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REVIEW

Biodegradable polymer Biolimus-eluting stent (Nobori®) for the treatment of coronary artery lesions: review of concept and clinical results

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Abstract: First-generation drug-eluting stents have raised concerns regarding the risk of late and very late stent thrombosis compared with bare metal stents and require prolonged dual antiplatelet therapy. Despite extensive investigations, the physiopathology of these late events remains incompletely understood. Aside from patient- and lesion-related risk factors, stent polymer has been cited as one of the potential causes. In fact, the persistence of durable polymer after complete drug release has been shown to be responsible for local hypersensitivity and inflammatory reactions. Third-generation drug-eluting stents with more biocompatible or biodegradable polymers have subsequently been developed to address this problem. In this article, we evaluate and discuss the concept and clinical results (safety and efficacy) of a third-generation drug-eluting stent with biodegradable polymer: the Nobori® stent.

Keywords: percutaneous coronary intervention, stent thrombosis, antiplatelet therapy

Introduction

Percutaneous transluminal coronary angioplasty was introduced by Gruntzig in the late 1970s as an alternative to coronary artery bypass graft surgery for coronary revascularization.[1] Since then, percutaneous coronary intervention (PCI) has been accepted as a safe, reliable, and effective treatment for coronary artery disease, and its use has spread worldwide. Nevertheless, in-stent restenosis (ISR), a complex phenomenon resulting in renewed symptoms, need for re-intervention, and poor patient outcome remained for many years the Achilles' heel of PCI.[2] The introduction, a decade ago, of first-generation drug-eluting stents (DESs) transformed the practice of PCI by drastically reducing the rate of this complication.[3] The efficacy of DESs has largely been demonstrated in large randomized trials, leading to their current widespread use in clinical practice. Even in high-risk populations, ISR incidence does not currently go above 5%–10%.[4–6] However, major concerns regarding the long-term safety of these first-generation DESs have progressively arisen, especially the increased risk of late/very late stent thrombosis (ST)[7–14] and the need for prolonged dual antiplatelet therapy (DAPT) with an inherent increase of bleeding complications. Aside from patient- and lesion-related factors, delayed re-endothelialization and recovery of endothelial function after stenting as well as inhibition of vascular repair after DES implantation, all of which promote inflammation and thrombotic pathways, have been implicated in the pathophysiology of late/very late ST. Of note, stent polymer has also been cited as one of the main causes of these late events. In fact, the persistence of a durable polymer

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after complete release of the anti-proliferative drug has been shown to be responsible for local hypersensitivity and inflammatory reactions.[15]

These safety concerns prompted additional research, new trial design, and development of new-generation DESs to reduce the rate of this rare but critical event.

Apart from the progress in stent platforms (thinner struts and stent designs), recent research in this field has subsequently been focused on the development of new more biocompatible durable polymers or completely biodegradable polymers. Third-generation DESs using biodegradable polymers, like the Biolimus-eluting stent (BES) (Nobori®; Terumo Corporation, Tokyo, Japan), have been developed to overcome the long-term adverse vascular reactions related to the durable polymer.

In this article, we present information on the concept and rationale behind this new stent generation. We then discuss the results of recent publications investigating the safety and effectiveness of the use of the third-generation BES (Nobori®) for the treatment of coronary artery lesions.

Rationale for new stent development

The two major complications of PCI, ISR and ST, have always been the trigger for new stent development.[16] Indeed, despite the fact that these events are multifactorial, stent "structure" has been suggested to be one of the leading causes of ISR and/or ST.[17–21]

