IN.PACT AV Access Study: 12-Month Primary Outcomes

Andrew Holden MBCHB, FRANZCR, EBIR, ONZM
Director of Interventional Radiology
Auckland Hospital, Auckland, New Zealand

Disclosures

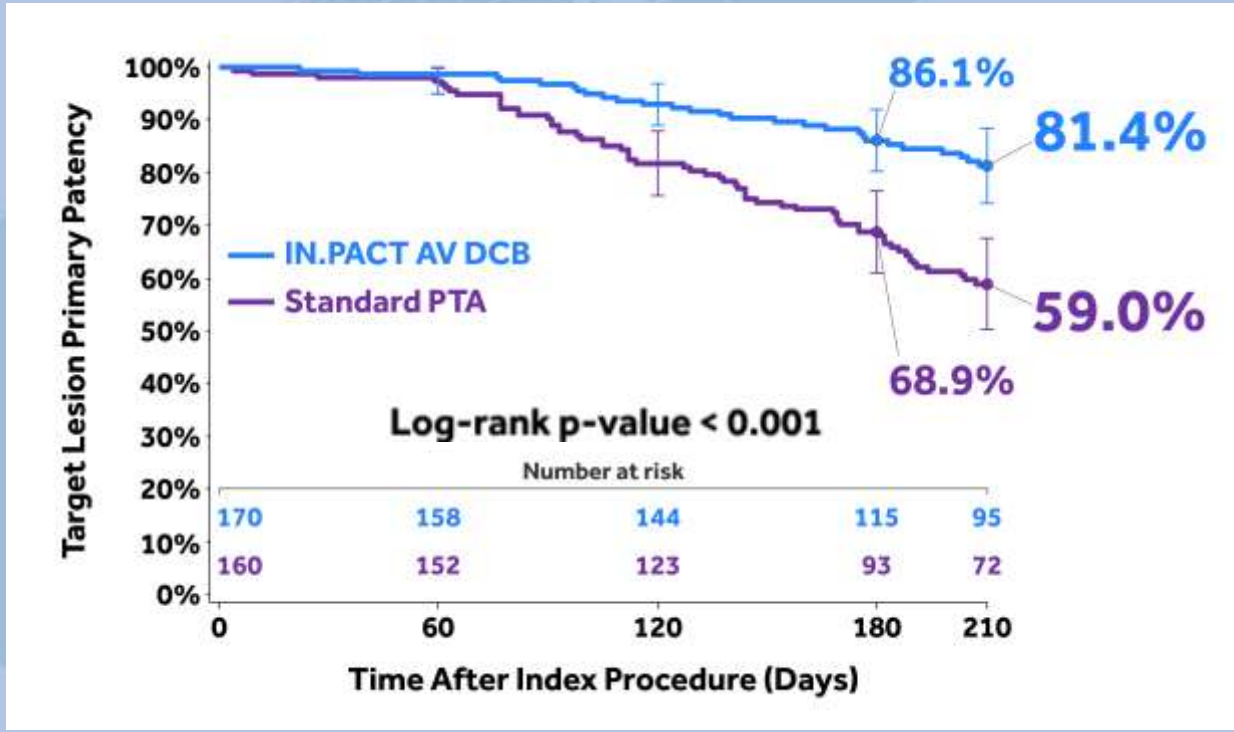
Speaker name: Andrew Holden, MBChB, FRANZCR, EBIR

I have the following potential conflicts of interest to report:

- ☒ Consulting – **Medical Advisory Board: Medtronic, Gore, Boston Scientific**
- ☐ Employment in industry
- ☐ Stockholder of a healthcare company
- ☐ Owner of a healthcare company
- ☐ Other(s)
- ☐ I do not have any potential conflict of interest

Current Data – Large Multicenter RCTs

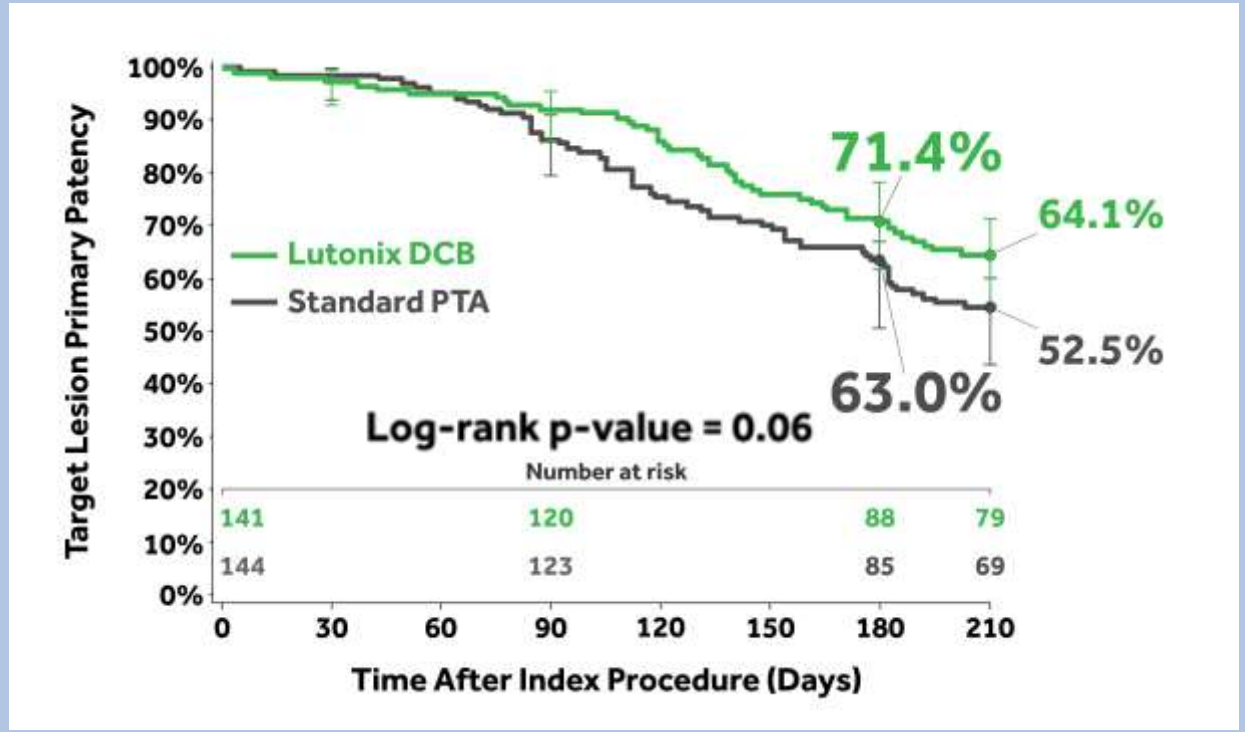
IN.PACT AV Access IDE[1]: Multicenter, global, prospective, randomized, core laboratory and clinical events committee adjudicated trial of 330 participants



The **primary effectiveness endpoint** was **target lesion primary patency at 6 months** defined as freedom from clinically driven reintervention of the target lesion or access circuit thrombosis

Primary efficacy endpoint MET

Lutonix AV IDE[2, 3]: Multicenter, prospective, randomized, core laboratory and clinical events committee adjudicated trial of 285 participants



The **primary effectiveness endpoint** was **target lesion primary patency at 6 months** defined as freedom from clinically driven reintervention of the target lesion or access circuit thrombosis

