Lutonix AV IDE Clinical Trial

Latest Lutonix AV Clinical Results

Skyi Pang
Vascular Surgeon
Hong Kong

Disclosure

Speaker name:

Skyi Yin Chun Pang

I have the following potential conflicts of interest to report:

- ☐ Consulting
- ☐ Employment in industry
- ☐ Stockholder of a healthcare company
- ☐ Owner of a healthcare company
- ☐ Other(s)

☑ I do not have any potential conflict of interest

Lutonix AV IDE Clinical Results

Objective

- Study design & published 6-month data
- Sub-group analysis
- 2-year outcome
- Safety and mortality data
- Current investigations
- Practical applications in 2019

Lutonix AV IDE Clinical Trial

Trial Design

Objective	To assess the safety and effectiveness of the LUTONIX® 035 AV Drug Coated Balloon PTA Catheter in the treatment of dysfunctional AV fistulae
Number of Patients/Sites	285 randomized subjects at 23 clinical sites
Primary Effectiveness Endpoint	Target Lesion Primary Patency (TLPP) - 6 months
Primary Safety Endpoint	Freedom from any serious adverse event(s) involving the AV access circuit through 30 days
Follow Up	1, 3, 6, 9, 12, 18, 24 month visits
Status	First Subject: June 2015 Enrollment Completion: March 2016

- ✓ Prospective
- ✓ Multi-Center
- ✓ Randomized (1:1)
- ✓ Core Lab Adjudicated
- ✓ Clinical Events Committee (CEC)
- ✓ Data & Safety Monitoring Board (DSMB)

Lutonix AV IDE Clinical Trial

Clinical Trial Sites

Investigator	Site Name	State	Investigator	Site Name	State
Balamuthusamy, Saravanan	Tarrant Vascular Clinic	TX	**Nadolski, Greg**	Hospital of the University of PA	PA
Waheed, Umar	Southwest Vascular Ctr	AZ	**Atray, Naveen**	Capital Nephrology Medical	CA
Lipkowitz, George	Renal &Transplant Assoc of NE	MA	**Bratton, Charles**	Medical University of SC	SC
Saad, Theodore	Nephrology Associates	DE	**Pflederer, Timothy**	Renal Care Associates, S.C.	IL
Hoggard, Jeffrey	Capital Nephrology Assoc.	NC	**Kamel, Ahmed**	University of Alabama at Birmingham (UAB)	AL
Peeler, David	University Vascular Access	TN	**Schultz, Scott**	Minnesota Vascular Surgery Ctr	MN
Neyra, Roxana	Arizona Kidney Disease and Hypertension Center	AZ	**Wilkins, Luke**	University of Virginia	VA
Lawless, Mike	Life Access Center	OK	**Irani, Zubin**	Massachusetts General Hospital	MA
Licht, Jonah	Providence Interventional	RI	**Tasse, Jordan**	Rush University	IL
Makris, Angelo	Chicago Access Care	IL	**Davanzo, William**	Phoebe Putney Memorial Hospital	GA
Molnar, Robert	San Antonio Kidney DiseaseCtr	TX	**Resnick, Scott**	Northwestern	IL
Kramer, Ari	Michigan Vascular Access	MI	**Ross, John**	Access Connections	SC
Chan, Micah	Spartanburg Regional Hpt	SC			

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Device Description

Study Device: LUTONIX® 035 DCB

- 2 µg/mm^2 paclitaxel + polysorbate and sorbitol excipients
- 4-12 mm diameters, 40-100 mm lengths
- .035” guidewire compatible, nylon, semi-compliant balloon
- Over the wire, co-axial shaft
- Nominal 6atm, RBP up to 12atm

