NEW GENERATIONS OF DRUG-ELUTING STENTS - A BRIEF REVIEW

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ABSTRACT

This review focuses on describing new generations of drug-eluting stents (DES) based on the use of novel stent platforms, coatings, and carrier systems, developed to enhance DES safety. Examples of various DES classes among the most clinically-used DES are briefly discussed.

Keywords: Drug-eluting stents (DES), biodegradable polymer DES, durable polymer DES, polymer-free DES, bioabsorbable vascular scaffolds.

BACKGROUND

Drug-eluting stents (DES) were designed to reduce in-stent neointimal proliferation, and thus, minimise in-stent restenosis (ISR), which is the major disadvantage of percutaneous coronary interventions with bare-metal stents (BMS). DES have revolutionised the treatment of coronary artery disease by reducing the rate of ISR from 20-40% with BMS to 6-8% with DES.

In recent years, however, concern has been raised regarding the long-term safety of DES and the risk of stent thrombosis (ST) and late restenosis due to neoatherosclerosis. This potential increased risk remains an area of uncertainty in the field of interventional cardiology. DES consist of a standard metallic stent, a polymer coating, and an antiproliferative drug that is embedded within a durable or biodegradable (bioabsorbable) polymer and released over time. Although the common basic concept of DES remains constant, all DES are not made equal and each type may vary significantly with respect to deliverability, efficacy, and safety (Table 1).

FIRST-GENERATION DES

First-generation DES include sirolimus-eluting stents (SES) and paclitaxel-eluting stents (PES).

Since their introduction into worldwide clinical practice in the years 2003 and 2004, first-generation DES - Cypher (SES; Cordis Corporation, Johnson & Johnson, Warren, NJ, USA) and Taxus (PES; Boston Scientific Corporation, Natick, MA, USA) - have dramatically reduced ISR and target vessel revascularisation (TVR) across virtually all lesion and patient subsets compared with BMS. However, their safety has been questioned because of suboptimal polymer biocompatibility leading to their propensity for late and very late ST,[1] and local drug toxicity. Concerns were based on human autopsy studies, which identified the durable polymers (DP) of these first-generation DES as possible triggers of chronic vessel wall inflammation, delayed hypersensitivity reactions, delayed arterial healing, incomplete stent strut re-endothelialisation due to inhibition of endothelial cell proliferation, stent malapposition, accelerated neoatherosclerosis, and polymer-induced increased risk of very late ST.[2–8] Also, DP used in first-generation DES have been associated with mechanical complications (polymer delamination and 'webbed' polymer surface leading to stent expansion issues) and nonuniform coating, resulting in unpredictable drug distribution and release.[9]

Table 1: Overview of first, second, and third-generation drug-eluting stents.

Series	Platform	Coating and Drug	Trials
Cypher®	316L stainless steel Bx Velocity stent (140 µm struts, 1.1176 mm crimped profile).	12.6 µm 3-layer coating (2 µm parylene C base coat, 10 µm main coat of PEVA, PBMA, and sirolimus, 0.6 µm top coat of PBMA). 80% of sirolimus elutes over ~30 days; remainder released by end of 90 days.	RAVEL, SAPPHIRE, SIRIUS
Taxus®	316L stainless steel Express2 stent (132 µm struts).	16 µm single-layer SIBS copolymer (nonresorbable elastomeric) coating containing paclitaxel, which elutes over ~90 days.	ELUTES, TAXUS II, ASPECT
Ion®	316L stainless steel PtCr alloy (81 µm struts for diameters 2.25–3.50 mm, 86-µm struts for 4.00 mm).	Triblock copolymer (composed of polystyrene and polyisobutylene units) coating containing paclitaxel.	PERSEUS
Promus®	L605 CoCr alloy ML Vision stent (81 µm struts, 1.0668 mm stent profile).	Durable PBMA, PVDF-HFP, and everolimus; 100% drug elution over 120 days.	SPIRIT I SPIRIT II
PROMUS Element™ Plus	PtCr alloy (minimum strut thickness 81 µm), open-cell stent design, short serpentine rings, helically distributed links, diameters of 2.25–4.0 mm, and lengths of 8–38 mm.	7 µm everolimus-eluting durable fluoropolymer coating.	DUTCH PEERS
Synergy®	Thin strut (74 µm) PtCr stent.	Ultrathin (4 µm) PLGA bioabsorbable polymer applied only to the abluminal surface, everolimus 38-179 µg, depending on stent length.	EVOLVE EVOLVE II
JACTAX®	Liberté (316 L) stainless steel stent, strut thickness of 96.5 µm.	Paclitaxel (0.6 µg/mm of stent length), bioabsorbable polymer DLPLA applied to the abluminal surface on premounted stent.	JACTAX Trial Drug Eluting Stent Trial
Xience V®	L605 CoCr ML Vision stent (81 µm struts).	7.6 µm fluoropolymer multilayer coating with 100 mcg/cm^2 everolimus.	SPIRIT III SPIRIT V EXCELLENT
Endeavor®	Cobalt chrome Driver stent (91 µm struts).	4.3 µm phosphorylcholine coating includes zotarolimus on 1 µm base coat.	ENDEAVOR I ENDEAVOR II
Resolute®	CoCr, open-cell stent design in a continuous, sinusoidal-helical pattern.	Biolinx polymer coating includes zotarolimus with extended release of 85% of zotarolimus within 60 days and almost 100% by 180 days.	TWENTE RESOLUTE All-Comers RESOLUTE International
Resolute Integrity®	CoCr, open-cell stent design, single, sinusoidal-formed, helically wrapped, locally laser-fused wire (strut thickness 91 µm), stent diameters of 2.25–4.0 mm, and lengths of 8–38 mm.	6 µm layer of coating that consists of zotarolimus and the BioLinx polymer system.	DUTCH PEERS

