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Engineering the extraordinary

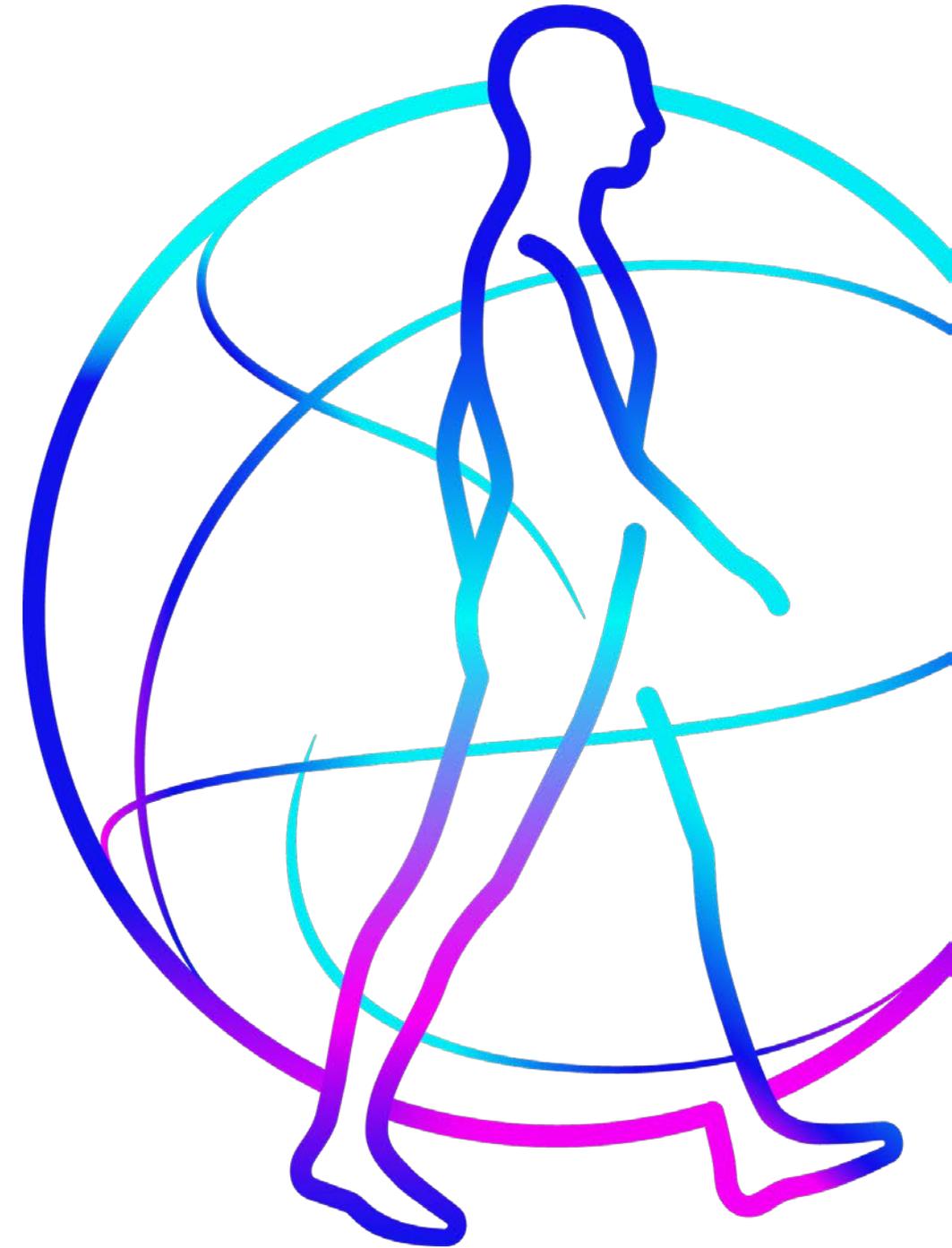
IN.PACT AV Access outcomes. We know which DCB to use!

Final 5-year Trial Outcomes

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Charing Cross Symposium, London – April 2024



Disclosures

Andrew Holden, MBChB, FRANZCR

I have the following potential conflicts of interest to report:

- ✓ Medical Advisory Board Member for: Boston Scientific, Gore, Medtronic, Philips
- ✓ Clinical Investigator for: Abbott, Bard-BD, Biotronik, Boston Scientific, Cagent, Cook, Efemoral, Endologix, Endospan, FluidX, Gore, Medtronic, Nectero, Philips, Reflow Medical, Shape Memory, Shockwave, Terumo, TriReme

Stockholder of a healthcare company

Owner of a healthcare company

Other(s)

I do not have any potential conflict of interest

Background

Long-term Follow-up of ESKD Patients – What do we know?

- We know a lot: population-level data collection worldwide (robust and recent yet inconsistent reporting)

Geography	Registry Name	Last Published	Data available through
United States	United States Renal Data Source (USRDS) https://www.niddk.nih.gov/about-niddk/strategic-plans-reports/usrds/news/2023/usrds-releases-2023-interactive-annual-data-report	2023	2021
Europe	European Renal Association (ERA) Registry https://www.era-online.org/research-education/era-registry/annual-reports/	2023	2021
Japan	Japanese Society for Dialysis Therapy (JSDT) Renal Data Registry https://www.jsdt.or.jp/english/2426.html / https://www.jstage.jst.go.jp/article/jsdt/56/12/56_473/_article/	2020 (En) 2023 (Jp)	2018 (En) 2022 (Jp)
Australia/New Zealand	Australia/New Zealand Dialysis and Transplant Registry (ANZDATA) https://www.anzdata.org.au/anzdata/publications/reports/	2024	2023

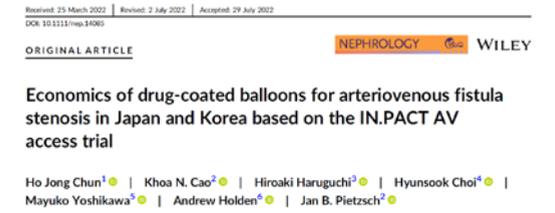
Yet unknowns remain on the individual level:

- Longitudinal patient data is scarce
- No ‘gold standard’ for fistula creation or maintenance; access to technology and algorithms of care vary widely
- Definitions of important characteristics and outcomes vary (eg lesion, intraprocedural techniques, outcomes)

ESKD, end stage kidney disease

IN.PACT AV Access IDE Study

Clinical Data Shared through the Years



Publication: 12-month Japanese/South Korean economic outcomes in Nephrology⁶

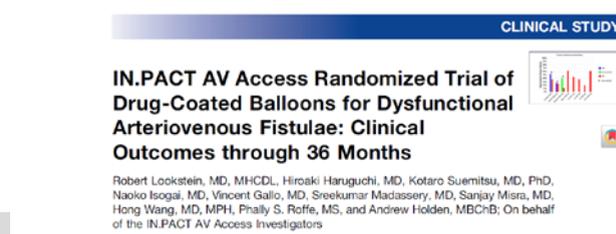


Publication: Primary Endpoints were Met - NEJM³



Publication: 12-month Japanese outcomes in TAD⁷

Primary Endpoint Presentation at CIRSE¹



Publication: 36-month outcomes in JVIR⁸

Study set-up

Study enrollment – April 2017 – May 2018

Approved by FDA in November²

Publications: 12-month clinical and economics manuscripts in JVIR^{4, 5}

2016	2017	2018	2019	2020	2021	2022	2023
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CIRSE, Cardiovascular and Interventional Radiological Society of Europe Annual Meeting; FDA, Food and Drug Administration; IDE, investigational device exemption; JVIR, Journal of Vascular and Interventional Radiology; NEJM, New England Journal of Medicine; TAD, Therapeutic Apheresis and Dialysis