Photo courtesy of BD

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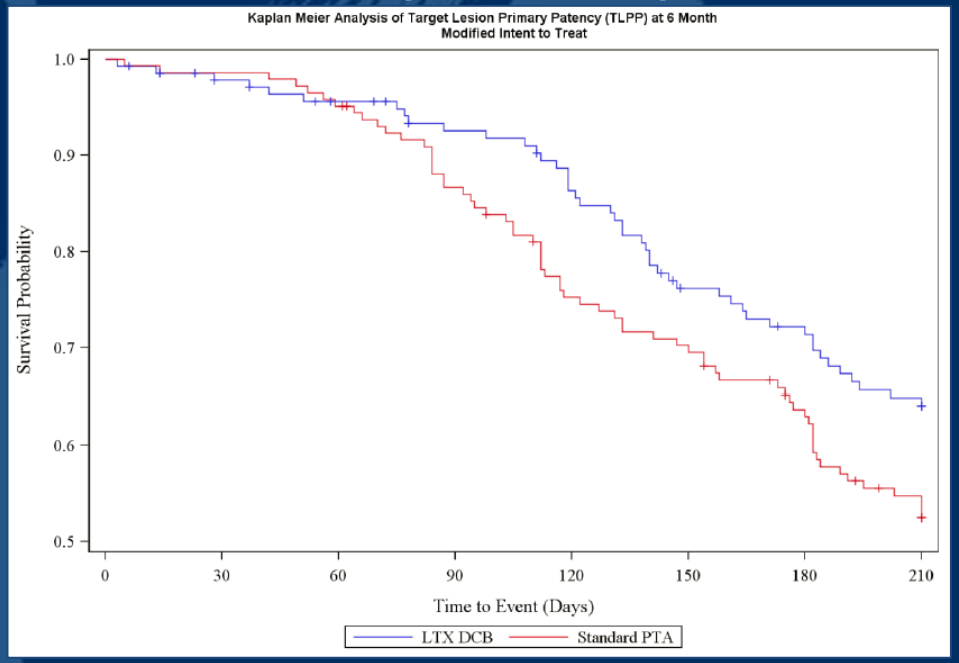
Primary Endpoint – 6 Month Results



Re-interventions	LTX DCB (n=141)	Standard PTA (n=144)	P	DCB vs. Control
Number of interventions, 180 days	44	64	0.034	31.3% Fewer
Number of interventions, 210 days	58	85	0.012	32.8% Fewer

Drug Coated Balloon Angioplasty in Failing AV Fistulas
A Randomized Controlled Trial

Scott O. Trerotola,[1] Jeffrey Lawson,[2,3] Prabir Roy-Chaudhury,[4] and Theodore F. Saad,[5] for the Lutonix AV Clinical Trial Investigators

Trerotola et al, *Clin JASN* 13:1215-1224, 2018

Drug-Coated Balloon Angioplasty for Hemodialysis Fistula Maintenance

Bharat Sachdeva and Kenneth Abreo
Clin J Am Soc Nephrol 13: 1140–1141, 2018. doi: https://doi.org/10.2215/CJN.07360618

Sachdeva B, Abreo K, *Clin JASN* 13:1140-1141, 2018

"The preliminary findings of this study are encouraging and hopefully, will be borne out over the 12 and 24 months of observation. It is our hope that DCB angioplasty will delay recurrent stenosis in AVFs and thereby, decrease morbidity and cost for patients on hemodialysis."

Lutonix AV IDE Clinical Trial
Subgroup Analyses

- Antiplatelet agents
- Fistula age
- Diabetes
- Previous intervention
- Fistula location
- Target lesion location

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Antiplatelet: Aspirin or Clopidogrel Post-Index Procedure

	6 Mo. TLPP		Diff.	P-val
Antiplatelet?	**LTX**	**Control**	**(95% CI)**	**n/s**
Yes- 6 months	47/67 (70.1%)	36/63 (57.1%)	**13.0%** (-3.4%, 29.4%)	
No	42/59 (71.2%)	52/77 (67.5%)	**3.7%** (-11.9%, 19.2%)	
Yes- 12 months	23/61 (37.7%)	15/62 (24.2%)	**13.5%** (-2.7%, 29.7%)	
No	23/53 (43.4%)	30/70 (42.9%)	**0.5%** (-17.1%, 18.2%)	
Yes- 24 months	13/64 (20.3%)	12/64 (18.8%)	**1.6%** (-12.2%, 15.3%)	
No	9/42 (21.4%)	13/61 (21.3%)	**0.1%** (-16.0%, 16.2%)	

- "Antiplatelet treatment protects fistula from thrombosis or loss of patency….."
  - Palmer et al, Antiplatelet therapy to prevent hemodialysis vascular access failure: Systematic review and meta-analysis. Am J Kidney Dis 2013; 61(1):112-122
- "… the use of antiplatelet agents prevented the loss of VA patency in a dose–response manner"
  - Hsu et al. Antiplatelet agents maintain arteriovenous fistula and graft function in patients receiving hemodialysis: A nationwide case-control study. PLoS one 2018; 13

