Supplementary data

Supplementary Appendix 1.

CONSORT 2010 checklist of information to include when reporting a randomised trial*

Section/Topic	Item No	Checklist item	Reported on page No
Title and abstract			
	1a	Identification as a randomised trial in the title	Yes
	1b	Structured summary of trial design, methods, results, and conclusions (for specific guidance see CONSORT for abstracts)	Yes
Introduction			
Background and objectives	2a	Scientific background and explanation of rationale	5
	2b	Specific objectives or hypotheses	Not included
Methods			
Trial design	3a	Description of trial design (such as parallel, factorial) including allocation ratio	6
	3b	Important changes to methods after trial commencement (such as eligibility criteria), with reasons	6
Participants	4a	Eligibility criteria for participants	P. 6 and published study design article (Micari, et al. *J Crit Limb Ischemia*. 2021)
	4b	Settings and locations where the data were collected	Suppl Table 1, p. 2
Interventions	5	The interventions for each group with sufficient details to allow replication, including how and when they were actually administered	7-8 and published study design article
Outcomes	6a	Completely defined pre-specified primary and secondary outcome measures, including how and when they were assessed	8-9
	6b	Any changes to trial outcomes after the trial commenced, with reasons	NA
Sample size	7a	How sample size was determined	Published study design article
	7b	When applicable, explanation of any interim analyses and stopping guidelines	Not included
Randomisation:			

Sequence generation	8a	Method used to generate the random allocation sequence	Not included
	8b	Type of randomisation; details of any restriction (such as blocking and block size)	Published study design article
Allocation concealment mechanism	9	Mechanism used to implement the random allocation sequence (such as sequentially numbered containers), describing any steps taken to conceal the sequence until interventions were assigned	Not included
Implementation	10	Who generated the random allocation sequence, who enrolled participants, and who assigned participants to interventions	Published study design article
Blinding	11a	If done, who was blinded after assignment to interventions (for example, participants, care providers, those assessing outcomes) and how	16-17
	11b	If relevant, description of the similarity of interventions	NA
Statistical methods	12a	Statistical methods used to compare groups for primary and secondary outcomes	10
	12b	Methods for additional analyses, such as subgroup analyses and adjusted analyses	10
Results			
Participant flow (a diagram is strongly recommended)	13a	For each group, the numbers of participants who were randomly assigned, received intended treatment, and were analysed for the primary outcome	P. 6, Figure 1, Tables 1 and 2
	13b	For each group, losses and exclusions after randomisation, together with reasons	Figure 1
Recruitment	14a	Dates defining the periods of recruitment and follow-up	Not included
	14b	Why the trial ended or was stopped	NA
Baseline data	15	A table showing baseline demographic and clinical characteristics for each group	Table 1
Numbers analysed	16	For each group, number of participants (denominator) included in each analysis and whether the analysis was by original assigned groups	Table 2 and Table 3
Outcomes and estimation	17a	For each primary and secondary outcome, results for each group, and the estimated effect size and its precision (such as 95% confidence interval)	Pp. 11-13, Tables 2 and 3
	17b	For binary outcomes, presentation of both absolute and relative effect sizes is recommended	NA
Ancillary analyses	18	Results of any other analyses performed, including subgroup analyses and adjusted analyses, distinguishing pre-specified from exploratory	NA, all pre-specified
Harms	19	All important harms or unintended effects in each group (for specific guidance see CONSORT for harms)	None reported
Discussion			
Limitations	20	Trial limitations, addressing sources of potential bias, imprecision, and, if relevant, multiplicity of analyses	16-17
Generalisability	21	Generalisability (external validity, applicability) of the trial findings	Not included

Interpretation	22	Interpretation consistent with results, balancing benefits and harms, and considering other relevant evidence	17-18
Other information			
Registration	23	Registration number and name of trial registry	Abstract (p. 2)
Protocol	24	Where the full trial protocol can be accessed, if available	Not included
Funding	25	Sources of funding and other support (such as supply of drugs), role of funders	18

*We strongly recommend reading this statement in conjunction with the CONSORT 2010 Explanation and Elaboration for important clarifications on all the items. If relevant, we also recommend reading CONSORT extensions for cluster randomised trials, non-inferiority and equivalence trials, non-pharmacological treatments, herbal interventions, and pragmatic trials. Additional extensions are forthcoming: for those and for up to date references relevant to this checklist, see www.consort-statement.org.

Supplementary Table 1. IN.PACT BTK randomised study sites and investigators.

