

## ARTS II

# Adjudication of events for FDA panel

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Arterial Revascularization Therapies Study II  
of the sirolimus-eluting Bx VELOCITY™ balloon  
expandable stent in the treatment of patients  
with de novo coronary artery lesions

# ARTS II Study Design

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## Design

- ■ Single arm, multicenter trial
- ■ 607 patients in 45 centers from 19 countries
- ■ The main goal of the ARTS II trial is to demonstrate non-inferiority in clinical effectiveness and cost-effectiveness with the CYPHER® stent

## Primary endpoint

- ■ Effectiveness of coronary stent implantation using the CYPHER™ sirolimus-eluting stent with that of surgery as observed in ARTS I measured as MACCE free survival at 1 year

## ARTS II Patient Population

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- ■ Patients between 18 and 80 years with Multivessel Disease (MVD)
- ■ Stable, unstable angina or silent ischemia
- ■ At least 2 lesions in different vessels and different territories
- ■ Patients will be stratified in order to reach a population with  $\geq 2.7$  lesions/ patient
- ■ No PCI or CABG in the past

# ARTS II Baseline Demographics and Clinical Characteristics

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	<b>ARTS II (N=607)</b>
Male	465 (77%)
Age (years)	63 $\pm$ 10
Previous MI	209 (34%)
Diabetes	159 (26%)
Hypertension	408 (67%)
Hypercholesterolemia	447 (74%)
Family history	217 (36%)
Current smokers	117 (19%)
Unstable angina	221 (36%)
2-VD	280 (46%)
3-VD	325 (54%)

## ARTS II Procedural Characteristics

### ARTS II (N=607, N=1925 treated lesions)

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Number of lesions treated	3.2 ± 1.1
Number of stents implanted	3.7 ± 1.5
Total stent length, mm	72 ± 32

## ARTS II Adjudication for FDA panel

- ■ The events reported in the ARTS II trial up to 3 years were (re-) adjudicated according to the definitions that were established in the Washington and Dublin meetings for the Academic Research Consortium (ARC)
- ■ Last patient 3 years follow-up is scheduled in December 2006
- ■ Status per mid November:
  - # patients with 3 year follow-up complete 399
  - # patients (with number of event triggers) 140 (233)
  - # events adjudicated according to ARC definitions 207

## ARC Definition of Stent Thrombosis

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### Timing

Acute stent thrombosis*	0 – 24 hours post stent implantation
Subacute stent thrombosis*	> 24 hours – 30 days post stent implantation
Late stent thrombosis**	> 30 days – 1 year post stent implantation
Very late stent thrombosis**	> 1 year post stent implantation

\* ***Acute or subacute can also be replaced by the term early stent thrombosis.***

\*\* ***including 'primary' as well as 'secondary' late stent thrombosis; 'secondary' late stent thrombosis is a stent thrombosis after a target segment revascularization.***

## ARC Definition of Stent Thrombosis

### ***Definite stent thrombosis***

Definite stent thrombosis is considered to have occurred by *either* angiographic or pathologic confirmation.

### ***Probable stent thrombosis***

Clinical definition of probable stent thrombosis is considered to have occurred after intracoronary stenting in the following cases:

- ■ Any unexplained death within the first 30 days.
- ■ Irrespective of the time after the index procedure any MI (MI), which is related to documented acute ischemia in the territory of the implanted stent without angiographic confirmation of stent thrombosis and in the absence of any other obvious cause.

### ***Possible stent thrombosis***

Clinical definition of possible stent thrombosis is considered to have occurred with any unexplained death from 30 days following intracoronary stenting until end of trial follow-up.