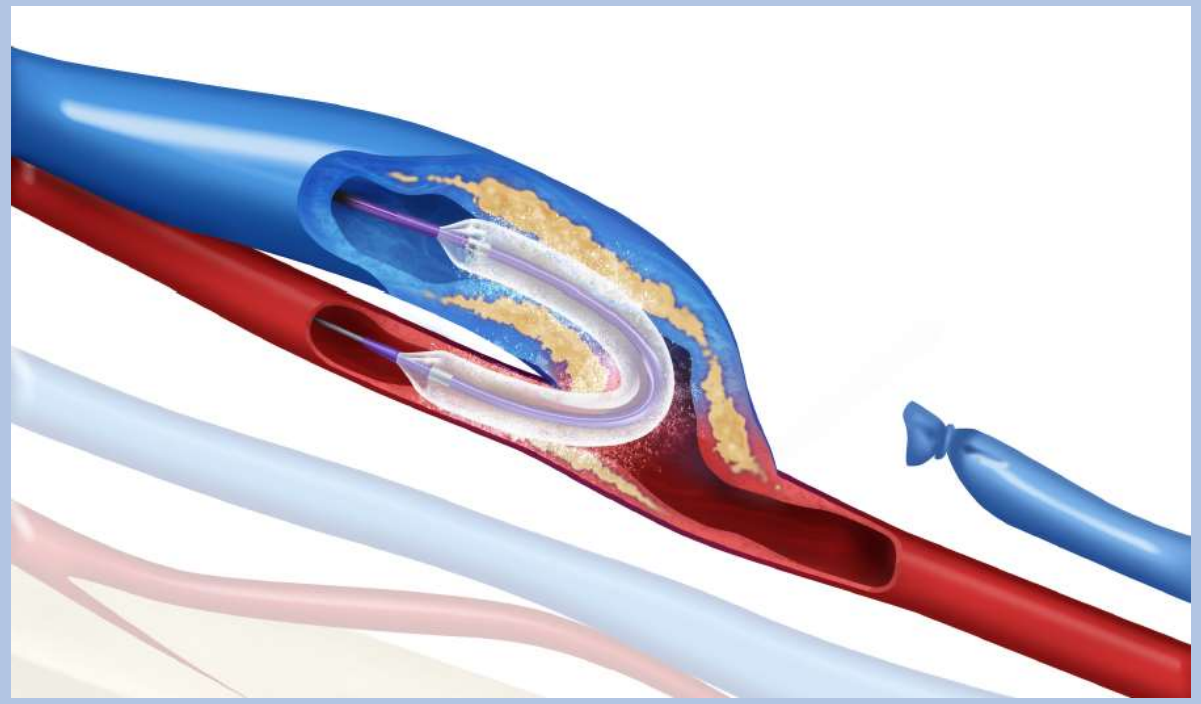
Primary efficacy endpoint NOT MET

1. Holden, A. CIRSE 2019
2. Trerotola SO, Lawson J, Roy-Chaudhury P, Saad TF, et al. Drug Coated Balloon Angioplasty in Failing AV Fistulas: A Randomized Controlled Trial. Clin J Am Soc Nephrol 2018;13:1215-1224.
3. LUTONIX® 035 Drug Coated Balloon PTA Catheter Model 9010 - BAW1400000 Rev4 Instructions for Use. Published October 2019.

IN.PACT AV Access IDE Study

Objective:

Evaluate the safety and effectiveness of the IN.PACT AV drug-coated balloon (DCB) compared to percutaneous transluminal angioplasty (PTA) for treatment of *de-novo* or *restenotic* obstructive lesions of *native* arteriovenous fistulae (AVF) in the upper extremity

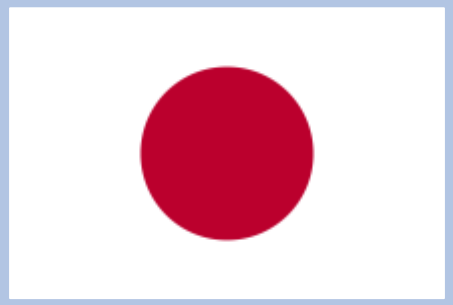


Principal Investigators:

- Robert Lookstein, MD *(USA)*
- Andrew Holden, MD *(New Zealand)*
- Hiroaki Haruguchi, MD *(Japan)*

IN.PACT AV Access IDE Study Design

- Prospective, global, multicenter, 1:1 randomized, single-blinded study
- 330 patients
- Follow-up to five years
- Lesions up to 10 cm in length in the native AVF
- Independent and blinded Duplex Ultrasound Core Lab[1], Angiographic Core Lab[2], and Clinical Events Committee[3]
- Patients enrolled at 29 Global Sites (United States, Japan and New Zealand)



1. VasCore DUS Core Laboratory
2. SYNTACTX Angiographic Core Laboratory
3. Clinical Events Committee and Data Safety Monitoring services provided by SYNTACTX

IN.PACT AV Access Key Inclusion/Exclusion Criteria

Inclusion

- Native AV fistula created ≥ 60 days prior to the index procedure
- Target vessel diameter of 4 – 12 mm
- Patient underwent successful crossing of the target lesion with the guide wire and pre-dilatation with a HP balloon:
  - stenosis of ≤ 30% in the absence of a flow limiting dissection (Grade ≥ C) or perforation
- Patient has a ***de novo and/or non-stented restenotic*** lesion located between the arteriovenous anastomosis and axillosubclavian junction with **≥ 50% stenosis**
- Target lesion or a tandem lesion that is **≤ 100 mm** in length

Exclusion

- Undergone prior intervention of access site within 30 days of index procedure
- Target AVF previously had or currently has a thrombosis
- Hemodynamically significant central venous stenosis that cannot be successfully treated prior to treatment of target lesion
- Presence of a stent located in the target AV access circuit
- Secondary non-target lesion requiring treatment within 30 days post index procedure
- Judged to have a lesion that prevents complete inflation of an angioplasty balloon or proper placement of the delivery system
- Presence of pseudoaneurysm or aneurysm requiring treatment at the lesion site

IN.PACT AV Access Key Inclusion/Exclusion Criteria

Inclusion

- Native AV fistula created ≥ 60 days prior to the index procedure
- Target vessel diameter of 4 – 12 mm
- Patient underwent successful crossing of the target lesion with the guide wire and pre-dilatation with a HP balloon:
  - stenosis of ≤ 30% in the absence of a flow limiting dissection (Grade ≥ C) or perforation
- Patient has a ***de novo and/or non-stented restenotic*** lesion located between the arteriovenous anastomosis and axillosubclavian junction with **≥ 50% stenosis**
- Target lesion or a tandem lesion that is **≤ 100 mm** in length

Exclusion

- Undergone prior intervention of access site within 30 days of index procedure
- Target AVF previously had or currently has a thrombosis
- Hemodynamically significant central venous stenosis that cannot be successfully treated prior to treatment of target lesion
- Presence of a stent located in the target AV access circuit
- Secondary non-target lesion requiring treatment within 30 days post index procedure
- Judged to have a lesion that prevents complete inflation of an angioplasty balloon or proper placement of the delivery system
- Presence of pseudoaneurysm or aneurysm requiring treatment at the lesion site

