Outcomes of 6 months versus 12 months dual antiplatelet therapy after implantation of biodegradable polymer Biolimus or durable polymer Zotarolimus-eluting stents: OPTIMA-C study and OCT sub-study, prospective, double-randomized, multicenter trial.

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Disclosure

- NOTHING TO DISCLOSE

Background - I

- Because one of strong predictor for stent thrombosis is early discontinuation of clopidogrel, prolonged dual antiplatelet therapy (DAPT) has been recommended. However, prolonged use of clopidogrel is associated with many potential risks and no additional benefits.
- On recent meta-analysis, compared with prolonged DAPT, short-term DAPT is associated with similar rates of MACE but lower rates of bleeding after DES placement, and optimal duration of DAPT was different depending on different types of DES, and Prolonging DAPT requires careful assessment of the trade-off between ischemic and bleeding complications.

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 ;24:217-23.
Valgimigli M, et al. Eur Heart J. 2013;34:909-19
Gennaro G, et al. J Am Coll Cardiol 2015;65:1298–310
Tullio P, et al. J Am Coll Cardiol 2015;65:1092–102

Background - II

- The effect of Shorter-DAPT on stent thrombosis was attenuated with the use of second-generation DES compared with the use of first-generation DES.

Martin G, et al. J Am Coll Cardiol 2015;65:777–86
Gennaro G, et al. J Am Coll Cardiol 2015;65:1298–310

- OCT study has been 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 clinical 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.

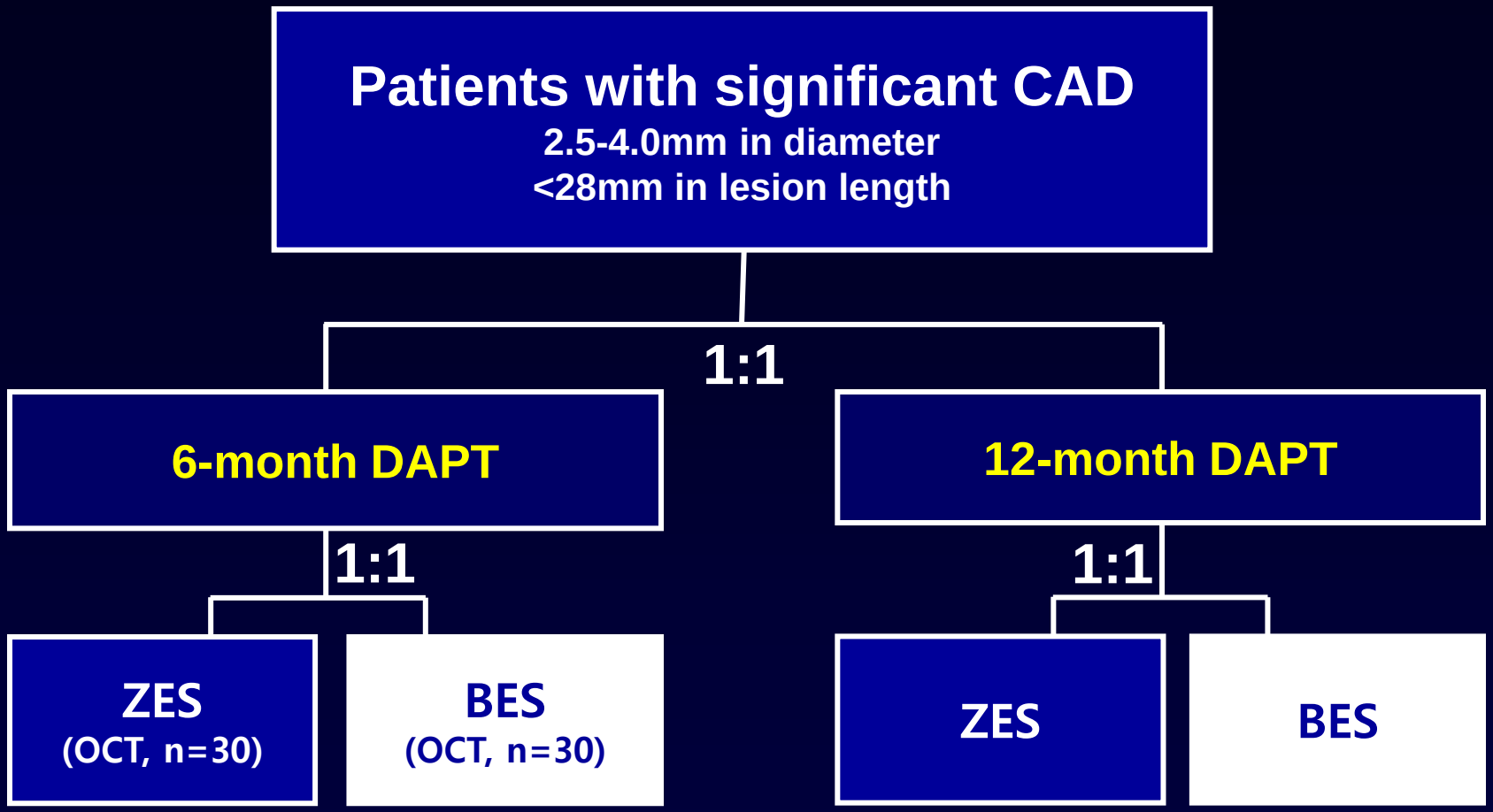
Study design and patients

- Prospective, open label, double-randomized trial
- Participating centers; conducted at 10 sites in Korea
- May, 2011~May, 2015

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.

