Drug-coated balloons for small coronary artery disease (BASKET-SMALL 2): an open-label randomised non-inferiority trial

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Summary

Background **Drug-coated balloons (DCB) are a novel therapeutic strategy for small native coronary artery disease. However, their safety and efficacy is poorly defined in comparison with drug-eluting stents (DES).**

Methods **BASKET-SMALL 2 was a multicentre, open-label, randomised non-inferiority trial. 758 patients with de-novo lesions (<3 mm in diameter) in coronary vessels and an indication for percutaneous coronary intervention were randomly allocated (1:1) to receive angioplasty with DCB versus implantation of a second-generation DES after successful predilatation via an interactive internet-based response system. Dual antiplatelet therapy was given according to current guidelines. The primary objective was to show non-inferiority of DCB versus DES regarding major adverse cardiac events (MACE; ie, cardiac death, non-fatal myocardial infarction, and target-vessel revascularisation) after 12 months. The non-inferiority margin was an absolute difference of 4% in MACE. This trial is registered with ClinicalTrials.gov, number NCT01574534.**

Findings **Between April 10, 2012, and February 1, 2017, 382 patients were randomly assigned to the DCB group and 376 to DES group. Non-inferiority of DCB versus DES was shown because the 95% CI of the absolute difference in MACE in the per-protocol population was below the predefined margin (–3·83 to 3·93%, p=0·0217). After 12 months, the proportions of MACE were similar in both groups of the full-analysis population (MACE was 7·5% for the DCB group *vs* 7·3% for the DES group; hazard ratio [HR] 0·97 [95% CI 0·58–1·64], p=0·9180). There were five (1·3%) cardiac-related deaths in the DES group and 12 (3·1%) in the DCB group (full analysis population). Probable or definite stent thrombosis (three [0·8%] in the DCB group *vs* four [1·1%] in the DES group; HR 0·73 [0·16–3·26]) and major bleeding (four [1·1%] in the DCB group *vs* nine [2·4%] in the DES group; HR 0·45 [0·14–1·46]) were the most common adverse events.**

Interpretation **In small native coronary artery disease, DCB was non-inferior to DES regarding MACE up to 12 months, with similar event rates for both treatment groups.**

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Introduction

Second-generation drug-eluting stents (DES) are the preferred treatment for percutaneous coronary intervention (PCI) in coronary artery disease.[1] However, the efficacy of stents is restricted in small coronary arteries.[2] This limitation applies to bare metal stents (BMS)[3] and first-generation and second-generation DES.[4]

Drug-coated balloons (DCB) are a novel concept for the treatment of coronary artery disease and an established therapeutic option for restenosis of BMS[5,6] and DES.[7,8] The technique is based on the fast delivery of highly lipophilic drugs to the vessel wall after single balloon inflation with a specific matrix.[9] To overcome the limitations of elastic recoil and flow-limiting dissections after balloon angioplasty, optimal lesion preparation is essential, as outlined in recommendations.[10] The feasibility of the technique in small-vessel coronary artery disease has been suggested in several pilot studies.[11–16]

However, to our knowledge, a large randomised trial comparing DCB with second-generation DES with clinical endpoints has not been done.

The Basel Kosten Effektivitäts Trial–Drug-Coated Balloons versus Drug-eluting Stents in Small Vessel Interventions (BASKET-SMALL) 2 trial aimed to test the non-inferiority of DCB versus second-generation DES in small vessel coronary artery disease using a 12-month composite clinical endpoint of major adverse cardiac events (MACE), consisting of cardiac death, non-fatal myocardial infarction, and target vessel revascularisation in a large all-comer population.

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Research in context

Evidence before this study

Second-generation drug-eluting stents (DES) are the standard treatment for coronary artery disease. However, their efficacy is restricted in small coronary arteries because of increased event rates compared with larger vessel sizes. Drug-coated balloons (DCB) are an established treatment option for in-stent restenosis in bare metal stents and DES, but there is scarce evidence about the efficacy and safety of DCB in native small coronary artery disease. Advantages of DCB include the potential for favourable vascular remodelling after angioplasty in the absence of a stent, the theoretical absence of any stent thrombosis, and the option of shortening dual antiplatelet therapy to only 4 weeks. Besides non-randomised data, only two small, randomised controlled trials have been done in this field, using angiographic endpoints and first-generation DES as comparators.

Added value of this study

BASKET-SMALL 2 is a pivotal multicentre randomised controlled study in a large all-comer population and shows the non-inferiority of DCB versus second-generation DES in the treatment of lesions in coronary arteries of less than 3 mm in diameter regarding major adverse cardiac events at 12 months. After successful predilatation of the lesion with a standard balloon, 758 patients were randomly assigned to one of the two treatment groups. The findings show that the use of DCB in small vessel coronary artery disease is safe if an acceptable angiographic result can be obtained after successful predilatation.

