Clinical impact of IVUS-guided CTO intervention on the clinical outcomes after new generation DES implantation; *Randomized CTO-IVUS study*

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On behalf of CTO-IVUS investigator

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Disclosure Statement of Financial Interest

I, (Yangsoo Jang) DO NOT have a financial interest/arrangement or affiliation with one or more organizations that could be perceived as a real or apparent conflict of interest in the context of the subject of this presentation.

Background

- **PCI for chronic total occlusion (CTO)** is still challenging and there are unmet needs even with the availability of DESs.

  ✓ Despite the development of novel techniques and technologies for CTO intervention, the increased clinical and angiographic risk factors accompanying complex procedures have been associated with worse clinical outcomes.

Patel MR, et al. JACC Cardiovasc Interv 2012;5:1054-61.
Van den Branden BJ, et al. EuroIntervention 2012;7:1189-96.

- The **use of intravascular ultrasound (IVUS)** has been recommended as one way to improve PCI clinical outcomes.

Fujii K, et al. Am J Cardiol 2006;97:1455-62.
Kimura T, et al. Circulation 2012;125:584-91.
Kim JS, et al. JACC Cardiovasc Interv 2013;6:369-76.

Role of IVUS for CTO intervention

- **For CTO wire crossing**
  - ✓ Detecting the proximal entry point in stumpless or ostial CTO lesions
  - ✓ Repositioning a guidewire after subintimal passage
  - ✓ Ensuring of the distal guidewire in the true lumen
- **For stenting**
  - ✓ Determination of lesion coverage
  - ✓ Stent optimization (expansion and apposition)
  - ✓ Detecting procedure-related complications (dissection, hematoma, rupture)
- **However, few data exists** regarding the **relationship between PCI by IVUS guidance after successful wire crossing and clinical outcomes** after stent implantation.

CTO IVUS (Chronic Total Occlusion InterVention with drUg-eluting Stents guided by IVUS) study

Objective

To test the hypothesis …

"IVUS-guided CTO intervention is superior to conventional angiography-guided CTO intervention"

we sought to conduct multi-center prospective randomized trial using new generation DES.

Methods

- Prospective, randomized trial conducted at 20 centers in Korea

1. Severance Cardiovascular Hospital, Yonsei University College of Medicine, Seoul, Korea
2. Kyungpook National University Hospital, Daegu, Korea
3. Korea University Guro Hospital, Seoul, Korea
4. Sejong General Hospital, Bucheon, Korea
5. SoonChunHyang University Hospital, Cheonan, Korea
6. The Catholic University of Korea Bucheon St. Mary's Hospital, Bucheon, Korea
7. Gangnam Severance Hospital, Yonsei University College of Medicine, Seoul, Korea
8. Gil Hospital, Gachon University College of Medicine, Incheon, Korea
9. Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, Korea
10. Kyung Hee University Hospital, Seoul, Korea
11. Kangwon National University Hospital, Chuncheon, Korea
12. Kangnam Sacred Heart Hospital, Seoul, Korea
13. Chonnam National University Hospital, Gwangju, Korea
14. Wonju Severance Christian Hospital, Yonsei University Wonju College of Medicine, Wonju, Korea
15. Myong Ji Hospital, Koyang-si, Korea
16. Kwangju Christian Hospital, Kwangju, Korea
17. St. Carollo Hospital, Sooncheon, Korea
18. Yeungnam University Hospital, Daegu, Korea
19. The Catholic university of Korea Daejeon St. Mary`s Hospital, Daejeon, Korea
20. The Catholic university of Korea Uijengbu St. Mary`s Hospital, Uijengbu, Korea

Principal investigator; Yangsoo Jang, MD, Ph D,

- **Major inclusion criteria;**
  - 20–80 years old with CTO and typical symptomatic angina or positive stress test
  - Reference vessel diameter of 2.5–4.0 mm by operator assessment
  - Total CTO lesion length ≤80 mm and number of stents implanted ≤4

CTO, defined as TIMI flow grade 0 with estimated occlusion duration ≥3 months

- **Major Exclusion criteria;**
  - Unprotected left main disease
  - Lesions with in-stent restenosis or graft vessel occlusion
  - History of PCI for the same CTO lesion within 2 weeks
  - Initial clinical presentation as acute MI
  - Cardiogenic shock or left ventricle ejection fraction <30%
  - Serum creatinine level ≥2.0 mg/dL or end-stage renal disease

Endpoints

- **Primary endpoint**
  - ✓ **Composite of cardiac death, MI, and target-vessel revascularization at 12 months**

- **Secondary endpoints**
  - ✓ Composite of cardiac death and MI
  - ✓ Individual components of the primary endpoint

Statistical analyses; Power calculation for sample size

Background; Randomized TULIP study (BMS for the diffuse long lesions)

- ✓ IVUS Guidance (n=73) vs. Angio Guidance (n=71)
- ✓ Composite rate of cardiac death, MI, and TLR at 12 months
  = 12% vs. 27% (p=0.026)

Oemrawsingh PV, et al. *Circulation* 2003;107:62-7

Two assumptions

1) Event rate of CTO would be similar to that of diffuse long lesions
2) The current DESs could reduce the TVR rate more than 50%.