Sample size and Statistics

- A non-inferiority comparison for MACE
- Overall incidence of the primary endpoint of two groups;
  - 12-month Standard therapy; 4.0%
  - non-inferiority margin of 4%
  - 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
  - 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).

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 <38mm 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 (cardiac death, MI, target vessel failure, stent thrombosis, 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

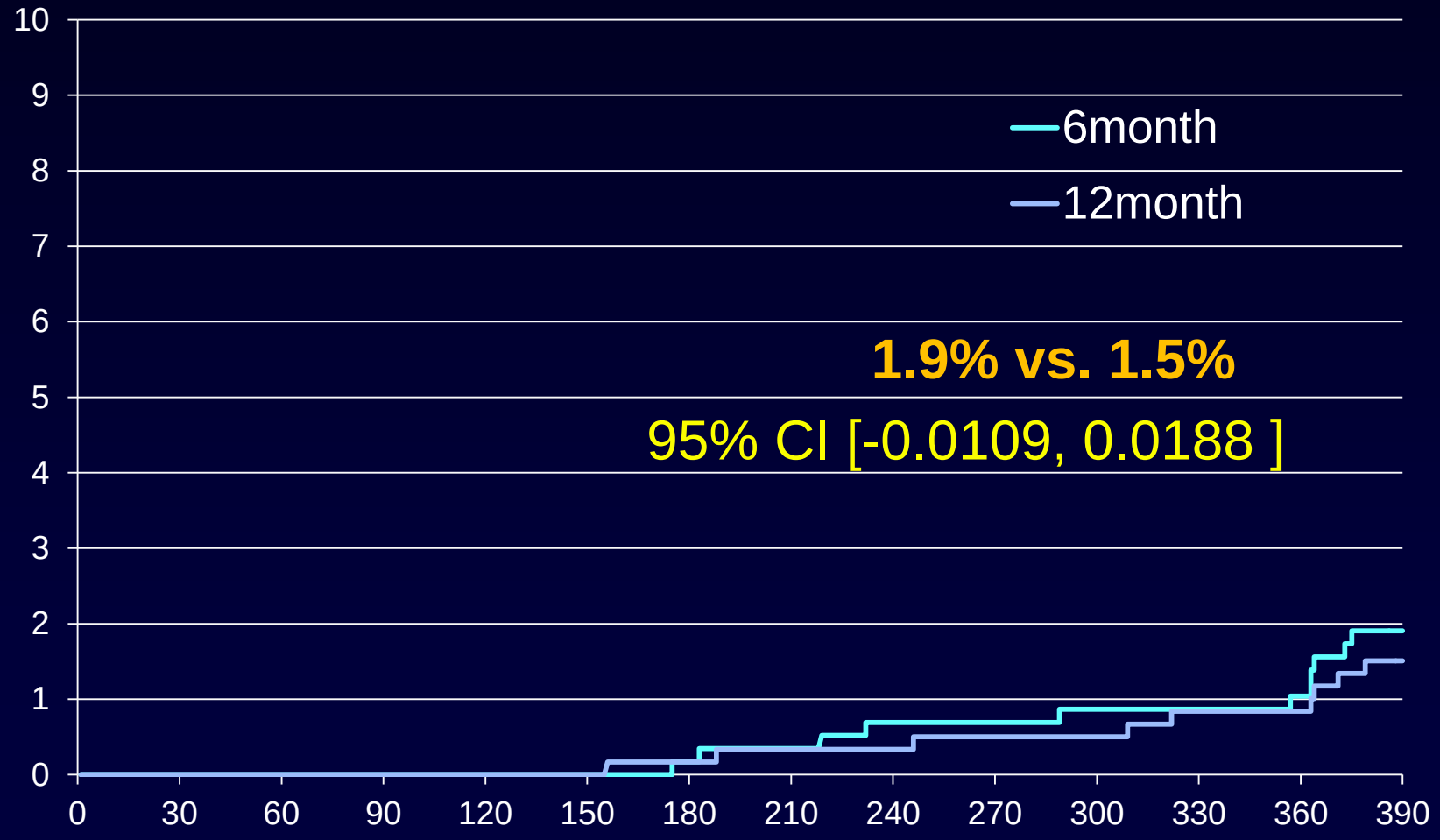
- To compare the lumen late loss by QCA at 1 year.
- To investigate 6 month neointimal coverage and uncovered stent struts between ZES and BES by OCT.