Implications of all the available evidence

A stent-free treatment of coronary artery disease with DCB is safe if an acceptable angiographic result can be obtained after predilatation of the lesion. To date, the technique is restricted to small coronary arteries, but might be expanded to larger vessel sizes with future research.

Methods

Study design

BASKET-SMALL 2 is an investigator-initiated, prospective, randomised, multicentre, open-label, non-inferiority trial.[17] The trial was done at 14 participating centres (appendix). The trial was done in accordance with the Declaration of Helsinki and Good Clinical Practice guidelines, and the protocol (appendix) was approved by the ethics committees in all participating centres.

See Online for appendix

Participants

All patients with an indication for PCI either due to acute coronary syndrome, chronic angina pectoris, or silent ischemia, and angiographic lesions in native coronary arteries with a diameter of 2 mm to less than 3 mm were eligible for enrolment. However, randomisation was only possible if predilatation of the lesion with an angioplasty balloon was successful—ie, if an acceptable angiographic result was obtained (no higher-grade dissections National Heart, Lung, and Blood Institute grade C to F,[18] no decreased blood flow (thrombolysis in myocardial infarction score ≤2), or no residual stenosis >30%) according to consensus group recommendations.[10] Exclusion criteria were concomitant PCI of large lesions of at least 3 mm in diameter in the same epicardial coronary artery, PCI of in-stent restenosis, life expectancy of less than 12 months, pregnancy, enrolment in another randomised trial for coronary intervention, or inability to give informed consent. All patients gave written informed consent before the intervention started. In urgent cases when the intervention could not be postponed, oral consent was given before the intervention started. Oral consent was documented by a second medical person not involved in the trial; written informed consent was given after the intervention.

Randomisation and masking

We used an interactive internet-based response system to randomly assign participants (1:1) to receive either angioplasty with DCB or implantation of a second-generation DES after successful predilatation.

This trial was open-label; therefore, participants or investigators were not masked to the treatment.

Procedures

Participants in the DCB group received the paclitaxel-coated balloon SeQuent Please (B Braun Melsungen AG, Melsungen, Germany), and those in the DES group received one of two second-generation DES: the everolimus-eluting Xience stent (Abbott Vascular, Santa Clara, CA, USA) or the paclitaxel-eluting Taxus Element stent (Boston Scientific, Natick, MA, USA). The study was started with Taxus Element as the comparator (to ensure that devices with similar agents were used), but later (between June 19, 2013, and Jan 24, 2014) had to be continued with Xience because the initial stent became unavailable.[17] The sample size was increased to conform to the different efficacy of the two DES. PCI was done strictly in accordance with established guidelines.[10] Specifically, the DCB, which had to be 2–3 mm longer on each side than the predilatation balloon, was inflated at nominal pressure for a minimal time of 30 s. In cases with flow-limiting dissections or residual angiographically significant stenosis (ie, >30% stenosis) after DCB treatment, additional spot stenting avoiding geographical mismatch was allowed. PCI was done under dual antiplatelet therapy with acetylsalicylic acid (100 mg per day) and either a thienopyridine (clopidogrel [75 mg per day] or prasugrel [10 mg per day]) or ticagrelor (90 mg twice per day). After PCI, dual antiplatelet therapy was continued in stable patients for 4 weeks (for DCB) or

6 months (for DES) and in patients with acute coronary syndrome for 12 months.[19] Dual antiplatelet therapy was given for 3 months in patients treated with a combination of DCB and BMS, and for 6 months in patients with DCB and DES. In patients on oral anticoagulation, we followed the guidelines,[1] irrespective of DCB or DES treatment.

All endpoints were adjudicated by an independent critical events committee. Follow-up was done after 6 and 12 months with structured clinical questionnaires or phone calls to assess clinical events, medication, and quality of life.

Outcomes

The primary objective of this trial was to show non-inferiority of DCB versus DES regarding MACE after 12 months. MACE was defined as the composite of cardiac death, non-fatal myocardial infarction, and target vessel revascularisation. Cardiac death was defined as any death that was not clearly of extracardiac origin, and myocardial infarction, according to guidelines.[20] Secondary endpoints were the single components of the primary endpoint, probable or definite stent thrombosis according to the Academic Research Consortium definition,[21] major bleeding (defined as Bleeding Academic Research Consortium type 3 to 5 bleeding),[22] and net clinical benefit (defined as the composite of MACE and major bleeding).

