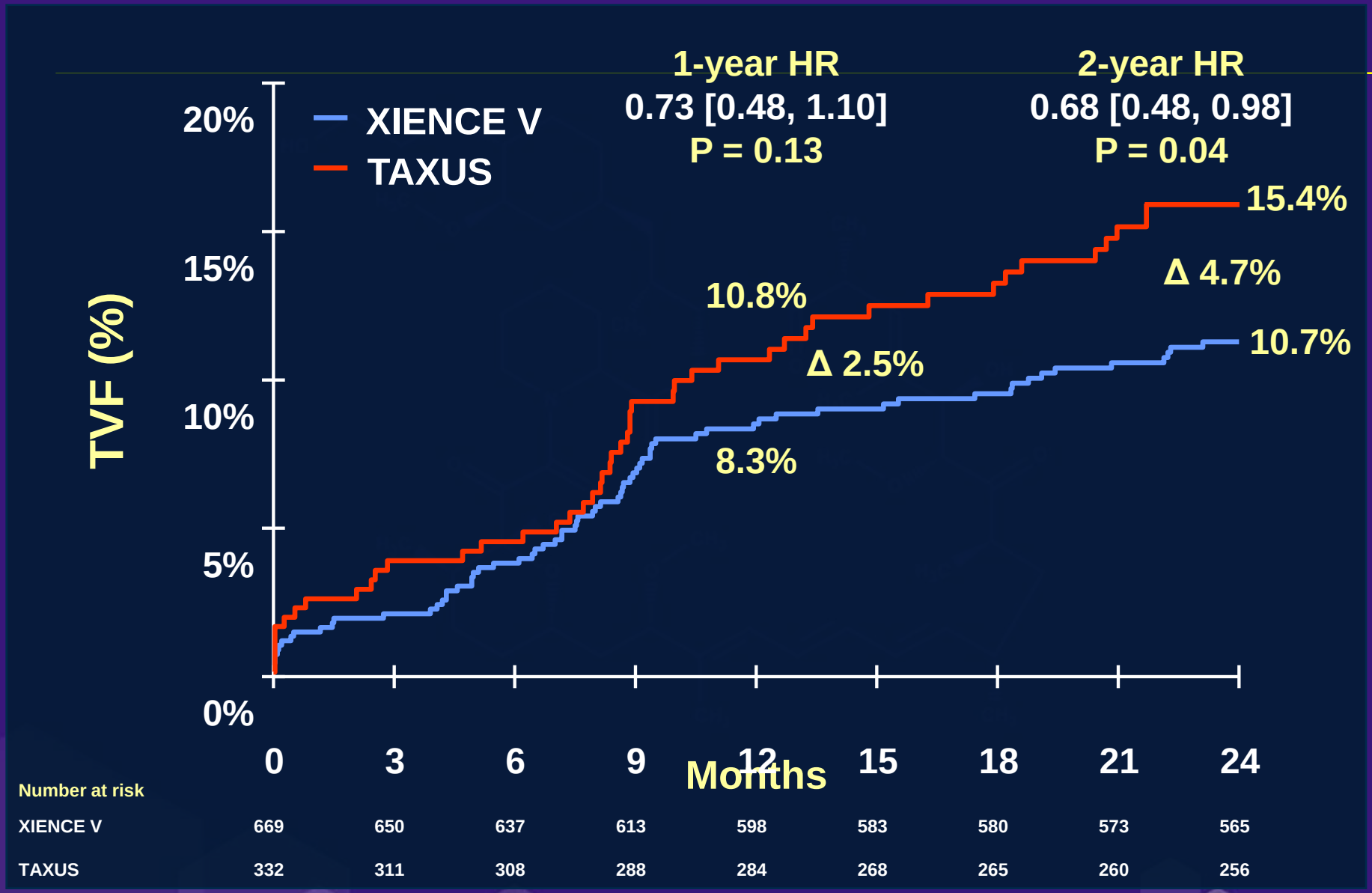
Everolimus-eluting
XIENCE V

Paclitaxel-eluting
TAXUS

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

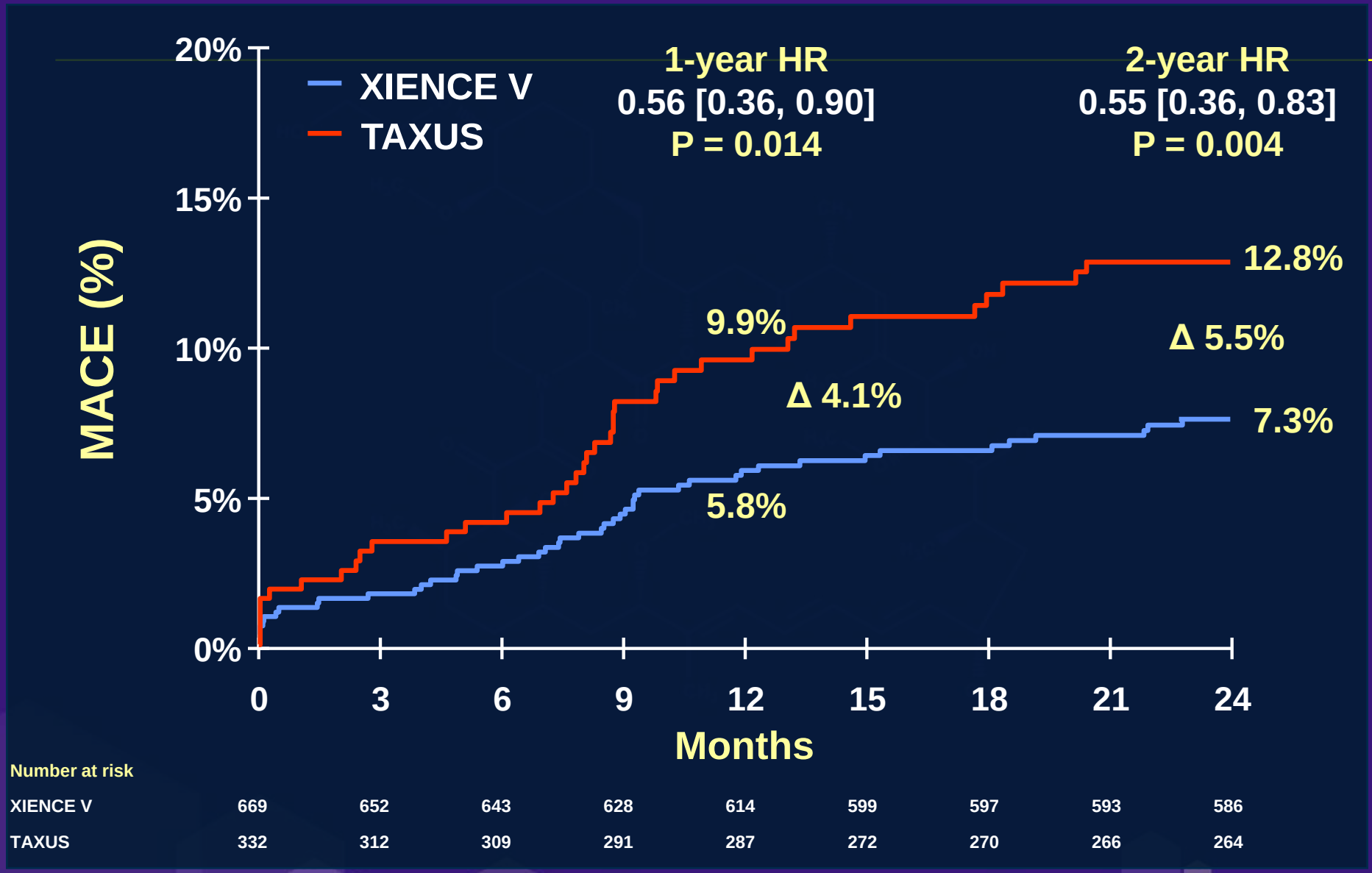
Clinical f/u: 1, 6, 9 months and yearly for 1-5 years