Baseline clinical characteristics

Variables	ZES 6 m DAPT (n=343)	BES 6 m DAPT (n=341)	ZES 12m DAPT (n=343)	BES 12 m DAPT (n=341)	P
Age (year)	63.1±10.9	62.7±11.3	64.2±10.2	64.6±10.6	0.069
Male sex, n (%)	241 (70.3)	237 (69.5)	235 (68.5)	229 (67.2)	0.836
Hypertension, n (%)	218 (63.6)	207 (60.7)	211 (61.5)	225 (66.0)	0.486
Diabetes mellitus, n (%)	101 (29.4)	98 (28.7)	104 (30.3)	99 (29.0)	0.972
Dyslipidemia, n (%)	107 (31.2)	97 (28.4)	94 (27.4)	101 (29.6)	0.726
Current smoker, n (%)	86 (25.1)	96 (28.0)	97 (28.4)	88 (25.8)	0.703
Ejection fraction, %	63.0±9.7	63.0±9.4	62.5±9.5	63.5±9.3	0.491
Prior myocardial infarction, n (%)	9 (2.6)	8 (2.3)	12 (3.5)	13 (3.8)	0.661
Prior percutaneous coronary intervention, n (%)	34 (9.9)	23 (6.7)	32 (9.3)	39 (11.4)	0.192
Clinical presentation, n (%)					
Stable angina	123 (35.9)	120 (35.2)	106 (31.1)	126 (37.1)	0.365
Unstable angina	134 (39.1)	121 (35.5)	130 (38.1)	123 (36.2)	0.756
NSTEMI	38 (11.1)	52 (15.2)	50 (14.7)	40 (11.8)	0.282
Medications at discharge					
Statins, n (%)	311 (90.7)	310 (90.4)	303 (88.9)	303 (88.9)	0.790
Beta blockers, n (%)	202 (58.7)	199 (58.0)	197 (57.8)	184 (54.0)	0.573
ACE inhibitors, n (%)	56 (16.3)	67 (19.6)	61 (17.8)	57 (16.7)	0.669
Angiotensin receptor blockers, n (%)	152 (44.3)	150 (44.0)	162 (47.2)	162 (47.5)	0.696