- Holden, A. CIRSE 2019
- <https://news.medtronic.com/2019-11-21-Medtronic-Drug-Coated-Balloon-Receives-U-S-FDA-Approval-to-Treat-Arteriovenous-Fistula-Lesionsv>. Accessed April 14, 2024.
- Lookstein R et al. N Engl J Med 2020;383:733-42
- Holden A et al. J Vasc Interv Radiol 2022;33(8):884-894 e7.
- Pietzsch JB et al. J Vasc Interv Radiol 2022;33(8):895-902.
- Chun H et. al. Neph (Carlton). 2022;27(11):859-868.
- Haruguchi H et al. Ther Apher Dial. 2023;27(4):682-69
- Lookstein R et al. J Vasc Interv Radiol 2023;34(12):2093-2102.e7

IN.PACT AV Access IDE Study

Objective and Study Characteristics†

Objective	Evaluate the safety and effectiveness of the IN.PACT™ AV drug-coated balloon compared to PTA for treatment of de-novo or restenotic obstructive lesions of native AVF in the upper extremity
Design	Prospective, global, multicenter, 1:1 randomized, single-blinded study of 330 participants
Sites	29 Global Sites in The United States, Japan and New Zealand
Adjudication	Independent and blinded Duplex Ultrasound Core Lab‡, Angiographic Core Lab§, and Clinical Events Committee ^Ω
Primary Safety Endpoint	Serious Adverse Event Rate within 30 Days Defined as the Serious Adverse Event (SAE) rate involving the AV access circuit through 30 days post-procedure
Primary Effectiveness Endpoint	Target Lesion Primary Patency Rate through 6 Months Defined as freedom from clinically-driven target lesion revascularization or access circuit thrombosis measured through 6 months post-procedure
Long-term Outcomes	
Through 36 months	Target lesion primary patency, access circuit primary patency, number of reinterventions, mortality
Through 60 months	Mortality with vital status follow-up

AVF, arteriovenous fistula; DCB, drug-coated balloon;
IDE, investigational device exemption; PTA, percutaneous transluminal angioplasty
Study sponsored by Medtronic, Inc
†Lookstein R et al. N Engl J Med 2020;383:733-42.

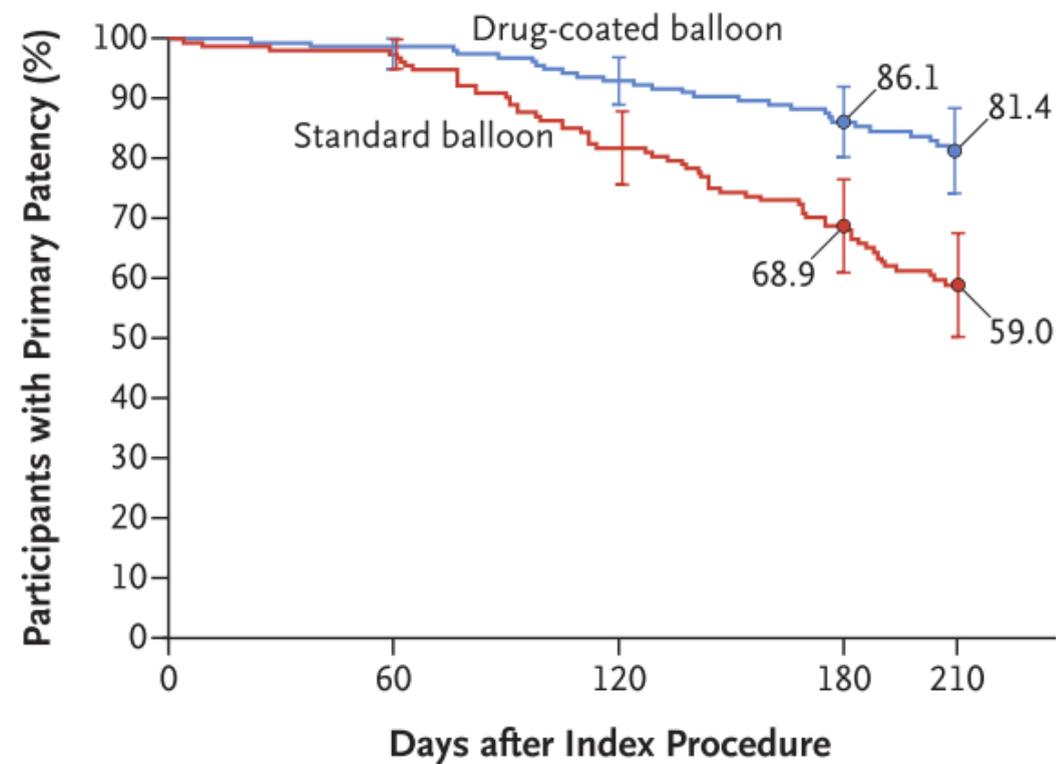
‡ VasCore DUS Core Laboratory
§ SYNTACTX Angiographic Core Laboratory
^Ω SYNTACTX Clinical Events Committee

IN.PACT AV Access IDE Study Outcomes Through 6 Months

Published in The New England Journal of Medicine in August 2020[†]

“Drug-coated balloon angioplasty was superior to standard angioplasty for the treatment of stenotic lesions in dysfunctional hemodialysis arteriovenous fistulas during the 6 months after the procedure and was noninferior with respect to access circuit–related serious adverse events within 30 days.”

