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Clinical Outcome and Benefits with Bio Absorbable Coronary Stent

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Abbreviations: BP: Bioabsorbable Polymer; BES: Biolimus-Eluting Stents; SES: Sirolimus-Eluting Stents; EES: Everolimus-Eluting; PES: Paclitaxel Eluting Stents; DES: Drug Eluting Stents; ZES: Zotarolimus-Eluting Endeavor

Introduction

Clinical trials including randomized clinical trial or nonrandomized (observational) can be categorized into comparative stent studies, either between

a) the two bioabsorbable stent generations; or

b) between bioabsorbable stent and other durable (or permanent, or biostable) stents; or

c) bioabsorbable stent assessment studies.

In most of studies the following bioabsorbable polymer-based drug eluting are used:

a) bioabsorbable polymer (BP)-based Biolimus-eluting stents (BP-BES);

b) bioabsorbable polymer-based Sirolimus-eluting stents (BP-SES);

c) bioabsorbable polymer Paclitaxel eluting stents (BP-PES);

d) Bioabsorbable polymer-based Everolimus-eluting (BP-EES); and

e) bioabsorbable Rapamycin-eluting stents (BP-RES).

The comparator durable polymer drug eluting stents (DP-DES) are:

a) durable polymer Sirolimus eluting stents (DP-SES);

b) durable polymer Paclitaxel eluting stents (DP-PES);

c) durable polymer cobalt chromium Everolimus eluting stents (DP-CoCr-EES);

d) durable polymer platinum chromium Everolimus eluting stents (DP-PC-EES);

e) durable polymer zotarolimus-eluting Endeavor(DP-ZES-E); and

f) Durable polymer Zotarolimus-eluting Resolute (DP-ZES-R). Some studies compared bioabsorbable DES with polymer free DES (PF-DES) [1]. The reported outcomes of the above mentioned clinical trials are major adverse cardiac events (MACE), which is a composite of adverse cardiac events including cardiac mortality, myocardial infarction (MI), and target lesion revascularization (TLR) and target vessel revascularization(TVR); all-cause-mortality; cardiac mortality; MI; stent thrombosis (ST); late stent thrombosis(LST); TLR; and TVR.

Non-Randomized (Observational)

The three non-randomized clinical trials, which we described in this review, are:

i) Igaki;

ii) ABSORB;

iii) BIOSOLVE I.

which are summarized in Table 1. Igaki is the first fully biodegradable stent [Igaki-Tamai stent (Kyoto Medical Planning Co, Ltd, Kyoto, Japan)] implanted in human coronary arteries. Preliminary and 6-month results of Igaki stent suggested feasibility, safety and not stent thrombosis and no major cardiac event occurred within 30 days and no major cardiac event developed within 6 months. The 6-month follow-up of all patients showed acceptable restenosis and target lesion revascularization rate, and no deaths, myocardial infarctions or CABGs were recorded [2]. The Igaki-Tamai stent required 3 years to disappear from human coronary arteries. Clinical follow up rate was 100% at 4 years; 98%

at 7 years and 96% at 10 years. Survival rates free of all-cause death, cardiac death and major adverse cardiac events (MACS) at 10 years were 87%, 98%, and 50% respectively [3]. The cumulative rates of TLR were 16% at 1 year,18% at 5 years and 28% at 10 years. Intravascular ultrasound data shows that the stent struts mostly disappeared within 3 years.

Table 1: Non-Randomized (Observational) Clinical Trials on Bioabsorbable Coronary Stents.