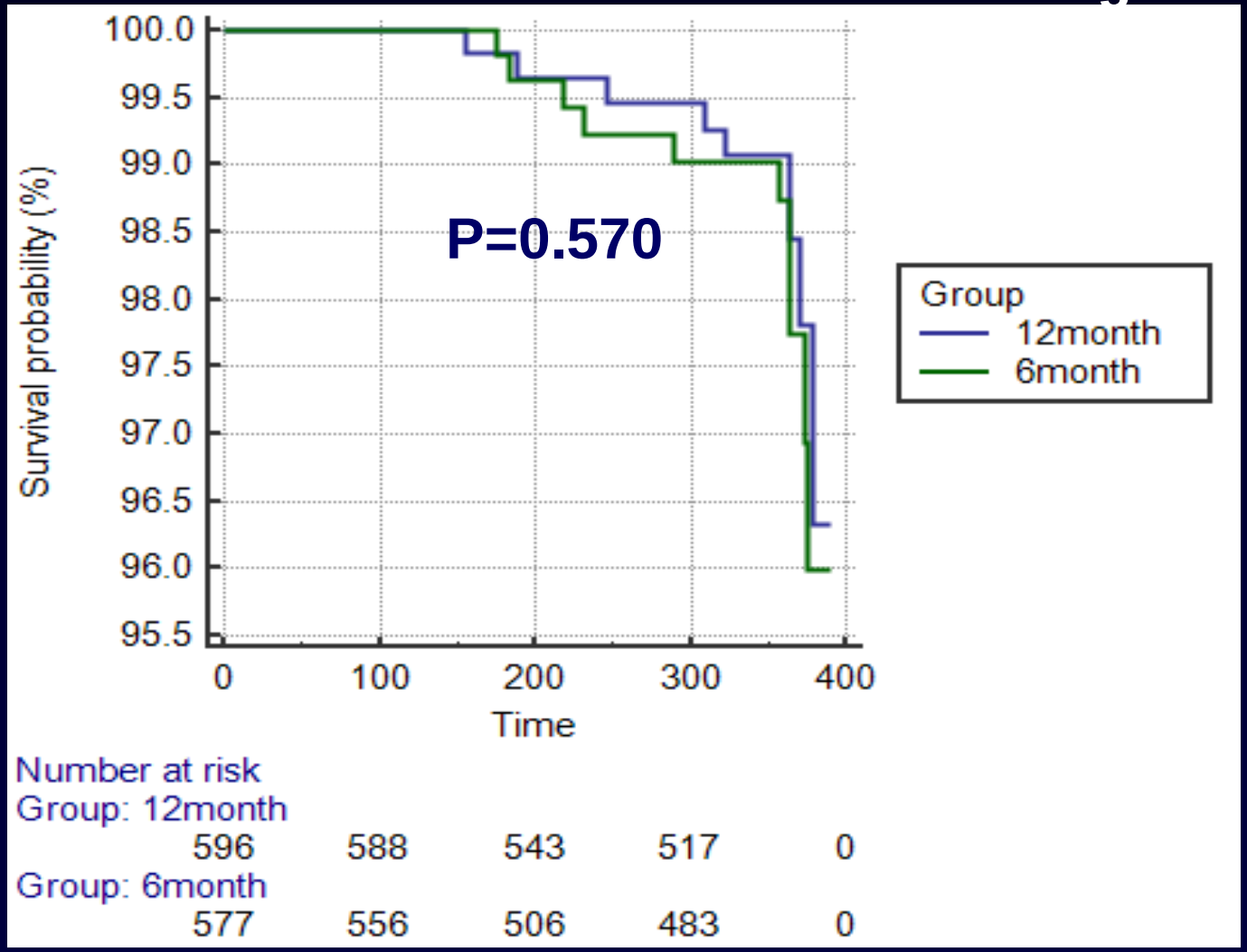
Results

MACE (cardiac death, MI, ST, TVF, Stroke) between 6month vs. 12month DAPT

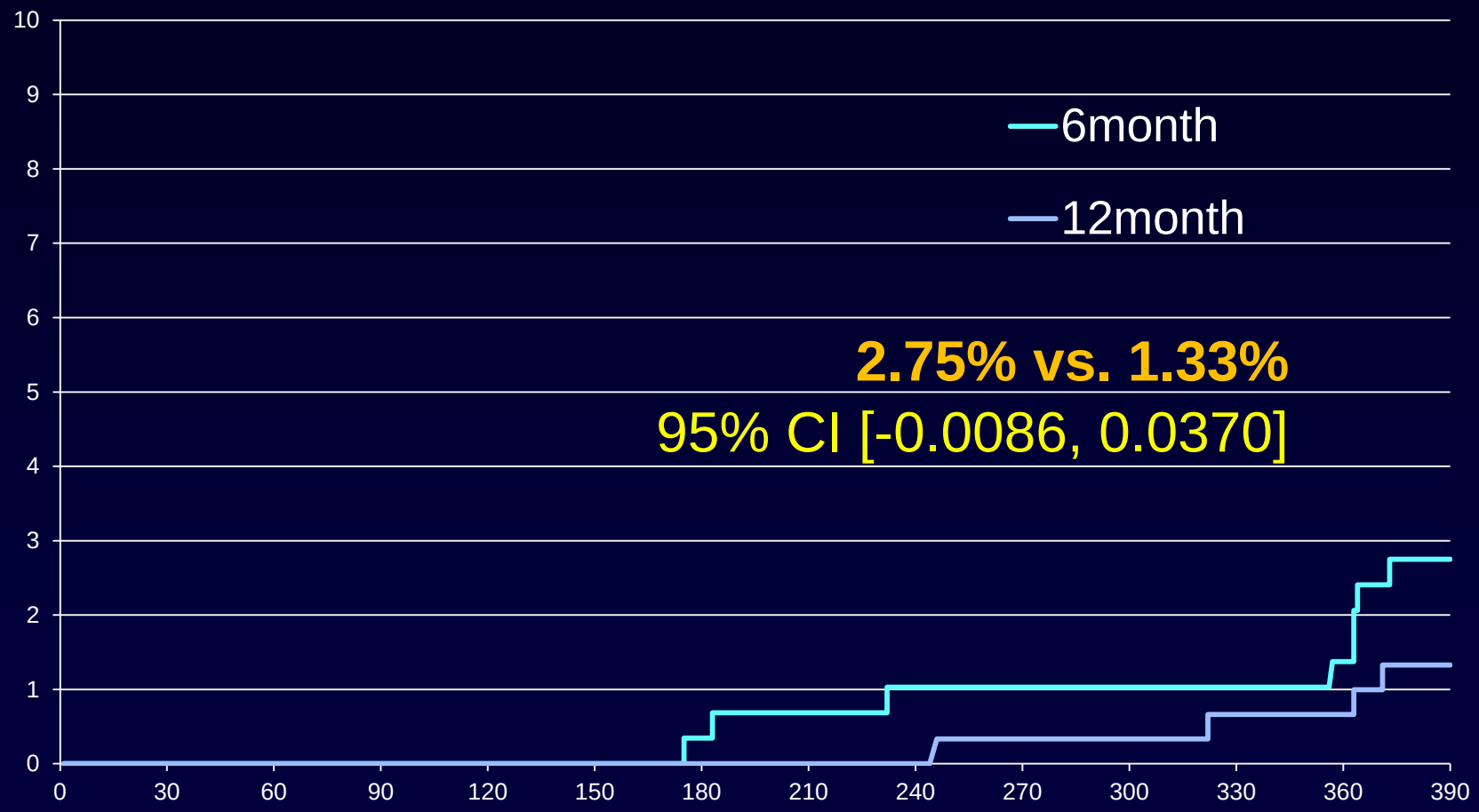