Series	Platform	Coating and Drug	Trials
Nobori®	Stainless steel, S-Stent™ strut thickness of 120 μm.	Bioabsorbable PLA, polymer thickness of 20 μm, biolimus A9, 15.6 μg/mm length.	NOBORI I, NOBORI I- 2nd Phase, NOBORI-JAPAN, COMPARE II NEXT
BioMatrix®	S-Stent platform, a thin, stainless steel, laser-cut, tubular stent, strut thickness of 137 μm.	Bioabsorbable PLA polymer applied to the abluminal surface, Biolimus A9 (15.6 μg/mm of stent length).	LEADERS
Yukon® Choice PC	Stainless steel, 316 LVM, modified microporous stent surface, strut thickness of 87 μm.	Abluminal coating with biodegradable PLA and shellac, polymer thickness of 5 μm, sirolimus.	ISAR-TEST 3 ISAR-TEST 4
Absorb BVS	Semicrystalline PLLA, strut thickness of 150 μm.	PDLA polymer, 8.2 μm/mm length, antiproliferative drug everolimus.	ABSORB Cohort A ABSORB Cohort B ABSORB II ABSORB Extend (ongoing)

PEVA: polyethylene vinyl acetate; PBMA: poly(n-butyl methacrylate); SIBS: styrene isoprene butadiene; PtCr: platinum chromium; CoCr: cobalt chromium; ML: multi-link; PVDF-HFP: poly(vinylidene fluoride-co-hexafluoropropylene); PLGA: poly(lactide-co-glycolide); DLPLA: D-lactic poly(lactic acid); PLA: poly(lactic acid); LVM: left ventricular mass; PLLA: poly-L-lactic acid; PDLA: poly(d-lactic acid).

SECOND-GENERATION DES

As a consequence, the extensive incentive towards the development of novel durable and absorbable (biodegradable) polymeric drug carrier systems and non-polymeric stent surfaces, and also the development of more modern stent platforms (ensuring better deliverability, radiopacity, flexibility, and radial strength), as well as the use of novel antiproliferative agents, resulted in the successful accomplishment of numerous second and third-generation DES.

The second-generation DES include the Endeavor (Medtronic, Minneapolis, MN, USA), Resolute (Medtronic), Xience V (Abbot Vascular, Santa Clara, CA, USA), and Promus (Boston Scientific, USA) stents, and utilise a more biocompatible DP. The Endeavor second-generation stents utilise a cobalt-chromium (CoCr) platform and a permanent phorylcholine polymer that facilitates the release of the sirolimus analogue, zotarolimus. The main representative of second-generation absorbable-polymer family of DES is the BioMatrix stent (Biosensors International, Singapore), which utilises a sirolimus analogue (Biolimus A9) and a biodegradable polylactic acid (PLA) polymer that completely dissolves over a 6-9 month period. CoCr, and later platinum chromium (PtCr), platforms used in second-generation DES permitted similar radial strength, enabling a thinner strut design and subsequently significantly improved deliverability.

