
2022 VASCULAR ACCESS FOR HEMODIALYSIS SYMPOSIUM
June 9 - 11, 2022
Charleston Marriott Hotel
Charleston, South Carolina
VASCULAR ACCESS SOCIETY OF THE AMERICAS
VASA

FLEX Vessel Prep System AV Registry Clinical Study Results

John E. Aruny, MD

Disclosures

Speaker name: John Aruny, MD

I have the following potential conflicts of interest to report:

Boston Scientific Advisory Board

Venture Medical Advisory

Merit Medical Investigator

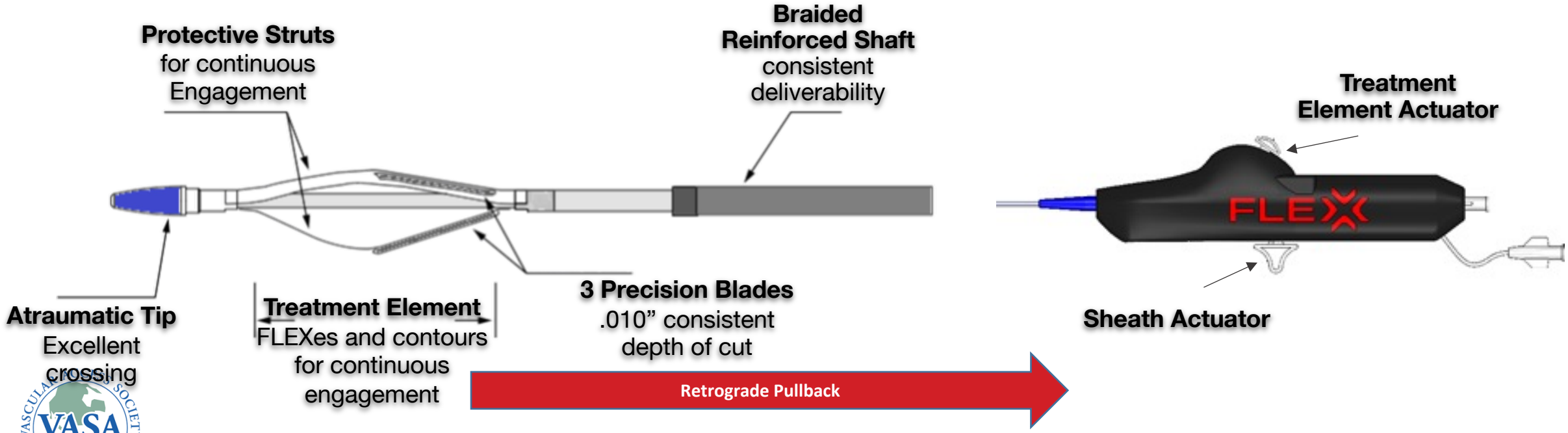
Background

- Maintaining functioning hemodialysis access for patients is challenging as failing fistulas and grafts prevent patients from life saving dialysis
- Registry results show real world patients with lesions that can be difficult to treat due to morphology, location like cephalic arch or patient characteristics
- Balloon angioplasty has been the gold standard with inconsistent patency results

FLEX Vessel Prep™ System - Easy To Use

Vessel Prep in AV Access

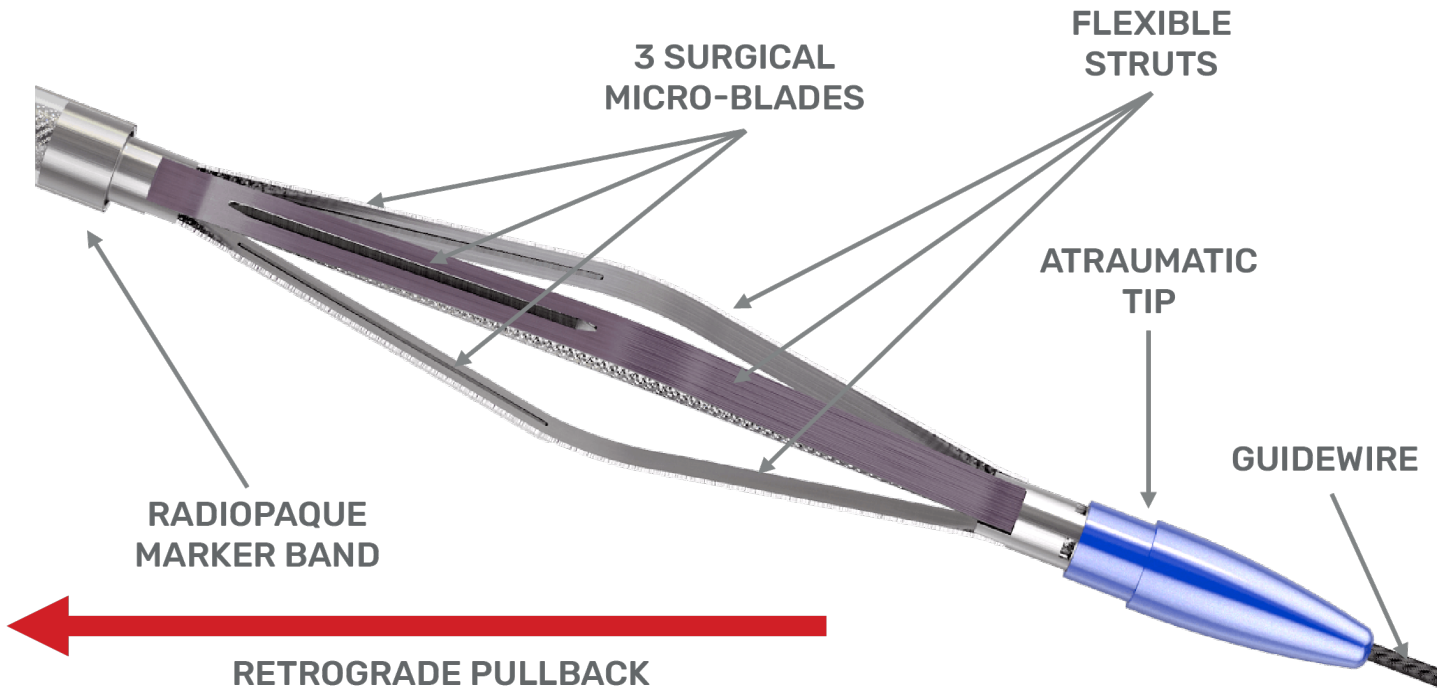
- 6Fr; .014” or .018” guidewire (OTW)
- 2 working lengths – 40cm (AV Access) & 120cm (FemPop)
- Braided shaft design for consistent deliverability
- Atraumatic tip for enhanced trackability & crossing profile