Hypothesis … "IVUS-guided CTO intervention is superior to conventional angiography guidance"

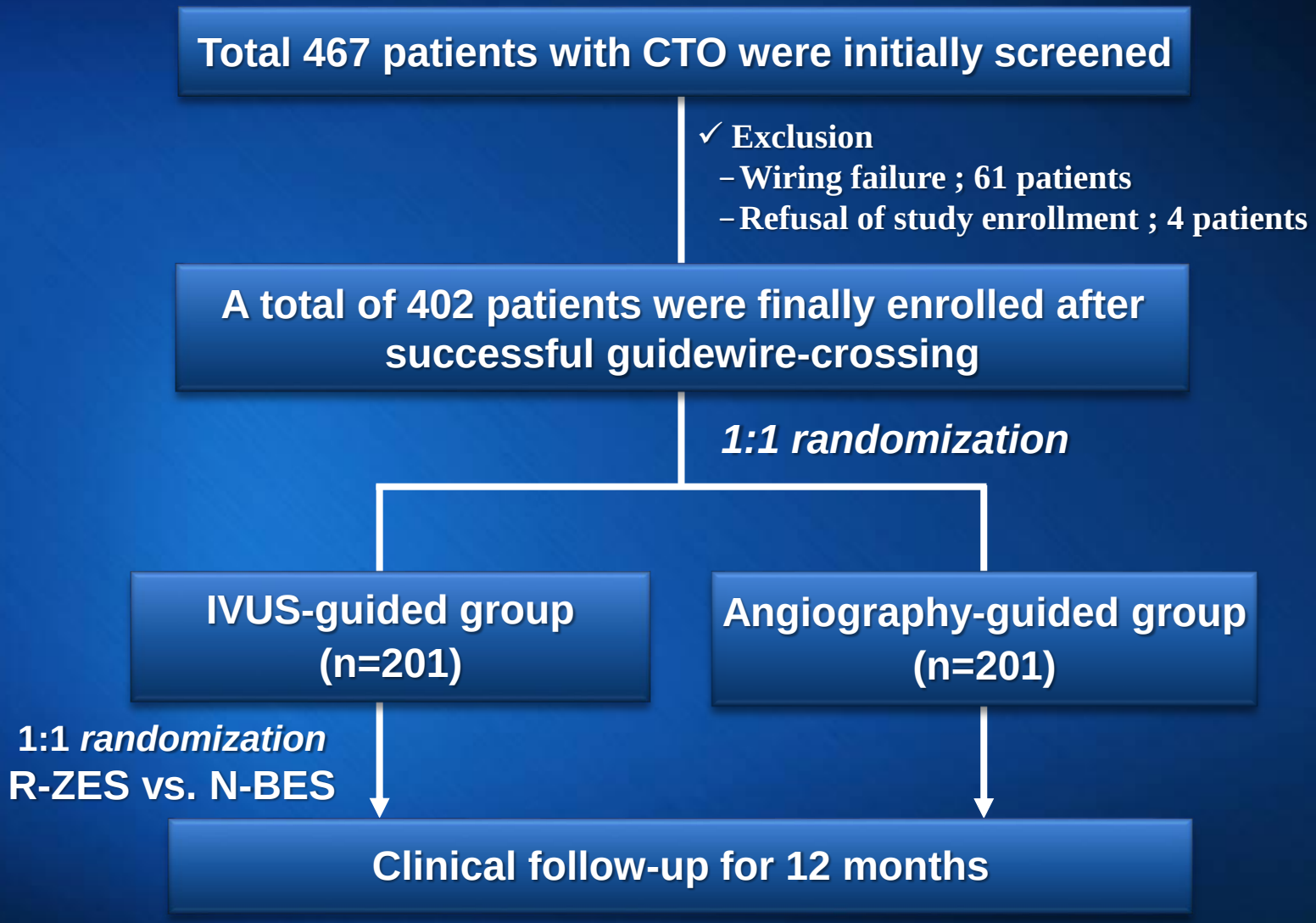
; Difference of the primary endpoint ≅ 9%.

→ A total of 400 patients would be sufficient.

(10% dropout rate, 90% power to detect a difference and an alpha error rate of 0.05)

- ✓ Compared by Kaplan–Meier method and log-rank test (hazard ratio, 95% CI)

Study at a glance and flow chart



Primary endpoint; Composite of Cardiac death, MI, & TVR at 12 months

Baseline characteristics

	IVUS-guided group (n=201)	Angiography-guided group (n=201)	p Value
Age, years	61.0 ± 11.1	61.4 ± 10.1	0.739
Male gender	162 (80.6%)	162 (80.6%)	1.000
Hypertension	126 (62.7%)	128 (63.7%)	0.836
Diabetes mellitus	70 (34.8%)	68 (33.8%)	0.834
History of heart failure	12 (6.0%)	10 (5.0%)	0.661
Ejection fraction, %	56.9 ± 13.1	56.7 ± 11.4	0.808
Prior MI	16 (8.0%)	16 (8.0%)	1.000
Prior PCI	31 (15.4%)	32 (15.9%)	0.891
Stable angina presentation	147 (73.1%)	147 (73.1%)	1.000
CTO lesion characteristics			
LAD	84 (41.8%)	94 (46.8%)	0.478
Stumpless CTO	23 (11.4%)	22 (10.9%)	0.874
Bridging collaterals	24 (11.9%)	29 (14.4%)	0.461

