Optimal Duration or Combination of Antiplatelet Therapy after PCI

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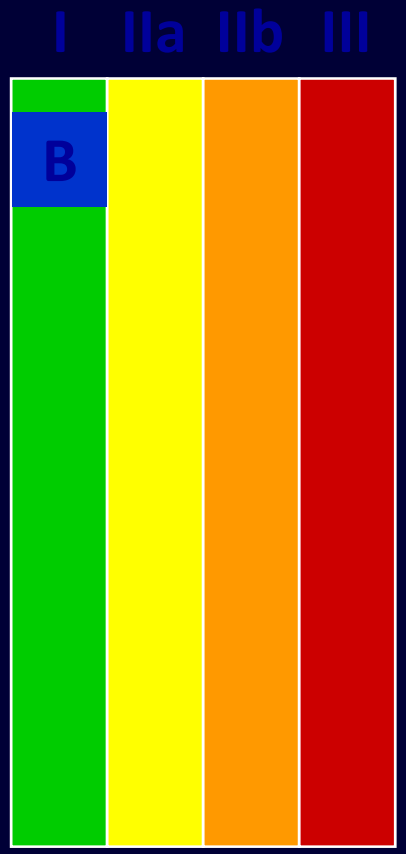
Optimal Duration of Dual Antiplatelet Therapy after PCI

ACC/AHA/SCAI 2007 Focused Update for PCI

Oral Antiplatelet Adjunctive Therapies

(Modified from 2005 PCI Guideline Recommendation)



For all post-PCI stented patients receiving a DES, clopidogrel 75 mg daily should be given for at least 12 months if patients are not at high risk of bleeding.

For post-PCI patients receiving a bare-metal stent, clopidogrel should be given for a minimum of 1 month and ideally up to 12 months (unless the patient is at increased risk of bleeding; then it should be given for a minimum of 2 weeks).

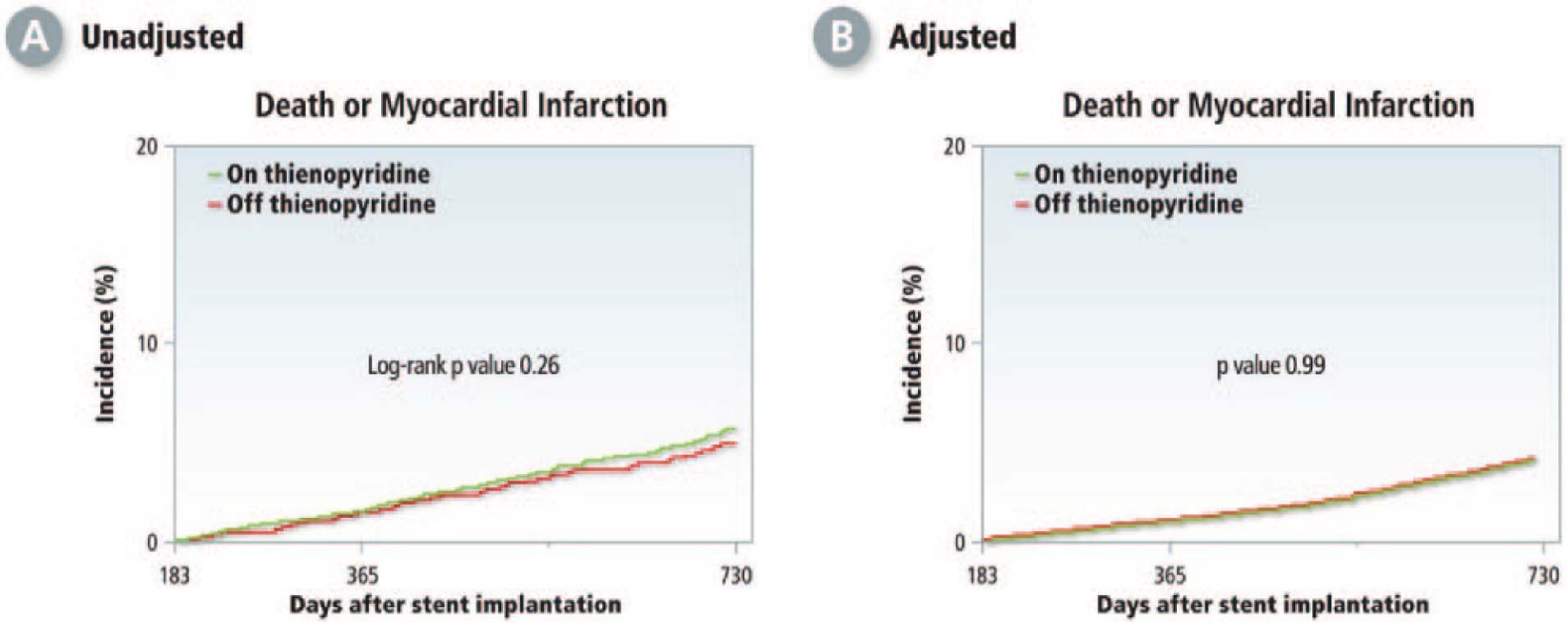
Hot Issues Regarding Clopidogrel

1. Data for and against long term use of dual antiplatelet therapy
    a. Cons
    b. Pros
2. Plavix vs. Aspirin after one year post-PCI
3. Which trials in the future will give us answers?

Discontinuation of Thienopyridine and Risk of Stent Thrombosis With Sirolimus-Eluting Stents

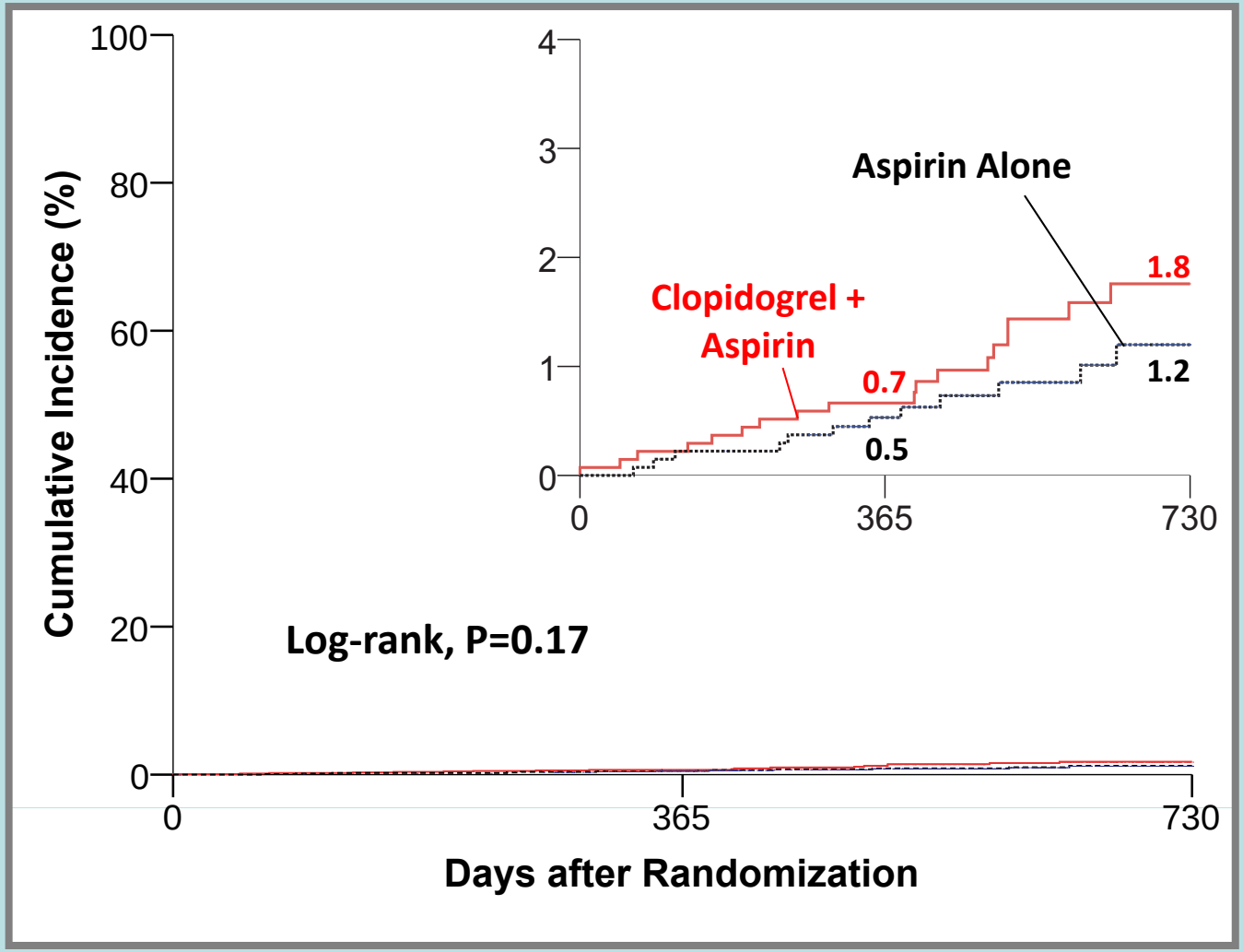
Kimura T et al. *Circulation* 2009;119:7987-995

Landmark Analysis on Thienopyridine Use Beyond 6 Months



Cardiac Death or Myocardial Infarction: DAT < 1y vs > 1y

(Real Late & ZEST Late. NEJM 2010)



No. at Risk			
Continuation group	1357	1122	299
Discontinuation group	1344	1100	301

Hot Issues Regarding Clopidogrel

1. **Data for and against long term use of dual antiplatelet therapy**
   - a. Cons
   - b. Pros
2. Plavix vs. Aspirin after one year post-PCI
3. Which trials in the future will give us answers?

Long-term DAT is helpful !

1. ‘CAPRIE-like subgroup’ in CHARISMA
   DAT for 30months ; better than ASA monotherapy

2. Duke Registry
   DAT > 6month or 12months ; better than DAT<6months

3. Denver, Seattle, Durham, & Richmond Network data
   DAT > 6m; better than DAT<6m

4. Europe data
   DAT> 1y ; better than DAT< 1y

5. Dutch ST registry
   Longer DAT is better than shorter DAT for ST

How long DAT?
not in conclusion

1. All studies are underpowered.
2. All studies are confounded and biased and have statistical limitations
3. Only one RCT data

   : interim data analysis from a unplanned pooled analysis of two unfinished studies.

   : inconclusive & causing confusion

Hot Issues Regarding Clopidogrel

1. Data for and against long term use of dual antiplatelet therapy
   a. Cons
   b. Pros
2. Plavix vs. Aspirin after one year post-PCI
3. **Which trials in the future will give us answers?**