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Age of Fistula

	6 Mo. TLPP		Diff.	12 Mo. TLPP		Diff.	24 Mo. TLPP		Diff.	P-val
Age of Fistula	**LTX**	**Control**	**(95% CI)**	**LTX**	**Control**	**(95% CI)**	**LTX**	**Control**	**(95% CI)**	**n/s**
<= 6 Months	2/3 (66.7%)	3/4 (75.0%)	**-8.3%** (-76.5%, 59.8%)	1/3 (33.3%)	3/4 (75.0%)	**-41.7%** (-100.0%, 26.5%)	0/2 (0%)	2/3 (66.7%)	**66.7%** (13.3%, 100.0%)	
6-12 Months	10/14 (71.4%)	14/26 (53.8%)	**17.6%** (-12.9%, 48.0%)	8/12 (66.7%)	7/24 (29.2%)	**37.5%** (5.2%, 69.8%)	4/11 (36.4%)	5/24 (20.8%)	**15.5%** (-17.2%, 48.3%)	
> 12 Months	77/109 (70.6%)	71/110 (64.5%)	**6.1%** (-6.3%, 18.5%)	37/99 (37.4%)	35/104 (33.7%)	**3.7%** (-9.4%, 16.9%)	18/93 (19.4%)	18/98 (18.4%)	**1.0%** (-10.1%, 12.1%)	

- "…the newer the AVF is at angioplasty, the shorter the post-intervention primary patency duration. Angioplasty in AVFs less than 6 months of age….significantly increased the risk of postintervention primary patency loss."
  - Neuen et al, Factors associated with patency following angioplasty of hemodialysis fistulae JVIR 2014;25:1419-1426

- "…the older the AVF, the smaller the probability of recurrence"
  - Heye et al, Factors influencing technical success and outcome of percutaneous balloon angioplasty in de novo native hemodialysis arteriovenous fistulas Eur J Rad 2012;81;2298-2303

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Diabetes

	6 Mo. TLPP		Diff.	12 Mo. TLPP		Diff.	24 Mo. TLPP		Diff.	P-val
	LTX	Control	(95% CI)	LTX	Control	(95% CI)	LTX	Control	(95% CI)	n/s
Yes	49/73 (67.1%)	57/91 (62.6%)	**4.5%** (10.2%,19.1%)	26/67 (38.8%)	30/88 (34.1%)	**4.7%** (-10.6%, 20.0%)	14/63 (22.2%)	15/82 (18.3%)	**3.9%** (-9.3%, 17.2%)	
No	40/53 (75.5%)	31/49 (63.3%)	**12.2%** (-5.6%, 30.0%)	20/47 (42.6%)	15/44 (34.1%)	**8.5%** (-11.4%, 28.4%)	8/43 (18.6%)	10/43 (23.3%)	**-4.7%** (-21.8%, 12.5%)	

- "The presence of diabetes mellitus predicted restenosis of AV fistulas after PTA…"
  - Wu et. al, Baseline plasma glycemic profiles but not inflammatory biomarkers predict symptomatic restenosis after angioplasty of arteriovenous fistulas in patients with hemodialysis, Atherosclerosis 2010;209:598-600
- "Patients with diabetes mellitus have higher risk for early dysfunction"
  - Heye et al, Factors influencing technical success and outcome of percutaneous balloon angioplasty in de novo native hemodialysis arteriovenous fistulas European Journal of Radiology 2012;81:2298-2303
- "Early dysfunction was positively correlated with diabetes"
  - Atkas et al, Percutaneous transluminal balloon angioplasty in stenosis of native hemodialysis arteriovenous fistulas: technical success and analysis of factors affecting post procedural fistula patency Diagn Interv Radiol 2015;21:160-166

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Previous Intervention

	6 Mo. TLPP		Diff.	12 Mo. TLPP		Diff.	24 Mo. TLPP		Diff.	P-val
	LTX	Control	(95% CI)	LTX	Control	(95% CI)	LTX	Control	(95% CI)	n/s
Yes	75/109 (68.8%)	72/121 (59.5%)	**9.3%** (-3.0%, 21.6%)	38/99 (38.4%)	35/115 (30.4%)	**7.9%** (-4.8%, 20.7%)	17/92 (18.5%)	18/109 (16.5%)	**2.0%** (-8.6%, 12.5%)	
No	14/17 (82.4%)	16/19 (84.2%)	**-1.9%** (-26.3%, 22.6%)	8/15 (53.3%)	10/17 (58.8%)	**-5.5%** (-39.9%, 28.9%)	5/14 (35.7%)	7/16 (43.8%)	**-8.0%** (-43.0%, 26.9%)	