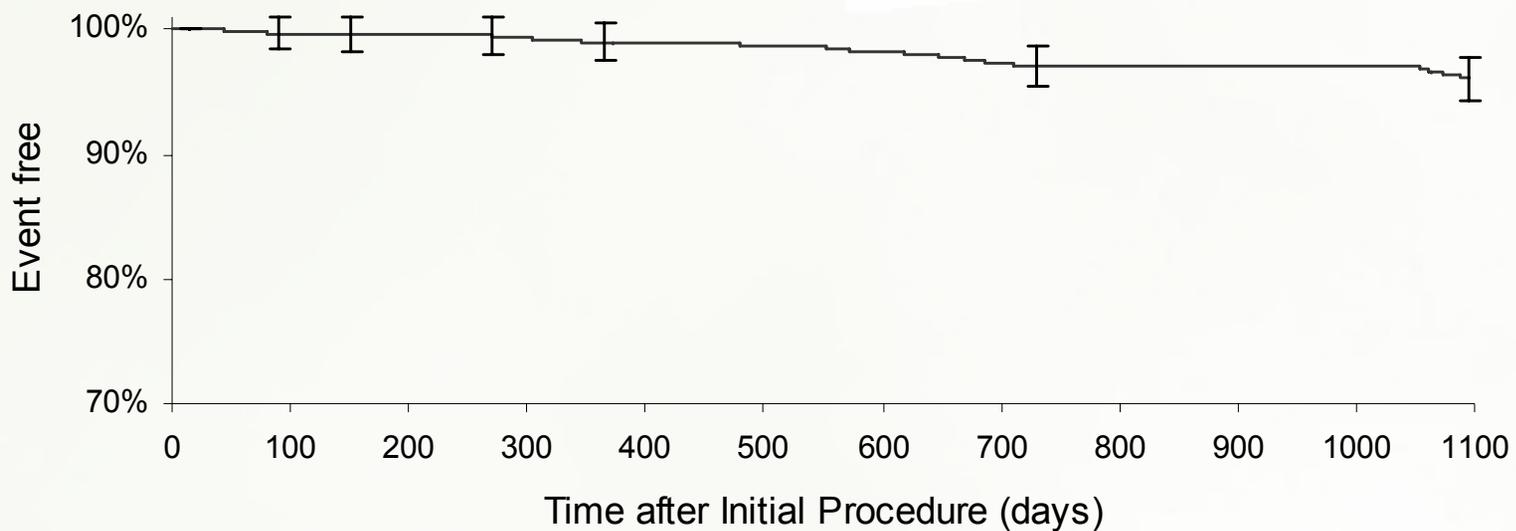
## Major Adverse Cardiac Events up to 1095 Days

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	Cypher™ N=607	95% Confidence Interval
<b><i>(hierarchical)</i></b>		
Death	19 (3.1%)	[1.9%, 4.8%]
MI w/o death	50 (8.2%)	[6.2%, 10.7%]
Q-wave MI	19 (3.1%)	[1.9%, 4.8%]
non Q-wave MI	31 (5.1%)	[3.5%, 7.2%]
Any revascularization w/o death or MI	39 (6.4%)	[4.6%, 8.7%]
<b><i>(composite)</i></b>		
Death/Q-wave MI	38 (6.3%)	[4.5%, 8.5%]
Death/all MI	69 (11.4%)	[9.0%, 14.2%]
MACE	108 (17.8%)	[14.8%, 21.1%]