Statistical analysis

The required sample size to show non-inferiority of DCB versus DES in the primary endpoint at 12 months was estimated to be 758 patients (appendix). This estimation was done after the comparator stents were changed (between June 19, 2013, and Jan 24, 2014) and was calculated on the basis of an expected MACE rate of 7% for DCB[14] and 10% for DES,[23] with non-inferiority established if the upper limit of the two-sided 95% CI% of the absolute risk difference was less than 4% (non-inferiority margin). Because the event rates of paclitaxel-eluting stents were expected to be higher than the rates of everolimus-eluting stents,[24] we calculated the sample size on the basis of the DES with expected lower event rates. Sample size was calculated with a resampling procedure (ie, we evaluated samples by sampling various sample sizes 9999 times from binomial distributions based on expected rates) and was set to ensure at least 90% power (1–β=0·9) at a significance level of α=5%. To account for an overall dropout rate of 5%, 758 patients were needed to ensure 720 analysable patients. After the enrolment of 75% of patients, a blinded re-assessment of sample size was done, which showed that the trial could be continued without an increase in sample size.[25] To test for non-inferiority, the absolute difference in MACE risk at 12 months between the DCB and DES groups and the two-sided 95% CI was analysed in the per-protocol population by applying a continuity corrected modification of Wilson's score method. We used the Z_{CU} method to calculate the p value for non-inferiority.[26] For sensitivity analyses, we repeated non-inferiority analyses on the full analysis population.

The full-analysis population was defined as all patients matching inclusion criteria who provided informed consent and were assigned to a treatment group. To form the per-protocol population, we excluded patients from the full-analysis population with major protocol violations (received neither DCB nor DES despite being randomised, unapproved procedures, received the opposite treatment than randomised due to complications) or patients lost to follow-up. Patients in the per-protocol population were analysed as treated. We used Cox proportional hazards models and Kaplan-Meier curves to analyse the time-dependent occurrence of events; hazard ratios (HRs) are presented with 95% CI. For baseline characteristics, continuous variables are reported as mean and SD, whereas categorical variables are reported as frequency and proportion. 95% CIs presented for secondary endpoints are not adjusted for multiple testing and inferences drawn from these might be not reproducible. The primary analysis in the per-protocol population had no missing values by definition. In sensitivity analyses on the full-analysis population, we assumed no event for patients who were lost to follow-up. We analysed secondary endpoints in the full-analysis population, according to the intention-to-treat principle with patients

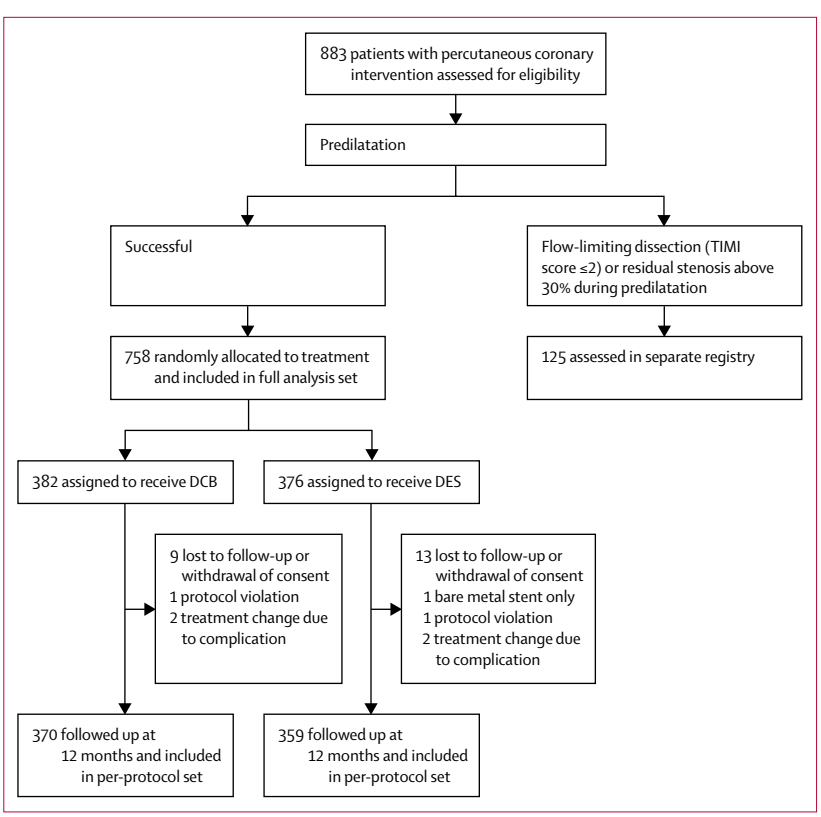

Figure 1: **Trial profile**
TIMI=thrombolysis in myocardial infarction. DCB=drug-coated balloons. DES=drug-eluting stents.

