CROSS and PERFECT Trials
Preliminary Results

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Current RCTs for Bifurcation Lesions

Evaluation of Optimal Stenting Technique

Trials	Comparison
NORDIC 1	Simple vs. Complex
NORDIC 2	Crush vs. Culotte
NORDIC 3	Kissing balloon vs. leave alone
BBC	Simple vs. Complex
CACTUS	Provisional T vs. Crush

Lessons From Trials

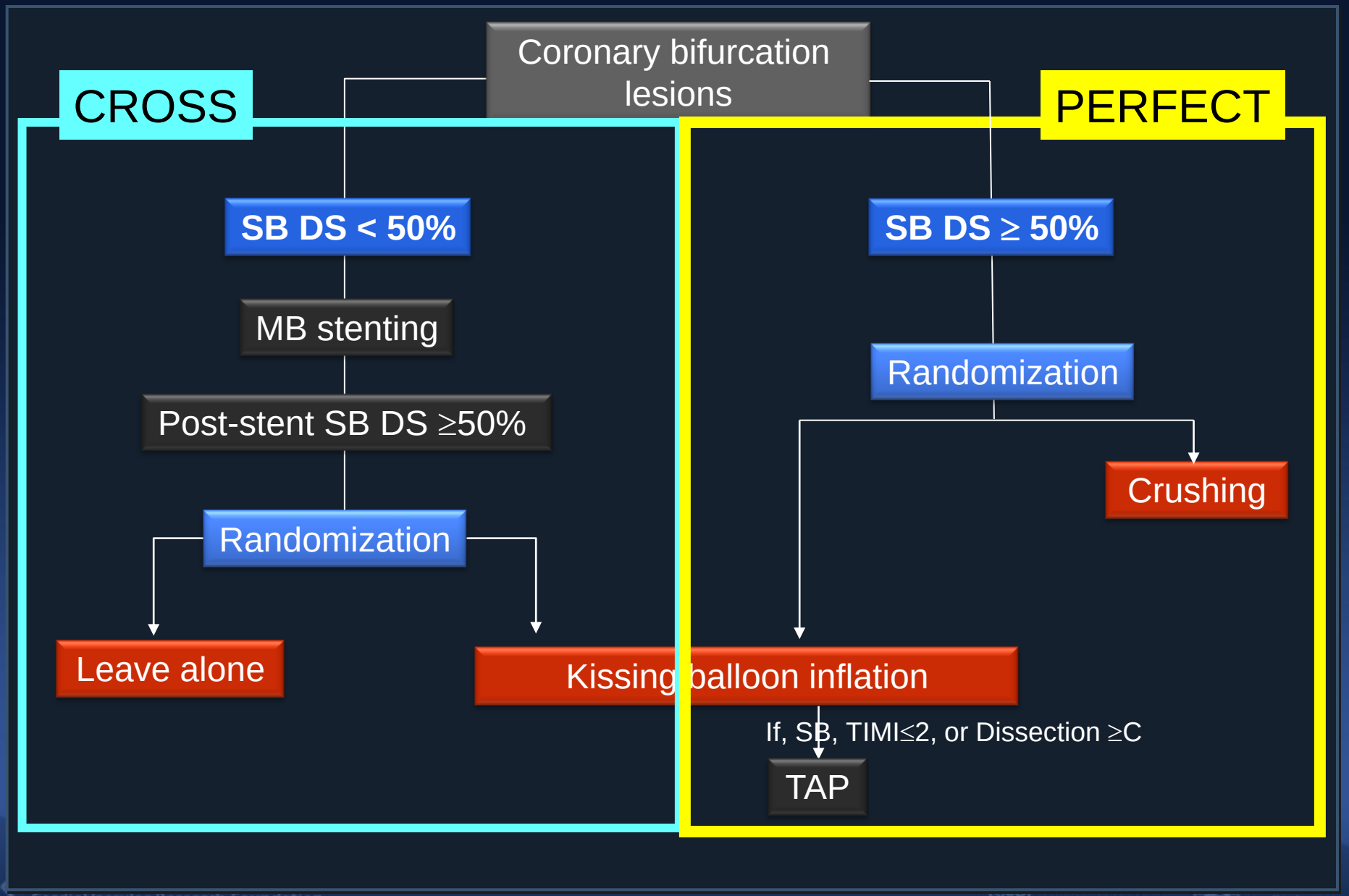
- No difference in the rate of death, spontaneous MI, and repeat revascularization rate
- Superiority of simple stenting in the rate of periprocedural MI
- Fewer stents in simple stenting

