Clinical Outcomes in 2481 Unselected Real-World Patients Treated With a Polymer-Free Sirolimus-Eluting Stent: 3 Years Results From the NANO Multicenter Registry

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Abstract

The long-term clinical data evaluating the safety and efficacy of the novel polymer-free sirolimus-eluting Nano plus stent (Lepu Medical, Beijing, China) is limited. We evaluated the 3-year clinical outcomes of a polymer-free sirolimus-eluting, Nano plus stent for the treatment of coronary artery disease in the NANO multicenter Registry. The NANO all-comers Registry trial was a prospective, multicenter clinical registry conducted in 26 centers between August 2016 and January 2017. A total of 2481 consecutive patients were exclusively treated with the Nano plus stent. The main clinical endpoint, target lesion failure (TLF, defined as cardiac death, target vessel nonfatal myocardial infarction, and clinically driven target lesion revascularization [CD-TLR]), was analyzed at 3 years. The incidence of TLF was 6.8% (168/2481). The rates of its individual components were as follows: cardiac death 3.8% (94/2481), target vessel nonfatal myocardial infarction 0.7% (18/2481), and CD-TLR 2.9% (68/2481). The rate of definite/probable stent thrombosis was 0.5% (13/2481). Diabetes mellitus, acute myocardial infarction, age, chronic renal failure, in-stent restenosis, chronic total occlusion and left ventricular ejection fraction <40% were the independent predictors of 3-year TLF. The TLF was relatively low in patients treated with polymer-free Nano plus stent at 3 years. The polymer-free Nano plus stent showed a favorable safety and efficacy profile in the real-world patients.

Clinical trial registration

URL: <https://www.clinicaltrials.gov/>. Unique identifier: [NCT02929030](#).

Introduction

Percutaneous coronary interventions (PCI) with drug-eluting stents (DES) is currently the most common revascularization treatment strategy for coronary artery disease worldwide. DES has dramatically improved clinical outcomes compared to bare metal stent (BMS)[1], however, current DES systems always need relatively long (> 6 months) dual antiplatelet therapy (DAPT)[2], which confined their usage on a significant proportion of patients with adherence restraints, such as those at high bleeding risk[3].

The durable polymer (DP) has been demonstrated to be associate with vessel wall inflammation, and contribute to delay arterial healing, which could lead to late thrombotic risk[4, 5]. Polymer-free (PF) coating technologies was then emerged. PF-DESs aim to prevent adverse events that caused by hypersensitivity reactions and chronic inflammation to polymer[6, 7]. In patients at high bleeding risk, PF-DES was found to be superior to BMS when used with a 1-month course of DAPT[8].

The Nano plus stent, a novel PF stent with nano-sized pores as drug carriers that contain the anti-proliferative drug sirolimus, is one of the most widely used DESs in China. Nano plus stent has an improved uniform distribution on the adluminal stent surface than microporous or textured rough surface stents. Nano plus stent has been demonstrated to have comparable safety and efficacy to DP-DES for the treatment of de novo coronary artery lesions in a selected randomized controlled trial population[9]. Previously, the outcomes of the real-world NANO Registry at 1 year have shown that the PF Nano plus

stent was associated with low TLF[10]. The current study reports the 3-year outcomes of the NANO all-comers Registry trial.

Methods

Study design and population

The NANO all-comers Registry trial (NCT02929030) was a prospective, multicenter trial conducted in 26 centers across China between August 2016 and January 2017 with a single arm design. A total of 2481 consecutive patients with symptomatic coronary artery disease scheduled for PCI were enrolled, with no specific inclusion or exclusion criteria[10]. The NANO Registry trial is planned to follow the patients up to 5 years.

The trial was performed in accordance with the Declaration of Helsinki and was approved by the ethics committees of the Xijing Hospital. All the patients signed the written informed consent prior to participation in the trial. Clinical outcomes were adjudicated by an independent clinical event committee.

Outcomes

The main clinical endpoint was target lesion failure (TLF), defined as cardiac death, target vessel nonfatal myocardial infarction (MI) and clinically driven target lesion revascularization (CD-TLR). The safety endpoint was definite and/or probable stent thrombosis (ST). MI was defined according to the third universal definition[11]. TLR was defined as any repeat revascularization by PCI or coronary artery bypass graft. ST was defined according to the Academic Research Consortium criteria[12].