ISR physiopathology has not yet been fully understood. Barotrauma induced by PCI is responsible for endothelial denudation and sub-intimal hemorrhages, leading to a local inflammatory response. This inflammatory process induced by vascular damage is thought to be one of the main contributors to the development of restenosis, by promoting vascular smooth muscular cell proliferation and extracellular matrix formation, resulting in neointimal hyperplasia. Beside these mechanical factors, other factors have been identified as predictors for ISR, including patient-related (eg, diabetes mellitus, smoking, and renal failure) and lesion-related (eg, minimal lumen diameter after PCI, severe calcifications, chronic total occlusions, tortuous vessel, and long lesion length) factors.[22] As mentioned above, ISR remained the Achilles' heel of PCI until the large use of DESs, which were specifically developed to overcome this complication. Before the introduction of bare-metal stents (BMSs), up to 50% of the patients treated by PCI experienced restenosis. Even in the BMS era, ISR remained one of the major limitations of this technique, with an average incidence of 20%, but that could increase up to 35% in complex lesions and diabetic patients.[4,5] The introduction, 10 years ago, of first- and then second-generation DESs transformed the practice of PCI by drastically reducing the incidence of this complication to less than 10%.[3]

DESs prevent restenosis by inhibiting vascular smooth muscle proliferation.[23–31] Unfortunately, they also delay re-endothelialization of stent struts, leading to the potential risk of late/very late ST and thereby the need for prolonged DAPT. Since the appearance of DESs, ST has become the major safety concern in contemporary PCI practice. ST is a rare adverse event (1% at 1 year and then 0.5% per year) but remains associated with high morbidity and mortality rates.[32] The overall prognosis is poor: most patients in whom ST occurs present with STEMI (ST-segment elevation myocardial infarction) or out-of-hospital death, and up to 30% of those who arrive alive at hospital die within the first month. Numerous factors have been implicated in ST physiopathology, but studies have also shown that these predictors vary over time. These data highlight the complex physiopathology of ST, depending on the timing of event occurrence. Acute (within 24 hours) and early ST (within 30 days) are likely related to mechanical issues concerning the stent (eg, minimum stent area and suboptimal stent expansion), inadequate platelet inhibition, or patient prothrombotic factors.[33] Late (up to 1 year) and very late ST (after 1 year) have been attributed to incomplete vascular healing and/or inadequate neointimal coverage, which in turn, promote inflammation and activation of thrombotic pathways[15] and late or acquired stent malapposition. DAPT associating aspirin with an oral P2Y12 inhibitor has been shown to be the standard therapy following coronary stenting in order to significantly reduce cardiac events, especially ST after PCI.[34] Current guidelines support the use of DAPT for 6–12 months after DES implantation.[35–39] In 2006, the potential risk of late/very late ST after DES implantation raised the question of prolonging DAPT even beyond the first year.[40–41] However, prolonged DAPT has also clearly been associated with an increased risk of bleeding.[42–47] Availability of new biodegradable polymers and/or stents may shorten the duration of necessary DAPT and therefore minimize the risk of major bleeding to which it is associated.

Stent "structure" and concept for new development

First- and second-generation DESs have three major components: the stent platform, the antiproliferative drug, and the polymer. All of these factors have been subject to

modification and have become a target for research and development. Improvement of each component could indeed lead to better patient outcomes.

The stent platform is the scaffold of the stent. It provides the radial force to prevent vessel occlusion provoked by vessel injury following PCI. First-generation DESs used stainless steel platforms. Cobalt-chromium and later platinum-chromium platforms used in second-generation DESs permitted similar stents' radial strength all the while enabling a thinner strut design and subsequently significantly improved deliverability and a reduced rate of ISR.[48–49] Unfortunately, the presence of a permanent scaffold in the vessel constitutes a stimulus for platelet aggregation and may lead to ST in patients with nonoptimal antiplatelet therapy and/or incomplete stent endothelialization. Recently, bioabsorbable platforms that biodegrade over a period of months have been developed, with the purpose of allowing the restoration of a normal vascular physiology and function over time. Ultimately, no foreign material is left exposed in the bloodstream. These stents may also potentially preserve reactive vasomotion and permit expansive remodeling.[50]