IN.PACT AV Access Primary Endpoints

Safety: 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

Effectiveness: Target Lesion Primary Patency Rate through 6 Months

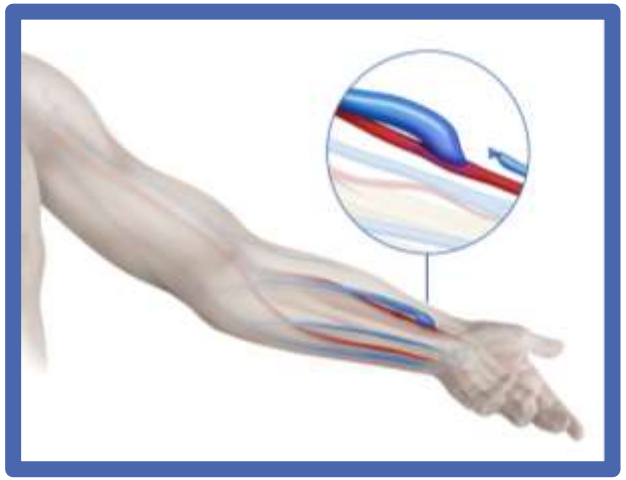
- Defined as freedom from clinically-driven target lesion revascularization (CD-TLR) or access circuit thrombosis measured through 6 months post-procedure
  - Clinically-Driven Target Lesion Revascularization (CD-TLR): Any re-intervention involving the target lesion in which:
    - The subject has a ≥ 50% diameter stenosis (per angiographic core lab assessment) in the presence of clinical or physiologic abnormalities that indicate dialysis access dysfunction OR
    - ≥ 70% stenosis without the presence of clinical or physiologic abnormalities indicating dialysis access dysfunction
  - IN.PACT AV access target lesion primary patency is measured out to 210 days endpoint (rather than 180 days)

IN.PACT AV Access Baseline Characteristics

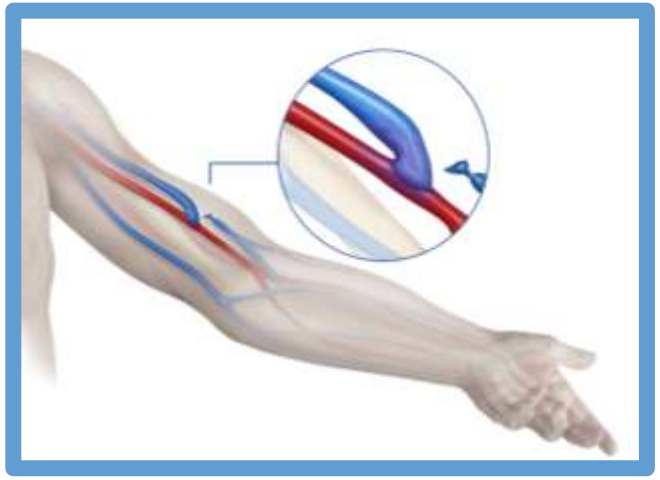
Baseline Demographics	IN.PACT AV DCB (n=170)	Standard PTA (n=160)	P-value
Age (yrs) (mean ± SD)	65.8 ± 13.1	65.5 ± 13.4	0.837
Male	65.9% (112/170)	63.1% (101/160)	0.646
Hypertension	**91.2% (155/170)**	**94.4% (151/160)**	**0.295**
Hyperlipidemia	**54.1% (92/170)**	**52.5% (84/160)**	**0.825**
Diabetes Mellitus - Type 1 **- Type 2**	2.4% (4/170) **60.6% (103/170)**	3.8% (6/160) **65.0% (104/160)**	0.532 **0.427**
Renal Insufficiency	100.0% (170/170)	100.0% (160/160)	> 0.999
Carotid Artery Disease	4.1% (7/170)	8.8% (14/160)	0.114
Congestive Heart Failure	22.9% (39/170)	24.4% (39/160)	0.796
Coronary Heart Disease	35.9% (61/170)	38.8% (62/160)	0.649
Peripheral Artery Disease	19.4% (33/170)	15.1% (24/159)	0.312
Smoker - Current - Former	11.2% (19/170) 37.6% (64/170)	16.3% (26/160) 28.1% (45/160)	0.201 0.079
Previous AV Access Endovascular Procedure	74.1% (126/170)	75.0% (120/160)	0.900

DCB, drug-coated balloon; PTA, percutaneous transluminal angioplasty

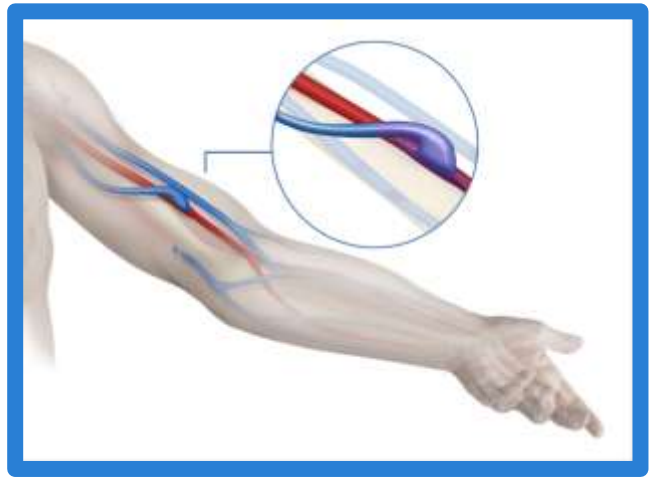
IN.PACT AV Access AVF Type



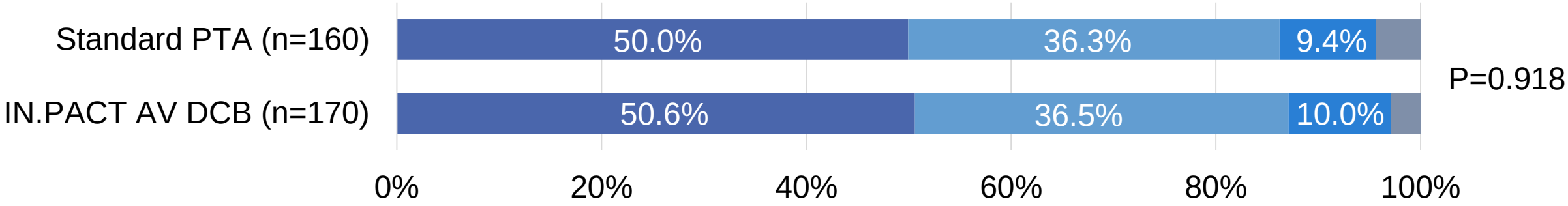
Radiocephalic



Brachiocephalic



Brachiobasilic



AVF type locations are site-reported ; AVF, arteriovenous fistula; DCB, drug-coated balloon; PTA, percutaneous transluminal angioplasty

*Other AVF types included radial-perforative vein (3), ulnar-basilica (2), basilobrachial, radialbasilic, high bifurcated ulnar artery to cephalic vein, distal radial artery to median vein, proximal radial artery to perforating vein, Gracz, left radiocephalic