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

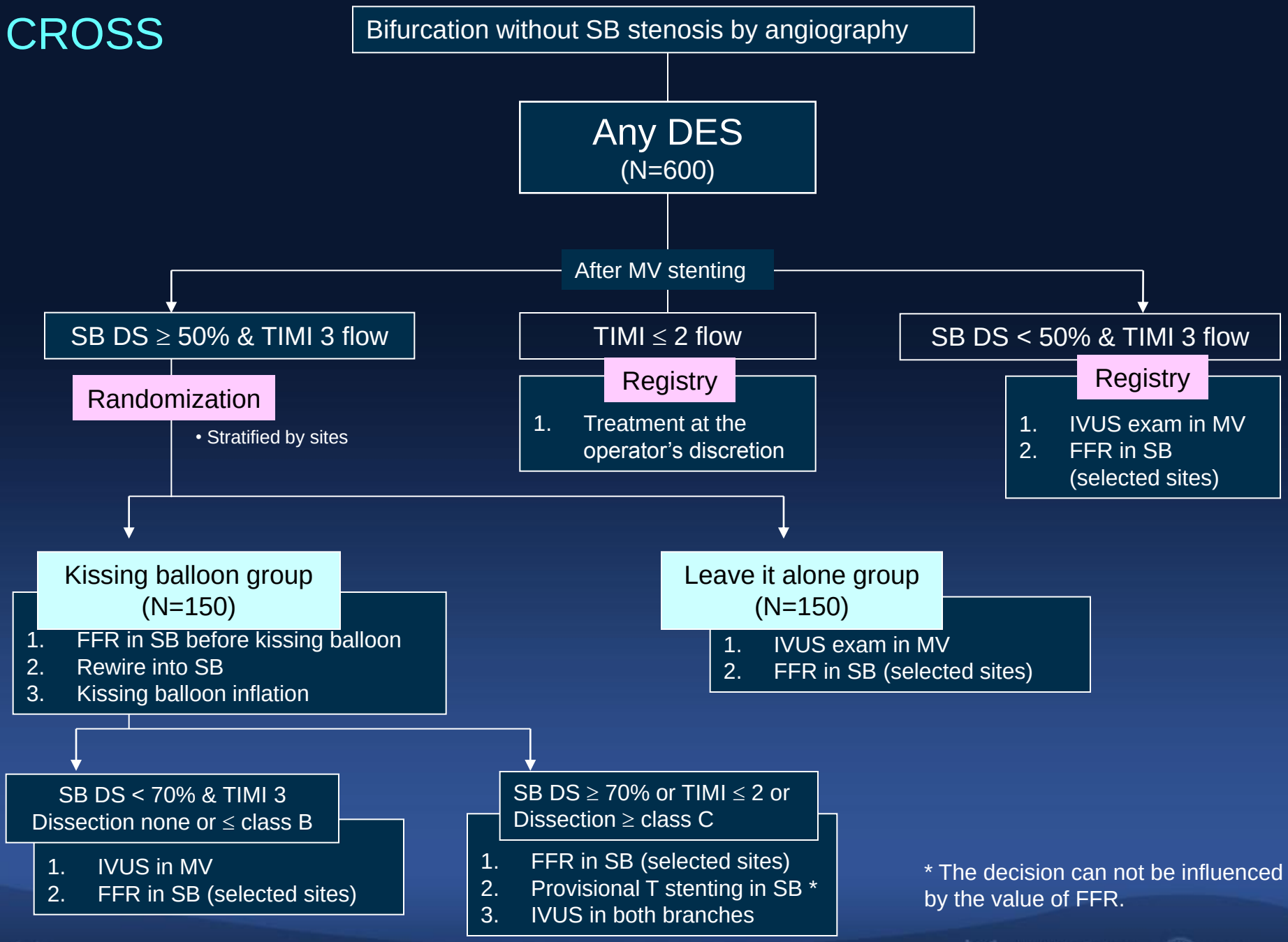
2. Angiographic

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

Exclusion Criteria

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

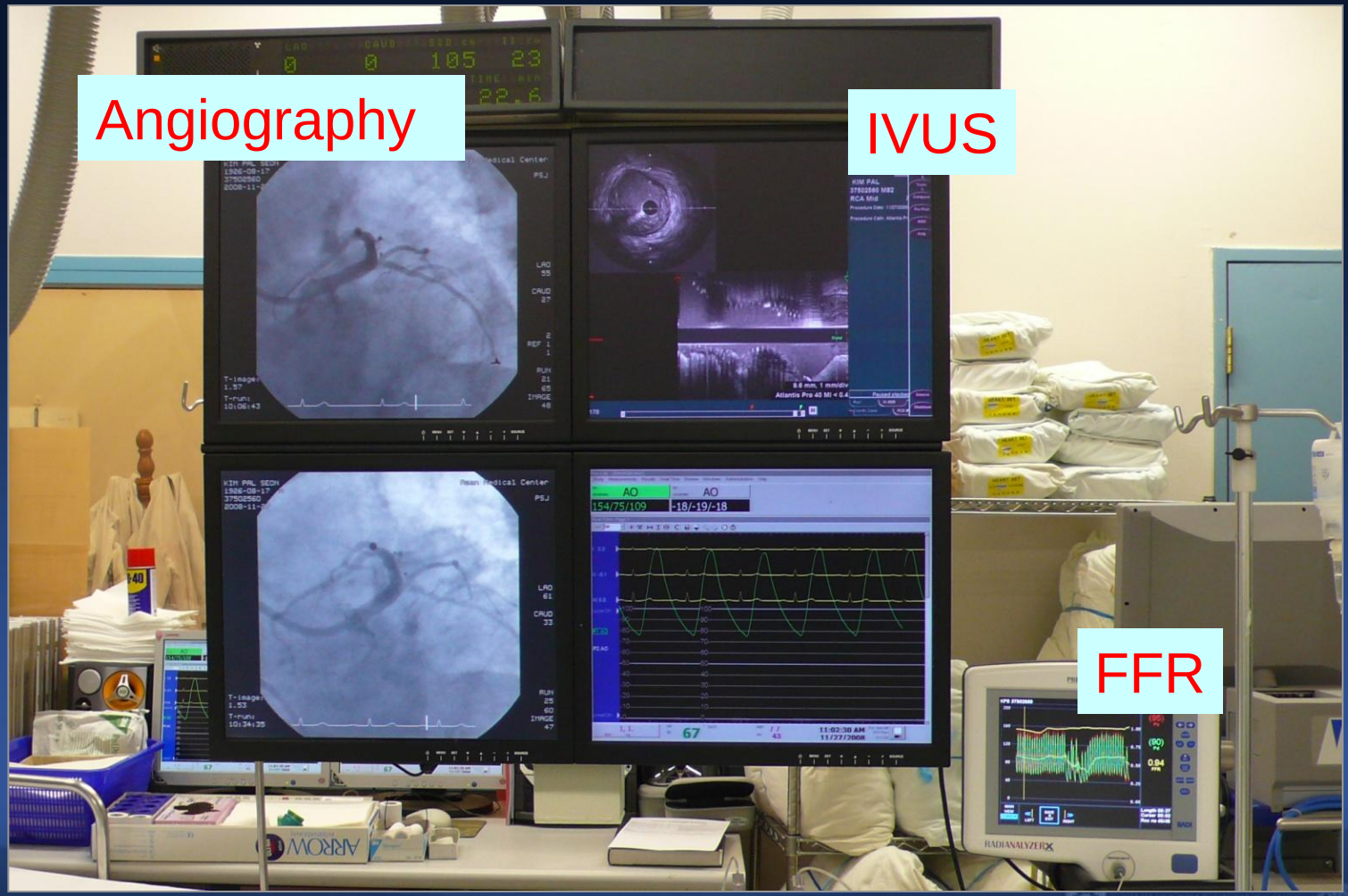
CROSS



* 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



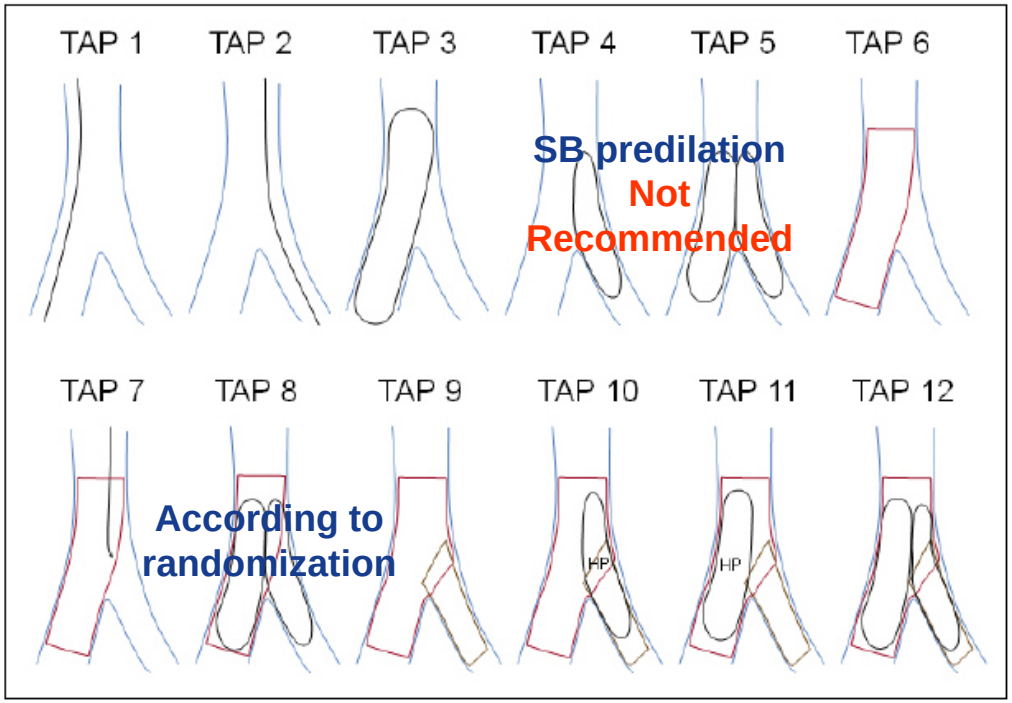
Procedures

Single Stent (Provisional T)

Angiographic & Procedural

Provisional T Stenting

Sequence	Procedure	Performance	Sequence	Procedure	Performance
TAP 1 *	MB wiring	Done ND	TAP 7 *	SB rewiring after MB stenting	Done ND
TAP 2 *	SB wiring	Done ND	TAP 8 *	Kissing after MB stenting	Done ND
TAP 3 *	MB predilation	Done ND	TAP 9 *	SB stenting	Done ND
TAP 4 *	SB predilation	Done ND	TAP10 *	SB balloon dilatation	Done ND
TAP 5 *	Kissing predilation	Done ND	TAP 11 *	MB balloon dilatation	Done ND
TAP 6 *	MB stenting	Done ND	TAP12 *	Final kissing	Done ND