There are several antiproliferative drugs with different modes of action. The goal of these drugs is to inhibit vascular smooth cell proliferation and migration, without affecting endothelial regeneration, and have anti-inflammatory/anti-thrombotic properties. Inhibitors of the mammalian target of rapamycin (mTOR) are the dominant class of antiproliferative drugs used for DESs. The first mTOR inhibitor used in clinical practice was sirolimus. Later derivatives include zotarolimus and everolimus. The mTOR inhibitors are cytostatic drugs resulting in arrest of the cell cycle at the G1 phase. Aside from mTOR inhibitors, tacrolimus, which acts as a calcineurin inhibitor, has also been used in DESs and is a cytostatic agent with both antiproliferative and anti-inflammatory activities. Finally, paclitaxel is a taxan drug, which acts as a cytotoxic drug through the stabilization of microtubules. However, all these antiproliferative agents have shown detrimental local effects on the vascular wall and on endothelial function recovery after stenting.[11] New drugs (biolimus, novolimus, and myolimus) have been developed and have shown promising results.[51–52] Compared with other mTOR inhibitors, biolimus shows better lipophilicity. Agents other than drugs are under investigation to limit restenosis, such as antibody-coated stents (CD34 antibody-coated stents) and nucleotide- or peptide-coated stents. The ultimate goal remains the inhibition of maladaptive neointimal proliferation, all the while promoting vascular healing.

Stent polymers control elution of the antiproliferative drug over a variable period of time. Once drug elution has been completed, most polymers exert limited functions and act as a potential trigger for local inflammation and hypersensitivity and subsequently late/very late ST. They promote an inflammatory response and eosinophilic infiltration in the arterial wall, causing hypersensitivity reactions and endothelial dysfunction responsible for delayed healing and lead to ST.[11,12,22,53] The biocompatibility, composition, formulation, degradation delay of the polymer, pharmacokinetics of the antiproliferative agent released by the polymer, and the management of variation in polymer degradation delay have become new difficult challenges for the development of stent polymers. An optimal polymer should mimic the endothelial lining in order to prevent late thrombotic complications, thus improving stent safety. Given the issue of polymer-induced inflammation and thrombosis, more biocompatible durable polymers have been developed. Second-generation DESs are composed of these polymers, thereby improving arterial healing and potentially reducing the rate of late ischemic events. The limited function of stent polymers once the drug is eluted has also fuelled research in biodegradable polymers. Third-generation DESs use polylactic acids (poly-L-lactic acid and poly D,L-lactide-co-glycolide) as bioabsorbable polymers. The BES with biodegradable polymer (Nobori®) is one of these third-generation DESs. Finally, another field of research is the development of stents that elute antiproliferative drugs without the need for polymers. These polymer-free stents could prevent the potential adverse physical effects of the polymer, leading to sustained intima inhibition, improved healing, and a lessened activation of the inflammatory/thrombotic pathways. Preclinical studies support their use, but robust data are still lacking.

The BES with biodegradable polymer (Nobori®) stent: design and clinical results

Safety, efficacy, and deliverability are the main sought-out properties for the development of new DESs. An optimal combination of these components, which are in part interdependent, is necessary for enhancing stent performance.

The BES stent with biodegradable polymer (Nobori®) is one of the third-generation DESs (Figure 1). The platform is composed of stainless steel, and the strut thickness is 112 μm. It is coated with a polylactic acid polymer on its abluminal surface, which is metabolized within 6–9 months to lactic acid, water, and carbon dioxide through interaction with the Krebs cycle. The stent elutes an antiproliferative drug,

