

# CROSS and PERFECT Trials

## Preliminary Results

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# Current RCTs for Bifurcation Lesions

## Evaluation of Optimal Stenting Technique

### **Trials**

### **Comparison**

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<b>NORDIC 1</b>	Provisional T vs. Systemic T stenting
<b>NORDIC 2</b>	Crush vs. Culotte
<b>NORDIC 3</b>	Kissing balloon vs. leave alone
<b>BBC</b>	Simple vs. Complex
<b>CACTUS</b>	Provisional T vs. Crush

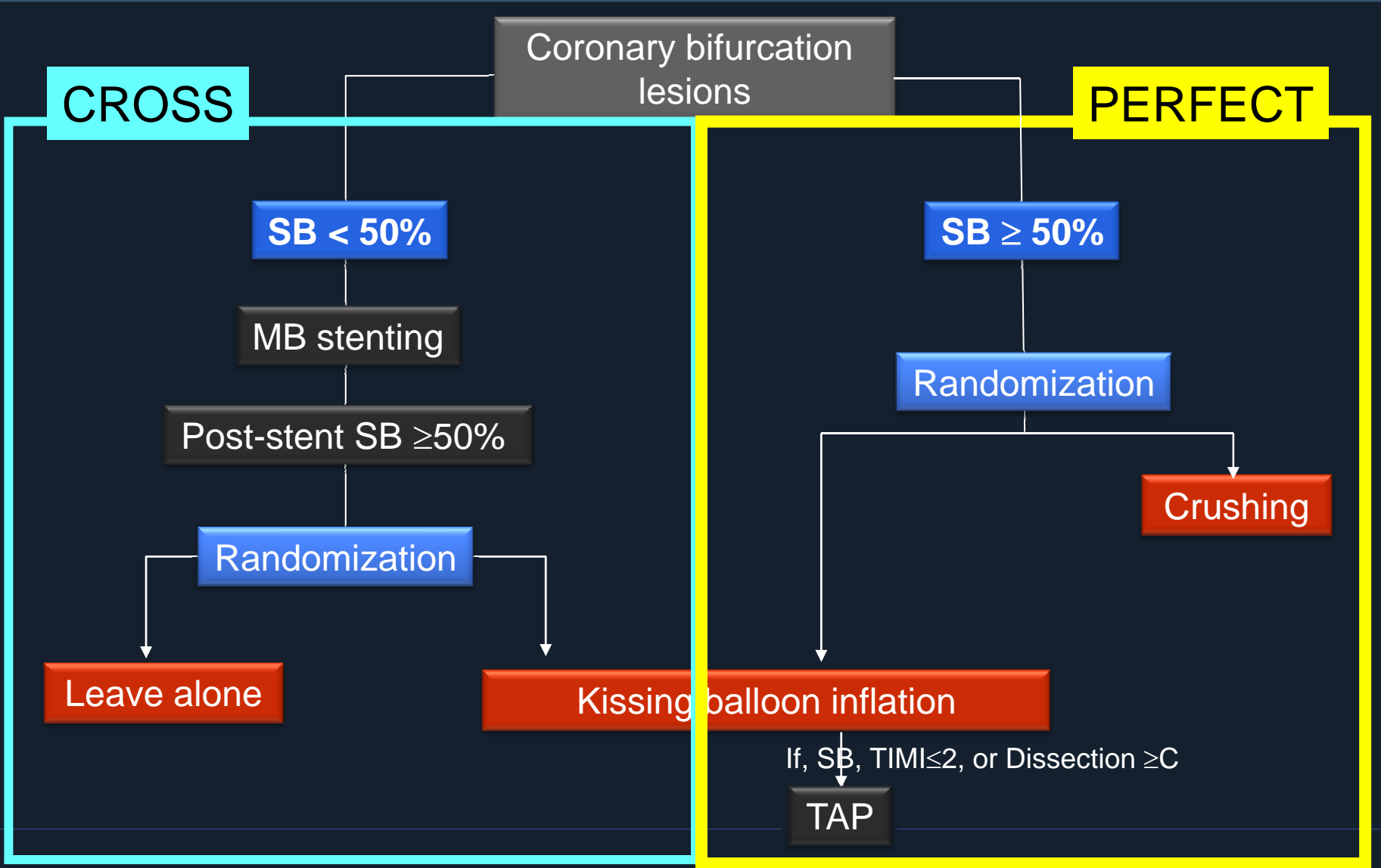
# Lessons From Trials

- No difference in the rate of death, spontaneous MI, and repeat revascularization rate
  - Superiority of simple stenting in the rate of periprocedural MI
  - Fewer stents in simple stenting
- BUT**, limited by selected inclusion, heterogeneous bifurcations, different procedures, and angiography-guidance

# Purposes of Trials

- To evaluate the outcomes of different stenting strategies for bifurcation lesions under the guidance of IVUS
- To understand the mechanism of acute and chronic compromise of side branch (SB) after bifurcation stenting with use of IVUS and FFR

# CROSS & PERFECT Trials



# Administration and Sites

## Sites

Asan Medical Center  
Aju University Hospital  
Busan Saint Mary's Hospital  
Busan University Hospital  
Catholic University, Kangnam St. Mary's Hospital  
Chungju Saint Mary's Hospital  
Chungnam National University Hospital  
Hallym University Sacred Heart Hospital  
Kangwon University Hospital  
Korea Veterans Hospital  
Kyungsang University Hospital  
Soonchunhyang University Seoul Hospital  
Soonchunhyang University Bucheon Hospital  
Soonchunhyang University Cheonan Hospital  
Ulsan University Hospital

## Principle investigator

Seung-Jung Park, MD

## Sponsor

KSCVI, CVRF

## Angiographic core lab

CVRF

## IVUS core lab

CVRF

## Data management

CVRF

## Clinical Event Committee

CVRF

Choice of optimal strategy for bifurcation lesions  
with normal side branch

# CROSS Trial

Bifurcations without SB Stenosis



# Inclusion Criteria

## 1. Clinical

- Ischemic symptom or sign
- Eligible lesion for intracoronary stenting
- Age >18 years, <75 ages

## 2. Angiographic

- De novo bifurcation with the MEDINA classification type 1.1.0, 1.0.0, or 0.1.0
- **MB:**  $\geq 2.5$  mm,  $\geq 50\%$  stenosis,  $\leq 50$  mm length covered with  $\leq 2$  stents
- **SB:**  $\geq 2.0$  mm,  $< 50\%$  stenosis



# Exclusion Criteria

- Serious comorbidity
- STEMI  $\leq$  2 weeks
- Left main disease
- In-stent restenosis
- Graft vessels
- TIMI flow  $\leq$  grade 2 in the side branch
- Chronic total occlusion
- Renal dysfunction, creatinine  $\geq$  2.0mg/dL

# CROSS

Bifurcation without SB stenosis by angiography

Any DES  
(N=600)