Survival Curve between 6 and 12 month DAPT

Log-rank test



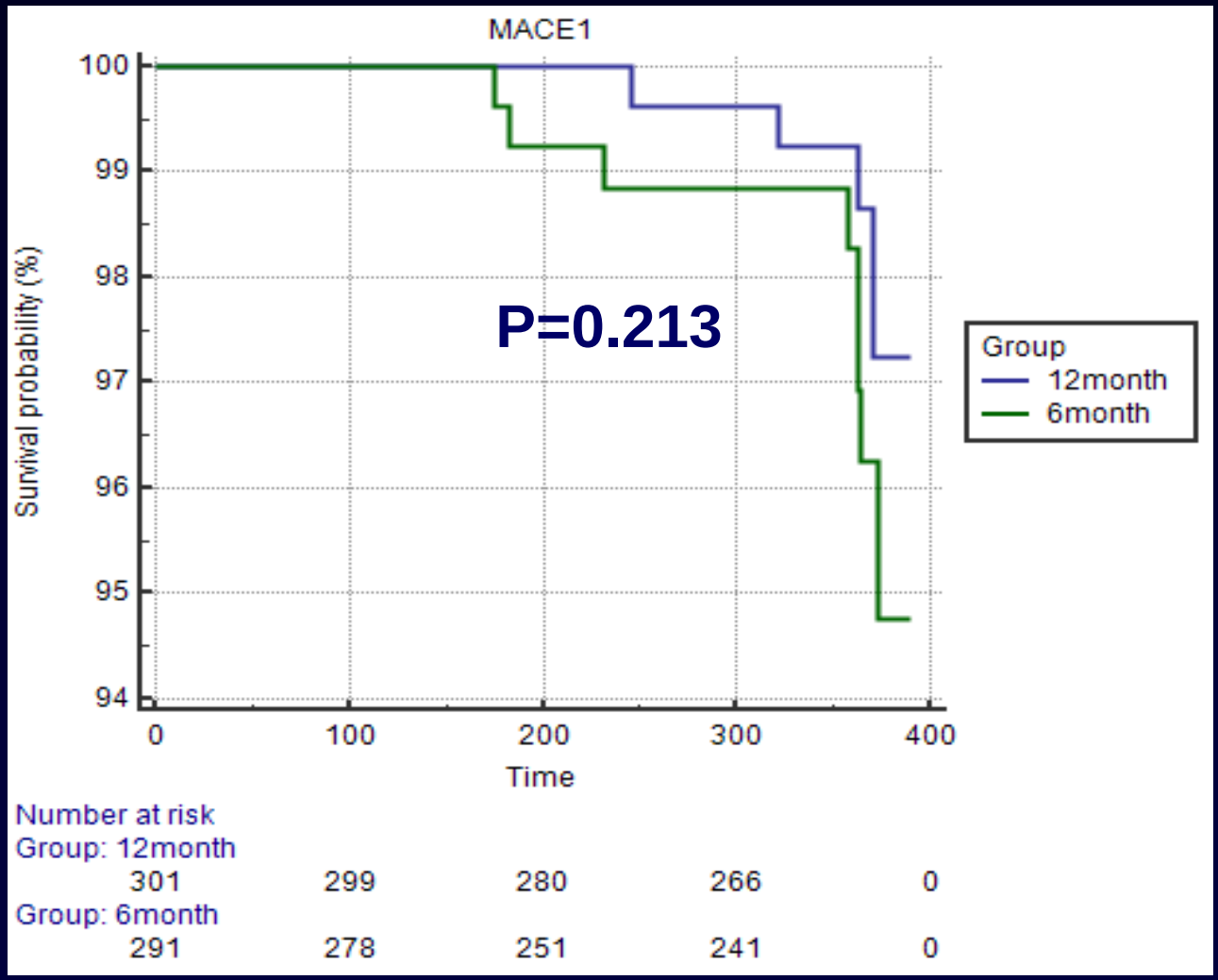
MACE in ZES
between 6month vs. 12month DAPT