Clinical trial name/ sample size	intervention/ comprator	Main outcome	Study design/length of study		Ref.
Igaki / N=50 10 years	IgaKI- Tamai stent (made in kyoto medical planning co, Ltd, kyoto, Japan)It is a coil stent made of PLLA monofilamenta and does not have any drug elution	all-cause death, cardiac death and major adverse cardiac events (MACS);TLR,definite/ probable scaffold thrombosis	observational prospective cohort study: single arm, single center	feasibility, safety and not stent thrombosis and no major cardiac event occurred within 30 days and no major cardiac event developed within 6 months.Acceptable MACS and scaffold thrombosis rates without stent recoil and vessel remodeling after 10 years suggested long-term safety	[Circulation_ Igaki_2000] [circulation_ Igaki_2012]
BIOSOLVE I/ n=46patients with 47 lesions	magnesium-based paclitaxel-eluting absorbable metal scaffold	Primary Outcome: Target Lesion Failure [Time Frame: a composite of cardiac death, target vessel myocardial infarction, and clinically driven target lesion revascularisation, at 6 and 12 months. Overall device and procedural success was 100%. target lesion failureat 6 months and 12 months were 4% and 7% respectively with no safety concern.	prospective, multicenter, Non-Randomized Single Group Assignment Open Label/12 months	feasibility, a good safety profile, and promising clinical and angiographic performance results up to 12 months	(BIOSOLVE-I)
ABSORB/cohort-A trial enrolled 30 patients /ABSORB cohort-B enrolled 101 patients/ 4 years	BP-EES poly-L-lactic acid that provides the support and a coating of poly-D, L-lactic acid that contain the antiproliferative agent everolimus	cardiac death, myocardial infarction, ischemia driven target lesion revascularization (TLR), ischemia-driven major advance cardiac event (MACE) and stent thrombosis	Prospective observational open-label consists of two different cohort studies (cohort-A and cohort-B)	At four years low ishamia-driven MACE rate of 3.4% without any late complications such as thrombosis and the device was safe with no cardiac deaths, no ischemic-driven target lesion revascularization or scaffold patency and target lesion restenosis	[ABSORB_ Lancet_2008].

Due to the small number of patients, it is difficult to comment on events that have a low incidence, especially scaffold thrombosis. Late angiography and IVUS (intravascular ultrasound) were not dedicated by the protocol but was based on clinical indications. Therefore, angiography and IVUS follow-up studies were performed in a relatively small number of patients so there is the potential for bias. Acceptable MACS and scaffold thrombosis rates without stent recoil and vessel remodeling suggested a long-term (>10 Years) safety of the Igaki-Tamai stent [3]. ABSORB cohort trial consists of two different cohort studies: i) cohort-A and ii) Cohort-B (B1, B2). The ABSORB cohort-A trial enrolled 30 patients with a single de novo native coronary artery lesion.

ABSORB cohort-B trial is the multi center, single-arm trial enrolled 101 patients with up to two de novo in a native coronary artery [ABSORB_Lancet_2008]. After two years, the stent was completely bio absorbed, vasomotion restored, and restenosis prevented with no compromise of luminal area, which means clinically safe, suggesting freedom from late thrombosis [4]. The four-year clinical outcomes of the ABSORB cohort-A trial demonstrated a low ischaemia-driven MACE rate of 3.4% without any late complications such as thrombosis and the device was safe with no cardiac deaths, no ischemic-driven target lesion revascularization or any scaffold patency and target lesion restenosis [5,6]. Due to the small late recoil compared with conventional metallic platform stents, the following improvements were introduced to the second-generation bioabsorbable stent:

i) Enhancing mechanical strength;

ii) More durable support to the vessel wall;

iii) Reducing maximum circular unsupported surface area; and

iv) Having a more uniform strut distribution and drug delivery.

The performance of this next- generation was subsequently investigated in the ABSORB Cohort B Trial, which was reported excellent clinical results up to 1-year follow-up [5,7]. There were no additional ID-MACE between six months and four years in the entire cohort; there was no instance of stent thrombosis according to either protocol or ARC definition [8,9]. Studying the clinical impact of acute scaffold disruption and late strut discontinuity of the second-generation revealed acute scaffold disruption was a rare phenomenon that has been associated with angina symptoms whereas late strut discontinuity was observed in approximately 40% of patients could be considered as an optical coherenc tomography finding of a normal bioresorption process without clinical implications [10].