Trials to answer the optimal duration of DAT

1. EXCELLENT RCT (Korea)
2. ISAR-SAFE (Germany)
3. OPTIMIZE (Brazil)
4. DAPT Trial (USA)

Efficacy of Xience/Promus versus Cypher to rEduce Late Loss in stENT

Hyo-Soo Kim MD, PhD

on behalf of the investigators

Seoul National University Hospital, Seoul, Korea

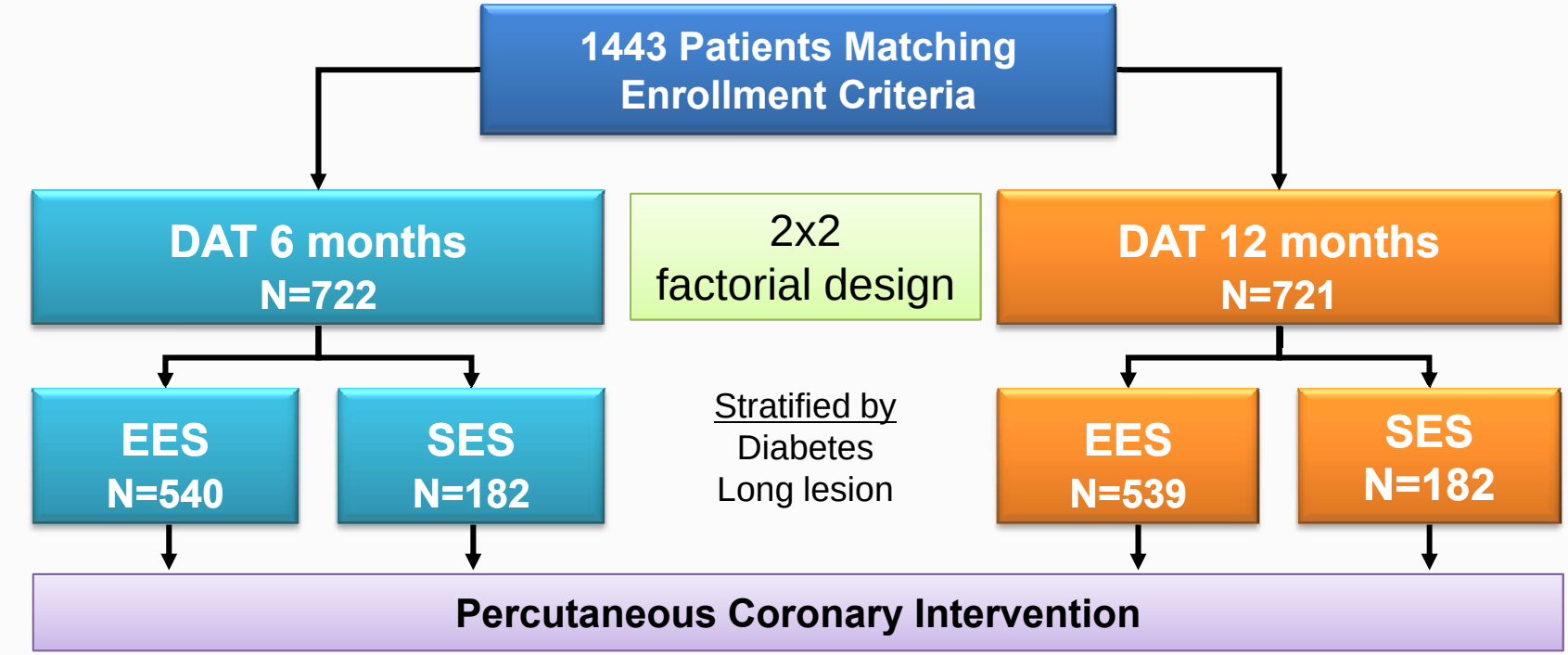
Participating Centers

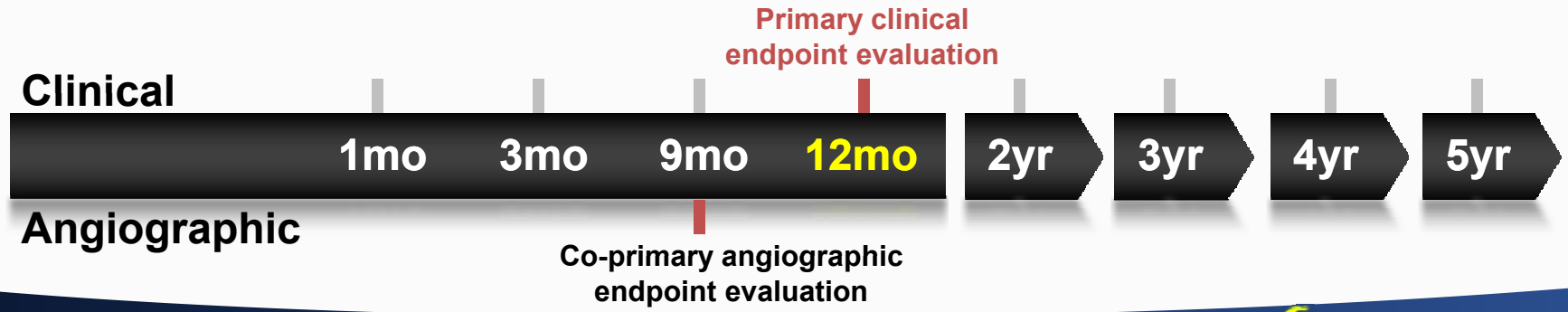
19 Hospitals in Republic of Korea

- Seoul National University Hospital
- Yonsei University Severance Hospital
- Samsung Medical Center
- Seoul National University Bundang Hospital
- Gachon University Gil Medical Center
- Yonsei University Wonju Christian Hospital
- Hallym University Sacred Heart Hospital
- Kandgong Sacred Heart Hospital
- Chonam National University Hospital
- Gangnam Severance Hospital
- NHIC Ilsan Hospital
- Inje University Sanggye Paik Hospital
- Korea University Anan Hospital
- Pusan National University Hospital
- Boramae Medical Center
- Kangnam Sacred Heart Hospital
- Uijeongbu St. Mary's Hospital
- Keimyung University Dongsan Hospital
- Ewha Womans University Mokdong Hospital

EXCELLENT-RCT Design

Investigator-initiated, multi-center, open label, prospective randomized trial



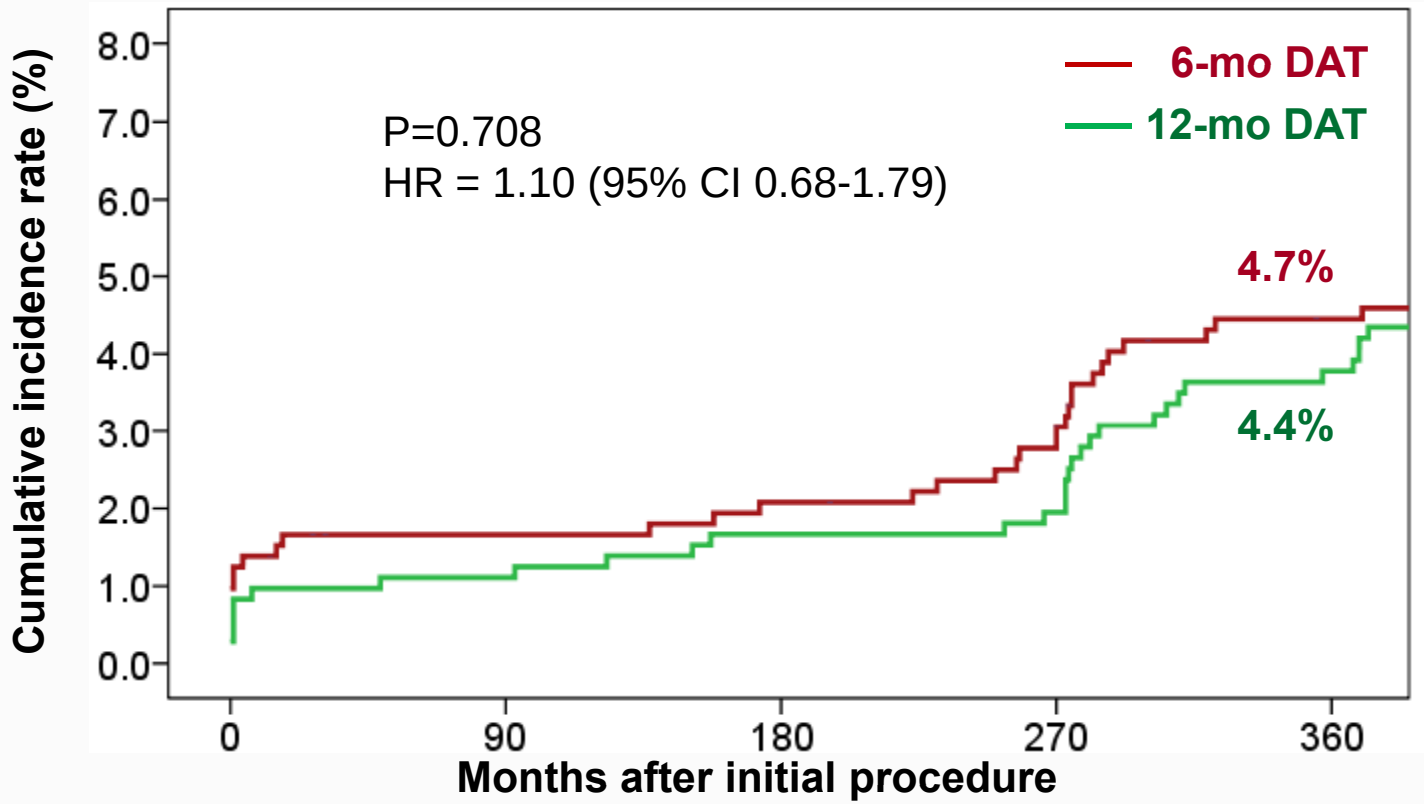


Am Heart J 2009 May;157:811-817.e1
www.clinicaltrials.gov (NCT00698607).

EXCELLENT-RCT

1° Endpoint

Target Vessel Failure



Patient Number at Risks

6-month	722	707	704	698	682
12-month	721	710	703	698	682

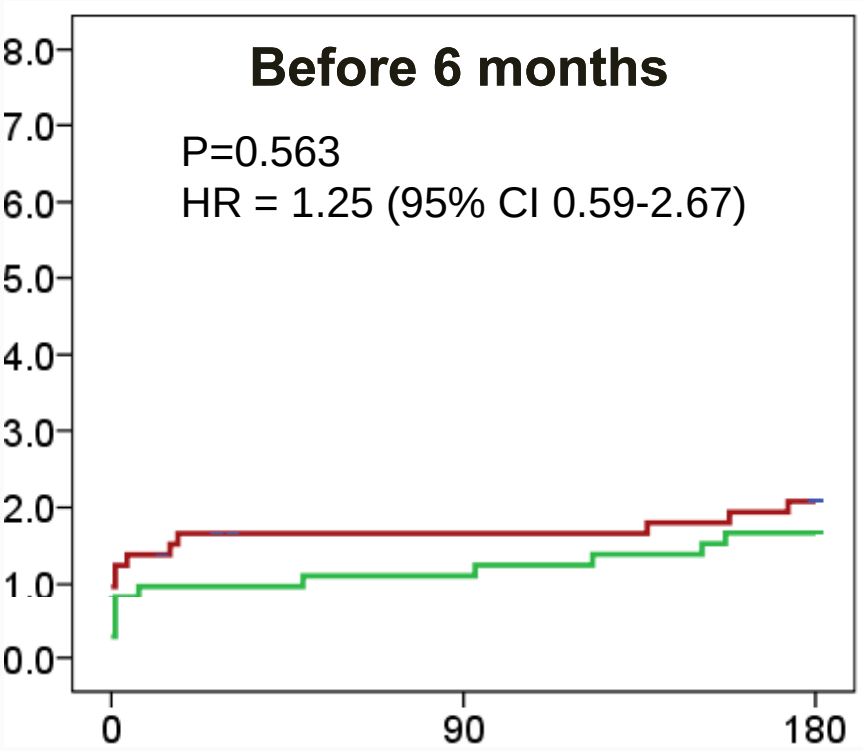
1° Endpoint

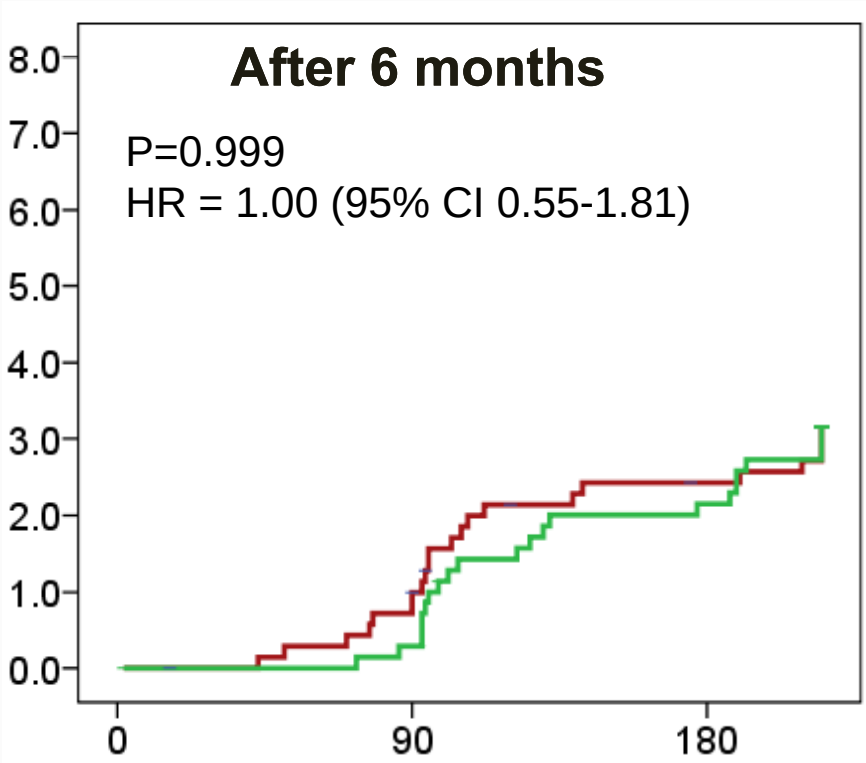
Target Vessel Failure

(6-month Landmark Analysis)

