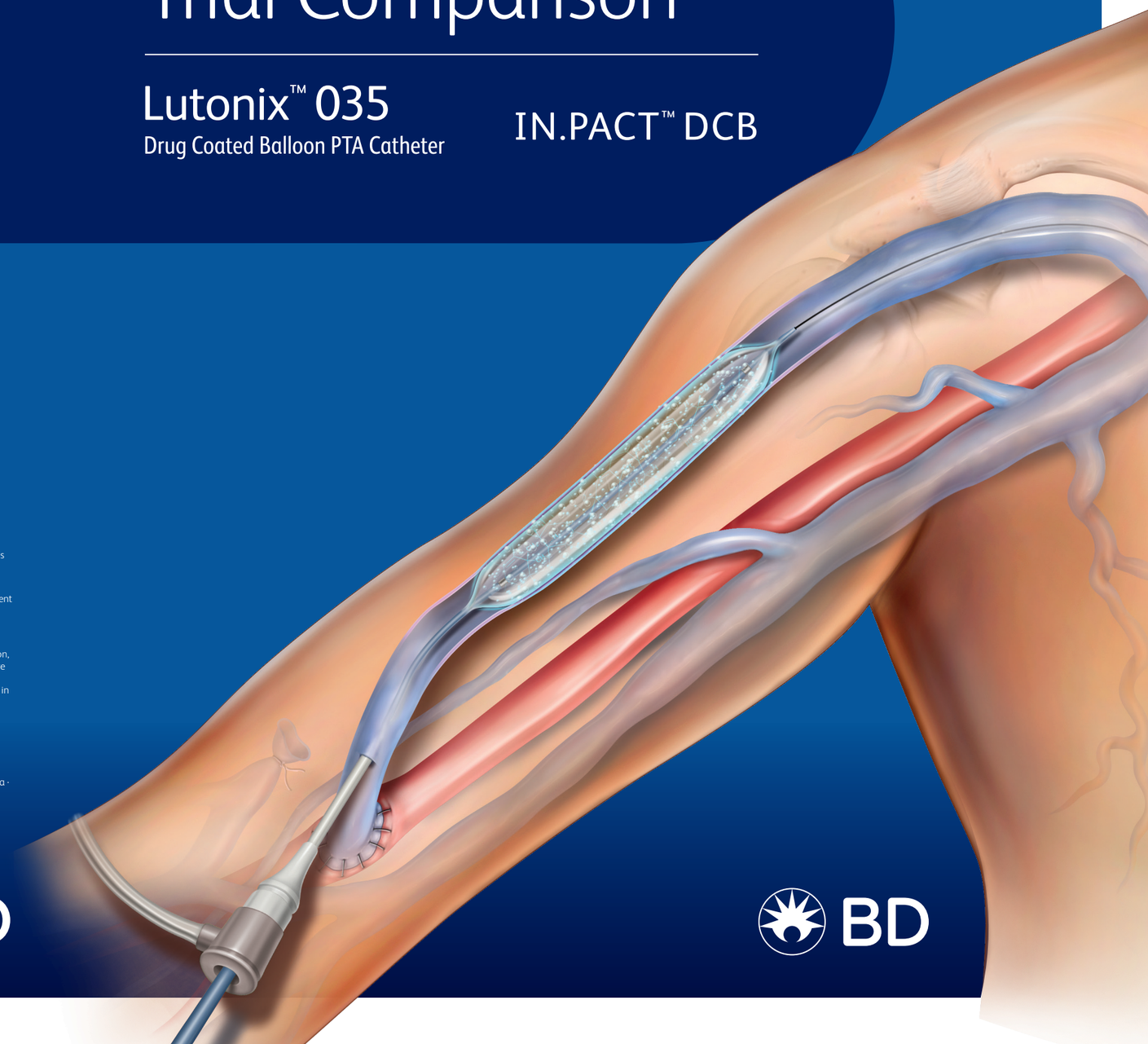
AV DCB IDE Trial Comparison

Lutonix™ 035
Drug Coated Balloon PTA Catheter

IN.PACT™ DCB



[1] Trerotola SO, Saad TF, Roy-Chaudhury P. The lutonix av randomized trial of paclitaxel-coated balloons in arteriovenous fistula stenosis: 2-year results and subgroup analysis. Journal of Vascular and Interventional Radiology. 2020;31(1). doi:10.1016/j.jvir.2019.08.035

[2] Trerotola SO, Lawson J, Roy-Chaudhury P, Saad TF, Lutonix AV Clinical Trial Investigators. Drug Coated Balloon Angioplasty in Failing AV Fistulas: A Randomized Controlled Trial. Clinical journal of the American Society of Nephrology: CJASN. 2018;13(8):1215-1224. doi:https://doi.org/10.2215/CJN.14231217

[3] Holden A, Haruguchi H, Suemitsu K, et al. IN.PACT AV Access Randomized Trial: 12-month clinical results demonstrating the sustained treatment effect of drug-coated balloons. Journal of Vascular and Interventional Radiology. 2022;33(8). doi:10.1016/j.jvir.2022.03.606

The Lutonix™ 035 Drug Coated Balloon PTA Catheter is indicated for percutaneous transluminal angioplasty (PTA), after pre-dilatation, for treatment of stenotic lesions of dysfunctional native arteriovenous dialysis fistulae that are 4 mm to 12 mm in diameter and up to 80 mm in length.