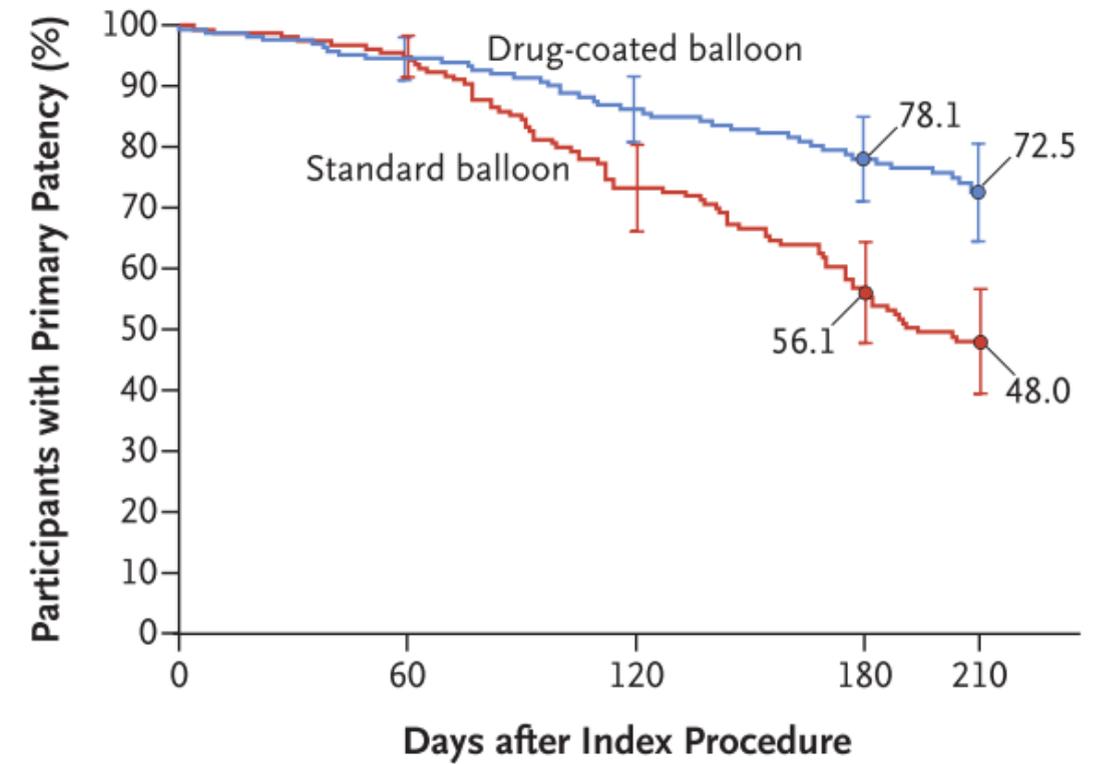
A Target-Lesion Primary Patency



No. at Risk

Drug-coated balloon	170	158	144	115	95
Standard balloon	160	152	123	93	72

B Access-Circuit Primary Patency



No. at Risk

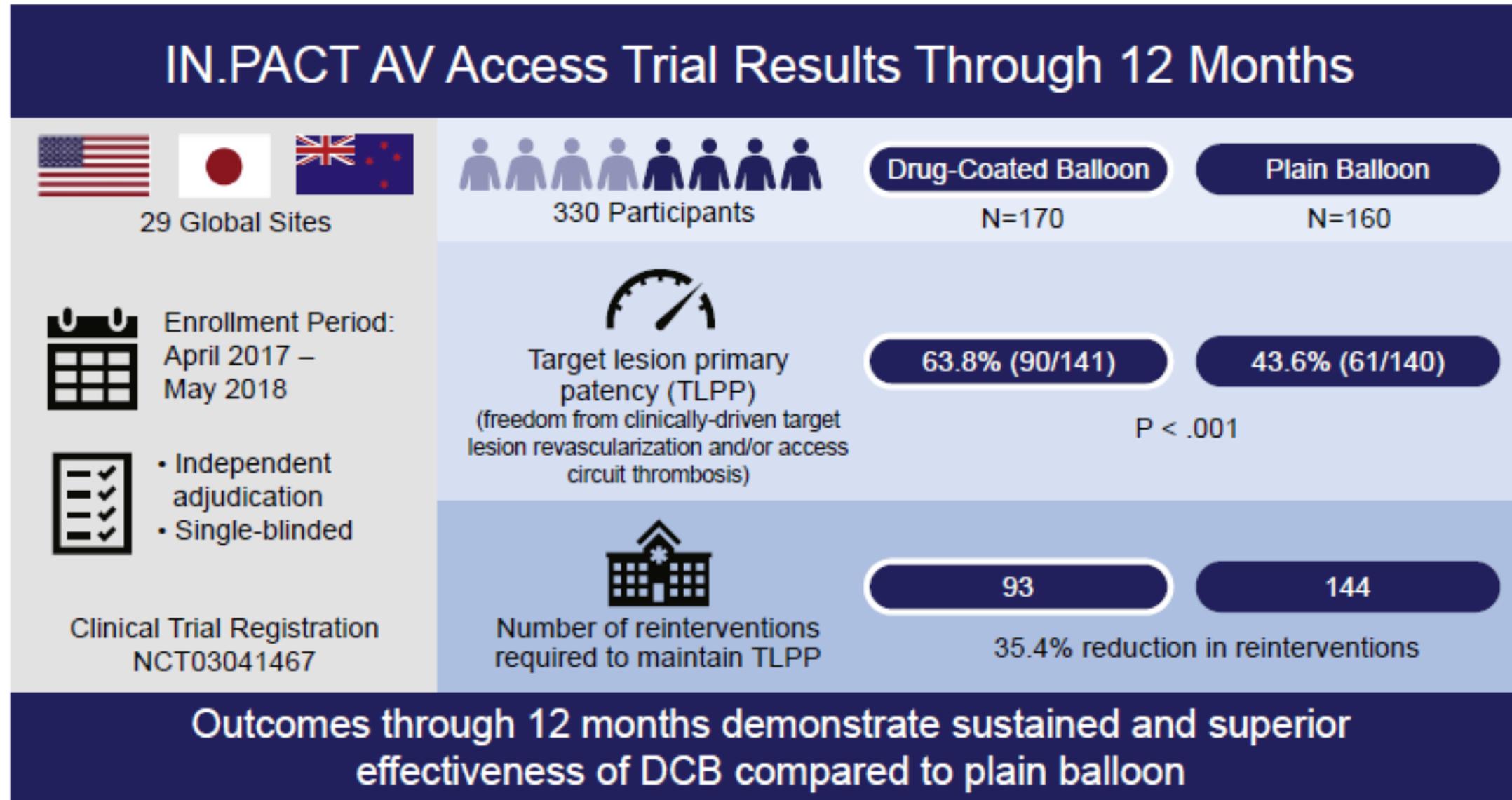
Drug-coated balloon	170	151	133	106	86
Standard balloon	160	148	110	78	62

IDE, investigational device exemption

[†] Lookstein R et al. N Engl J Med 2020;383:733-42.

IN.PACT AV Access IDE Study Outcomes Through 12 Months

Published in The Journal of Vascular and Interventional Radiology in 2022[†]



Winner of 2022
JVIR Editor's
Award for
Outstanding
Clinical Study

DCB, drug-coated balloon; IDE, investigational device exemption; JVIR, Journal of Vascular and Interventional Radiology

[†] Holden A et al. J Vasc Interv Radiol 2022;33(8):884-894 e7.

Accessed April 14, 2024. <https://irq.sirweb.org/sirtoday/2022-jvir-awards/>

IN.PACT AV Access IDE Study Outcomes Through 12 Months - Economics

Published in JVIR in 2022[†] (US) and Nephrology in 2023[‡] (Japan/Korea analyses)

Projected economic impact based on 12M reintervention/primary patency burden (DCB: 0.65, PTA: 1.05) suggests sizable reduction in resource use can be expected with DCB over time

- **United States:**

- Cost savings between **\$3,893** and **\$4,263** per patient at 2.5 and 3 years respectively, depending on analysis approach
- These savings can help to accommodate incremental reimbursement for DCB



- **Japan and Korea:**

- With added DCB-specific reimbursement, cost savings was reached at one year in Korea and between 3-5 years in Japan



Similar directional findings might be expected in other healthcare systems

DCB, drug-coated balloon; IDE, investigational device exemption; JVIR, Journal of Vascular and Interventional Radiology; US, United States