# ARTS II Survival

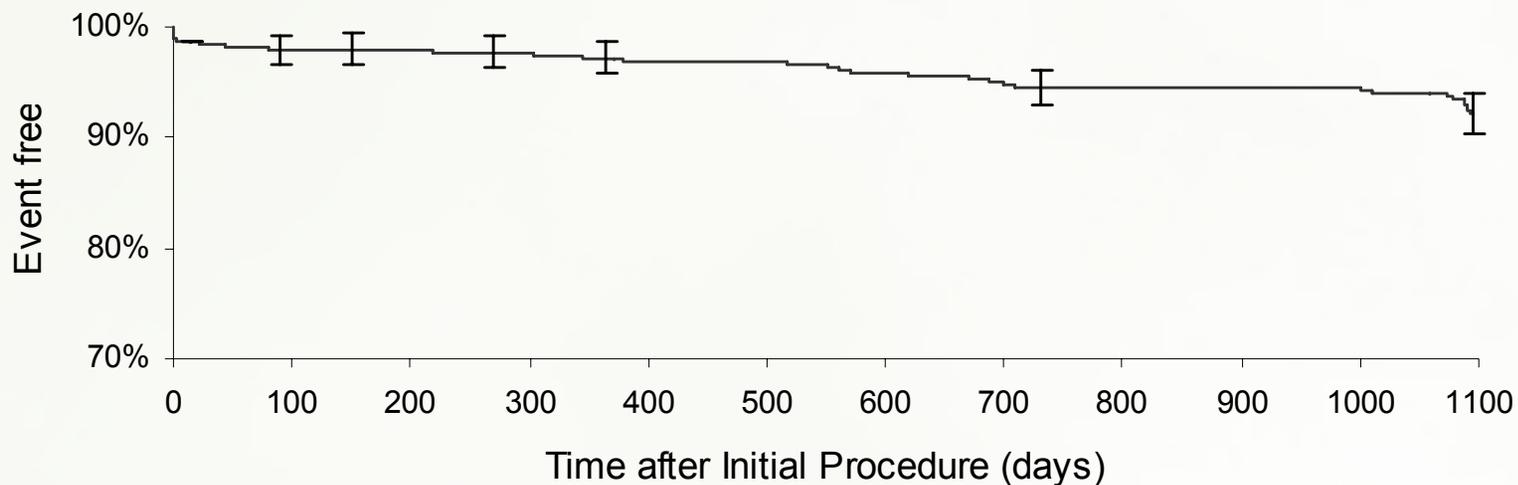


Interval ending day	0	365	730	1095
# At risk	607	585	504	351
Cume. Survival rate (%)	100.0	99.0	97.0	96.0

# ARTS II Survival Free from Death/Q-wave MI

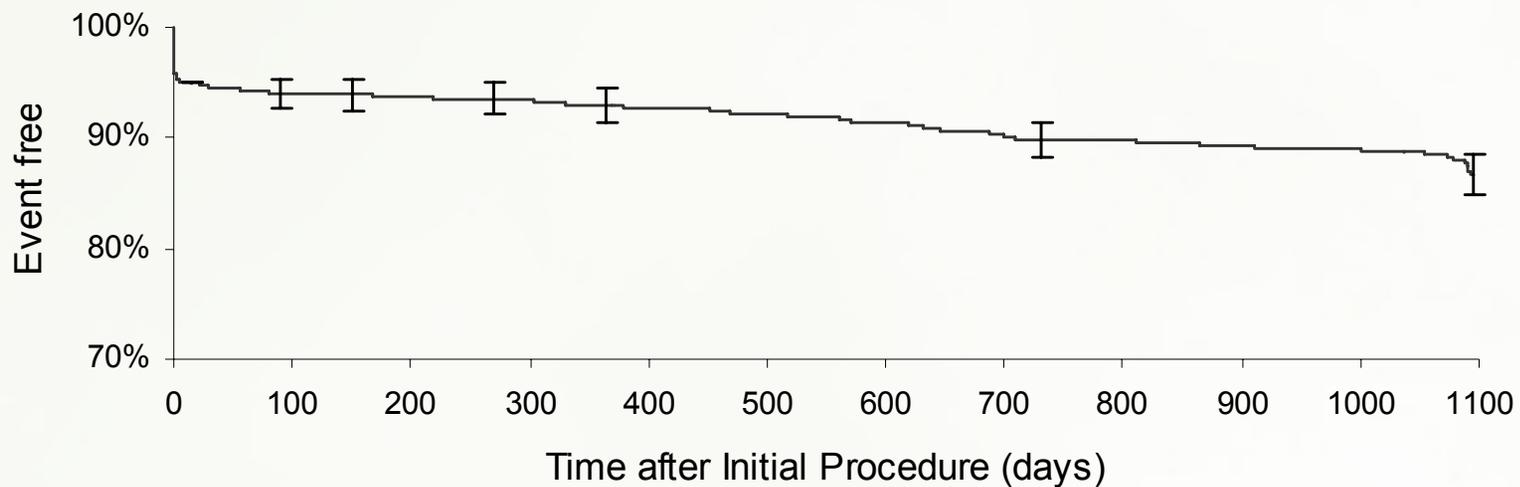


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Interval ending day	0	365	730	1095
# At risk	607	574	495	344
Cume. Survival rate (%)	100.0	97.2	94.6	92.2

