AVeNEW Trial: 12-Month Update

Bart Dolmatch, MD FSIR
(on behalf of the AVeNEW Investigators)

Disclosure

Bart Dolmatch MD FSIR:

.....

I have the following potential conflicts of interest to report:

- [x] 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

Objective

To compare Covera™ Vascular Covered Stent to PTA for treating stenotic lesions in upper extremity AV fistulae (AVF's)

- **Prospective, Multicenter, Randomized**
  - 280 patients
  - 1:1 randomization of PTA vs PTA/Covera™
  - 24 International Sites
- **Follow-up**
  - Primary safety end-point at 30 days
  - Primary efficacy end-point at 6-month
  - 12-month data presented today
  - Ongoing through 3 years

AVeNEW: 24 Study Centers

U.S.

Investigator	Site Name	State
Robert Mendes	N Carolina Heart & Vascular Res.	NC
John Aruny	Yale University	CT
Vaqar Ali	First Coast Cardiovascular Inst.	FL
Pablo Pergola	Clinical Advancement Center	TX
Erin Moore	River City Clinical Research	FL
Himanshu Shah	Indiana University	IN
Dominic Yee	Radiology Imaging Associates	CO
Wang Teng	Alliance Research Centers	CA
Randy Cooper	Southwest Clinical Research	AZ
Saravanan Balamuthusamy	Tarrant Vascular Clinic	TX
George Lipkowitz	Kidney Care & Transplant Serv.	MA
Theodore Saad	Nephrology Associates	DE
Jonah Licht	Providence Interventional Assoc.	RI
Angelo Makris	Chicago Access Care	IL
Tim Rogers	Discovery Medical Research	FL
Jeffery Hoggard	North Carolina Nephrology	NC

Europe, Australia, New Zealand

Investigator	Site Name	Country
Stewart Hawkins	Middlemore Clinical Trials	NZ
Ewan Macaulay	Royal Adelaide Hospital	AUS
Ian Spark	Southern Adelaide Local Health Network	AUS
Rick De Graaff	Maastricht Univers Medisch	NL
Hannes Deutschmann	LKH-Univ. Klinikum Graz	AT
Ralph Kickuth	Universitätsklinikum Würzburg	DE
Geert Maleux	University Hospitals Leuven	BE
Thomas Pfammatter	Universität Zürich	CH

AVeNEW Study Criteria

Key Inclusion Criteria

- Upper extremity AV fistula
- ≥ 1 successful dialysis session
- Angiographic stenosis ≥ 50%
- Clinical or hemodynamic fistula dysfunction in the venous outflow circuit
- Target lesion(s): ≤ 9 cm in length
- Vessel diameter: 5.0 - 9.0mm

Key Exclusion Criteria

- Lesion across elbow, in cannulation zone, within a stent, or in a thoracic central vein

Study Device: COVERA™ Vascular Covered Stent

Flared & Straight Covered-Stent configurations

- ePTFE encapsulated nitinol stent
- Diameters: 6-10 mm
- Lengths: 40, 60, 80, and 100 mm (30 mm straight only)

Thumbwheel Delivery System:

- Sheath compatibility: 8-9 F
- Working length: 80 & 120 cm
- 0.035” over-the-wire system with atraumatic tip

U.S. Indication (FDA Approved): for use in hemodialysis patients to treat stenoses in the venous outflow of an arterio-venous (AV) fistula and at the venous anastomosis of an ePTFE or other synthetic AV graft.

EU Indication: for the treatment of stenoses in the upper extremity venous outflow of patients dialyzing with an arterio-venous (AV) access graft or fistula.

Patient Demographics

	Covered Stent Group	PTA Group	p-value
Number of Patients (ITT), N	142	138	
Mean Age, years ± SD	63 ± 13.2	62 ± 11.5	0.70
Male/Female, %/%	62.7/37.3	60.9/39.1	0.76
Race, % (n)			0.08
Caucasian	70.4 (100)	66.7 (92)	
African American	25.4 (36)	26.1 (36)	
Mean BMI, kg/m^2 ± SD	30.8 ± 6.3	28.9 ± 5.8	0.01
Risk Factor, % (n)			0.54
Hypertension	97.9 (139)	96.4 (133)	
Smoker (Current & Former)	43/7 (62)	44.9 (62)	
Diabetes (Type 2)	71.1 (101)	68.1 (94)	
Congestive Heart Failure, % (n)	24.6 (35)	29.0 (40)	0.41
Coronary Artery Disease, % (n)	32.4 (46)	37.7 (52)	0.35
Peripheral Artery Disease, % (n)	16.9 (24)	21.0 (29)	0.38