SPIRIT III - 1° Clinical Endpoint: Target vessel failure



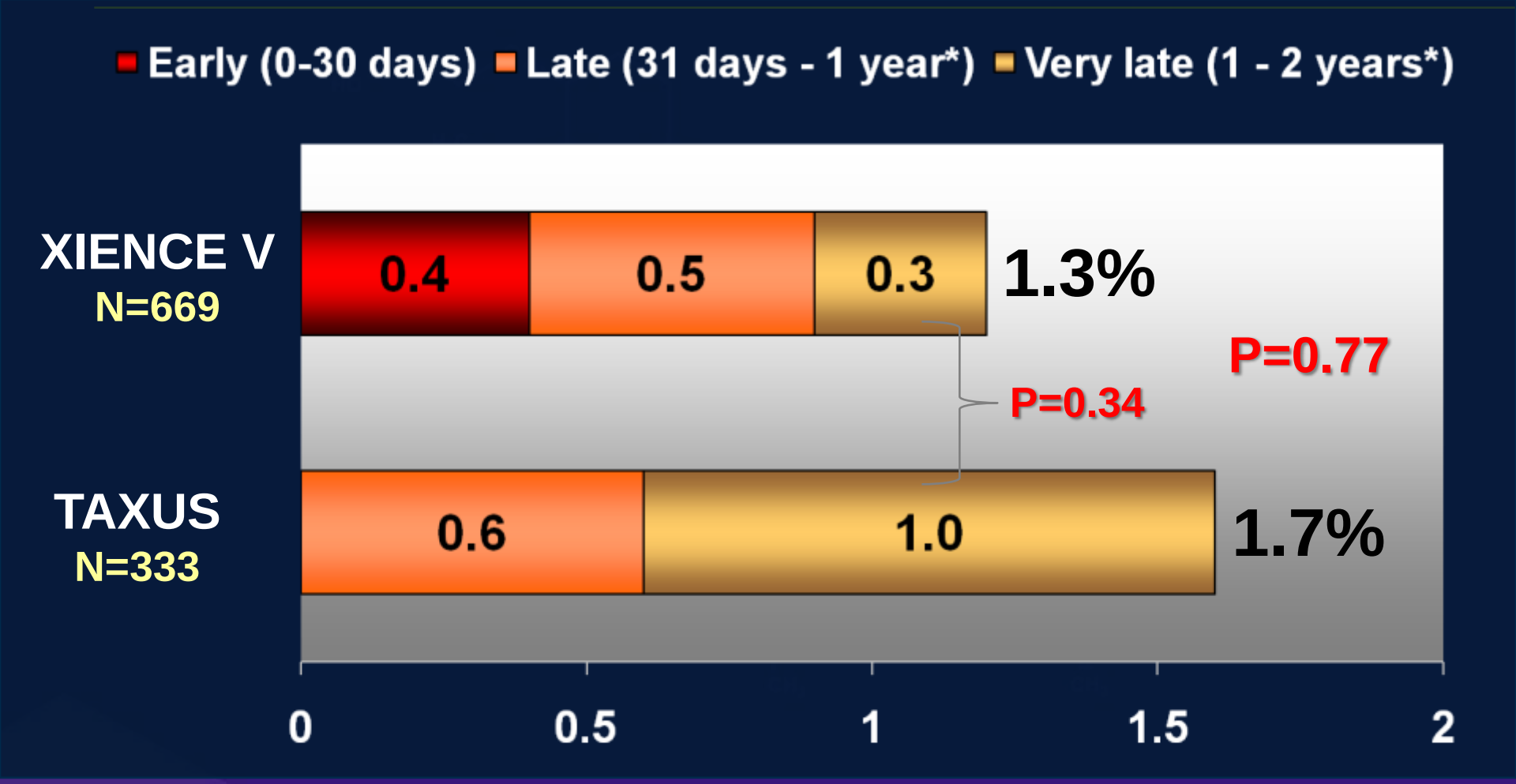
TVF = cardiac death, MI, or ischemia-driven TVR