	Drug-coated balloon (n=382)	Drug-eluting stent (n=376)
Mean age, years	67·2 (10·3)	68·4 (10·3)
Sex		
Male	295 (77%)	262 (70%)
Female	87 (23%)	114 (30%)
Mean body-mass index	28·4 (4·5)	28·2 (4·6)
Smoking status*		
Current smoker	82 (22%)	72 (20%)
Former smoker	144 (39%)	123 (34%)
No smoker	148 (40%)	172 (47%)
Hypercholesterolaemia†	262 (69%)	259 (70%)
Arterial hypertension‡	324 (85%)	332 (89%)
Family history of CAD	150 (43%)	128 (38%)
Diabetes§		
Insulin dependent	48 (13%)	47 (13%)
Non-insulin dependent	74 (19%)	83 (22%)
No diabetes	259 (68%)	243 (65%)
Previous myocardial infarction	160 (42%)	133 (35%)
Previous PCI	235 (62%)	241 (64%)
Previous CABG	37 (10%)	34 (9%)
Cerebrovascular insult¶		
No	352 (92%)	339 (90%)
Stroke	16 (4%)	23 (6%)
Transient ischaemic attack	13 (3%)	14 (4%)
PAOD	27 (7%)	26 (7%)
COPD	28 (7%)	36 (9%)
Renal failure	54 (14%)	59 (16%)
Presentation		
STEMI	11 (3%)	4 (1%)
NSTEMI	53 (14%)	56 (15%)
Unstable angina	48 (13%)	42 (11%)
Stable angina	270 (70%)	274 (73%)
Oral anticoagulation	33 (9%)	31 (8%)
LVEF, median (IQR)	60% (50–60)	60% (55–65)

Data are n (%) or mean (SD) unless otherwise stated. CAD=coronary artery disease. PCI=percutaneous coronary intervention. CABG=coronary artery bypass graft. PAOD=peripheral arterial occlusive disease. COPD=chronic obstructive pulmonary disease. STEMI=ST-elevation myocardial infarction. NSTEMI=non-ST-elevation myocardial infarction. LVEF=left ventricular ejection fraction. *Data were only available for 374 participants in the drug-coated balloon group and 367 in the drug-eluting stent group. †Data were only available for 381 in the drug-coated balloon group and 370 in the drug-eluting stent group. ‡Data were only available for 374 in the drug-eluting stent group. §Data were only available for 381 in the drug-coated balloon group and 373 in the drug-eluting stent group. ¶Data were only available for 381 in the drug-coated balloon group.

Table 1: **Baseline characteristics**

	Drug-coated balloon	Drug-eluting stent
Target vessel		
Left anterior descending artery	128 (34%)	116 (31%)
Left circumflex artery	179 (47%)	183 (49%)
Right coronary artery	75 (20%)	77 (20%)
Multivessel disease	313 (82%)	285 (76%)
Bifurcation lesion	22 (6%)	29 (8%)
Mean procedural success, n (SD)	96% (19)	98 (13)
Mean number of DCB or DES, n (SD)	1·68 (0·82)	1·26 (0·55)
Mean length of DCB or DES, mm (SD)	23·93 (11·74)	23·18 (12·85)
Mean effective size of DCB or DES, mm (SD)	2·75 (2.14)	2·57 (0.25)
Mean inflation pressure, atm (SD)	11·06 (3·54)	13·58 (3·90)
Mean duration of inflation, sec (SD)	48·45 (28.24)	23·36 (18.92)
Compliant balloon for predilatation	282 (73%)	276 (74%)

Data are n (%) or mean (SD). DCB=drug-coated balloons. DES=drug-eluting stents.

Table 2: **Angiographic data**

analysed as randomised. We used R (version 3.5.0) for all statistical analyses.[27]

Role of the funding source

The funders of the study had no role in study design, data collection, data analysis, and data interpretation, or writing of the report, and did not participate in the decision to submit the manuscript for publication. The principle investigator (RVJ) and NG had full access to all data. The corresponding author had final responsibility for the decision to submit for publication.

Results

Between April 10, 2012, and February 1, 2017, 883 patients were enrolled, of which 758 (86%) were randomly assigned to treatment and 125 (14%) entered a separate registry. Randomisation ended once the calculated sample size was reached. Of the patients who were randomly assigned treatment, 382 were assigned to the DCB group and 376 to the DES group. Overall, 729 (96%) of 758 patients had complete data for the primary endpoint (figure 1). The two treatment groups were well balanced in terms of baseline demographic and clinical characteristics of patients (table 1) and angiographic data (table 2). However, there was a higher proportion of men in the DCB group than in the DES group (p=0·0232; table 1).