FLEX Vessel Prep™ System: Extends Patency for Hemodialysis patients

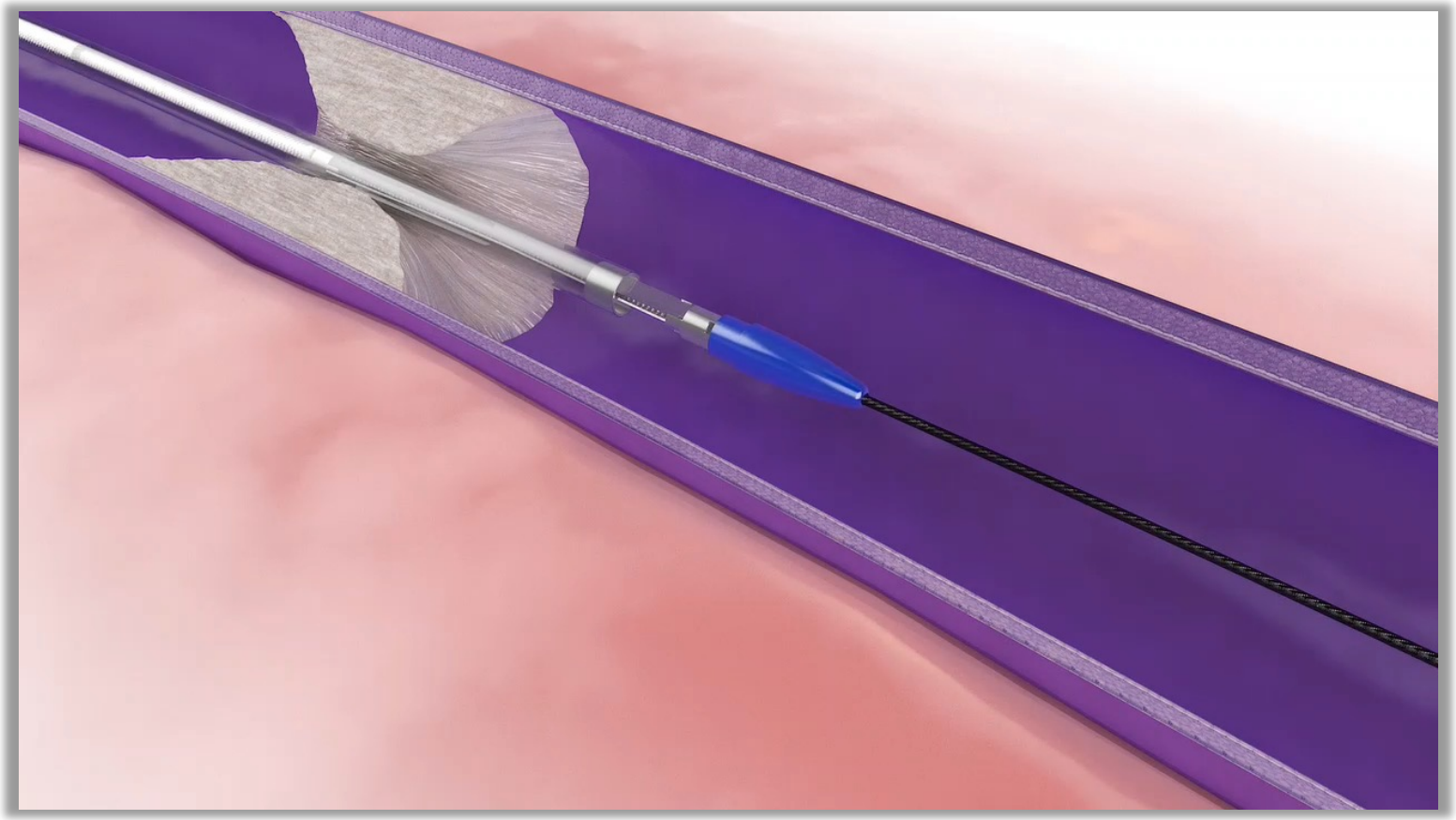
Mechanism of Action: 3 micro-surgical blades mounted on the back pf independent skids:

- Improves vessel compliance by releasing circumferential tension
- Enables lower uniform balloon inflation pressures for less barotrauma
- Treats single or multiple stenoses in an AV circuit with one device



FLEX VP prepares the vessel prior to angioplasty to maximize the outcome, while minimizing complications

FLEX Vessel Prep™ System



3 surgical blades mounted on independent skids

- Consistent engagement in stenoses
- Releases circumferential & fibro-muscular tension in resistant stenoses

FLEX-AV Registry Overview

- **Study Design:** Multi-Center, Single-Arm, Prospective Study
- **Study Population:** Patients with AVF/AVG stenosis, eligible for FLEX/Angioplasty treatment.
- **Enrollment:** 114
- **Sites:** 8 Sites

Follow-Up: Phone call to the patient and/or dialysis center at 6, 9, and 12 months.

FLEX-AV Registry Overview

- **Primary Endpoint**

  Anatomic Success defined as the angiographic percentage of stenosis post procedure as <30% at the completion of the index procedure.

- **Additional Assessments**

  - Target Lesion Primary Patency: The time interval of uninterrupted patency from initial study treatment to the next thrombosis or intervention performed on the target lesion.
  - Circuit Primary Patency: The time interval from initial study treatment to the next access thrombosis or intervention performed within the vascular access circuit.

FLEX-AV Registry

✓ Inclusion Criteria

- Hemodialysis patient currently scheduled to undergo an intervention of their arteriovenous fistula or graft due to clinical or hemodynamic abnormalities.
- The patient is ≥18 years of age. Patient is legally competent, has been informed of the study, voluntarily agrees to participate, and has signed the informed consent form.
- The patient has a reasonable expectation of remaining on hemodialysis for 12 months.
- The patient understands the study and is willing and able to comply with follow-up requirements.
- The patient is willing to provide informed consent.