After MV stenting

SB DS  $\geq$  50% & TIMI 3 flow

Randomization

- Stratified by sites

TIMI  $\leq$  2 flow

Registry

1. Treatment at the operator's discretion

SB DS < 50% & TIMI 3 flow

Registry

1. IVUS exam in MV
2. FFR in SB (selected sites)

Kissing balloon group  
(N=150)

1. FFR in SB before kissing balloon
2. Rewire into SB
3. Kissing balloon inflation

Leave it alone group  
(N=150)

1. IVUS exam in MV
2. FFR in SB (selected sites)

SB DS < 70% & TIMI 3  
Dissection none or  $\leq$  class B

1. IVUS in MV
2. FFR in SB (selected sites)

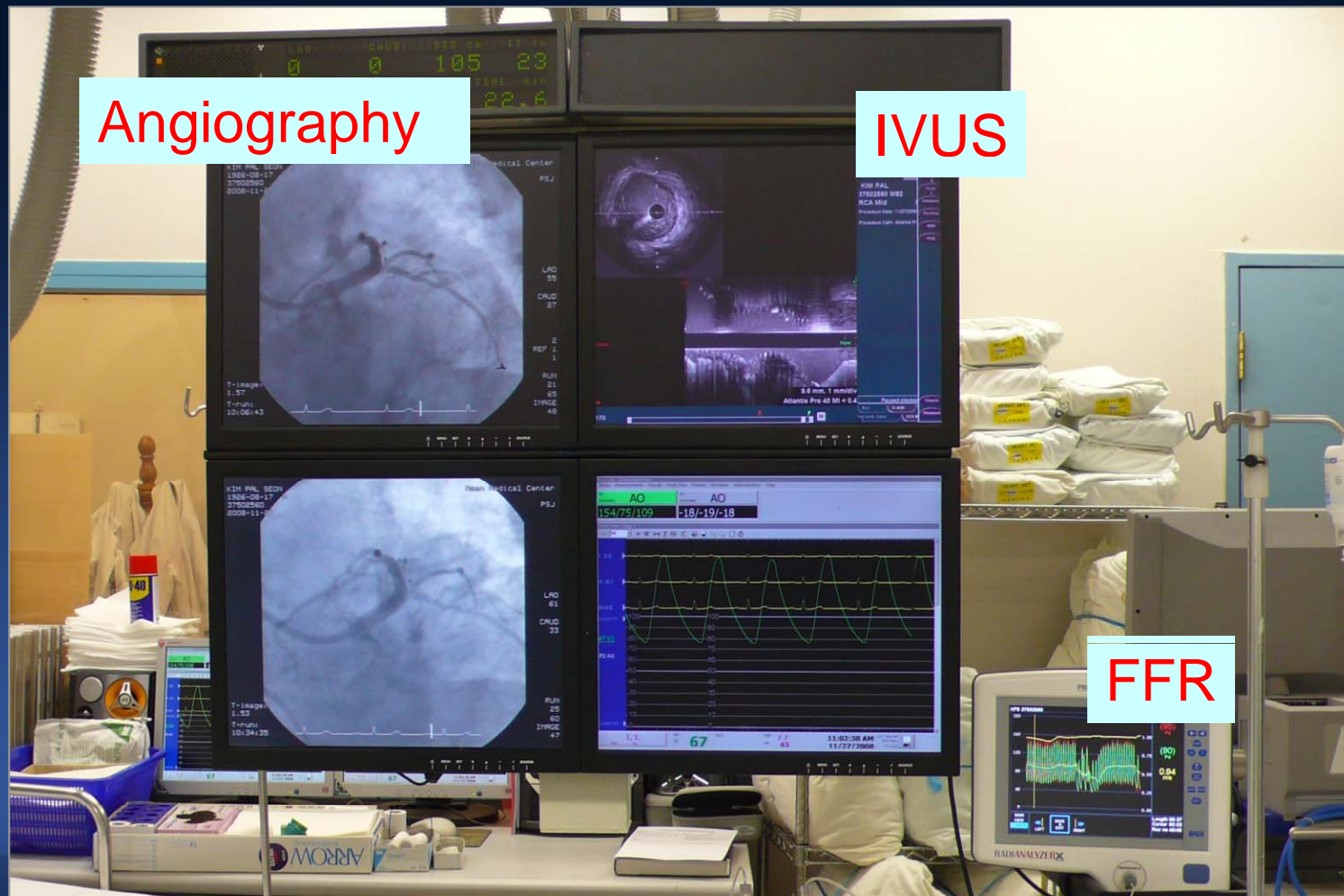
SB DS  $\geq$  70% or TIMI  $\leq$  2 or  
Dissection  $\geq$  class C

1. FFR in SB (selected sites)
2. Provisional T stenting in SB \*
3. IVUS in both branches

\* The decision can not be influenced by the value of FFR.