- "…the only predictor of secondary patency was a previously failed and abandoned AVF"
  - Neuen et al, Factors associated with patency following angioplasty of hemodialysis fistulae JVIR 2014;25:1419-1426

- "…early dysfunction was significantly higher…in failed vascular access groups after initial PTA…"
  - Kim et al, Factors affecting patency following successful percutaneous intervention for dysfunctional hemodialysis vascular access Ann Vasc Surg 2018;47:54-61

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Previous Intervention by Time

	6 Mo. TLPP		Diff.	12 Mo. TLPP		Diff.	24 Mo. TLPP		Diff.	P-val
Previous Intervention	**LTX**	**Control**	**(95% CI)**	**LTX**	**Control**	**(95% CI)**	**LTX**	**Control**	**(95% CI)**	**n/s**
> 90 days	59/82 (72.0%)	65/101 (64.4%)	**7.60%** (-5.9%, 21.1%)	29/73 (39.7%)	33/96 (34.4%)	**5.4%** (-9.4%, 20.1%)	13/67 (19.4%)	17/90 (18.9%)	**0.5%** (-11.9%, 13.0%)	
< = 90 days	16/27 (59.3%)	7/20 (35.0%)	**24.30%** (-3.7%, 52.2%)	9/26 (34.6%)	2/19 (10.5%)	**24.1%** (1.2%, 47.0%)	4/25 (16.0%)	1/19 (5.3%)	**10.7%** (-6.8%, 28.3%)	
No previous intervention	14/17 (82.4%)	16/19 (84.2%)	**-1.90%** (-26.3%, 22.6%)	8/15 (53.3%)	10/17 (58.8%)	**-5.5%** (-39.9%, 28.9%)	5/14 (35.7%)	7/16 (43.8%)	**-8.0%** (-43.0%, 26.9%)	

- "…early occurrence was associated with a lower secondary patency rate"
  - Atkas et al, Percutaneous transluminal balloon angioplasty in stenosis of native hemodialysis arteriovenous fistulas: technical success and analysis of factors affecting post procedural fistula patency Diagn Interv Radiol 2015; 21:160-166

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Fistula Location

	6 Mo. TLPP		Diff.	12 Mo. TLPP		Diff.	24 Mo. TLPP		Diff.	P-val
Location	**LTX**	**Control**	**(95% CI)**	**LTX**	**Control**	**(95% CI)**	**LTX**	**Control**	**(95% CI)**	**n/s**
Across Antecubital Fossa	4/6 (66.7%)	5/7 (71.4%)	**-4.8%** (-55.2%, 45.7%)	1/6 (16.7%)	3/6 (50.0%)	**-33.3%** (-83.2%, 16.6%)	1/6 (16.7%)	2/5 (40.0%)	**-23.3%** (-75.6%, 28.9%)	
Forearm	30/41 (73.2%)	22/31 (71.0%)	**2.2%** (-18.8%, 23.2%)	16/36 (44.4%)	11/29 (37.9%)	**6.5%** (-17.5%, 30.5%)	7/34 (20.6%)	6/26 (23.1%)	**-2.5%** (-23.6%, 18.7%)	
Upper Arm	55/79 (69.6%)	60/101 (59.4%)	**10.2%** (-3.7%, 24.2%)	29/72 (40.3%)	31/96 (32.3%)	**8.0%** (-6.7%, 22.7%)	14/66 (21.2%)	17/93 (18.3%)	**2.9%** (-9.7%, 15.5%)	

- "Upper arm fistulae were associated with reduced postintervention primary patency"
  - Neuen et al, Factors associated with patency following angioplasty of hemodialysis fistulae JVIR 2014;25:1419-1426
- Upper-arm AVFs predicted shorter primary patency after angioplasty compared with forearm AVF
  - Rajan et al, Dysfunctional autogenous hemodialysis fistulas: Outcomes after angioplasty- Are there clinical predictors of patency? Radiology 2004;232:508-515