Study device

The Nano plus stent is a novel PF sirolimus-eluting stent (Lepu Medical, Beijing, China) with the nanoporous stent surface technology used to carry drug and control drug release. The Nano plus stent system is based on a 316L stainless steel platform and has a high-pressure delivery system with a semi-compliant rapid exchange balloon catheter. The delivery system presents a crossing profile of 0.9-1.2 mm with two radiopaque markers at the ends of the balloon to facilitate correct stent placement. The two ends of the stent have a sinusoidal curve shape, while the center of the stent is composed of a specialized cyclic structure that aligns into a helix. Nano-sized pores (mean pore diameter: 400 nm, 1/800 of the stent thickness) are uniformly distributed on the abluminal stent surface.

Statistical analysis

Continuous variables are presented as mean $\pm$ standard deviation. Categorical data are expressed as percentages. Cumulative event curves were generated using the Kaplan-Meier method. Multivariable Cox proportional hazards model was used to identify the independent predictors of the 3-year TLF. Baseline clinical and procedural variables that were considered clinically relevant or that showed a univariate relationship with TLF ($p < 0.10$) were entered into the multivariate Cox proportional hazards model. All

statistical analyses were performed using the SAS 9.1 software package (SAS Institute, Cary, NC). All tests were 2-sided, and a p value <0.05 was considered statistically significant.

Results

Baseline demographics and clinical characteristics

Patient baseline and lesion characteristics are reported previously and also in **Table 1** and **Table 2**[10]. The mean age of the patients was 62.8 ± 10.1 years. 40.2% of patients presented acute myocardial infarction (AMI) and 22.8% of patients had diabetes mellitus. 11.6% of patients had multiple vessel PCI, and 63.9% of lesions were American College of Cardiology/American Heart Association (ACC/AHA) type B2 or C lesions, including 17.0% ultra-long lesions (lesion length ≥ 40 mm), 14.5% chronic total occlusions (CTO), 11.7% bifurcations, 5.8% severe calcifications, 2.7% severe tortuosity, and 4.1% referenced vessel diameter <2.5 mm.

Clinical outcomes up to 3 years follow-up

The cumulative rate of TLF at 3 years was 6.8% (n=168) among all patients (**Figure 1**), with cardiac death occurred in 3.8% (n=94) (**Figure 2a**), target vessel nonfatal MI in 0.7% (n=18) (**Figure 2b**), and CD-TLR in 2.9% (n=68) (**Figure 2c**) of patients (**Table 3**). In total, at 3 years, the rate of definite or probable ST was 0.5% (n=13) (**Figure 2d and Table 3**). The rates of clinical outcomes within 1 year, 1 to 2 year and 2 to 3 year are shown in **Table 3**.

Predictors of TLF at 3 years follow-up

Multivariate analyses of TLF at 3 years using the Cox proportional hazard model showed that the independent predictors of 3-year TLF included diabetes mellitus, AMI, age, chronic renal failure, in-stent restenosis, CTO and left ventricular ejection fraction <40% (**Table 4**).

Discussion

Results of the 3 years analysis of the NANO all-comers Registry trial show that patients treated with PF Nano plus stent had a relatively low rate of TLF, which was mainly driven by cardiac death. The rate of definite or probable ST was low suggesting the PF Nano plus stent was safe and effective in a real-world population.

Stent design, anti-proliferative drug and the presence and type of polymer are essential factors of a DES platform relate to its clinical efficacy. Durable polymer was related to inflammatory responses and delayed arterial healing[4], but important to facilitate loading and controlling the release of anti-proliferative drugs. Without a drug carrier might be associated with lesser efficacy on inhibiting neointimal hyperplasia, most probably due to insufficient and/or uncontrolled drug delivery at the target lesion[13,14]. The Nano plus stent is a novel PF sirolimus-eluting stent that employs nanoporous stent

surface technology to control drug delivery and release. Numerous nano-sized pores are uniformly distributed on the abluminal stent surface, which functions as a drug reservoir for prolonged release of anti-proliferative drug[15]. It has been demonstrated that DES efficacy is closely associated with the release kinetics of the anti-proliferative drug in the first 30 days. The Nano plus stent has a sirolimus dose of 2.2 µg/mm² and 85% of the drug is released within 30 days[9], which allows it to have enough concentration of the anti-proliferative drugs to inhibit neointimal hyperplasia. We previously reported that the PF Nano plus stent showed similar safety and efficacy compared with the DP sirolimus-eluting stent in terms of angiographic outcomes at 9 months and clinical outcomes at 2 years [9]. In the current analysis, using PF Nano plus stent for the treatment of relatively complex lesions in the unselected population had a low and acceptable rate of 3-year TLF.