# Evaluation of IVUS & FFR

*to assess the mechanisms of phenomena occurring in bifurcations after stenting*



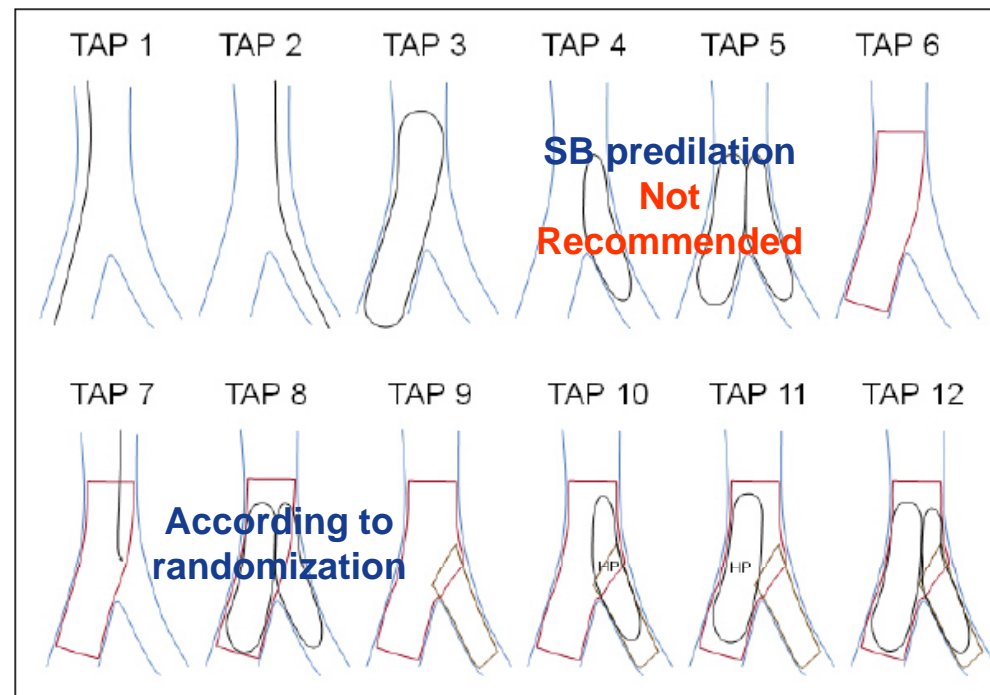
# Procedures

## Single Stent (Provisional T)



### Angiographic & Procedural Provisional T Stenting

Sequence	Procedure	Performance	Sequence	Procedure	Performance
TAP 1 *	MB wiring	<input type="radio"/> Done <input type="radio"/> ND	TAP 7 *	SB rewiring after MB stenting	<input type="radio"/> Done <input type="radio"/> ND
TAP 2 *	SB wiring	<input type="radio"/> Done <input type="radio"/> ND	TAP 8 *	Kissing after MB stenting	<input type="radio"/> Done <input type="radio"/> ND
TAP 3 *	MB predilation	<input type="radio"/> Done <input type="radio"/> ND	TAP 9 *	SB stenting	<input type="radio"/> Done <input type="radio"/> ND
TAP 4 *	SB predilation	<input type="radio"/> Done <input type="radio"/> ND	TAP10 *	SB balloon dilatation	<input type="radio"/> Done <input type="radio"/> ND
TAP 5 *	Kissing predilation	<input type="radio"/> Done <input type="radio"/> ND	TAP 11 *	MB balloon dilatation	<input type="radio"/> Done <input type="radio"/> ND
TAP 6 *	MB stenting	<input type="radio"/> Done <input type="radio"/> ND	TAP12 *	Final kissing	<input type="radio"/> Done <input type="radio"/> ND



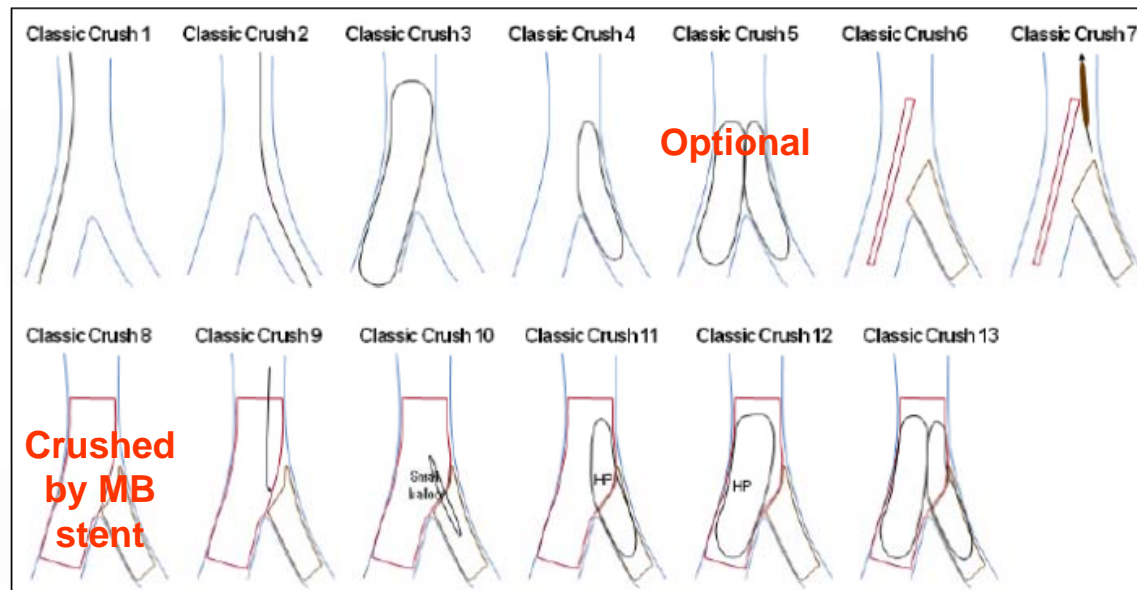
# Procedures

## Crush: Classic Stent Crushing



### Angiographic & Procedural Classic Crush

Sequence	Procedure	Performance	Sequence	Procedure	Performance
Classic Crush 1 *	MB wiring	<input type="radio"/> Done <input type="radio"/> ND	Classic Crush 8 *	MB stenting (Crush SB stent)	<input type="radio"/> Done <input type="radio"/> ND
Classic Crush 2 *	SB wiring	<input type="radio"/> Done <input type="radio"/> ND	Classic Crush 9 *	SB rewiring	<input type="radio"/> Done <input type="radio"/> ND
Classic Crush 3 *	MB predilation	<input type="radio"/> Done <input type="radio"/> ND	Classic Crush 10 *	SB ballooning by small balloon	<input type="radio"/> Done <input type="radio"/> ND
Classic Crush 4 *	SB predilation	<input type="radio"/> Done <input type="radio"/> ND	Classic Crush 11 *	SB high pressure dilatation	<input type="radio"/> Done <input type="radio"/> ND
Classic Crush 5 *	Kissing predilation	<input type="radio"/> Done <input type="radio"/> ND	Classic Crush 12 *	MB high pressure dilatation	<input type="radio"/> Done <input type="radio"/> ND
Classic Crush 6 *	SB stenting (MB stent backup)	<input type="radio"/> Done <input type="radio"/> ND	Classic Crush 13 *	Final kissing dilatation	<input type="radio"/> Done <input type="radio"/> ND
Classic Crush 7 *	SB balloon and wire retrieval	<input type="radio"/> Done <input type="radio"/> ND			