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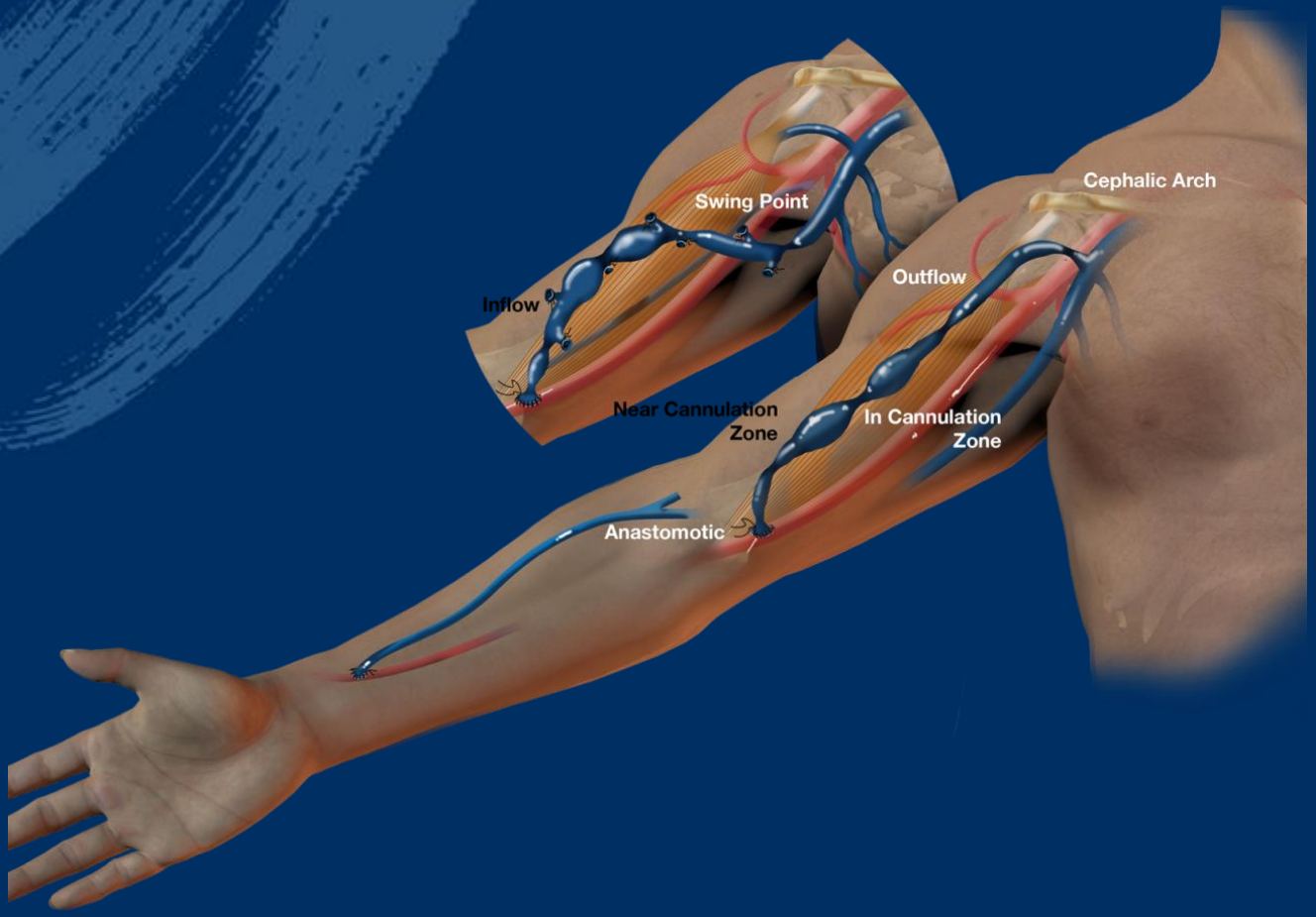
Target Lesion Location