6-mo DAT

12-mo DAT

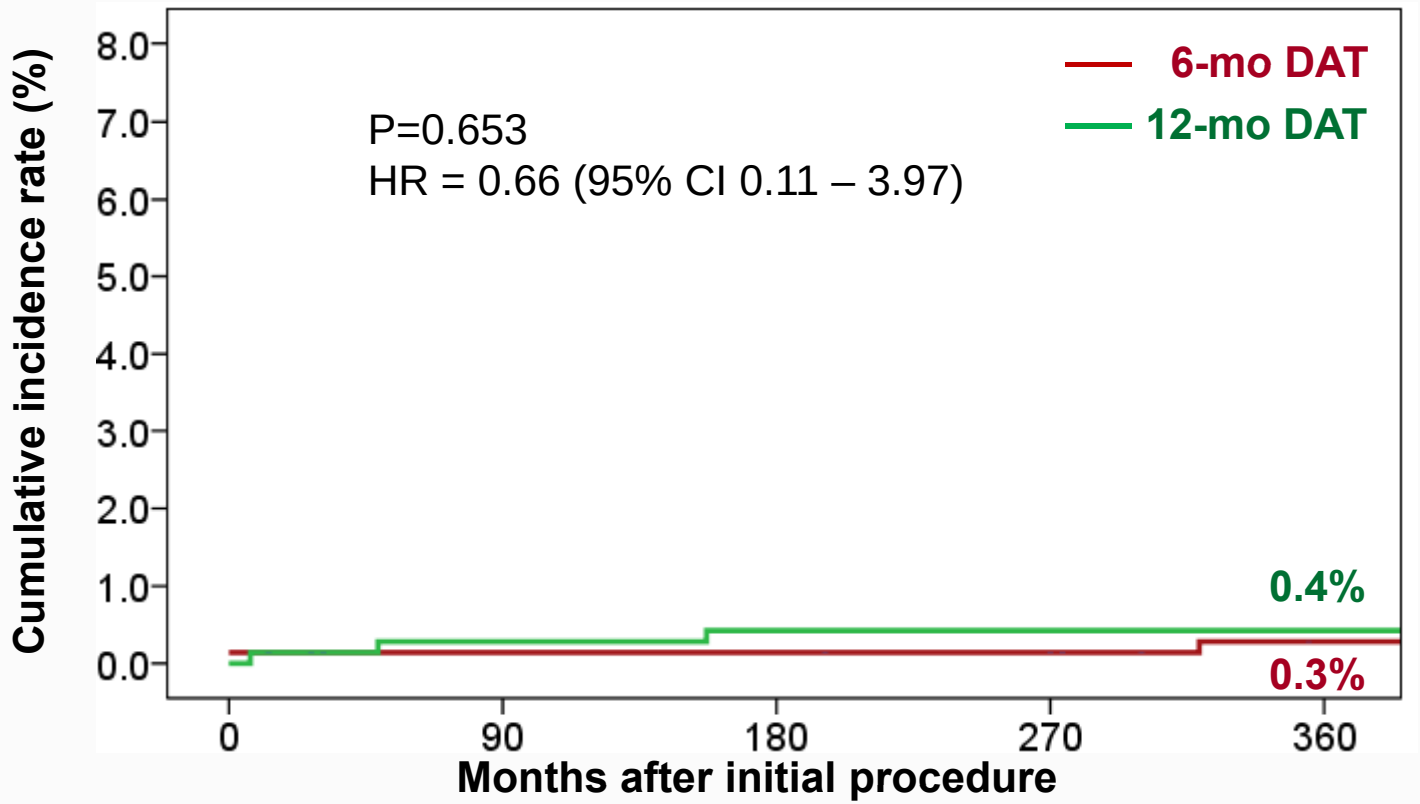




Patient Number at Risks			
6-mo	722	707	701
12-m0	721	710	699

Patient Number at Risks		
701	697	681
699	698	680

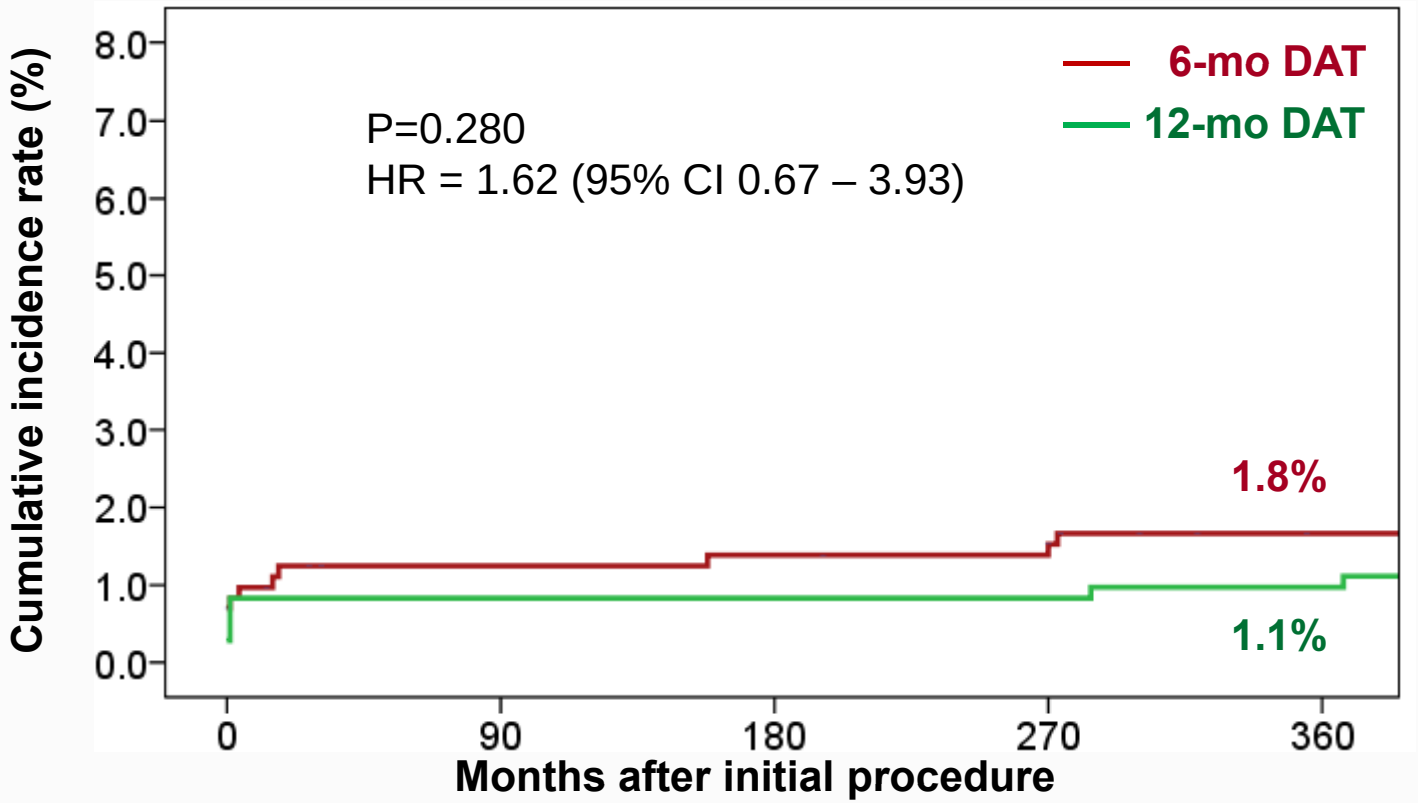
Cardiac Death



Patient Number at Risks

6-month	722	718	718	717	712
12-month	721	716	712	710	705

Myocardial Infarction

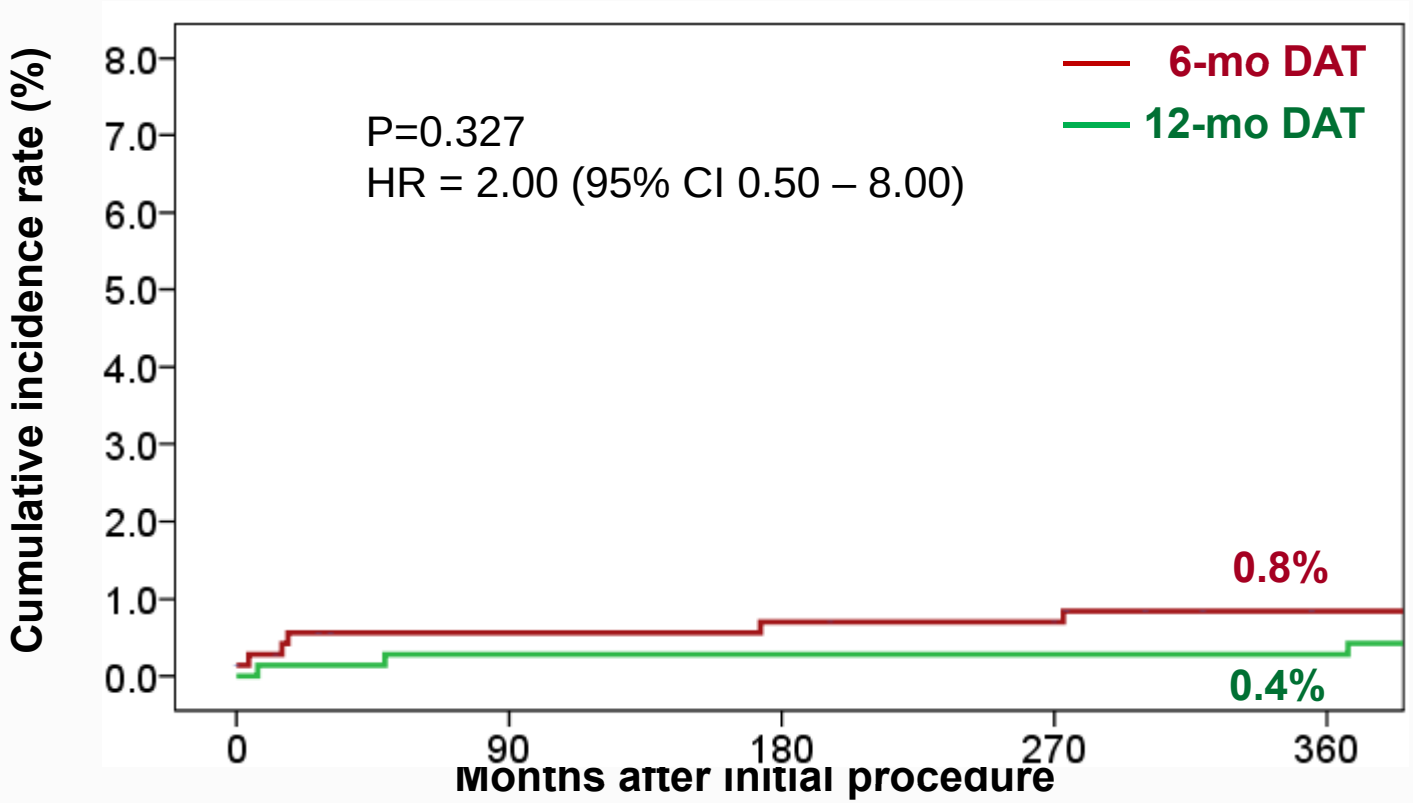


Patient Number at Risks

6-month	722	709	708	697	700
12-month	721	710	706	704	698

Stent Thrombosis

(Definite or probable stent thrombosis by ARC definition)