BIOSOLVE-1 assessed the safety and performance of a new magnesium-based paclitaxel-eluting absorbable metal scaffold (DREAMS) in symptomatic patients with de-novo coronary lesions. Overall device and procedural success was 100%.
Target lesion failure at 6 months and 12 months were 4% and 7%, respectively, with no safety concern. No cardiac death or scaffold thrombosis occurred [11].

Randomized Clinical Trials

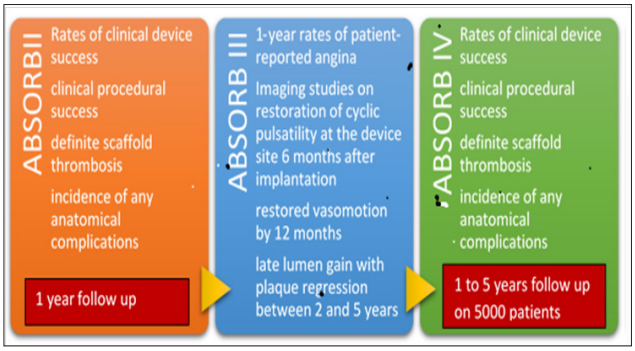

Figure 1: Clinical trial parameters for evaluate the safety and efficacy of the BP-EES Vs. metallic Everolimus-eluting stent XIENCE stent (CoCr-EES).

Figure 1. shows the Clinical trial parameters for evaluate the safety and efficacy of the BP-EES Vs. metallic Everolimus-eluting stent XIENCE stent (CoCr-EES) in ABSORB II, ABSORB III, ABSORB IV studies. ABSORB II study aiming to evaluate the safety and efficacy the BP-EES/metallic Everolimus-eluting stent XIENCE stent (CoCr-EES) [11]. Rates of clinical device success, clinical procedural success, definite scaffold thrombosis and the overall rate of definite or probable scaffold thrombosis and the incidence of any anatomical complications assessed by angiography were not significant between two treated groups. (ABSORB ii one year). In a post-hoc analysis, cumulative angina rates at 1 year were significantly lower in the bioresorbable scaffold group than in the metallic stent group. The BP-EES group also demonstrated less use of nitrates and less revascularization, which may have been driven by the reduction in angina [13] (Figure 1).

ABSORB III is much larger randomized trial compared with ABSORB II. As a result, the power of ABSORB III to detect differences in either efficacy or safety between the control metallic platform and BP-EES is going to be much greater [14]. The 1-year rates of patient-reported angina were also nearly identical with the two devices [15]. Imaging studies support the novel attributes of bioresorbable scaffolds with restoration of cyclic pulsatility at the device site 6 months after implantation, restored vasomotion by 12 months, and late lumen gain with plaque regression between 2 and 5 years, benefits that are not possible with permanent metallic stents [15-18]. However, if there are benefits from these attributes, they are likely to become evident only in the longer term. The ongoing ABSORB IV trial [ClinicalTrials.gov number, NCT02173379], which will enroll approximately 5000 patients, has a powered primary endpoint of improved rates of target-lesion failure at 1 to 5 years after implantation, an outcome that is designed to address this question. ABSORB IV is the continuation of ABSORB III and the data from ABSORB III and ABSORB IV will be pooled to support the ABSORB IV primary endpoint.

