6 month vs. 12 month DAPT After 2nd Generation DES (BES vs. ZES)
: Prospective, Randomized, Multicenter Trial

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Disclosure

- **Personal Disclosure(s)**
  - NOTHING TO DISCLOSE
- **Additional Disclosure(s)**
  - NOTHING TO DISCLOSE
- **Expert Witness Disclosure(s)**
  - NOTHING TO DISCLOSE

Background - I

- Because one of strong predictor for stent thrombosis is early discontinuation of clopidogrel, prolonged dual antiplatelet therapy (DAPT) is highly recommended.

Iakovou I, et al. JAMA 2005;293:2126-30.
Pfisterer M, et al. J Am Coll Cardiol 2006;48:2584-91.
Brar SS, et al. J Am Coll Cardiol 2008;51:2220-7.

- However, prolonged use of clopidogrel is associated with many potential risks and no additional benefits.

Stone GW, et al. Am J Cardiol 2008;102:1017-22.
Kandzari DE, et al. JACC Cardiovasc Interv. 2009 ;2:1279-85.

- Optimal duration of DAPT was different depending on different types of DES.

Leon MB, et al. J Am Coll Cardiol 2010;55:543-54.
Kim BK et al. J Am Coll Cardiol. 2012;60:1340-8.
Yu X et al. Coron Artery Dis. 2013 May;24:217-23.
Valgimigli M, et al. Eur Heart J. 2013;34:909-19

Background - II

Recent OCT study reported sufficient strut coverage and outcome following ZES implantation

Kim JS, et al. J Am Coll Cardiol Intv 2009;2:1240-7.
Hahn JY, et al. Circ J 2010;74:2314-21.
Kim BK et al. J Am Coll Cardiol. 2012;60:1340-8.

More complete strut coverage of BES as compared with SES

Gutiérrez-Chico JL et al, Am Heart J 2011;162:922-31.
Kim BK. et al, Int J Cardiol. 2013 Oct 12;168:4617-23.

Hypothesis & Objective

Hypothesis;

- 6-month DAPT after 2nd generation DES implantation (ZES, BES) may be non-inferior to 12-month DAPT (standard therapy).
- 6-month DAPT may be sufficient on the bases of neointimal coverage.

Objectives;

- To compare the efficacy and safety between 6-months and 12-months DAPT after implantation of ZES and BES.
- To compare the neointimal coverage between ZES and BES at 6month.