To improve DES safety, second-generation DES have more biocompatible DPs, or bioabsorbable polymers, which are eventually bioresorbed, rendering the stent surface similar to BMS free of a chronic inflammatory stimulation. Some studies have shown that bioabsorbable polymer-based DES are more effective than BMS[10] and, by reducing the risk of very late ST, perhaps safer than first-generation DES.[11] However, second-generation fluorinated DP-based CoCr everolimus-eluting stents (Xience V, Abbott Vascular, and Promus, Boston Scientific) and PtCr everolimus-eluting stents (Promus Element, Boston Scientific) have been associated with lower rates of early, late, and very late ST compared with first-generation DES and BMS,[12] challenging the widespread belief that bioabsorbable polymers are necessary to minimise the risk of ST.

A recent meta-analysis[13] compared the short-term (1 month) and mid-term (1 year) performance of sirolimus, biolimus A9, and paclitaxel biodegradable-polymer DES, as well as the 1-year performance of biodegradable polymer DES with DP DES. The incidence of target lesion revascularisation (TLR) at 30 days was 0.4% in the biodegradable polymer SES, 0.7% in the biodegradable polymer PES, and 1.4% in the biodegradable polymer biolimus-eluting stents (BES). These incidences were statistically significantly different (overall p=0.01). At 1-year follow-up clinical endpoints were assessed in seven randomised controlled studies comparing biodegradable polymer DES with DP DES. It was observed that the risk of developing TLR at 1-year follow-up was not significantly different in DP DES compared to biodegradable polymer DES (OR=0.8, 95% CI=0.5-1.4, p=0.5). Similarly, the 1-year risk of definite ST was not significantly different in DP DES compared to biodegradable polymer DES (OR=0.7, 95% CI=-0.2-2.4, p=0.5). These results suggest that biodegradable, polymer DES do not necessarily perform better than DP DES, and that short, mid, and long-term results should be carefully judged for newly emerging biodegradable polymer DES before they become a new clinical standard.

Another, more recent, large-scale network meta-analysis[14] documented bioabsorbable polymer BES to be associated with superior clinical outcomes compared with BMS and first-generation DES, and similar rates of cardiac death/myocardial infarction (MI), and TVR compared with second-generation DP DES. The same paper from Palmerini et al.[14] highlighted, however, higher rates of definite ST with bioabsorbable polymer BES than with CoCr everolimus-eluting stents. The increased risk for definite ST with bioabsorbable polymer BES compared with CoCr everolimus-eluting stents was apparent both in the early period (before 30 days) and the late period (between 30 days and 1 year). These data demonstrate that the use of currently available bioabsorbable polymers is not associated with the lowest risk of ST, especially within the first year after stent implantation.

Polymers requiring active bioresorption have historically been associated with greater rates of inflammation than DPs.[15] Among all new generation DES the concept of non-polymeric or polymer-free DES deserves to be mentioned. A good example is Yukon Choice DES (Translumina, Germany), the first stent especially designed for nonpolymeric application of antiproliferative, anti-inflammatory, and/or antithrombotic drugs. The surface of the YUKON Choice DES contains micropores to enable the adsorption of different organic substances. The coating solution (biodegradable polylactide and shellac) fills the pores completely and creates a uniform layer. After the drug (sirolimus) is fully released, the microporous PEARL surface favours the adhesion of endothelial cells.

THIRD-GENERATION DES

Bioabsorbable Drug-Eluting Vascular Scaffolds (BVS)

Dramatic advances in bioabsorbable materials and technology have delivered the potential for a fully absorbable scaffold, which is able to mechanically support the coronary artery for a predetermined time period. BVS represent a new concept of providing transient vessel support with drug delivery capability but theoretically without the long-term limitations of metallic DES, such as permanent vessel caging and possible malapposition, risk of late ST, neoatherosclerosis, and local inflammation.[16-21] Also, permanent metallic stenting precludes the possibility of later surgical revascularisation, prevents late lumen enlargement, results in jailing of side-branches, and inhibits non-invasive imaging of coronary arteries using computed tomography (CT) and magnetic resonance imaging (MRI).[22-26] On the contrary, BVS have the unique ability of restoration of vascular physiology and anatomical integrity, such as native tortuosity and angulation, as they provide only a temporary scaffold necessary to maintain the patency of the vessel after intervention.