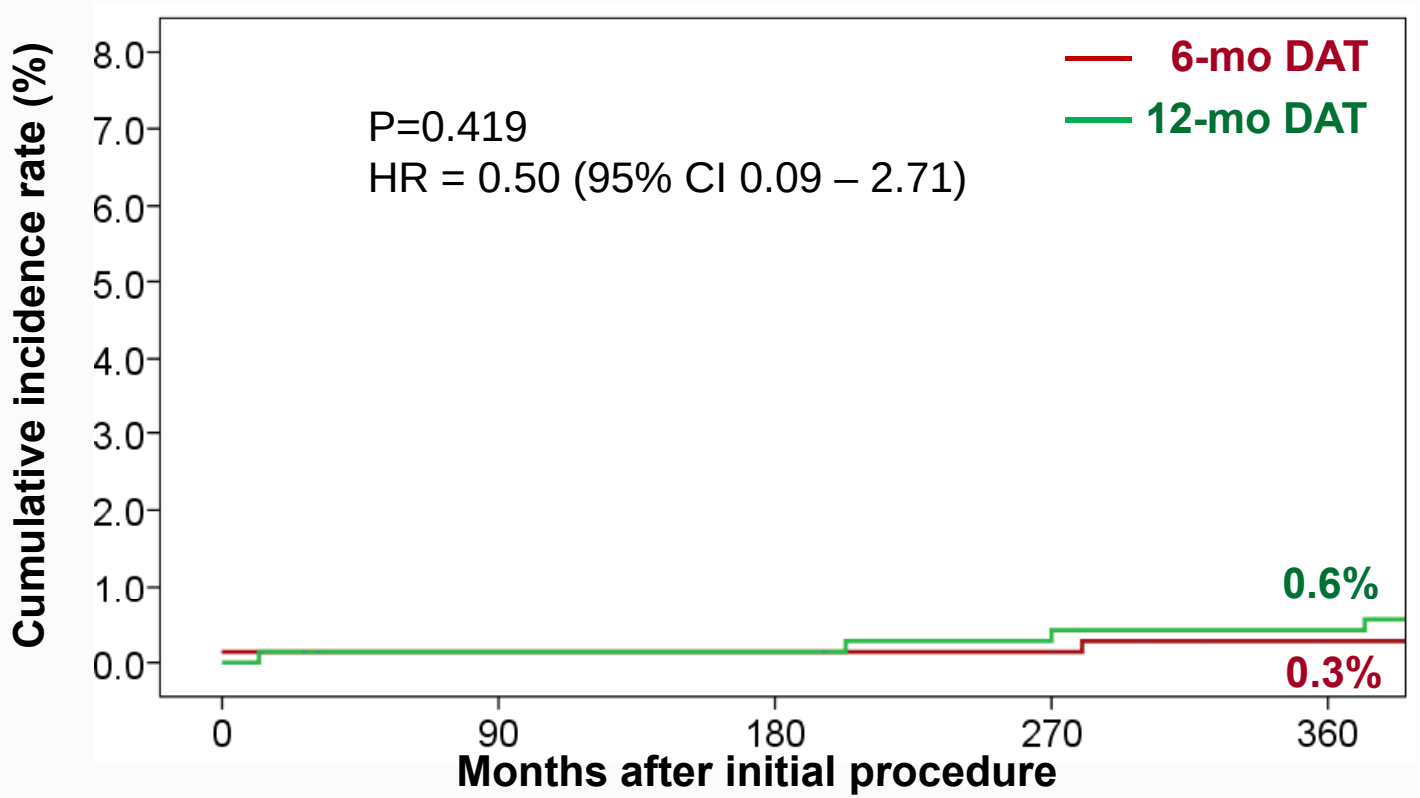


Patient Number at Risks

6-month	722	713	712	712	706
12-month	721	716	712	710	705

TIMI Major Bleeding

(Overt clinical bleeding with a drop of Hb > 5 g/dl or Hct > 15%)

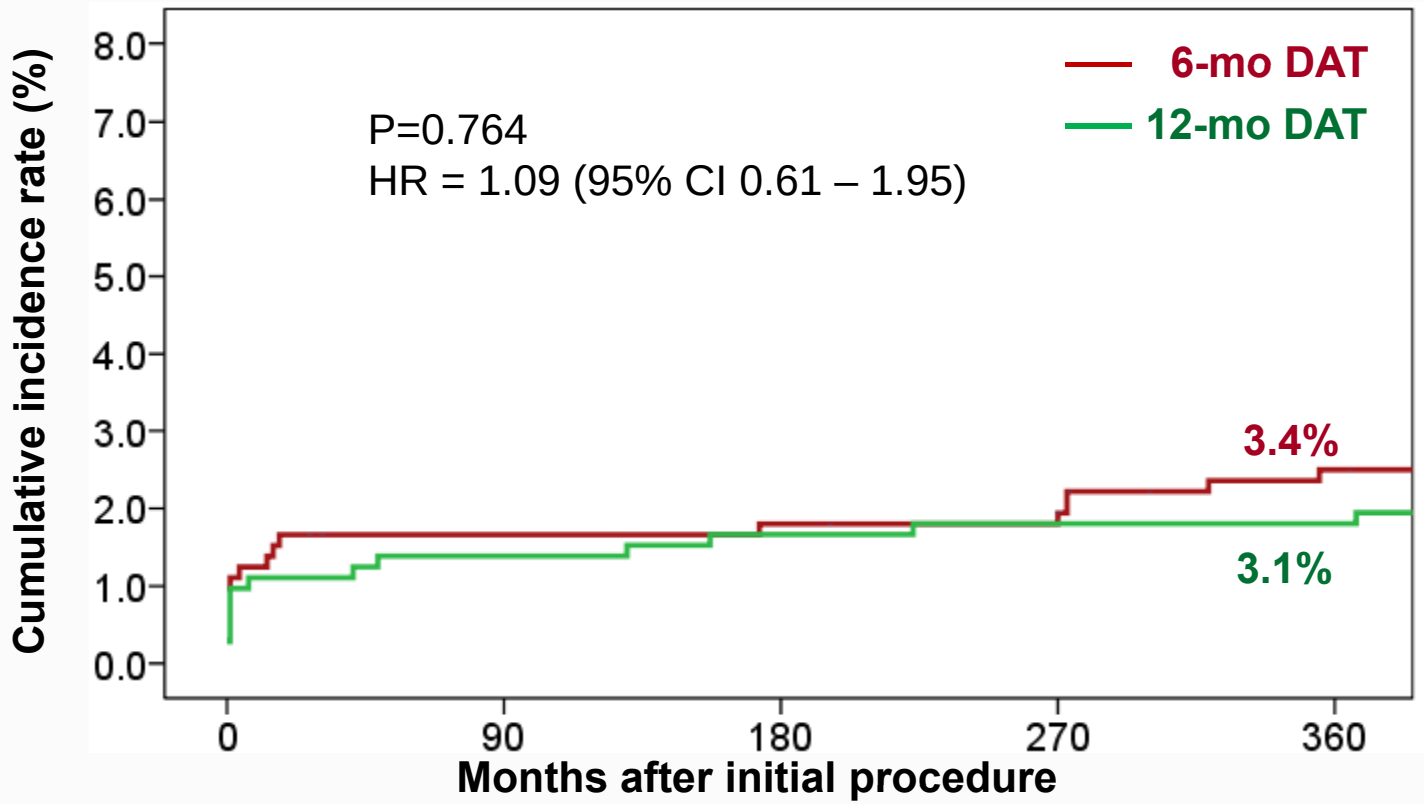


Patient Number at Risks

6-month	722	717	717	716	710
12-month	721	716	712	711	703

Safety Endpoint

(Death, MI, stent thrombosis, CVA, or TIMI major bleeding)

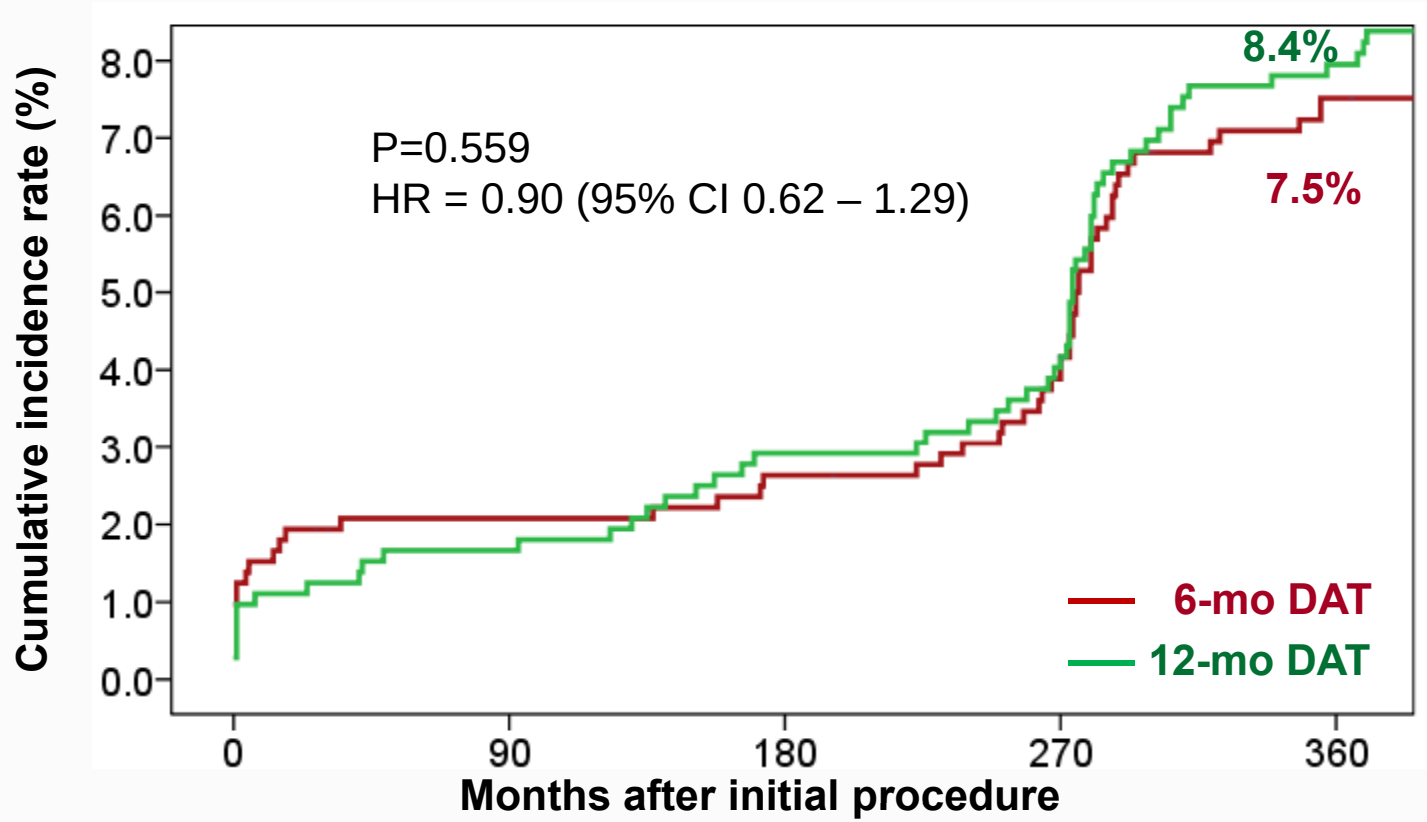


Patient Number at Risks

6-month	722	708	707	706	698
12-month	721	710	706	704	699

MACCE

(Death, MI, CVA, or any revascularization)