Currently, there is ongoing debate over potential beneficial antithrombogenic effects of polymer coatings. The antiproliferative drugs, the presence and type of polymer, the metallic stent platform, geometry, and strut thickness may contribute to the following controversy results. PF-DESs were designed to attempt to prevent adverse events that caused by chronic inflammation to polymer. However, Shiratori et al. found that compared with DP-paclitaxel-eluting stent, PF-paclitaxel-eluting stent was associated with increased neointimal proliferation and subsequent clinical restenosis[16]. The ISAR-TEST-3 (Intracoronary Stenting and Angiographic Restenosis Investigators – Test Efficacy of Rapamycin-eluting Stents with Different Polymer Coating Strategies) study showed that the PF stent provided an inferior efficacy, the BP stent is at least as effective as the DP stent in terms of antirestenotic efficacy[14].

Inconsistent with these findings, most studies demonstrated that compared to DP-DES, PF-DES has a favorable safety and efficacy profile either in a selected population[17,18] or in a real-world clinical setting[19,20], even follow up to 10 years[21]. Compared to the latest-generation DP-DES, PF-DES also provided a noninferior efficacy regarding TLF at 12 months[22]. Someone may argue that recently the SORT OUT IX observed inconsistent results as compared to those above studies. The SORT OUT IX found that the PF BioFreedom stent did not meet criteria for non-inferiority for MACE (major adverse cardiac events) at 12 months when compared with the ultrathin strut BP sirolimus-eluting Orsiro stent, and the BioFreedom stent had a higher incidence of TLR[23]. Of note, several limitations and the feature of the BioFreedom stent should be considered. Around 90% of biolimus A9 released from the BioFreedom stent within 48 hours of implantation, the relatively fast drug release may contribute to less efficacy on inhibiting neointimal hyperplasia. Strut thickness is associated with in-stent restenosis[24]. The BioFreedom stent is with a strut thickness of 112 µm, which is thicker than most other newer-generation DES (60-90 µm). In our present analysis, the Nano plus stent is a relatively thin strut stent (91 µm), which may partly contribute to the low TLF for the 1-year and 3-year results of NANO Registry.

PF-DES were initially designed out of hopes that, without the polymer, the risk of late thrombotic events would be decreased, allowing shorten the DAPT durations. The LEADERS FREE trial showed that PF-DES has an efficacy and safety advantage over BMS at 1 year in patients at high bleeding risk treated with 1 month of DAPT[8]. And the benefits of PF-DES over BMS were maintained up to 2 years[25]. LEADERS FREE II trial reproduced the results of LEADERS FREE in an independent, predominantly North American

cohort of high bleeding risk patients[26]. However, this advantage seems to be questioned recently. The ONYX ONE trial observed that among patients at high bleeding risk who received 1 month of DAPT after PCI, DP-DES was noninferior to PF-DES in terms of safety and effectiveness composite outcomes[27]. Notably, PF-DES (BioFreedom stent: 112 μm) was thicker than DP-DES (Resolute Onyx stent: 81 μm) in the ONYX ONE trial, while the strut thickness potentially impacts on clinical outcomes in patients following PCI[24,28,29]. To date, the majority of the studies demonstrated that PF-DES has a favorable safety and efficacy profile as compared to DP-DES[17-22]. PF-DES may be an acceptable alternative to DP-DES, especially for patients with the need for an early interruption of DAPT.

Stent failure remains to occur, which may lead to adverse cardiac events, despite the improvement of the contemporary DES. To identify the related factors that may predict TLF was of paramount importance. However, predictors of TLF vary in the different postprocedural periods[30]. Previously, we identified that diabetes mellitus, AMI, left ventricular ejection fraction <40%, and long lesions (>40 mm) independently predicted 1-year TLF. At 3 years, the independent predictors of TLF included diabetes mellitus, AMI, age, chronic renal failure, in-stent restenosis, CTO and left ventricular ejection fraction <40%, the predictors identified in the present analysis are highly consistent with previous studies[31,30,32]. Identifying and intensive managing these predictors may help to reduce the rate of TLF and improve the long-term clinical outcomes.