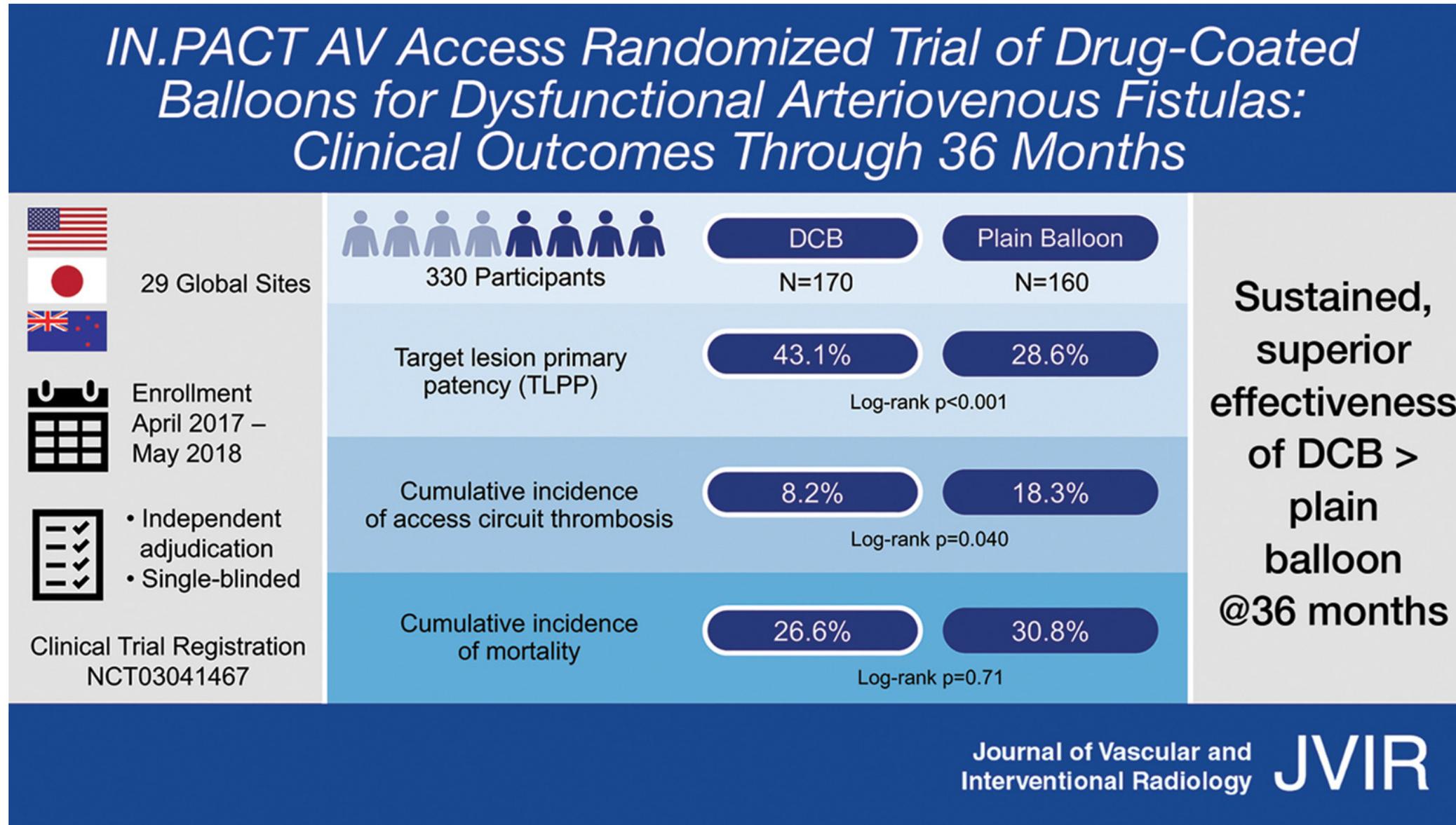
PTA, percutaneous transluminal angioplasty

[†] Pietzsch JB et al. J Vasc Interv Radiol 2022;33(8):895-902.

[‡] Chun HJ et al. Nephrology (Carlton) 2022 Nov;27(11):859-868.

IN.PACT AV Access IDE Study Outcomes Through 36 Months

Published in The Journal of Vascular and Interventional Radiology in 2023[†]



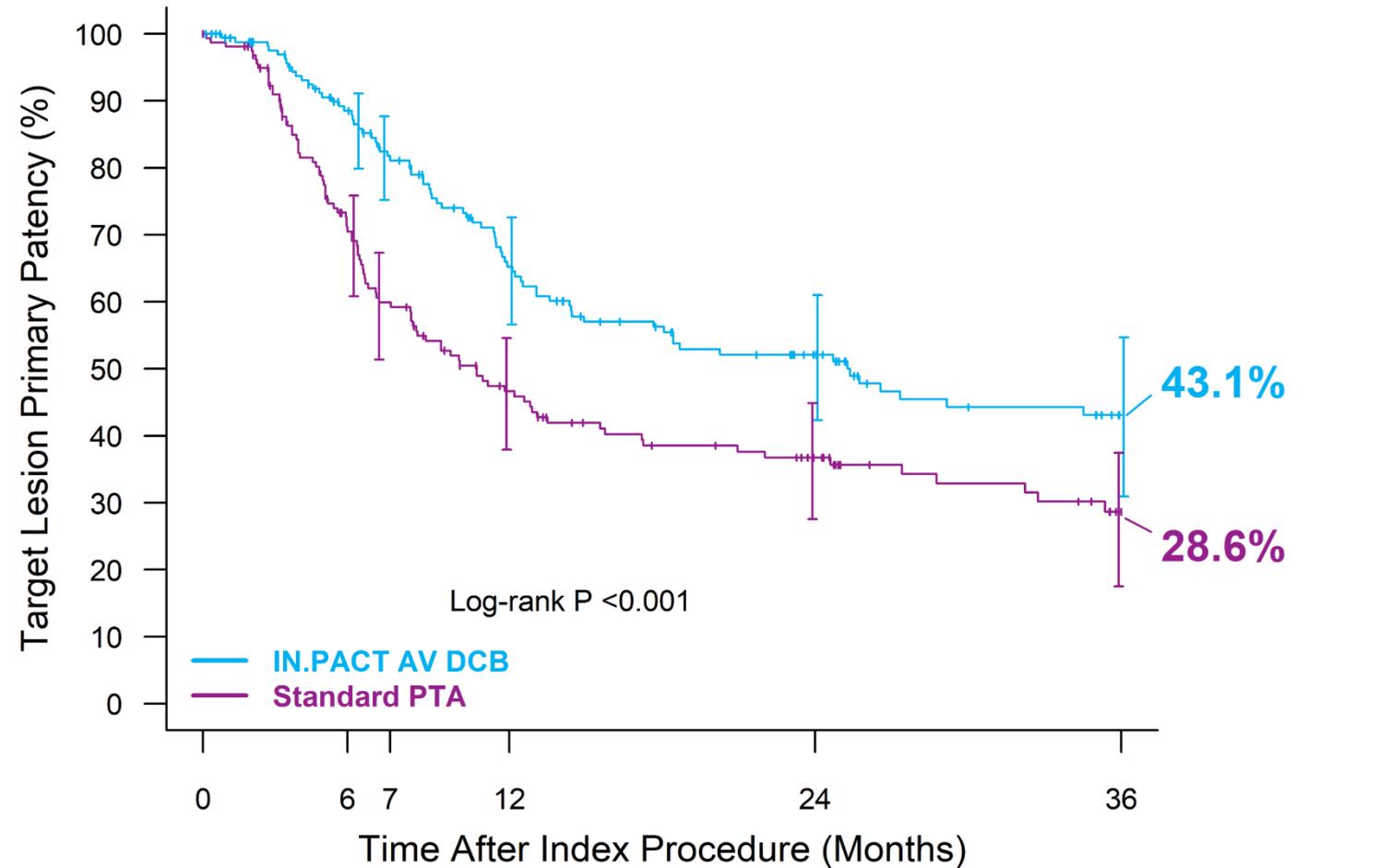
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† Lookstein R et al. J Vasc Interv Radiol 2023;34(12):2093-2102.e7.
Accessed April 14, 2024. https://irq.sirweb.org/sirtoday/2023-jvir-awards_1/

IN.PACT AV Access IDE Study Outcomes Through 36 Months

Published in The Journal of Vascular and Interventional Radiology in 2023[†]