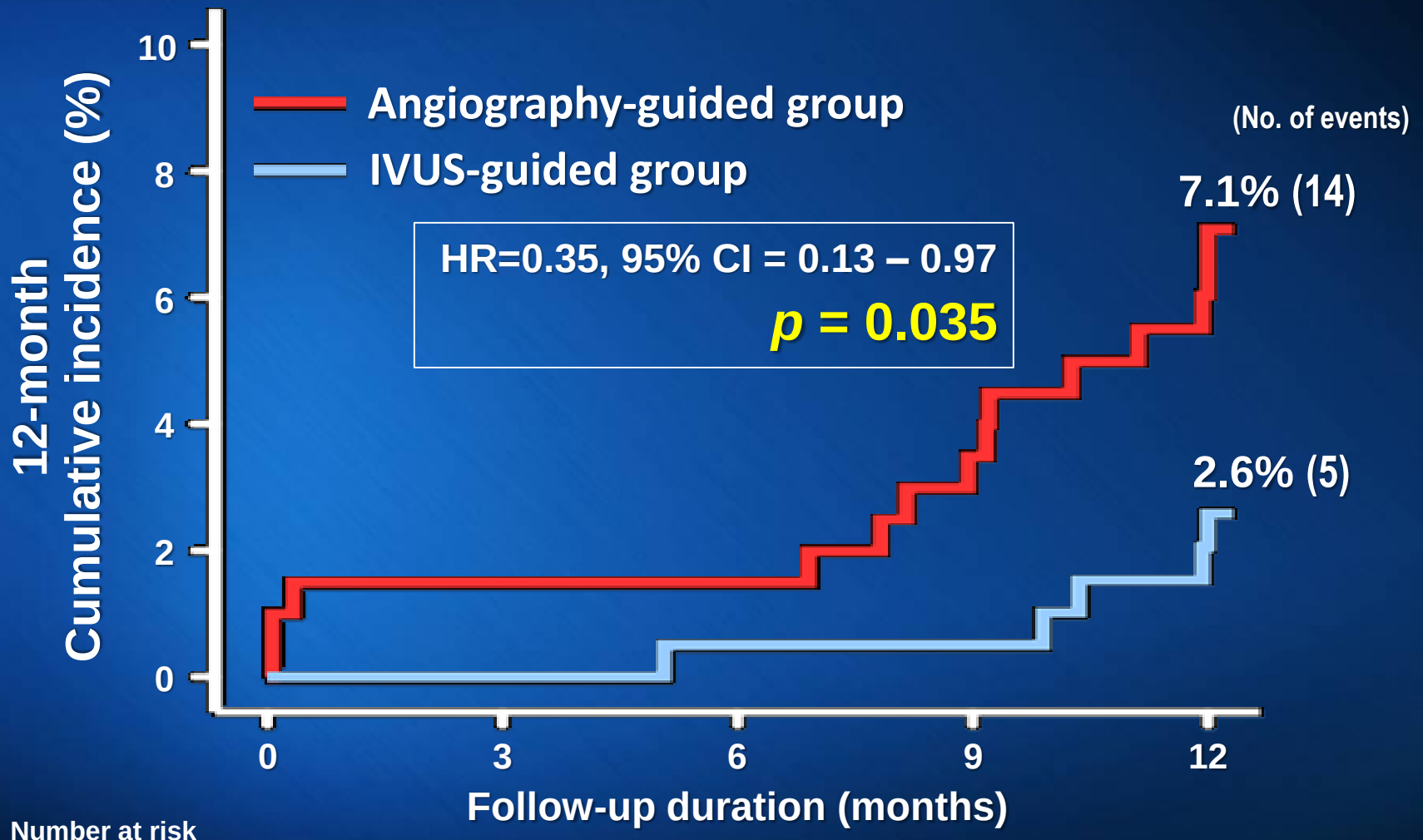
Procedural summary for CTO intervention

	IVUS-guided (n=201)	Angiography-guided (n=201)	p Value
Procedure success	199 (99.0%)	197 (98.0%)	0.411
Femoral artery access	149 (74.1%)	145 (72.1%)	0.653
Contralateral angiogram	101 (50.2%)	92 (45.8%)	0.369
Retrograde approach	14 (7.0%)	19 (9.5%)	0.364
Total number of stents, n	1.7 ± 0.8	1.6 ± 0.7	0.198
Mean stent diameter, mm	2.91 ± 0.52	2.85 ± 0.41	0.228
Total stented length, mm	43.6 ± 18.7	41.5 ± 17.6	0.245
High-pressure post-stent dilation	103 (51.2%)	83 (41.3%)	0.045
Maximum post-stent balloon pressure, atm	14.6 ± 3.7	13.8 ± 3.8	0.040
Total procedure time, min	95 ± 50	88 ± 47	0.167
Total fluoroscopic time, min	41 ± 26	37 ± 24	0.155
Total contrast volume used, mL	299 ± 128	295 ± 123	0.728
Balloon angioplasty without stent	2 (1.0%)	1 (0.5%)	0.562