Currently, there are four materials used in BVS, of which lactide polymers, particularly poly-levo-lactic acid (PLLA), form the basis of several devices and are the most extensively investigated. Other materials include magnesium, polyanhydrides (salicylic acid and adipic acid), and polycarbonates (amino acids, e.g. tyrosine).

The absorbable metallic stent (Biotronik, Berlin, Germany) is composed of magnesium and some other rare metals, and is the only bioresorbable metallic stent implanted in humans. The device has a high mechanical strength and similar properties to the other metallic stents. The stent resorption is completed within 4 months, producing inorganic salts without causing a

significant inflammatory response.[27-31] The efficacy of the first-generation of magnesium stents was examined in the PROGRESS AMS trial, revealing a high incidence of TLR (45%) at 12 months and an increased late luminal loss (LLL) on angiograms at 4 months follow-up (1.08±0.49 mm). Intravascular ultrasound (IVUS) at 4 months follow-up revealed almost complete resorption of the device and a significant reduction in luminal dimensions due to neointima formation (45%), negative remodelling (42%), and to an increase in the plaque area outside the stent (13%). The negative remodelling was attributed to an early reduction of the scaffold radial force caused by too fast a resorption of the device. Thus, significant modifications using a different magnesium alloy, with increased radial strength and prolonged duration of the resorption, as well as the incorporation of paclitaxel elution within a biodegradable matrix to control the release of the antiproliferative drug, were necessary. The drug-eluting absorbable metallic stent (DREAMS) was tested in a clinical setting in the BIOSOLVE-I study, which showed TLR rate at 6 months of 4.3%, and LLL of 0.64±0.50 mm.[32] DREAMS was further modified to create the next generation DREAMS 2 with radiopaque markers at both ends and sirolimus elution instead of paclitaxel.[33] Further progress of this exciting project is eagerly awaited.

One of the most clinically widely used - and, to date, most widely investigated - BVS is ABSORB (Abbott Vascular). This fully resorbable BVS has been tested in the ABSORB cohort A study, and demonstrated excellent long-term clinical results up to 3 years with a major adverse cardiac event rate (MACE) of 3.4%.[34-36]

The scaffold consisted of a backbone of PLLA coated with poly-DL-lactide (PDLLA), which contained and controlled the release of the antiproliferative drug everolimus. The first-generation of BVS showed slightly higher acute recoil than conventional metallic platform stents, and at 6 months, an 11.8% reduction in scaffold area and a 24.3% decrease in minimal luminal area (late recoil).[37]

Although the short and long-term results of the ABSORB cohort A trial were favourable, reinforcement of the mechanical performance of the device and prolongation of its mechanical integrity up to 6 months were necessary. To enhance the mechanical strength of the struts and to reduce immediate and late recoil, the strut design

and the manufacturing process of the polymer were modified in the revised version, BVS 1.1., with more uniform strut distribution, reduced maximum circular unsupported surface area, more uniform vessel wall support, and drug transfer. Also, the modified manufacturing has resulted in a lower hydrolysis rate of the polymer, thus preserving its mechanical integrity for a longer period of time. Clinical outcomes in Cohort B demonstrate a MACE rate of 8.9% at 2 years follow-up.[38]

CONCLUSION

In summary, based on available data at the time this review was written, the newer biocompatible DP everolimus-eluting stents and Resolute zotarolimus-eluting stents, and the biodegradable polymer biolimus-eluting stents, maintain the efficacy of gold standard SES. However, and disappointingly, with respect to safety endpoints, second-generation biodegradable polymer-based DES fell short of high expectations, and differences when compared with second-generation DP DES become obvious, with everolimus-eluting stents and Resolute zotarolimus-eluting stents emerging as the safest stents to date.[39] Moreover, second-generation DES, particularly the everolimus-eluting stent (Xience V, Abbot; Promus, Boston Scientific), significantly reduced the risk of TVR in patients with ST-segment-elevation MI (STEMI) without increasing the risk of adverse safety outcomes, including rates of ST, when compared with BMS.[40] BVS is a relatively new technology introduced to address the limitations of the traditional metallic stents.

However, these devices still have limited applications, and to date they do not outperform the current generation of high performance metallic drug-eluting devices. Evidence from the validation of the second-generation BVS indicates that they have overcome the drawbacks of the first-generation (e.g. rapid bioresorption and device shrinkage) and that they are able to compete with the metallic stents in terms of safety and efficacy. However, it remains to be demonstrated from the ongoing and upcoming clinical studies whether BVS can truly restore vascular integrity and function.