Contraindications: 1) Women who are breastfeeding, pregnant or are intending to become pregnant or men intending to father children over the next 2 years. It is unknown whether paclitaxel will be excreted in human milk and there is a potential for adverse reaction in nursing infants from paclitaxel exposure. 2) Patients judged to have a lesion that prevents complete inflation of an angioplasty balloon or proper placement of the delivery system.

Warnings: 1) Contents supplied STERILE using ethylene oxide (EO) process. Do not use if sterile barrier is damaged or opened prior to intended use. 2) Do not use after the "Use by" date. 3) Do not use if product damage is evident. 4) The Lutonix™ Catheter is for use in one patient only; do not reuse in another patient, reprocess or resterilize. Risks of reuse in another patient, reprocessing, or resterilization include: · Compromising the structural integrity of the device and/or device failure which, in turn, may result in patient injury, illness or death. · Creating a risk of device contamination and/or patient infection or cross-infection, including, but not limited to, the transmission of infectious disease(s) from one patient to another. Contamination of the device may lead to patient injury, illness or death. 5) Do not exceed the Rated Burst Pressure (RBP) recommended for this device. Balloon rupture may occur if the RBP rating is exceeded. To prevent over-pressurization, use of a pressure monitoring device is recommended. 6) Use the recommended balloon inflation medium of contrast and sterile saline (≤50% contrast). Never use air or any gaseous medium to inflate the balloon as this may cause air emboli in case of balloon burst. 7) This product should not be used in patients with known hypersensitivity to paclitaxel or structurally related compounds as this may cause allergic reaction (difficulty in breathing, skin rash, muscle pain).

Potential Adverse Events: Potential adverse events which may be associated with a PTA balloon dilation procedure include, but are not limited to, the following: · Additional intervention · Allergic reaction to drugs or contrast medium · Aneurysm or pseudoaneurysm · Arrhythmias · Embolization · Hematoma · Hemorrhage, including bleeding at the puncture site · Hypotension/hypertension · Inflammation · Loss of permanent access · Occlusion · Pain or tenderness · Sepsis/infection · Shock · Stroke · Steal Syndrome · Thrombosis · Vessel dissection, perforation, rupture, or spasm. Although systemic effects are not anticipated, refer to the Physicians' Desk Reference for more information on the potential adverse events observed with paclitaxel. Potential adverse events, not described in the above source, which may be unique to the paclitaxel drug coating include, but are not limited to, the following: · Allergic/immunologic reaction to the drug coating (paclitaxel) · Alopecia · Anemia · Blood product transfusion · Gastrointestinal symptoms · Hematologic dyscrasia (including leukopenia, neutropenia, thrombocytopenia) · Hepatic enzyme changes · Histologic changes in vessel wall, including inflammation, cellular damage, or necrosis · Myalgia/Arthralgia · Myelosuppression · Peripheral neuropathy

The products referenced herein do not have the exact same indications for use. **Please consult respective product labels and instructions for use for indications, contraindications, hazards, warnings, and precautions. Lutonix™ Catheter is** $\mathbb{R}_{x\ only}$

BD

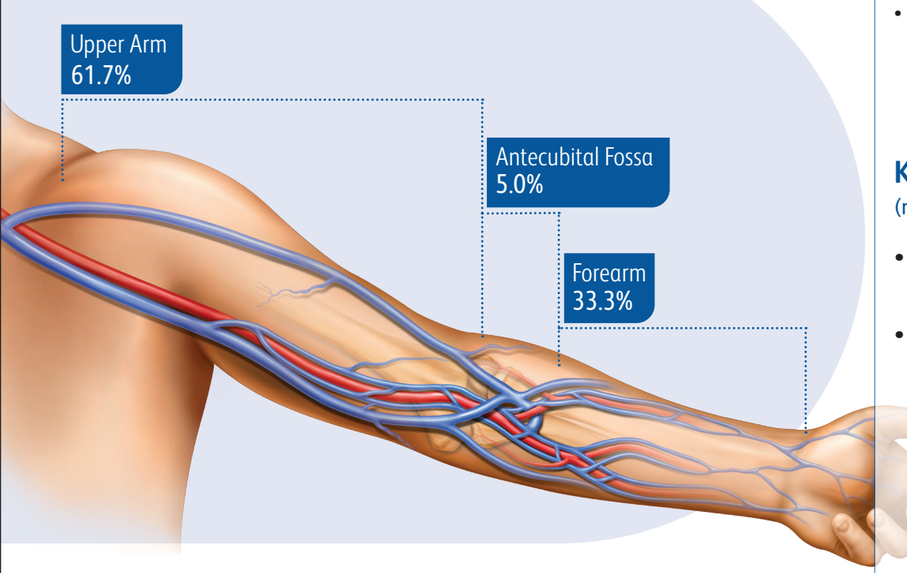
BD

Lutonix AV IDE Trial[1,2]