Quantitative & qualitative angiographic analyses

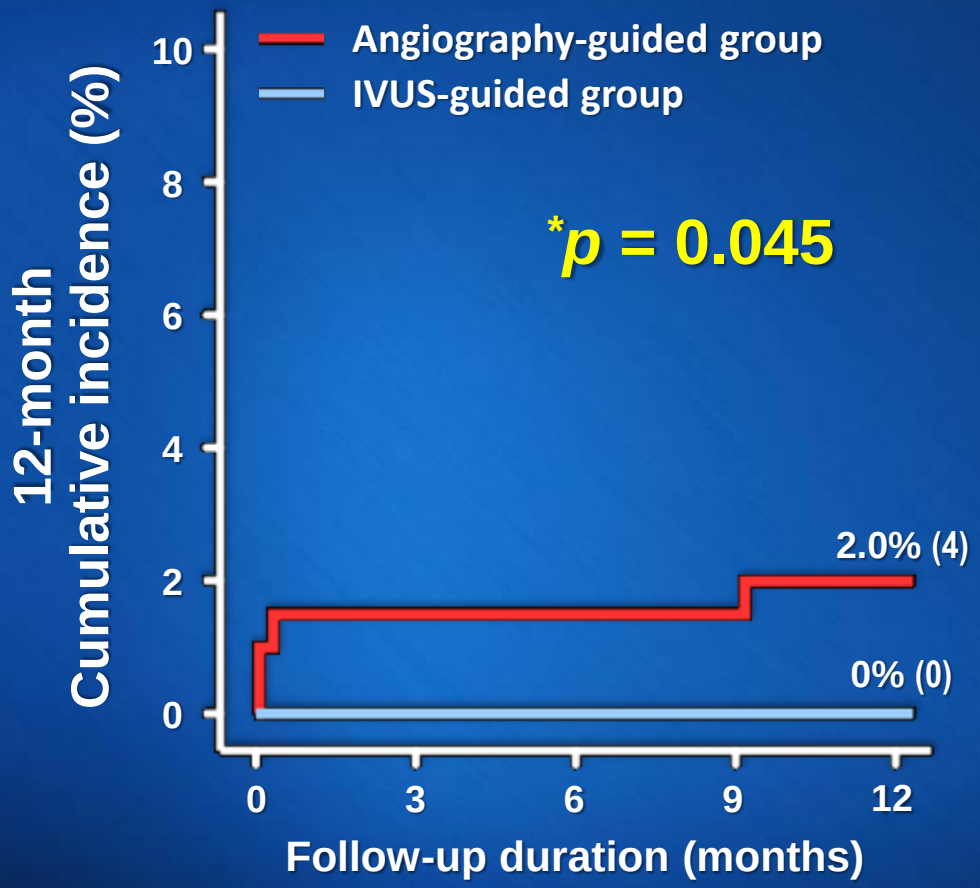
	IVUS-guided (n=201)	Angiography-guided (n=201)	p Value
Length of CTO, mm	26.8 ± 17.3	26.4 ± 17.6	0.860
Total lesion length, mm	36.3 ± 17.1	35.5 ± 17.0	0.615
Pre-procedural Reference vessel diameter, mm	2.69 ± 0.44	2.64 ± 0.55	0.346
Post-procedure			
Reference vessel diameter, mm	2.92 ± 0.39	2.86 ± 0.45	0.144
Minimum luminal diameter, mm	2.64 ± 0.35	2.56 ± 0.41	0.025
Percent diameter stenosis, %	9.0 ± 9.8	10.2 ± 10.9	0.272
Stent edge dissection	18 (9.0%)	27 (13.4%)	0.155

Primary endpoint (Cardiac death, MI, TVR)