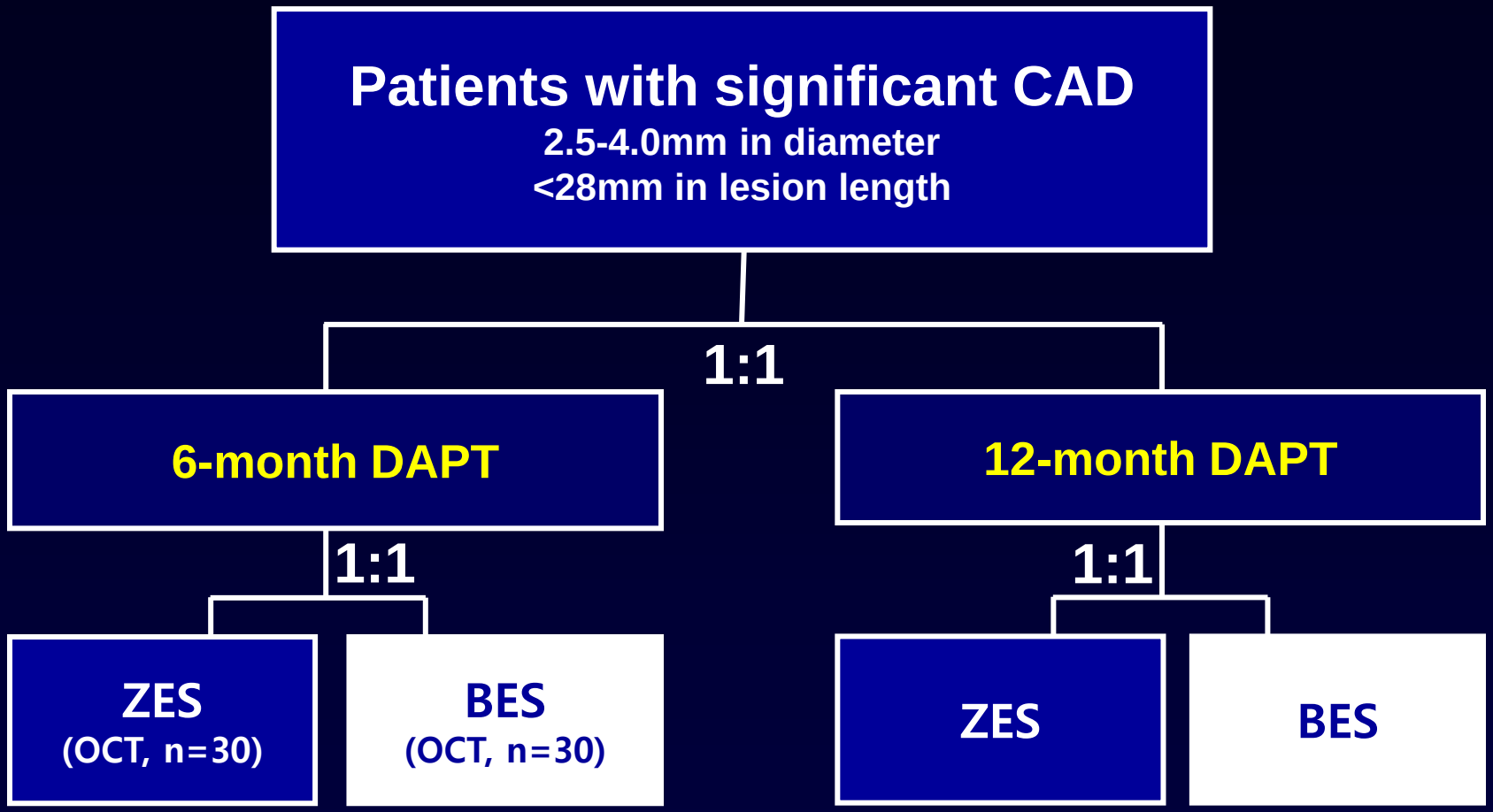
Study design and patients

- Prospective, open label, double-randomized trial
- Participating centers; conducted at 10 sites in Korea

Randomization

- Using an interactive web-based response system, study participants were randomly assigned in a 1:1 ratio to receive either 6-month DAPT or 12-month DAPT, and the ZES or BES.
- Among them, 60 patients were randomly assigned (ZES, BES) to be evaluated at 6month OCT.

Study at a glance



ZES = Endeavor Resolute Integrity, zotarolimus-eluting stent ; BES = Biomatrix, Biolimus A9-eluting stent
OCT: optical coherance tomography, 6month angiography was done in patients assigned OCT.

Inclusion criteria

- Patients with stable angina, unstable angina, or NSTEMI.
- Diameter stenosis ≥ 50%, reference vessel diameter of 2.5 to 4.0 mm , and lesion length of <28mm by visual estimation.
- Elective PCI, eligible for participation.

Exclusion criteria

- Prior history of cerebral vascular accidents, peripheral artery diseases, thromboembolic disease or stent thrombosis
- Left ventricular ejection fraction < 40%
- Lesions with in-stent restenotic lesion, chronic total occlusion, bifurcation, or significant left main disease requiring intervention
- Cardiogenic shock
- Acute ST-elevation MI
- Contraindication to antiplatelet agents
- Severe hepatic (≥3 times normal values) or renal dysfunction (serum creatinine >2.4 mg/dl)

End-points

Primary

- Major cardiac adverse events (death, MI and ischemia driven-TVR, Stroke) at 12 months for comparison between 6-months and 12-months maintenance of DAPT in patients undergoing PCI using Resolute Integrity (ZES) or BioMatrix stent (BES).

Secondary

- Late loss in 12 month Angiographic Follow up
- To investigate 6 month neointimal coverage and uncovered stent struts between ZES and BES by OCT.

Sample size and Statistics

- A non-inferiority comparison
- Overall incidence of the primary endpoint of two groups;
  6-month DAPT; 11.7%
  12-month Standard therapy; 9.7%
  - non-inferiority margin of 1%
  - 20% drop out rate, this required an estimated sample size of 1,368 patients (684 for each group) to achieve 80% power for non-inferiority test and a one-sided type I, II error of 5%.
- P-value <0.05 were considered statistically significant.
- Statistical Analysis System software (SAS; 9.1.3., SAS Institute, NC) and R version 2.12.2 (R Development Core Team, Vienna, Austria).