Circuit/Lesion Characteristics & Procedural Details

	Covered Stent Group	PTA Group
Outflow Vein, % (n)		
Cephalic	73.9 (105)	68.8 (95)
Basilic	24.6 (35)	30.4 (42)
Lesion Location, % (n)		
Cephalic Arch	54.9 (78)	50.7 (70)
Cephalic Vein Outflow	17.6 (25)	17.4 (24)
Basilic Vein Swing Point & Outflow	20.4 (29)	23.9 (33)
Mean Lesion Length, mm ± SD	28.8 ± 17.4	29.7 ± 17.0
Flared/Straight Stent Graft Configuration, %/%	46.1/53.9	na
Final Mean Residual Stenosis, % ± SD	2.2 ± 5.8	15.0 ± 18.0
Dialysis Resumed at 30 Days, % (n)	96.5 (137)	97.8 (135)
Acute Technical Success[1]	100%	na
Acute Procedural Success[2]	98.6%	98.4%

[1]Successful deployment to the intended location

[2]Anatomic success (residual stenosis ≤ 30%) and resolution of the pre-procedure clinical indicators of stenosis

Primary Endpoints

Freedom from a Primary Safety Event (30 days)*

Covered Stent Group	PTA Group	Difference [90% CI]	p-value[1]
95.0% (133/140)	96.4% (132/137)	-1.4% [-7.3%, 4.6%]	0.002

Safety with COVERA was *non-inferior* to PTA

*Binary/proportional Analysis

Target Lesion Primary Patency (TLPP) at 6 months^

Covered Stent Group [95% CI]	PTA Group [95% CI]	Hazard Ratio [95% CI]	p-value[2]
78.7% [70.8%, 84.7%]	47.9% [38.7%, 56.6%]	0.322 [0.213, 0.519]	<0.001