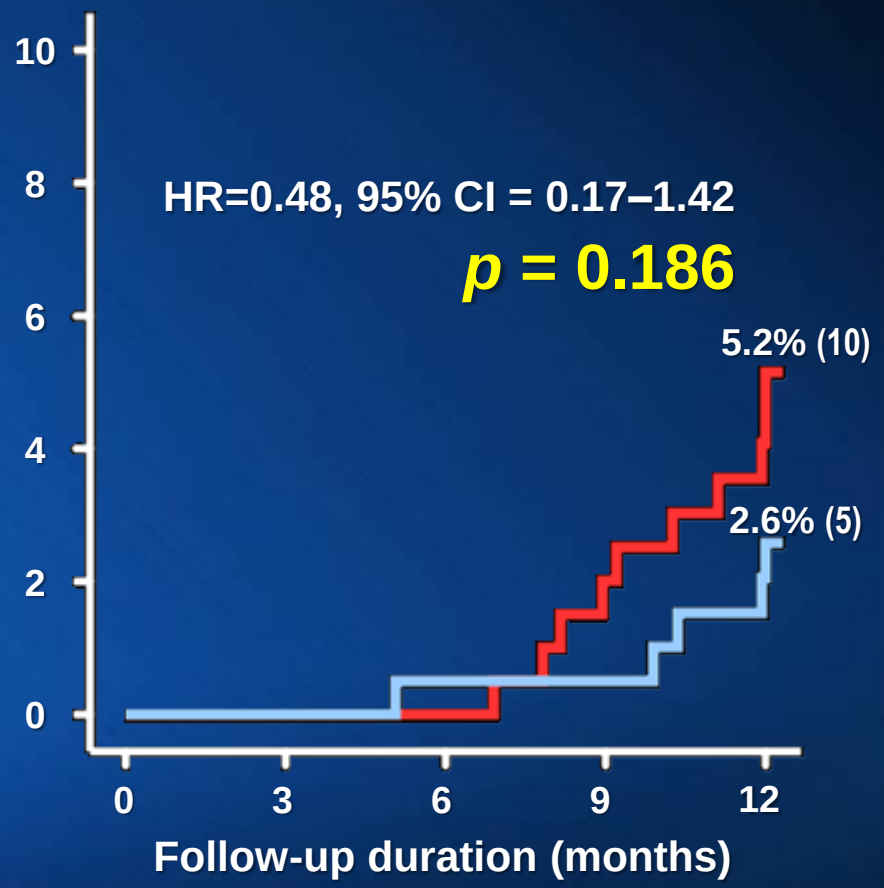


Number at risk			
Angiography-guided	201	198	179
IVUS-guided	201	198	186

Cardiac death or MI



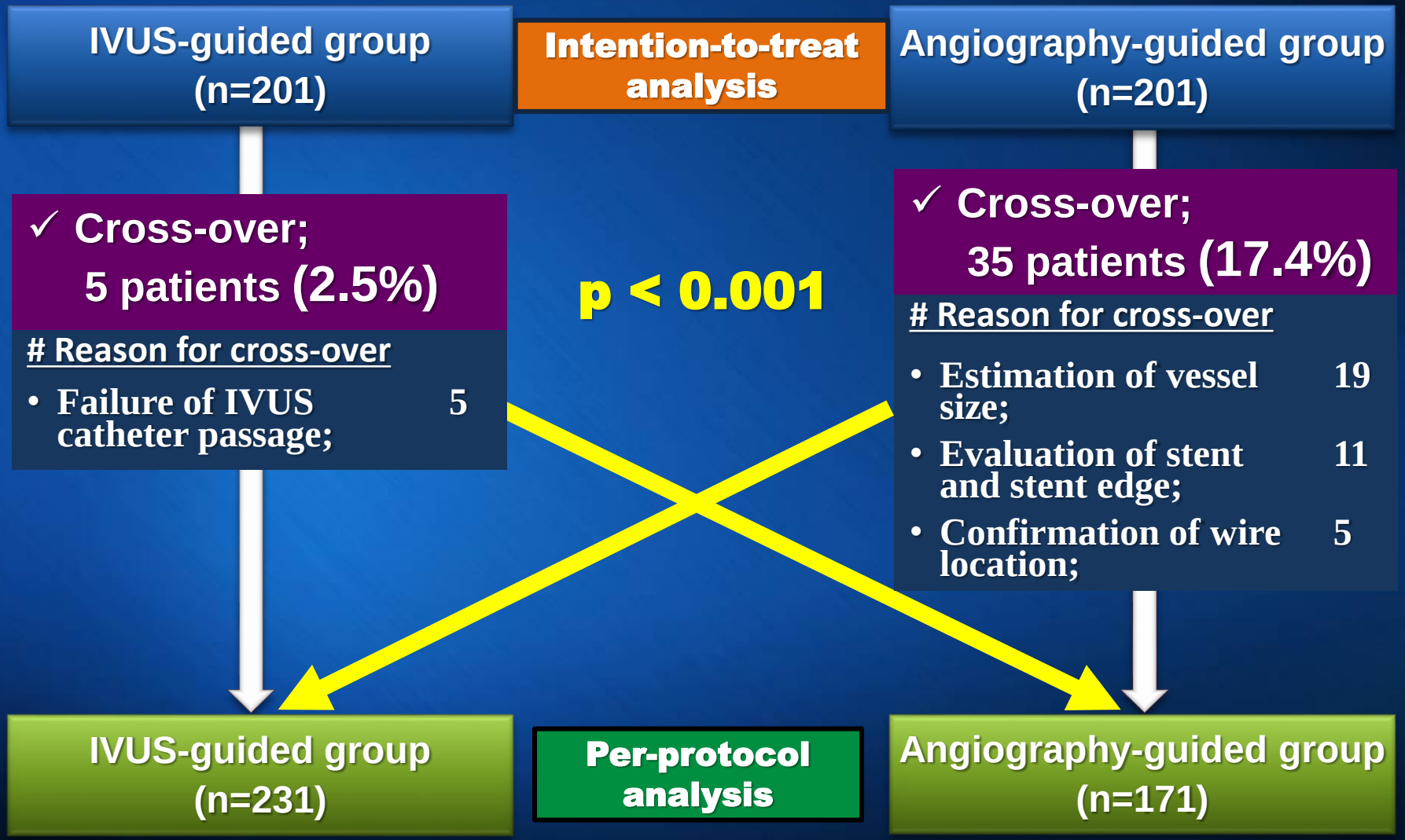
TVR



Number at risk						
Angiography-guided	201	198	187	201	199	180
IVUS-guided	201	199	190	201	198	186