LEADER is a randomized Trial of Biolimus-eluting Stents with a Biodegradable Polymer versus Sirolimus-eluting Stents with a Durable Polymer [19]. (The safety benefit of the BP-BES compared with DP-SES was related to a significant reduction in very late ST (>1 year) and associated composite clinical outcomes [20]. Biodegradable polymer BES maintained non-inferiority and improved long-term clinical outcomes compared to SES through 5 years (P= 0.071) with 74% relative risk reduction in very late definite stent thrombosis. The benefit of biodegradable polymer BES emerged in the very late phase [19,21]. COSTAR II (Cobalt chromium Stent with Antiproliferative for Restenosis) trial is designed to compare BP-PES/DP-PES stent in single and multivessel percutaneous coronary intervention [22]. Paclitaxel elution from a stent coated with biostable polymer (TAXUS) reduces restenosis after PCI. The COSTAR DES is a novel stent with laser-cut reservoirs containing bioresorable polymer loaded to elute 10g paclitaxel/30 days [23]. The COSTAR II study demonstrates that the COSTAR DES is no inferior in clinical and angiographic performance compared with the TAXUS DES. The relative benefit attributable to the TAXUS stent is predominantly due to lower rates of clinically driven TVR, with no differences observed in the incidences of death, MI, or stent thrombosis by the end of 9 months' follow-up [24].

NEVO RES-1 compared the NEVOTM sirolimus-eluting coronary stent system (NEVO SES) and the TAXUS LibertéTM paclitaxel-eluting stent. Six-month angiographic results demonstrated the superiority of the NEVO SES over the TAXUS PES for the primary endpoint, in-stent late loss [nevores 6]. No stent thrombosis occurred in the NEVO SES group.No definite or probable stent thrombosis was recorded in the NEVO SES group at two years. Numerical differences favouring the NEVO SES that were observed at six months continued to increase over the 24 months of follow-up [25]. EVOLVE II (DP-PtCr-EES(PROMUS)/(SYNERGY) BP-PtCr-EES)

supports the premise that the safety and efficacy of SYNERGY are at least comparable to the predicate PtCr durable polymer EES [26]. COMPARE II study is the first adequately powered trial to compare a biodegradable polymer-coated DES with Everolimus-eluting Xience as a gold standard, showed that a biodegradable polymer DES is at least as efficacious and safe as the Everolimus-eluting stent up to 12 months after implantation [27,28].

Results of randomised trials and meta-analyses have shown that the second generation Eeverolimus-eluting stent significantly reduces the need for repeat revascularization and is also better at preventing stent thrombosis and myocardial infarction than are the early-generation sirolimus-eluting or paclitaxel-eluting stents. Therefore, the Everolimus-eluting Xience or Promus stents are the gold standard to which new stent designs should be compared [29]. SORT OUT V the effects of a biodegradable polymer biolimus-eluting stent compared with a durable polymer-coated sirolimus-eluting stent in 1229 patients (1532 lesions). The definite stent thrombosis at 12 months was significantly more in the biolimus-eluting stent group than in the sirolimus-eluting stent group. At 1-year follow-up, the biodegradable polymer biolimus-eluting Nobori stent did not improve clinical results compared with a first-generation sirolimus-eluting stent. Long-term data and result are needed to make recommendations for the role of this biolimus-eluting stent in routine clinical practice [30]. Table 2 presented summerized outcomes in randomized clinical trial (Table 2).

Table 2: Randomized Clinical Trials on Bioabsorbtion Stents.