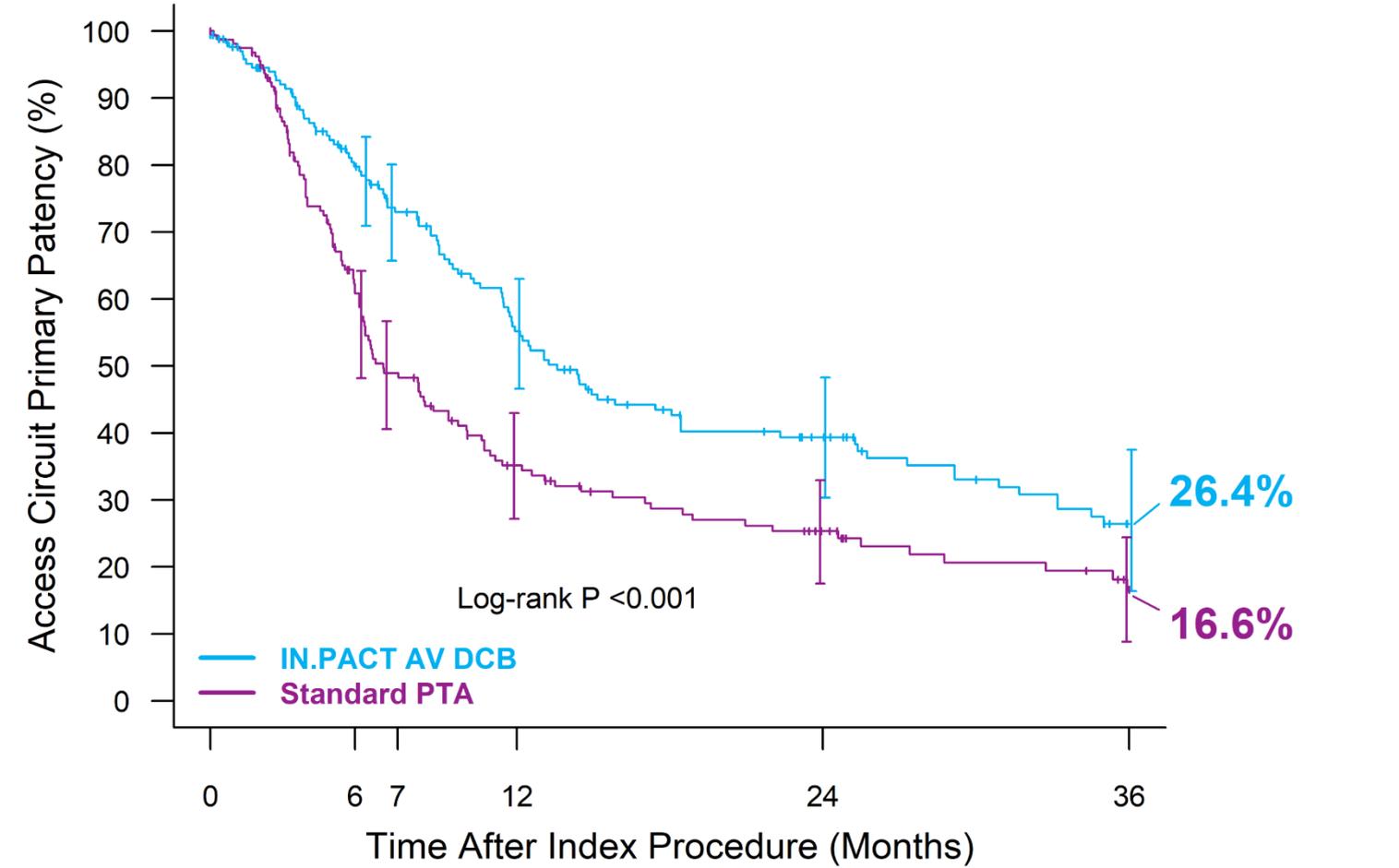
Target Lesion Primary Patency



Number at Risk

Time (Months)	0	6	7	12	24	36
IN.PACT AV DCB	170	129	120	89	56	28
Standard PTA	160	98	85	60	37	16

Access Circuit Primary Patency



Number at Risk

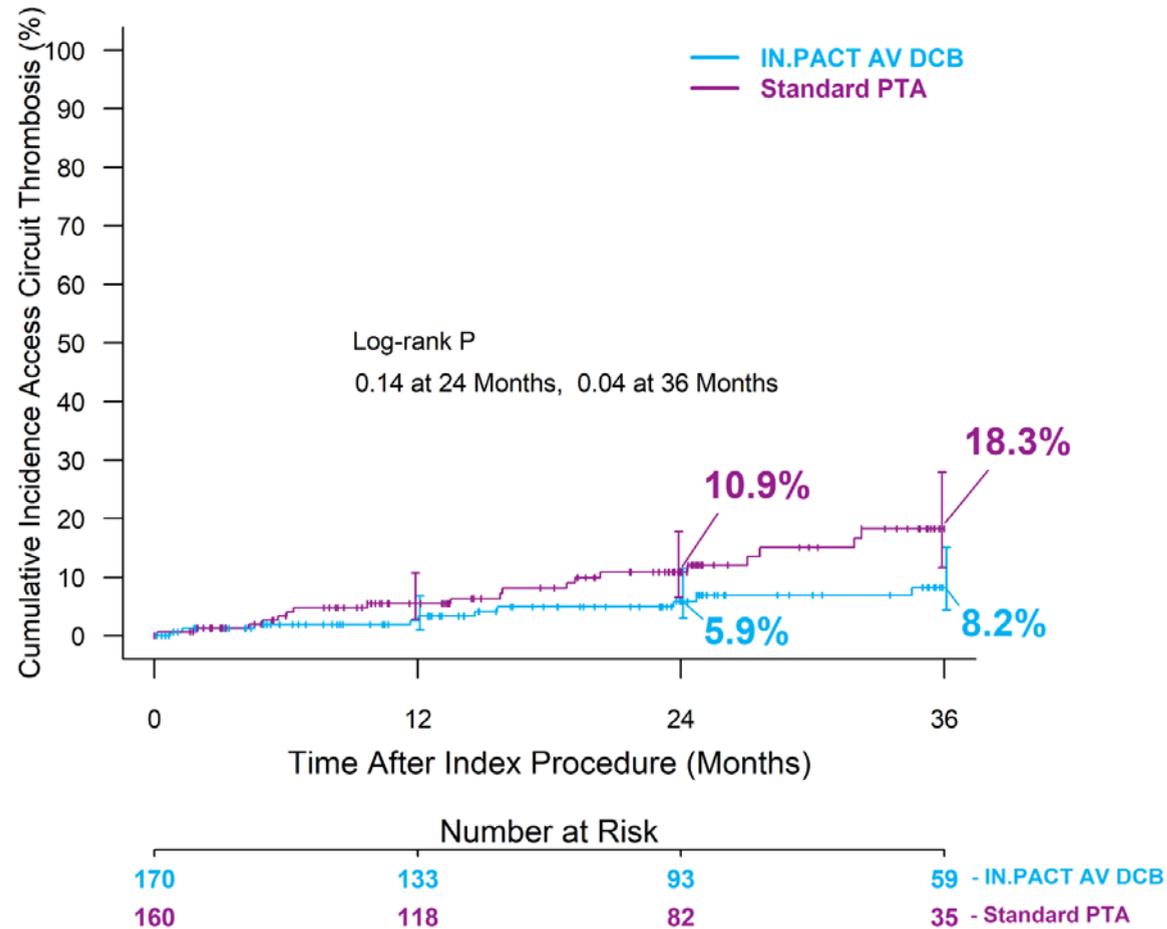
Time (Months)	0	6	7	12	24	36
IN.PACT AV DCB	170	117	107	77	44	17
Standard PTA	160	82	70	46	26	11

DCB, drug-coated balloon; IDE, investigational device exemption; JVIR, Journal of Vascular and Interventional Radiology
[†] Lookstein R et al. J Vasc Interv Radiol 2023;34(12):2093-2102.e7.