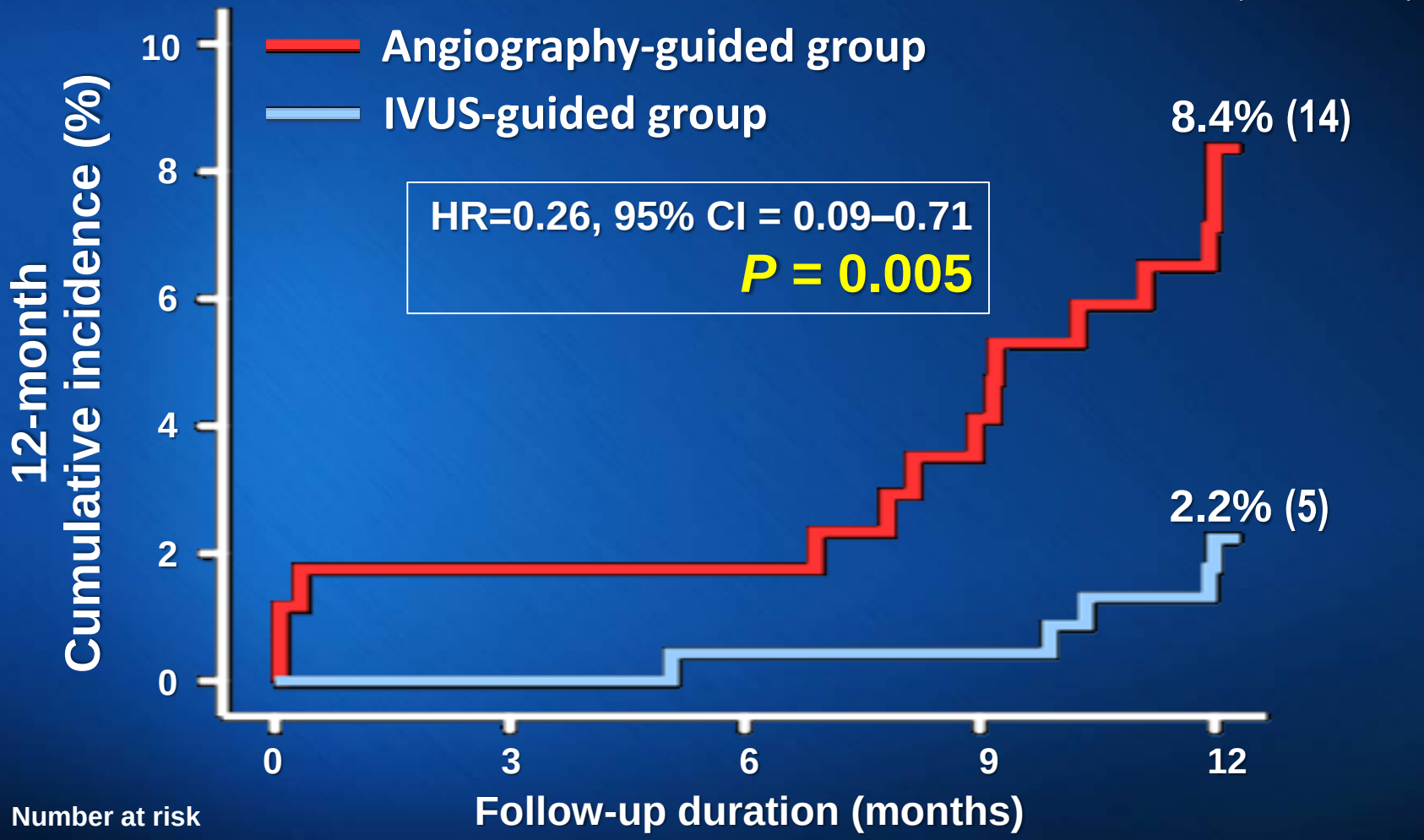
*Not calculable HR or CI because of no occurrence of the event

Cross-over


IVUS-guided group (n=201)
Intention-to-treat analysis
Angiography-guided group (n=201)
✓ Cross-over; 5 patients (2.5%)
Reason for cross-over
• Failure of IVUS catheter passage; 5
p < 0.001
✓ Cross-over; 35 patients (17.4%)
Reason for cross-over
• Estimation of vessel size; 19
• Evaluation of stent and stent edge; 11
• Confirmation of wire location; 5
IVUS-guided group (n=231)
Per-protocol analysis
Angiography-guided group (n=171)