Limitations

The present study was a single arm, non-randomized study with inherent limitations. However, the current analysis highlights the safety and efficacy of Nano plus stent in an unselected population in a real-world setting. Although the results of the analysis showed that PF Nano plus stent has a favorable safety and efficacy profile, head-to-head comparisons with the newer-generation of DES are needed in future studies.

Conclusion

An extended follow-up to 3 years, TLF was relatively low in patients treated with PF Nano plus stents in the multicenter NANO Registry trial. The PF Nano plus stents showed promising safety and efficacy in the real-world patients, although longer follow-up is needed for further evaluation.

Declarations

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Disclosures The authors certify that: (1) the paper is not under consideration elsewhere, (2) no part of the paper has been previously published, (3) all of the authors have read and approved the manuscript, and (4) none of the authors has any relevant disclosures.

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Compliance with ethical standards

Conflict of interest All authors declare no conflicts of interest.

Ethical approval This study was approved by the local ethics committee of our institution.

References

1. Stefanini GG, Holmes DR, Jr. (2013) Drug-eluting coronary-artery stents. *N Engl J Med* 368 (3):254-265. doi:10.1056/NEJMra1210816
2. Neumann FJ, Sousa-Uva M, Ahlsson A, Alfonso F, Banning AP, Benedetto U, Byrne RA, Collet JP, Falk V, Head SJ, Juni P, Kastrati A, Koller A, Kristensen SD, Niebauer J, Richter DJ, Seferovic PM, Sibbing D, Stefanini GG, Windecker S, Yadav R, Zembala MO, Group ESCSD (2019) 2018 ESC/EACTS Guidelines on myocardial revascularization. *Eur Heart J* 40 (2):87-165. doi:10.1093/eurheartj/ehy394
3. Moussa ID, Colombo A (2009) Antiplatelet therapy discontinuation following drug-eluting stent placement: dangers, reasons, and management recommendations. *Catheter Cardiovasc Interv* 74 (7):1047-1054. doi:10.1002/ccd.22167
4. Hezi-Yamit A, Sullivan C, Wong J, David L, Chen M, Cheng P, Shumaker D, Wilcox JN, Udipi K (2009) Impact of polymer hydrophilicity on biocompatibility: implication for DES polymer design. *J Biomed Mater Res A* 90 (1):133-141. doi:10.1002/jbm.a.32057
5. Joner M, Finn AV, Farb A, Mont EK, Kolodgie FD, Ladich E, Kutys R, Skorija K, Gold HK, Virmani R (2006) Pathology of drug-eluting stents in humans: delayed healing and late thrombotic risk. *J Am Coll Cardiol* 48 (1):193-202. doi:10.1016/j.jacc.2006.03.042
6. Costa RA, Abizaid A, Mehran R, Schofer J, Schuler GC, Hauptmann KE, Magalhaes MA, Parise H, Grube E, BioFreedom FIMCTI (2016) Polymer-Free Biolimus A9-Coated Stents in the Treatment of De Novo Coronary Lesions: 4- and 12-Month Angiographic Follow-Up and Final 5-Year Clinical Outcomes of the Prospective, Multicenter BioFreedom FIM Clinical Trial. *JACC Cardiovasc Interv* 9 (1):51-64. doi:10.1016/j.jcin.2015.09.008
7. Baquet M, Jochheim D, Mehilli J (2018) Polymer-free drug-eluting stents for coronary artery disease. *J Interv Cardiol* 31 (3):330-337. doi:10.1111/joic.12499
8. Urban P, Meredith IT, Abizaid A, Pocock SJ, Carrie D, Naber C, Lipiecki J, Richardt G, Iniguez A, Brunel P, Valdes-Chavarri M, Garot P, Talwar S, Berland J, Abdellaoui M, Eberli F, Oldroyd K, Zambahari R, Gregson J, Greene S, Stoll HP, Morice MC, Investigators LF (2015) Polymer-free Drug-Coated Coronary Stents in Patients at High Bleeding Risk. *N Engl J Med* 373 (21):2038-2047. doi:10.1056/NEJMoa1503943
9. Zhang Y CF, Muramatsu T, et al. (2014) Nine-month angiographic and two-year clinical follow-up of polymer-free sirolimus-eluting stent versus durable-polymer sirolimus-eluting stent for coronary artery disease: the Nano randomized trial. *Chin Med J (Engl)* 127:2153-2158. doi:10.3760/cma.j.issn.0366-6999.20133148