The difference in absolute risk of MACE between the two treatment groups was 0·0005 (95% CI –0·038 to 0·039) in the per-protocol population (figure 2). Since the margin of the 95% CI did not cross the predefined value of 4% (p=0·0217), non-inferiority of DCB versus DES was shown (figure 2). A sensitivity analysis in the full-analysis population gave similar results, with a difference in risk of –0·0012 (–0·040 to 0·037; figure 2). In the full-analysis population, proportion of MACE events after 12 months was 7·3% in the DCB group and 7·5% in the DES group (0·97, 0·58–1·64; p=0·9180; figure 3).

Rates of cardiac death (12 patients [3·1%] for the DCB group *vs* five patients [1·3%] for the DES group; HR 2·33 [95% CI 0·82–6·61]; p=0·1131), non-fatal myocardial infarction (1·6% *vs* 3·5%; 0·46 [0·17–1·20]; p=0·1123), and target vessel revascularisation (3·4% *vs* 4·5%; 0·75 [0·36–1·55]; p=0·4375) did not differ between the groups (appendix). Probable or definite stent thrombosis occurred

in both treatment groups since stents were also implanted in patients in the DCB group, mostly in other parts of the coronary vasculature; however, rates were low and not statistically different between the DCB and DES groups (0·79% *vs* 1·60%; 0·73 [0·16–3·26]). There was no acute vessel closure in DCB lesions. Rates of major bleeding were low and similar between the DCB and DES groups (1·1% *vs* 2·4%; 0·45 [0·14–1·46]) and rates of the net clinical benefit were similar in the DCB and DES groups (7·9% *vs* 9·6%; 0·81 [0·50–1·32]). None of the subgroups showed strong differential effects between the treatment groups (interaction tests; figure 4).

MACE proportions after 12 months were generally higher in men than in women but were similar within both treatment groups (figure 4). The interaction did not differ between sex and treatment (interaction term 0·93 [0·25–3·41]; p=0·9127).

Within the two treatment groups, we did specific post-hoc analyses regarding the combination of DCB with stents (DCB group) and the different stent types (DES group; per-protocol population; figure 5). In the DCB group, 19 (5·1%) patients were treated with a combination of DCB and stents in the index lesion (mostly DES). MACE rates for DCB and stents were numerically higher than for DCB only (DCB with stent *vs* DCB only, 15·8% *vs* 7·0%; HR 2·11 [95% CI 0·62–7·19]; p=0·2306). In the DES group, 94 (28%) of 341 patients were treated with paclitaxel-eluting stents, which had numerically higher MACE rates than did everolimus-eluting stents (12·8% *vs* 5·7%, HR 2·04 [0·88–4·76]; p=0·0987). The specific HR for the comparison between DCB and everolimus-eluting stents was 1·21 (0·63–2·32; p=0·5751) and was 0·52 (0·26 to 1·04; p=0·0649) for the comparison between DCB and paclitaxel-eluting stents.

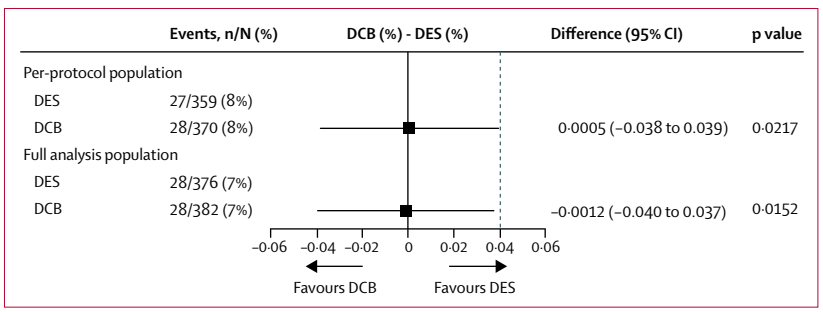

Figure 2: **Major adverse cardiac events by study group**
Data are absolute difference in event rates between the DCB and DES groups. The p-value tests whether the absolute difference in rates is equal to the pre-defined non-inferiority margin (0·04). DCB=drug-coated balloons. DES=drug-eluting stents.

