Network Meta-Analysis

Durable-Polymer DES vs. Biodegradable-Polymer DES vs. BMS

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Interventional cardiology

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Biodegradable-polymer drug-eluting stents vs. bare metal stents vs. durable-polymer drug-eluting stents: a systematic review and Bayesian approach network meta-analysis

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Background	The aim of this study was to compare the safety and efficacy of biodegradable polymer (BP) drug-eluting stents (DES), how each it ents (BMS), and durable polymer DES in patients undergoing coronary revascularization, we performed
	a systematic review and network meta-analysis using a bisyesian network of the systematic review and network meta-analysis using a bisyesian network of the systematic review and network meta-analysis using a bisyesian network of the systematic review and network meta-analysis using a bisyesian network of the systematic review and network meta-analysis using a bisyesian network of the systematic review and network meta-analysis using a bisyesian network of the systematic review and network meta-analysis using a bisyesian network of the systematic review and network meta-analysis using a bisyesian network of the systematic review and network meta-analysis using a bisyesian network of the systematic review and network meta-analysis using a bisyesian network of the systematic review of the
Methods and results	Study stents included BMs, parlitaxel-eluting (FCS), salves and the stent of the stent stend stent stent stend stent stend stent stend ste
	to the Academic Research Consortium within 1 year.
Results	Biodegradable polymer-biolimus-eluting stensis [OR, 036; 5936 Cables Collection] Grl, 0.38–0.73), Co-Cr-EES (OR, 034; 95% Crl, 0.23–0.52), and PCCr-EES (OR, 0.31;95% Crl, 0.10–0.90) were all super- life to the terms of definite or probable ST within 1 year. Cobalt –chromium everolimus-eluting stents demonstrated lor to BMS in terms of definite or probable ST within 1 year. Cobalt –chromium everolimus-eluting stents and the lowest risk of ST of all stents at all times after stent implantation. Biodegradable polymer-biolimus-eluting stents was the lowest risk of ST of all stents at all times after stent implantation. Biodegradable polymer-biolimus-eluting stents was the lowest risk of ST of all stents at all times after stent implantation. Biodegradable polymer-biolimus-eluting stents was the lowest risk of ST of all stents at all times after stent implantation. Biodegradable polymer-biolimus-eluting stents was the lowest risk of ST of all stents at all times after stent implantation. Biodegradable polymer-biolimus-eluting stents was the lowest risk of ST of all stents at all times after stent implantation. Biodegradable polymer-biolimus-eluting stents was the lowest risk of ST of all stents at all times after stent implantation. Biodegradable polymer-biolimus-eluting stents was the lowest risk of ST of all stents at all times after stent implantation. Biodegradable polymer-biolimus-eluting stents was the lowest risk of ST of all stents at all times after stent implantation. Biodegradable polymer biolimus-eluting stents was the lowest risk of ST of all stents at all times after stents at a stent implantation. Biodegradable polymer biolimus-eluting stents was the lowest risk of ST of all stents at all times after stents at a stent implantation. Biodegradable polymer biolimus-eluting stents at a stent implantation in the stents at a stent stents at a stent implantation. Biodegradable polymer biologite stents at a stent implantation in the stent stent implantation. Biodegradable polymer implantation im
	the need for repeat revascularization, and all but PES reduced or retaining of ST within 1 year. Cobalt-chromium everolimus-eluting
Conclusions	All DESs but PES and ZES-E were superior to BMS in terms of 31 ways suggest that not only the biodegradability of polymer, stents was safer than any DES even including BP-BES. Our results suggest that not only the biodegradability of polymer, but the optimal combination of stental oy, design, strut thickness, polymer, and drug all combined determine the safety of but the optimal combination of stental oy, design, strut thickness, polymer, and drug all combined determine the safety of
	DES. Biodegradable polymer drug-eluting stents Meta-analysis
Keywords	Bare metal stents . Drug-eluting stents . Drug-eluting stents .

1 The first two authors contributed equally to the study. Published on behalf of the European Society of Candidogy. All rights reserved. © The Author 2014. For permissions please email: (ournals permissions@oup.com

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Restenosis

Requiring repeat revascularization Relatively soft adverse event



Stent Thrombosis

Results in death/MI Relatively hard adverse event





VS.