SPIRIT III - Major Adverse Cardiac Events



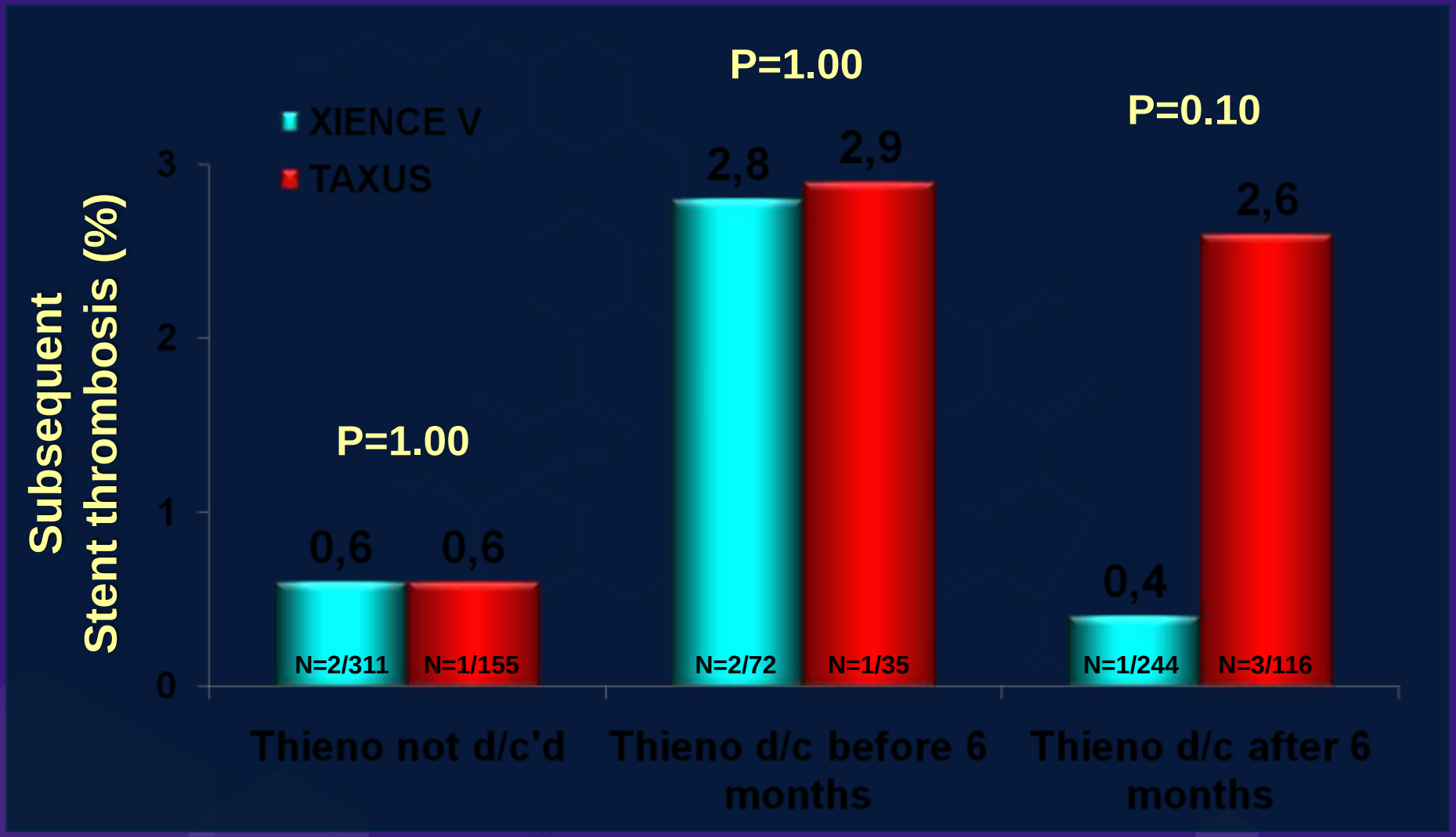
MACE = cardiac death, MI, or ischemia-driven TLR

SPIRIT III - Stent Thrombosis (ARC Def/Prob)



*Includes F/U window of ±28 days

SPIRIT III - Subsequent Stent Thrombosis* According to Thienopyridine Discontinuation



*Protocol definition

SPIRIT II + III: 1-year Pooled Patient Level Meta-Analysis in Vessels <2.765mm

SPIRIT II + III

Similar inclusion and exclusion criteria: Up to two de novo lesions, maximum of one lesion per epicardial vessel
RVD <2.765 mm
LL ≤ 28 mm