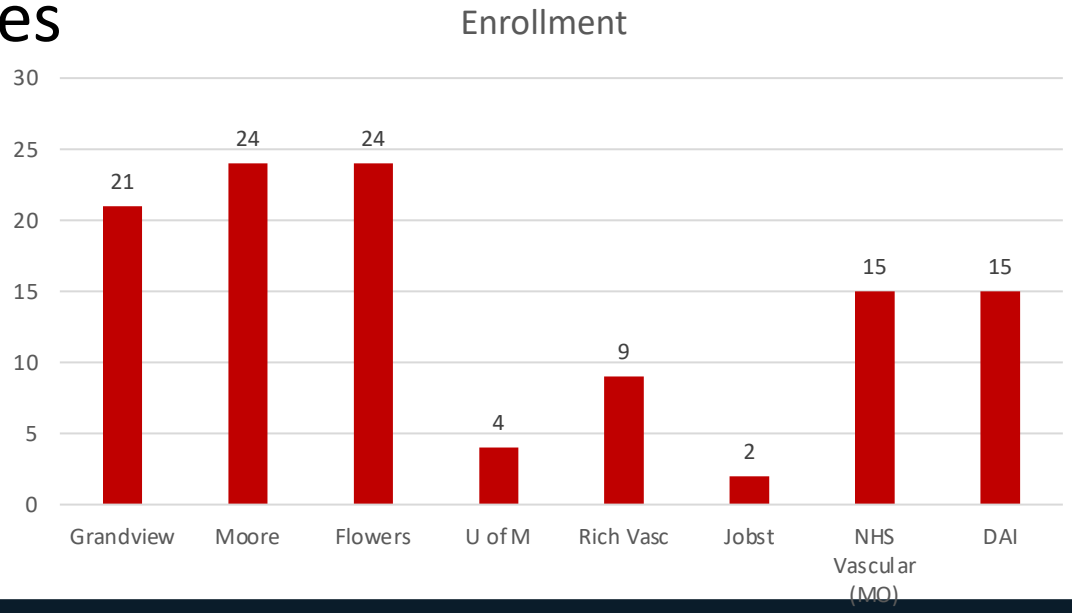
FLEX-AV Registry

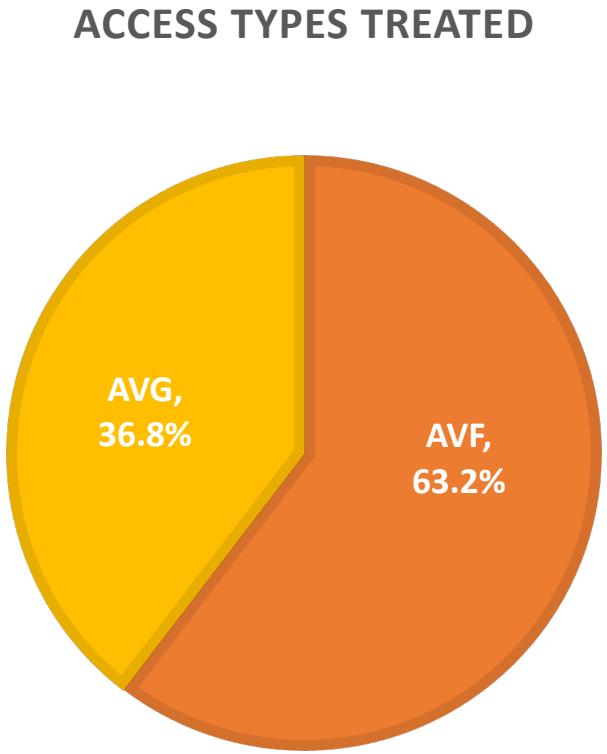
❌ Exclusion Criteria

- The patient has a known or suspected systemic infection.
- The patient has a known or suspected infection of the hemodialysis graft.
- The patient has an untreatable allergy to radiographic contrast material.
- In the opinion of the operating physician, the patient's hemodialysis access is unsuitable for endovascular treatment.

Overview

- 114 patients treated- Fistulas dominating access type
- Number of target lesion treated, n= 114
- Total number of lesions treated, n= 148, 28% of patients had secondary lesions
- 8 clinical sites





Patient Demographics

Variable	114 Subjects
Age (years)	63.3 ± 12.7 (114) 31.0-88.0
Gender	
Female	61/114 (53.5%)
Male	53/114 (46.5%)
Race	
American Indian or Alaska Native	2/114 (1.8%)
Asian	1/114 (0.9%)
Black or African American	75/114 (65.8%)
White	36/114 (31.6%)
Smoking History	
Current	17/114 (14.9%)
Never	60/114 (52.6%)
Past	37/114 (32.5%)

Medical History

Variable	114 Subjects
Diabetes	71/114 (62.3%)
Hypertension	105/114 (92.1%)
Congestive Heart Failure	44/114 (38.6%)
Prior AV Access Interventions (count)	4.9 ± 5.8 (104) 0.0-29.0
Years since AV Access Creation (years)	3.1 ± 2.6 (114) 0.1-13.9
Years since Started Hemodialysis (years)	4.7 ± 4.0 (114) 0.1-19.3
Days since last dialysis (days)	2.3 ± 11.1 (113) 0.0-119.0

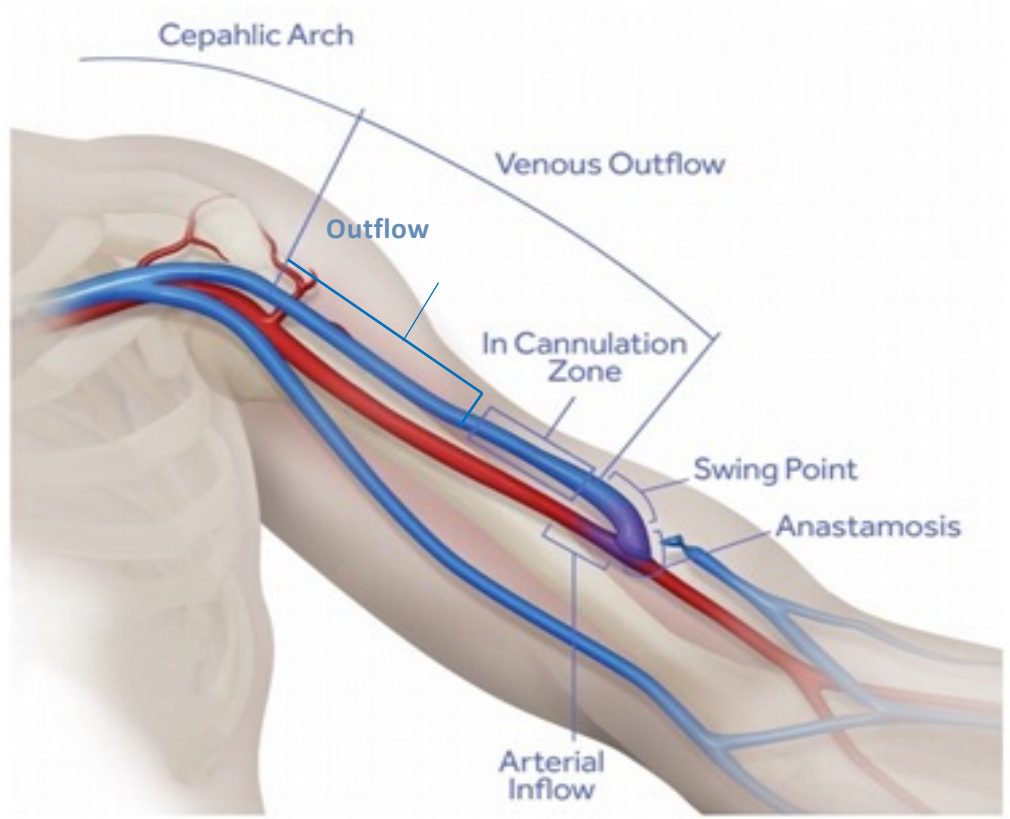
Access Characteristics

Variable	114 Subjects
Fistula Type	
Arteriovenous Fistula	72/114 (63.2%)
Arteriovenous Graft	42/114 (36.8%)
Location	
Forearm	11/114 (9.6%)
Other	4/114 (3.5%)
Upper Arm	99/114 (86.8%)

Access Sites- Detailed	114 Subjects
Basilic -Cephalic trans fistula	1/114 (0.9%)
Brac-Basil Fistula	27/114 (23.7%)
Brach-Axill Graft	36/114 (31.6%)
Brach-Ceph Fistula	37/114 (32.5%)
Brachial-Antecub Graft	3/114 (2.6%)
Left thigh graft	1/114 (0.9%)
Radial Artery-Cephalic Vein Fistula	3/114 (2.6%)
Radial-Ceph Fistula	5/114 (4.4%)
Right Thigh Graft	1/114 (0.9%)

Lesion Characteristics

Variable	114 Subjects
Target Vessel Diameter (mm)	7.8 ± 2.2 (114)
Number of Lesions	
1	82/114 (71.9%)
2	30/114 (26.3%)
3	1/114 (0.9%)
4	1/114 (0.9%)
Target Lesion Location	
Anastomosis	6/114 (5.3%)
Cannulation Zone (Up to 1st large collateral vein)	3/114 (2.6%)
Cephalic Arch	25/114 (21.9%)
Inflow (2 cm from Anastomosis)	2/114 (1.8%)
Outflow (Above Cannulation Zone)	57/114 (50.0%)
Peri-Anastomosis	3/114 (2.6%)
Swing Segment	18/114 (15.8%)
Target Lesion Length (mm)	21 ± 25 (113)
Target Lesion Pre-Procedure Stenosis (%)	75.2 ± 14.7 (114)