DES?

THE LANCET

Stent thrombosis with drug-eluting and bare-metal stents: $\Im \mathscr{W}^{\dagger}$ evidence from a comprehensive network meta-analysis

Tullio Palmerini, Giuseppe Biondi-Zoccai, Diego Della Riva, Christoph Stettler, Diego Sangiorgi, Fabrizio D'Ascenzo, Takeshi Kimura, Carlo Briguori, Manel Sabatè, Hyo-Soo Kim, Antoinette De Waha, Elvin Kedhi, Pieter C Smits, Christoph Kaiser, Gennaro Sardella, Antonino Marullo, Ajay J Kirtane, Martin B Leon, Gregg W Stone

Lancet 2012; 379: 1393-402

Articles

Tullio Palmerini et at. Lancet 2012

HOSPITAL

Stent Thrombosis Network Meta-analysis Primary EP: ARC Definite ST (FU through 2 years)

49 RCTs, 50,844 pts



Palmerini T et al. Lancet 2012

Stent Thrombosis Network Meta-analysis Primary EP: ARC Definite ST (FU through 2 years) 49 RCTs, 50,844 pts

1-year definite st	ent thromb	oosis*		Odds Ratio [95%]
CoCr-EES vs BMS			•	0.23 (0.13-0.41)
CoCr-EES vs PES		⊢−● −	-	0.28 (0.16-0.48)
CoCr-EES vs SES		(0.41 (0.24-0.70)
CoCr-EES vs Res-2	ZES	└───	-	0.14 (0.03-0.47)
CoCr-EES vs End-2	ZES	⊢ −●−	4	0.21 (0.10-0.44)
SES vs BMS		I	- - 	0.57 (0.36-0.88)
End-ZES vs SES			·	1.92 (1.07-3.90)
	0.01	0.1	1	10
		Favors Ste	nt 1 Favor	s Stent 2

Palmerini T et al. Lancet 2012

Interventional Cardiology

Short- and Long-Term Outcomes With Drug-Eluting and Bare-Metal Coronary Stents

A Mixed-Treatment Comparison Analysis of 117 762 Patient-Years of Follow-Up From Randomized Trials

Sripal Bangalore, MD, MHA; Sunil Kumar, MD; Mario Fusaro, MD; Nicholas Amoroso, MD; Michael J. Attubato, MD; Frederick Feit, MD; Deepak L. Bhatt, MD, MPH; James Slater, MD

Bangalore et at. Circulation 2012

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Network of Treatment Comparisons



Any Stent Thrombosis

Control	Treatment	Treatment Control	Rate Ratio	95%	Crl
BMS (Ref)					
	Sirolimus		0.87	0.71	1.07
	Paclitaxel	· · · · · · · · · · · · · · · · · · ·	1.19	0.92	1.51
	Everolimus	↓ '	0.51	0.35	0.73
	Zotarolimus	_	0.90	0.59	1.34
	Zotarolimus-R		0.75	0.38	1.49
Sirolimus (Ref)					
	Paclitaxel	_ _	1.36	1.07	1.72
	Everolimus		0.59	0.41	0.83
	Zotarolimus	· · · · · · · · · · · · · · · · · · ·	1.04	0.67	1.54
	Zotarolimus-R		0.87	0.44	1.71
Paclitaxel (Ref)		Ť			
	Everolimus	_ _	0.44	0.31	0.60
	Zotarolimus	·	0.78	0.50	1.10
	Zotarolimus-R	•	0.64	0.33	1.24
Everolimus (Ref)		· · · ·			
	Zotarolimus	↓	1.73	1.08	2.87
	Zotarolimus-R		1.45	0.82	2.66
Zotarolimus (Ref)					
	Zotarolimus-R	\	0.82	0.39	1.83
	0.10	1.00	10.00		
		RR (95% Crl)			

Bangalore et al. Circulation. 2012;125:2873-2891

Background

- <u>Biodegradable-polymer (BP) DES</u> has been developed with an aim to reduce the risk of late stent thrombosis.
- While BP-DES have yet to receive approval in the United States, they are widely used across the world including Asia and Europe.
- Recent meta-analyses (Palmerini et al. Lancet 2012; Bangalore et al. Circ 2012) have shown improved safety as well as efficacy of newer-generation DES.
- However, they have limitations in that the number of patients with newer-generation DES was relatively small and that <u>BP-DES were not included in the analyses</u>.