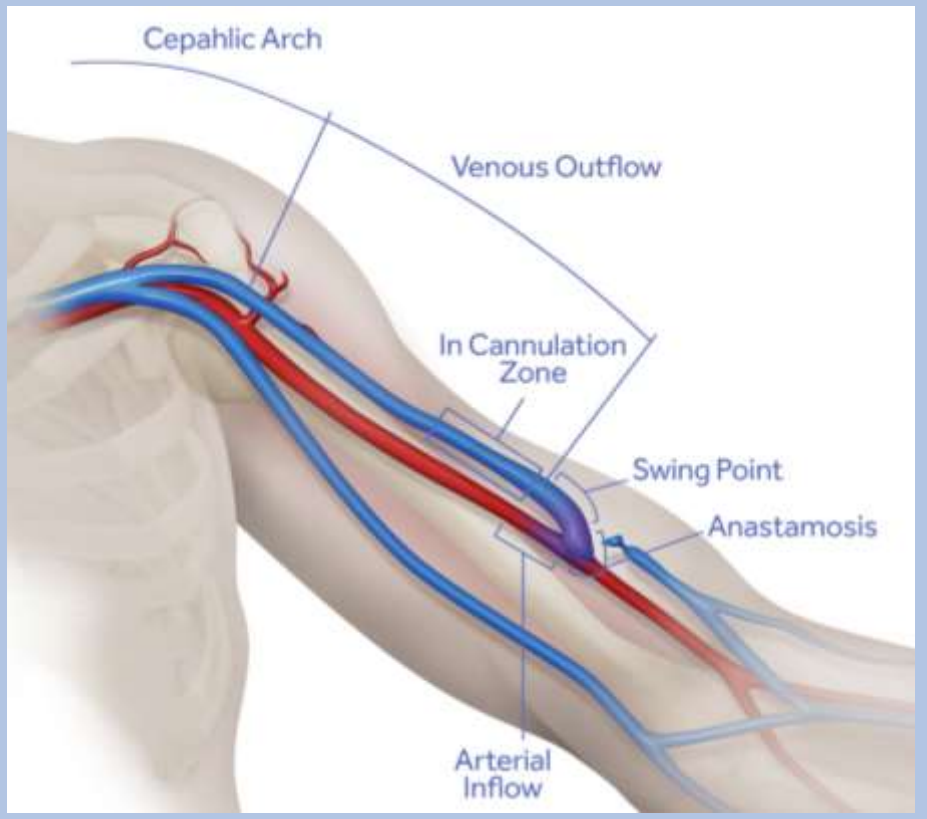
IN.PACT AV Access AVF Characteristics

AVF Characteristics[1]	IN.PACT AV DCB (n=170)	Standard PTA (n=160)	P-value
Lesion Length (mm; mean ± SD)	**46.9 ± 28.1**	**40.0 ± 25.7**	**0.021**
Target Arm			0.449
Right	23.5% (40/170)	27.5% (44/160)	
Left	76.5% (130/170)	72.5% (116/160)	
Dominant Arm	22.4% (38/170)	24.4% (39/160)	0.697
Age of AVF (years; mean ± SD)	3.2 ± 3.0	3.5 ± 3.8	0.436
Years of Hemodialysis (mean ± SD)	4.3 ± 5.1	4.2 ± 5.2	0.755

AVF, arteriovenous fistula
DCB, drug-coated balloon
PTA, percutaneous transluminal angioplasty
1. These AVF characteristics were site-reported.

IN.PACT AV Access Lesion Characteristics

Lesion Characteristics	IN.PACT AV DCB (n=170)	Standard PTA (n=160)	P-value
Lesion Type			0.905
De Novo	30.0% (51/170)	30.6% (49/160)	
Restenotic	**70.0% (119/170)**	**69.4% (111/160)**	
Target Lesion Location[1, 2]			0.310
Arterial Inflow	2.4% (4/170)	4.4% (7/160)	
Anastomosis	**25.9% (44/170)**	**25.0% (40/160)**	
Swing Point	8.2% (14/170)	7.5% (12/160)	
In Cannulation Zone	14.7% (25/170)	7.5% (12/160)	
Venous Outflow	**31.2% (53/170)**	**33.1% (53/160)**	
Cephalic Arch	**17.6% (30/170)**	**22.5% (36/160)**	



DCB, drug-coated balloon; PTA, percutaneous transluminal angioplasty

1. Target lesion location was site-reported

2. Lesion definitions:

Arterial Inflow: treated segment is isolated to the arterial side
Anastomosis: treated segment crosses or meets the AV anastomosis
Swing Point: treated segment includes the curved segment of mobilized vessel
In Cannulation Zone: treated segment is isolated to straight segment of vessel where cannulation is performed
Venous Outflow: treated segment is in basilic vein (non-mobilized) or distal to the cephalo-axillary junction
Cephalic Arch: treated segment includes curved segment of cephalic vein as the vein crosses between the pectoralis major and deltoid muscles

IN.PACT AV Access Procedural Characteristics

Procedural Characteristics[1]	IN.PACT AV DCB (n=170)	Standard PTA (n=160)	P-value
Minimum Lumen Diameter (mm)			
Pre-procedure	2.7 ± 1.6 (170)	2.8 ± 1.7 (159)	0.731
After pre-dilatation	4.9 ± 1.9 (167)	5.2 ± 2.0 (159)	0.269
After index procedure	5.5 ± 1.9 (170)	5.7 ± 2.1 (158)	0.584
Percent Diameter Stenosis			
Pre-procedure	64.8 ± 13.3 (170)	64.8 ± 14.5 (159)	0.986
After pre-dilatation	34.6 ± 14.0 (167)	32.4 ± 13.5 (159)	0.160
After index procedure	26.8 ± 10.8 (170)	26.3 ± 10.9 (158)	0.653
Device Success[2]	**100.0% (212/212)**	**100.0% (162/162)**	**> 0.999**
Procedural Success[3]	**73.5% (125/170)**	**76.9% (123/160)**	**0.482**
Clinical Success[4]	**100.0% (159/159)**	**100.0% (154/154)**	**> 0.999**

1. Procedural characteristics were core-lab reported.
2. Device Success is successful delivery, inflation, deflation and retrieval of the intact study balloon device without burst at or below rated burst pressure (RBP) at index procedure.
3. Procedural Success is maintenance of patency (≤ 30% residual stenosis as reported by the core lab or by investigator if core lab data is not available) in the absence of peri-procedural serious adverse device effect.
4. Clinical Success is resumption of successful dialysis for at least one session after index procedure.

IN.PACT AV Access – 6-Month Effectiveness Endpoint

6-Month Effectiveness Endpoint	IN.PACT AV DCB (n=170)	Standard PTA (n=160)	Difference [95% CI]	P-value[1]
Target Lesion Primary Patency[2, 3]	82.2%	59.5%	22.8% [12.8%, 32.8%]	< 0.001
Clinically-driven target lesion revascularization	16.4%	38.5%	-22.1% [-31.9%, -12.3%]	< 0.001
Access circuit thrombosis	2.0%	3.4%	-1.4% [-5.1%, 2.3%]	0.222

1. P-values for the primary effectiveness endpoint were based on one-sided Z-test
2. Target lesion primary patency is defined as freedom from clinically-driven target lesion revascularization or access circuit thrombosis post index procedure.
3. For 6-month endpoints, all participants with events or participants without events but had at least 150 days of clinical follow-up were counted as evaluable participants. If a participant had no event and abandoned arteriovenous access circuit within 150 days the participant will be considered not evaluable for 6-months effectiveness endpoints. “Through 6 months” refers to 210 days for the patency-related endpoints and their components, including target lesion primary patency, CD-TLR, access circuit thrombosis, access circuit primary patency and re-intervention in access circuit; 180 days was used for all the other endpoints through 6 months.