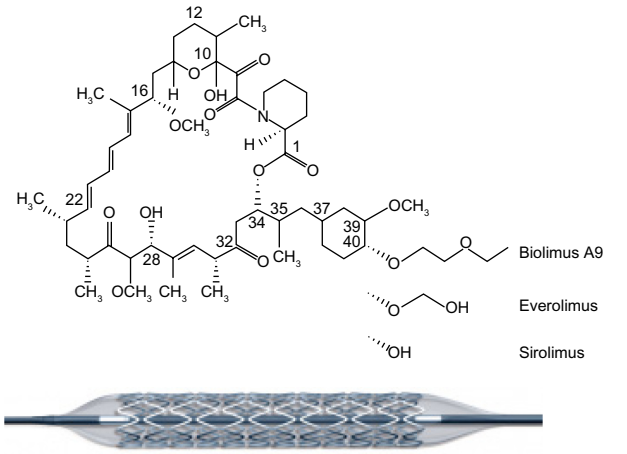

Figure 1 The Biolimus-eluting stent (Nobori®; Terumo Corporation, Tokyo, Japan): chemical structure of Biolimus A9 and stent design. Replacement of hydrogen by alkoxy-alkyl group at 40-O position increases its lipophilicity.

biolimus (15.6 µg/mm), for up to 30 days. The coating design of the stent combined with the lipophilicity of the drug is thought to optimize local drug distribution and to reduce its release into the general circulation. At the end, the Nobori® stent will leave only a BMS in place.

The Nobori® stent has already been compared with first- and second-generation DESs with promising results. The NOBORI CORE trial[54] reported late-loss with the Nobori® stent at 9 months, similar to that found using the sirolimus-eluting stent (SES, Cypher®; Cordis Corporation, Bridgewater, NJ, USA): 0.10 and 0.12 mm, respectively (P=0.66). However, the use of the Nobori® stent results in better endothelial recovery, with normal coronary vasodilatation in the adjacent stent segments after implantation, contrasting with the paradoxical vasoconstriction seen with first-generation DESs.[55,56] The NOBORI I trial showed non-inferiority to and subsequent superiority of the Nobori® stent over the paclitaxel-eluting stent (Taxus®, Boston Scientific, Maple Grove, MN, USA): late-loss 0.11 versus 0.32 mm, $P<0.001$. Moreover, this trial demonstrated a lower rate of ST with the Nobori® stent after a 9-month follow-up.[57]

Three recent large randomized trials have compared safety and efficacy of this third-generation DES with that of first- and second-generation DESs with durable polymer (Table 1).[58]

The SORT OUT V trial[59] enrolled 2,468 patients who underwent PCI in Denmark and randomized them 1:1 using the Nobori® and Cypher® stents. This trial was a multicenter, prospective, non-inferiority trial (non-inferiority margin chosen at 2%) comparing the BES using biodegradable polymer with the SES using permanent polymer. A total of 1,229 patients were assigned to the BES group (1,532 lesions)

Table 1 Characteristics and principal results of recent trials with the Nobori® (Terumo Corporation, Tokyo, Japan) stent as compared with first- and second-generation DESs

Trial	Date	Number of patients	Design of the study and comparator	Longer follow-up available and results
NOBORI CORE[54]	2008	43 Stable angina 100%	Prospective, multicenter, and comparative. Vasomotion study after implantation of a BES Nobori® stent and an SES	Nine months follow-up. Endothelium-dependent vasomotion is preserved after BES implantation as compared with SES and may reduce thrombotic events.
NOBORI I[57]	2009	243 UA 28% Stable angina 72%	RCT BES Nobori® stent versus PES Taxus® Liberté	Nine months follow-up. Nobori® stent showed greater degree of neointimal hyperplasia inhibition. Reduction of ISR. No ST up to 9 months.
SORT OUT V[59]	2013	2,458 STEMI 18% NSTEMI and UA 30% Stable angina 52%	RCT BES Nobori® stent versus first-generation SES Cypher® stent to treat coronary artery stenosis	Twelve months follow-up. BES did not show non-inferiority and did not improve clinical outcomes when compared with SES. Higher early ST in the BES group.
COMPARE II[60]	2013	2,707 STEMI 22% NSTEMI 27% UA 10% Stable angina 41%	RCT BES Nobori® stent versus second-generation EES Xience® or Prime®	At 12 months follow-up, BES Nobori® stent showed non-inferiority as compared with EES. Procedural failure higher in the BES group.
NEXT[61]	2013	3,235 STEMI and NSTEMI 5% UA 12% Stable angina 83%	RCT BES Nobori® stent as compared with EES Xience® or Prime®	Twelve months follow-up. Outcome after implantation of BES is non-inferior to EES, with very low rate of ST.