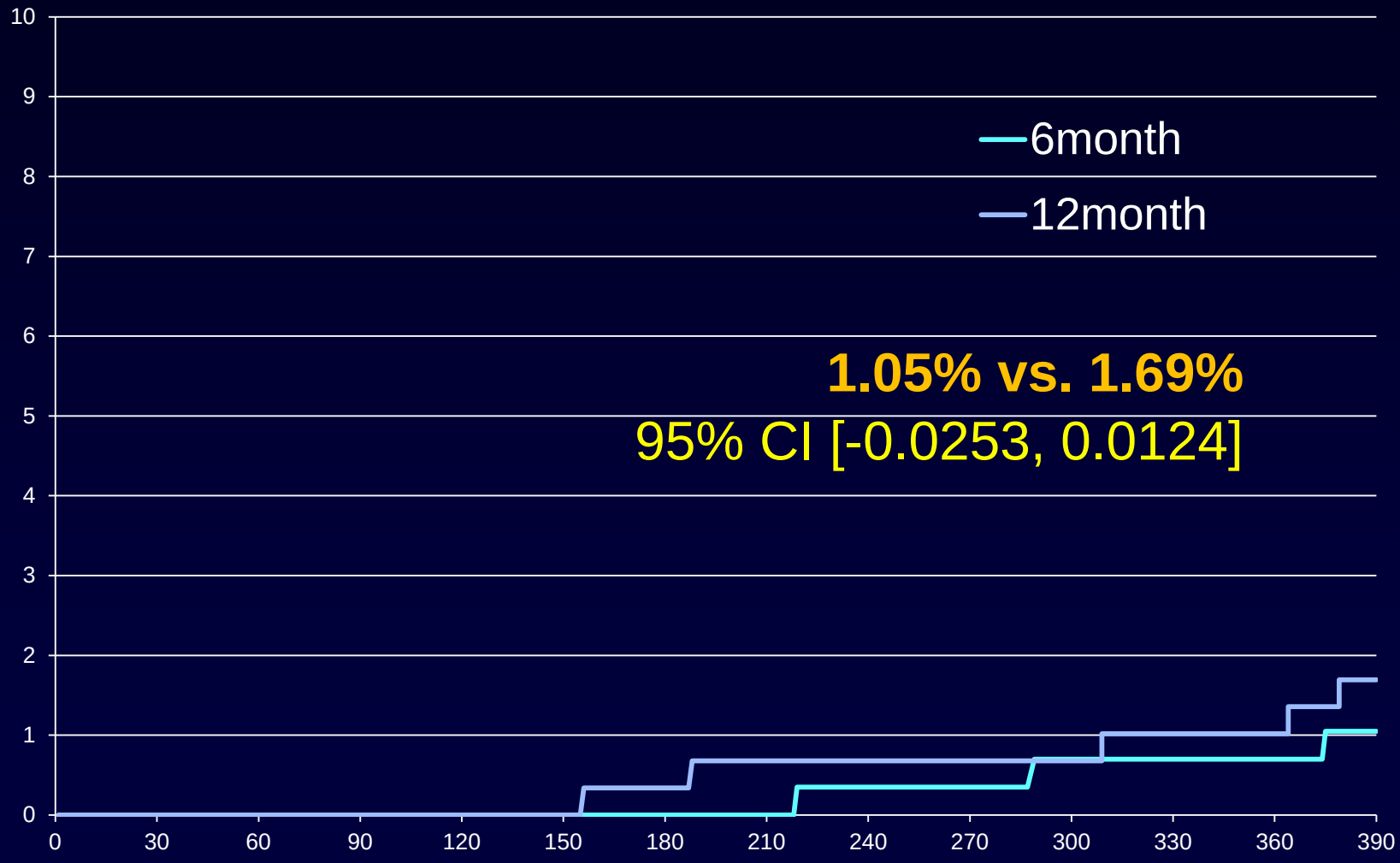
Survival Curve between 6 and 12 month DAPT

Log-rank test

ZES



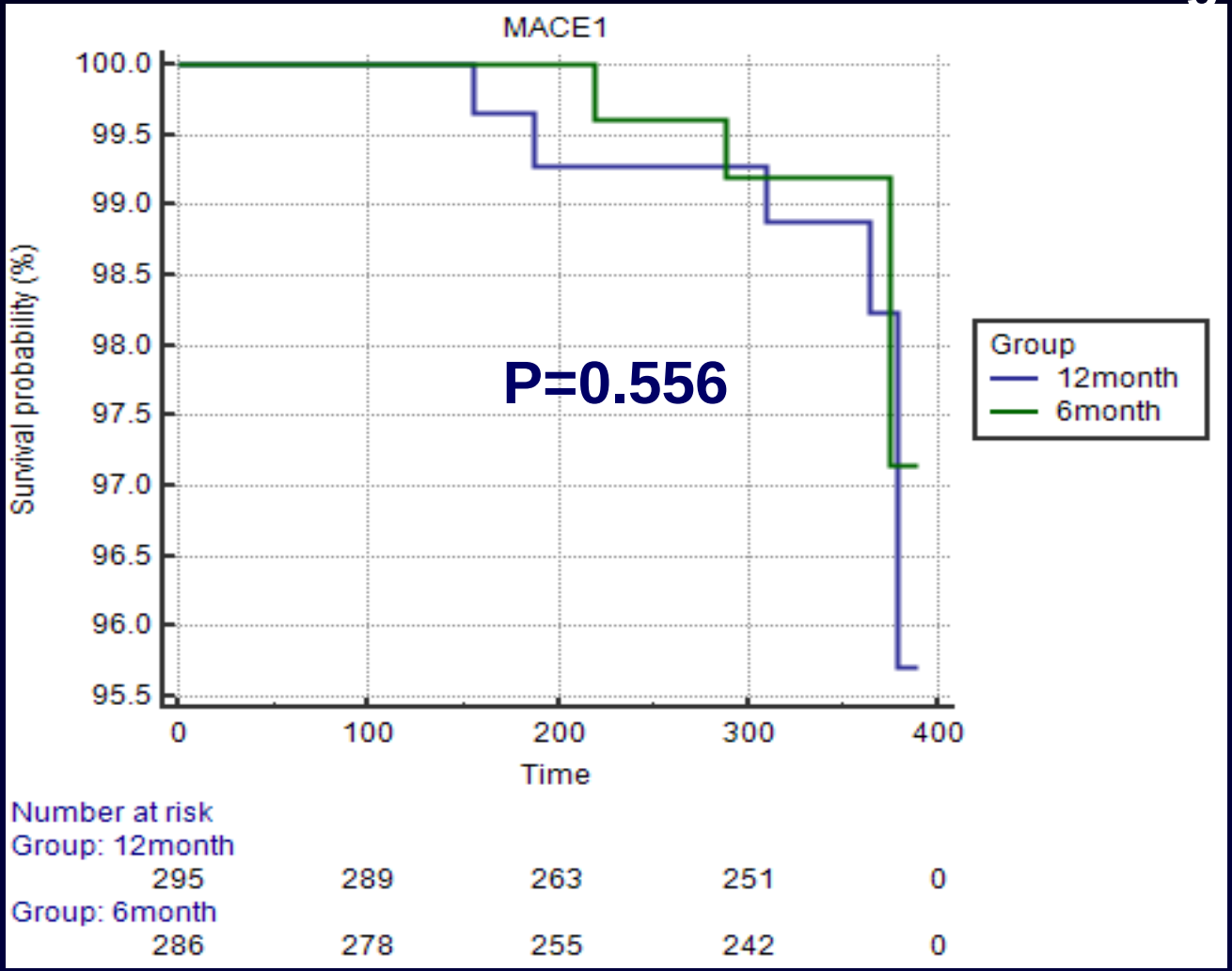
MACE in BES
between 6month vs. 12month DAPT