CROSS Trial
Study Design

- **Primary end points**
  - 8-month diameter stenosis in SB

- **Hypothesis: non-inferiority**
  - H_a : Leave alone ≥ Kissing balloon

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 : superiority**
  - H_a : Provisional T ≥ 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:** ≥ 2.5 mm, ≥ 50% stenosis, ≤ 50 mm length covered with ≤ 2 stents
- **SB:** ≥ 2.0 mm, ≥ 50% stenosis, ≤ 30 mm length covered with 1 stent

PERFECT Trial

True bifurcation by angiography

Wire insertion into both branches

Randomization with any DES

Crush group (N=240)

1. Preprocedural IVUS in both branches
2. Predilation in the MV and SB
3. SB stenting while keeping MB stent
4. Removal of SB stent and wire
5. MV stenting
6. Rewire into the SB stent
7. Sequential high pressure balloon dilatation in both in-stent areas
8. Kissing balloon inflation
9. Postprocedural IVUS in both branches

Crossover to crush

Serious dissection necessitating urgent stenting in SB after predilation*

Provisional T stenting group (N=240)

1. Preprocedural IVUS in both branches
2. Predilation in the MV
3. MV stenting while keeping jailed wire in the SB
4. Rewire into the SB
5. Kissing balloon inflation with low pressure at SB

Indication of SB Stenting

Angiography at SB

- TIMI ≤ 2 flow or
- DS ≥ 70% or
- Dissection ≥ NHLBI class C

1.

4. Kissing balloon inflation
5. Postprocedural IVUS in both branches

* Predilation in SB is strongly discouraged.