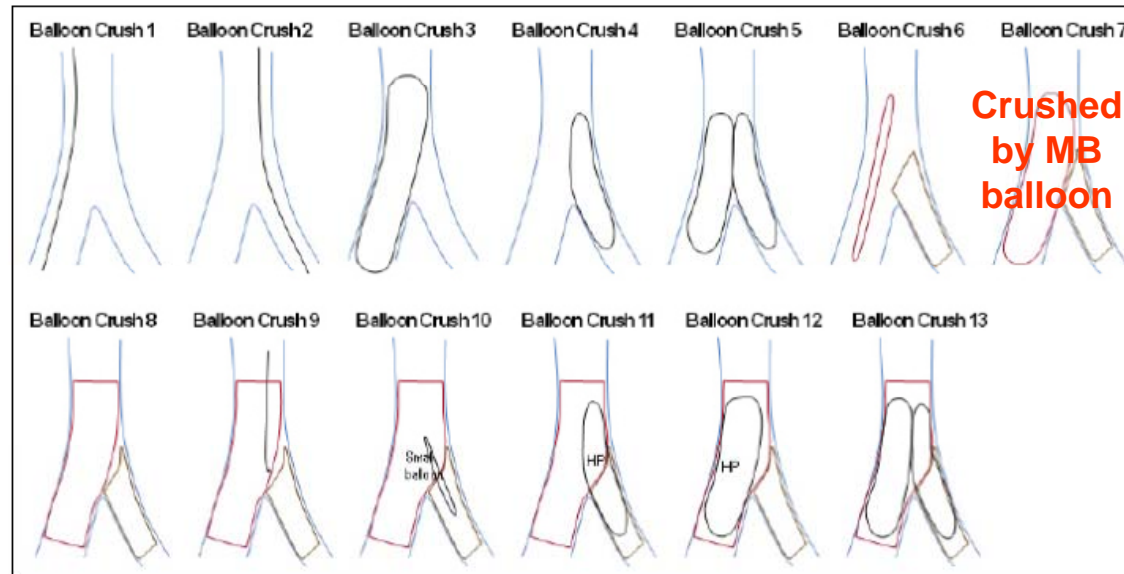
# Procedures

## Crush: Balloon Crushing



### Angiographic & Procedural Balloon Crush

Sequence	Procedure	Performance	Sequence	Procedure	Performance
Balloon Crush 1 *	MB wiring	<input type="radio"/> Done <input type="radio"/> ND	Balloon Crush 8 *	MB stenting	<input type="radio"/> Done <input type="radio"/> ND
Balloon Crush 2 *	SB wiring	<input type="radio"/> Done <input type="radio"/> ND	Balloon Crush 9 *	SB rewiring	<input type="radio"/> Done <input type="radio"/> ND
Balloon Crush 3 *	MB predilation	<input type="radio"/> Done <input type="radio"/> ND	Balloon Crush 10 *	SB ballooning by small balloon	<input type="radio"/> Done <input type="radio"/> ND
Balloon Crush 4 *	SB predilation	<input type="radio"/> Done <input type="radio"/> ND	Balloon Crush 11 *	SB high pressure dilatation	<input type="radio"/> Done <input type="radio"/> ND
Balloon crush 5 *	Kissing predilation	<input type="radio"/> Done <input type="radio"/> ND	Balloon Crush 12 *	MB high pressure dilatation	<input type="radio"/> Done <input type="radio"/> ND
Balloon Crush 6 *	SB stenting (MB stent backup)	<input type="radio"/> Done <input type="radio"/> ND	Balloon Crush 13 *	Final kissing dilatation	<input type="radio"/> Done <input type="radio"/> ND
Balloon Crush 7 *	Crush SB stent by MB balloon	<input type="radio"/> Done <input type="radio"/> ND			



# CROSS Trial Study Design

- **Primary end points**
  - 8-month diameter stenosis in SB
- **Hypothesis: non-inferiority**
  - $H_a$  : Leave alone  $\geq$  Kissing balloon