Abbreviations: BES, biolimus-eluting stent; DES, drug-eluting stent; EES, everolimus-eluting stent; ISR, in-stent restenosis; NSTEMI, non-ST-segment elevation myocardial infarction; PES, paclitaxel-eluting stent; RCT, randomized clinical trial; SES, sirolimus-eluting stent; ST, stent thrombosis; STEMI, ST-segment elevation myocardial infarction; UA, unstable angina.

and 1,239 to the SES group (1,555 lesions). DAPT was pursued at least 12 months after the procedure. The primary endpoint was a composite of safety (cardiac death, myocardial infarction [MI], and ST) and efficacy (target lesion revascularization [TLR]) within 9 months of stent implantation (intention-to-treat analysis). There were 75% male, and only 15% of the patients had a history of diabetes. Altogether, 17% had undergone a previous coronary intervention. PCI was performed in an acute setting in 49% of cases in both groups. The main target vessel location was the left anterior descending (LAD) artery (40.8%). Procedure characteristics were similar between the two groups, except for maximum stent pressure, which was significantly higher in the SES group (18 versus 16 atm, $P<0.0001$). Composite primary endpoint occurred in 4.1% of cases in the BES group and 3.1% of cases in the SES group (one-sided $P_{\text{non-inferiority}}=0.06$, and $P=0.22$ for superiority). Cardiac death and TLR were not significantly different between the BES and SES groups (0.7% versus 1%, $P=0.38$; 3.3% versus 2.1%, $P=0.07$). Of note, ST occurred more frequently in the BES group (especially within the first month), with no clear explanation, and the rate of ST was particularly low in the SES group: 0.7% versus 0.2%, $P=0.03$. The authors concluded that the BES did not show non-inferiority when compared with the first-generation SES at 9 months.

The COMPARE II trial[60] was a multicenter, open-label, randomized, controlled, non-inferiority trial (non-inferiority margin chosen at 4%) and aimed to compare the safety and efficacy of the BES using biodegradable polymer with a second-generation everolimus-eluting stent (EES) using durable biocompatible polymer (Xience V® [Abbott Vascular, Santa Clara, CA, USA] or Prime® [Boston Scientific Corporation, Natick, MA, USA]). Altogether, 2,707 patients were enrolled and assigned 2:1. A total of 1,795 patients (2,638 lesions) received a BES, and 912 patients (1,387 lesions) an EES. DAPT was continued for a minimum of 12 months. The primary endpoint was a composite of safety (cardiac death and non-fatal MI) and efficacy (TLR) at 12 months. There were 74% male, 21.7% diabetics, and 20% had a previous history of MI. PCI was performed in an acute setting in 57.9% of cases. The LAD artery was the main target vessel (40.3%). Only 6.5% of the lesions were bifurcation lesions. Procedure characteristics were not significantly different between the groups but the rate of non-allocated stent implantation was higher in the BES group. Primary endpoint occurred in 5.2% of cases in the BES group and 4.8% in the EES group (one-sided $P_{\text{non-inferiority}}<0.0001$, and $P=0.69$ for superiority). There was no difference in the rates of cardiac death (0.8% in each group, $P=0.97$) and MI (2.8% in the BES group versus 2.5% in the EES group; $P=0.63$). The rate of definite ST (0.7% versus 0.4%, $P=0.38$) and definite/probable ST (0.8% versus 1%, $P=0.58$) were very low and comparable between the two groups. Target vessel revascularization did not differ between the BES group (2.9%) and the EES group (2.6%, $P=0.69$). The authors concluded that the BES was shown to be non-inferior to the EES in terms of safety and efficacy at 1-year follow-up after PCI. The 5-year follow-up of the study should answer the question of long-term safety and efficacy of the BES compared with second-generation DESs.