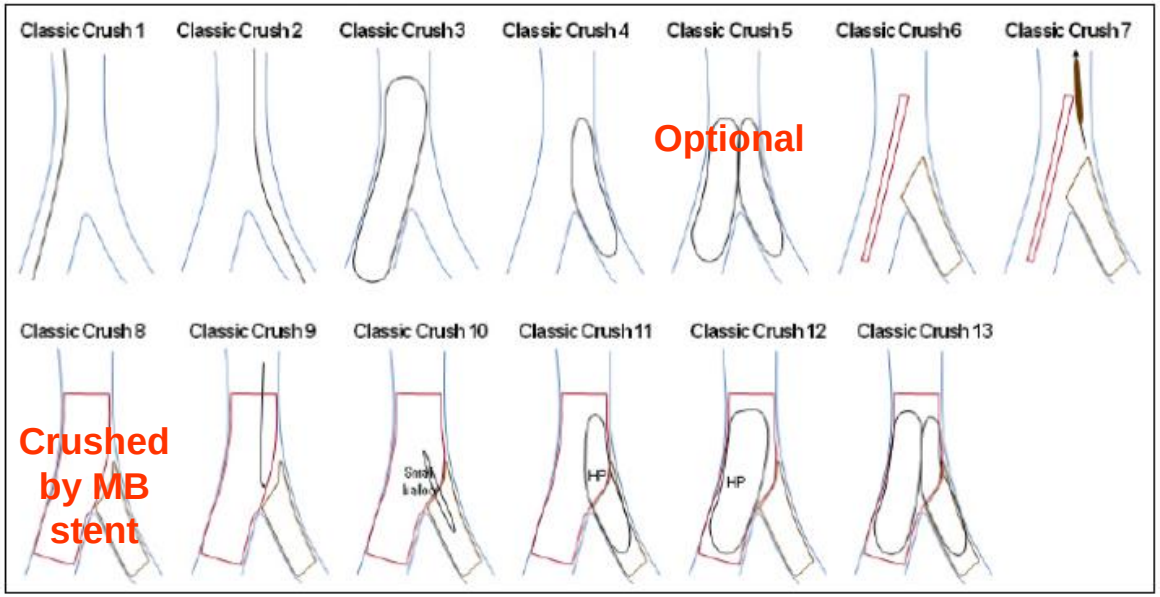
Procedures

Crush: Classic Stent Crushing

Angiographic & Procedural

Classic Crush

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



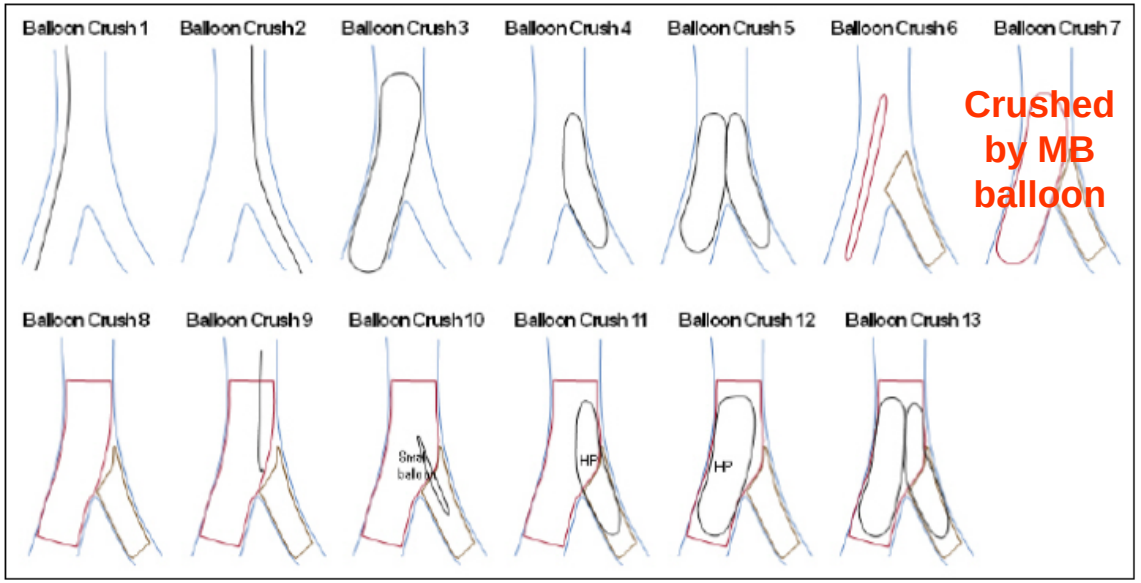
Procedures

Crush: Balloon Crushing

Angiographic & Procedural

Balloon Crush

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



Power Calculation

CROSS

- Non-inferiority design
- H_a : no kissing < kissing
- Assumed FU diameter stenosis: 45% in kissing
- δ: relative 30% (absolute 15%)
- Alpha: 0.05 one-sided
- Power: 90%
- Drop out rate : 0.2
- Sample in random group: 360
- Overall cohort: 600

PERFECT

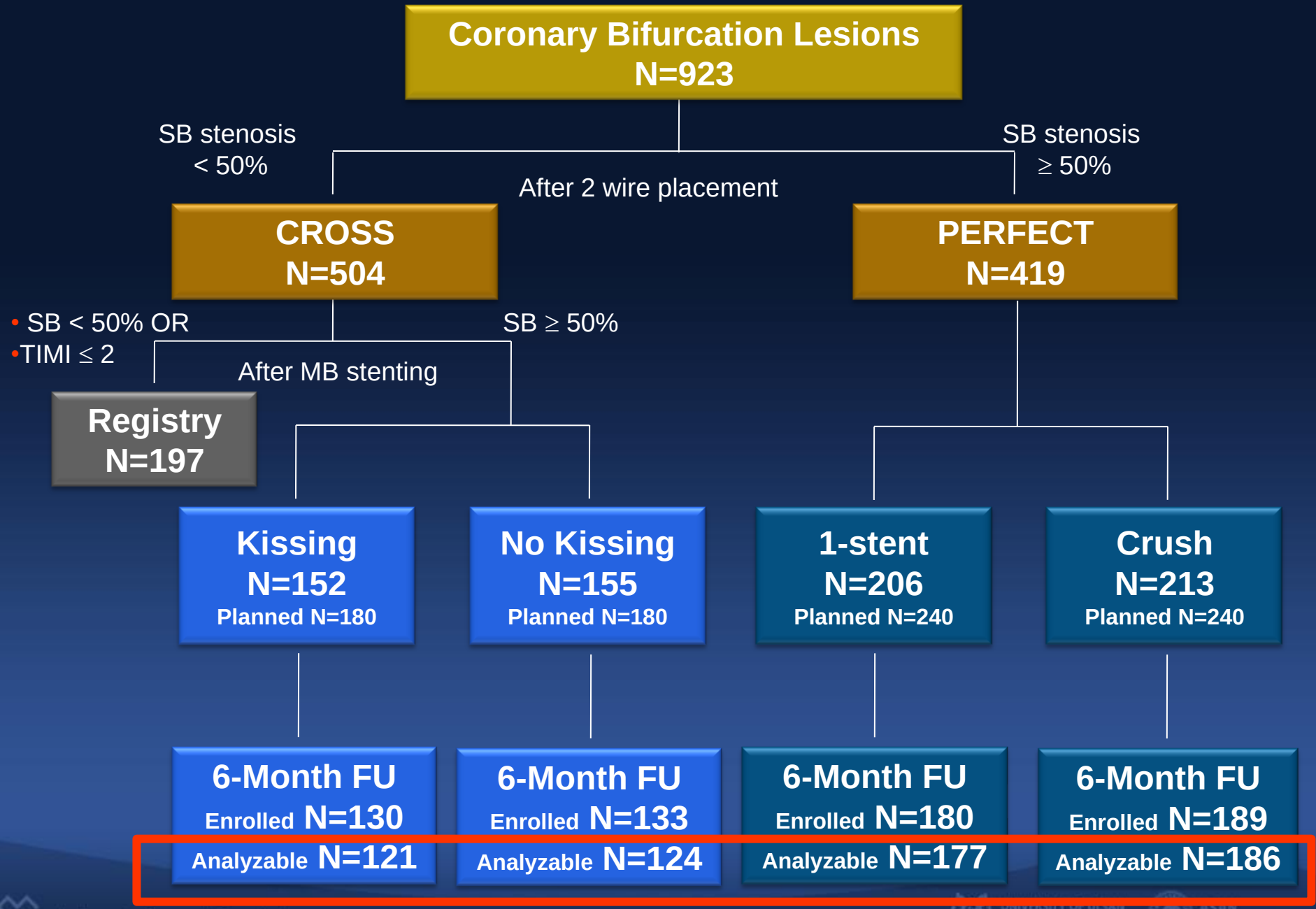
- Superiority design
- H_a : Crush $\leq$ 1-stent
- Assumed FU restenosis: Crushing, 11%; 1-stent, 23%
- Alpha: 0.05 two-sided
- Power : 90%
- Drop out rate : 0.15
- Overall cohort: 240