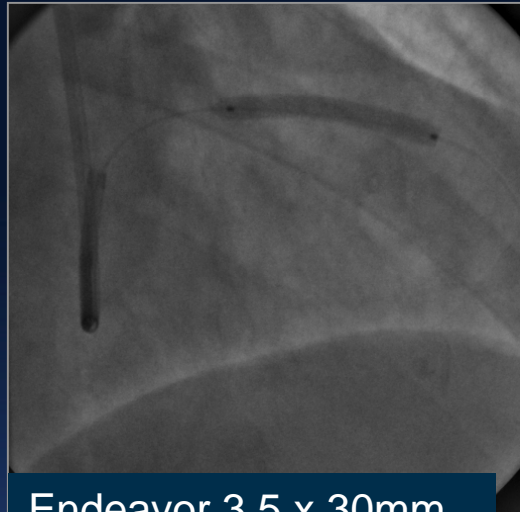
# Intermediate Stenosis at SB

## CROSS Patient

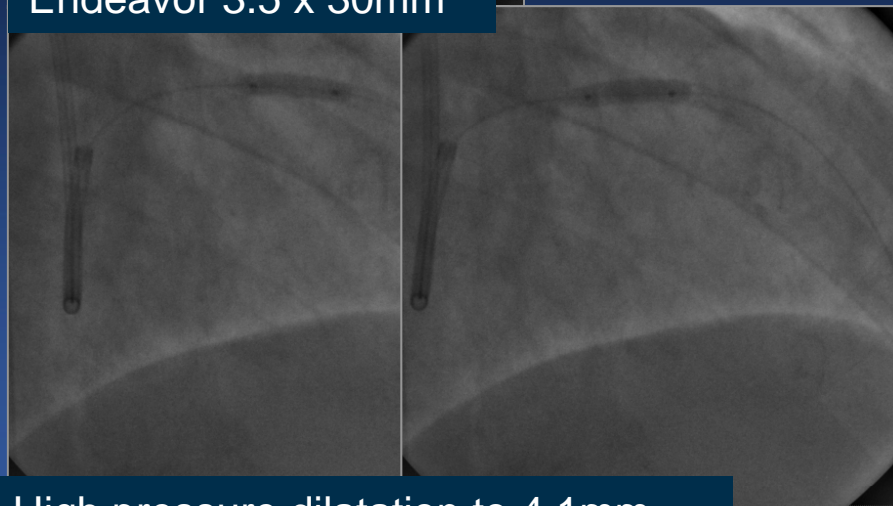




# Main Branch Stenting Randomized to Endeavor Stent



Endeavor 3.5 x 30mm

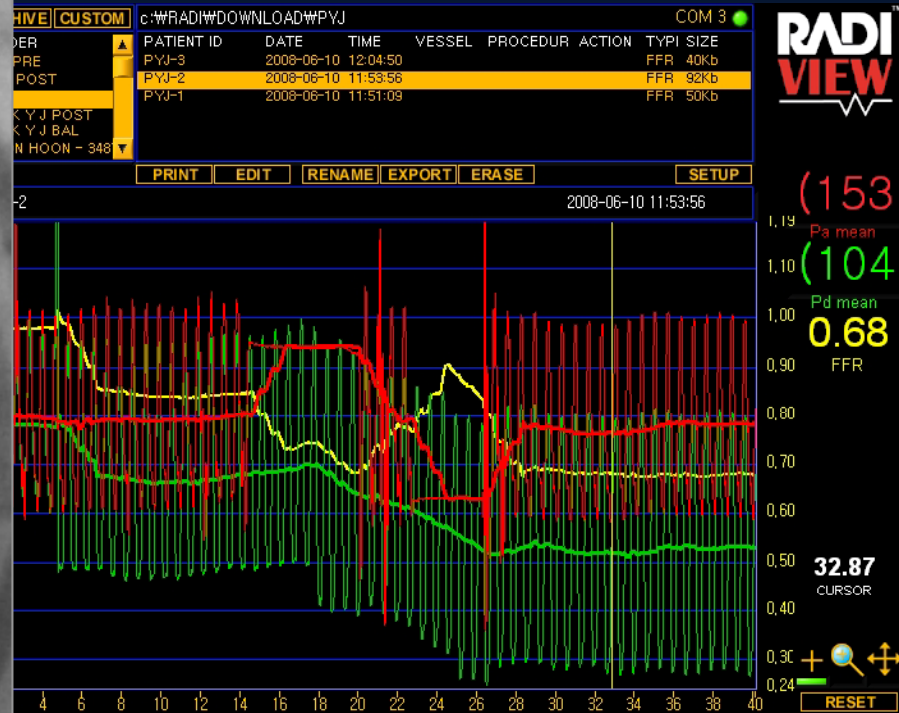


High pressure dilatation to 4.1mm



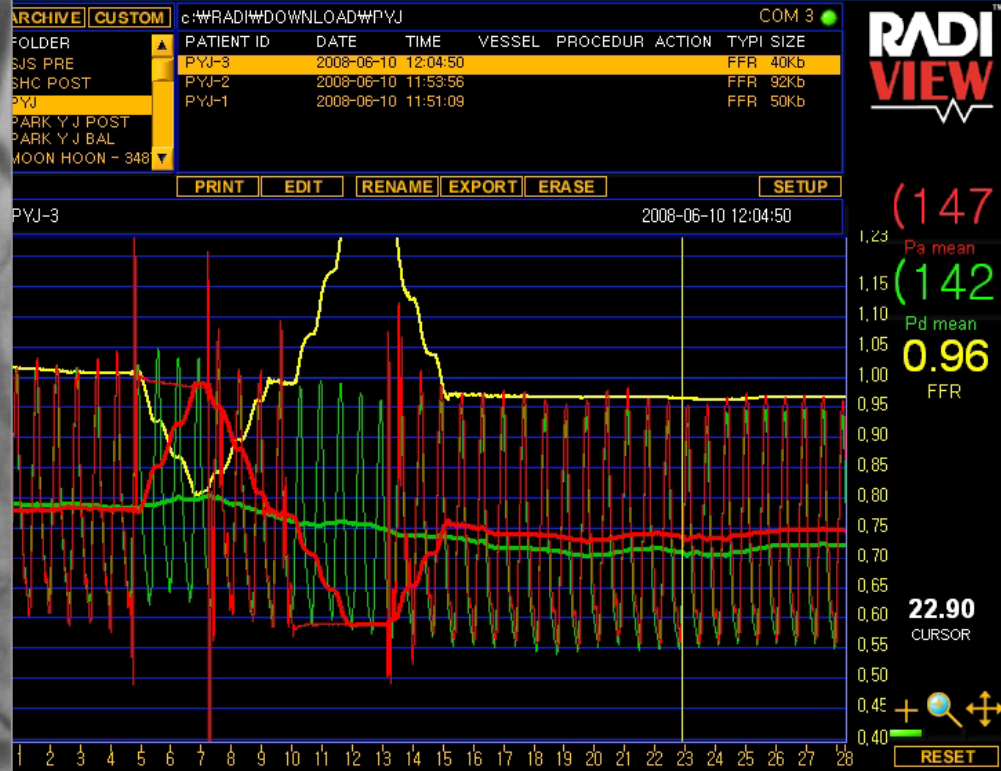
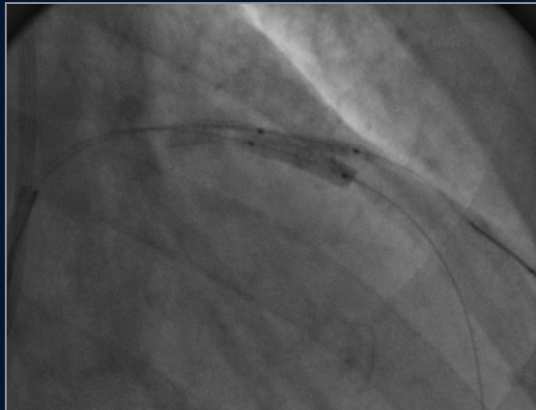
# Significant SB jail with TIMI 3 flow

- FFR before kissing
- Randomization to kissing balloon



# Final FFR after Kissing

- Post-procedure FFR



# Final Angiogram



OPTimal StEnting StRategy For TruE BifurCaTion

# PERFECT Trial

## Bifurcations with SB Stenosis



# PERFECT Trial Study Design

- **Primary end point**
  - 8-month overall angiographic restenosis rate
  
- **Hypothesis : non-inferiority**
  - $H_a$  : Provisional T  $\geq$  Crush technique

# Inclusion Criteria

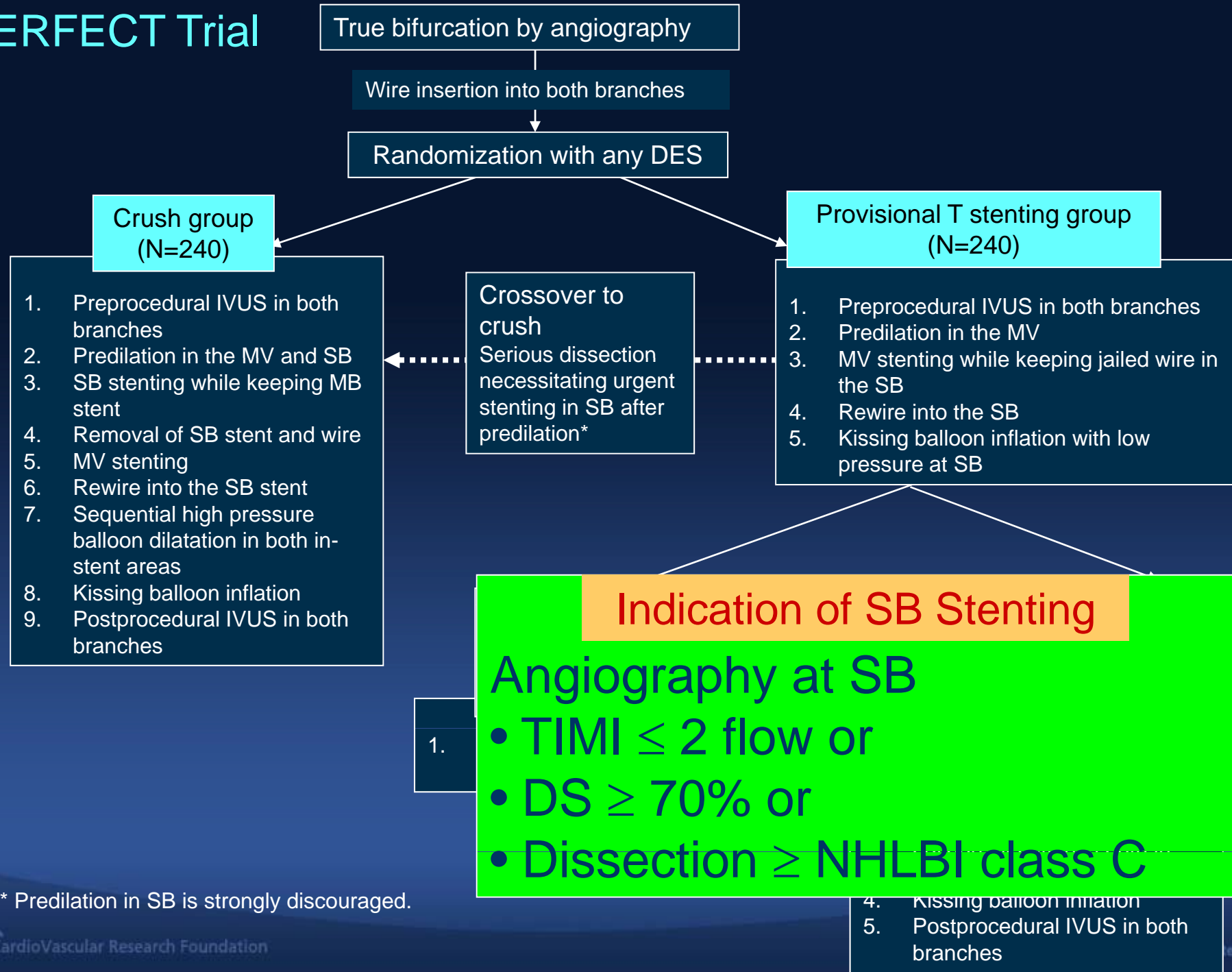
## 1. Clinical

- Ischemic symptom or sign
- Eligible lesion for intracoronary stenting
- Age >18 years, <75 ages