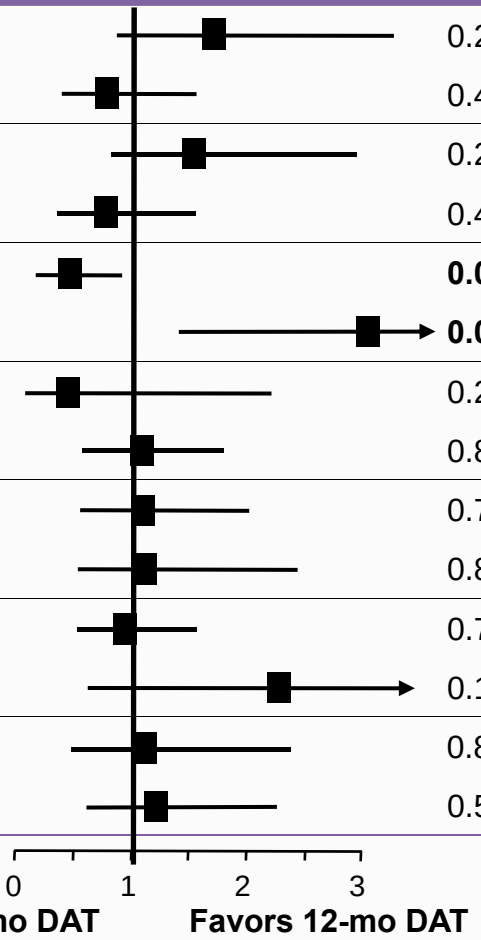


Patient Number at Risks

6-month	722	705	701	691	662
12-month	721	708	697	688	655

Subgroup Analysis for TVF

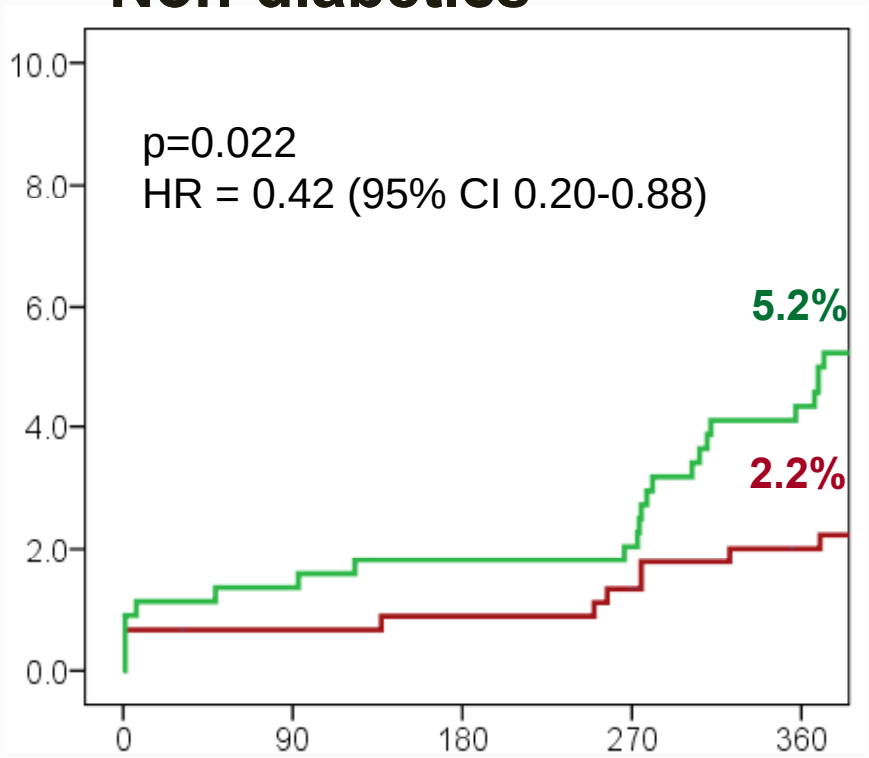
		N	6-mo DAT	12-mo DAT	X^2 p-value	Cox HR	Cox p-value	P for interaction
Age	< 65	761	19 (5.0%)	12 (3.2%)	0.202		0.202	0.155
	≥ 65	667	15 (4.5%)	19 (5.7%)	0.465		0.473	
ACS*	No	694	21 (6.9%)	14 (4.1%)	0.252		0.243	0.186
	Yes	734	13 (3.6%)	17 (4.6%)	0.474		0.471	
Diabetes	No	884	10 (2.2%)	23 (5.3%)	0.018		**0.022**	**<0.001**
	Yes	544	24 (8.8%)	8 (2.9%)	0.003		**0.005**	
LVEF	< 50%	123	3 (3.0%)	4 (7.1%)	0.286		0.290	0.287
	≥ 50%	1086	26 (4.8%)	25 (4.6%)	0.833		0.808	
Bifurcation	No	959	23 (4.7%)	20 (4.3%)	0.769		0.757	0.998
	Yes	469	11 (4.9%)	11 (4.5%)	0.830		0.830	
Stent	EES	1067	25 (4.7%)	27 (5.1%)	0.739		0.764	0.168
	SES	361	9 (5.0%)	4 (2.2%)	0.149		0.168	
Multi-stent	No	854	14 (3.2%)	12 (2.9%)	0.819		0.816	0.871
	Yes	563	20 (7.5%)	19 (6.4%)	0.601		0.585	



**ACS = unstable angina, NSTEMI, or STEMI*

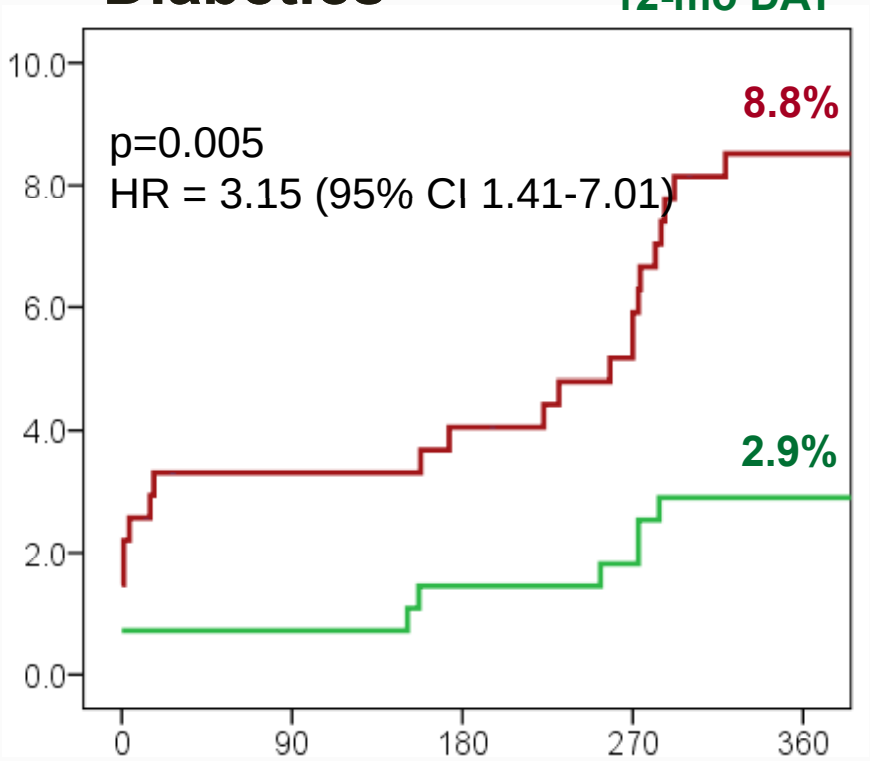
TVF according to Diabetes

Non-diabetics



Patient Number at Risks					
6-mo	450	446	445	443	437
12-mo	443	435	432	429	416

Diabetics



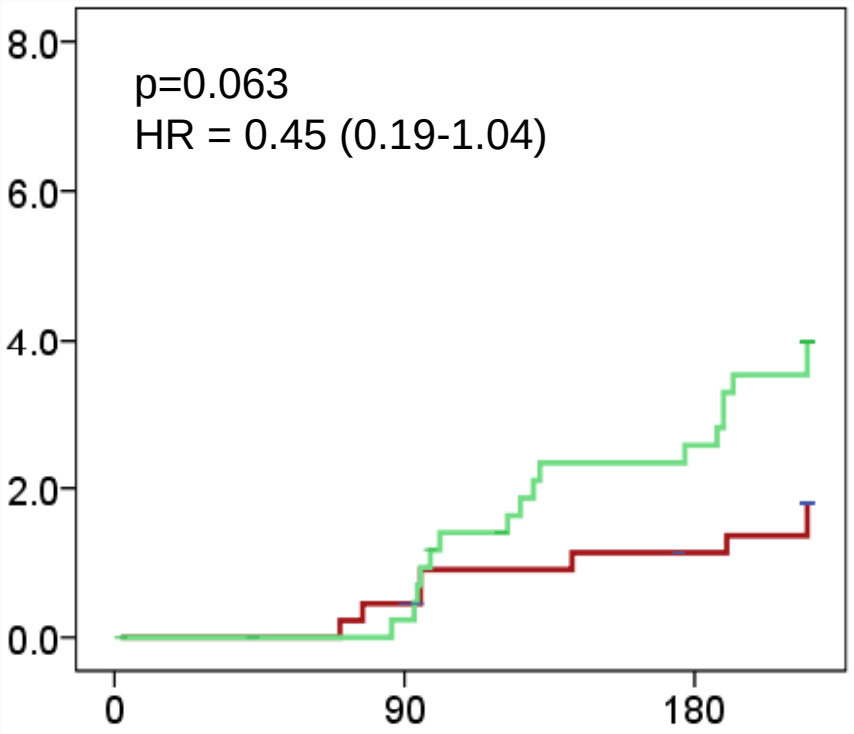
Patient Number at Risks					
272	261	259	255	245	
278	275	271	270	265	

TVF according to Diabetes

Landmark Analysis after 6 months

6-mo DAT
12-mo DAT

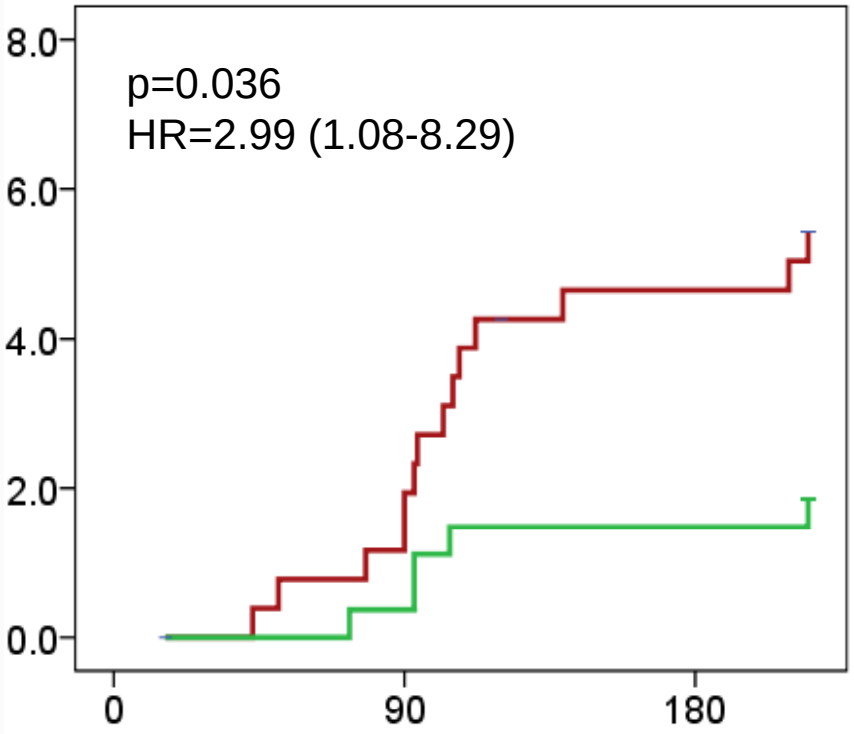
Non-diabetics



Patient Number at Risks

6-mo	444	442	436
12-mo	431	428	415

Diabetics



Patient Number at Risks

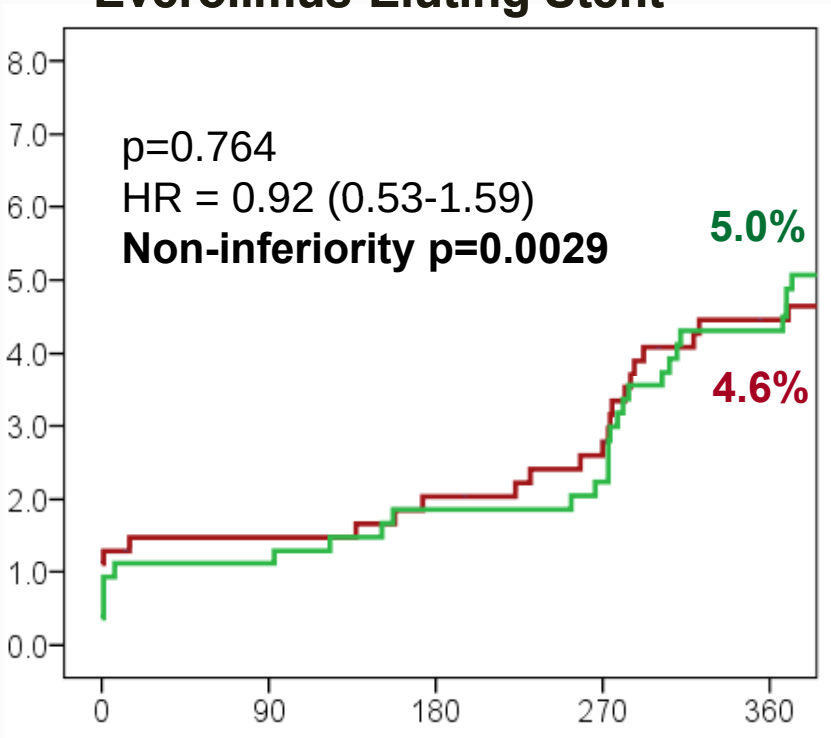
259	255	245	
271	270	265	

TVF in Stent Subgroups

(Randomized to EES vs. SES in 3:1 fashion)