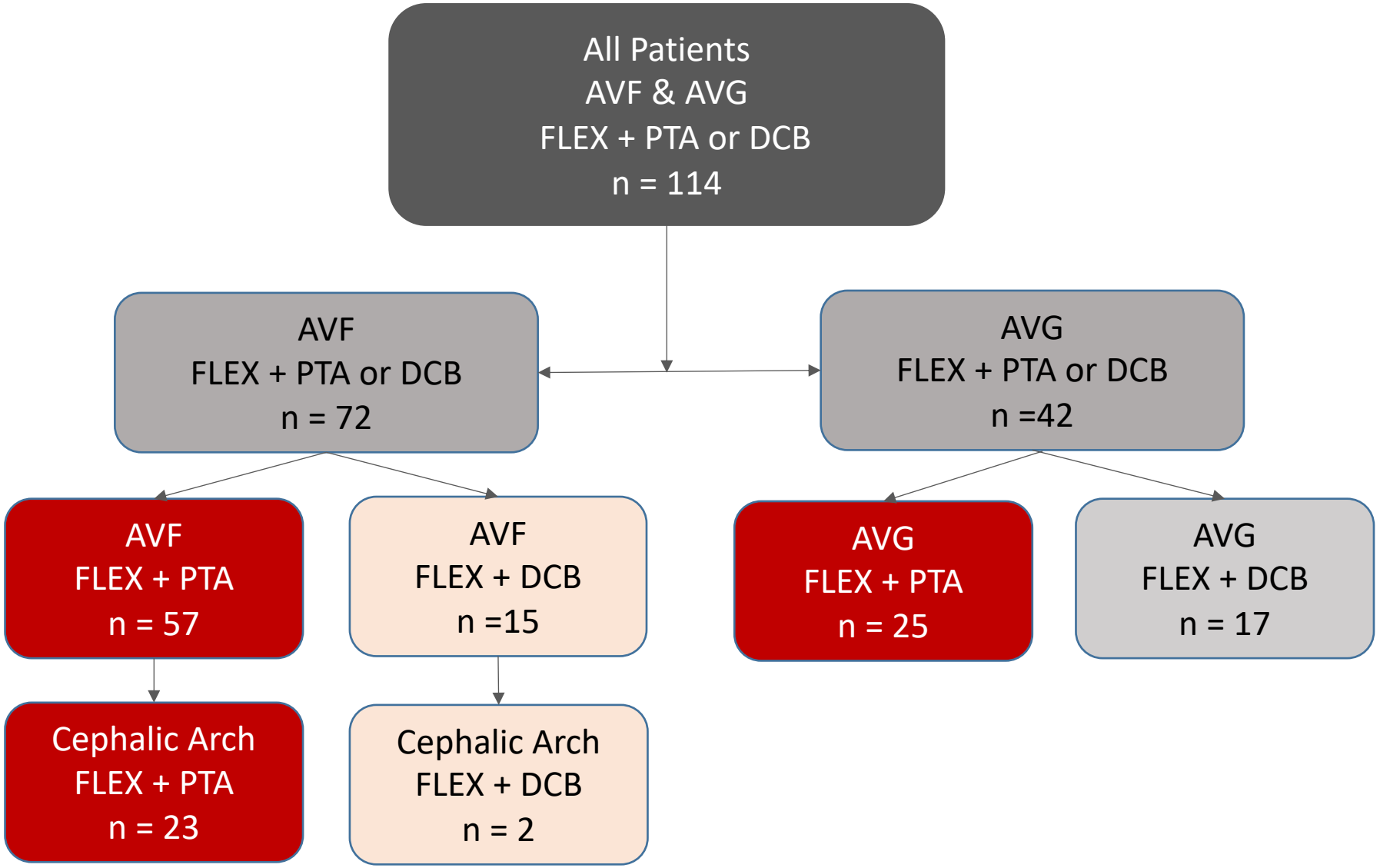


Procedure Characteristics

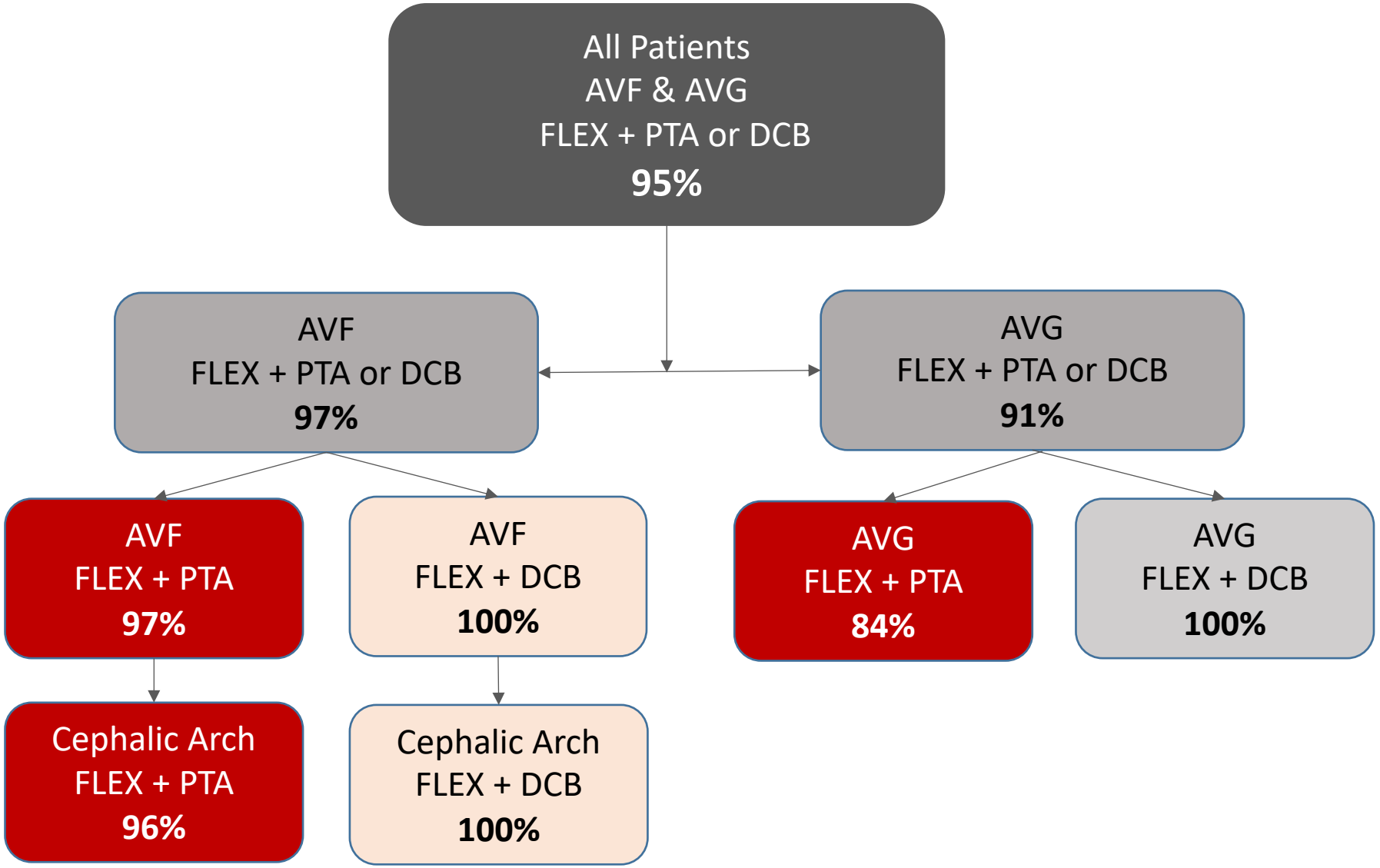
Variable	114 Subjects
Target Lesion FLEX passes (count)	5.1 ± 1.0 (114) 2.0-8.0
Target Lesion Post FLEX Stenosis (%)	53.4 ± 22.1 (114) 0.0-95.0
Number of balloon inflations (count)	
1	67/114 (58.8%)
2	38/114 (33.3%)
3	6/114 (5.3%)
4	1/114 (0.9%)
5	1/114 (0.9%)
6	1/114 (0.9%)