Biodegradable Polymer DES

Developed with an aim to reduce the risk of late stent thrombosis

Abluminal biodegradable coating

No drug carrier or drug inside the stent:

- Early BMS-like endothelial coverage¹
- More targeted drug release
- Reduced systemic exposure



Biodegradable polymer \rightarrow vanish within 6-9 months



Aim of Study

- In this study, we sought to compare the clinical outcome of various types of coronary stents including BMS, durable-polymer DES (DP-DES), and biodegradable-polymer DES (BP-DES).
- A systematic literature review of ulletrandomized controlled trials comparing coronary stents was performed, and the data from the review was the basis of a multipletreatments network metaanalysis using a Bayesian framework.





Flow Diagram of Systematic Review



RCTrials finally included (N=113)

Network Plot of Included Trials

- Polygonal network configuration with mixed connections
- Almost fully closed loops with limited comparisons of PtCr-EES and ZES-R



Study Characteristics



- A total of 113 trials with 90,584 patients
 - 6 studies: 3-arm design
 - 1 study: 2-phase enrollment
 - 10 studies: DM
 - 21 studies: STEMI
 - 5 studies: CTO
 - 3 studies: uLMCA disease
 - 3 studies: in-stent restenosis
 - 2 studies: bypass graft
- Estimated median F/U duration
 = 19.1 months (3 months 5 years)

SNU-Hospital (Seoul National University)

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Main Characteristics of Included Trials

Trials	Stent Comparison (Patient Number)	Primary Endpoint	Design Major Inclusion Criteria		Main Results	Follow-Up
Published in 2002						
RAVEL	SES vs. BMS (120:118)	In-stent LL at 6 months	Multicenter, superiority	Stable or unstable angina	SES superior to BMS	5 years
Published in 2003						
ASPECT	PES vs. BMS (117:58)	% stenosis at 4-6 months	Three-center, superiority	Stable or unstable angina	PES superior to BMS	6 months
E-SIRIUS	SES vs. BMS (175:177)	MLD at 8 months	Multicenter, superiority	Stable or unstable angina	SES superior to BMS	9 months
SIRIUS	SES vs. BMS (533:525)	TVF at 9 months	Multicenter, superiority	Stable or unstable angina	SES superior to BMS	5 years
TAXUS I	PES vs. BMS (31:30)	MACE (death Q-wave MI, TVR, ST) at 30 days	Three-center, feasibility	Stable or unstable angina	Promising results of PES	2 years
TAXUS II	BMS vs. PES (270:266)	%NIH by IVUS at 6 months	Multicenter, superiority	Stable or unstable angina	PES superior to BMS	5 years
Published in 2004						
C-SIRIUS	SES vs. BMS (50:50)	MLD at 8 months	Multicenter, superiority	Stable or unstable angina	SES superior to BMS	9 months
SES-SMART	SES vs. BMS (129:128)	In-segment binary restenosis at 8 months	Multicenter, superiority	Stable angina, ACS	SES superior to BMS	2 years
TAXUS IV	BMS vs. PES (652:662)	TVR at 9 months	Multicenter, superiority	Stable or unstable angina	PES superior to BMS	5 years
Published in 2005						
BASKET	SES vs. PES (264:281)	Cost-effectiveness after 6 months	Single-center, superiority	All-comer design	DES (SES and PES) not superior to BMS	18 months
ISAR						
С	ontinued					



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Rankogram

Definite or Probable ST within 1 Year

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Definite or Probable ST of DES with Reference to BMS