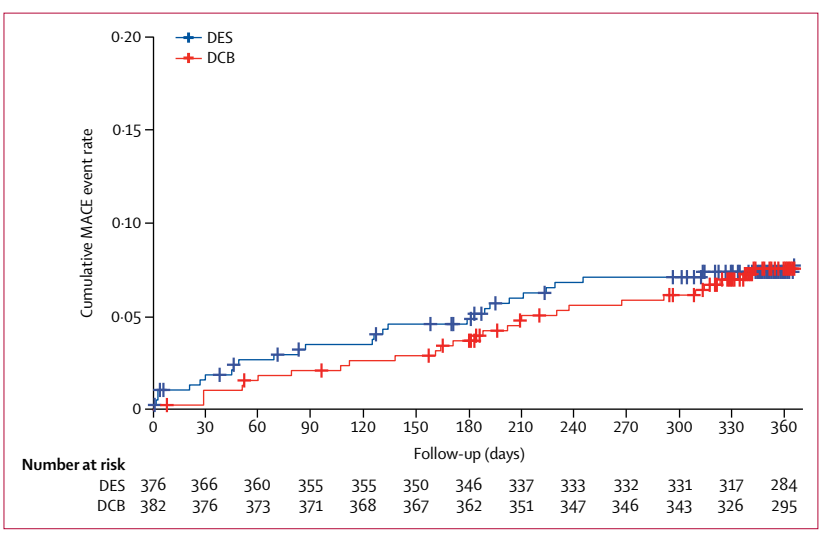

Figure 3: **Cumulative incidence rates for MACE**
Full analysis population. MACE=major adverse cardiac events. DCB=drug-coated balloons. DES=drug-eluting stents.

Discussion

The BASKET-SMALL 2 trial showed the non-inferiority of DCB versus DES regarding clinical events in a large all-comer population undergoing PCI in native small-vessel coronary artery disease. After 12 months, MACE rates were low and similar between the groups.

The DCB technique is based on the interaction of a highly lipophilic drug with a coating matrix and allows for fast and homogenous drug delivery into the vessel wall. Although many devices exist on the market, balloons coated with paclitaxel and iopromide have shown favourable clinical results and are the most widely used to date.[9] DCB is an established treatment option for the treatment of in-stent restenosis,[5–8] but, in native small-vessel coronary artery disease, the technique has been tested in smaller studies only.[15,16] Advantages of DCB are the potential for favourable vascular remodelling after angioplasty in the absence of a stent, the theoretical lack of any stent thrombosis, and the option of shortening dual antiplatelet therapy to only 4 weeks. Possible limitations relate to the early days of interventional cardiology, in which the method of plain balloon angioplasty—at that time in the absence of dual antiplatelet therapy—was restricted by acute vessel closure due to elastic recoil and flow-limiting dissections.[28] Therefore, in our study, rigorous lesion preparation according to established recommendations[10] to achieve an acceptable angiographic result before use of DCB was mandatory to avoid complications.

So far, only two randomised controlled trials have assessed the efficacy and safety of DCB versus DES in native small-vessel coronary artery disease.[15,16] The PICCOLETO study[15] tested the effect of a paclitaxel-eluting balloon (Dior; Eurocor, Bonn, Germany), in which the drug adhered to the roughened surface without matrix, compared with a first-generation paclitaxel-eluting stent (Taxus Liberté) and was prematurely stopped after 57 patients were enrolled. The findings showed an increase in the primary angiographic endpoint (% diameter stenosis) in the DCB group versus the DES group after 6 months and also an increase in the combined clinical endpoint, which was mainly attributed