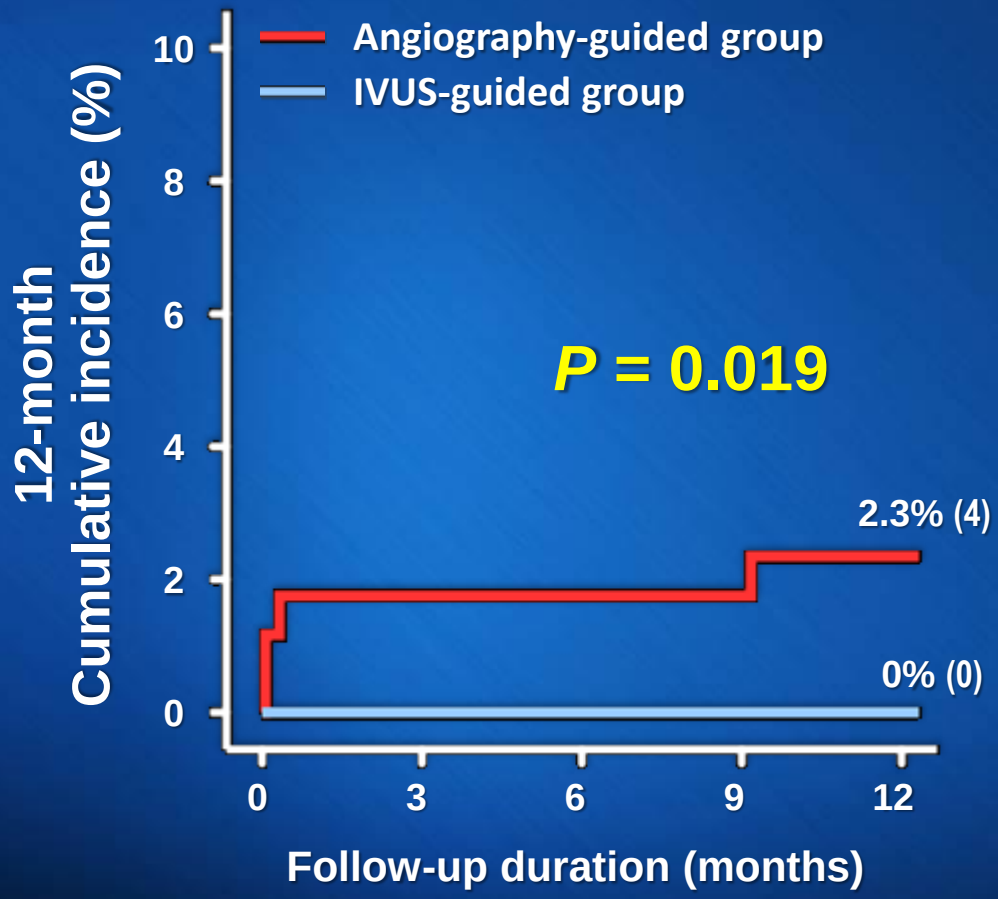
Primary endpoint (Cardiac death, MI, TVR)