IN.PACT AV Access IDE Study Outcomes Through 36 Months

Access Circuit Thrombosis^{†, ‡}

Access circuit thrombosis was higher in the PTA group compared to the DCB group through 36 months



	IN.PACT AV DCB	Standard PTA	Total Participants
Participants with a Thrombosis	10	19	29
Participants without a Thrombosis	160	141	301

Clinically-relevant predictors of access circuit thrombosis using multivariable analysis

High previous reintervention rate

Higher pre-procedure percent diameter stenosis

Upper arm AVF type

Use of PTA rather than DCB

AVF, arteriovenous fistula; DCB, drug-coated balloon; IDE, investigational device exemption; PTA, percutaneous transluminal angioplasty

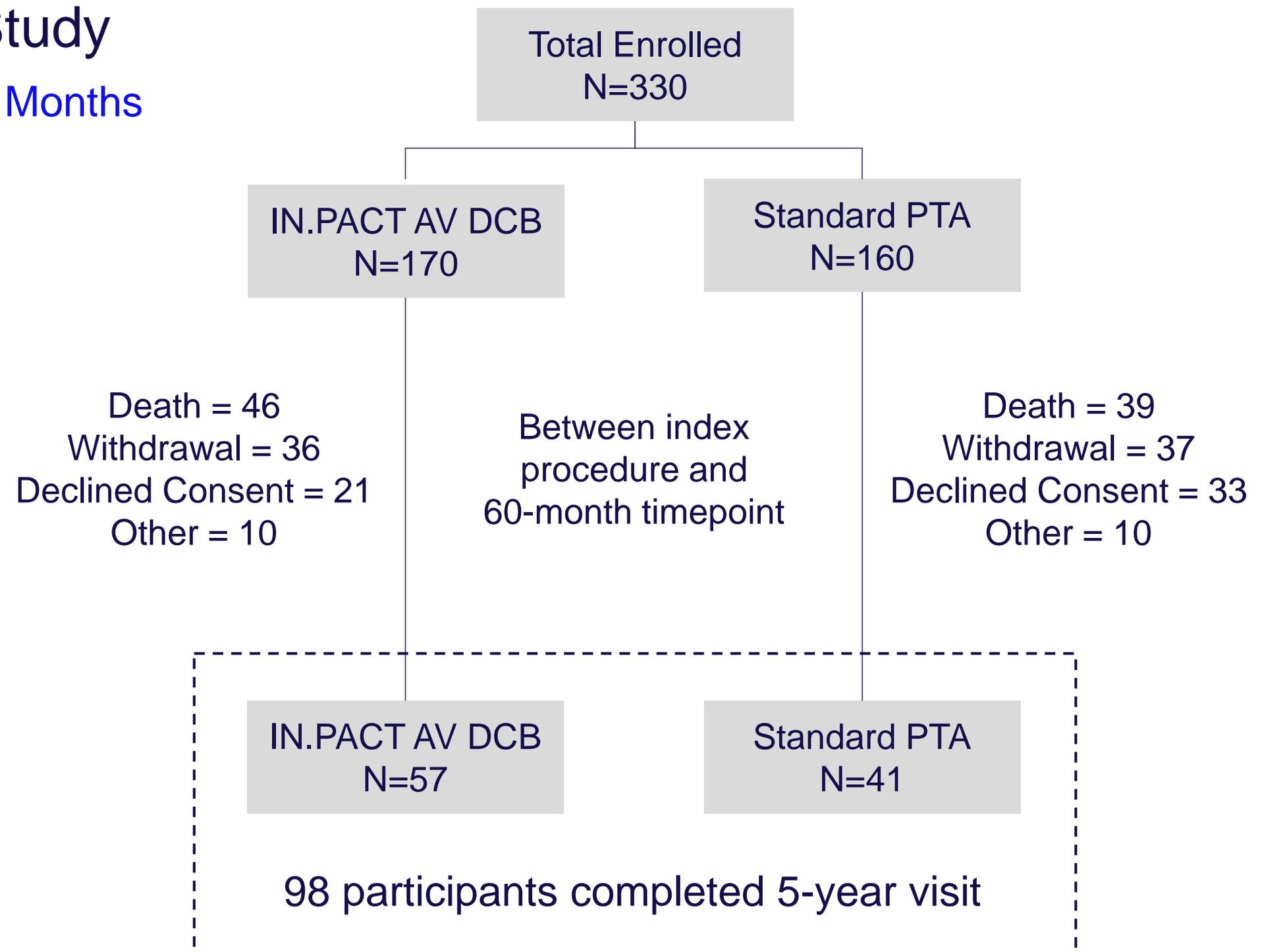
[†] Lookstein R et al. J Vasc Interv Radiol 2023;34(12):2093-2102.e7.

[‡] Lookstein, R. VIVA 2023.

IN.PACT AV Access IDE Study

Follow-up Compliance Through 60 Months

- Study originally planned to go through 24 months
- 5-year extension required reconsenting
- Smaller pool of participants completed later follow-up visits:
 - Death
 - Decline to re consent
 - Withdrawal
 - Other reasons[†]

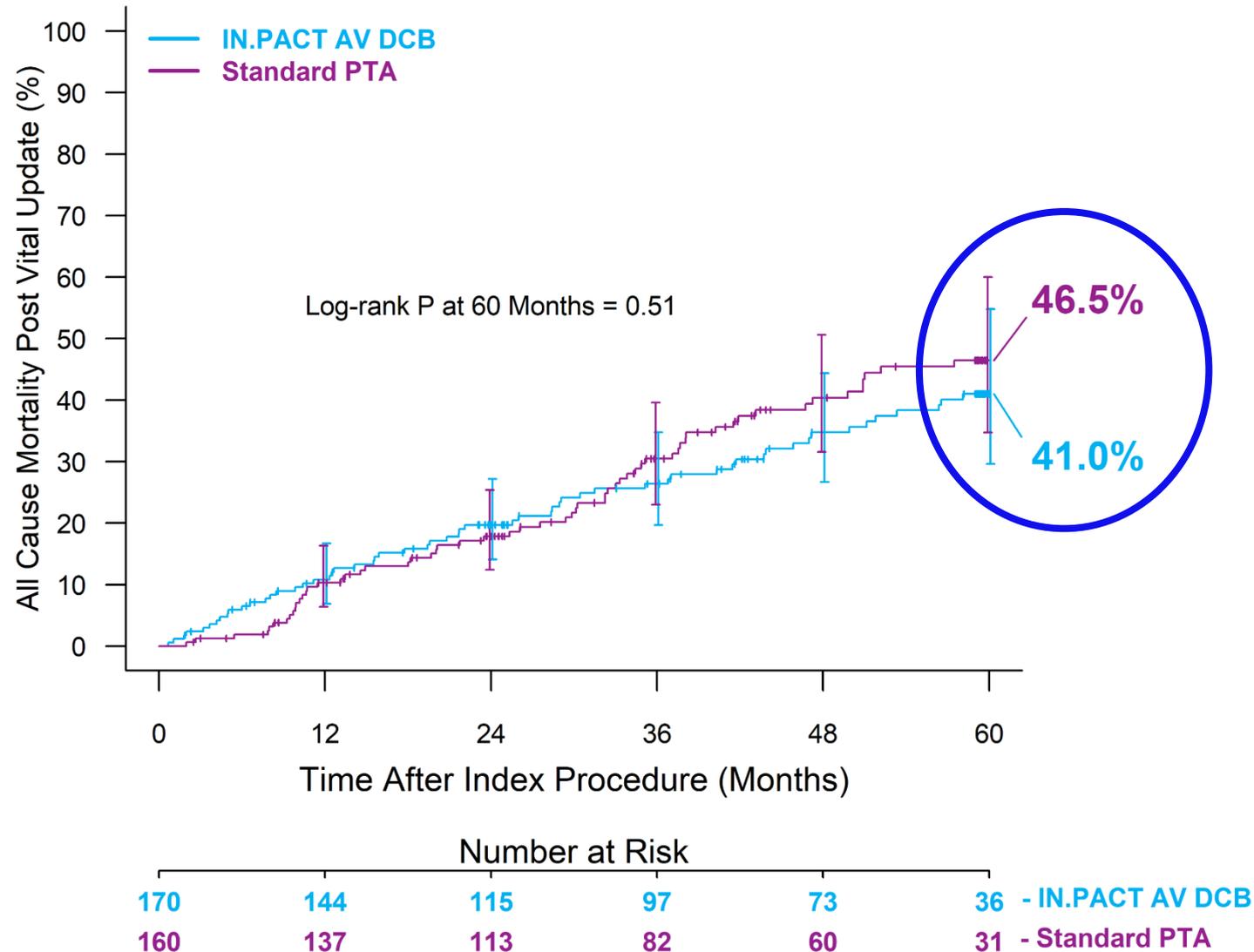


DCB, drug-coated balloon; IDE, investigational device exemption; PTA, percutaneous transluminal angioplasty
[†] Other includes lost-to-follow-up, receiving a kidney transplant, site closure, or participant did not complete follow-up visit