Finally, when assessing the efficacy and safety of any DES, obviously everything matters; biodegradability of polymer, the optimal combination of stent alloy, design, strut thickness,

polymer, and the drug. Nonetheless, however important the quality and performance of DES may seem, stents are only one of numerous, often underestimated but complex and critically relevant, interplaying factors influencing the individual clinical outcome (e.g. lesion complexity, coronary anatomy, comorbidities, operator technical skill, and experience etc.). Thus, effective management of patients undergoing percutaneous coronary intervention requires focus on clinical and angiographic data to guide optimal device choice in the continuously expanding scenario of coronary stents.

REFERENCES

1. Stettler C et al. Outcomes associated with drug-eluting and bare-metal stents: a collaborative network meta-analysis. Lancet. 2007;370:937-48.

2. Bertrand OF et al. Biocompatibility aspects of new stent technology. J Am Coll Cardiol. 1998;32(3):562–71.

3. Nakazawa G et al. Drug-eluting stent safety: findings from preclinical studies. Expert Rev Cardiovasc Ther. 2008;6(10):1379–91.

4. Nakazawa G et al. Delayed arterial healing and increased late stent thrombosis at culprit sites after drug-eluting stent placement for acute myocardial infarction patients: an autopsy study. Circulation. 2008;118(11):1138–45.

5. Cook S et al. Incomplete stent apposition and very late stent thrombosis after drug-eluting stent implantation. Circulation. 2007;115(18):2426–34.

6. Siqueira DA et al. Late incomplete apposition after drug-eluting stent implantation: incidence and potential for adverse clinical outcomes. Eur Heart J. 2007;28(11):1304 –9.

7. Joner M et al. Pathology of drug-eluting stents in humans: delayed healing and late thrombotic risk. J Am Coll Cardiol. 2006;48(1):193-202.

8. Kounis NG et al. Coronary stents, hypersensitivity reactions, and the Kounis syndrome. J Interv Cardiol. 2007;20(5):314–23.

9. Hossainy S, Prabhu S. A mathematical model for predicting drug release from a biodurable drug-eluting stent coating. J Biomed Mater Res A. 2008;87(2):487–93.

10. Raber L et al. Effect of biolimus-eluting stents with biodegradable polymer vs bare-metal stents on cardiovascular events among patients with acute myocardial infarction: the COMFORTABLE AMI randomized trial. JAMA. 2012;308(8):777-87.

11. Stefanini GG et al. Biodegradable polymer drug-eluting stents reduce the risk of stent thrombosis at 4 years in patients undergoing percutaneous coronary intervention: a pooled analysis of individual patient data from the ISAR-TEST 3, ISAR-TEST 4, and LEADERS randomized trials. Eur Heart J. 2012;33(10):1214-22.

12. Palmerini T et al. Stent thrombosis with drug-eluting and bare-metal stents: evidence from a comprehensive network meta-analysis. Lancet. 2012;379(9824):1393-402.

13. Ahmed TA et al. Clinical performance of drug-eluting stents with biodegradable polymeric coating: a meta-analysis and systematic review. EuroIntervention. 2011;7(4):505-16.

14. Palmerini T et al. Clinical outcomes with bioabsorbable polymer versus durable polymer-based drug-eluting and bare-metal stents: evidence from a comprehensive network meta-analysis. J Am Coll Cardiol. 2014;63(4):299-307.

15. De Scheerder IK et al. Biocompatibility of biodegradable and nonbiodegradable polymer-coated stents implanted in porcine peripheral arteries. Cardiovasc Intervent Radiol. 1995;18(4):227-32.

16. Ormiston JA and Serruys PWS. Bioabsorbable coronary stents. Circ Cardiovasc Interv. 2009;2(3):255–60.

17. Waksman R. Biodegradable stents: they do their job and disappear. J Invasive Cardiol. 2006;18(2):70–4.

18. Finn AV et al. Pathological correlates of late drug-eluting stent thrombosis: strut coverage as a marker of endothelialization. Circulation. 2007;115(18):2435–41.

19. Hoffmann R et al. Patterns and mechanisms of in-stent restenosis: a serial intravascular ultrasound study. Circulation. 1996;94(6):1247–54.

20. Togni M et al. Sirolimus-eluting stents associated with paradoxic coronary vasoconstriction. J Am Coll Cardiol. 2005;46(2):231–6.