(A) Early ST (\leq 30 days) (D) Very Late ST (>365 days) BMS vs. BMS reference BMS vs. BMS reference 0.78 (0.46-1.34) PES vs. BMS PES vs. BMS 1.54 (0.89-2.66) 0.61 (0.30-1.22) ZES-E vs. BMS ZES-E vs. BMS 0.54 (0.21-1.35) **BP-BES vs. BMS** 0.34 (0.13-0.82) 0.44 (0.11-1.52) **BP-BES vs. BMS** SES vs. BMS 0.53 (0.32-0.88) 1.82 (1.05-3.13) SES vs. BMS 0.27 (0.08-0.81) ZES-R vs. BMS 0.49 (0.09-2.57) ZES-R vs. BMS 0.29 (0.14-0.55) CoCr-EES vs. BMS CoCr-EES vs. BMS 0.49 (0.20-1.17) 0.14 (0.03-0.59) PtCr-EES vs. BMS 1.15 (0.07-45.92) PtCr-EES vs. BMS (B) Late ST (31-365 days) (E) Late and Very Late ST (>30 days) BMS vs. BMS reference reference BMS vs. BMS PES vs. BMS 1.10 (0.54-2.34) PES vs. BMS 1.31 (0.81-2.04) 0.82 (0.41-1.76) ZES-E vs. BMS 1.51 (0.47-5.26) ZES-E vs. BMS 0.38 (0.08-1.71) **BP-BES vs. BMS BP-BES vs. BMS** 0.42 (0.15-1.10) SES vs. BMS 0.35 (0.15-0.76) SES vs. BMS 1.16 (0.73-1.78) ZES-R vs. BMS 1.59 (0.24-10.30) ZES-R vs. BMS 0.94 (0.30-3.22) CoCr-EES vs. BMS 0.31 (0.11-0.80) 0.42 (0.22-0.78) CoCr-EES vs. BMS PtCr-EES vs. BMS 2.20 (0.12-86.66) PtCr-EES vs. BMS 1.21 (0.19-10.72) (F) ST at the Longest Follow-Up (C) ST within 1 Year (-365 days) BMS vs. BMS reference BMS vs. BMS reference 1.08 (0.84-1.38) PES vs. BMS 0.85 (0.60-1.19) PES vs. BMS ZES-E vs. BMS 0.70 (0.48-1.01) 0.75 (0.45-1.19) ZES-E vs. BMS **BP-BES vs. BMS** 0.55 (0.32-0.89) 0.59 (0.39-0.89) **BP-BES vs. BMS** SES vs. BMS 0.82 (0.64-1.05) 0.53 (0.39-0.73) SES vs. BMS

ZES-R vs. BMS

0.125 0.25

Favors first treatment

0.5

2

4

Favors second treatment

CoCr-EES vs. BMS

PtCr-EES vs. BMS

0.62 (0.32-1.22)

0.42 (0.29-0.60)

0.40 (0.16-1.15)

Favors second treatment

2

ZES-R vs. BMS

0.125 0.25 0.5

Favors first treatment

CoCr-EES vs. BMS PtCr-EES vs. BMS 0.52 (0.24-1.18)

0.35 (0.23-0.52)

0.31 (0.10-0.89)

Random sequence generation Allocation concealment Blinding (study patient) Blinding (treating physician) Blinding of clinical outcome assessment Incomplete outcome data addressed Free of selective reporting Free of other bias

Risk of Bias in all 113 RCTs (8 aspects)

- All trials were randomized controlled trials
- Allocation concealment: adequate in 86/113 trials
- A double-blind design
 - some studies in early period (2003-2006)
 - no studies since 2007
- Blinding of clinical event adjudication: adequate in 2/3
- Yes (Low risk of bias)
- Unclear
- No (High risk of bias)

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Risk of Bias from 8 Aspects

- Among a total of 113 trials included
- Proportion of studies with each of the judgments for each entry (according to the Cochrane Collaboration's tool)

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Sensitivity Analysis Definite or Probable ST within 1 Year

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Studies with Low Risk of Bias : 48 Trials; 60,911 Patients

Definite ST Within 1 Year Kang SH, Park KW,, Kim HS. Euro Heart J 2014

$CoCr-EES > (PtCr-EES \ge SES \ge BP-BES \ge PES \ge ZES-R \ge ZES-E \ge BMS)$

- CoCr-EES superior to BMS, ZES-E, ZES-R, PES, BP-BES, and SES
- SES superior to BMS
- SES tended to be superior to ZES-E and PES