10. Liu Y, Zhang Y, Li Y, Qi T, Pan D, Wang H, Liu C, Ma D, Fang Z, Zhang R, Mou F, Tao L, Investigators NA-CR (2020) One-year clinical results of the NANO registry: A multicenter, prospective all-comers registry study in patients receiving implantation of a polymer-free sirolimus-eluting stent. *Catheter Cardiovasc Interv* 95 Suppl 1:658-664. doi:10.1002/ccd.28734
11. Thygesen K, Alpert JS, Jaffe AS, Simoons ML, Chaitman BR, White HD, Joint ESCAAHAWHFTFftUDoMI, Katus HA, Lindahl B, Morrow DA, Clemmensen PM, Johanson P, Hod H, Underwood R, Bax JJ, Bonow RO, Pinto F, Gibbons RJ, Fox KA, Atar D, Newby LK, Galvani M, Hamm CW, Uretsky BF, Steg PG, Wijns W, Bassand JP, Menasche P, Ravkilde J, Ohman EM, Antman EM, Wallentin LC, Armstrong PW, Simoons ML, Januzzi JL, Nieminen MS, Gheorghiade M, Filippatos G, Luepker RV, Fortmann SP, Rosamond WD, Levy D, Wood D, Smith SC, Hu D, Lopez-Sendon JL, Robertson RM, Weaver D, Tendera M, Bove AA, Parkhomenko AN, Vasilieva EJ, Mendis S (2012) Third universal definition of myocardial infarction. *Circulation* 126 (16):2020-2035. doi:10.1161/CIR.0b013e31826e1058
12. Cutlip DE, Windecker S, Mehran R, Boam A, Cohen DJ, van Es GA, Steg PG, Morel MA, Mauri L, Vranckx P, McFadden E, Lansky A, Hamon M, Krucoff MW, Serruys PW, Academic Research C (2007) Clinical end points in coronary stent trials: a case for standardized definitions. *Circulation* 115 (17):2344-2351. doi:10.1161/CIRCULATIONAHA.106.685313
13. Lansky AJ, Costa RA, Mintz GS, Tsuchiya Y, Midei M, Cox DA, O'Shaughnessy C, Applegate RA, Cannon LA, Mooney M, Farah A, Tannenbaum MA, Yakubov S, Kereiakes DJ, Wong SC, Kaplan B, Cristea E, Stone GW, Leon MB, Knopf WD, O'Neill WW, Investigators DCT (2004) Non-polymer-based paclitaxel-coated coronary stents for the treatment of patients with de novo coronary lesions: angiographic follow-up of the DELIVER clinical trial. *Circulation* 109 (16):1948-1954. doi:10.1161/01.CIR.0000127129.94129.6F
14. Mehilli J, Byrne RA, Wieczorek A, Iijima R, Schulz S, Bruskina O, Pache J, Wessely R, Schomig A, Kastrati A, Intracoronary S, Angiographic Restenosis Investigators–Test Efficacy of Rapamycin-eluting Stents with Different Polymer Coating S (2008) Randomized trial of three rapamycin-eluting stents with different coating strategies for the reduction of coronary restenosis. *Eur Heart J* 29 (16):1975-1982. doi:10.1093/eurheartj/ehn253
15. Tsujino I AJ, Honda Y, Fitzgerald PJ (2007) Drug delivery via nano-, micro and macroporous coronary stent surfaces. *Expert Opin Drug Deliv* 4:287-295
16. Shiratori Y, Cola C, Brugaletta S, Alvarez-Contreras L, Martin-Yuste V, del Blanco BG, Ruiz-Salmeron R, Diaz J, Pinar E, Marti V, Garcia-Picart J, Sabate M (2014) Randomized comparison between polymer-free versus polymer-based paclitaxel-eluting stent: two-year final clinical results. *Circ Cardiovasc Interv* 7 (3):312-321. doi:10.1161/CIRCINTERVENTIONS.113.000800
17. Massberg S, Byrne RA, Kastrati A, Schulz S, Pache J, Hausleiter J, Ibrahim T, Fusaro M, Ott I, Schomig A, Laugwitz KL, Mehilli J, Intracoronary S, Angiographic Results: Test Efficacy of S, Probucol-Eluting Versus Zotarolimus- Eluting Stents I (2011) Polymer-free sirolimus- and probucol-eluting versus new generation zotarolimus-eluting stents in coronary artery disease: the Intracoronary Stenting and