The NEXT trial[61] was a prospective, multicenter, randomized, open-label, non-inferiority trial (non-inferiority margin chosen at 3.4%) comparing the BES (Nobori®) with the EES (Xience V® or Prime®) in terms of TLR at 1 year. DAPT was continued at least 3 months after the procedure. From May to October, 2011, in 98 Japanese centers, 3,235 patients were randomized 1:1 without any exclusion criteria to undergo PCI with either the BES or the EES. Altogether, 30% of included patients were over 75 years old, and 46% of the population in each group were diabetic. PCI was performed in a stable clinical setting for 83% of patients. The target vessel location was the LAD artery in 48% of cases. Efficacy endpoint was any TLR at 1 year, whereas the primary safety endpoint was a composite of death and MI. Primary efficacy endpoint occurred in 4.2% in both the BES group and the EES group (one-sided $P_{\text{non-inferiority}}<0.0001$, and $P=0.93$ for superiority). The rate of any MI and stroke was similar between the two groups (3.3% versus 3.1 [$P=0.77$] and 1.4% versus 1.5% [$P=0.89$]). No difference was observed in terms of mortality, 2.6% and 2.5% in the BES and EES groups, respectively, $P=0.9$. With regard to the rate of ST, the incidence was extremely low, and there was no difference between the BES group and the EES group (0.25% and 0.06%, $P=0.18$). The angiographic sub-study shows that the difference in in-segment late loss between the two groups was −0.03 mm, demonstrating non-inferiority of the BES, with a margin of 0.195 mm. Of note, the rate of stent fracture was significantly higher in the BES group (3.1% versus 0%; $P=0.004$). The authors concluded in the non-inferiority of the BES over the EES in the setting of stable coronary artery disease. Clinical outcomes were excellent, with a low rate of TLR and extremely low rate of ST in each group.

Discussion

Third-generation DESs using biodegradable polymer such as the Nobori® stent have been developed to overcome long-term adverse effects observed with first-generation DESs

related to the use of durable polymers, and to thereby shorten the duration of DAPT and the ensuing risk of hemorrhagic complications. Biodegradable BESs should nonetheless possess similar efficacy to actual DESs in preventing ISR (lower rate of TLR as compared with BMSs).

First studies evaluating BES efficacy and safety have shown promising results, with significantly lower in-stent late loss than with paclitaxel-eluting stents, and similar in-stent late loss as SESs.[54,57] However, the recent COMPARE-II, SORT OUT V, and NEXT trials, all three of which were sufficiently powered to compare clinical outcomes, showed contrasting results. To date, only the COMPARE-II and the NEXT trials have evaluated a new third-generation DES versus a second-generation DES (Xience V® or Prime®). The COMPARE-II trial demonstrated non-inferiority of the BES relative to second-generation EESs, but procedural failure was significantly higher in the BES group.[60] By contrast, non-inferiority of the BES relative to the first-generation SES was not shown in the SORT OUT V trial due to a higher risk of early ST without a clear explanation for this phenomenon.[59] In fact, the rate of ST was particularly low in the SES group in this study. The NEXT trial is the largest trial, to date, evaluating the efficacy and safety of the BES as compared with the EES.[61] In this trial, clinical and angiographic outcomes of the BES group were non-inferior to the EES group, and the device implantation success rate was comparable in both groups. Of note, a higher rate of stent fracture was seen in the BES group in the angiographic substudy of the NEXT trial, but its imputability in very late ST or TLR is uncertain and needs further exploration.