Baseline clinical characteristics

Variables	ZES 6 m DAPT (n=343)	BES 6 m DAPT (n=340)	ZES 12m DAPT (n=344)	BES 12 m DAPT (n=341)	P
Age (year)	63.6±9.6	62.3±9.4	62.5±10.0	62.3±9.8	0.94
Male sex, (n)	235	231(69.6)	191 (63.7)	193 (64.3)	0.47
Body mass index, kg/m^2	25.0±3.1	24.9±3.2	25.1±3.1	24.9±3.1	0.50
Hypertension, (n)	215	201	207	218	0.52
Diabetes mellitus, (n)	87	77	89	86	0.37
Dyslipidemia, (n)	108	103	99	108	0.31
Current smoker, (n)	158	142	152	154	0.29
Ejection fraction, %	62.2±8.7	63.4±9.4	64.2±9.1	62.9±9.7	0.56
Prior myocardial infarction, (n)	12	11	14	14	0.78
Prior percutaneous coronary intervention, (n)	33	29	32	39	0.73
Clinical presentation, (n)					0.56
Stable angina	153	156	152	151	
Unstable angina	132	128	129	131	
NSTEMI	58	56	63	59	
Medications at discharge					
Statins, no. (%)	329	331	332	330	0.71
Beta blockers, no. (%)	321	319	320	323	0.59
ACE inhibitors, no. (%)	149	152	147	150	0.51
Angiotensin receptor blockers, no. (%)	162	159	161	157	0.49

Primary end point
Clinical follow-up at 1 year

- Clinical follow-up at 1 year: 849/1,368 (61.1%)
- Angiographic follow-up at 1 year; 747/849 (87.9%)
- MACE (death, MI and ischemic driven-TVR, stroke)
  - between 6- and 12-month DAPT was 4.7 % vs. 3.6 % (p=n.s)
  - between ZES and BES was 4.7 % vs. 3.6 % (p=n.s)

	ZES 6m (n=212)	BES 6m (n=213)	ZES 12m (n=214)	BES 12m (n=210)
Death	0 (0.0%)	1 (0.5%)	1 (0.5%)	0 (0.0%)
MI	1 (0.5%)	1 (0.5%)	1 (0.5%)	1 (0.5%)
Ischemic driven TVR	11 (5.2%)	5 (2.3%)	5 (2.4%)	6 (2.9%)
Stroke	0 (0.0%)	1 (0.5%)	1 (0.5%)	0 (0.0%)

Secondary end point: QCA data

	ZES 6m DAPT (n=343)	BES 6m DAPT (n=340)	ZES 12m DAPT (n=344)	BES 12m DAPT (n=341)	p
Stent diameter (mm)	3.31±0.42	3.37±0.42	3.39±0.42	3.44±0.47	0.283
Stent length (mm)	20.2±4.3	19.9±4.1	19.8±4.4	20.4±4.4	0.673
MLD (mm)					
Pre	0.97±0.41	0.99±0.37	0.97±0.47	0.92±0.57	0.570
Post	3.31±0.45	3.30±0.47	3.31±0.44	3.31±0.55	0.477
12 month Follow-up	3.03±0.48 (n=191)	2.99±0.47 (n=189)	2.98±0.48 (n=186)	2.97±0.49 (n=181)	0.347
Late loss (mm), 12month	0.28±0.28	0.31±0.27	0.33±0.29	0.34±0.25	0.611

Secondary endpoint: OCT findings at 6month

Cross-section-level analysis	ZES (n=30)	BES (n=30)	p
Time to follow-up OCT, days	184.6±22.5	189.7±24.9	0.412
Stent diameter, mm	3.33±0.41	3.41±0.50	0.482
Stent length, mm	17.7±4.2	17.6±4.4	0.929
Total No. of cross sections, n	491	488	-
Mean stent CSA, mm^2	7.90±2.14	8.19±2.35	0.620
Mean lumen CSA, mm^2	7.48±2.14	7.65±2.38	0.769
Mean NIH CSA, mm^2	0.42±0.24	0.48±0.30	0.373
Cross sections with any uncovered strut, %	11.0±13.1	15.9±22.2	0.410
Cross sections with a ratio of uncovered to total strut >0.3, %	0.2±1.0	1.9±6.8	0.776
Cross sections with any malapposed strut, %	4.8±8.5	5.0±14.2	0.777