Enrollment

- Since 2009
- Targeted final enrollment date: end of 2010
- Early termination of enrollment on DEC 2012
  - Slow enrollment
  - Cumulative evidence supporting 1-stent over 2-stent
  - Improvement of outcomes with the development of new DES
  - Over 80% of targeted population

Clinicaltrialgov.com, NCT00694005

Clinicaltrialgov.com, NCT00693251



Preliminary Results in Intention-to-Treat Principle

Baseline Characteristics

	CROSS			PERFECT		
	Kissing (N=121)	No Kissing (N=124)	p	Single (N=177)	Crush (N=186)	p
Age, yrs	60.6 ± 9.3	61.4 ± 7.4	0.46	60.5 ± 8.9	60.7 ± 9.0	0.88
Male	70.2	64.5	0.34	73.4	74.7	0.78
Diabetics	30.6	30.6	0.99	25.4	25.8	0.93
Smoking	33.1	22.6	0.067	33.9	26.9	0.15
Hyperlipidemia	48.8	47.6	0.85	59.9	65.1	0.31
Hypertension	56.2	57.3	0.87	56.5	55.9	0.91
Family history	7.4	14.5	0.077	14.7	15.6	0.81
Prior PCI	5.8	9.7	0.26	6.2	8.6	0.39
Prior MI	1.7	4.8	0.28	5.1	4.3	0.72
Renal failure	1.7	0	0.24	1.1	0	0.24
LV EF, %	61.0 ± 7.0	62.4 ± 5.6	0.11	59.3 ± 7.4	60.4 ± 7.0	0.19
Sinus rhythm	95.9	96.8	0.75	96.0	98.4	0.21

Preliminary Results in Intention-to-Treat Principle

Baseline Characteristics

	CROSS			PERFECT		
	Kissing (N=121)	No Kissing (N=124)	p	Single (N=177)	Crush (N=186)	p
Presentation			0.35			0.89
SA	38.0	37.9		50.3	52.2	
UA	43.8	39.5		31.6	32.8	
NSTEMI	5.8	4.0		5.1	2.7	
Disease extent			0.059			0.65
1 VD	61.2	51.6		52.5	50.5	
2 VD	28.1	41.9		32.8	31.2	
3 VD	10.7	6.5		14.7	18.3	

Preliminary Results in Intention-to-Treat Principle

Lesion Characteristics

	CROSS			PERFECT		
	Kissing (N=121)	No Kissing (N=124)	p	Single (N=177)	Crush (N=186)	p
Site			0.95			0.78
LAD	90.1	88.7		90.4	92.5	
LCX	6.6	8.1		7.9	5.4	
RCA	3.3	3.2		0.6	1.1	
MEDINA *			0.4			0.002
1: 0: 0	4.1	8.1		0	0.5	
0: 1: 0	14.0	8.9		0	0	
1: 1: 0	55.4	63.7		5.6	0	
1: 1: 1	19.8	13.7		85.3	93.0	
0: 0: 1	0.8	0		0	0	
1: 0: 1	2.5	2.4		1.7	2.2	
0: 1: 1	3.3	3.2		7.3	4.3	
No. of lesions	1.6 ± 0.8	1.7 ± 0.7	0.36	1.8 ± 0.9	1.8 ± 0.9	0.81

* Reported by independent physicians in sites

Preliminary Results in Intention-to-Treat Principle

Procedures

	CROSS			PERFECT		
	Kissing (N=121)	No Kissing (N=124)	p	Single (N=177)	Crush (N=186)	p
Radial approach	30.6	31.5	0.88	10.2	9.7	0.88
DES types			0.63			0.87
Cypher	36.4	29.0		63.8	63.4	
Taxus (Liberte)	12.4	16.1		1.1	1.1	
Endeavor	30.6	35.5		7.3	8.1	
Xience, Promus	13.2	14.5		20.9	18.8	
Nobori, Biomatrix	6.6	4.8		4.0	3.2	
Others	0.8	0		2.8	5.4	
Stents per lesion	1.4 ± 0.6	1.4 ± 0.6	0.82	2.0 ± 1.0	2.7 ± 1.0	<0.001
IVUS in MB	93.4	96.0	0.37	94.9	95.7	0.72
IVUS in SB	48.8	34.7	0.025	81.4	91.9	0.003

Preliminary Results in Intention-to-Treat Principle

Procedures

	CROSS			PERFECT		
	Kissing (N=121)	No Kissing (N=124)	p	Single (N=177)	Crush (N=186)	p
Stents in MB	100	100		100	100	
No.	1.3 ± 0.5	1.3 ± 0.5	0.91	1.4 ± 0.6	1.4 ± 0.5	0.89
Length, mm	33.0 ± 13.3	32.8 ± 13.1	0.86	37.6 ± 15.6	37.5 ± 14.3	0.97
Size, mm	3.5 ± 2.4	3.3 ± 0.3	0.28	3.3 ± 0.3	3.3 ± 0.3	0.36
Stents in SB	3.3	0.8	0.21	28.8	97.8	<0.001
No.	-	-	-	0.3 ± 0.5	1.0 ± 0.2	<0.001
Length, mm	-	-	-	21.7 ± 7.0	21.7 ± 7.1	0.99
Size, mm	-	-	-	2.7 ± 0.2	2.8 ± 1.7	0.55
Strategy			0.49			<0.001
Provisional T	99.2	100		95.5	11.3	
Crush	0	0		4.0	88.2	
Final kissing	96.7	5.6	<0.001	79.7	95.7	<0.001
FFR after proc.	42.1	50.0	0.22			
< 0.8	5.9	24.2	0.008			