TLPP with COVERA was *superior* to PTA

^ Kaplan-Meier Analysis

[1] Farrington Manning non-inferiority test

[2] One-sided p-value calculated using the log-rank test

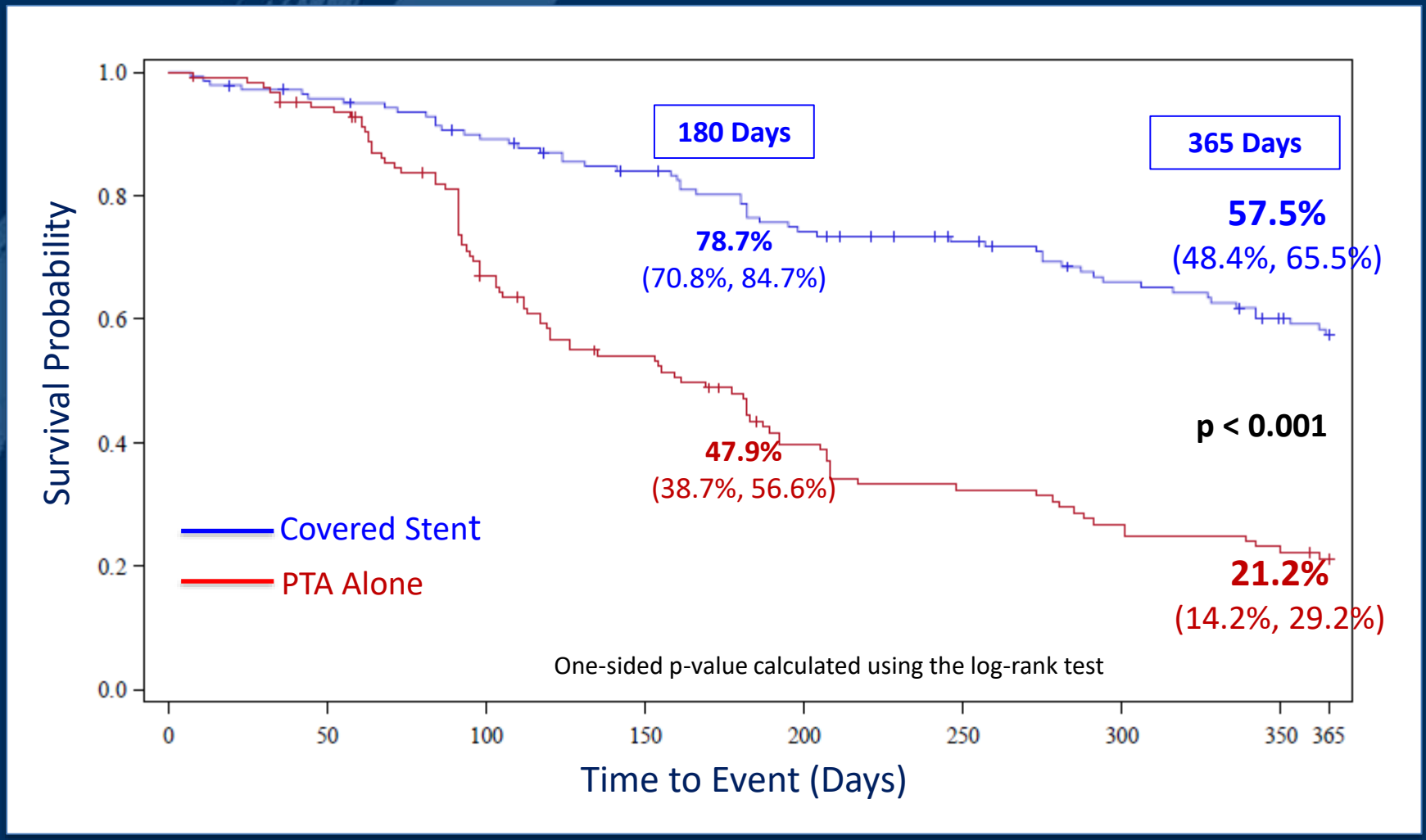
12-Month Outcomes

Outcomes	Covered Stent Group	PTA Group	Difference
Target Lesion Primary Patency (TLPP) (proportional analysis), (n/N)	55.6%	20.2%	35.5%
Target Lesion IPF (IPF-T) [1], days ± SD	259.8 ± 115.4	160.6 ± 87.3	99.1 ± 13.4

Follow-up at 12 Months: 83.9% (235/280 patients)

[1] IPF-T: Index of Patency – Target Lesion; the time from the initial study procedure to study completion or access abandonment divided by the number of reinterventions at the target lesion to maintain vascular access.

Freedom from Loss of TLPP (through 365 Days)