# ARTS II Survival Free from Death/MI



Interval ending day	0	365	730	1095
# At risk	607	549	471	327
Cume. Survival rate (%)	100.0	92.9	89.8	86.7

# ARTS II and Dublin/ARC Event Adjudication

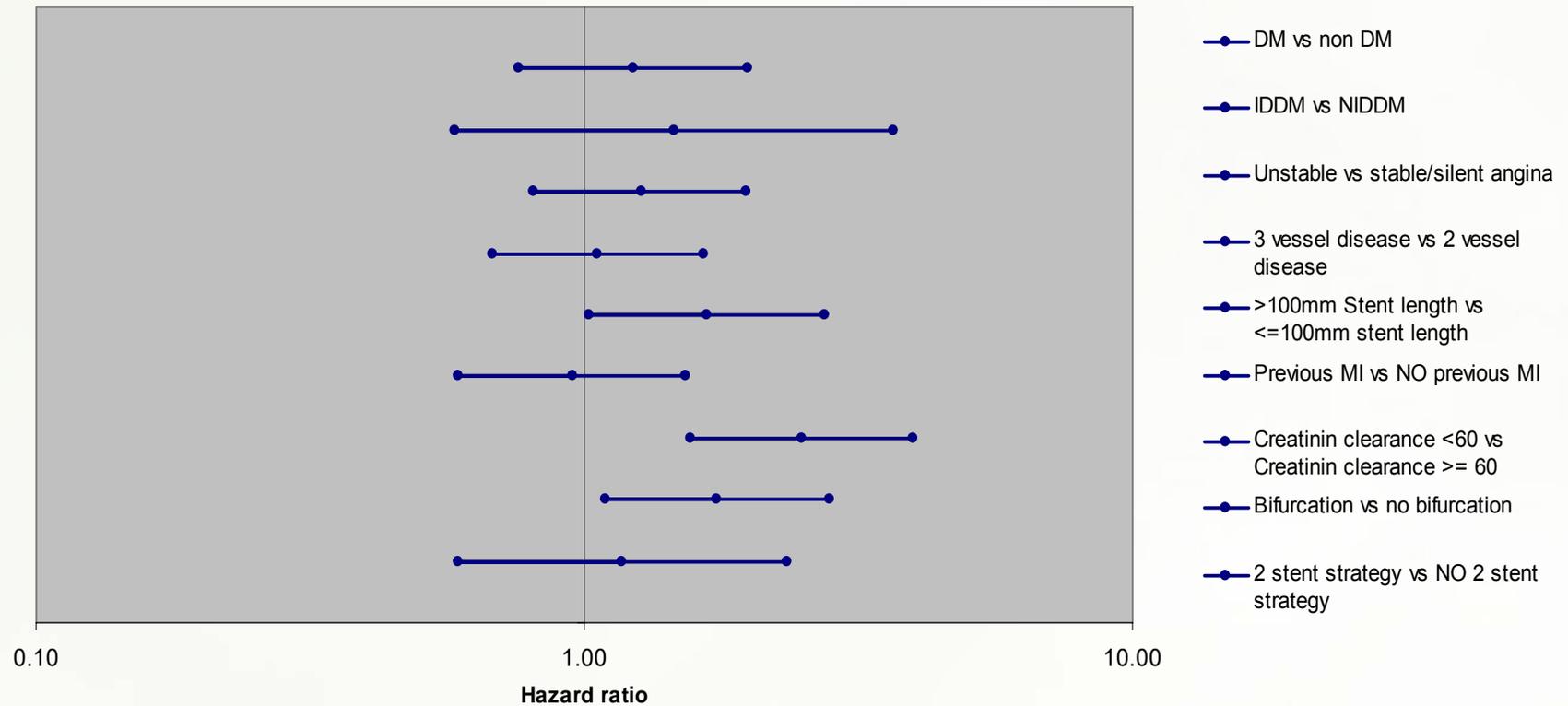


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	ARTS II N=607	Dublin ARC N=607
<b>(non hierarchical)</b>		
Death adjudicated	18	19
Death, pending adjudication	1	0
Death adjudicated:		
■ ■ cardiac	8 (1.3%)	9 (1.5%)
■ ■ non-cardiac/non-cardiovascular	10 (1.6%)	9 (1.5%)
■ ■ vascular	0	1 (0.2%)
MI <u>triggers</u> adjudicated		
MI confirmed as "MI"	14	57
MI, confirmed as "no MI"	42	29
MI, pending adjudication	7	1
<u>Patients</u> with confirmed MI:		
■ ■ Q-wave	6 (1.0%)	21 (3.5%)
■ ■ non Q-wave	8 (1.3%)	33 (5.4%)

# Potential Risk Factors for Death/MI

Arts II population: death/MI  
Hazard Ratios and 95% Confidence Intervals of risk factors