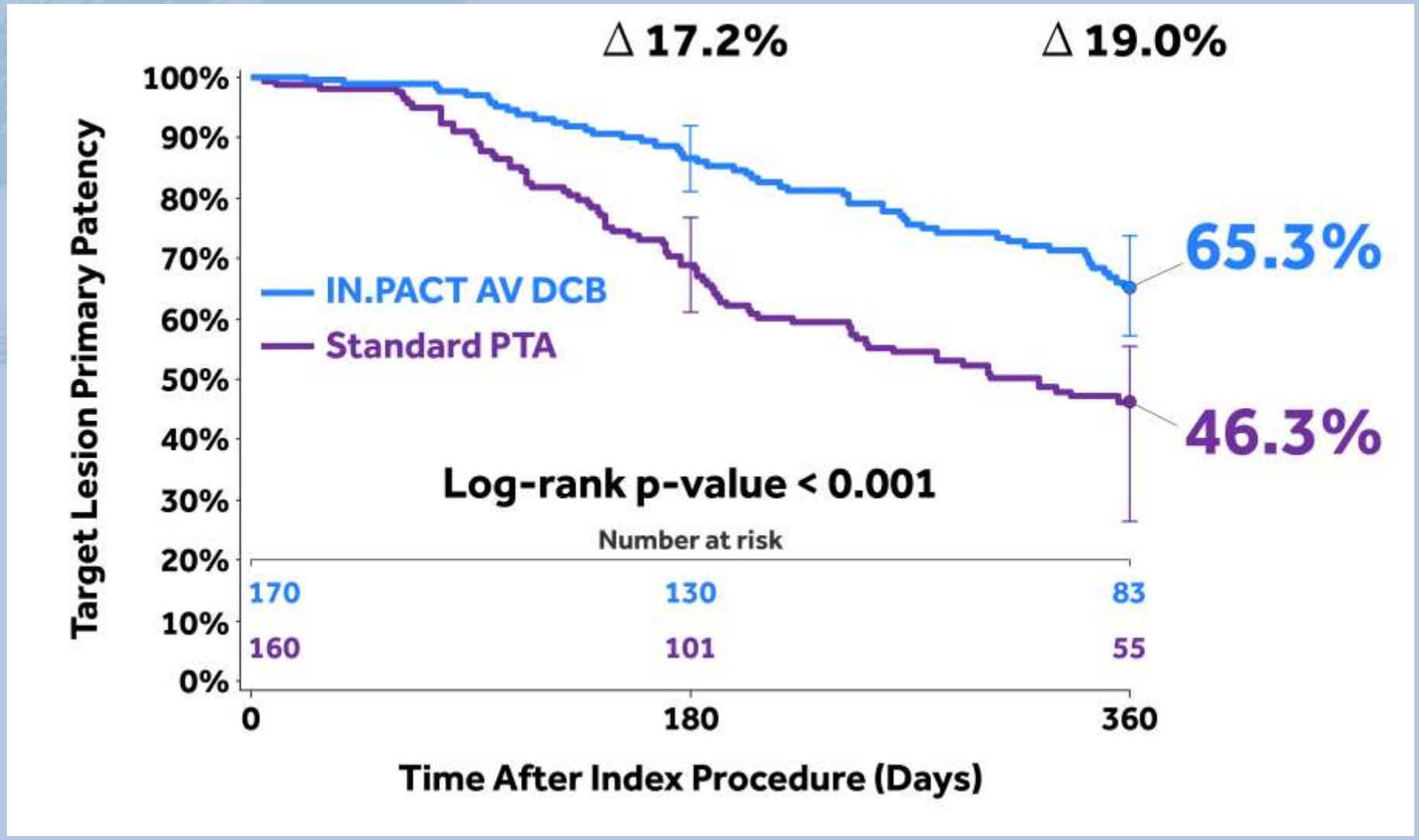
IN.PACT AV Access – 12-Month Effectiveness Endpoint

12-Month Effectiveness Endpoint	IN.PACT AV DCB (n=170)	Standard PTA (n=160)	Difference [95% CI]	P-value[1]
Target Lesion Primary Patency[2, 3]	63.8%	43.6%	20.3% [8.8%, 31.7%]	< 0.001
Clinically-driven target lesion revascularization	35.0%	54.3%	-19.3% [-30.8%, -7.9%]	0.001
Access circuit thrombosis	2.9%	6.2%	-3.3% [-8.3%, 1.7%]	0.193

1. P-values for the primary effectiveness endpoint were based on two-sided Chi-square test
2. Target lesion primary patency is defined as freedom from clinically-driven target lesion revascularization or access circuit thrombosis post index procedure.
3. For 12-months endpoints, all participants with events or participants without events but had at least 330 days of clinical follow-up were counted as evaluable participants. If a participant had no event and abandoned arteriovenous access circuit within 330 days the participant will be considered not evaluable for 12-months effectiveness endpoints. “Through 12 months” refers to 360 days for the patency-related endpoints and their components, including target lesion primary patency, CD-TLR, access circuit thrombosis, access circuit primary patency and re-intervention in access circuit.

IN.PACT AV Access – 12-Month Effectiveness Endpoint

Kaplan-Meier Plot



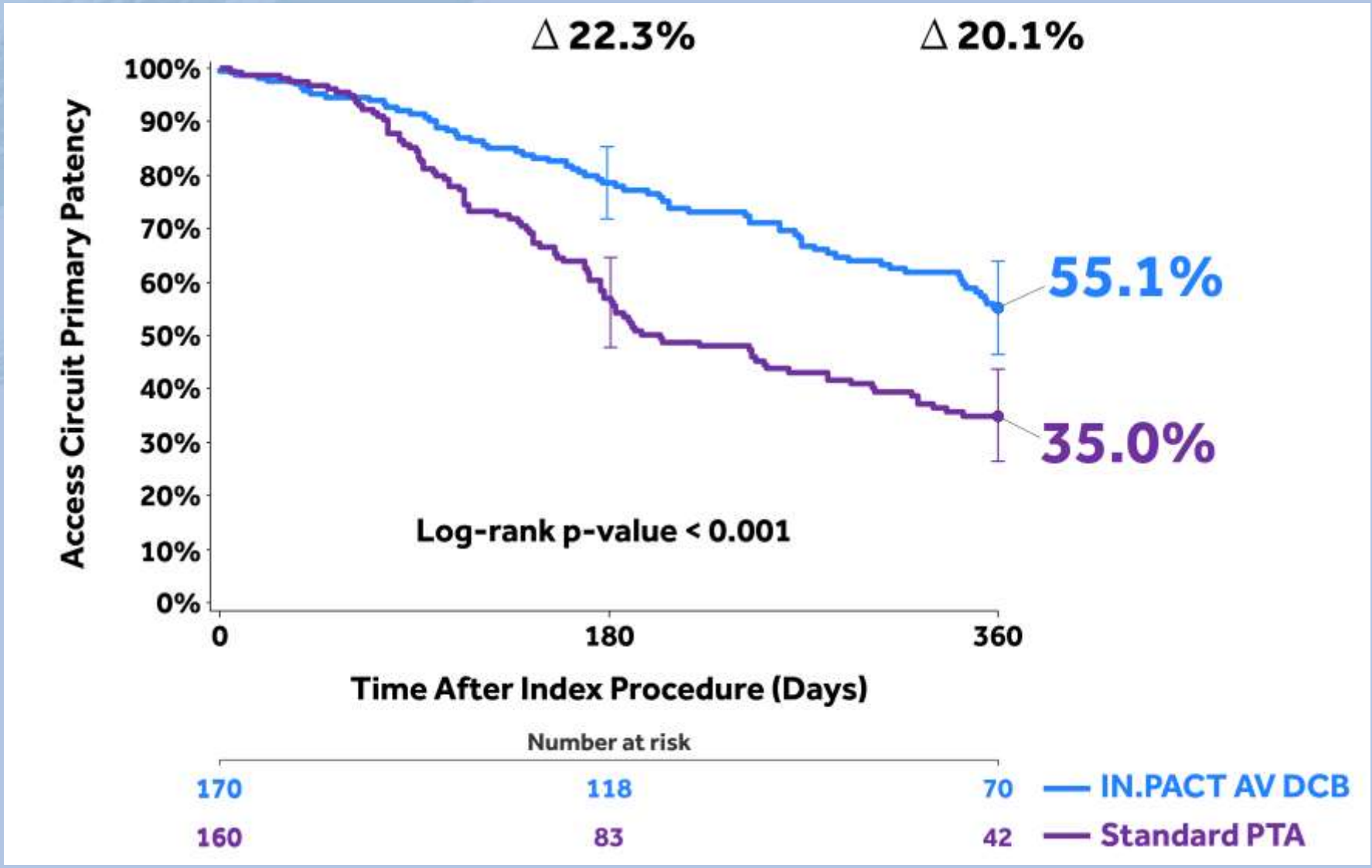
IN.PACT AV Access – 12-Month Access Circuit Patency