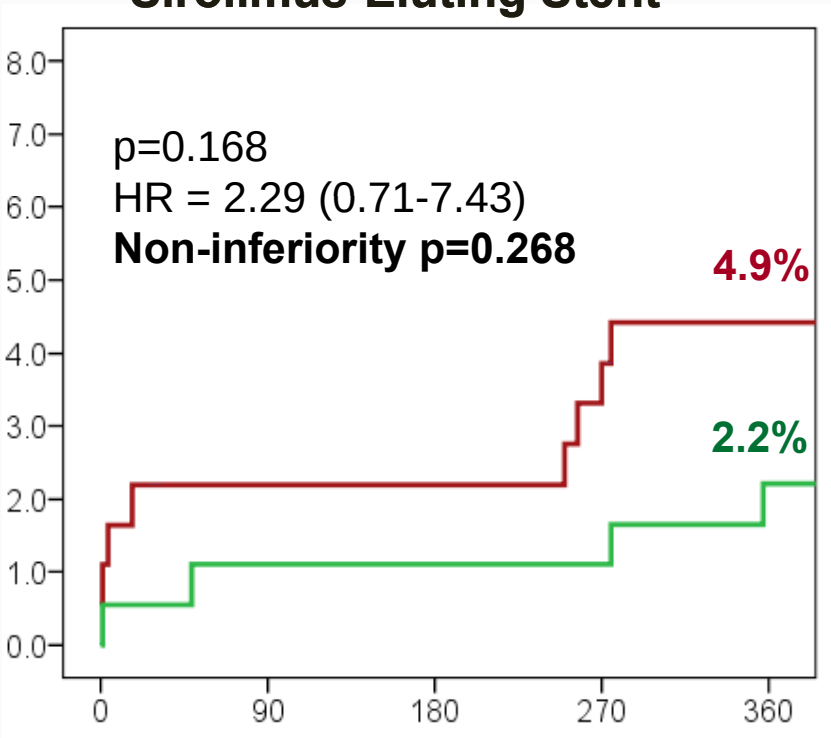
6-mo DAT
12-mo DAT

Everolimus-Eluting Stent



Patient Number at Risks					
6-mo	540	531	528	524	511
12-mo	539	531	524	521	505

Sirolimus-Eluting Stent



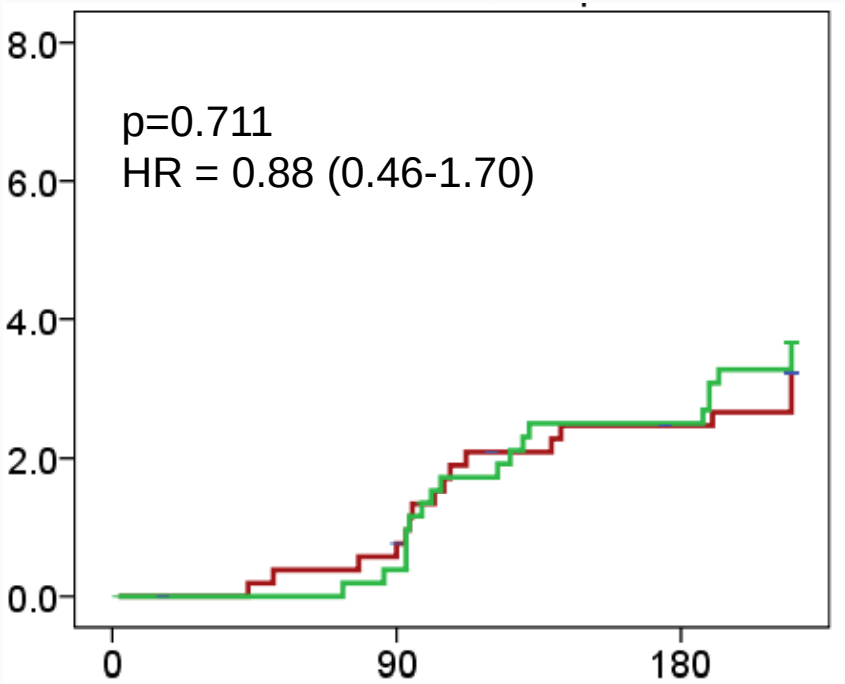
Patient Number at Risks					
182	176	176	174	171
182	179	179	178	176

TVF in Stent Subgroups

Landmark Analysis after 6 months

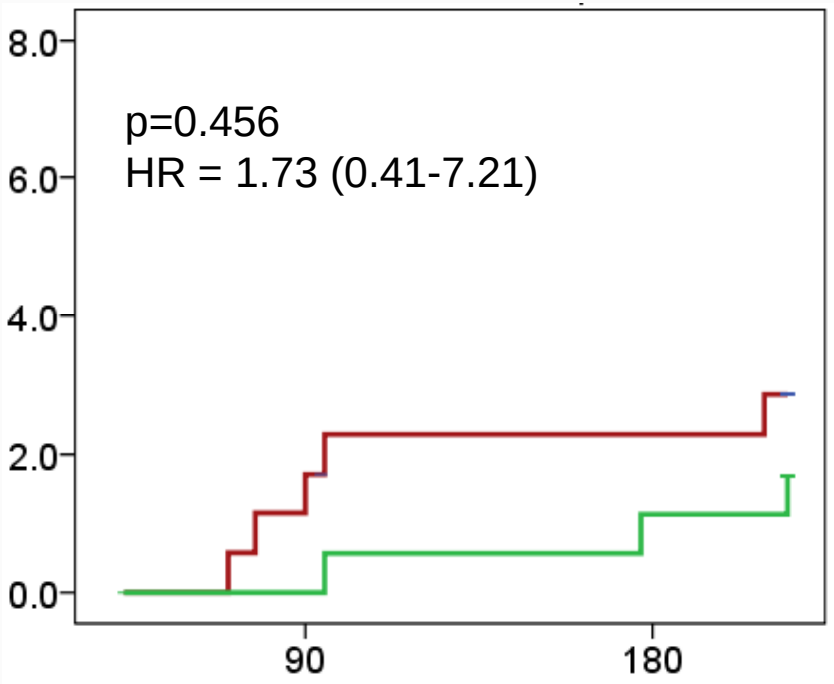
6-mo DAT
12-mo DAT

Everolimus-Eluting Stent



Patient Number at Risks			
6-mo	528	524	511
12-mo	523	520	504

Sirolimus-Eluting Stent



Patient Number at Risks			
175	173	170	
179	179	176	

Conclusions

- Six-month DAT is non-inferior to 12-month DAT with regard to the risk of TVF at 12 months after DES implantation.
- The safety of the 6-month DAT was heterogeneous and not proved in some subgroups, which suggests that the discontinuation of clopidogrel should be attempted considering the clinical and procedural risk profiles of the patients.
- A larger-scale randomized controlled trial is required to test the impact of shorter duration of clopidogrel therapy on the hard endpoints.

Ongoing Trials on the DAT Duration

Trial name	Subjects	DAT duration	DES type	1° EP
DAPT	20,645 12-mo event free	12-mo vs. 30-mo	All DES and BMS	33-mo D/MI/CVA
ISAR-SAFE	6,000 6-mo event free	6-mo vs. 12-mo	All DES	15-mo D/MI/CVA/Bleed
CYPRESS	2,500 All comer	12-mo vs. 30-mo	All DES	D/MI
Optimal…	1,966 All comer	12-mo vs. longer?	All DES	3-year D/MI/CVA/Bleed
SCORE	280 Myocardial infarction	12-mo vs. 24-mo	All DES	1-year D/MI
OPTIMIZE	3,120 Non-STEMI	3-mo vs. 12-mo	ZES	12-mo D/MI/CVA/Bleed
PRODIGY	1,700 All-comer	6-mo vs. 24-mo	EES, PES, ZES, BMS	24-mo D/MI/CVA

DAT = dual antiplatelet thearpy, EP = end point,
D/MI/CVA = death, myocardial infarction, cerebrovascular accident

(from www.clinicaltrials.gov)

Optimal Combination of Antiplatelet Therapy after PCI

Optimal Combination

of Antiplatelet Therapy after PCI

aspirin & Plavix

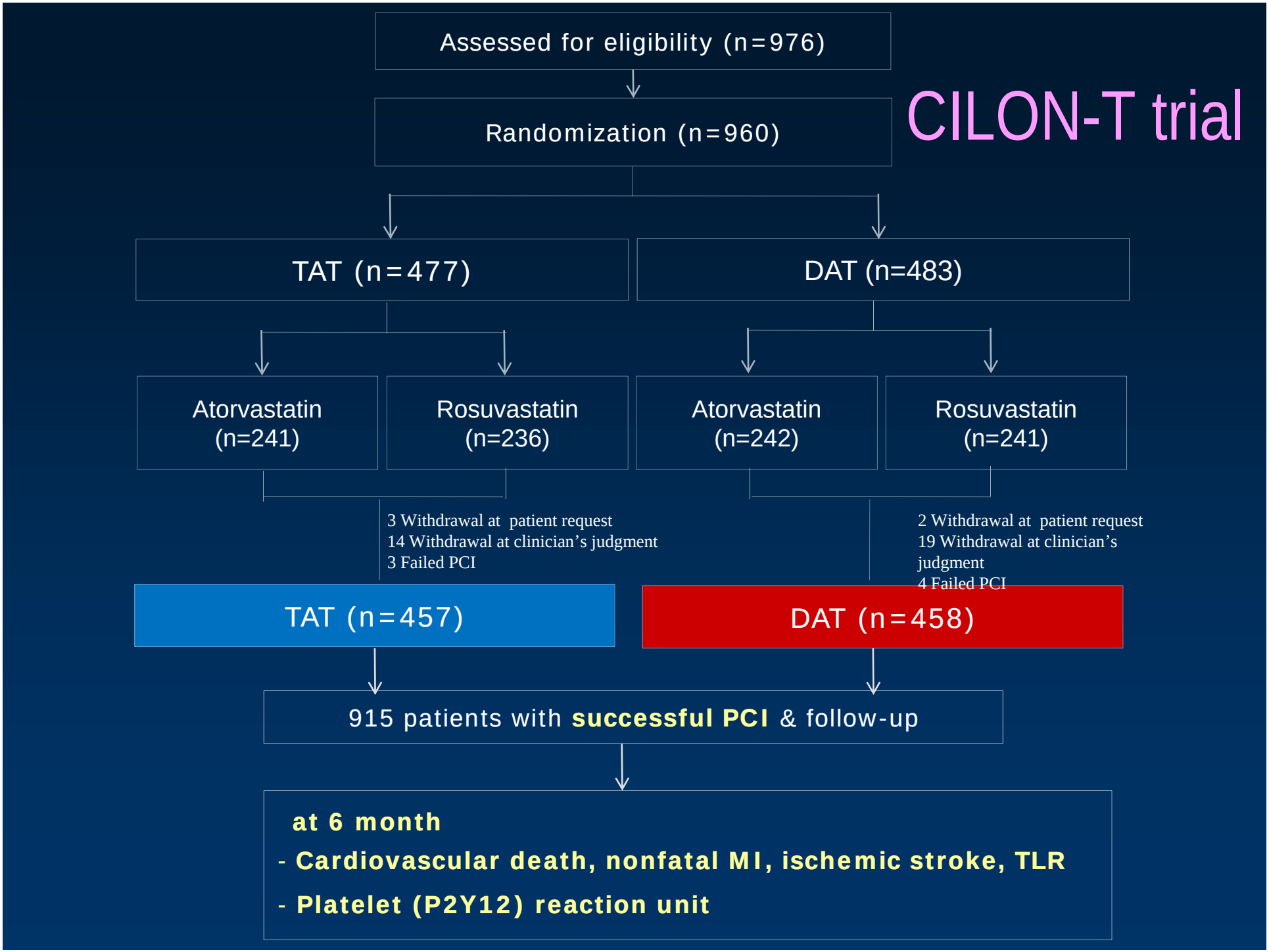
: standard one with huge evidences

: but, prevalent Plavix resistant

: do we need something stronger?