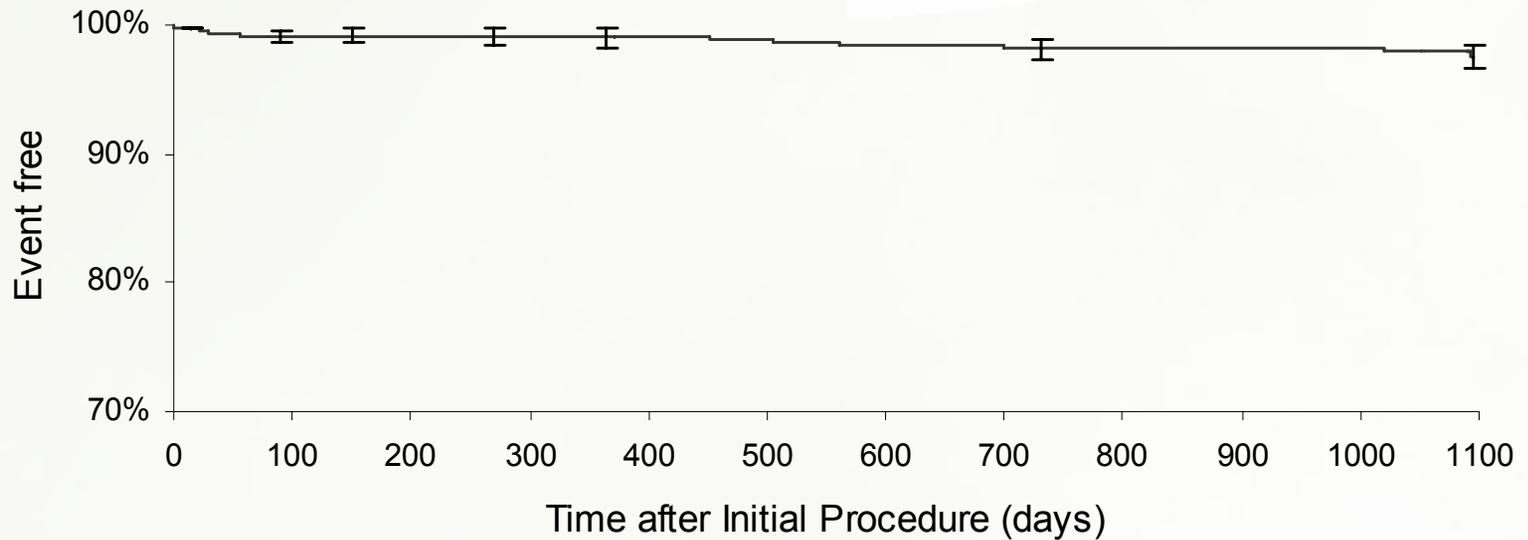
## Stent Thrombosis up to 1095 Days

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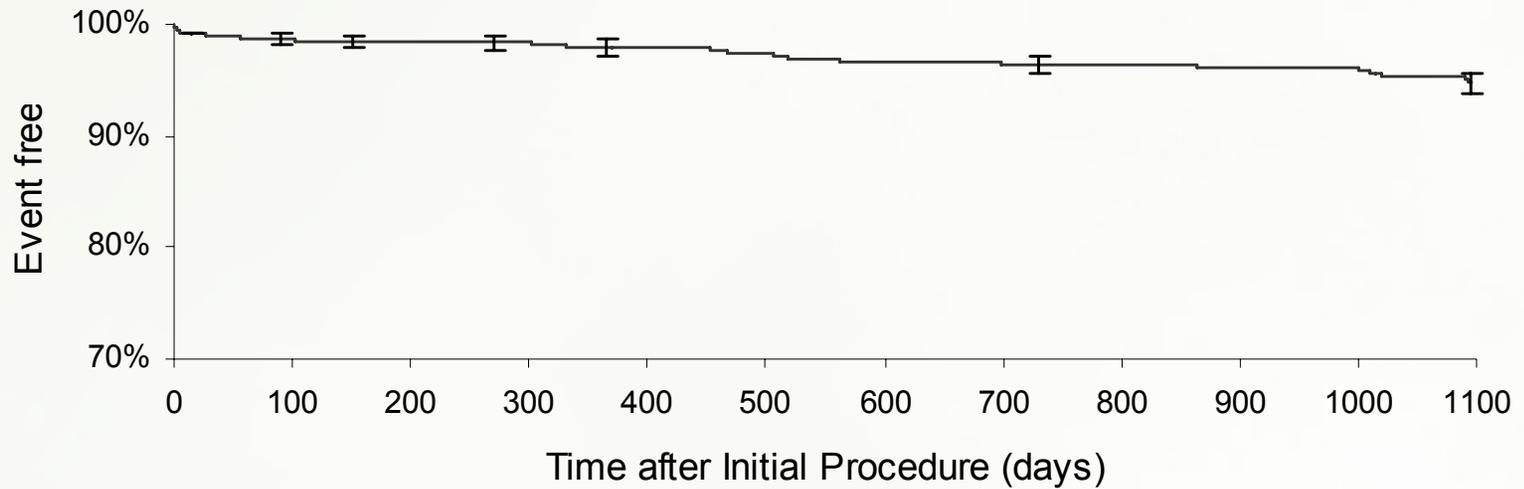
<b>N=607</b>	<b>0-30 days</b>	<b>0-365 days</b>	<b>0-1095 days</b>
<b>(hierarchical)</b>			
<b>Stent thrombosis</b>			
Definite	4 (0.7%)	6 (1.0%)	12 (2.0%)
Probable	3 (0.5%)	7 (1.2%)	14 (2.3%)
Possible	0	3 (0.5%)	7 (1.2%)
Definite/probable	7 (1.2%)	13 (2.1%)	26 (4.3%)

# ARTS II Survival free from Stent Thrombosis (Definite)



Interval ending day	0	365	730	1095
# At risk	607	578	497	345
Cume. Survival rate (%)	100.0	99.0	98.1	97.6