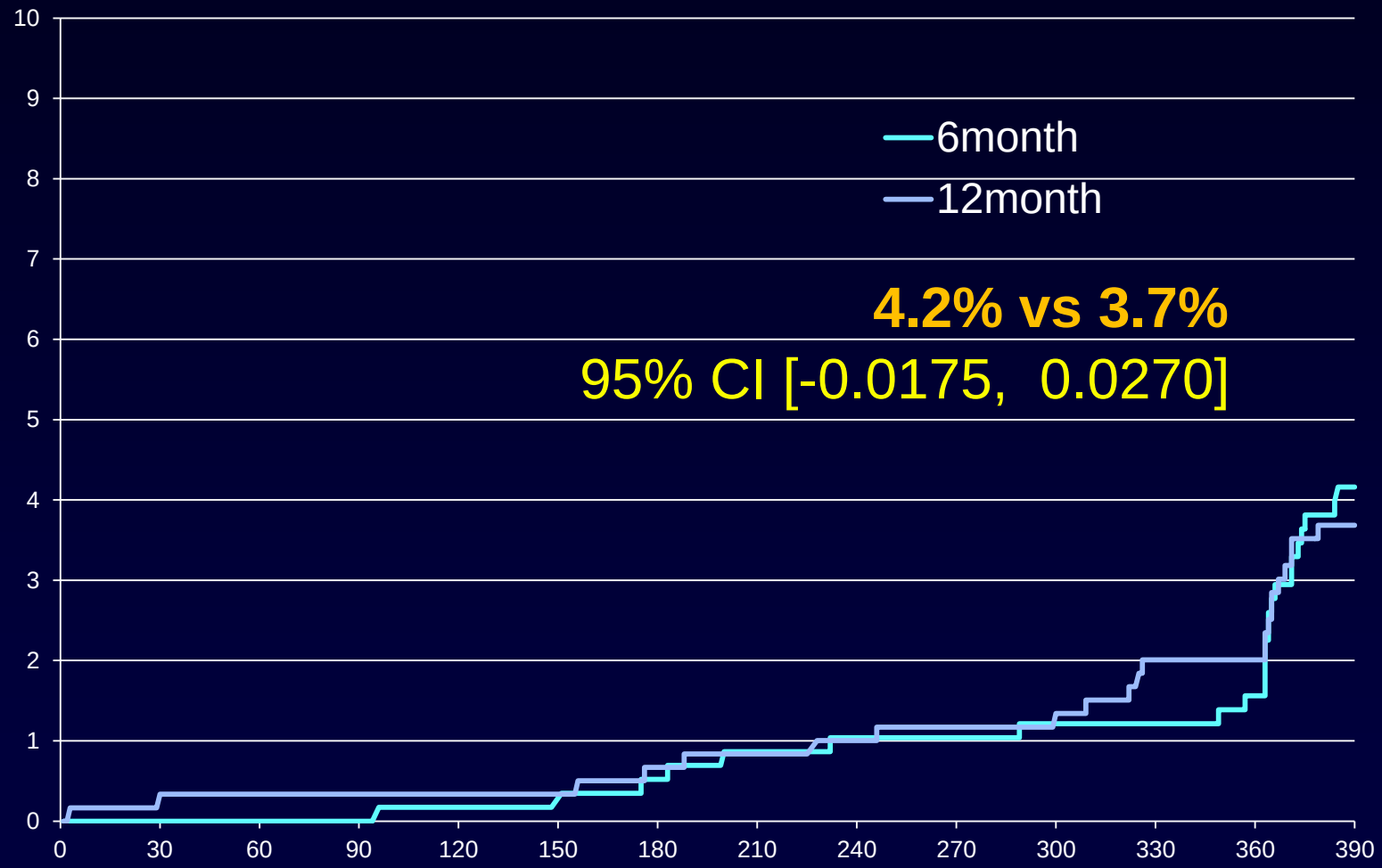
Survival Curve between 6 and 12 month DAPT