Variable	114 Subjects
PTA / DCB	
DCB	32/114 (28.1%)
PTA	82/114 (71.9%)
Maximum Pressure (atm)	15.2 ± 5.9 (114) 4.0-32.0
Maximum Effacement Pressure (atm)	9.5 ± 10.9 (114) 0.0-50.0

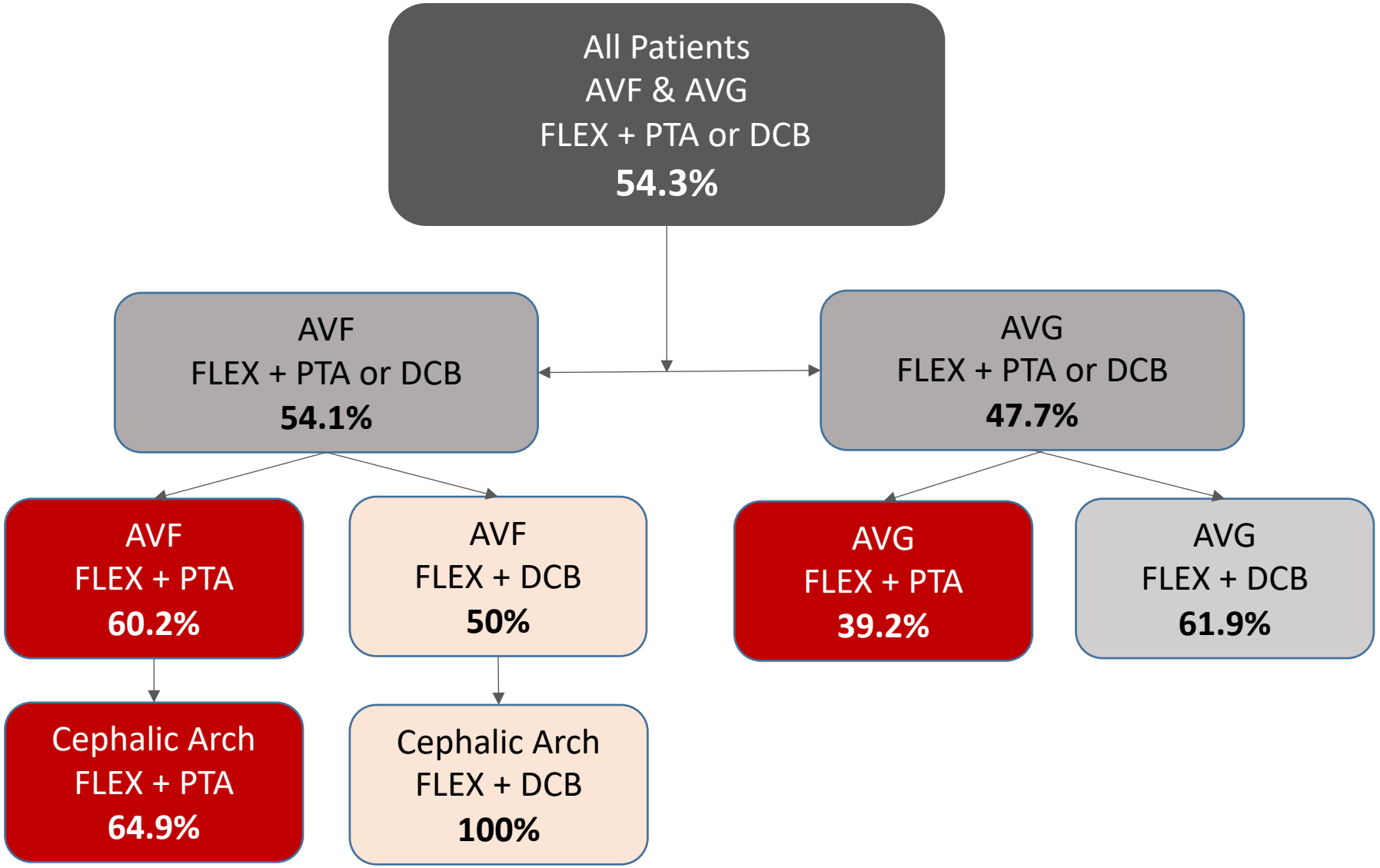
Patient Cohorts



Primary Endpoint – Anatomic Success per Cohort



6-month Circuit Primary Patency per Cohort



Functional Primary Patency
6 months

Freedom from Target Lesion Reintervention

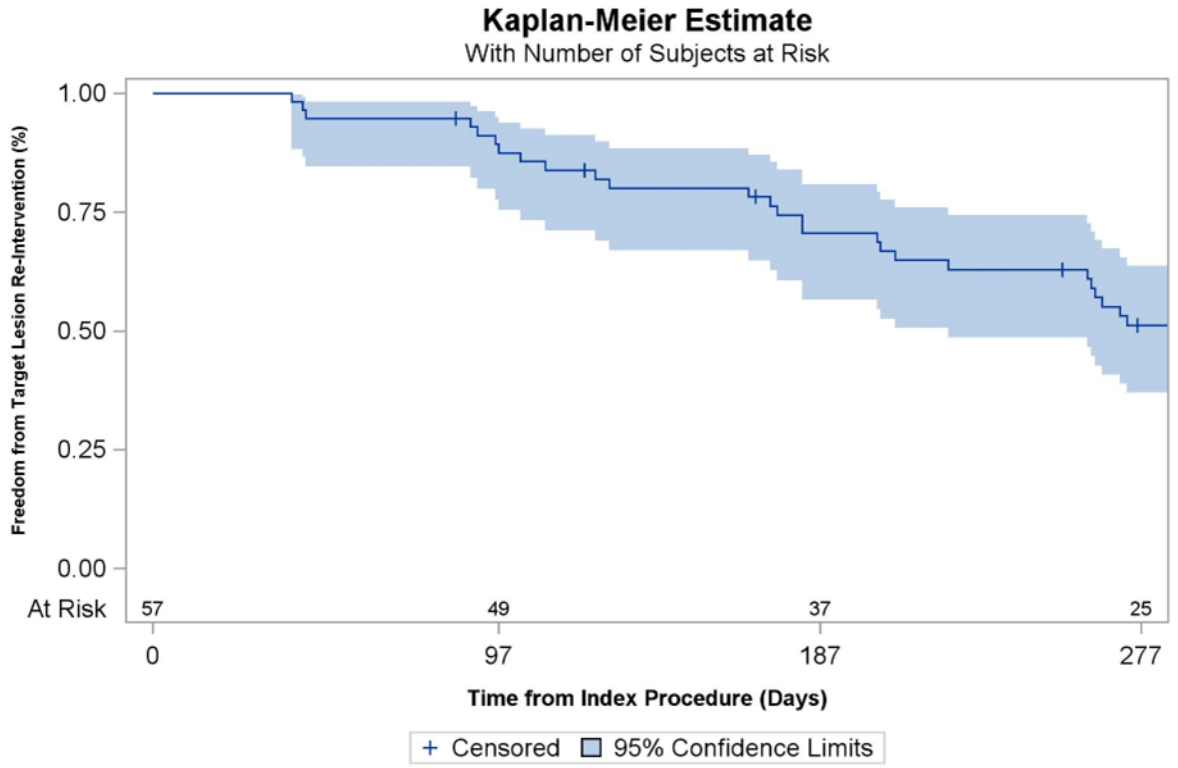
6-month Functional Primary Patency Analysis