Such as ASA-PLAVIX-PLETAAL

CILON-T trial

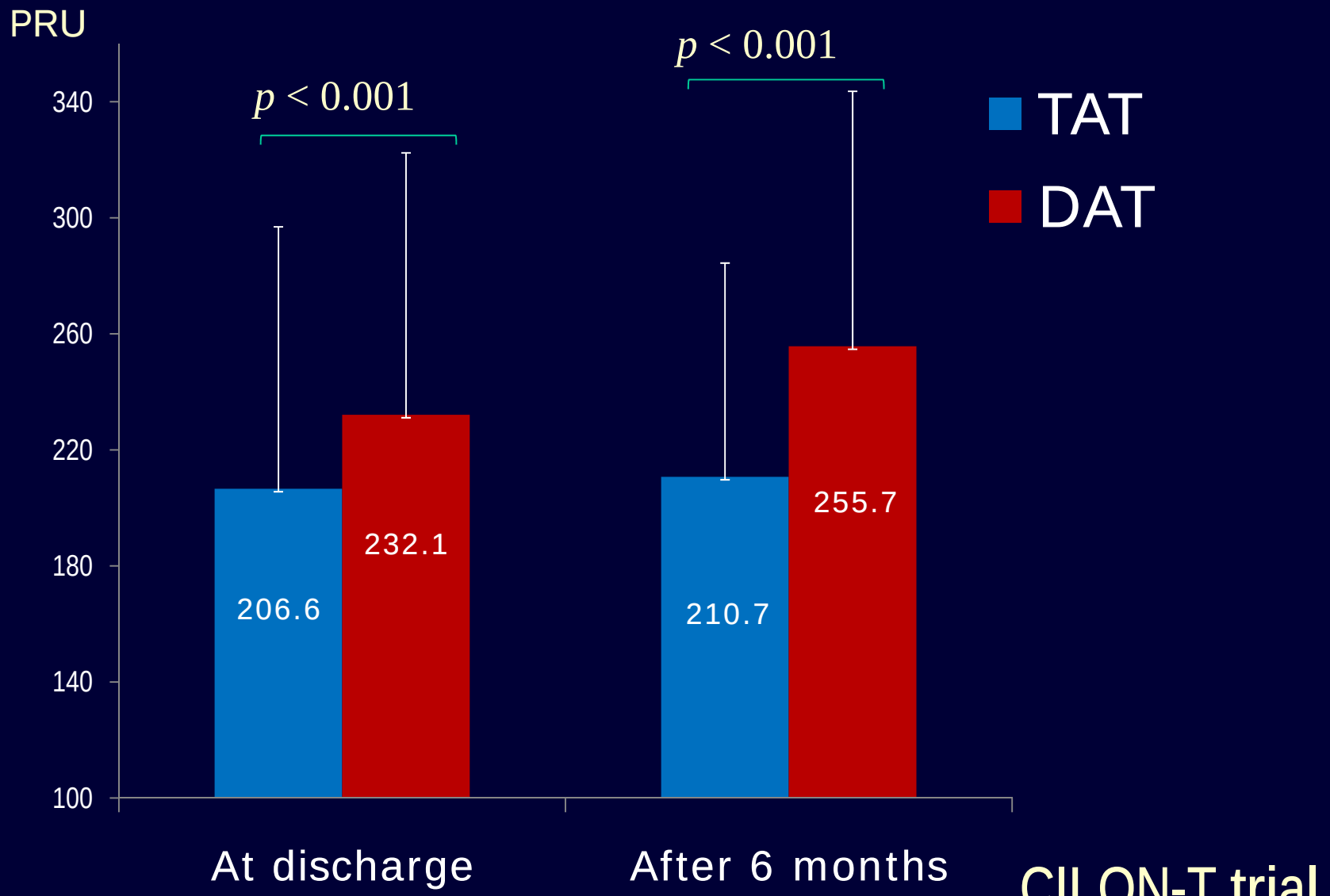


CILON-T trial : participating centers

Centers	Investigators
Seoul National University Hospital	Hyo-Soo Kim, MD, PhD
Seoul National University Bundang Hospital	In-Ho Chae, MD, PhD
Konyang University Hospital	Jang-Ho Bae, MD, PhD
Korea University Guro Hospital	Seung-Woon Rha, MD, PhD
Chungbuk University Hospital	Myeong-Chan Cho, MD, PhD

P2Y12 reaction unit (PRU): TAT vs DAT

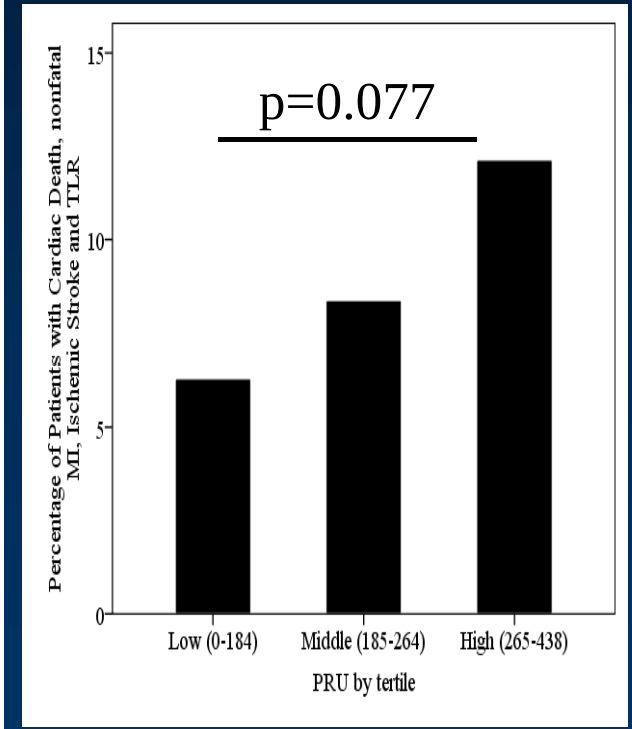
(JW Seo,,, HS Kim. CILON-T trial. JACC 2011)



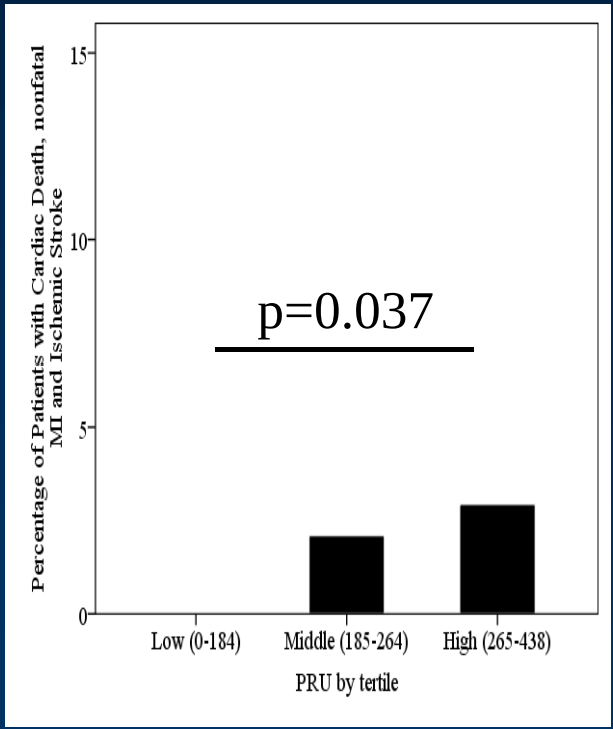
CILON-T trial

Results: Clinical outcomes depending on PRU value

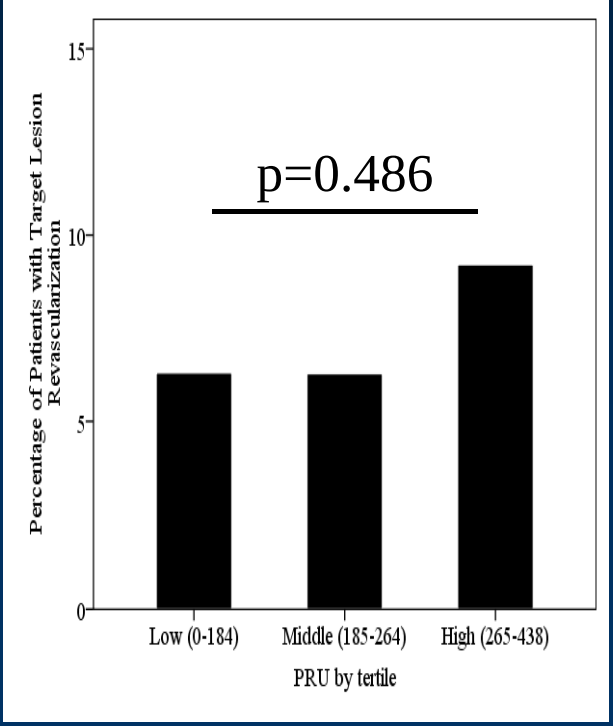
Composite of CD, nonfatal MI, ischemic stroke & TLR



Composite of CD, nonfatal MI & ischemic stroke



TLR



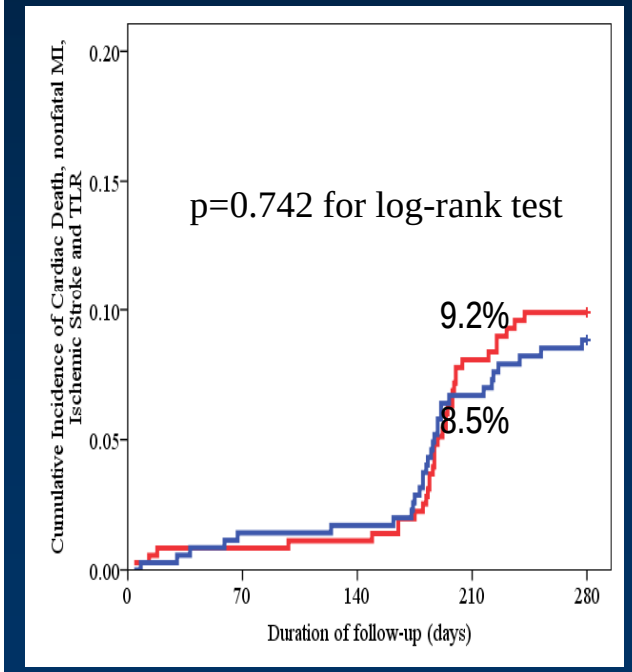
(JW Seo,,, HS Kim. CILON-T trial. JACC 2011)

Results: Clinical outcomes depending on anti-plt regimen

(JW Seo,,, HS Kim. CILON-T trial. JACC 2011)

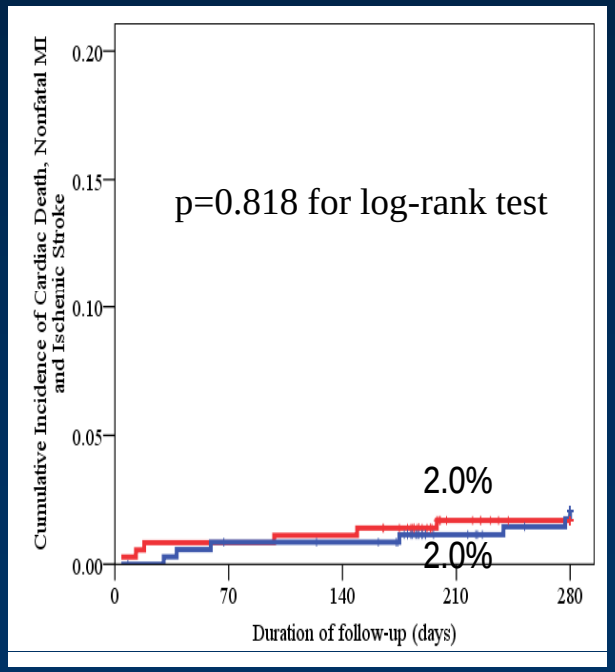
Double anti-PLT regimen Triple anti-PLT regimen

Composite of CD, nonfatal MI, ischemic stroke & TLR



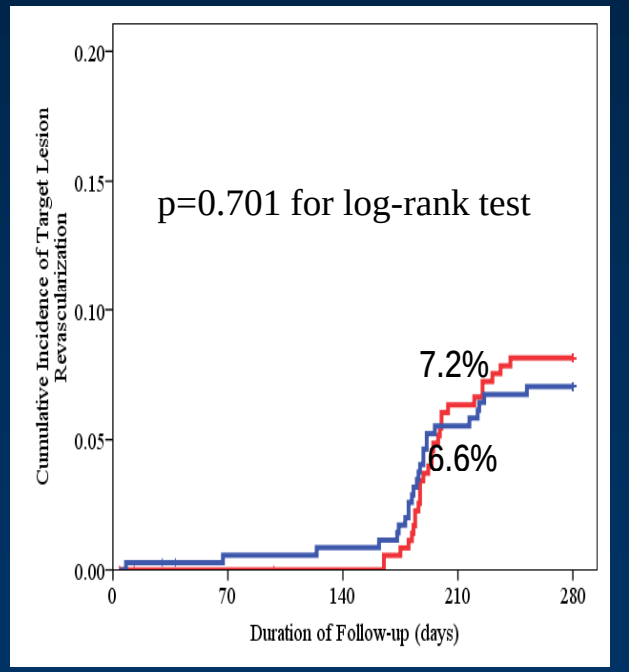
DAT	458	452	450	425	416
TAT	457	450	449	428	418