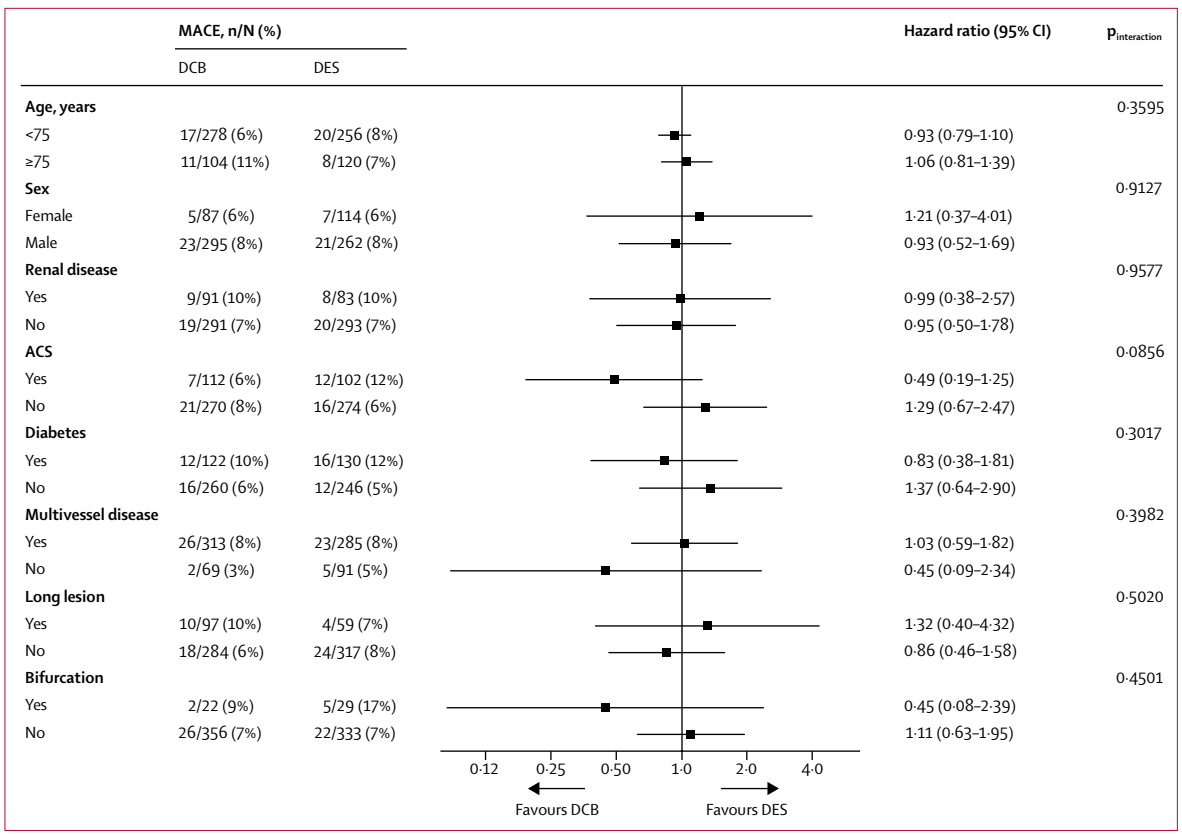

Figure 4: **Subgroup analyses of MACE and hazard ratios**
Cox proportional hazards models were fitted with time-to-MACE as outcome and with patients censored at last observation if experiencing no event. All analyses were done on the full analysis population with the treatment group as assigned to patients at randomisation. MACE=major adverse cardiac events. DCB=drug-coated balloons. DES=drug-eluting stents. ACS=acute coronary syndrome.

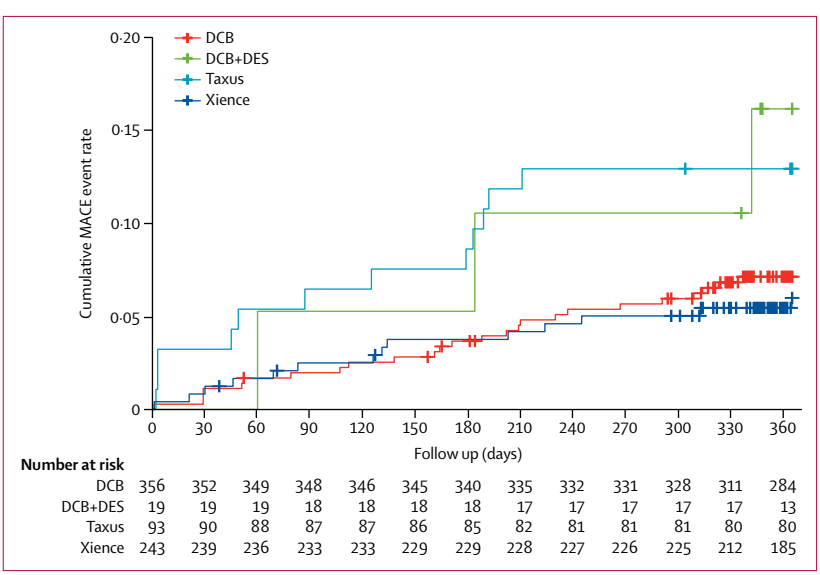

Figure 5: **Cumulative incidence rates for MACE**
According to the actual treatment that patients received. MACE=major adverse cardiac events. DCB=drug-coated balloons. DES=drug-eluting stents.

to the type of DCB and the fact that geographical mismatch was not prevented.[29] By contrast, the BELLO study[16] tested the efficacy of a paclitaxel-eluting balloon using urea as matrix (IN.PACT Falcon; Medtronic, Santa Rosa, CA, USA) against a first-generation paclitaxel-eluting stent (Taxus Liberté) and enrolled 182 patients. The primary angiographic endpoint of non-inferiority regarding angiographic in-stent or in-balloon late loss after 6 months was met, and the combined clinical endpoint showed similar event rates for both groups after 6 and 36 months.[30] Although more than 95% of lesions were treated with optimal lesion preparation in BELLO, this measurement was true for only 25% of lesions in PICCOLETO. Therefore, the use of a DCB with favourable clinical data, the prevention of geographical mismatch and an optimal lesion preparation might have contributed to the positive result of BASKET-SMALL 2. The study was not powered to detect differences in the single components of the primary endpoint. The potential long-term benefit of DCB over permanently implanted stents might not be seen until after 2–5 years.[30] Long-term follow-up data of the current study are still being collected and will be reported in due time.