Meta-Analysis of Patient Level Data
N = 541

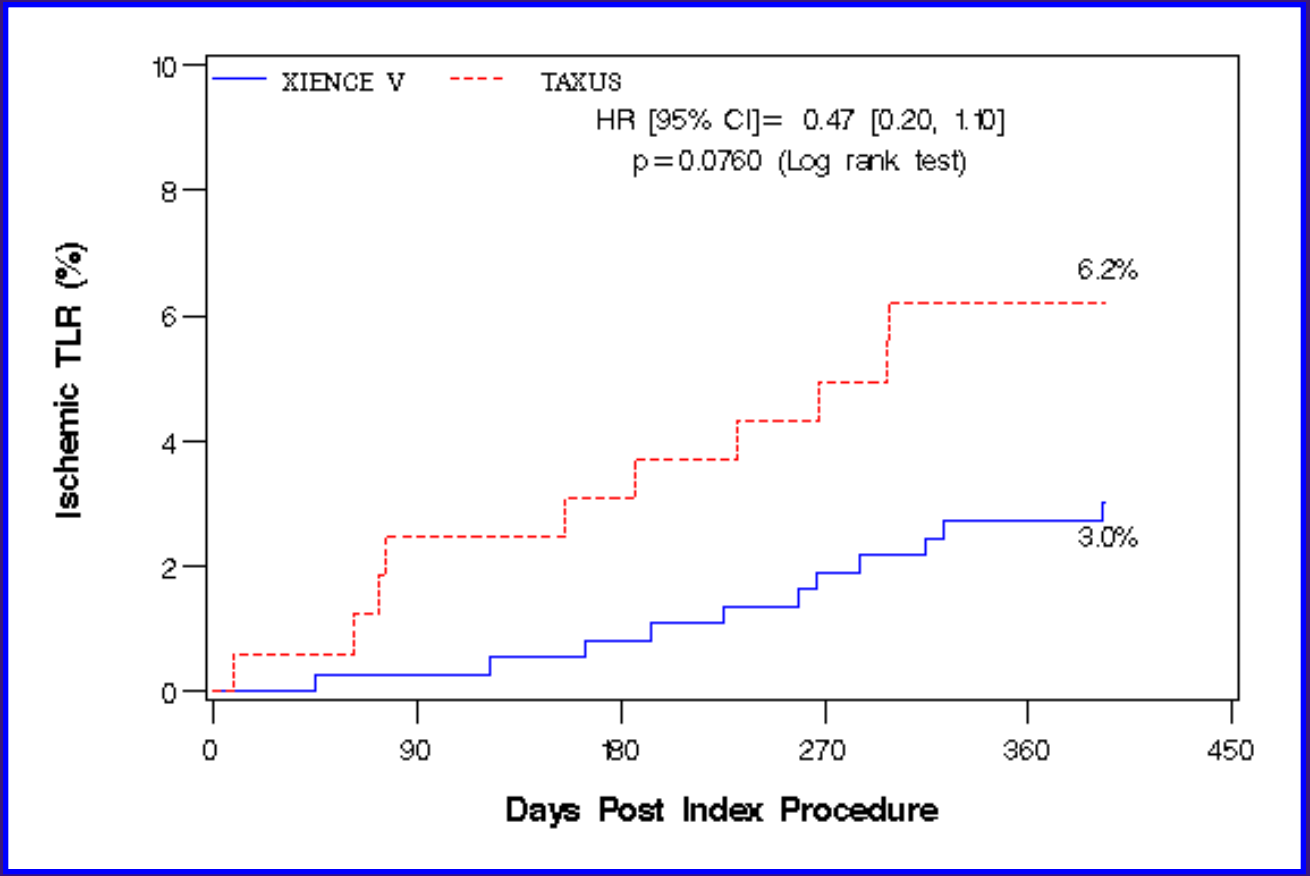
XIENCE V
N = 376

TAXUS®
N = 165

- Independent Meta-Analysis done by CRF
- SPIRIT II and SPIRIT III have similar inclusion and exclusion criteria
- Pooled, patient level analysis of combined SPIRIT II and SPIRIT III data

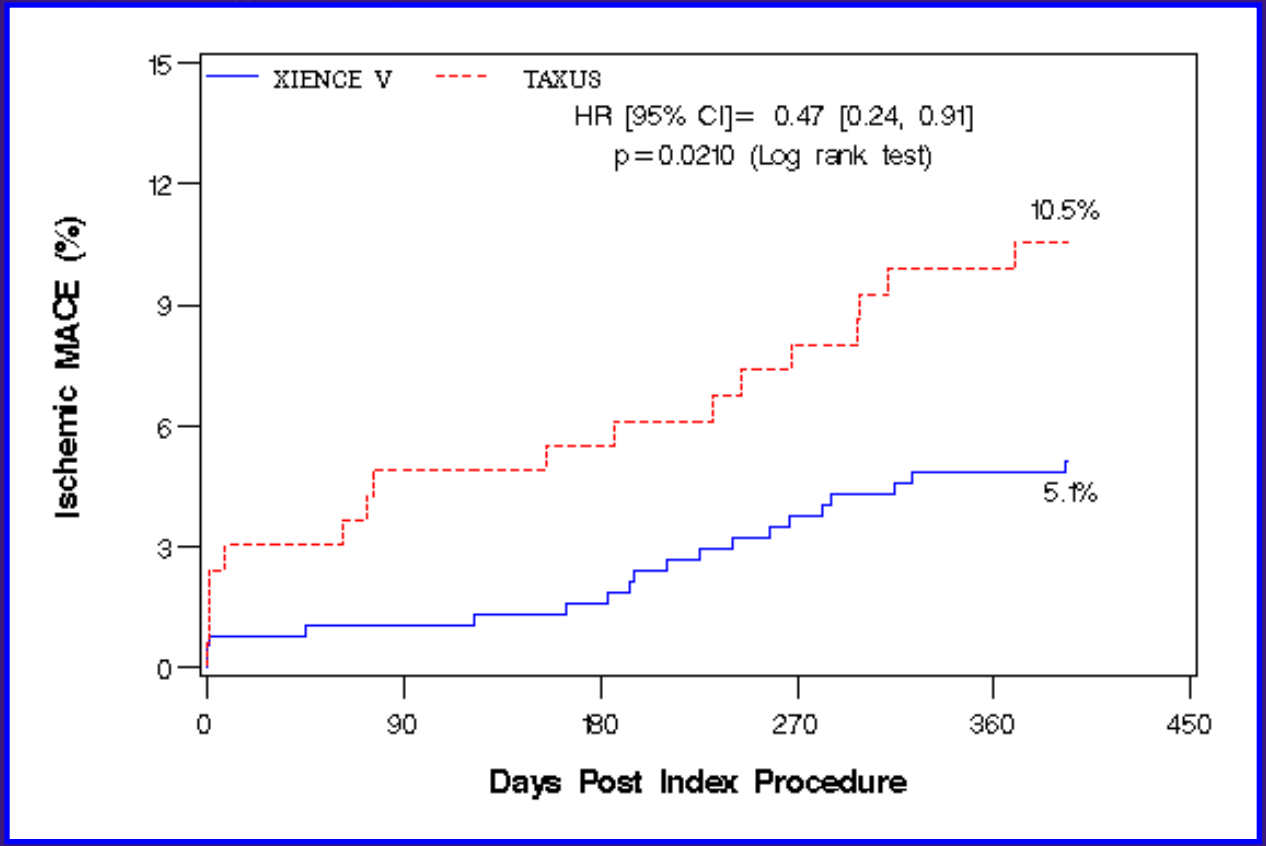
*SPIRIT II was up to 4.0mm

SPIRIT II + III: 1-year Pooled Patient Level Meta-Analysis in Vessels <2.765mm - Ischemic TLR (393 Days)



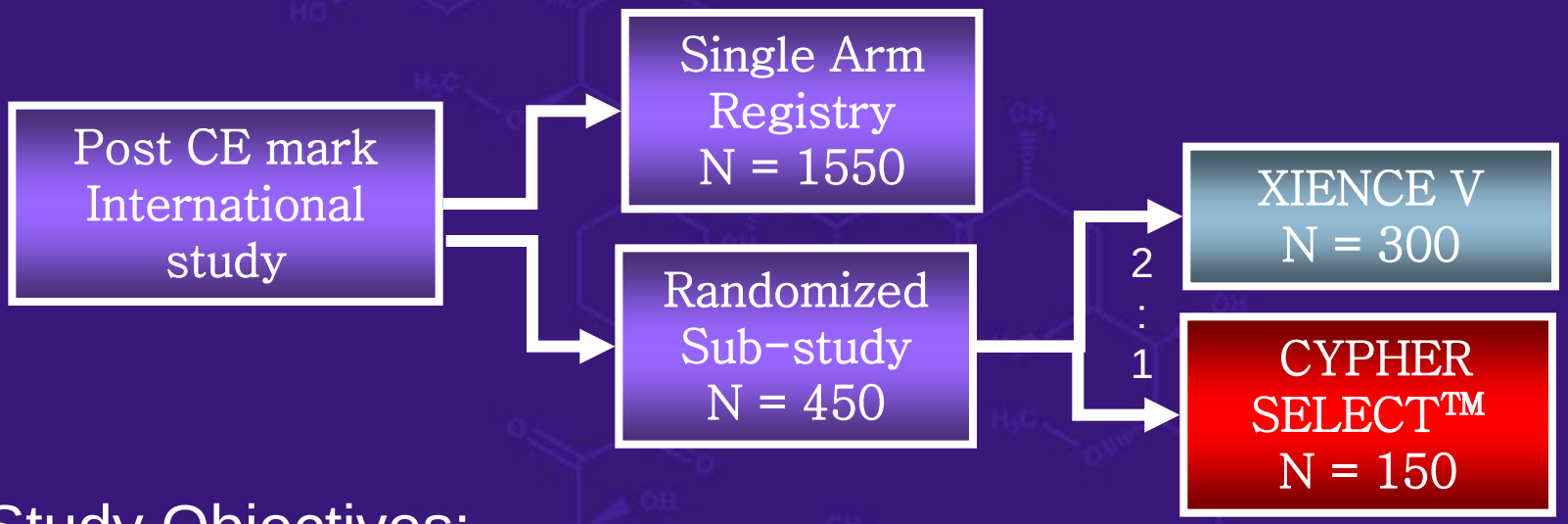
	0	90	180	270	360	393
Number at Risk						
XIENCE V	**376**	**370**	**367**	**357**	**352**	**351**
TAXUS®	**165**	**158**	**157**	**151**	**149**	**148**