Composite of CD, nonfatal MI & ischemic stroke



DAT	458	452	451	449	447
TAT	457	452	452	451	448

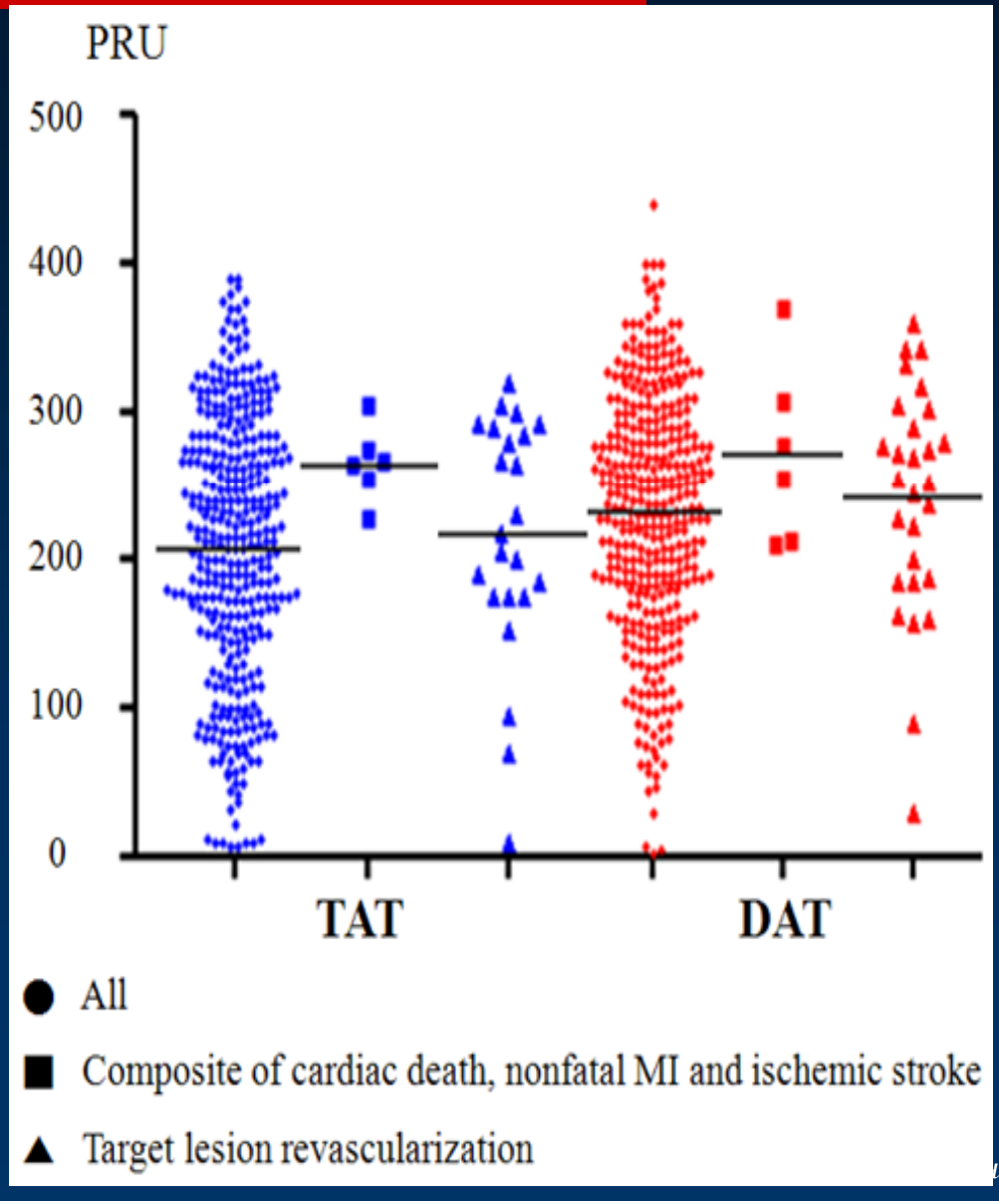
TLR



DAT	458	458	449	426	418
TAT	457	450	449	429	421

Distribution of PRU in pts with TAT vs DAT

(JW Seo,,, HS Kim. CILON-T trial. JACC 2011)

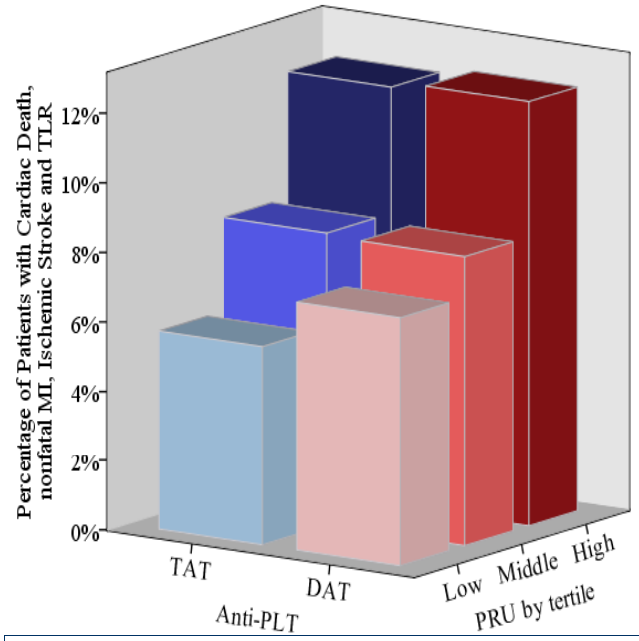


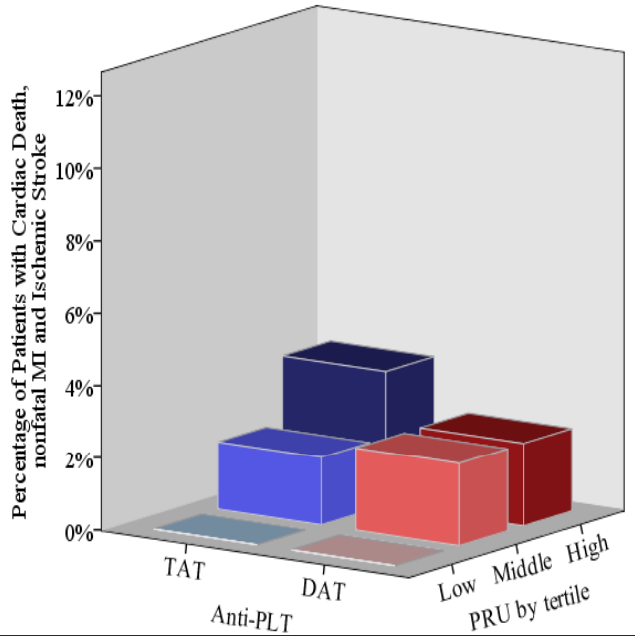
PRU value versus Anti-PLT regimen to predict MACCE

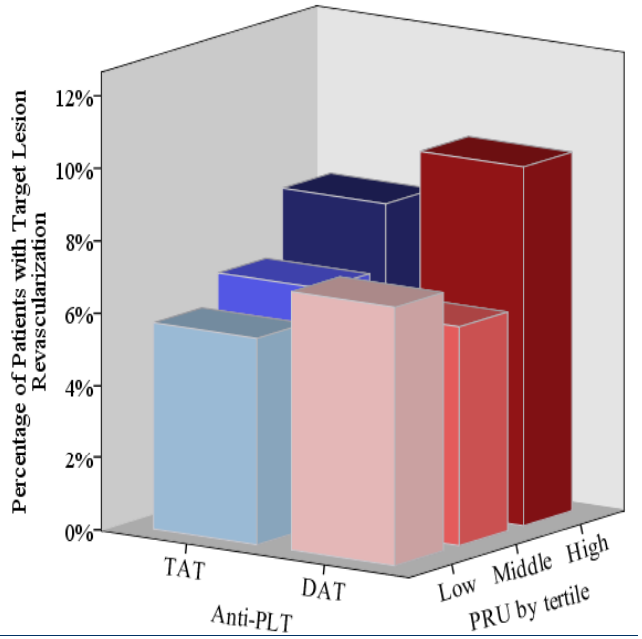
Composite of CD, nonfatal MI, ischemic stroke & TLR

Composite of CD, nonfatal MI & ischemic stroke

TLR







(JW Seo,,, HS Kim. CILON-T trial. JACC 2011)

Summary of CILON-T randomized controlled trial

- TAT achieved lower PPR (post-treatment platelet reactivity) than DAT.
- But it did not necessarily reduce MACCE within six months after DES implantation,
- because there were substantial numbers of hypo-responders even to TAT.
- The importance of PPR is reflected by the finding that the patients with low PPR (PRU < 210 unit) did not develop any thrombotic event (CD, MI, or ischemic stroke) irrespective of anti-platelet regimen.

Optimal Combination

- ASA / Plavix
- ASA / double-dose Plavix ?
- ASA / Plavix / Pletaal ?
- ASA / Prasugrel
- ASA / Ticagrelor

HOST-ASSURE trial

- Harmonizing Optimal Strategy for

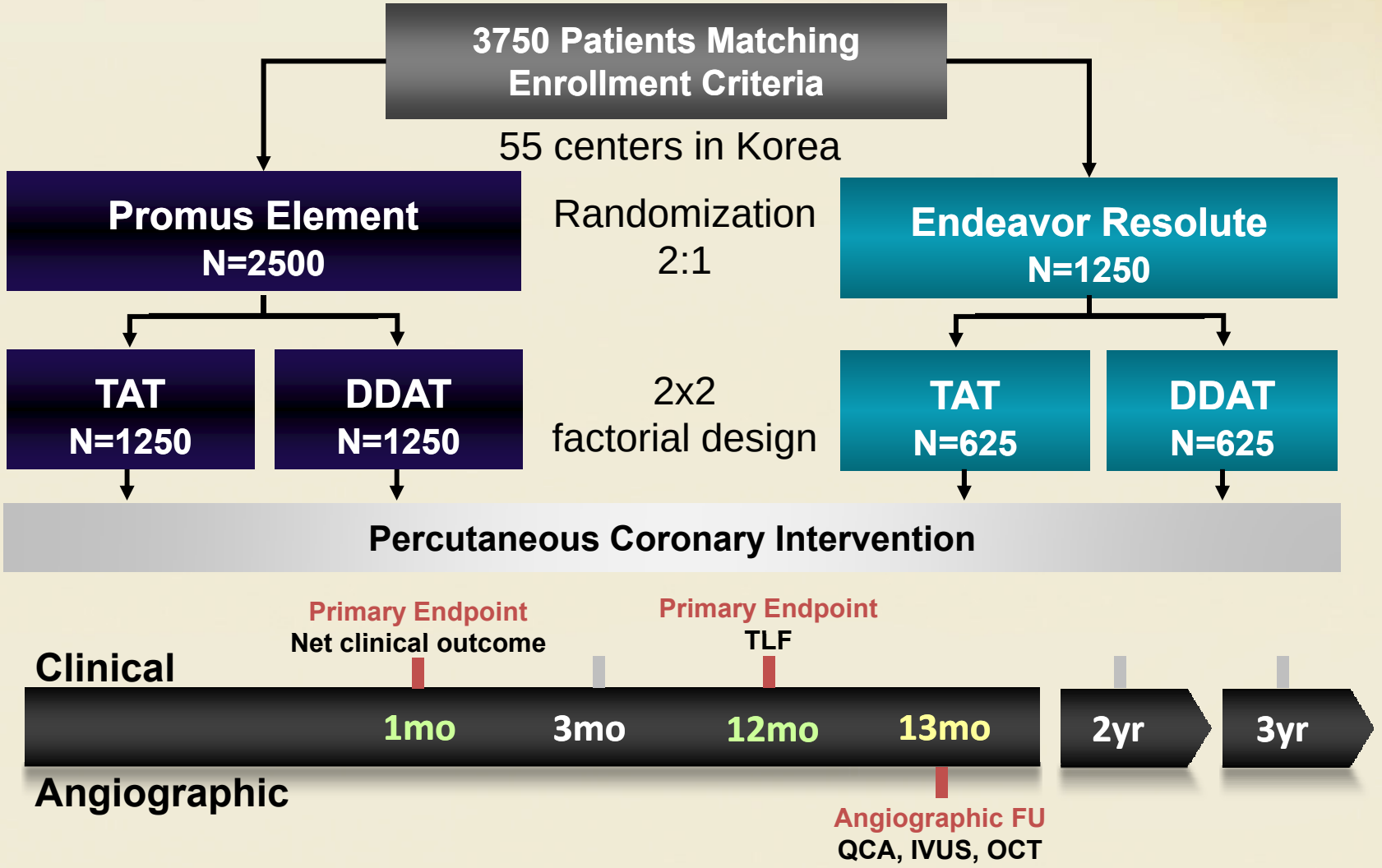
Treatment of coronary artery stenosis –

SAfety & EffectiveneSS of Drug-ElUting

Stents & Anti-platelet REgimen -

HOST-ASSURE: Trial Design

Prospective, open label, two-arm, randomized multi-center trial



Options for Combination of anti-plt therapy

Choose one depending on comorbid condition or PPR (Post-tx Platelet Reactivity)

- ASA / Plavix
- ASA / double dose Plavix
- ASA / Plavix / Pletaal
- ASA / Prasugrel
- ASA / Ticagrelor