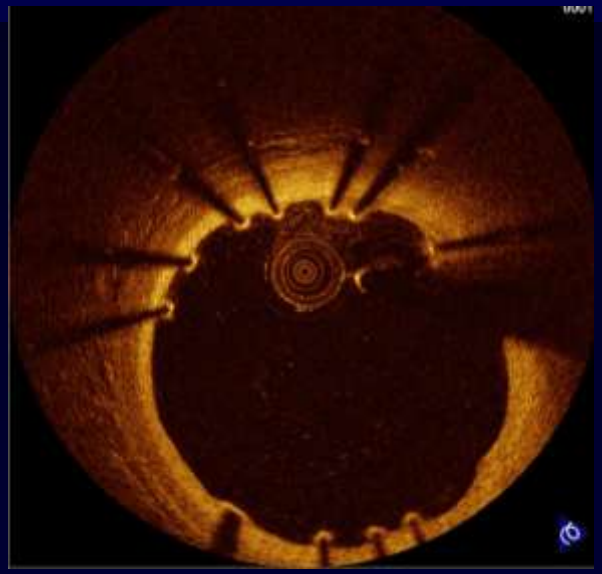
Secondary endpoint: OCT findings at 6month

Strut-level analysis	ZES (n=30)	BES (n=30)	p
Total No. of analyzable struts (n)	5,721	5,231	-
Mean NIH thickness (μm)	61.9 ± 39.6	81.6 ± 57.1	0.126
% of uncovered strut	3.0 ± 5.2	2.4 ± 5.3	0.636
% of malapposed strut	1.0 ± 3.4	0.7 ± 2.1	0.636
Both of malapposed and uncovered strut (%)	0.7 ± 2.8	0.2 ± 0.8	0.358
Presence of intra-stent thrombi, n (%)	0 (0.0)	0 (0.0)	-

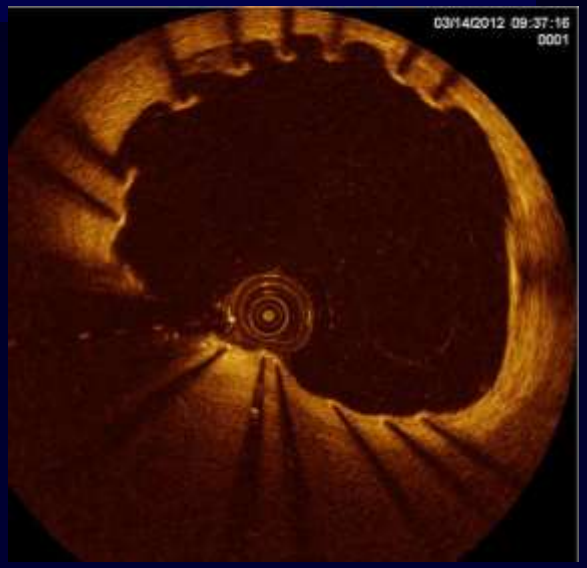
OCT Sample Images

ZES

Covered

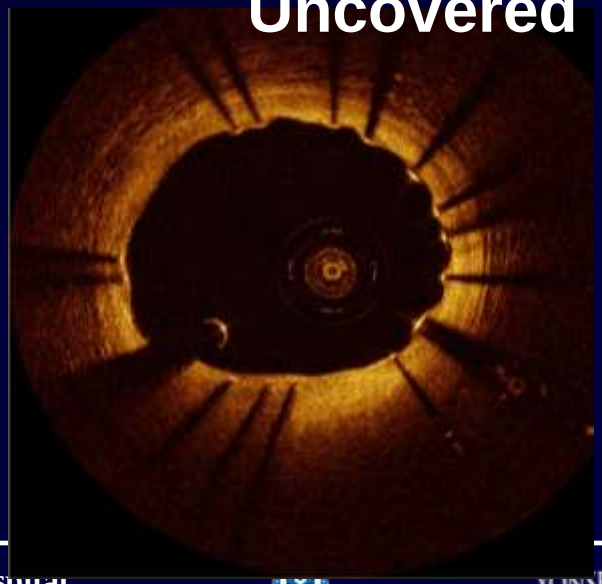


Uncovered



Malapposed

BES



Summary

- On clinical follow up, there were no significant different in MACE including death, myocardial infarction, or target vessel failure, Stroke between 6-month and 12-month DAPT, and between ZES and BES.

- Angiographic follow up data were not different also.

- 6 month OCT follow up data showed that slightly decreased tendency of malapposed strut in BES, but not significant. Further OCT studies will provide more insights into clinical implications of observations from OCT-imaging after newer DES implantation.

Limitations

- This is an interim result in on-going study. Final results will be reported.
- One year of clinical follow-up may not be sufficient to assess the fatal late outcomes (e.g, very late stent thrombosis).
- Because the patients with very high risks were not included, the generalized application of these results to the entire population demands careful attention.

Conclusion

- Shorter duration of DAPT may be suggestive for the newer generation DES.
- BES with biodegradable polymer has comparable clinical, angiographic, and OCT outcome with ZES with durable polymer.