12-Month Access Circuit Patency	IN.PACT AV DCB (n=170)	Standard PTA (n=160)	Difference [95% CI]	P-value[1]
Access circuit primary patency[2]	53.8%	32.4%	21.4% [10.2%, 32.6%]	< 0.001
Re-intervention in access circuit	45.1%	66.7%	-21.5% [-32.8%, -10.3%]	< 0.001
Access circuit thrombosis	2.9%	6.2%	-3.3% [-8.3%, 1.7%]	0.193

1. P-values for access circuit patency were based on two-sided Chi-square test
2. Access circuit primary patency is defined as freedom from re-intervention in the access circuit or access circuit thrombosis post index procedure

IN.PACT AV Access – 12-Month Access Circuit Patency

Kaplan-Meier Plot



IN.PACT AV Access – 12-Month Safety Endpoint

12-Month Safety Endpoint	IN.PACT AV DCB (n=170)	Standard PTA (n=160)	Difference [95% CI]	P-value[1]
Serious adverse events involving the AV access circuit within 360 days	**46.9%**	**69.2%**	**-22.3% [-33.3%, -11.2%]**	**<0.001**
Total number of subjects with at least one serious adverse event	**68**	**101**		
Anastomotic stenosis	1	0		
Arteriovenous fistula aneurysm	4	5		
Arteriovenous fistula occlusion	4	5		
Arteriovenous fistula operation	0	2		
Arteriovenous fistula site complication	**62**	**93**		
Arteriovenous fistula site haematoma	1	0		
Arteriovenous fistula site haemorrhage	0	3		
Arteriovenous fistula thrombosis	3	4		
Arteriovenous graft site stenosis	1	0		
Brachiocephalic vein stenosis	0	1		
Haemodialysis complication	2	0		
Peripheral swelling	0	1		
Steal syndrome	1	3		
Subclavian artery stenosis	0	1		
Subclavian vein stenosis	0	3		
Subclavian vein thrombosis	0	1		
Vasospasm	0	1		
Vessel puncture site haematoma	0	1		

1. P-values for the binary endpoints were based on two-sided chi-square test.

IN.PACT AV Access – 12-Month Revascularizations

Revascularizations	IN.PACT AV DCB (n=170)	Standard PTA (n=160)	Difference [95% CI]	P-value[1]
Any target lesion revascularization	40.1%	62.4%	-22.3% [-33.6%, -10.9%]	< 0.001

1. P-values for the endpoints on number of interventions required were based on two-sided Wilcoxon sum rank test
2. Number of interventions required to maintain target lesion patency is defined as number of target lesion revascularizations post index procedure
3. Number of interventions required to maintain access circuit patency is defined as number of re-interventions in the target lesion and/or access circuit post index procedure

IN.PACT AV Access – 12-Month Revascularizations

Revascularizations	IN.PACT AV DCB (n=170)	Standard PTA (n=160)	Difference [95% CI]	P-value[1]
Any target lesion revascularization	40.1%	62.4%	-22.3% [-33.6%, -10.9%]	< 0.001
Number of interventions required to maintain target lesion patency through 360 days[2]				
Total number of reinterventions	93	144		
Mean ± SD	0.5 ± 0.9	0.9 ± 1.0		
Subjects with at least one intervention	57	88		

1. P-values for the endpoints on number of interventions required were based on two-sided Wilcoxon sum rank test
2. Number of interventions required to maintain target lesion patency is defined as number of target lesion revascularizations post index procedure
3. Number of interventions required to maintain access circuit patency is defined as number of re-interventions in the target lesion and/or access circuit post index procedure

IN.PACT AV Access – 12-Month Revascularizations

Revascularizations	IN.PACT AV DCB (n=170)	Standard PTA (n=160)	Difference [95% CI]	P-value[1]
Any target lesion revascularization	40.1%	62.4%	-22.3% [-33.6%, -10.9%]	< 0.001
Number of interventions required to maintain target lesion patency through 360 days[2]				
Total number of reinterventions	93	144	**35.4% reduction**	
Mean ± SD	0.5 ± 0.9	0.9 ± 1.0	-0.4 [-0.6, -0.1]	< 0.001
Subjects with at least one intervention	57	88		

1. P-values for the endpoints on number of interventions required were based on two-sided Wilcoxon sum rank test
2. Number of interventions required to maintain target lesion patency is defined as number of target lesion revascularizations post index procedure
3. Number of interventions required to maintain access circuit patency is defined as number of re-interventions in the target lesion and/or access circuit post index procedure

IN.PACT AV Access – 12-Month Revascularizations

Revascularizations	IN.PACT AV DCB (n=170)	Standard PTA (n=160)	Difference [95% CI]	P-value[1]
Any target lesion revascularization	40.1%	62.4%	-22.3% [-33.6%, -10.9%]	< 0.001
Number of interventions required to maintain target lesion patency through 360 days[2]				
Total number of reinterventions	93	144	**35.4% reduction**	
Mean ± SD	0.5 ± 0.9	0.9 ± 1.0	-0.4 [-0.6, -0.1]	< 0.001
Subjects with at least one intervention	57	88		
Number of interventions required to maintain access circuit patency through 360 days[3]				
Total number of reinterventions	110	168		
Mean ± SD	0.6 ± 1.0	1.1 ± 1.2		
Subjects with at least one intervention	65	94		

1. P-values for the endpoints on number of interventions required were based on two-sided Wilcoxon sum rank test
2. Number of interventions required to maintain target lesion patency is defined as number of target lesion revascularizations post index procedure
3. Number of interventions required to maintain access circuit patency is defined as number of re-interventions in the target lesion and/or access circuit post index procedure