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Target Lesion Location

	6 Mo. TLPP		Diff.	12 Mo. TLPP		Diff.	24 Mo. TLPP		Diff.	P-val
Target Lesion Location	**LTX**	**Control**	**(95% CI)**	**LTX**	**Control**	**(95% CI)**	**LTX**	**Control**	**(95% CI)**	**n/s**
Anastomotic	13/17 (76.5%)	8/14 (57.1%)	**19.3%** (-13.5%, 52.2%)	7/16 (43.8%)	3/13 (23.1%)	**20.7%** (-12.7%, 54.1%)	3/16 (18.8%)	1/13 (7.7%)	**11.1%** (-12.9%, 35.0%)	
Cephalic arch	13/25 (52.0%)	14/31 (45.2%)	**6.8%** (-19.4%, 33.1%)	5/23 (21.7%)	9/31 (29.0%)	**-7.3%** (-30.5%, 15.9%)	1/22 (4.5%)	1/29 (3.4%)	**1.1%** (-9.9%, 12.0%)	
In cannulation zone	8/11 (72.7%)	11/16 (68.8%)	**4.0%** (-30.8%, 38.7%)	6/10 (60.0%)	7/15 (46.7%)	**13.3%** (-26.2%, 52.8%)	3/9 (33.3%)	5/14 (35.7%)	**-2.4%** (-42.1%, 37.3%)	
Inflow	13/17 (76.5%)	22/28 (78.6%)	**-2.1%** (-27.4%, 23.1%)	9/16 (56.3%)	11/25 (44.0%)	**12.3%** (-18.9%, 43.4%)	5/14 (35.7%)	8/23 (34.8%)	**0.9%** (-30.8%, 32.7%)	
Near cannulation zone	8/11 (72.7%)	7/8 (87.5%)	**-14.8%** (-49.7%, 20.1%)	3/9 (33.3%)	3/5 (60.0%)	**-26.7%** (-79.5%, 26.2%)	1/8 (12.5%)	1/4 (25.0%)	**-12.5%** (-60.7%, 35.7%)	
Outflow	25/31 (80.6%)	20/34 (58.8%)	**21.8%** (0.2%, 43.4%)	11/28 (39.3%)	9/34 (26.5%)	**12.8%** (-10.6%, 36.2%)	7/26 (26.9%)	6/33 (18.2%)	**8.7%** (-12.8%, 30.3%)	
Swing point	9/14 (64.3%)	6/9 (66.7%)	**-2.4%** (-42.1%, 37.3%)	5/12 (41.7%)	3/9 (33.3%)	**8.3%** (-33.2%, 49.9%)	2/11 (18.2%)	3/9 (33.3%)	**-15.2%** (-53.5%, 23.2%)	

- Cannulation zone…..more than intimal hyperplasia?
  - Roy-Chaudhury et al, Hemodialysis vascular access dysfunction: A cellular and molecular viewpoint JASN 2006;17(4):1112-1127
- "Swing-segment lesions predispose to early fistula failure"
  - Badero et al, Frequency of swing-segment stenosis in referred dialysis patients with angiographically documented lesions Am J Kidney Dis 2008;51(1):93-98
- Cephalic arch lesions more difficult to treat
  - Rajan et al, Prevalence and Treatment of Cephalic Arch Stenosis in Dysfunctional Autogenous Hemodialysis Fistulas JVIR 2003;14:567-573