TLR Within 1 Year

$(BP-BES \ge CoCr-EES \ge SES \ge PtCr-EES \ge ZES-R) > (PES \ge ZES-E) > BMS$

- All DES superior to BMS
- BP-BES, CoCr-EES and SES superior to ZES-E and PES

All-Cause Death in 1 Year Kang SH, Park KW,, Kim HS. Euro Heart J 2014

No significant difference between any comparisons

Conclusions

- All DESs but PES and ZES-E were superior to BMS in terms of ST within 1 year.
- CoCr EES (in large sample size) was superior to any DES even including BP-BES in terms of ST.
- PtCr EES (in small sample size) showed a promising tendency to be superior to any DES in terms of ST.
- Our results suggest that not only the biodegradability of polymer, but the optimal combination of stent alloy, design, strut thickness, polymer, and drug all combined determine the safety of DES.

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Network Meta-Analysis

Durable-Polymer DES vs. Biodegradable-Polymer DES vs. BMS

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Eligible Study Criteria

Inclusion criteria

- RCT comparing 2 or more coronary stents in patients undergoing PCI
- Study stents
 - (1) BMS (Bare metal stents)
 - (2) PES (Paclitaxel-eluting stents, Boston Scientific)
 - (3) SES (Sirolimus-eluting stents, Cordis)
 - (4) **ZES-E** (Endeavor zotarolimus-eluting stents, Medtronic)
 - (5) CoCr-EES (Cobalt-chromium everolimus-eluting stents, Abbott Vascular and Boston Scientific)
 - (6) **PtCr-EES** (Platinum-chromium everolimus-eluting stents, Boston Scientific)
 - (7) ZES-R (Resolute zotarolimus-eluting stents, Medtronic)
 - (8) **BP-BES** (BP biolimus A9-eluting stents, Biosensors and Terumo)

Exclusion criteria

- 1) Studies comparing two stents with different stent design within the same category described above,
- 2) Studies in which specific type of DES was not predefined and the choice among available DES was left to the investigators' discretion (for example, BMS versus any DES)
- 3) Studies published in a language other than English.
- * No restrictions were imposed on study period, sample size, or publication status as well as patient or lesion criteria.

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Data Sources

- Electronic search (from the inception to March 2013)
 - PubMed
 - Embase
 - Cochrane Central Register of Controlled Trials (CENTRAL)
 - Relevant websites (www.crtonline.org, www.clinicaltrialresults.com, www.tctmd.com, www.cardiosource.com, and www.pcronline.com)

Study Outcomes

- Principal safety endpoint: definite or probable ST ≤ 1 year (defined according to the ARC consensus)
- Other safety endpoints
 - definite ST
 - cardiac death
- Efficacy endpoints
 - TLR

- all-cause death
- myocardial infarction
- TVR

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Data Analysis

Bayesian random effects model

- Bayesian extension of the hierarchical random-effects model proposed by Lumley for networks of multi-arm trials
- Markov chain Monte Carlo samplers in WinBUGS
 - Running 3 chains with different starting values
 - A burn-in phase of 20,000 iterations were followed by 50,000 updates
- Noninformative prior distributions
- Odds ratios (OR) with 95% credible intervals (Crls)
- Results for which the CrIs of the ORs did not include 1 were considered significant

Sensitivity analysis

- (1) Excluding studies with any potential risk of bias
- (2) Excluding studies with exclusive enrollment of diabetic patients
- (3) Excluding studies with exclusive enrollment of STEMI
- (4) Excluding studies with mandatory angiographic follow-up

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Consistency Between Direct And Indirect Estimates of Stent Thrombosis

BP-BES Versus BMS

CoCr-EES Versus BP-BES

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Cardiac Death in 1 Year

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No significant difference between any comparisons

MI Within 1 Year

- PtCr-EES, ZES-R, CoCr-EES, ZES-E, SES, and BP-BES superior to BMS
- PtCr-EES, ZES-R, CoCr-EES, ZES-E, and SES superior to PES
- CoCr-EES tended to be superior to BP-BES and SES

TVR Within 1 Year

BMS << (PES ≒ ZES-E) < (ZES-R ≒ BP-BES ≒ SES ≒ CoCr-EES ≒ PtCr-EES)

- All DES superior to BMS
- CoCr-EES, SES, and BP-BES superior to PES
- CoCr-EES, SES, and BP-BES superior to ZES-E