- Angiographic Results: Test Efficacy of Sirolimus- and Probucol-Eluting versus Zotarolimus-eluting Stents (ISAR-TEST 5) trial. *Circulation* 124 (5):624-632. doi:10.1161/CIRCULATIONAHA.111.026732
18. Kufner S, Sorges J, Mehilli J, Cassese S, Repp J, Wiebe J, Lohaus R, Lahmann A, Rheude T, Ibrahim T, Massberg S, Laugwitz KL, Kastrati A, Byrne RA (2016) Randomized Trial of Polymer-Free Sirolimus- and Probucol-Eluting Stents Versus Durable Polymer Zotarolimus-Eluting Stents. *JACC: Cardiovascular Interventions* 9 (8):784-792. doi:10.1016/j.jcin.2016.01.009
 19. Sardella G, Stefanini GG, Briguori C, Tamburino C, Fabbicocchi F, Rotolo F, Tomai F, Paggi A, Lombardi M, Gioffre G, Sciafani R, Rolandi A, Sciahbasi A, Scardaci F, Signore N, Calcagno S, Mancone M, Chiarito M, Giordano A (2018) Safety and efficacy of polymer-free biolimus-eluting stents in all-comer patients: the RUDI-FREE study. *EuroIntervention* 14 (7):772-779. doi:10.4244/EIJ-D-18-00148
 20. Chiarito M, Sardella G, Colombo A, Briguori C, Testa L, Bedogni F, Fabbicocchi F, Paggi A, Pallosi A, Tamburino C, Margonato A, Pivato CA, Baber U, Calcagno S, Giordano A, Godino C, Stefanini GG (2019) Safety and Efficacy of Polymer-Free Drug-Eluting Stents. *Circ Cardiovasc Interv* 12 (2):e007311. doi:10.1161/CIRCINTERVENTIONS.118.007311
 21. Kufner S, Ernst M, Cassese S, Joner M, Mayer K, Collieran R, Koppa T, Xhepa E, Koch T, Wiebe J, Ibrahim T, Fusaro M, Laugwitz K-L, Schunkert H, Kastrati A, Byrne RA (2020) 10-Year Outcomes From a Randomized Trial of Polymer-Free Versus Durable Polymer Drug-Eluting Coronary Stents. *Journal of the American College of Cardiology* 76 (2):146-158. doi:10.1016/j.jacc.2020.05.026
 22. R. Rozemeijer MS, M. Voskuil, et al (2019) Randomized all-comers evaluation of a permanent polymer zotarolimus-eluting stent versus a polymer-free amphilimus-eluting stent. *Circulation* 139 67–77
 23. Jensen LO EJ, Veien KT, Ahlehof O, Hansen KN, Aziz A, et al (2020) Randomized comparison of the polymer-free biolimus-coated biofreedom stent with the ultrathin strut biodegradable polymer sirolimus-eluting orsiro stent in an all-comers population treated with percutaneous coronary intervention: the SORT out IX Trial. *Circulation* 141:2052–2063
 24. Kastrati A MJ, Dirschinger J, et al (2001) Intracoronary stenting and angiographic results: strut thickness effect on restenosis outcome (ISAR-STEREO) trial. *Circulation* 103:2816–2821. doi:10.1161/01.CIR.103.23.2816
 25. Garot P, Morice M-C, Tresukosol D, Pocock SJ, Meredith IT, Abizaid A, Carrié D, Naber C, Iñiguez A, Talwar S, Menown IBA, Christiansen EH, Gregson J, Copt S, Hovasse T, Lurz P, Maillard L, Krackhardt F, Ong P, Byrne J, Redwood S, Windhövel U, Greene S, Stoll H-P, Urban P, Urban P, Morice M-C, Abizaid A, Meredith IT, Pocock SJ, Carrié D, Naber C, Greene S, Stoll H-P (2017) 2-Year Outcomes of High Bleeding Risk Patients After Polymer-Free Drug-Coated Stents. *Journal of the American College of Cardiology* 69 (2):162-171. doi:10.1016/j.jacc.2016.10.009
 26. Krucoff MW, Urban P, Tanguay J-F, McAndrew T, Zhang Y, Rao SV, Morice M-C, Price MJ, Cohen DJ, Abdel-Wahab M, Mehta SR, Faurie B, McLaurin B, Diaz C, Stoll H-P, Pocock S, Leon MB (2020) Global Approach to High Bleeding Risk Patients With Polymer-Free Drug-Coated Coronary Stents. *Circulation: Cardiovascular Interventions* 13 (4). doi:10.1161/circinterventions.119.008603