Study site	Location	Investigators
Universitair Ziekenhuis Gent	Gent, Belgium	Frank Vermassen, MD, PhD
UniversitätsSpital Zürich	Zurich, Switzerland	Martin Banyai, MD Frederic Baumann, MD Robert Kreuzpointer, MD
Ziekenhuis Oost Limburg – Campus Sint-Jan	Genk, Belgium	Wouter Lansink, MD
Hôpital Guillaume et René Laënnec – CHU de Nantes	Nantes, France	Yann Gouëffic, MD, PhD Philippe Chaillou, MD
IRCCS Multimedica	Sesto San Giovanni, Italy	Flavio Airoldi, MD
University General Hospital of Patras	Patras, Greece	Konstantinos Katsanos, MD, PhD
AZ Sint-Blasius – Campus Dendermonde	Dendermonde, Belgium	Koen Deloose, MD
Maria Cecilia Hospital	Cotignola, Italy	Antonio Micari, MD, PhD Paolo Sbarzaglia, MD
Ospedale San Donato	Arezzo, Italy	Francesco Liistro, MD

Supplementary Table 2. Procedural characteristics and outcomes from the IN.PACT BTK randomised study.

	DCB (N=23 participants) (N=25 lesions*)	PTA (N=27 participants) (N=30 lesions*)	*p*-value
Inflow lesion treatment during index procedure†,§	43.5 (10/23)	51.9 (14/27)	0.584
Predilation†	100.0 (25/25)	100.0 (30/30)	>0.999
Number of predilations per lesion†			0.087
1	16.0 (4/25)	6.7 (2/30)	
2	36.0 (9/25)	20.0 (6/30)	
3	32.0 (8/25)	26.7 (8/30)	
>3	16.0 (4/25)	46.7 (14/30)	
Maximum predilation pressure per lesion, atm†	12.3±2.9 (25)	13.2±2.5 (30)	0.295
Number of DCB balloons per participant†			–
1	0.0 (0/23)	NA	
2	26.1 (6/23)	NA	
3	56.5 (13/23)	NA	
>3	17.4 (4/23)	NA	
Maximum DCB pressure per balloon, atm†	12.6±2.4 (68)	NA	–
DCB balloon diameter, mm†	3.1±0.4 (25)	NA	–
Post-dilation†	36.0 (9/25)	10.0 (3/30)	0.026
Overall balloon diameter (all balloons used), mm†	3.0±0.3 (25)	2.9±0.4 (30)	0.187
Provisional stent†	8.0 (2/25)	3.3 (1/30)	0.586
Dissections‡			0.108
0	45.8 (11/24)	72.4 (21/29)	
A	0.0 (0/24)	0.0 (0/29)	
B	45.8 (11/24)	24.1 (7/29)	
C	4.2 (1/24)	3.4 (1/29)	
D	4.2 (1/24)	0.0 (0/29)	
E–F	0.0 (0/24)	0.0 (0/29)	
MLD, mm‡	1.945±0.412 (24)	1.797±0.462 (29)	0.230
Diameter stenosis, %‡	31.843±10.959 (24)	34.124±14.368 (29)	0.703
Final residual stenosis, %†	5.1±7.6 (25)	6.8±8.5 (30)	0.432
Device success†,¶	94.1 (64/68)	NA	–
Clinical success‡,#	52.2 (12/23)	40.7 (11/27)	0.570

Values are mean±SD (N) or % (n/N).

* The study sites and core laboratory identified different numbers of target lesions in each treatment group. Study sites identified 25 target lesions in the DCB group and 30 in the PTA group. Therefore, all site-reported lesion characteristics use 25 as the denominator for the DCB group and 30 as the denominator for the PTA group. The core laboratory identified 24 target

lesions in the DCB group and 29 in the PTA group. Therefore, all core laboratory-reported lesion characteristics use 24 as the denominator for the DCB group and 29 as the denominator for the PTA group.

† Site reported.

‡ Core laboratory reported.

§ Significant inflow lesions in the ipsilateral iliac, superficial femoral artery and popliteal arteries needed to be treated successfully prior to enrolment in the study. No other non-target lesions (including outflow lesions) in the target limb were allowed to be treated.

¶ Device success is defined as successful drug delivery, balloon inflation, deflation and retrieval of the intact study device without burst below the rated burst pressure (balloon-based assessment, DCB group only).