Stent Thrombosis Network Meta-analysis Primary EP: ARC Definite ST (FU through 2 years) 49 RCTs, 50,844 pts

Palmerini T et al. Lancet 2012

Myocardial Infarction

Sirolimus		0.82	0.71	0.95									
Paclitaxel		1.02	0.90	1.20									
Everolimus		0.63	0.51	0.80									
Cotarolimus		0.69	0.52	0.89									
otarolimus-R		0,69	0.45	1.03	io	95%	Crl						
Paclitaxel		1.26	1.11	1.43	.89	0.79	1.09						
verolimus		0.77	0.64	0.95	89	0.78	1.07						
otarolimus		0.84	0.66	1.08	.81	0.64	1.01	lariza	tion				
otarolimus-R		0.84	0.57	1.22	94	0.73	1.24	141124					
		1200		100	71	0.31	1.09			10000			
verolimus		0.61	0.51	0.75				tate Ratio	95%	Crl			
otarolimus		0.66	0.52	0.86	00	0.87	1.15						
otarolimus-R		0.67	0.02	0.00	.00	0.07	1.15	0.32	0.27	0.38			
otaroninus-re		0.07	0.40	0.50	.07	0.71	1.07	0.48	0.41	0.58	rizat	tion	
automacioni		(1993)	2422	0404448	.05	0.65	1.27	0.28	0.22	0.38			
totarolimus		1.09	0.81	1.49	./6	0.38	1.22	0.56	0.43	0.72		0.5%	
totarolimus-R		1.09	0.76	1.51		222	1.1	0.39	0.23	0.66	Ratio	95%	Cri
					.87	0.71	1.08						
otarolimus-R	_	1.01	0.65	1.51	.05	0.82	1.29	1.50	1.30	1.76	0.39	0.34	0.45
0.10	Zotarolimus-R	10.00			0.77	0.37	1.23	0.88	0.69	1.15	0.61	0.53	0.69
Everolimus (Ref)	1.00	10.00						1.73	1.35	2.23	0.39	0.31	0.48
	Zotarolimus		* -		1.22	0.88	1.54	1.20	0.74	2.04	0.61	0.48	0.77
	Zotarolimus-R				0.87	0.45	1.32				0.44	0.27	0.68
Zotarolimus (Ref	0							0.59	0.45	0.76			
	Zotarolimus-R	• • • • • • • • • • • • • • • • • • •			0.74	0.33	1.23	1.14	0.88	1 /9	1.54	1.36	1.75
			Zotaro	limue-B	10.00			0.80	0.00	1 33	0.98	0.79	1.20
	0.10		uzotaro	iiiiiius-n	10.00	•		0.00	0.43	1.30	1.55	1.25	1.94
	Eve	rolimus (Ret)	i% Crl)	0.000				102-022	0.225	100.000.000	1.11	0.70	1.74
			Zotaro	limus				1.96	1.39	2.75			
			Zotaro	limus-R			•	1.36	0.90	2.11	0.63	0.52	0.78
	Zot	arolimus (Ref)									1.01	0.80	1.27
			Zotaro	limus-R	-			0.70	0.41	1.22	0.72	0.45	1.12
				Everoli	mus (Re	ef) 4.00		10.00					
				-a, que thi	map fin	Zota	irolimus	10.00	-		1.58	1 20	2 11
						RR 196%	Crilinus-	R			1 13	0.76	1.68
				7-1		E0ta	noninda-	1995 (S	and the second second		1.10	0.10	1.00
				Zotarol	imus (R	er) Toto		-	10 10		0.70	0.40	
						Zota	irolimus-	R			0.72	0.43	1.17
	irolimus aclitaxel verolimus otarolimus-R 'aclitaxel verolimus otarolimus otarolimus otarolimus-R totarolimus-R totarolimus-R totarolimus-R totarolimus-R totarolimus-R totarolimus-R totarolimus-R	irolimus aclitaxel verolimus otarolimus-R 'aclitaxel verolimus otarolimus otarolimus-R verolimus otarolimus-R totarolimus-R cotarolimus-R totarolimus-R cotarolimus-R totarolimus-R cotarolimus-R cotarolimus-R totarolimus-R cotarolimus-R	irolimus aclitaxel verolimus otarolimus-R iotarolimus-R verolimus otarolimus-R iotarolimus-R verolimus otarolimus-R iotarolimus-R otarolimus-R iotarolimus-R	irolimus actitaxel verolimus otarolimus co	irolimus 0.82 0.71 0.95 aclitaxel 1.02 0.90 1.20 verolimus 0.63 0.51 0.80 otarolimus-R 0.69 0.45 1.03 aclitaxel 1.26 1.11 1.43 verolimus 0.77 0.64 0.95 otarolimus-R 0.84 0.66 1.08 otarolimus-R 0.84 0.66 1.08 otarolimus-R 0.61 0.51 0.75 totarolimus-R 0.61 0.51 0.75 otarolimus-R 0.66 0.52 0.86 otarolimus-R 0.61 0.51 0.75 otarolimus-R 0.67 0.45 0.96 otarolimus-R 1.09 0.81 1.49 otarolimus-R 1.09 0.76 1.51 totarolimus-R 1.01 0.65 1.51 zotarolimus-R 1.00 1.002 204arolimus-R zotarolimus-R 2.01 1.002 