- 111/114 target lesions were considered for the Kaplan-Meier estimate
  - 2 subjects did not contribute to any follow-up analysis
  - 1 subject dropped out at 26 days
- Patients analyzed in following cohorts:
  - AVF with PTA alone
  - AVG with PTA alone
  - Cephalic Arch target lesions with PTA alone
- Statistical Analysis
  - ✓Functional Patency estimation via Kaplan-Meier analysis at the close of the 6-month FU visit
  - ✓Freedom from TLR (time) was determined using restricted mean survival time analysis (RMST) restricted to 270 days

6-month Functional Patency
FLEX + PTA in AVF

AVF's

FLEX+ PTA
70.6% (n=57)
Avg. time FF-TLR = ***219.7 days***



Literature Comparisons 6-month Functional Patency after PTA –AVF Results

Published Results	FLEX Registry FLEX + PTA	Rajan, et al[1]	Liao, et al[2]	Hu, et al[3]	Ng, et al[4]	Phang, et al[5]
6-month Functional Patency AVF	**70.6% (n=57)**	55%* (n=53) *ref. Clark et al	55.4%* (n=275) *Only studies for AVFs - reported as event rate of 44.6%	37.5% (n=501) *AVFs only Calculated from table	0%-34%* (n=143) *Only studies for AVFs from table	21.3% (n= 94)

Note: Articles selected that best represented the real-world population for cohort.

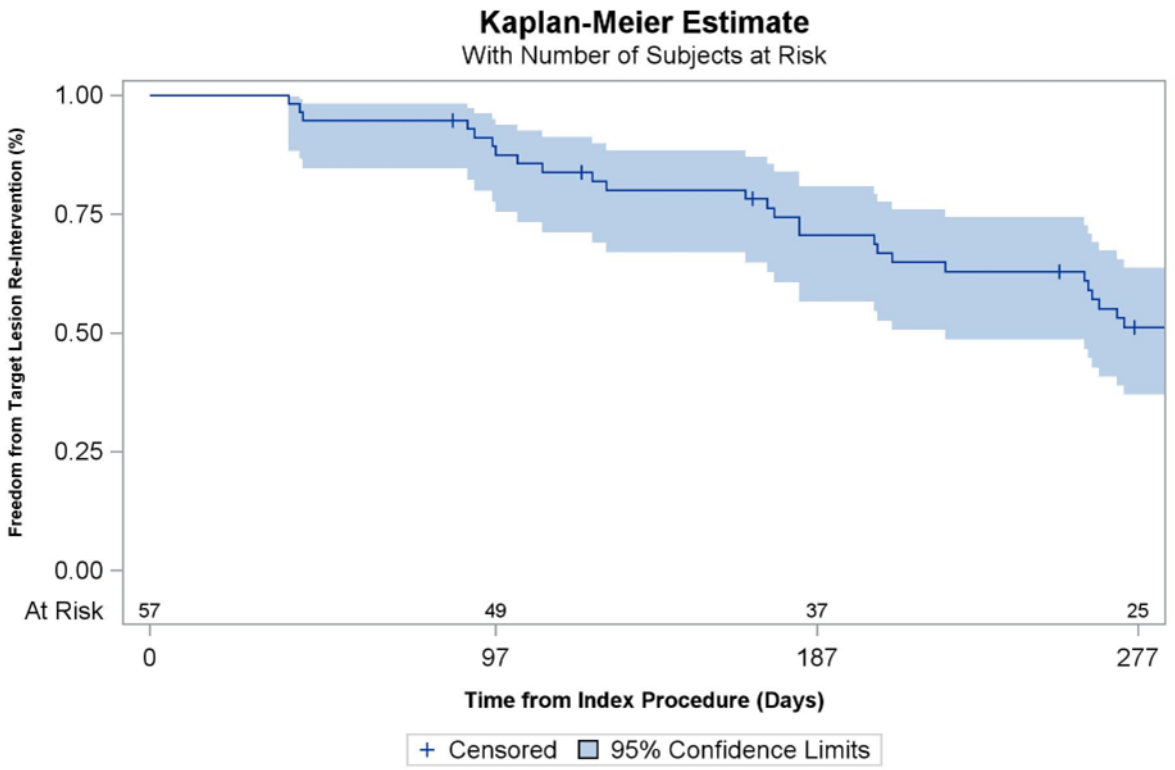
[1] Rajan D., et al., Dysfunctional Autogenous Hemodialysis Fistulas: Outcomes after Angioplasty – Are There Clinical Predictors of Patency? Radiology. Sept 2004.
[2] Liao M-T, Chen M-K, Hsieh M-Y, Yeh N-L, Chien K-L, Lin C-C, et al. Drug-coated balloon versus conventional balloon angioplasty of hemodialysis arteriovenous fistula or graft: A systematic review and meta-analysis of randomized controlled trials. PLOS One; 2020 15(4).
[3] Hu H, Tan Q, Wang J, Liu Y, Yang Y, Zhao J. Drug-coated balloon angioplasty for failing haemodialysis access: meta-analysis of randomized clinical trials. Br J Surg. 2021 Nov 11;108(11):1293-1303.
[4] Ng B, Fugger M, Onakpoya IJ, et al. Covered stents versus balloon angioplasty for failure of arteriovenous access: a systematic review and meta-analysis. BMJ Open 2021;11
[5] Phang, C., et. Al, Paclitaxel-coated balloon in the treatment of recurrent dysfunctional arteriovenous access, real-world experience and longitudinal follow up, Nephology, 24 (2019) 1290-1295.

6-month Functional Patency FLEX + PTA in Cephalic Arch

AVF's

FLEX+ PTA
70.6% (n=57)
Avg. time FF-TLR = ***219.7 days***

Cephalic Arch Lesions
FLEX+ PTA
69.3% (n=23)
Avg. time FF-TLR = ***211.0 days***



Literature Comparisons 6-month Functional Patency after PTA – Cephalic Arch Results

Published Results	FLEX Registry FLEX + PTA	D'Cruz, et al[1,5]	Tng et al.[2]	Vasanthamohanm, et al.[3]	Miller, et al.[4]
6-month Functional Patency Cephalic Arch	**69.3%** (n=23) Avg time to TLR = 211	23%* (n=224) *Pooled multi-studies (0-70.8%)	51.6% (n=62)	8%-42%* (n=11-25) * multi-studies small sample sizes	27% (n=50)* * Historical controls