Clinical Trial Name/ Sample Size	Intervention/ Comprator	Main Outcome	Study Design/Length of Study		Ref.
ABSORB II n=501 (2:1) ratio/ 3 years	BP-EES/ metallic everolimus-eluting stent XIENCE stent (CoCr-EES)	Primary outcome (vasomotion;minimum lumen diameter at 3 years after nitrate admin-istration minus minimum lumen diameter post procedureafter nitrate administration; Intravascular ultrasound secondary endpoints; composite clinical secondary endpoints;Scaff old or stent thrombosis timing)	randomized, active-controlled, single-blinded, multicenter (40 center two-arm)	At 2 years there were no significant differences in the clinical outcomes between the two groups regarding PoCE (all death, all MI and all revascularization) and DoCE (cardiac death, TV-MI and TLR)	
ABSORB III/ n=2008(2:1 ratio)	BP-EES / everolimus-eluting cobalt–chromium (Xience)CoCr-EES;	noninferiority (margin, 4.5 percentage points for the risk difference) and superiority, was target-lesion failure (cardiac death, target-vessel myocardial infarction, or ischemia-driven target-lesion revascularization) at 1 year.	multicenter, single-blind, active-treatment, controlled clinical trial/ 5 years	target-lesion failure at 1 year were 1.7 percentage points higher in the Absorb group than in the Xience group, a nonsignificant difference that met the study criteria for noninferiority The 1-year rates of patient-reported angina were also nearly identical with the two devices.	[ABSORB III DESIGN]
COMPARE II/n=2707// 5. years	BP-BES (Nobori)/ DP- Co Cr-EES (Xience V)	composite of safety (cardiac death and non-fatal myocardial infarction) and efficacy (clinically indicated target vessel revascular- isation) at 12 months. Secondary endpoints were a composite of major adverse cardiac events (cardiac death, non-fatal myocardial infarction, and clinically driven target-lesion revascularisation within a 12 month follow- up) and a composite of cardiac death, non-fatal myocardial infarction, and target vessel revascularisation at 3 and 5 years.	open-label, prospective, randomised, controlled, non-inferiority trialat 12 sites with no restrictions on the number of lesions or vessels to be treated, the location of lesions, or lesion length The only inclusion criteriawere age older than 18 years, life expectancy of 5 years or longer(	Not any significant difference fortheprimary composite endpoint between stent types, nor did the individual primary endpoint components or the stent thrombosis rates after 12 months. BP-BES (Nobori) stent are as safe and efficacious as the current standard of a thin-strut everolimus-eluting stent with a durable biocompatible polymer. DP- Co Cr-EES(Xience V)	
COMPARE II/n=2707/ (2; 1)/ 5 years	BP-BES (Nobori)/ DP- Co Cr-EES(Xience V)	composite of safety (cardiac death and non-fatal myocardial infarction) and efficacy (clinically indicated target vessel revascular- isation) at 12 months. Secondary endpoints were a composite of major adverse cardiac events (cardiac death, non-fatal myocardial infarction, and clinically driven target-lesion revascularisation within a 12 month follow- up) and a composite of cardiac death, non-fatal myocardial infarction, and target vessel revascularisation at 3 and 5 years.	open-label, prospective, randomised, controlled, non-inferiority trial (02;1) /5 years follow up	Not any significant difference for the primary composite endpoint between stent types, nor did the individual primary endpoint components or the stent thrombosis rates after 12 months. BP-BES (Nobori) stent are as safe and efficacious as the current standard of a thin-sturteverolimus-eluting stent with a durable biocampatible polymer. DP-Co Cr-EES (Xience V)	

(LEADERS) (N = 1,707)/ 5 years	BP-BES/DP-SES	Assessed at 5 years) MACE TLR, TVR;cardiac mortality, MI, and ST	Multi-center (10 center), assessor-blind, noninferiority, "all-comers"clinical trial	After 3 year follow-up, there was not any statistically significant difference between BP-BES and DP-SES in overall major adverse cardiac events (MACE: a composite of cardiac death, MI, TVR), cardiac mortality, MI, TLR and TVR, and ST. After5-year follow-up, a statistically significant reduction reported in very late ST (> 1year) with BP-BES P = 0.0034)]	[LEADER 3 year] (LEADER 5 year)
(NEVORes-Elution IDuration: 2 years months/394	BP-SES/DP-PES	Assessed at 6-month) MACE; Death MI; ST; TLR	prospective multicentrerandomised study, (single de novo lesions.)	Proved the superiority of NEVOSES over TAXUS Liberte PES for the primary angiographic end point of in-stent late loss	[nevores 2 year] [nevores 6]
COSTAR II Duration:9 Month N= 1700 single- and multivessel (3:2 ratio)	BP-PES/DP-PES	Assessed at 8-month) MACE; TVR	prospective, multicenter, noninferiority (0 COSTAR versus TAXUSstudy design	CoStar DES is noninferior in clinical and angiographic performance compared with the TAXUS DES	
EVOLVE II n=1684 (1:1)	platinum chromium (PtCr) metal alloy stent that elutes everolimus DP-PtCr-EES(PROMUS)/ (SYNERGY) BP-PtCr-EES	The primary end pointwas the rate of 12-month target lesion failure (TLF); Secondary clinical end points included individual components of TLF,, all-cause death, and stent thrombosis	prospective, multicenter (125 clinical sites) randomizedsingle-blindnoninferiority trial	supports the premise that the safety and efficacy of SYNERGY are at least comparable to the predicate PtCr durable polymer EES.	
SORT OUT V /n=2468	BP-BES (nobori)/DP-SES (Cypher Select Plus)	the primary endpoint—a composite of safety (cardiac death, myocardial infarction, defi nite stent thrombosis) and effi cacy (target vessel revascularisation)		At 1-year follow-up, the biodegradable polymer biolimus-eluting Nobori stent did not improve clinical results compared with a first-generation sirolimus-eluting stent.	