## 2. Angiographic

- De novo bifurcation with the MEDINA classification type 1.1.1, 1.0.1, or 0.1.1
- **MB:**  $\geq 2.5$  mm,  $\geq 50\%$  stenosis,  $\leq 50$  mm length covered with  $\leq 2$  stents
- **SB:**  $\geq 2.0$  mm,  $\geq 50\%$  stenosis,  $\leq 30$  mm length covered with 1 stent

# PERFECT Trial

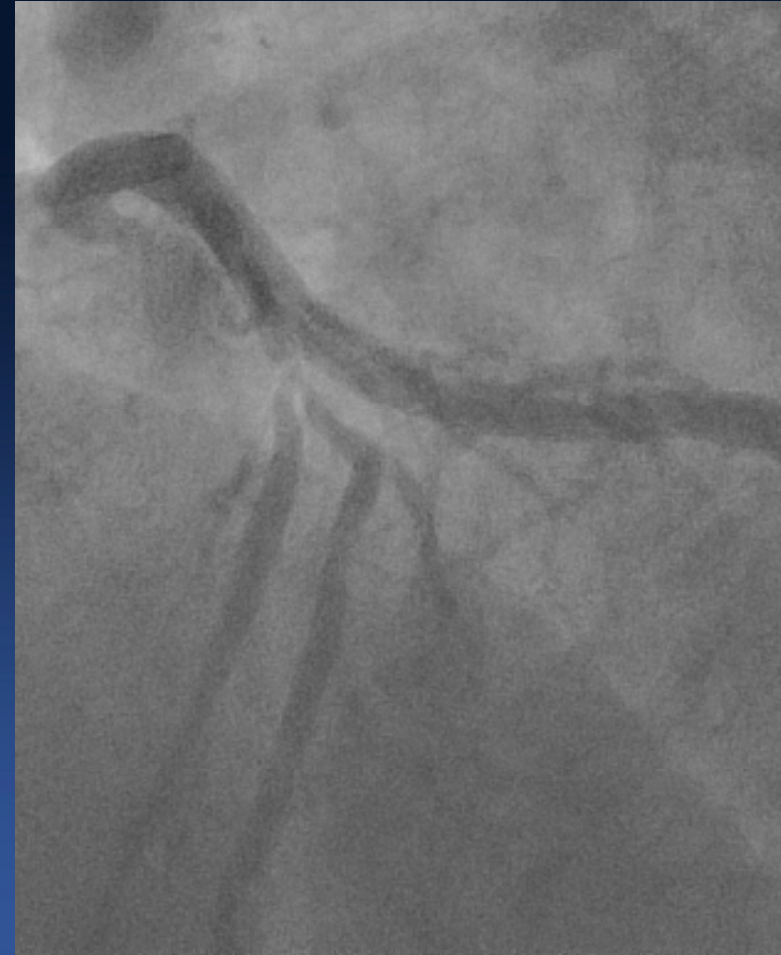


\* Predilation in SB is strongly discouraged.