27. Windecker S, Latib A, Kedhi E, Kirtane AJ, Kandzari DE, Mehran R, Price MJ, Abizaid A, Simon DI, Worthley SG, Zaman A, Hudec M, Poliacikova P, Abdul Ghapar AKB, Selvaraj K, Petrov I, Mylotte D, Pinar E, Moreno R, Fabbiochi F, Pasupati S, Kim HS, Aminian A, Tie C, Wlodarczak A, Hur SH, Marx SO, Jankovic I, Brar S, Bousquette L, Liu M, Stone GW, Investigators OO (2020) Polymer-based or Polymer-free Stents in Patients at High Bleeding Risk. *N Engl J Med* 382 (13):1208-1218. doi:10.1056/NEJMoa1910021
28. Iglesias JF, Muller O, Heg D, Roffi M, Kurz DJ, Moarof I, Weilenmann D, Kaiser C, Tapponnier M, Storteky S, Losdat S, Eeckhout E, Valgimigli M, Odutayo A, Zwahlen M, Jüni P, Windecker S, Pilgrim T (2019) Biodegradable polymer sirolimus-eluting stents versus durable polymer everolimus-eluting stents in patients with ST-segment elevation myocardial infarction (BIOSTEMI): a single-blind, prospective, randomised superiority trial. *The Lancet* 394 (10205):1243-1253. doi:10.1016/s0140-6736(19)31877-x
29. Byrne RA, Stone GW, Ormiston J, Kastrati A (2017) Coronary balloon angioplasty, stents, and scaffolds. *The Lancet* 390 (10096):781-792. doi:10.1016/s0140-6736(17)31927-x
30. Konigstein M, Madhavan MV, Ben-Yehuda O, Rahim HM, Srdanovic I, Gkargkoulas F, Mehdipoor G, Shlofmitz E, Maehara A, Redfors B, Gore AK, McAndrew T, Stone GW, Ali ZA (2019) Incidence and predictors of target lesion failure in patients undergoing contemporary DES implantation-Individual patient data pooled analysis from 6 randomized controlled trials. *Am Heart J* 213:105-111. doi:10.1016/j.ahj.2019.03.011
31. Taniwaki M, Stefanini GG, Silber S, Richardt G, Vranckx P, Serruys PW, Buszman PE, Kelbaek H, Windecker S (2014) 4-Year Clinical Outcomes and Predictors of Repeat Revascularization in Patients Treated With New-Generation Drug-Eluting Stents. *Journal of the American College of Cardiology* 63 (16):1617-1625. doi:10.1016/j.jacc.2013.12.036
32. Ananthakrishna R, Kristanto W, Liu L, Chan SP, Loh PH, Tay EL, Chan KH, Chan MY, Lee CH, Low AF, Tan HC, Loh JP (2018) Incidence and predictors of target lesion failure in a multiethnic Asian population receiving the SYNERGY coronary stent: A prospective all-comers registry. *Catheter Cardiovasc Interv* 92 (6):1097-1103. doi:10.1002/ccd.27577

Tables

Table 1. Baseline demographics and clinical characteristics.

Clinical characteristics	N = 2,481
Age, years (mean $\pm$ SD)	62.76 $\pm$ 10.07
Sex (male)	1,763 (71.1%)
DM	564 (22.8%)
Insulin treatment for DM	158 (28.0%)
Hypertension	1,388 (56.0%)
Chronic renal failure	41(1.7%)
Hypercholesterolemia	1,046 (42.2%)
Previous MI	320 (12.9%)
Previous PCI	278 (11.2%)
Previous CABG	17 (0.7%)
Current smoker	56.82 $\pm$ 9.25
Clinical presentation	
Silent ischemia	54 (2.2%)
Stable angina	170 (6.7%)
Unstable angina	1,298 (52.4%)
Non-ST-elevation MI	324 (13.1%)
ST-elevation MI	672 (27.1%)

DM, diabetes mellitus; MI, myocardial infarction; PCI, percutaneous coronary intervention; CABG, coronary artery bypass graft.