Discussion

In the LEADERS (Limus Eluted from A Durable versus ERodable Stent coating) trial, a biolimus-eluting bioabsorbable polylactic-acid polymer-coated stent was compared with a first-generation sirolimus-eluting stent with a durable vinyl-acrylate copolymer showed non-inferiority between both stent types at 9 months and 12 months,(LEADERS) but after 4 years follow-up the definite very late (>1 year) stent thrombosis rate and the number of patients reaching the primary endpoint (composite of cardiac death, myocardial infarction, and clinically indicated target vessel revascularization) were significantly lower with the biolimus-eluting stent than with the sirolimus-eluting stent [21]. This finding is particularly relevant because definite late stent thrombosis is associated with serious events such as myocardial infarction and mortality. Longer-term follow-up of the COMPARE II trial will show whether the beneficial effect of the biodegradable polymer biolimus-eluting stent on late stent thrombosis also applies when compared with newer-generation DES. A comprehensive network meta-analysis compared major differences in safety and efficacy of BP-BES with BMS and durable polymer eluting stents including DP-PES, DP-SES, DP-EES (DP-CoCr-EES, DP-PtCr-EES) and DP-ZES (DP-PC-ZES, DP-Re- ZES) [31].

In this large-scale network meta-analysis, BP-BES were associated with superior clinical outcomes compared with BMS and first-generation DES and similar rates of cardiac death/MI, MI, and TVR compared with second-generation DP-DES but higher rates of definite ST than CoCr-EES(31).Risk for definite ST with BP-BES compared with CoCr-EES was apparent both in the early period (before 30 days) and the late period (between 30 days and 1 year) but conversely, a nonsignificant trend was present for a

reduced rate of very late ST (beyond 1 year) with BP-BES compared with CoCr-EES . These data demonstrate that use of BP might not be associated with the lowest risk of ST, especially within the first year after stent implantation. Polymers requiring active bio resorption have historically been associated with greater rates of inflammation than DP. Moreover, although polylactic acid (the BP used in the Biomatrix and Nobori stents [Terumo Corporation] in the present report) induces relatively low levels of inflammation, other BP might theoretically be more inert and/or completely resorb faster (e.g., in 3 months compared with 6 to 9 months in the current BP-BES), permitting the late benefits of BP-DES to emerge at an earlier time period.

Therefore, any potential advantages of BP-based DES over biocompatible DP-based stents might not emerge until the late follow-up period after biodegradation of the polymer and large-scale studies will be required to determine whether the potential late benefits of a BP can more than offset the early benefits of a thromboresistant DP. SES and PES were associated with the highest rates of ST beyond 1 year, significantly higher than with BMS, BP-BES, CoCr-EES, and PC-ZES. Thus, some of the late benefit seen in randomized trials of BP-BES compared with first-generation DES such as LEADERS, NEVORes-Elution and COSTAR might relate more to the poor safety profile of the comparator stent rather than to specific benefits of the BP itself. The best-in-class second-generation DES to determine meaningful differences is CoCr-EES then the result of COMPARE II AND ABSORB III and ABSORB IV will be conclusive.