21. Barlis P et al. Coronary bioabsorbable magnesium stent: 15-month intravascular ultrasound and optical coherence tomography findings. Eur Heart J. 2007;28(19):2319.

22. Cademartiri F et al. Usefulness of 64-slice multislice computed tomography coronary angiography to assess in-stent restenosis. J Am Coll Cardiol. 2007;49(22):2204–10.

23. Erbel R et al. Temporary scaffolding of coronary arteries with bioabsorbable magnesium stents: a prospective, non-randomised multicentre trial. Lancet. 2007;369(9576):1869–75.

24. Eggebrecht H et al. Images in cardiovascular medicine. Novel magnetic resonance-compatible coronary stent: the absorbable magnesium-alloy stent. Circulation. 2005;112(18):e303–4.

25. Okamura T et al. 3-Dimensional optical coherence tomography assessment of jailed side branches by bioresorbable vascular scaffolds: a proposal for classification. JACC Cardiovasc Interv. 2010;3(8):836–44.

26. Serruys PW et al. A bioabsorbable everolimus-eluting coronary stent system (ABSORB): 2-year outcomes and results from multiple imaging methods. Lancet. 2009;373(9667):897–910.

27. Serruys PW et al. From metallic cages to transient bioresorbable scaffolds: change in paradigm of coronary revascularization in the upcoming decade? Eur Heart J. 2012;33(1):16–25b.

28. Waksman R. Biodegradable stents: they do their job and disappear.

J Invasive Cardiol. 2006;18(2):70–4.

29. Waksman R et al. Safety and efficacy of bioabsorbable magnesium alloy stents in porcine coronary arteries. Catheter and Cardiovasc Interv. 2006;68(4):607-17.

30. Waksman R. Current state of the absorbable metallic (magnesium)

stent. EuroIntervention. 2009;5(Suppl F):F94–7.

31. Waksman R et al. Early- and long-term intravascular ultrasound and angiographic findings after bioabsorbable magnesium stent implantation in human coronary arteries. JACC: Cardiovasc Interv. 2009;2(4):312–20.

32. Haude M. From PROGRESS to DREAMS. PCR focus group on bioresorbable vascular scaffolds. Session 6: CLINICAL DATA: Current status – Part I. Presented at EuroPCR, March 2012, Rotterdam, the Netherlands.

33. Waksman R. Lessons learned from preclinical studies of magnesium scaffolds (Biotronik's DREAMS program). PCR focus group on bioresorbable vascular scaffolds. Session 3: Understanding the basics of polymer bioresorption in vivo – Part II. EuroPCR, March 2012, Rotterdam,

the Netherlands.

34. Ormiston JA et al. A bioabsorbable everolimus-eluting coronary stent system for patients with single de-novo coronary artery lesions (ABSORB): a prospective open-label trial. Lancet. 2008;371(9616):899–907.

35. Onuma Y et al. Three-year results of clinical follow-up after a bioresorbable everolimus-eluting scaffold in patients with de novo coronary artery disease: the ABSORB trial. EuroIntervention. 2010;6(4):447–53.

36. Tanimoto S et al. Late stent recoil of the bioabsorbable everolimus-eluting coronary stent and its relationship with plaque morphology. J Am Coll Cardiol. 2008;52(20):1616–20.

37. Okamura T et al. In vivo evaluation of stent strut distribution patterns in the bioabsorbable everolimus-eluting device: an OCT ad hoc analysis of the revision 1.0 and revision 1.1 stent design in the ABSORB clinical trial. EuroIntervention. 2010;5(8):932–8.

38. Dudek D. Evaluation of the absorb everolimus eluting bioresorbable vascular scaffold (ABSORB BVS) in the treatment of patients with de novo native coronary artery lesions: 2 year clinical results of ABSORB cohort B trial. J Am Coll Cardio. 2012;59(13s1):E319.

39. Navarese EP et al. Safety and efficacy outcomes of first and second generation durable polymer drug eluting and biodegradable polymer biolimus eluting stents in clinical practice: comprehensive network meta-analysis. BMJ. 2013;347:f6530.

40. Bangalore S et al. Outcomes with various drug-eluting or bare-metal stents in patients with ST-segment elevation myocardial infarction: a mixed treatment comparison analysis of trial level data from 34 068 patient-years of follow-up from randomized trials. Circ Cardiovasc Interv. 2013;6(4):378-90.