IN.PACT AV Access IDE Study Outcomes Through 60 Months

Podium First

Incidence of All-Cause Mortality Post Vital Status Update



Mortality rate of patients on hemodialysis in the United States (dialysis onset 2017; includes COVID-19 pandemic[†])

1 year	2 years	3 years	4 years	5 years
18.8%	30.1%	40.9%	51.8%	60.4%

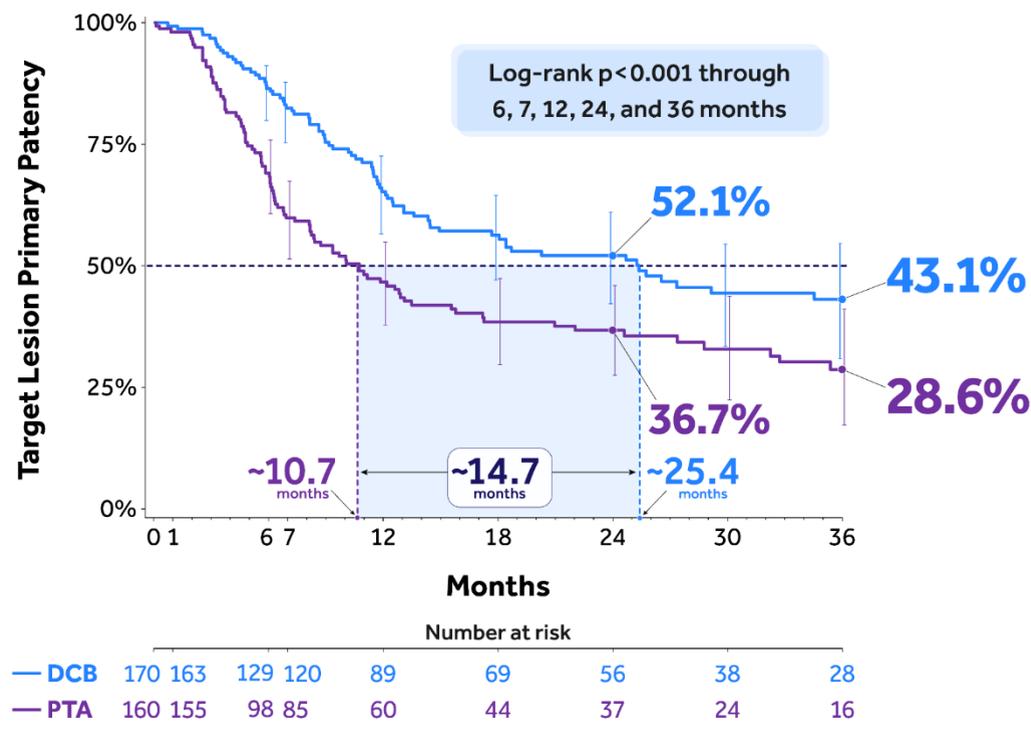
Vital status collection only legal to collect in US. DCB, drug-coated balloon; IDE, investigational device exemption; PTA, percutaneous transluminal angioplasty

[†] USRDS 2023 Annual Report, Figure 6.7. <https://usrds-adr.niddk.nih.gov/2023/end-stage-renal-disease/6-mortality>. Adjusted survival of incident ESRD patients after onset of ESRD in patients treated with hemodialysis with the year of ESRD onset being 2017 (same numbers for 2007 onset are 23.0% at 1 year, 35.0% at 2 years, 44.9% at 3 years, 53.5% at 4 years and 60.6% at 5 years; 2012 onset is 20.8% at 1 year, 32.1% at 2 years, 41.9% at 3 years, 50.5% at 4 years and 58.3% at 5 years)

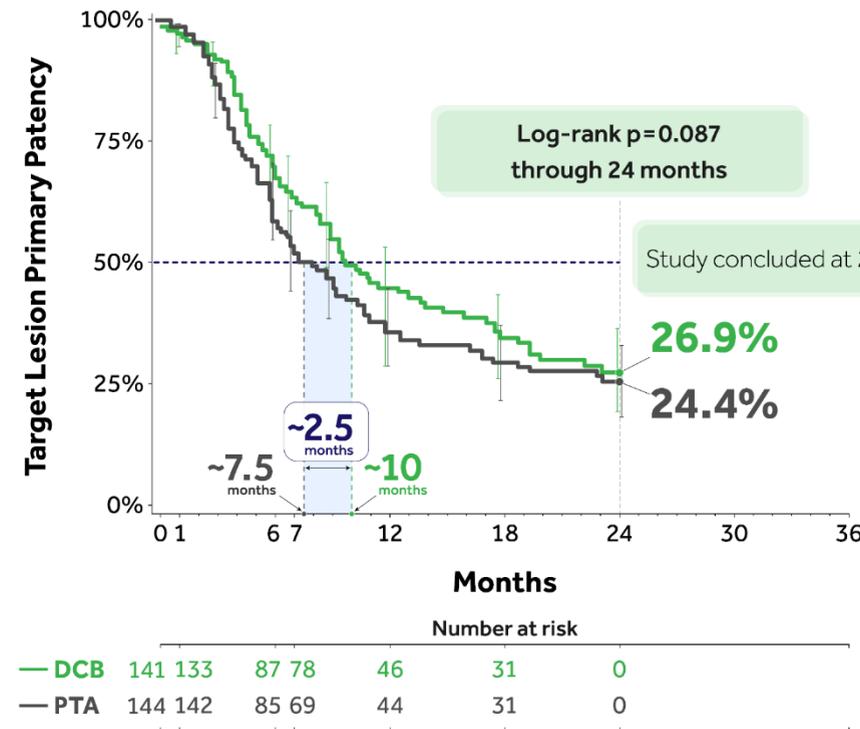
How Does this Compare to Other Devices?