Comparison with other studies

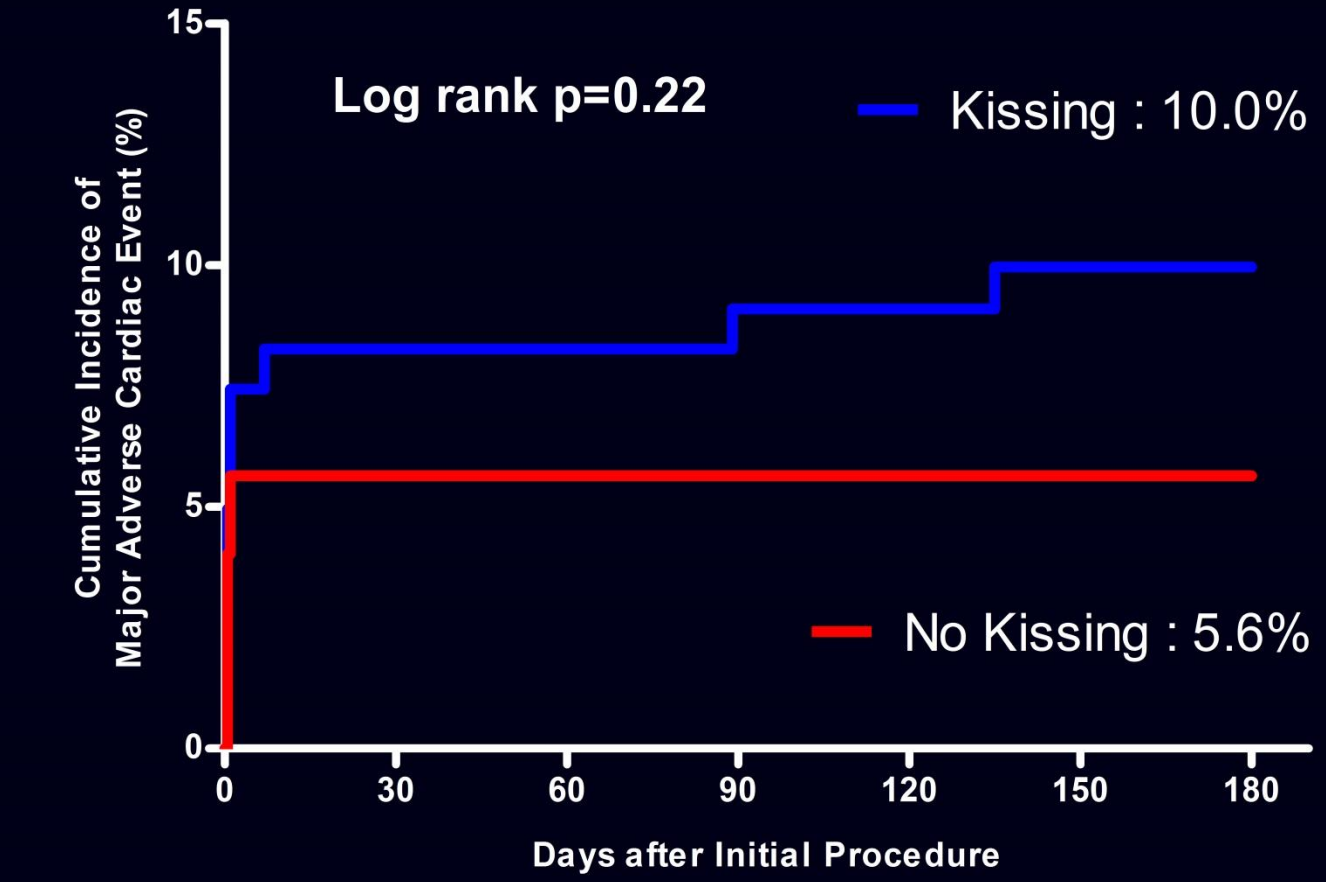
	Nordic I		Nordic II		CACTUS		BBC-one		CROSS		PERFECT	
	1-stent	Cru,culo, T	crush	culotte	1-stent	Crush	1-stent	crus, culo	Kiss	No kiss	1-stent	crush
Age, yr	63	62	65	65	67	65	64	67	61	61	61	61
Male, %	77	79	71	72	76	80	77	77	70	65	73	75
DM, %	13	12	13	15	22	24	13	11	31	31	25	26
MVD	-	-	-	-	-	-	31	27	39	48	47	49
Prior MI	-	-	-	-	35	45	23	25	2	5	5	4
Medina 1.1.1	-	-	-	-	-	-	60	60	20	14	85	93
FKB, %	32	74	85	92	90	92	29	76	97	6	80	96
SB stent, %	4.3	95.1	99.0	97.7	31	-	-	-	3.3	0.8	28.8	97.8
No. stent	1.3	2.2	-	-	-	-	-	-	1.4	1.4	2.0	2.7