Per-protocol Analysis

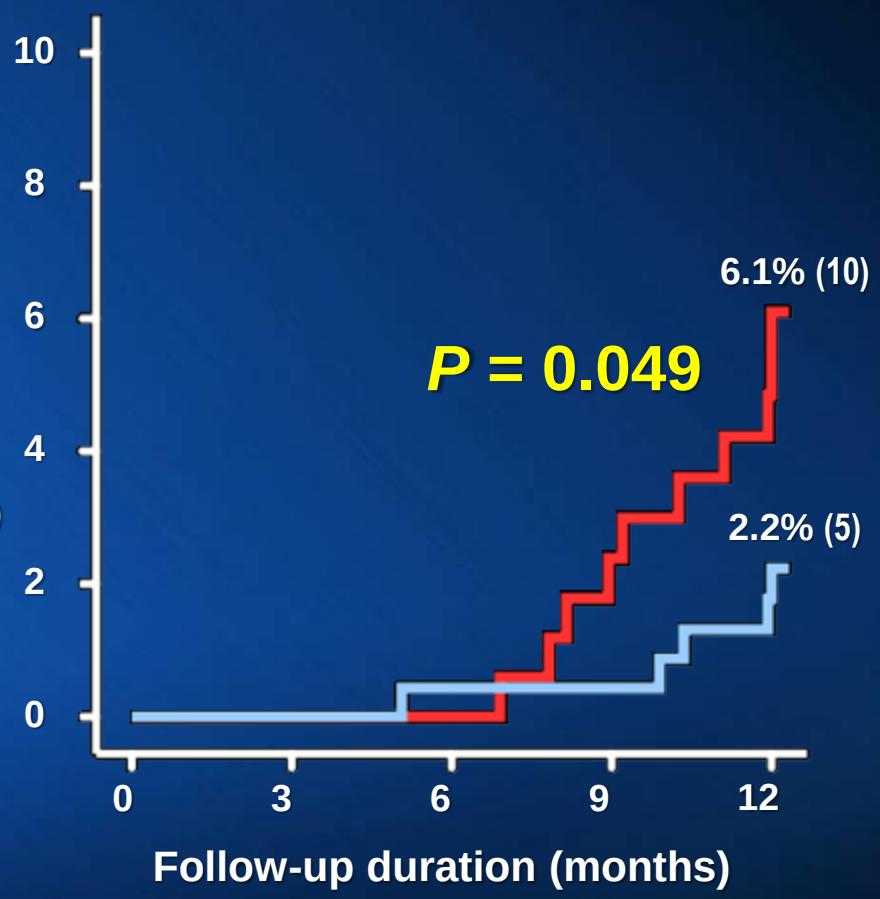


Per-protocol Analysis

Cardiac death or MI



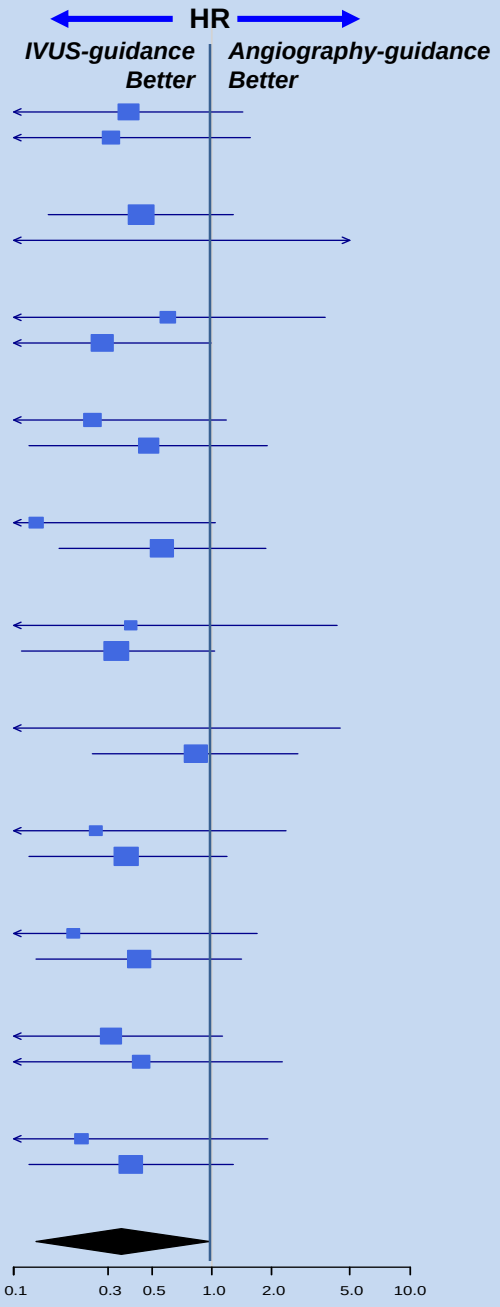
TVR



Number at risk						
Angiography-guide	171	167	159	171	168	152
IVUS-guide	231	230	218	231	229	214

Subgroup analysis of the primary endpoint (Cardiac death, MI, TVR)

Subgroup	HR	95% CI	p-value	p-for-interaction
Age				**0.857**
< 65 (n=233)	0.38	0.10~1.43	0.154	
≥ 65 (n=169)	0.31	0.06~1.56	0.156	
Gender				**0.956**
Male (n=324)	0.44	0.15~1.28	0.131	
Female (n=78)	0.02	0.00~164.9	0.378	
Diabetes mellitus				**0.465**
Yes (n=138)	0.60	0.10~3.72	0.601	
No (n=264)	0.28	0.08~0.99	0.045	
Hypertension				**0.547**
Yes (n=254)	0.25	0.05~1.18	0.080	
No (n=148)	0.48	0.12~1.9	0.293	
Three-vessel disease				**0.225**
Yes (n=140)	0.13	0.02~1.04	0.054	
No (n=262)	0.56	0.17~1.87	0.350	
Heart failure				**0.978**
Yes (n=22)	0.39	0.04~4.27	0.438	
No (n=380)	0.33	0.11~1.03	0.057	
Type of drug-eluting stents				**0.834**
R-ZES (n=201)	0.02	0.00~4.43	0.148	
N-BES (n=201)	0.83	0.25~2.71	0.754	
Total number of stents implanted				**0.778**
≤1 (n=175)	0.26	0.03~2.36	0.233	
≥2 (n=227)	0.37	0.12~1.19	0.097	
CTO length				**0.533**
≤28 (n=160)	0.20	0.02~1.69	0.139	
>28 (n=242)	0.43	0.13~1.41	0.163	
Reference vessel diameter				**0.745**
<3.0 mm (n=244)	0.31	0.08~1.13	0.077	
≥3.0 mm (n=158)	0.44	0.09~2.26	0.324	
LAD intervention				**0.653**
LAD (n=178)	0.22	0.03~1.91	0.172	
Non-LAD (n=224)	0.39	0.12~1.28	0.120	
Overall	**0.35**	**0.13~0.97**	**0.035**	



Summary of CTO-IVUS study

- This CTO-IVUS study is the first randomized trial investigating the clinical benefits of IVUS guidance for CTO intervention after successful guidewire crossing in the era of new generation DES.

- This study demonstrated that …
  - ✓ As compared to conventional angiography-guided CTO intervention, IVUS-guided CTO intervention
    - caused a more frequent use of high-pressure post-dilation and a larger post-procedural MLD
    - finally, significantly improved clinical outcomes after DES implantation

Limitation

- Some assumptions for power calculation were arbitrary.
- For the comparison of acute procedure results, only QCA analysis was available.
- Follow-up duration of this study was only 12 months.

Conclusion

- Compared to conventional angiography-guided CTO intervention, **IVUS-guided CTO intervention** significantly **improved clinical outcomes during the 12 months** following new generation DES implantation.


Thank you for your attention