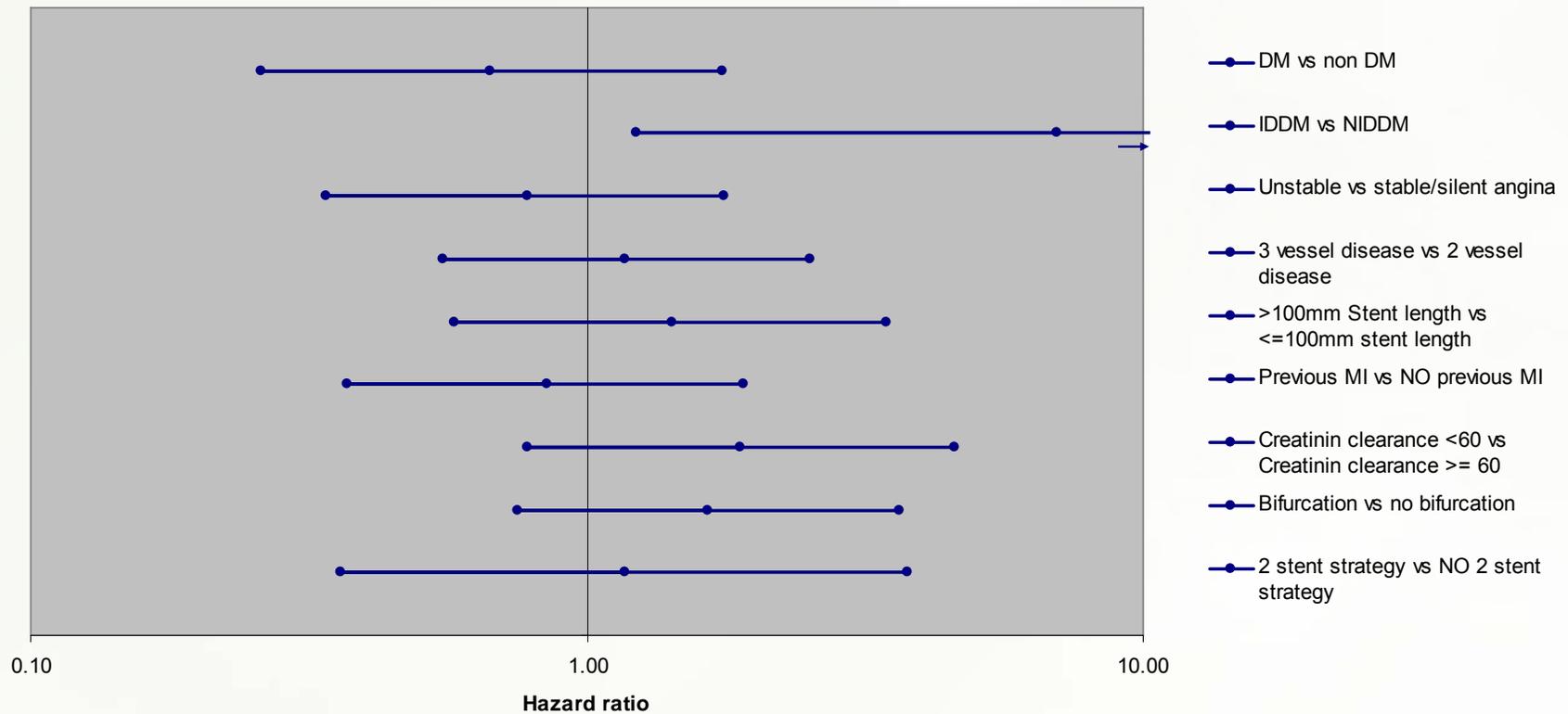
# ARTS II Survival Free from Stent Thrombosis (Definite/Probable)



Interval ending day	0	365	730	1095
# At risk	607	573	490	340
Cume. Survival rate (%)	100.0	97.8	96.5	94.7

# Potential Risk Factors for Stent Thrombosis

Arts II population: Stent thrombosis  
Hazard Ratios and 95% Confidence Intervals of risk factors



## Conclusion

In ARTS II in patients with 2-or 3 vessel disease events up to 3 years were adjudicated according to the ARC definitions. For definite/probable stent thrombosis (ST) the following numbers were observed:

■ ■ (Sub)acute ST	0-30 days	7/607 (1.2%)
■ ■ Late ST	30 days-1 year	6/607 (1.0%)
■ ■ Very late ST	1-3 years	14/607 (2.3%)

Complete 3 years follow-up and event adjudication will be presented on ACC 2007.

Potential risk factors for ST observed in a post hoc analysis are:

- ■ Insulin dependent diabetes mellitus
- ■ Renal function
- ■ Bifurcation stenting

These findings can only be verified in prospective randomised controlled clinical trials.