Table 2. Lesion and procedural characteristics.

Variable	N = 2,904
Target vessel	
LMCA	96 (3.3%)
LAD	1,278 (44.0%)
LCX	586 (20.2%)
TIMI flow grade preprocedure	
0	599 (20.7%)
1	206 (7.1%)
2	218 (7.5%)
3	1871 (64.7%)
Thrombus present	474 (19.1%)
Thrombus aspiration	114 (5.7%)
Lesion complexity	
AHA/ACC classification	
A	428 (15.0%)
B1	428 (15.0%)
B2	506 (17.8%)
C	1,315 (46.1%)
In-stent restenosis, n (%)	57 (2.0%)
Calcified lesion	169 (5.8%)
Bifurcated lesions	340 (11.7%)
Chronic total occlusion	422 (14.5%)
Severe tortuosity	79 (2.7%)
Lesion length $\geq$ 40 mm	460 (17.0%)
RVD <2.5 mm	115 (4.1%)
Total stent diameter	3.11 $\pm$ 1.34
Total stent length, mm	25.99 $\pm$ 8.59
Post dilatation	2050 (70.6%)
Average maximal pressure (atm)	17.45 $\pm$ 3.82

Multiple vessel PCI	287 (11.6%)
Number of stents per lesion	1.33 ± 0.60
Number of stents per patient	1.56 ± 0.79
Device success	2,385 (96.1%)
Procedural success	2,368 (95.4%)
P2Y12 at discharge	
Clopidogrel	1,785 (71.9%)
Ticagrelor	696 (28.1%)

Values are expressed as mean ± SD or n (%). ACC, American College of Cardiology; AHA, American Heart Association; LAD, left anterior descending artery; LCX, left circumflex artery; LMCA, left main coronary artery; PCI, percutaneous coronary intervention; RCA, right coronary artery; TIMI, thrombolysis in myocardial infarction; RVD, referenced vessel diameter.

Table 3. Clinical outcomes up to 3 years follow-up.

Endpoint	0-1 year n(%)	1-2 year n(%)	2-3 year n(%)	0-3 years n(%)
Target Lesion Failure	76 (3.1%)	57 (2.3%)	35 (1.4%)	168 (6.8%)
Cardiac death	44 (1.8%)	24 (1.0%)	26 (1.0%)	94 (3.8%)
Target non-fatal vessel MI	9 (0.4%)	6 (0.2%)	3 (0.1%)	18 (0.7%)
Clinically driven TLR	34 (1.3%)	30 (1.2%)	9 (0.4%)	73 (2.9%)
Definite stent thrombosis	5 (0.2%)	0 (0%)	1 (0.04%)	6 (0.2%)
Definite/Probable stent thrombosis	10 (0.4%)	2 (0.1%)	1 (0.04%)	13 (0.5%)

Table 4. Predictors of TLF at 3 years follow-up.

Predictors	Univariate		Multivariate	
	HR (95% CI)	P value	HR (95% CI)	P value

Age	1.04 (1.02-1.06)	<0.01	1.03 (1.01-1.05)	0.003
DM	1.79 (1.30-2.47)	<0.01	1.78 (1.20-2.56)	0.003
AMI	1.46 (1.08-1.97)	0.015	1.47 (1.02-2.12)	0.038
Chronic renal failure	2.93 (1.21-7.15)	0.018	2.80 (1.12-7.01)	0.028
LVEF<40%	3.70 (2.32-5.92)	<0.01	3.02 (1.88-4.87)	<0.01
ISR	2.48 (1.22-5.05)	0.012	2.32 (1.12-4.81)	0.024
CTO	1.74 (1.22-2.47)	<0.01	1.53 (1.003-2.33)	0.048

AMI, acute myocardial infarction; CTO, chronic total occlusion; DM, diabetes mellitus; ISR, n-stent restenosis; LVEF, left ventricular ejection fraction.

Figures

Figure 1

Cumulative incidence of target lesion failure up to 3 years.

Figure 2

Cumulative incidence of cardiac death (a), target vessel nonfatal MI (b), clinical driven TLR (c), and ST (d) up to 3 years. TLR, target lesion revascularization; MI, myocardial infarction; ST, stent thrombosis.