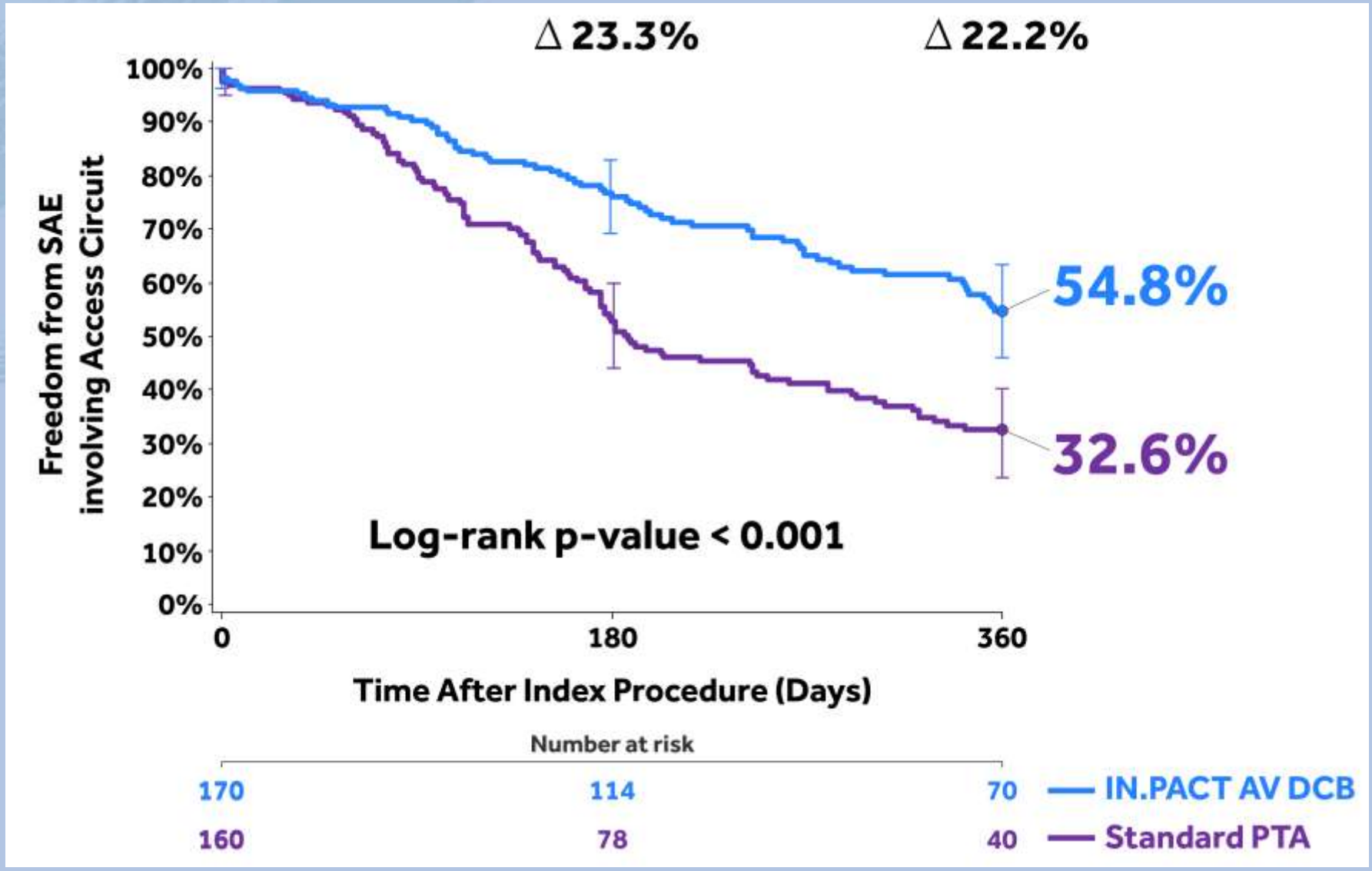
IN.PACT AV Access – 12-Month Revascularizations

Revascularizations	IN.PACT AV DCB (n=170)	Standard PTA (n=160)	Difference [95% CI]	P-value[1]
Any target lesion revascularization	40.1%	62.4%	-22.3% [-33.6%, -10.9%]	< 0.001
Number of interventions required to maintain target lesion patency through 360 days[2]				
Total number of reinterventions	93	144	**35.4% reduction**	
Mean ± SD	0.5 ± 0.9	0.9 ± 1.0	-0.4 [-0.6, -0.1]	< 0.001
Subjects with at least one intervention	57	88		
Number of interventions required to maintain access circuit patency through 360 days[3]				
Total number of reinterventions	110	168	**34.5% reduction**	
Mean ± SD	0.6 ± 1.0	1.1 ± 1.2	-0.4 [-0.6, -0.2]	< 0.001
Subjects with at least one intervention	65	94		

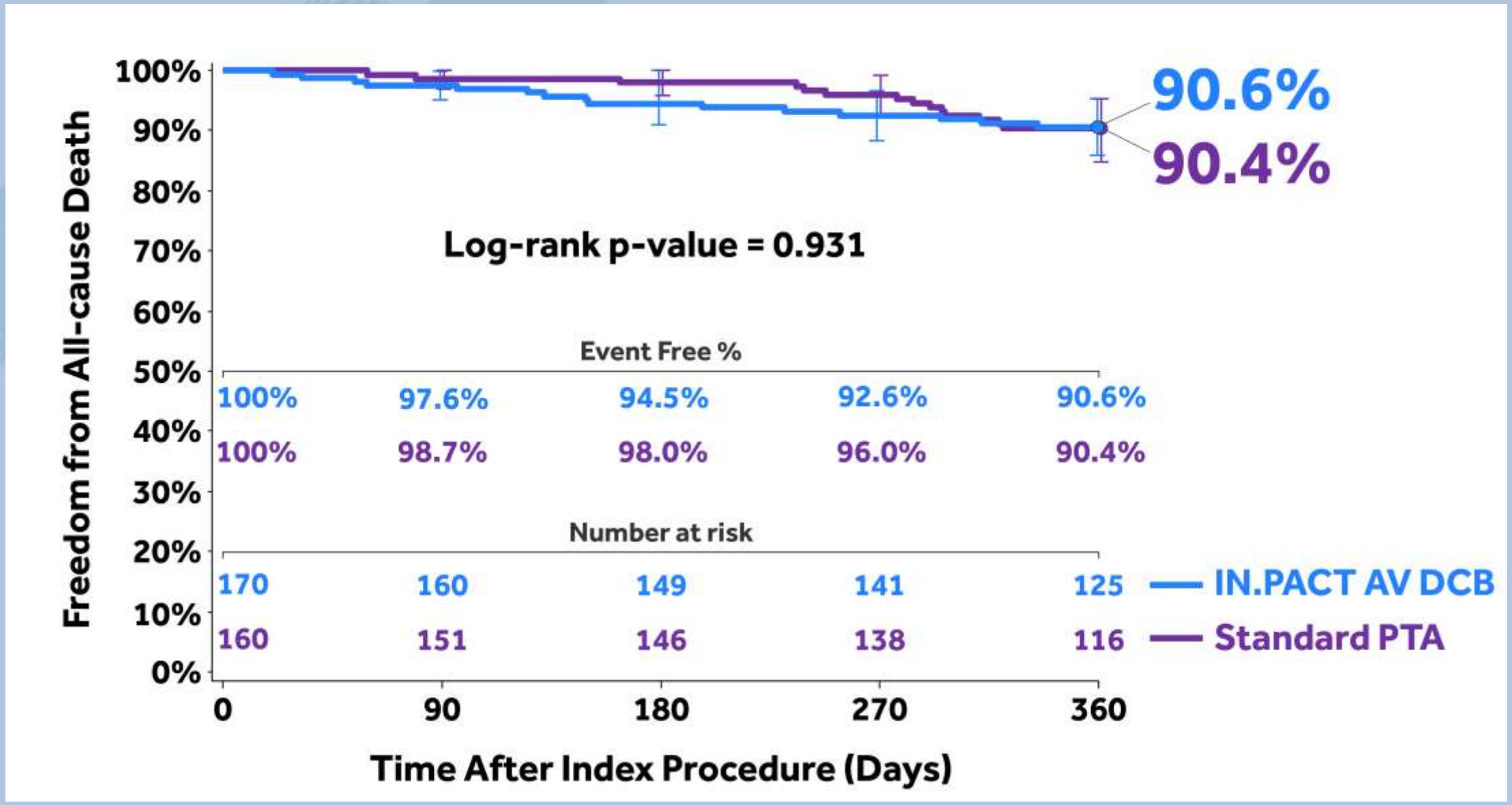
1. P-values for the endpoints on number of interventions required were based on two-sided Wilcoxon sum rank test
2. Number of interventions required to maintain target lesion patency is defined as number of target lesion revascularizations post index procedure
3. Number of interventions required to maintain access circuit patency is defined as number of re-interventions in the target lesion and/or access circuit post index procedure