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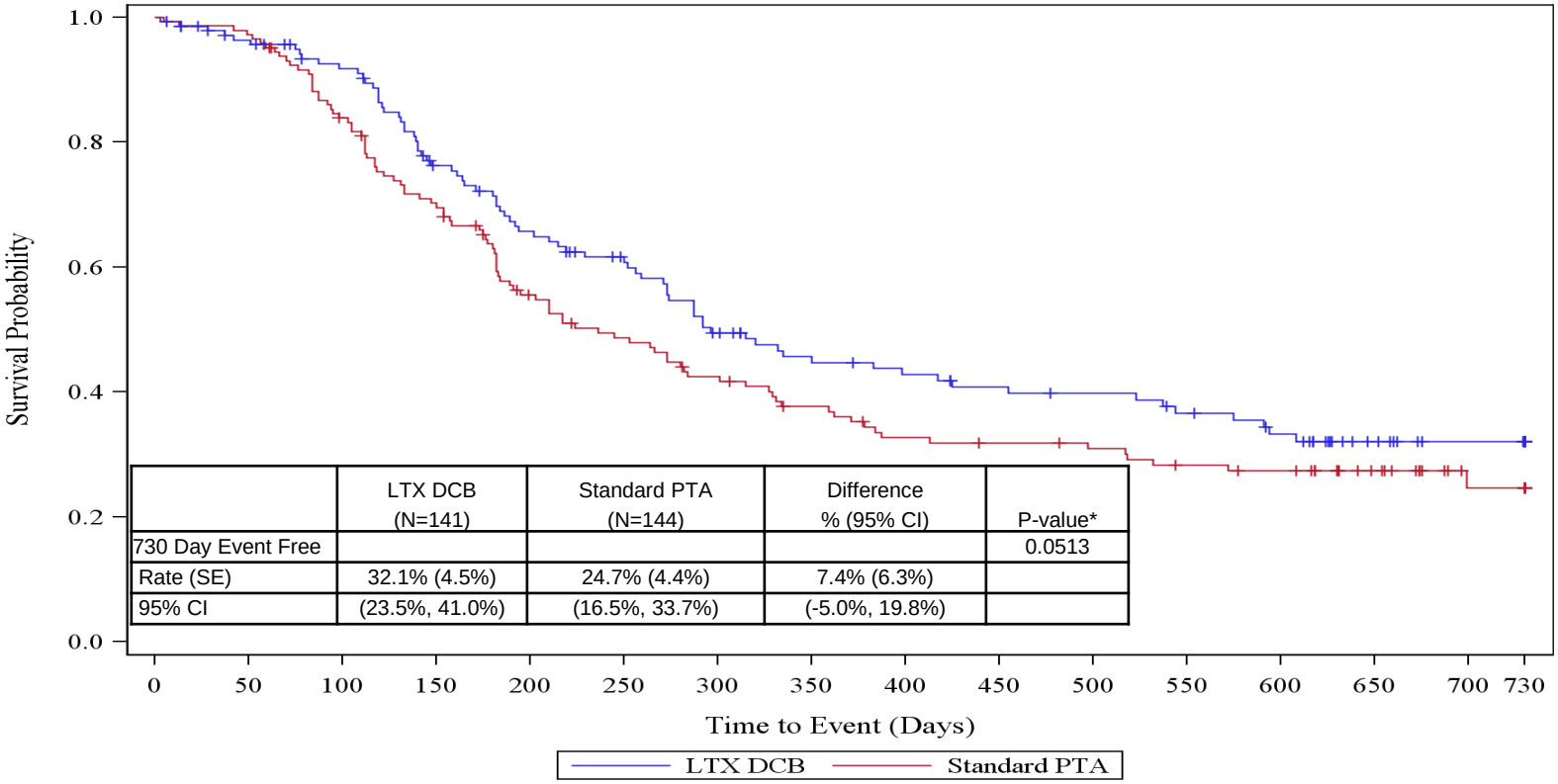
24 Month Data

Lutonix AV IDE Clinical Trial

Efficacy- Interim 24 Month TLPP

C.R.Bard Inc.
Protocol: CL0023-01

Figure 14.2.1.1.1.D730
Kaplan Meier Analysis of Target Lesion Primary Patency (TLPP) at 24 Month
Modified Intent to Treat



	LTX DCB (N=141)	Standard PTA (N=144)	Difference % (95% CI)	P-value*
730 Day Event Free				0.0513
Rate (SE)	32.1% (4.5%)	24.7% (4.4%)	7.4% (6.3%)	
95% CI	(23.5%, 41.0%)	(16.5%, 33.7%)	(-5.0%, 19.8%)	

Target Lesion Primary Patency (TLPP) ends with a clinically driven re-intervention of the target lesion or access thrombosis.
Data Source: ADSL, ADEF
Program name: fpce_km.sas

Output for DEC 1, 2017 Data Cut Report

Date: 02JAN2018 10:24

Data shown are interim, site reported and subject to change

*One-sided p-value

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Mortality at 24 Months

Description	Lutonix (n=141)	Control (n=144)	P Value
Number of Deaths at 24 Months	33 (23.4%)	26 (18.1%)	**P=0.265**

N= 4 voluntarily withdrew from dialysis- Lutonix
N= 1 voluntarily withdrew from dialysis- Control

U.S. 2 year mortality on hemodialysis- 33.2%[1]

1. USRDS 2018 Chapter 5 Mortality, Table 5.3

Lutonix AV Clinical Trial

Lutonix AV Clinical Program

Title	Number of Subjects
Lutonix AV Clinical Trial - Complete	N=285
Lutonix AV Real World Global Registry - Enrolled	N=324
Lutonix AV Post Approval Study – Enrolling	N=213
Total	**N=822**