Non-adjudicated Results in Intention-to-Treat Principle at 6 months

No Significant Difference

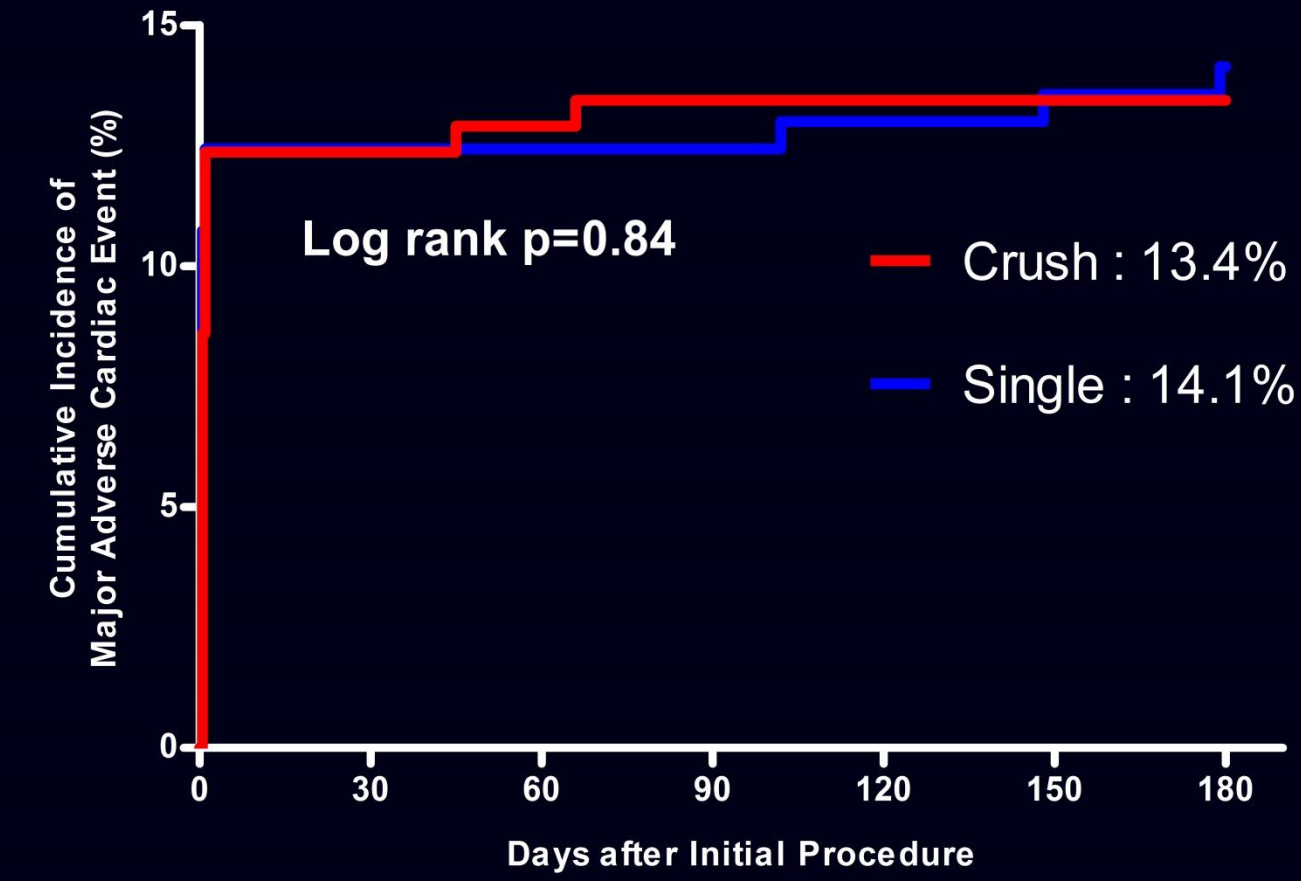
	CROSS			PERFECT		
	Kissing (N=121)	No Kissing (N=124)	p	Single (N=177)	Crush (N=186)	p
Months	175.0 ± 22.4	177.6 ± 13.3	0.27	179.3 ± 7.2	177.5 ± 15.9	0.15
Death	0.8	0	0.31	0.6	1.1	0.59
Cardiac	0.8	0	0.31	0.6	0.5	0.98
Non-cardiac	0	0		0	0	
MI	8.3	5.6	0.42	11.9	12.4	0.9
Q MI	0	0.8	0.32	0	0	
Non-Q MI	8.3	4.8	0.28	11.9	11.8	0.98
Any revasculare	1.7	0.8	0.54	2.3	0.6	0.16
TVR	0.9	0	0.31	1.7	0	0.076
TLR	0.9	0	0.31	1.7	0	0.076
Stent thrombosis	0	0		0.6	1.1	0.59

MACE at 6 months: CROSS



No. at risk				
Kissing	121	112	108	103
No Kissing	124	119	117	113

MACE at 6 months: PERFECT



No, at risk				
Single	177	158	154	151
Crush	186	162	161	158

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.