SPIRIT II + III: 1-year Pooled Patient Level Meta-Analysis in Vessels <2.765 - Ischemic MACE (393 Days)



	0	90	180	270	360	393
Number at Risk						
XIENCE V	376	367	364	352	347	346
TAXUS®	165	154	153	146	143	141

XIENCE V SPIRIT WOMEN



Study Objectives:

- Characterization of the female population undergoing stent implantation with XIENCE V
- Continued assessment of XIENCE V with the primary focus on clinical outcomes in the treatment of female patients

Women and Cardiovascular Disease

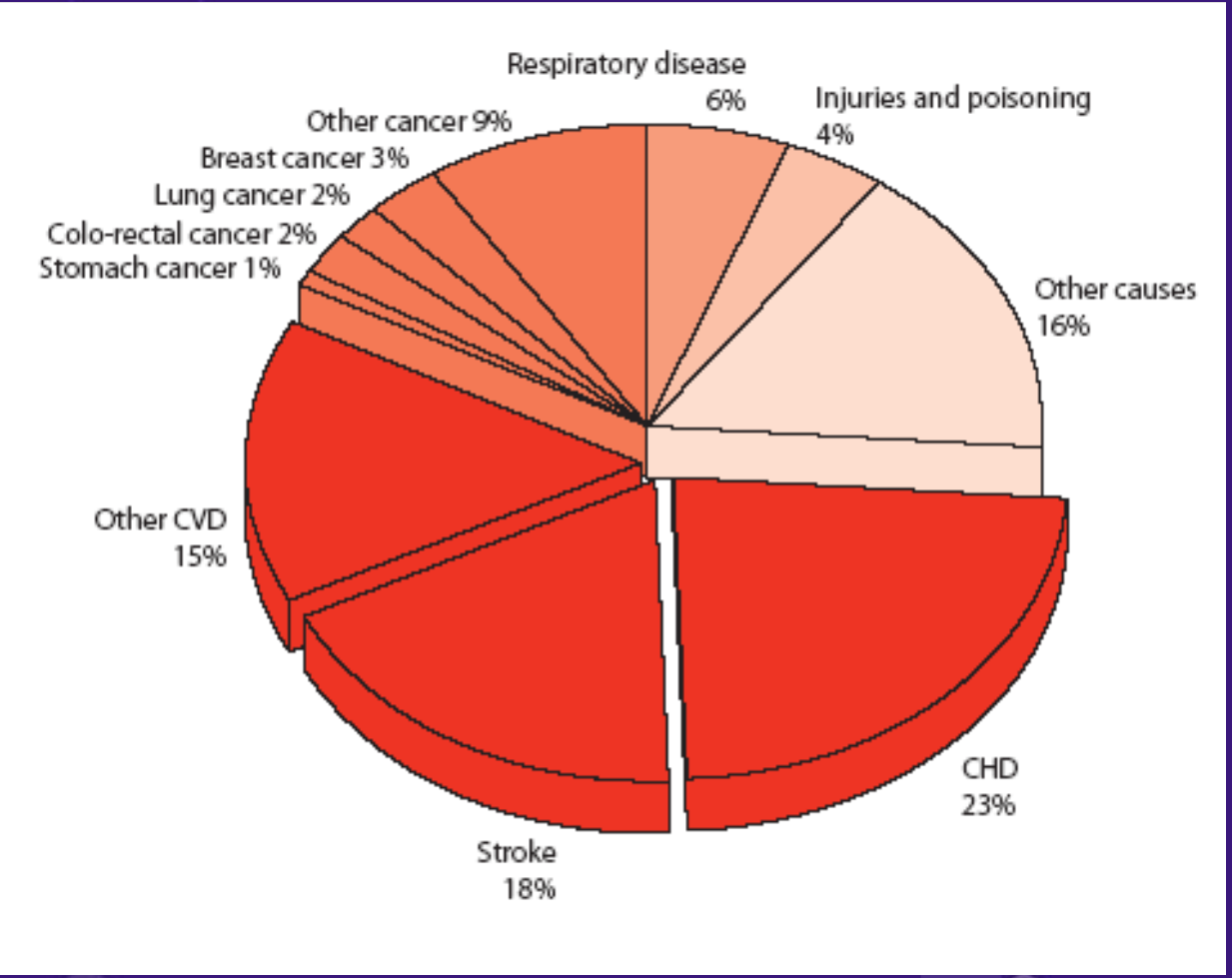
- Data show that the **majority of all deaths** in women are the result of cardiovascular disease.
- However, a **physician awareness** survey found that fewer than 1 in 5 physicians know that more women than men die each year from CVD.
- Symptoms are **different** in women.[1,3]
- Treatment strategy, options, and outcome in CVD are **less favourable** for women than for men.[2,4]
- Women and their physicians need to be **aware** of women's risks to better embrace **preventive** measures.
- Women are **under-represented** in clinical trials.[2]

1. World Heart Federation
2. National Center on Health Statistics; National Heart, Lung and Blood Institute; and American Heart Association's 2002 Heart and Stroke Statistical Update
3. MayoClinic.com Tools for Healthier Lives, "Hearth Disease in Women: A Mayo Clinic Specialist Answers Questions", Sharonne Hayes, M.D., director of the Women's Heart Clinic at Mayo Clinic.
4. American Acadamy of Family Physicians

Death By Cause in Women (2004)

- ***CVD is responsible for 55% of deaths in women (43% in men)***

- ***18 x Mortality compared to Breast cancer***



World Health Organization 2004 (Europe)

Women in Clinical Trials – SPIRIT III

Gender Based Evaluation of the XIENCE V

- ACC 2008 Congress - Dr. A. Lansky

Summary Conclusions:

• XIENCE V significantly reduced in-stent / in-segment late loss in women at 8 months.