In the metaanalysis (from 126 randomized trials Twenty-eight trials randomized patients to a biodegradable polymer drug eluting stent, and the rest used durable polymer drug eluting stents) reported a statistically significant decrease in stent thrombosis (ST) events in BP-BES compared with DP-SES and statistically significant less MI, TVR and ST events were reported in BP- BES compared with DP-PES. It was also observed that BP-BES had statistically significant lower TVR compared with DP-ZES-E: The results of this study, showed that biodegradable polymer drug eluting stents are superior to first generation durable polymer drug eluting stents but are not superior to newer generation durable polymer drug eluting stents for either efficacy or safety outcomes. Newer generation durable polymer stents (cobalt chromium everolimus eluting stents, platinum chromium everolimus eluting stents, and zotarolimus eluting stent-Resolute) were the most effective stents in having the lowest rate of repeat revascularization, no increase in very late stent thrombosis, and a significant decrease in the risk of myocardial infarction. But one of the most important point is that the following time is mean of 2.3 (range 0.5-5) years, that means the result is not conclusive [32].

A meta-analysis of 5834 patients revealed not any significant differences in terms of overall mortality, MI, late ST, and TLR between bioabsorbable DES including BP-BES or BP-SES, and durable DES including DP-PES, DP-SES, DP- ZES [33]. In a meta-analysis comprising data for 3738 patients in six trials (ABSORB China, ABSORB Japan, EVERBIO II, TROFi II) randomized to receive either an everolimus-eluting bioresorbable vascular scaffold (n=2337) or an everolimus-eluting metallic stent (n=1401) and median follow-up 12 months (IQR 9–12) are analyzed. Metallic stent was either a cobalt–chromium stent (Xience V, Xience Prime, or Xience Expedition, Abbott Vascular, Santa Clara, CA, USA; n=1321) or a platinum–chromium stent (Promus Element, Boston Scientific, Natick, MA, USA; n=80) [34]. Findings showed that bioresorbable vascular scaffolds had a similar risk of repeat revascularization as metallic stents, a higher risk of stent (scaffold) thrombosis at 1 year of follow-up, and an inferior mid-term angiographic performance. The primary benefit of biodegradable versus metallic stents is expected to emerge several years after percutaneous coronary interventions, when the elution of anti-restenotic drug is completed and the bioresorbable scaffold is dissolved.

At least similar efficacy and safety versus the existing best-in-class drug-eluting stent at 12 months is important. The rate and the timing of definite or probable stent thrombosis in patients who received a bioresorbable vascular scaffold was consistent with that reported in other studies, with most events occurring within 30 days [34]. Studies with extended follow-up in a larger number of patients are needed to fully assess the expected long-term advantages of everolimus-eluting bioresorbable vascular scaffolds. A summary of meta-analysis results on Bioabsorbable Polymer/Durable Polymer-Based Drug-Eluting and Metal Stents are presented in (Table 3). Randomized clinical trials (SPIRIT and COMPARE) and meta-analyses have revealed that the second generation everolimus-eluting stent significantly reduces the need for repeat revascularization and better prevent stent thrombosis and myocardial infarction than are the early-generation sirolimus-eluting or paclitaxel-eluting stents(35,36). Therefore, the Everolimus-eluting Xience or Promus stents are the gold standard to which new stent designs should be compared [29]. (Table 3)

Table 3: Clinical Outcomes With Bioabsorbable Polymer/Durable Polymer-Based Drug-Eluting and Metal Stents From Meta-Analysis.