Two distinct interventional treatment entities in our trial are of specific interest. The numerically (not significantly) higher event rate with the combination of DCB and stents might be explained by accidental angiographic mismatch and is consistent with previous data, wherein rates of restenosis increased when DCB were combined with BMS.[14,15] Therefore, guidelines on DCB therapy advocate the use of DES in case of unplanned stent implantation,[10] and current generation limus-DES should be preferred.[31] However, the combination of DCB with stents in the same lesion should be avoided whenever possible. Second, the MACE rates of patients on DES who are receiving paclitaxel-eluting stents compared with that of patients receiving everolimus-eluting stents is consistent with previous non-randomised data.[23,24] However, a randomised controlled pilot study in small-vessel coronary artery disease reported a numerically lower event rate for paclitaxel-eluting versus zotarolimus-eluting stents.[32] On the basis of our data, paclitaxel seems to be more efficient in the setting of the DCB than the DES technique.

DCB require a shorter dual antiplatelet therapy than do DES in stable patients (ie, 4 weeks only instead of 6 months), which might reduce the risk of major bleeding.[10,19] The shorter duration of dual antiplatelet therapy might be of additional benefit, which was not accounted for in the current non-inferiority trial.

Our study has some limitations. First, the trial was initially designed with a second-generation paclitaxel-eluting stent as comparator to the paclitaxel-eluting balloon to use the same drug and make comparisons possible. However, since the stent became unavailable during the study, the comparator was changed to an everolimus-eluting stent and the sample size was increased. Therefore, the trial was switched from a pure comparison of two different devices to a more comprehensive comparison of two interventional strategies. Second, there was an imbalance in sex distribution among the randomised groups, with more male patients randomly assigned to the DCB group than to the DES group. However, a specific analysis revealed that male patients had higher event rates than women did, thus underlining the efficacy of DCB and that there was no significant interaction between sex and treatment. Third, extrapolation of our findings to other types of DCB may not be justified. Finally, there was no routine angiographic follow-up in the study; therefore, event rates could have been underestimated. Since this was a clinical trial, there was no routine core-lab analysis of the angiographies at trial entry and at follow-up.

In summary, to our knowledge, BASKET-SMALL 2 is the first large randomised controlled trial testing the efficacy of a paclitaxel-iopromide-coated DCB versus second-generation DES in a large all-comer population regarding clinical endpoints. Our study showed that DCB are non-inferior to DES in lesions of small native coronary arteries regarding MACE up to 12 months, with similar event rates for both treatment groups. Therefore, small native coronary artery disease might safely be treated with DCB after successful predilatation.

Contributors

RVJ, NG, CK, and BS designed the study, collected and interpreted the data, and drafted the manuscript. AF, M-AO, NM, SM-W, GL, DW, JW, SR, MS, FM, AL, F-PS, CM, PR, and SO collected the data and critically revised the work for important intellectual content. MC designed the study and analysed the data. All authors approved the final version.

Declaration of Interests

RVJ has received lecture honoraria and travel support from B Braun. M-AO has received proctoring honoraria and travel support from Biosensors and research support from Terumo. NM has received speaker's honoraria from Edwards and Medtronic and consultant honoraria from Biotronik. GL is a medical user advisory board member for REVA Medical and has relationships with drug and device companies, including Terumo, Acrostak, Bionsensors, Boston Scientific, Abbott Vascular, Impuls Medical, and Orbus Neich. FM is supported by Deutsche Gesellschaft für Kardiologie, Deutsche Hochdruckliga, and Deutsche Forschungsgemeinschaft (SFB TRR 219), and has received grant support and personal fees from Medtronic and Recor Medical. AL has received speaker honoraria or served as a consultant for the following companies: Medtronic, St Jude Medical, Claret Medical Inc, Boston Scientific, Edwards Lifesciences, Symetis, and Bard, and holds stock options from Claret Medical, Emboline, and Transverse Medical. AL has also received grant support from Medtronic and Claret Medical and speaker honoraria from Novartis and Bayer. NG has received travel support from B Braun. BS is a shareholder of InnoRa GmbH and was named as co-inventor on patent applications submitted by Charité University Hospital, Berlin, Germany. All other authors declare no competing interests.

Data sharing

As secondary analyses are in progress, data collected for the study, including individual participant data and a data dictionary defining each field in the set, will not be made available to others.

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