IN.PACT AV Access Freedom from SAE

12-month Kaplan-Meier Plot

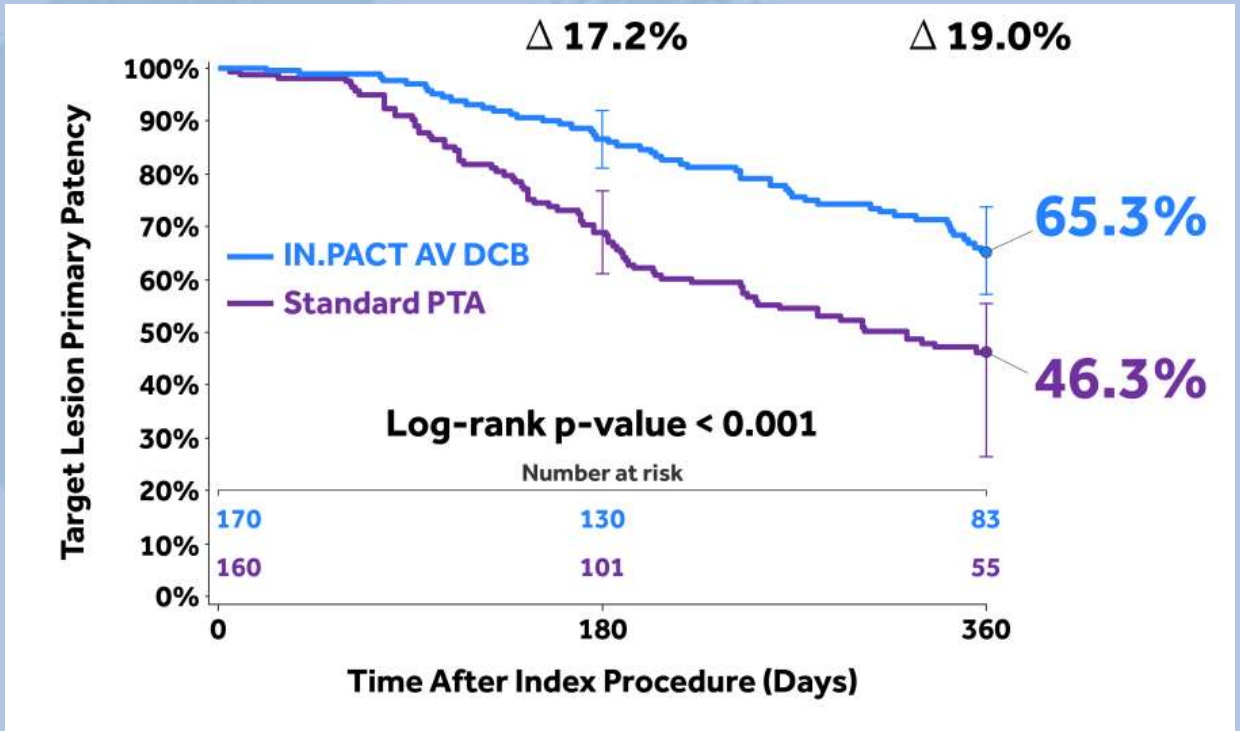


IN.PACT AV Access KM Mortality Through 12 Months

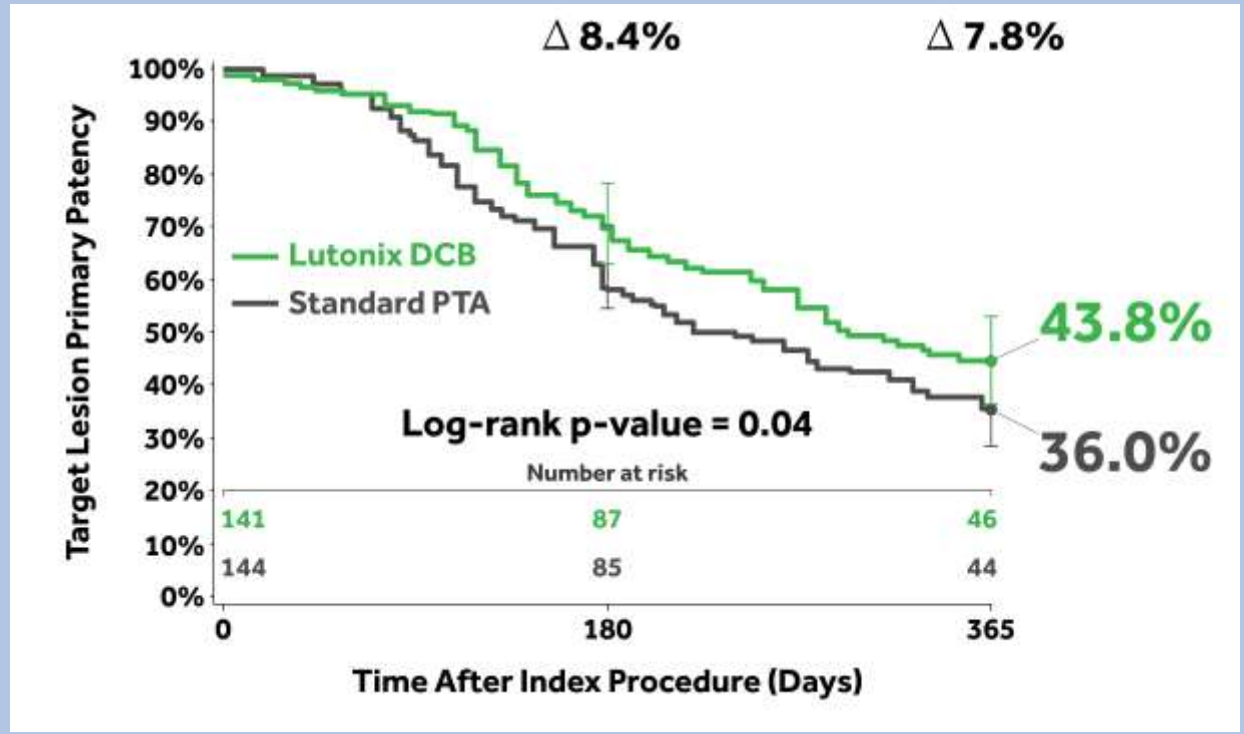


Data as of January 2020 – Large Multicenter RCTs Target Lesion Primary Patency Through 12 Months

IN.PACT AV Access IDE[1]: Multicenter, global, prospective, randomized, core laboratory and clinical events committee adjudicated trial of 330 subjects



Lutonix AV IDE[2]: Multicenter, prospective, randomized, core laboratory and clinical events committee adjudicated trial of 285 subjects



1. Holden, A. LINC 2020.
2. Trerotola SO, Lawson J, Roy-Chaudhury P, Saad TF, et al. Drug Coated Balloon Angioplasty in Failing AV Fistulas: A Randomized Controlled Trial. Clin J Am Soc Nephrol 2018;13:1215-1224.

Conclusions

- First time seen sustained patency advantage for a DCB over PTA using quality vessel prep with high pressure balloon over 12 months
  - Target lesion primary patency: 63.8% DCB, 43.6% PTA ($p<0.001$)
- Fewer reinterventions to maintain target lesion primary patency in the DCB group compared to PTA group
  - 56.0% at 6 months
  - 35.4% at 12 months
- Lower rate of access circuit thrombosis in the DCB group compared to the PTA group through 12 months
  - 2.9% DCB, 6.2% PTA ($p=0.193$)
- No difference in mortality out to 12 months

THANK YOU

IN.PACT AV Access Study: 12-Month Primary Outcomes

Andrew Holden MBCHB, FRANZCR, EBIR, ONZM
Director of Interventional Radiology
Auckland Hospital, Auckland, New Zealand