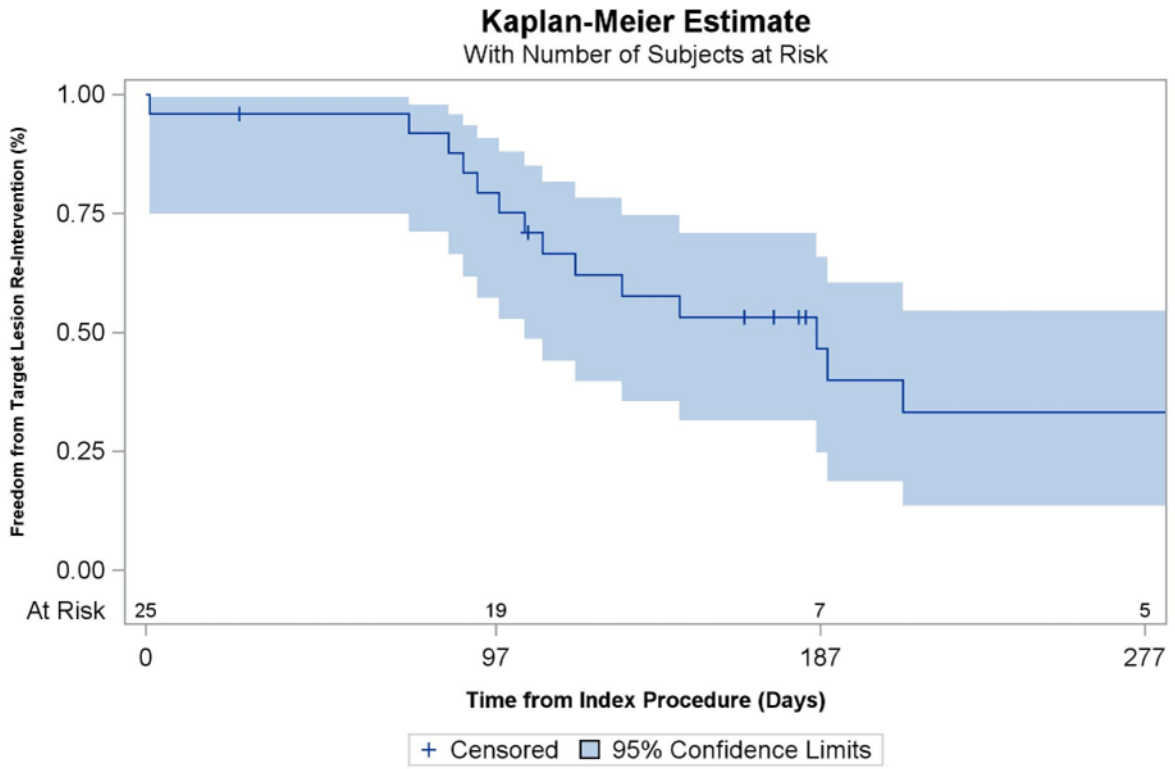
Note: Articles selected that best represented the real-world population for cohort.

[1] D'Cruz RT, Leong SW, Syn N, et al. Endovascular treatment of cephalic arch stenosis in brachiocephalic arteriovenous fistulas: a systematic review and meta-analysis. J Vasc Access 2019; 20: 345.
[2] Tng RK, et al., Treatment of cephalic arch stenosis in dysfunctional arteriovenous fistulas with paclitaxel-coated versus conventional balloon angioplasty, CVIR Endovascular, (2021) f:80.
[3] Vasanthamohanm, L., et al. The Management of Cephalic Arch Stenosis in Arteriovenous Fistulas for Hemodialysis: A Systematic ReviewCardiovasc Intervent Radiol (2015) 38:1179–1185
[4] Miller GA, Preddie DC, Savransky Y, Spergel LM. Use of the Viabahn stent graft for the treatment of recurrent cephalic arch stenosis in hemodialysis accesses. J Vasc Surg. 2018.
[5] Beathard et al., End Points for Interventional Studies for AV Access,Clin J Am Soc Nephrol 13: 501–512, March 2018.

6-month Functional Patency
FLEX + PTA in AVG

AVG's

FLEX+ PTA
46.6% (n=25)
Avg. time FF-TLR = ***173.9 days***



Literature Comparisons 6-month Functional Patency after PTA – AVG Results

Published Results for PTA of AVGs	FLEX Registry FLEX + PTA	Vesely, et al[1]	Haskel, et al [2]	Yang, et al[3]	Liao, et al.[4]	Ng, et al.[5]	Phang, et al.[6]
6-month Functional Patency AVG	**46.6%** (n=25)	34% (n=148)	23% (n=86)	28% (n=49)	9% (n=22)	8% – 34.2%* (N=293) *Meta-analysis of RCTs of covered stents – AVGs	5.7% (n=53)

Note: Articles selected that best represented the real-world population for cohort.

[1] Vesely T, DaVanzo W, Behrend T, et al. Balloon angioplasty versus Viabahn stent graft for treatment of failing or thrombosed prosthetic hemodialysis grafts. J Vasc Surg. 2016;64:1400-1410.e1.4

[2] Haskel, Z., et al. Stent Graft versus Balloon Angioplasty for Failing Dialysis-Access Grafts N Engl J Med 2010;362:494-503.

[3] Yang HT, Yu SY, Su TW, Kao TC, Hsieh HC, Ko PJ. A prospective randomized study of stent graft placement after balloon angioplasty versus balloon angioplasty alone for the treatment of hemodialysis patients with prosthetic graft outflow stenosis. J Vasc Surg. 2018 Aug;68(2):546-553.

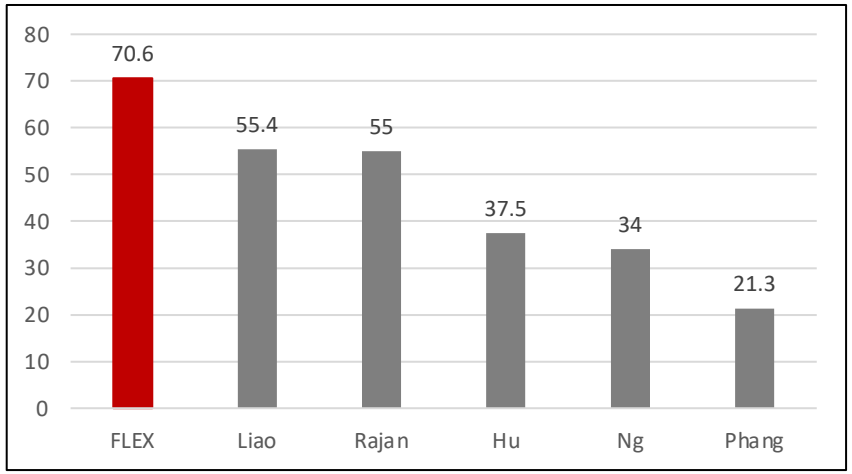
[4] Liao M-T, Chen M-K, Hsieh M-Y, Yeh N-L, Chien K-L, Lin C-C, et al. Drug-coated balloon versus conventional balloon angioplasty of hemodialysis arteriovenous fistula or graft: A systematic review and meta-analysis of randomized controlled trials. PLOS One; 2020 15(4).

[5] Ng B, Fugger M, Onakpoya IJ, *et al*. Covered stents versus balloon angioplasty for failure of arteriovenous access: a systematic review and meta-analysis. *BMJ Open* 2021;11

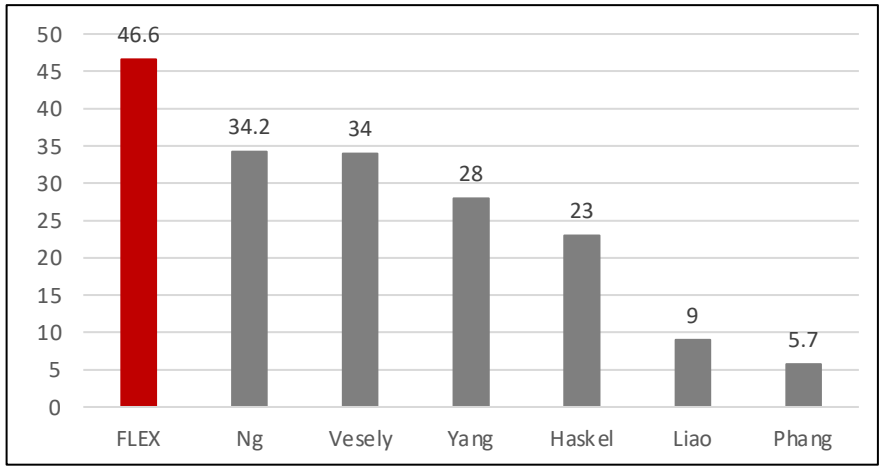
[6] Phang, C., et al., Paclitaxel-coated balloon in the treatment of recurrent dysfunctional arteriovenous access, real-world experience and longitudinal follow up, Nephology, 24 (2019) 1290-1295.