• The beneficial effects of XIENCE V compared to TAXUS in reducing MACE was statistically significant among women.

• XIENCE V may have a trend toward reduced ischemia-driven target lesion revascularization and any target lesion revascularization.

Women in Clinical Trials

ESC Recommendation: Conduct trials in female patients

- Statement from Policy Conference on Cardiovascular Diseases in Women (2006)[1]

- Only 15 – 35% of the subjects in PCI trials are women[2]
- Only 1 in 5 patients in arrhythmia and HF trials is a woman[2]
- 8 out of 10 withdrawn prescription drugs (since 1997) caused more adverse events in women than in men[2]

1. Stramba-Badiale M, Fox KM, Priori SG, Collins P, Daly C, Graham I, Jonsson B, Schenck-Gustafsson K, Tendera M. Cardiovascular diseases in women: a statement from the policy conference of the European Society of Cardiology. Eur. Heart J. 2006: 27: 994-1005.
2. National Center on Health Statistics; National Heart, Lung and Blood Institute; and American Heart Association's 2002 Heart and Stroke Statistical Update

XIENCE V SPIRIT WOMEN

First prospective study designed to:

- Study DES in female patients
- Compare treatment outcomes to a similar male population (SPIRIT V trial)
- Understand challenges in referral pathway

Through this initiative – Our goal is to increase awareness among physicians and patients on cardiovascular disease in women

XIENCE V SPIRIT WOMEN
Global Site Distribution

Argentina (2)
Brazil (4)
Venezuela (2)

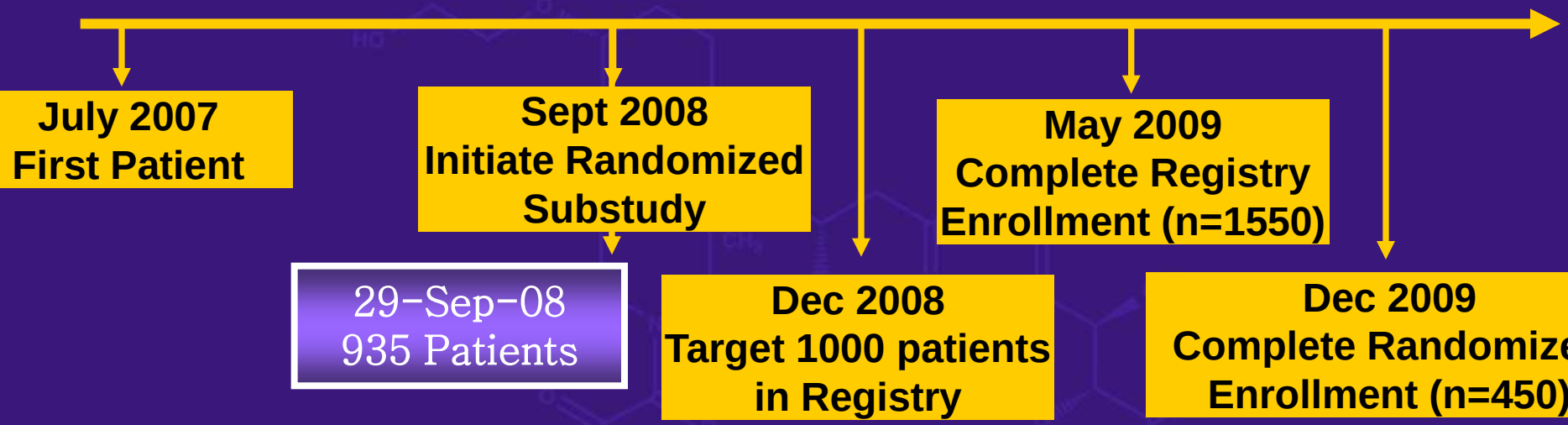
Austria (2)
Belgium (3)
Denmark (1)
France (8)
Germany (15)
Greece (2)

Hungary (2)
Israel (1)
Italy (12)
Latvia (1)
Netherlands (5)
Norway (2)
Poland (2)

Portugal (3)
Russia (1)
South Africa (2)
Spain (5)
Switzerland (4)
UK (3)

Australia (3)
Hong Kong (4)
India (6)
Malaysia (1)
China (6)