Of major importance, all these trials have enrolled low risk patients, and notably a low incidence of diabetics, with relatively simple angiographic lesions (eg, large vessels, low rate of bifurcations, and lesion length <20 mm). PCI was also performed in the majority of cases in a stable clinical setting. These facts are critical regarding the interpretation of the results and the low rate of adverse events observed in these three trials: the primary efficacy endpoint was lower than 5% in all studies, and any conclusion must be interpreted with caution, especially in non-inferiority trials. In addition, a safety comparison of modern DESs is challenging. Indeed, ST, especially very late ST, is a rare complication, and although 12-month results of standard trials usually enable safety or efficacy to be assessed, longer follow-up (5 years or more) and large trials are mandatory in the present case in regard of late-event exploration. The rate of ST in the present studies is particularity low (around 0.5% at 1 year), and these trials are not powered enough to evaluate such a low frequency event. Finally, if present, the expected benefit of third-generation DESs like the Nobori® stent over older DESs would logically appear only after 1 year. To date, no very late ST with the Nobori® stent has been reported in the literature, with the limitation that long-term follow-up is currently only available for very few patients.

The LEADERS trial was the first randomized study to evaluate BESs against durable polymer first-generation DESs. This trial included higher risk patients, and the rate of events was on average twice as high as compared with the COMPARE II, SORT OUT V, and NEXT trials. The LEADERS study compared another third-generation BES (Biomatrix Flex®, Biosensors, Newport Beach, CA, USA) with SESs. The only difference between the Biomatrix Flex® and the Nobori® stent is the presence of an ultra-thin non-degradable parylene coating between the stent and the polymer on the Nobori® stent to assure polymer attachment to the stent struts, which do not exist on the Biomatrix Flex®. The final 5-year report has just been published[62] and demonstrates that the BES is non-inferior to the SES with regard to the primary endpoint (cardiovascular death, MI, and clinically driven target vessel revascularization) (22.3% in the BES group versus 26.1% in the SES group; P=0.071). In addition, even though no significant difference was observed between the BES and the SES in total definite ST at 5 years, the BES was associated with a significantly lower rate of very late ST and secondary composite endpoint (all cause death, any MI, any revascularization) (0.6% in the BES group versus 2.2% in the SES group for very late ST [P=0.003], and 35.1% versus 40.4% for secondary composite endpoint [P=0.02]).[62]

A recently pooled analysis based on patient individual data from the ISAR-TEST 3, the ISAR-TEST 4, and the LEADERS trial[63] has demonstrated that biodegradable polymer DESs (including: biodegradable polymer BES [Biomatrix Flex®], n=857; and biodegradable polymer SES, n=1,501) improve safety and efficacy over first-generation SESs during long-term follow-up. The three trials separately showed no differences between BESs and DESs in the past, highlighting the lack of statistical power of these studies (taken alone) to detect relevant differences in very low frequency events such as ST. In this meta-analysis, the benefit of BESs was seen in the rate of ST (0.2% versus 1.3%, P=0.004), MI (1.5% versus 3%, P=0.03), and cardiac death (3.9% versus 4.9%, P=0.05). Of note, BESs also showed a significant reduction in TLR in this meta-analysis (12% versus 13.7%, P=0.029). These trials were performed with sirolimus first-generation DESs as control, and results cannot be extended to other second-generation DESs. Further studies using second-generation DESs as control are required to make any conclusions. Interestingly, such a

meta-analysis of trials that have evaluated the Nobori® stent may carry interesting conclusions in the next future.

Conclusion

BMSs and DESs have changed the landscape of current PCI by significantly reducing the rate of ISR. However, first-generation DESs have been associated with a higher rate of late or very late ST. The physiopathology of this rare but serious event is multifactorial, but inflammation and delayed arterial healing, of which the durable polymer may be a putative mechanism, has an important role. The concept of biodegradable polymer and totally bioresorbable scaffolds looks, in consequence, very interesting. Data currently available have shown promising but contrasting results. Long-term follow-up is mandatory to see if the implantation of these third-generation DESs will improve clinical outcomes with a lower rate of ST and MI. Further studies and results of their long-term follow-up would definitely shed light on patient outcomes with the use of such devices.

Disclosure

The authors report no conflicts of interest in this work.

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