Published Results vs FLEX Registry
6-month Functional Patency

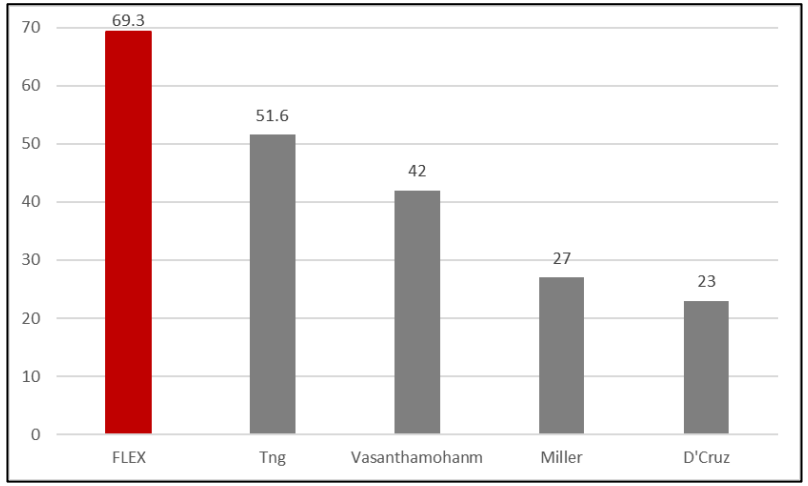
Published Results vs FLEX + PTA for AVF



Published Results vs FLEX + PTA for AVG



Published Results vs FLEX + PTA for Cephalic Arch



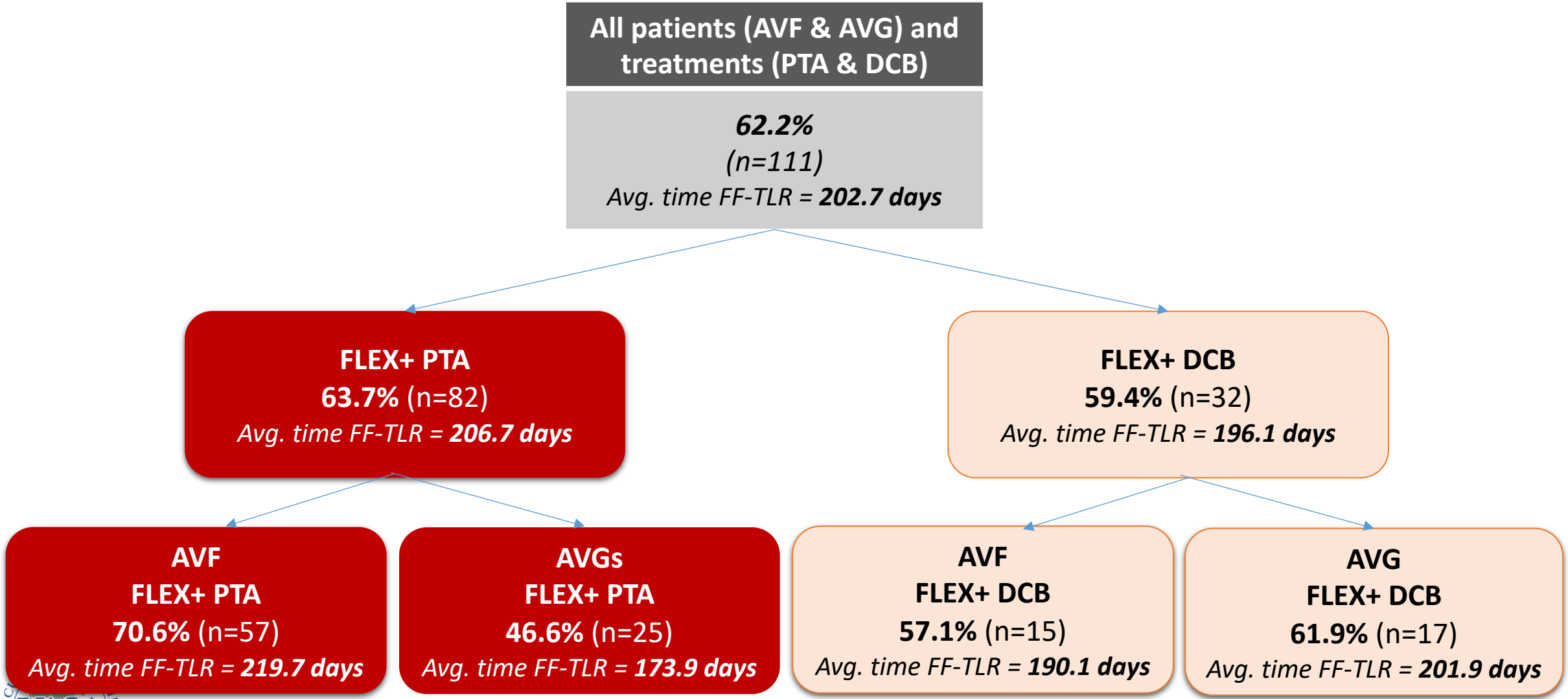
Procedure Complications Reported

- **No Serious Adverse Events**
- 4.3% Minor Procedure Complications

Classification	Reported Complication	Number	Reported Cause	Treatment	%	JVIR Quality Improvement Guideline[1] Thresholds
Major	None	0	N/A	N/A	0%	2% (AVF) 7% (AVG)
Minor	Dissection, Grade B,C	4	Angioplasty	1 – No treatment 3 – Balloon inflation	4.3%	8% (AVF) 4% (AVG)
	Balloon burst	1	Balloon Rupture	Embolectomy		

[1] Daruiushnia, S. et al. Quality Improvement Guidelines for Percutaneous Image-Guided Management of the Thrombosed or Dysfunctional Dialysis Circuit, J Vasc Interv Radiol 2016;27:1518–1530

6-month Functional Primary Patency Analysis
FLEX + PTA vs FLEX + DCB



Conclusions

- The FLEX AV Registry 6-month outcomes demonstrate sustained patency across most patients and impressive results specifically in the **Cephalic Arch and AV Grafts**.
- Result highlights PTA only:
  - 71% patency for all AVF patients
  - 69% patency for Cephalic arch lesions
  - 47% patency for all AVG patients (as compared with other published data of 23%, 28%, 34% respectively)
  - AVG Days, Freedom from TLR
    - All patients 203
    - All (AVF & AVGs) Flex + PTA 207
    - All AVF, FLEX + PTA 220
    - All CA + PTA 211
    - All AVG, Flex + PTA 174
  - Lower PTA max inflation pressures 15.2 ATM
  - No observed SAEs (only acute observations)

Implications from FLEX AV Registry Results

The FLEX Vessel Prep System may

- Maximize HP-PTA outcome
  - Offer superior solution to AVF and AVG treated with stand alone HP PTA
- Offer an attractive alternative to DCB for AV access repair
  - FLEX + PTA exhibits similar patency as PTA + DCB
  - Likely impressive implication of product cost and access center throughput
- Offer safer procedure than stand alone HP-PTA (n=114 lesion treatment with no adverse events)
- Introduce a better solution to treat cephalic arches
- In AVG – FLEX + HP-PTA yields better results than historic HP-PTA alone

Indications For Use

The FLEX Vessel Prep™ System is indicated for use with percutaneous transluminal angioplasty (PTA) catheters to facilitate dilation of stenoses in the femoral and popliteal arteries and treatment of obstructive lesions of native or synthetic arteriovenous dialysis fistulae. The device is also indicated for treatment of in-stent restenosis of balloon expandable and self-expanding stents in the peripheral vasculature.