204arolimus-R zotarolimus-R 2.01 1.002 204arolimus	irolimus 0.82 0.71 0.95 aclitaxel 1.02 0.90 1.20 verolimus 0.63 0.51 0.80 otarolimus-R 0.69 0.45 1.03 io raclitaxel 1.26 1.11 1.43 .89 verolimus 0.77 0.64 0.95 .83 otarolimus-R 0.84 0.66 1.08 .81 otarolimus-R 0.84 0.66 1.08 .81 otarolimus-R 0.61 0.51 0.77 .84 .95 otarolimus-R 0.66 0.52 0.86 .00 otarolimus-R 0.61 0.51 0.75 .05 otarolimus-R 0.67 0.45 0.96 .87 .05 .05 .05 .05 .05 cotarolimus-R 1.09 0.81 1.49 .76 cotarolimus-R 1.01 0.65 1.51 .05 cotarolimus-R 1.01 0.65 1.51 .05 zotarolimus-R 2.02 .037	irolimus 0.82 0.71 0.95 acitaxel 1.02 0.90 1.20 verolimus 0.63 0.51 0.80 otarolimus 0.69 0.45 1.03 10 otarolimus 0.69 0.45 1.03 10 95% otarolimus 0.84 0.66 0.95 89 0.79 otarolimus-R 0.84 0.66 1.05 0.71 0.31 otarolimus-R 0.66 0.52 0.86 00 0.87 otarolimus-R 0.66 0.52 0.86 00 0.87 otarolimus-R 0.66 0.52 0.86 0.0 0.87 otarolimus-R 1.09 0.81 1.49 76 0.38 o	irolimus 0.82 0.71 0.95 acitaxel 1.02 0.90 1.20 verolimus 0.63 0.51 0.80 otarolimus-R 0.69 0.45 1.03 io 95% Crl acitaxel 1.26 1.11 1.43 verolimus 0.69 0.45 1.03 io 95% Crl verolimus 0.66 0.64 0.95 otarolimus-R 0.84 0.66 1.08 otarolimus-R 0.84 0.67 1.22 otarolimus-R 0.84 0.57 1.22 otarolimus-R 0.61 0.51 0.77 otarolimus-R 0.61 0.51 0.77 otarolimus-R 0.67 0.45 0.96 otarolimus-R 0.67 0.45 0.96 otarolimus-R 1.09 0.81 1.49 76 0.38 1.22 otarolimus-R 1.09 0.76 1.51 05 0.82 1.23 otarolimus-R 1.01 0.65	irolimus acilitaxel verolimus otarolimus-R acilitaxel verolimus otarolimus-R otarol	irolimus aciitaxel verolimus otarolimus-R otarolimus otarolimus otarolimus otarolimus otarolimus otarolimus otarolimus otarolimus otarolimus otarolimus otarolimus otarolimus otarolimus otarolimus otarolimus otarolimus otarolimus cotarolimus cotarolimus cotarolimus R totarolimus R totarolimus cotarolimus cotarolimus R totar	irolimus 0.82 0.71 0.95 acitaxel 1.02 0.90 1.20 verolimus 0.63 0.52 0.89 0.69 0.45 1.03 0 95% Cri acitaxel 1.26 1.11 1.43 89 0.79 1.09 verolimus 0.61 0.651 0.89 0.78 1.07 otarolimus 0.84 0.657 1.22 94 0.73 1.24 otarolimus 0.61 0.51 0.75 1.22 94 0.73 1.24 verolimus 0.61 0.51 0.75 0.32 0.27 0.38 otarolimus-R 0.66 0.52 0.86 00 0.87 1.15 otarolimus-R 0.66 0.52 0.86 0.038 1.27 0.38 otarolimus-R 1.09 0.81 1.49 76 0.38 1.22 otarolimus-R 1.09 0.81 1.49 77 0.37 1.23 otarolimus-R 0.00 1.51 0.52 0.	irolimus 0.82 0.71 0.95 aciitaxel 1.02 0.90 1.20 verolimus 0.63 0.51 0.80 0tarolimus-R 0.69 0.45 1.03 100 95%, Crit aciitaxel 1.26 1.11 1.43 .89 0.79 1.09 verolimus 0.61 0.64 0.68 0.73 1.09 1.01 otarolimus-R 0.84 0.66 1.08 .81 0.64 1.01 otarolimus 0.61 0.51 0.77 0.38 0.27 0.38 otarolimus-R 0.61 0.51 0.76 0.57 0.38 0.22 0.38 otarolimus-R 0.61 0.51 0.76 0.51 0.38 1.27 0.28 0.22 0.38 otarolimus-R 1.09 0.76 1.51 05 0.38 1.22 0.38 0.59 0.43 0.72 otarolimus-R 1.09 0.76 1.51 0.50 0.38 1.22 0.38 0.45 0.51 0.51	irclimus 0.92 0.71 0.95 aciltaxel 0.63 0.51 0.80 otarolimus-R 0.669 0.52 0.89 otarolimus-R 0.669 0.45 1.03 verolimus-R 0.669 0.45 1.03 otarolimus-R 0.669 0.45 1.03 otarolimus-R 0.66 1.11 1.43 .69 0.79 1.09 verolimus 0.61 0.51 0.75 1.07 1.07 1.04 0.64 1.04 otarolimus-R 0.61 0.51 0.75 0.22 0.38 0.27 0.38 otarolimus-R 0.667 0.45 0.96 87 0.71 1.07 otarolimus-R 0.67 0.45 0.96 87 0.71 1.07 otarolimus-R 0.667 0.45 0.96 87 0.71 1.08 0.39 0.23 0.66 otarolimus-R 1.09 0.81 1.49 76 0.38 1.22 0.38 0.43 0.59 0.43 0.39 0.31 </td