Clinical Trial Design

Study Design	Prospective, Multi-Center, Randomized (1:1), Angiography Core Lab Blinded
Number of Patients/Sites	285 randomized subjects at 23 U.S. clinical sites
Primary Effectiveness Endpoint	Target Lesion Primary Patency (TLPP) at 180 days TLPP defined as freedom from a clinically driven re-intervention of the target lesion or access thrombosis
Primary Safety Endpoint	Freedom from SAE(s) involving the AV access circuit through 30 days

Lutonix™ 035 DCB Fistula Locations



Target Lesion Locations

Target Lesion Location	Lutonix™ 035 AV DCB (N=141)	Control PTA (N=144)
Inflow	33.8%	29.6%
Outflow	24.5%	22.5%
Cephalic Arch	18.7%	22.5%
Swing Point	14.4%	12.0%
Cannulation Zone	4.3%	9.9%
Anastomotic	4.3%	3.5%

Key Inclusion Criteria
(not all-encompassing)

- Target lesion located from anastomosis to axillosubclavian junction
- Mature AV fistula created ≥30 days prior to the index procedure
- ≥50% stenosis
- Target lesion diameter of 4–12 mm
- Target lesion length of ≤10 cm
  - **Note:** tandem lesions allowed if separated by a gap of ≤2 cm

Key Exclusion Criteria
(not all-encompassing)

- Target lesion located central to axillosubclavian junction
- Bare metal or covered stent in target or secondary non-target lesion
  - **Note:** Patent stents within the access circuit at locations not treated as target or secondary non-target lesion **were allowed**
- Thrombosed access or an access with a thrombosis treated ≤30 days prior to the index procedure
- Secondary non-target lesion that cannot be successfully treated

IN.PACT AV Access Trial[3]

Key Inclusion Criteria
(not all-encompassing)

- Target lesion located from: anastomosis to axillosubclavian junction **+2** cm upstream into arterial side
- Mature AV fistula created ≥60 days prior to index procedure
- ≥50% stenosis
- Target lesion diameter of 4–12 mm
- Target lesion length of ≤10 cm
  - **Note:** tandem lesions allowed if separated by a gap of ≤3 cm

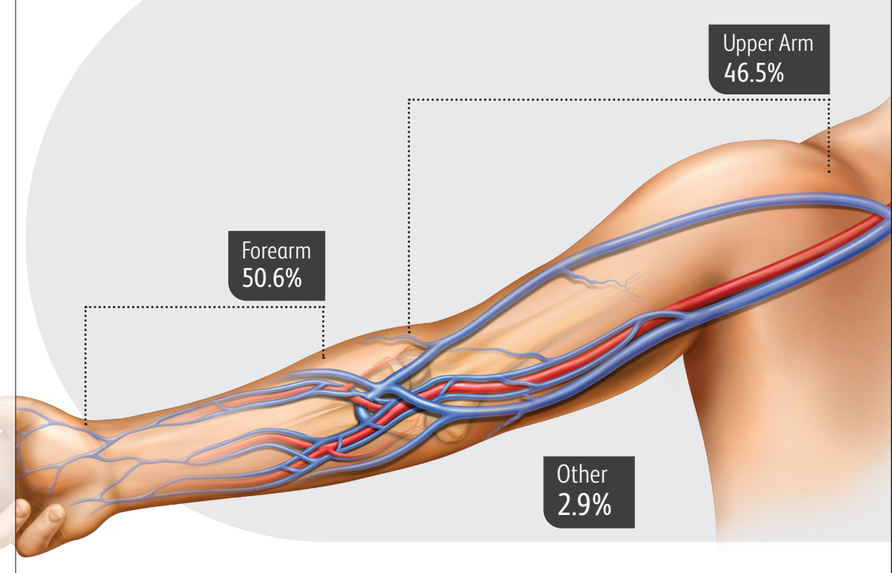
Key Exclusion Criteria
(not all-encompassing)

- Target lesion located central to axillosubclavian junction
- Stent located in target AV access circuit
- Undergone prior intervention of access site within 30 days of index procedure
- AVF or access circuit which previously had or currently has a thrombosis
- Secondary non-target lesion that requires treatment within 30-days post index procedure

Clinical Trial Design

Study Design	Prospective, Global, Multi-Center, Randomized (1:1), Angiography Core Lab Blinded
Number of Patients/Sites	330 randomized subjects at 29 clinical sites across the U.S., New Zealand, and Japan
Primary Effectiveness Endpoint	Target Lesion Primary Patency (TLPP) at 180 days TLPP defined as freedom from clinically driven target lesion revascularization or access circuit thrombosis
Primary Safety Endpoint	Freedom from SAE(s) involving the AV access circuit through 30 days

IN.PACT™ AV DCB Fistula Locations



Target Lesion Locations

Target Lesion Location	IN.PACT™ DCB (N=170)	Control PTA (N=160)
Inflow	2.4%	4.4%
Outflow	31.2%	33.1%
Cephalic Arch	17.6%	22.5%
Swing Point	8.2%	7.5%
Cannulation Zone	14.7%	7.5%
Anastomotic	25.9%	25.0%