Large RCT Outcomes

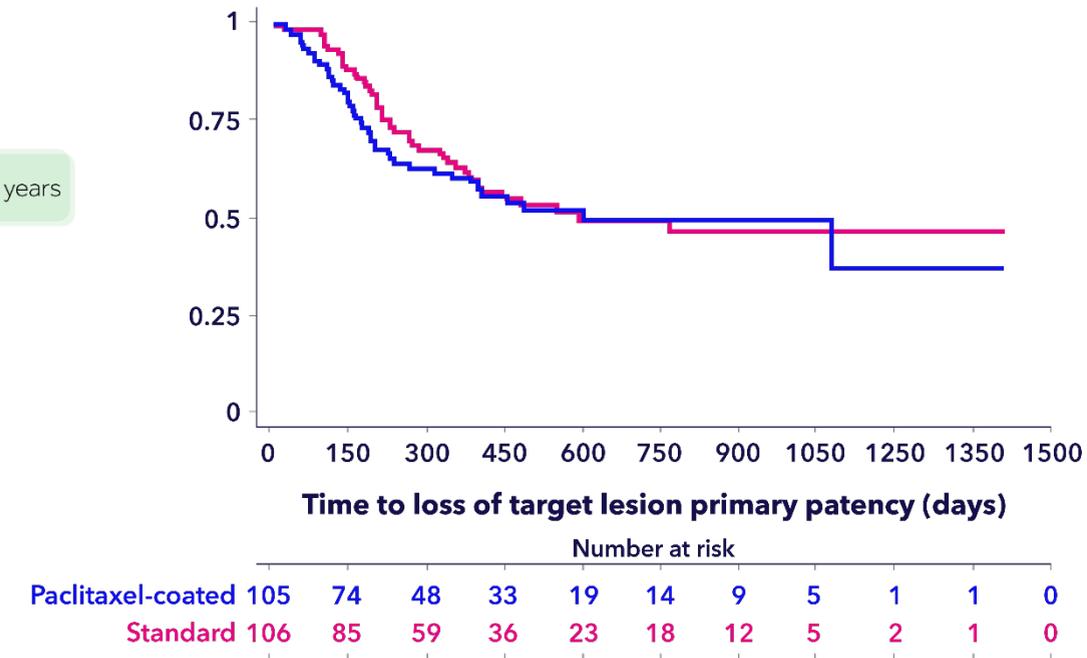
IN.PACT AV Access IDE¹



Lutonix AV IDE²



PAVE³



Results are not directly comparable. Primary patency rates may be defined differently. Information provided is for illustration purposes only, and may differ in head-to-head comparison

DCB, drug-coated balloon; IDE, investigational device exemption; PTA, percutaneous transluminal angioplasty; RCT, randomized controlled trial

1. Lookstein R et al. J Vasc Interv Radiol 2023;34(12):2093-2102.e7.
2. Trerotola SO et al. J Vasc Interv Radiol 2020;13:1-14 e5.
3. Karunanithy N et al. Kidney Int 2021;100(2):447-456.

Differences in DCB Outcomes

Potential Reasons

Patient Characteristics

- Age
- Type of kidney disease
- Fistula age
- Fistula type
- Fistula location

Device

- Excipient type
- Drug type
- Drug concentration
- Coating procedure

Trial Design

- Geography
- Inclusion/exclusion criteria

Procedure

- Vessel preparation
- Length of DCB inflation

IN.PACT AV Access IDE Study Outcomes Through 60 Months

Summary

- The IN.PACT AV Access Study is the only randomized pivotal trial of a device treating dysfunctional arteriovenous fistulas to demonstrate consistent and sustained clinical benefit through 36 months
- All-cause mortality remained comparable between DCB and PTA through 60 months
- Durable long-term data suggests the use of IN.PACT AV DCB as a standard of care for AVF maintenance in patients with ESKD

Thank you

IN.PACT™ AV Paclitaxel-coated PTA balloon catheter

Brief Statement

Indications for Use:

The IN.PACT™ AV Paclitaxel-coated PTA Balloon Catheter is indicated for percutaneous transluminal angioplasty, after appropriate vessel preparation, for the treatment of obstructive lesions up to 100 mm in length in the native arteriovenous dialysis fistulae with reference vessel diameters of 4 to 12 mm.

Contraindications

- The IN.PACT AV DCB is contraindicated for use in the following anatomy and patient types:
- Coronary arteries, renal arteries, and supra-aortic/cerebrovascular arteries
- Patients who cannot receive recommended antiplatelet and/or anticoagulant therapy
- Patients judged to have a lesion that prevents complete inflation of an angioplasty balloon or proper placement of the delivery system
- Patients with known allergies or sensitivities to paclitaxel
- Women who are breastfeeding, pregnant, or are intending to become pregnant, or men intending to father children. It is unknown whether paclitaxel will be excreted in human milk and whether there is a potential for adverse reaction in nursing infants from paclitaxel exposure

Warnings

- Use the product prior to the Use-by date specified on the package.
- Contents are supplied sterile. Do not use the product if the inner packaging is damaged or opened.
- Do not use air or any gaseous medium to inflate the balloon. Use only the recommended inflation medium (equal parts contrast medium and saline solution).
- Do not move the guidewire during inflation of the IN.PACT AV DCB.
- Do not exceed the rated burst pressure (RBP). The RBP is based on the results of in vitro testing. Use of pressures higher than RBP may result in a ruptured balloon with possible intimal damage and dissection.
- The safety of using multiple IN.PACT AV DCBs with a total drug dosage exceeding 15,105 µg paclitaxel has not been evaluated clinically.

IN.PACT™ AV Paclitaxel-coated PTA balloon catheter

Brief Statement

Precautions

- This product should only be used by physicians trained in percutaneous transluminal angioplasty (PTA).
- Assess risks and benefits before treating patients with a history of severe reaction to contrast agents. Identify allergic reactions to contrast media and antiplatelet therapy before treatment and consider alternatives for appropriate management prior to the procedure.
- This product is not intended for the expansion or delivery of a stent.
- Do not use the IN.PACT AV DCB for pre-dilatation or for post-dilatation.
- This product is designed for single patient use only. Do not reuse, reprocess, or resterilize this product. Reuse, reprocessing, or resterilization may compromise the structural integrity of the device and/or create a risk of contamination of the device, which could result in patient injury, illness, or death.
- The use of this product carries the risks associated with percutaneous transluminal angioplasty, including thrombosis, vascular complications, and/or bleeding events
- The safety and effectiveness of the IN.PACT AV DCB used in conjunction with other drug-eluting stents or drug-coated balloons in the same procedure has not been evaluated.
- The extent of the patient's exposure to the drug coating is directly related to the number of balloons used. Refer to the Instructions for Use (IFU) for details regarding the use of multiple balloons and paclitaxel content.
- Appropriate vessel preparation, as determined by the physician to achieve residual stenosis of $\leq 30\%$, is required prior to use of the IN.PACT AV DCB. Vessel preparation of the target lesion using high-pressure PTA for pre-dilatation was studied in the IN.PACT AV Access clinical study. Other methods of vessel preparation, such as atherectomy, have not been studied clinically with IN.PACT AV DCB.

Potential Adverse Effects

- Potential adverse effects which may be associated with balloon catheterization may include, but are not limited to, the following: abrupt vessel closure, allergic reaction, arrhythmias, arterial or venous aneurysm, arterial or venous thrombosis, death, dissection, embolization, hematoma, hemorrhage, hypotension/hypertension, infection, ischemia or infarction of tissue/organ, loss of permanent access, pain, perforation or rupture of the artery or vein, pseudoaneurysm, restenosis of the dilated vessel, shock, stroke, vessel spasms or recoil.
- Potential complications of peripheral balloon catheterization include, but are not limited to, the following: balloon rupture, detachment of a component of the balloon and/or catheter system, failure of the balloon to perform as intended, failure to cross the lesion. These complications may result in adverse effects.
- Although systemic effects are not anticipated, potential adverse effects not captured above that may be unique to the paclitaxel drug coating include, but are not limited to, the following: allergic/immunologic reaction, alopecia, anemia, gastrointestinal symptoms, hematologic dyscrasia (including leucopenia, neutropenia, thrombocytopenia), hepatic enzyme changes, histologic changes in vessel wall, including inflammation, cellular damage, or necrosis, myalgia/arthralgia, myelosuppression, peripheral neuropathy.
- Refer to the Physician's Desk Reference for more information on the potential adverse effects observed with paclitaxel. There may be other potential adverse effects that are unforeseen at this time.
- Please reference appropriate product *Instructions for Use* for a detailed list of indications, warnings, precautions and potential adverse effects. This content is available electronically at www.manuals.medtronic.com.

CAUTION: Federal law (USA) restricts this device to sale by or on the order of a physician.



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