Bangalore et al. Circulation. 2012;125:2873-289TR (95% Crl)

Stent Thrombosis Network Meta-analysis Primary EP: ARC Definite ST (FU through 2 years) 49 RCTs, 50,844 pts

SEOUL NATIONAL UNIVERSITY

Palmerini T et al. Lancet 2012

DES and Late Stent Thrombosis

- DES → repeat revascularization ↓
- DES → delayed vessel wall healing
 - \rightarrow abnormal vascular response \rightarrow potential for stent thrombosis
- Polymer in DES → Thrombogenic nidus

Joner et at. JACC 2006

Development of Newer Generation DES

	Drug	Stent	Strut Thickness	Polymer	Polymer Thickness
SES	Sirolimus	Stainless steel	140 µm	PEVA/PBMA	13.7 µm
PES	Paclitaxel	Stainless steel	97 µm	SIBS	17.8 µm
ZES-E	Zotarolimus	Cobalt Nickel	91 µm	Biolinx	4.8 µm
CoCr-EES	Everolimus	Cobalt Chromium	81 µm	PVDF	7.8 µm
PtCr-EES	Everolimus	Platinum Chromium	81 µm	Fluorinated copolymer	8 µm
ZES-R	Zotarolimus	Cobalt Chromium	89 µm	Biolinx	6 µm
BP-BES	Biolimus A9	Stainless Steal	120 µm	PLA	10 µm
			SNU-H	ospital (Seoul Na	tional University)