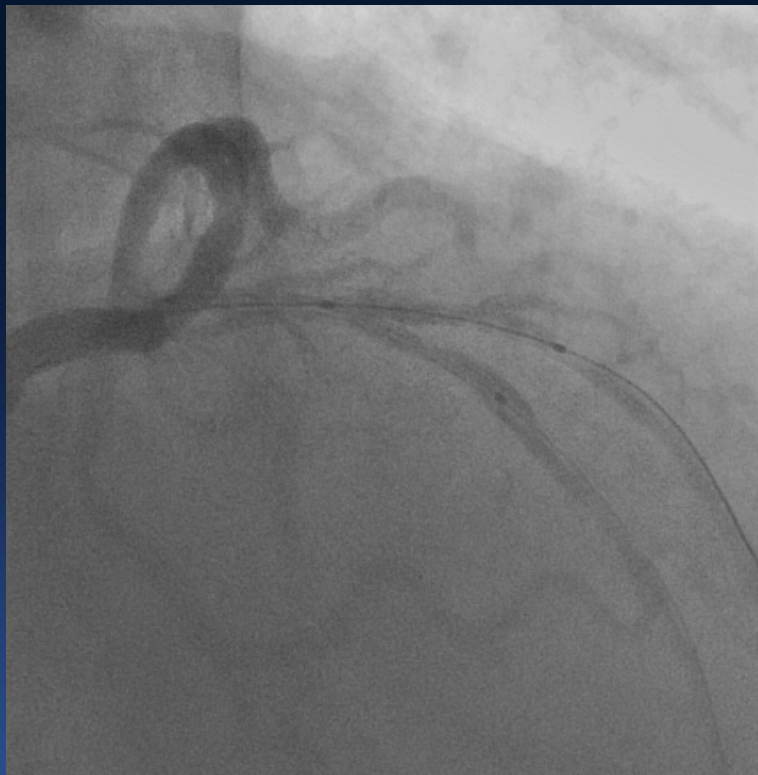


# Significant Stenosis at SB

## PERFECT Patient

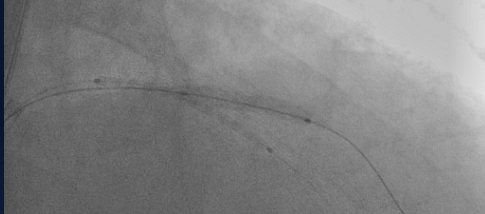


# Randomized to Crush

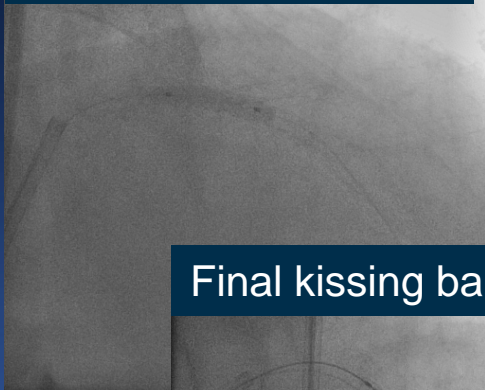


Cypher 3.5 x 28 & 3.0 x 18mm

SB stenting at 14atm



MB non-compliant balloon to 4.1mm



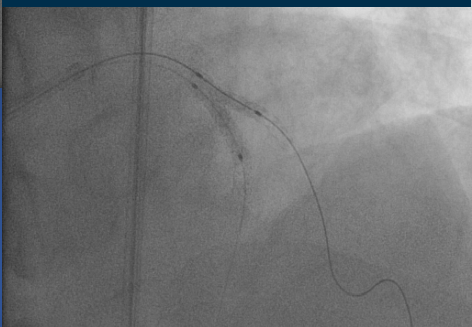
MB stenting at 8atm



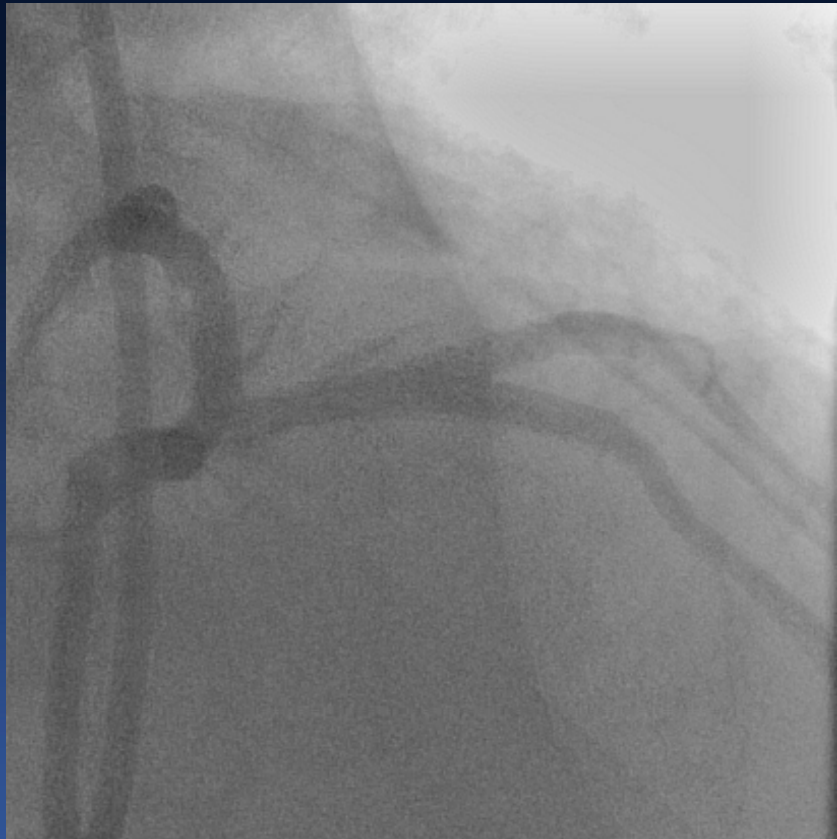
SB non-compliant balloon to 3.3mm



Final kissing balloon



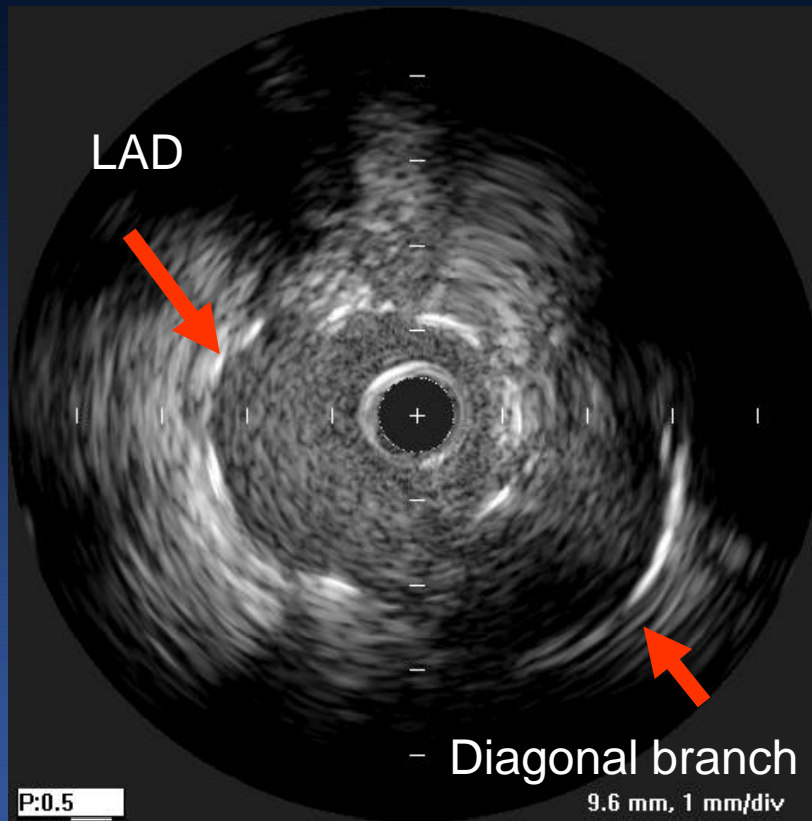
# Final Angiogram



# IVUS Finding

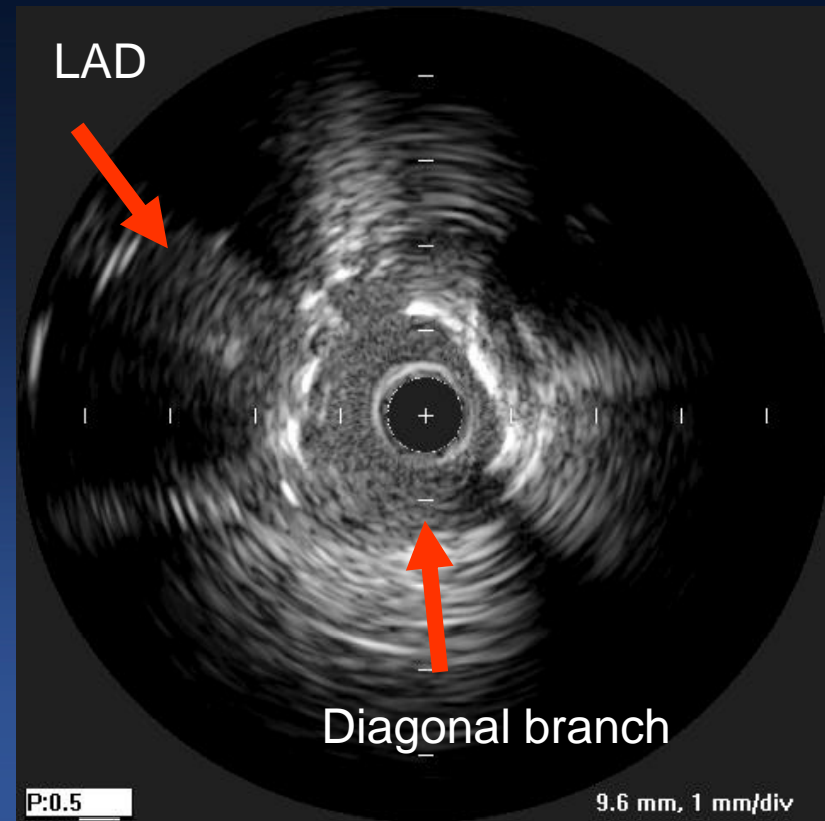
From LAD

Stent area 7.49 mm<sup>2</sup>



From Diag.