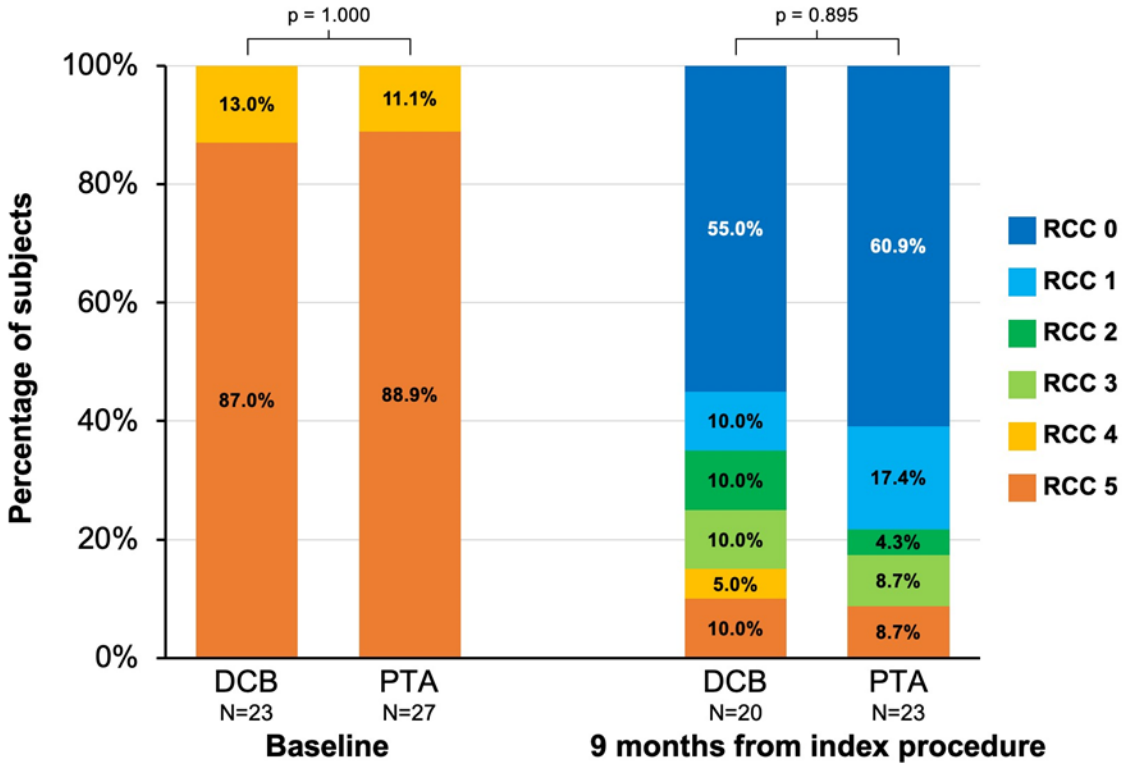
Clinical success is defined as residual stenosis ≤30% without procedural complication (death, major target limb amputation, thrombosis of target lesion, or target vessel revascularisation) prior to discharge (participant-based assessment).

DCB: drug-coated balloon; MLD: minimal lumen diameter; PTA: percutaneous transluminal angioplasty

Supplementary Table 3. Functional flow assessment by duplex ultrasound up to nine months from the IN.PACT BTK randomised study.

	DCB (N=24 lesions*)	PTA (N=29 lesions*)	Difference [95% CI]	*p*-value
Lesions with functional flow at 3 months, %†	93.8 (15/16)	66.7 (14/21)	27.1 [-0.3, 49.0]	0.104
Lesions with functional flow at 6 months, %†	88.2 (15/17)	72.2 (13/18)	16.0 [-11.2, 40.6]	0.402
Lesions with functional flow at 9 months, %†	84.6 (11/13)	60.0 (6/10)	24.6 [-10.9, 55.4]	0.341

Values are % (n/N) unless otherwise indicated.
* Core laboratory analysis determined a total of 24 target lesions in the DCB group and 29 target lesions in the PTA group. All core laboratory-based assessments use these values for counts and proportions.
† Functional flow defined as the absence of target lesion occlusion (no flow) as assessed by duplex ultrasound.
CI: confidence interval; DCB: drug-coated balloon; PTA: percutaneous transluminal angioplasty



Supplementary Figure 1. Rutherford clinical category at baseline and month 9 in the IN.PACT BTK randomised study.

Participants in both groups showed clinical improvement in RCC from baseline to nine months after the index procedure. The distribution of participants among RCC categories was not significantly different between groups at baseline (p=1.000) or nine months (p=0.895).

DCB: drug-coated balloon; PTA: percutaneous transluminal angioplasty; RCC: Rutherford clinical category