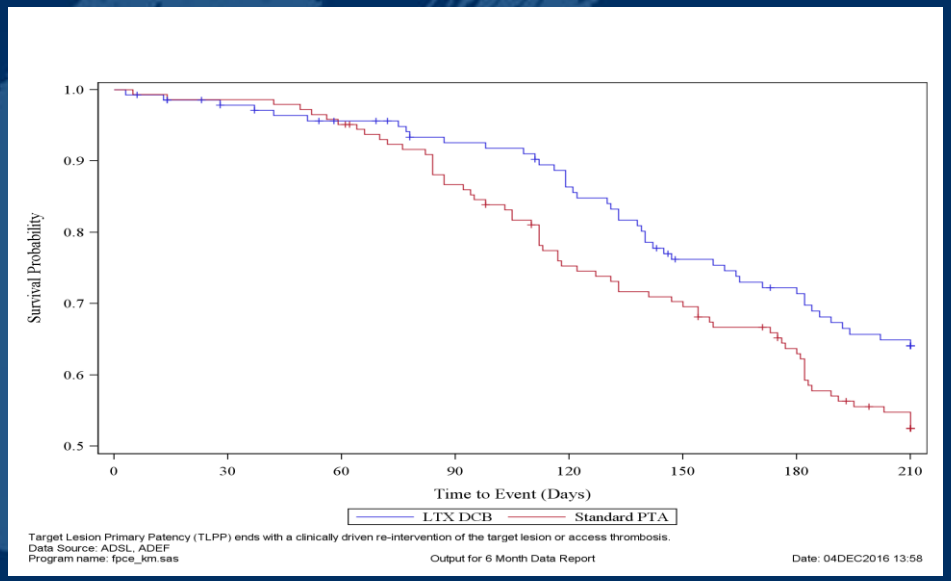
Lutonix AV Global Registry

6 Month Data

6 Month TLPP Results

Lutonix AV IDE Clinical Trial

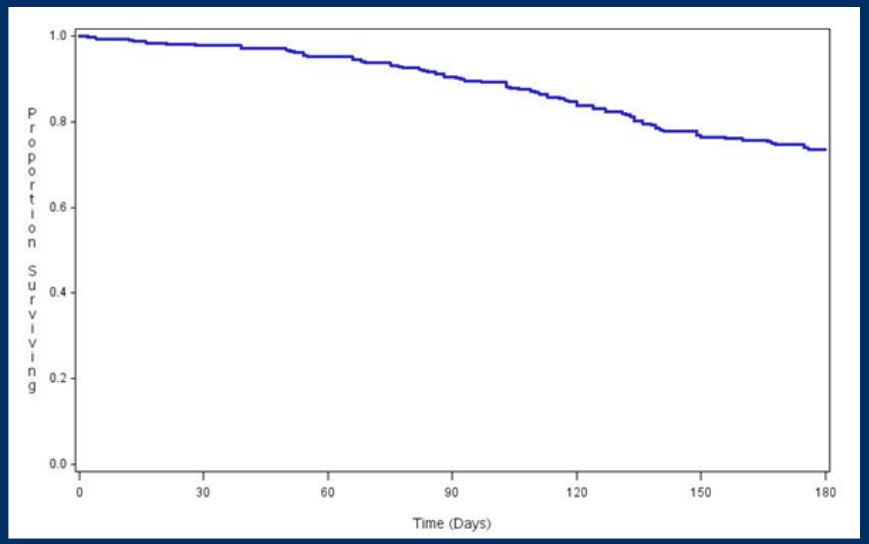
71.4% TLPP at 6 Months



Mature, dysfunctional fistulae. Central vein and ISR excluded. Restenotic and previous thrombosis included.

Lutonix AV Global Registry

73.5% TLPP at 6 Months



Real World treated lesions; Central vein, ISR, AVG/AVF, Cephalic Arch, Restenotic, etc.

TLPP ends with a clinically driven re-intervention of the target lesion or access thrombosis. Kaplan Meier modified intent to treat.

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Summary

DCB effect was not statistically different between subgroups

- *DCB appears to work equivalently across access history/lesion location*

Mortality rate was comparable to control arm

- *None of the deaths were related to the test device or the procedure*

Additional analyses to follow

- *> 800 subjects part of a Lutonix AV protocol*

Thank You

Lutonix AV IDE Clinical Trial

Latest Lutonix AV Clinical Results

Skyi Pang
Vascular Surgeon
Hong Kong