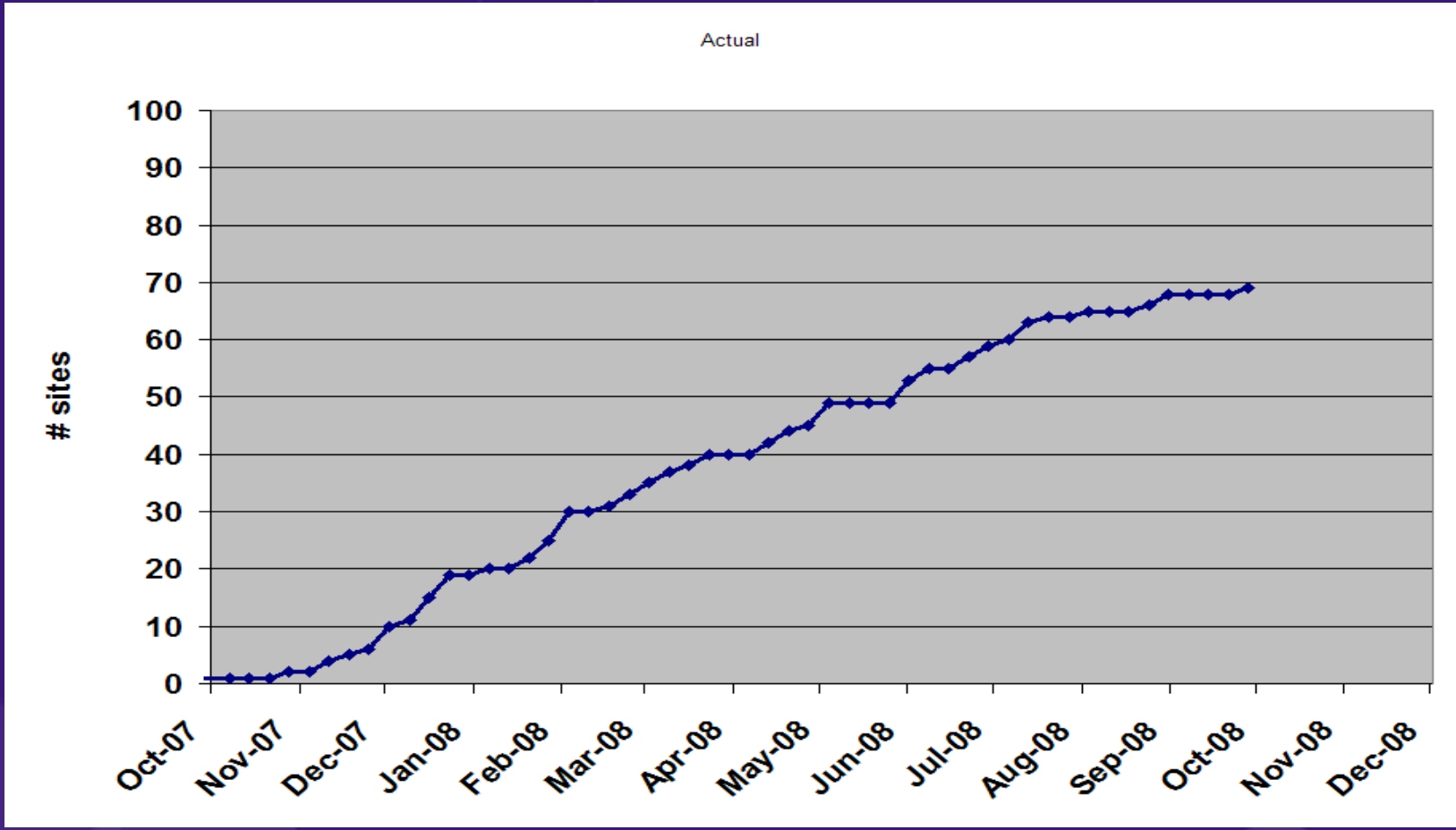
XIENCE V SPIRIT WOMEN Timeline



- Continue to enroll in the Single Arm Study in 2009

Site Opening Status

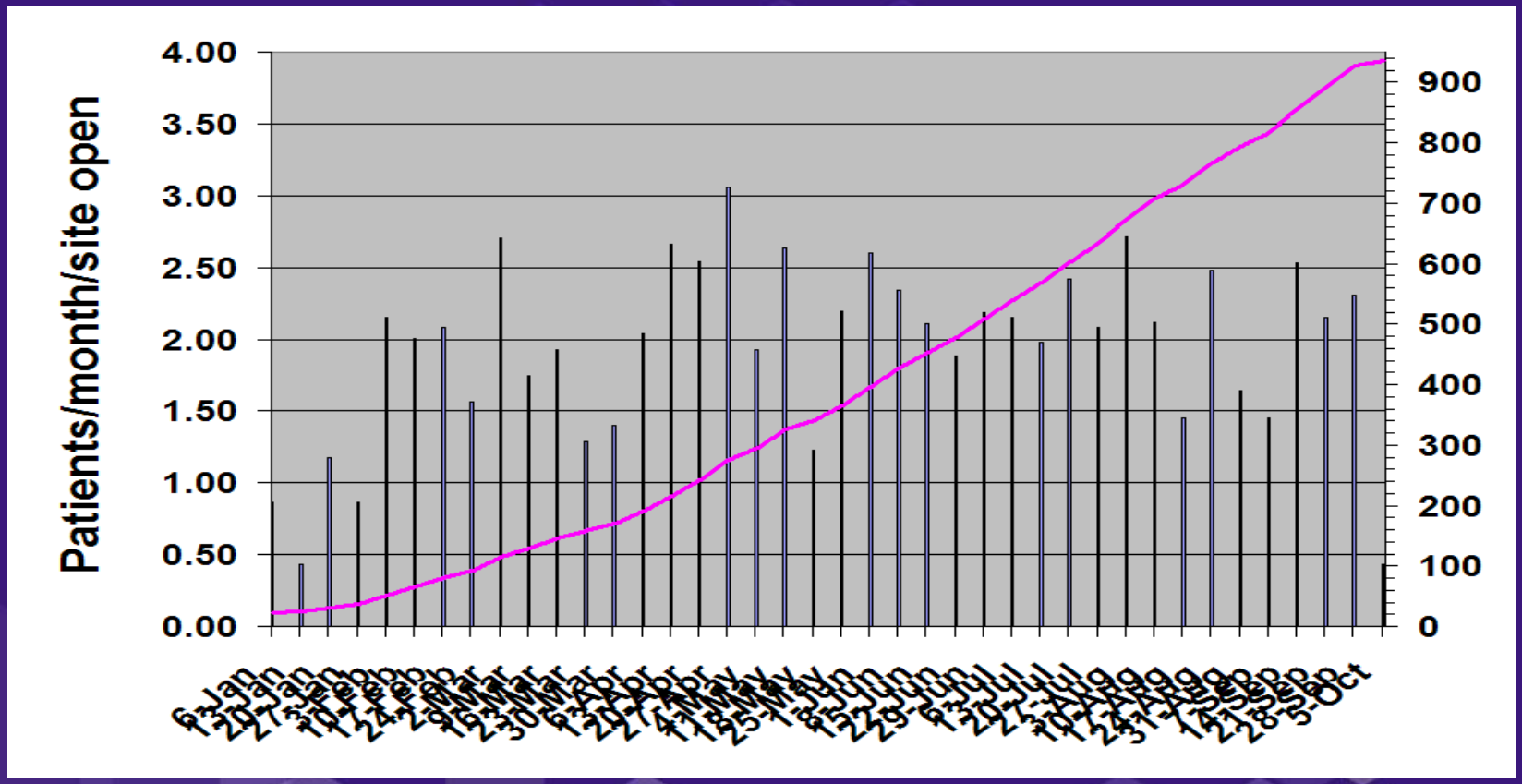
Current Status: 69 Sites Open



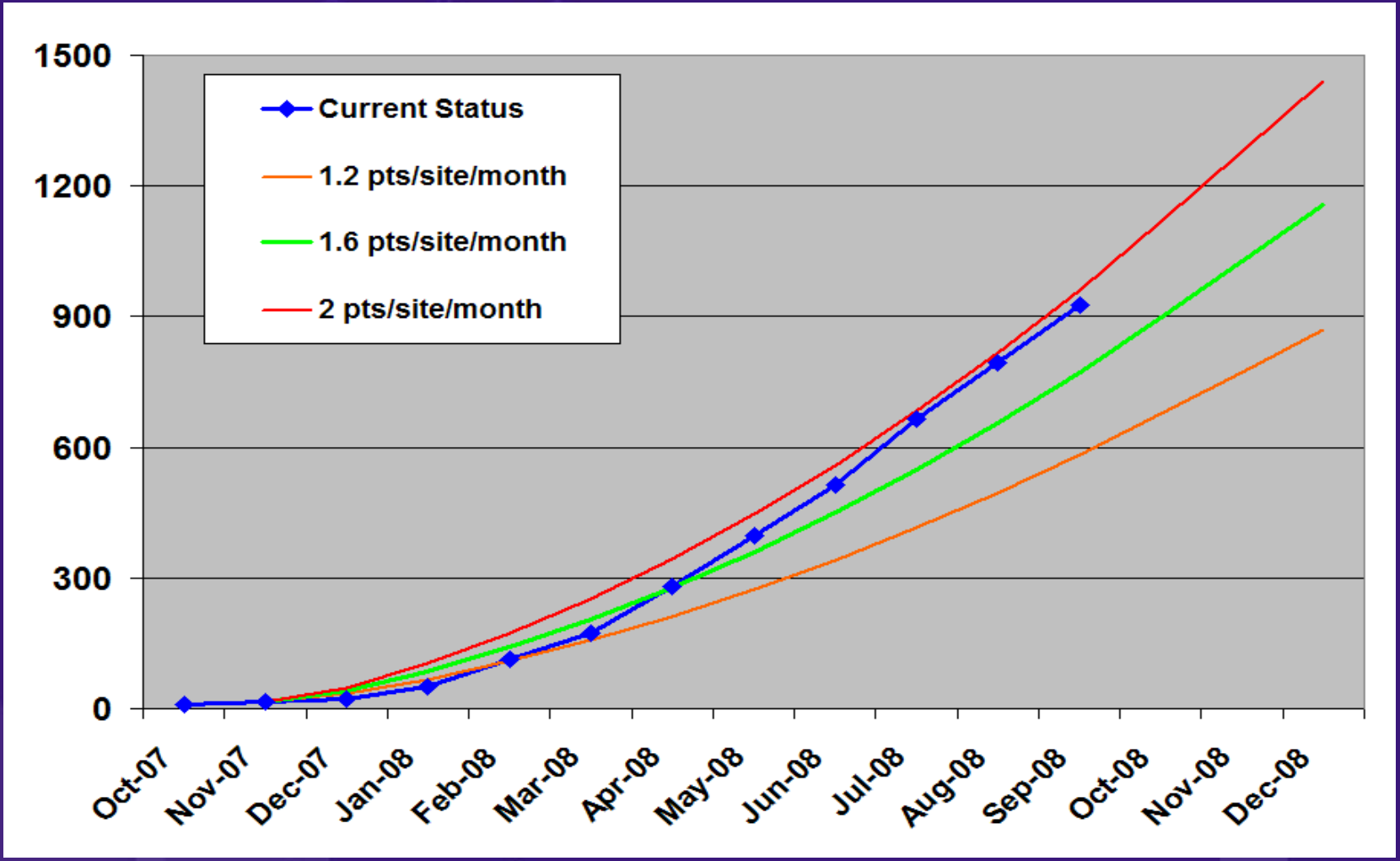
Registry Enrollment Projections

Target Recruitment: 2.0 patients/site/month

- Current Rate = 2.07 patients/site/month
- Active Sites – 80% of open sites are enrolling



Enrolment Projections



High Enrolling Sites

Top Enrollers

Total Number of Patients

	# Patients
Care Hospital (Dr. Kumar, IND)	53
OLVG (Dr. Amoroso, NED)	50
ICPS (Dr. Morice, FRA)	49
Centro Cardio Lugano (Dr. Pasotti, SWI)	48
Hospital General de Alicante (Dr. Mainar, ESP)	41
Hosp. Trias y Puyol (Dr. Mauri, ESP)	33
Hôp. Universit. de Genève (Dr. Noble, SWI)	32
St. Antonius (Dr. Suttorp, NED)	31
Latvian Center Cardiology (Dr. Erglis, LAT)	31
H. H. Ziekenhuis Roeselare (Dr. Stammen, BEL)	30

Top Enrollment Rate

Enrollment Rate = Patients/Month

	# Patients	Patients last
Centro Cardio Lugano (Dr. Pasotti, SWI)	48	9
Semmelweis University (Dr. Merkely, HUN)	23	7
Instituto Dante Pazzanese (Dr. Abizaid, BRA)	15	7
Feiringkliniken (Dr. Molstad, NOR)	12	7
Care Hospital (Dr. Kumar, IND)	53	6
Allgem. Krankenhaus Wien (Dr. Glogar, AUS)	17	6
University of Pécs (Dr. Horvath, HUN)	6	6
H. H. Ziekenhuis Roeselare (Dr. Stammen, BEL)	30	5
Ospedale di Modena (Prof. Modena, ITA)	5	5
ICPS (Dr. Morice, FRA)	49	4

Overall Status – Randomized Sub-Study

- Sites Invited: 21
- Sites ready for activation: 13

- 5 planned/performed SIV:
  - Dr. Morice: 23/Sep/08
  - Prof. Nordrehaug: 16/Sep/08
  - Prof. Witkowkski: 22/Sep/08
  - Dr. Pasotti: 24/Sep/08
  - Dr. Helqvist: 30/Sep/08

- Enrollment start foreseen for end of September/beginning of October

SPIRIT WOMEN - Protocol Amendment

Protocol amendment has been approved and signed off.

The major modifications included in the amendment are as follows:

- The treatment strategy will be determined by the Investigator; however it is **recommended** that each enrolling Investigator review the most recent IFU
- Adverse event collection following the 2 year follow up visit will be limited to cardiac and serious adverse events only
- Blood work requirements and study endpoint defenitions have been updated to ensure alignment with ARC definitions.

Women Specific Data Collected

- Gender-Specific Symptoms- Hormonal Status, Risk Factors
- Referral Path- Time from referring physician(s) to interventional cardiologist
- These questions have also been added to SPIRIT V
  - Data from both studies will provide data on gender differences across geographical areas

Conclusions

1. First prospective study designed to focus on female population
   - Goal is to increase awareness among physicians and patients on cardiovascular disease in women

2. Clinical Studies that target specific patient groups require more effort than “all-comer” registries
   - Only 15 – 35% of the subjects in PCI trials are women

3. Commitment needed from all sites to actively recruit women
   - Target enrollment rate: 2 patients/site/month