Log-rank test

BES

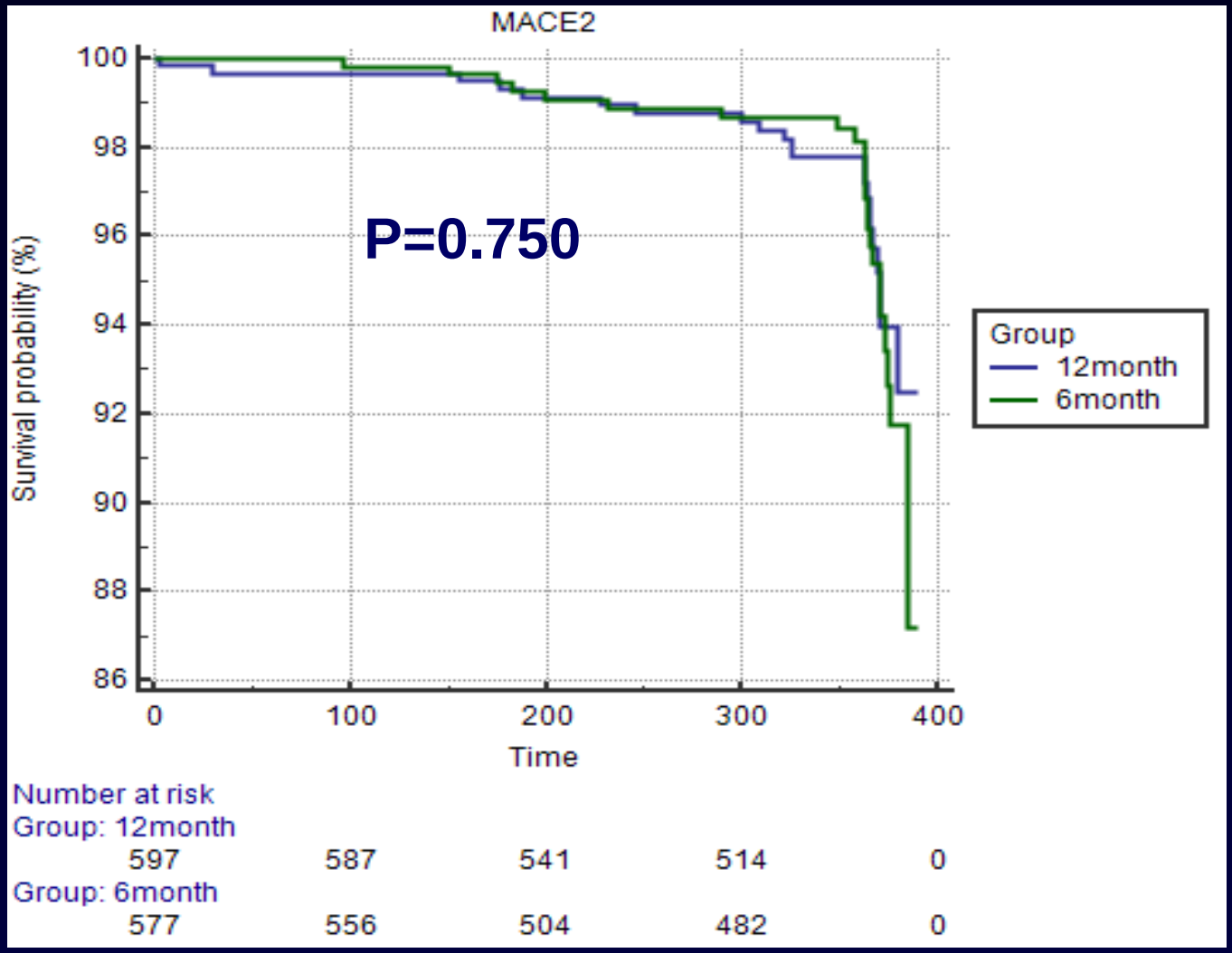


MACE (all death, any PCI, Stroke, major bleeding) between 6mon vs. 12mon DAPT



Survival Curve between 6 and 12 month DAPT

Log-rank test



Secondary end point-QCA data

	ZES 6m DAPT (n=343)	BES 6m DAPT (n=341)	ZES 12m DAPT (n=343)	BES 12m DAPT (n=341)	p
Stent diameter (mm)	3.12±0.42	3.14±0.44	3.16±0.43	3.18±0.49	0.367
Stent length (mm)	21.0±5.06	20.8±5.20	20.2±5.00	20.0±4.73	0.030
MLD (mm)					
Pre	0.90±0.46	0.92±0.47	0.91±0.46	0.95±0.50	0.514
Post	3.02±0.44	3.05±0.45	3.04±0.45	3.05±0.49	0.801
12 month Follow-up	2.73±0.89	2.79±0.84	2.80±0.87	2.84±0.83	0.582
Late loss (mm), 12month	0.30±0.77	0.27±0.81	0.26±0.83	0.28±080	0.949

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)	-

Summary

- On clinical follow up, there were no significant different in MACE including death, myocardial infarction, or target vessel failure, stroke, and non-target PCI in 6-month and 12-month DAPT.
- 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

- 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

- Even though patients with the high ischemic risk such as ACS-NSTEMI, 2nd generation DESs have relative safety zone of MACE, stent thrombosis at least 6 months DAPT.

- To validate for our conclusions, Further study and meta-analysis would be required.