4.62 mm<sup>2</sup>



# Current Status

Till April 2012

**CROSS Study**  
(Target N=600)

- **478 (80%)** enrolled
- 288 (60%) randomization to kissing vs. leave alone

**PERFECT Study**  
(Target N=480)

- **394 (82%)** enrolled

# Preliminary Results in Intention-to-Treat Principle

## Baseline Characteristics

	CROSS		PERFECT	
	Kissing (143)	No kissing (145)	Single (191)	Crush (201)
Age, yrs	60.9 ± 9.2	60.9 ± 7.8	60.8 ± 8.8	60.9 ± 9.0
Male	72.0	66.2	75.4	75.1
Diabetics	29.9	29.5	24.5	25.1
Smoking	31.3	23.7	30.9	22.8
Hyperlipidemia	32.8	36.0	40.4	43.9
Hypertension	48.5	52.5	50.5	53.5
Family history	4.5	5.8	9.6	9.1
Prior PCI	5.2	7.9	5.3	8.6
Prior MI	1.5	2.2	3.7	3.0
Renal failure	0.7	0	0.5	0
LV EF, %	61.0 ± 7.6	62.9 ± 5.6	59.2 ± 8.0	60.4 ± 7.2
Sinus rhythm	97.0	97.1	98.4	98.5

# Preliminary Results in Intention-to-Treat Principle

## Baseline Characteristics

	CROSS		PERFECT	
	Kissing (143)	No kissing (145)	Single (191)	Crush (201)
<b>Presentation</b>				
Stable angina	56.0	56.1	63.6	64.3
Unstable angina	36.6	39.6	28.9	32.7
NSTEMI	7.4	4.3	7.5	3.1
<b>Disease extent</b>				
1 VD	64.4	54.6	53.4	51.0
2 VD	25.2	39.0	32.5	31.0
3 VD	10.4	6.4	14.1	18.0

# Preliminary Results in Intention-to-Treat Principle

## Lesion Characteristics

Site	CROSS		PERFECT	
	Kissing (143)	No kissing (145)	Single (191)	Crush (201)
LAD	91.9	88.7	92.1	94.0
LCX	5.9	8.5	7.3	4.5
RCA	2.2	2.8	0.5	1.5
MEDINA *				
1: 0: 0	3.7	8.5	0	0.5
0: 1: 0	14.1	10.6	0.5	0
1: 1: 0	<b>45.9</b>	<b>51.1</b>	0	0.5
1: 1: 1	25.9	20.6	<b>85.3</b>	<b>86.0</b>
0: 0: 1	0	0	0	0
1: 0: 1	5.2	5.0	3.1	4.0
0: 1: 1	5.2	4.3	11.0	9.0
No. of lesions	1.5 ± 0.8	1.6 ± 0.7	1.7 ± 9	1.8 ± 0.9

\* Reported by independent physicians in sites



# Preliminary Results in Intention-to-Treat Principle Procedures

	CROSS		PERFECT	
	Kissing (143)	No kissing (145)	Single (191)	Crush (201)
Radial approach	33.3	34.8	11.5	11.5
DES types				
Cypher	34.8	25.7	61.3	63.0
Taxus (Liberte)	11.0	15.0	1.6	1.5
Endeavor	28.1	31.4	8.4	7.5
Xience, Promus	15.6	16.4	24.6	24.5
Nobori, Biomatrix	5.2	5.7	3.7	3.0
Others	5.2	5.7	0.5	0.5
Stents per lesion	1.6 ± 0.8	1.6 ± 0.8	2.0 ± 1.0	2.6 ± 1.0
IVUS in MB	95.6	96.5	95.8	94.5
IVUS in SB	47.4	33.3	80.1	91.0

# Preliminary Results in Intention-to-Treat Principle Procedures

	CROSS		PERFECT	
	Kissing (143)	No kissing (145)	Single (191)	Crush (201)
Stents in MB	100	100	99.5	100
No.	1.3 ± 0.5	1.3 ± 0.5	1.4 ± 0.6	1.4 ± 0.5
Length, mm	33.1 ± 13.2	32.6 ± 13.2	36.9 ± 15.7	37.7 ± 14.8
Size, mm	3.3 ± 0.3	3.3 ± 0.3	3.3 ± 0.3	3.3 ± 0.4
Stents in SB	<b>3.7</b>	<b>0.7</b>	<b>29.8</b>	<b>96.5</b>
No.	-	-	0.3 ± 0.5	1.0 ± 0.2
Length, mm	-	-	8.9 ± 11.7	20.5 ± 8.1
Provisional T	100	100	<b>79.6</b>	3.5
Crush	0	0	20.4	<b>95.6</b>
Final kissing	<b>92.5</b>	<b>5.0</b>	<b>81.0</b>	<b>97.0</b>
FFR after proc.	52.6	45.4	15.1	0
< 0.8	<b>18.5</b>	<b>23.3</b>	<b>58.6</b>	-

# Preliminary Non-adjudicated Results in Intention-to-Treat Principle

## No Significant Difference

	CROSS		PERFECT	
	Kissing (143)	No kissing (145)	Single (191)	Crush (201)
Months	27.4 ± 15.7	28.2 ± 15.6	29.9 ± 13.9	28.9 ± 14.1
Death	2 (1.6)	0	1 (0.5)	3 (1.5)
Cardiac	1	0	1	2
Non-cardiac	1	0	0	1
MI	7 (5.0)	7 (4.9)	18 (9.4)	19 (9.4)
STEMI	0	0	0	1
Non-STEMI	7	7	18	18
Any revasc.	14 (12.1)	9 (7.4)	6 (3.4)	11 (6.2)
TVR	9 (7.8)	5 (4.1)	3 (1.7)	5 (2.2)
TLR	7 (6.0)	4 (3.0)	3 (1.7)	3 (1.6)
Stent thrombosis	0	1 (0.7) late	0	1 (0.5) late
Death, MI or TVR	16 (12.9)	12 (9.0)	22 (11.6)	26 (13.3)

# Conclusion

- Patients with SB stenosis enrolled in PERFECT trial had more extensive CAD than those without SB stenosis enrolled in CROSS trial.
- IVUS-guided bifurcation stenting leads to excellent initial and long-term outcomes.
- In patients without SB stenosis, functional SB jail after MB stenting does not occur frequently.
- In contrast, in patients with SB stenosis, functional SB jail after MB stenting is not uncommon.
- Long-term outcomes of all patients adjudicated by independent CEC will be available in 2013.
- The CROSS and PERFECT trials will provide insight into the mechanism of initial and long-term SB compromise with anatomical and functional evaluations.