Considered stents	Reasults	Ref.
	superior clinical outcomes of BP-BES compared with BMS and first-generation DES. similar rates of cardiac death/MI, MI, and TVR in BP-BES compared with second-generation DP-BES -higher rates of definite ST ofBP-DES than CoCr-EES	

BP-BES/DP-DES	decrease in stent thrombosis (ST) events in BP-BES compared with DP-SESand statistically significant less MI, TVR and ST events were reported in BP- BES compared with DP-PES. It was also observed that BP- BES had statistically significant lower TVR compared with DP-ZES-E:	Bangalore
BP-BES/ Newer generation durable polymer stents (cobalt chromium everolimus eluting stents, platinum chromium everolimus eluting stents, and zotarolimus eluting stent-Resolute)	Newer generation durable polymer stents were the most effective stents in having the lowest rate of repeat revascularization, no increase in very late stent thrombosis, and a significant decrease in the risk of myocardial infarction.	Bangalore
bioabsorbable DES (BP-BES or BP-SES)/durable DES (DP-PES, DP-SES, DP- ZES)	not any significant differences in terms of overall mortality, MI, late ST, and TLR	LUPI

A pooled analysis from three large-scale multicenter randomized clinical trials (ISAR-TEST 3, ISAR-TEST 4, and LEADERS) included 4062 patients of which 2358 patients had been randomly assigned to treatment with biodegradable polymer DES (1501 patients with sirolimus- eluting and 857 patients with Biolimus-eluting stents) and 1704 patients to treatment with durable polymer SES assessed clinical outcomes for 4 years follow-up. The efficacy endpoint was target lesion revascularization and the safety endpoint was definite stent thrombosis. The risk of target lesion revascularization and the risk of definite stent thrombosis were significantly lower among patients treated with biodegradable polymer DES vs. durable polymer SES. In landmark analysis between 1 and 4 years, the incidence of myocardial infarction was significantly lower for patients treated with biodegradable polymer DES vs. durable polymer. Importantly, this difference was not apparent when the trials included in this study were analyzed separately. The result showed improved safety and efficacy of Biodegradable polymer DES compared with durable polymer SES during long-term follow-up to 4 years [37,38].

Although the one of the limitation of this pooled analysis is that only sirolimus - eluting durable polymer were included in this study and the result cannot be extended to other available stents and may be overestimated.

A pooled analysis of three RCTs (ISAR-TEST 3, ISAR-TEST 4, and LEADERS) comparing BP-DES (BP-BES and BP-SES), with DP-SES reported, BP- DES was associated with a statistically significant lower rate of MI and ST compared with DP-DES. However, no difference between BP-DES and DP-DES was indicated in other clinical outcomes such as all-cause mortality, cardiac mortality, cardiac mortality/ML and TLR up to 4 years follow- up [38]. The comparative effectiveness of BP-DES with DP-DES in patients with coronary artery disease who have undergone PCI is inconsistent and inconclusive, depending on the types of stents and the eluting drugs. Better designed RCTs and cost-effectiveness analysis in Canadian settings are needed to determine whether BP-DES could replace DP-DES in the treatment of patients with CAD requiring PCI. No studies were identified evaluating the cost-effectiveness of bioabsorbable polymer DES compared with durable polymer or polymer free DES for adult's CAD. No guidelines regarding the use of bioabsorbable stents for adults with CAD were found.

Conclusion

Clinical outcome and benefits of bioabsorbable and durable stent was considered by non-randomized and randomized clinical trial. large-scale network meta-analysis showed that there are not any significant differences in terms of overall mortality, MI, late ST, and TLR between Bioabsorbable DES including BP-BES or BP-SES, and durable DES including DP-PES, DP-SES, DP- ZE and bioresorbable vascular scaffolds had a similar risk of repeat revascularization as metallic stent. However, the risk of target lesion revascularization and the risk of definite stent thrombosis were significantly lower among patients treated with biodegradable polymer DES vs. durable polymer SES. Also, lower rate of MI and ST was observed in patient with BP-BES compared those with DP-DES. Studies with extended follow-up in a larger number of patients are needed to fully assess the expected long-term advantages of everolimus-eluting bioresorbable vascular scaffolds.

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