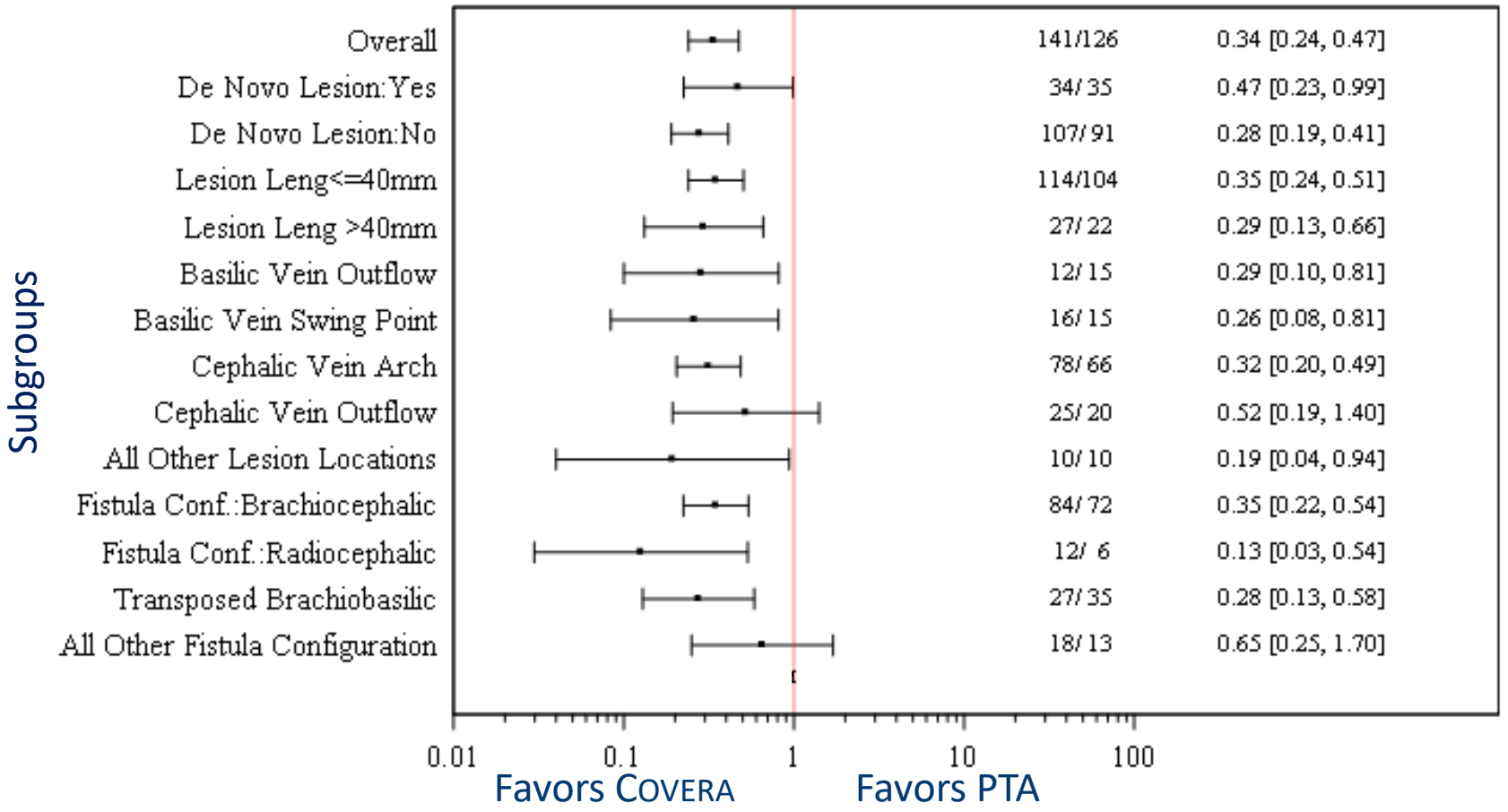


Rates are estimated using the Kaplan-Meier method, and the 95% confidence intervals are estimated using Greenwood's formula

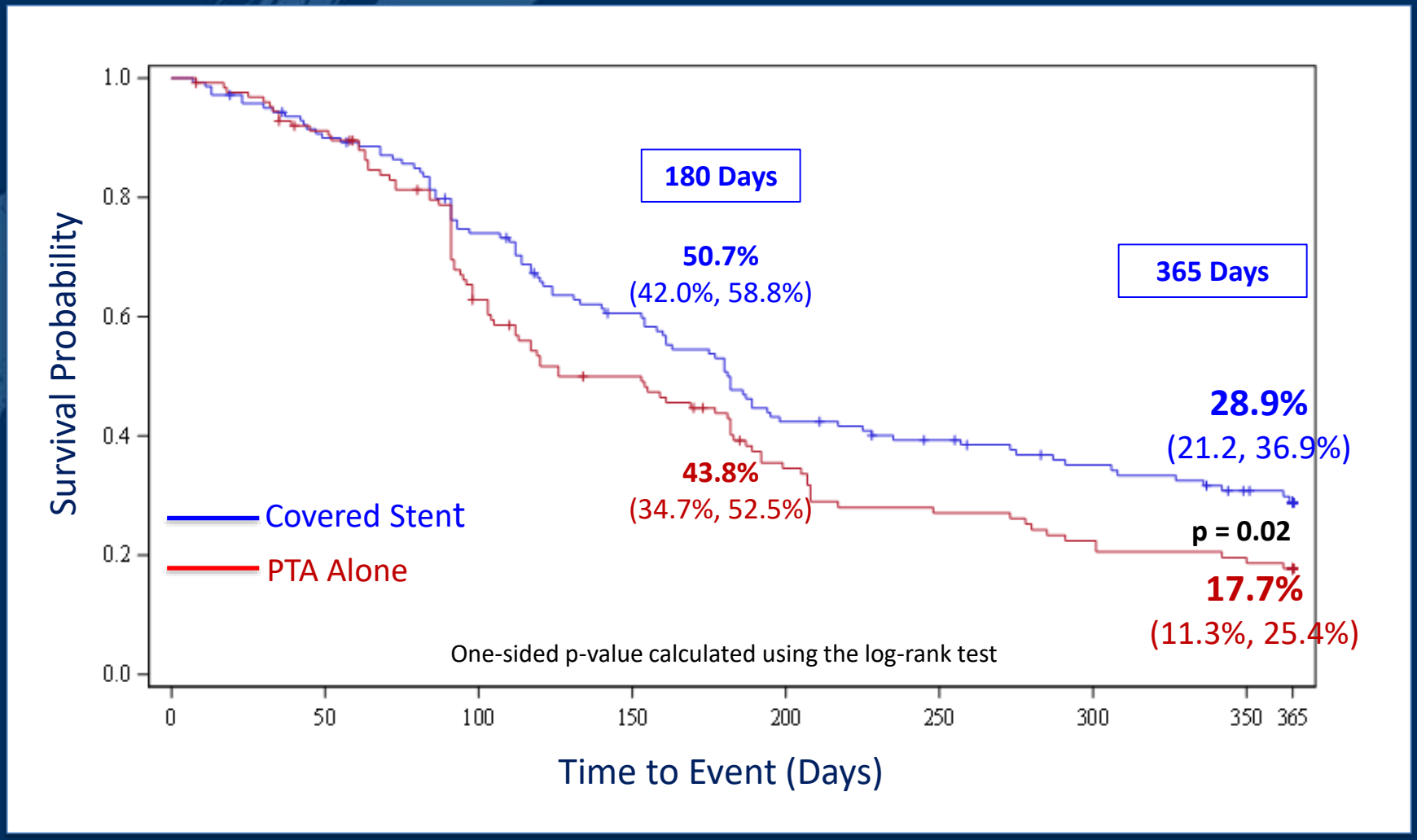
12-Month Exploratory Subgroup Analysis

TLPP by Lesion Characteristics

(Forest Plot Hazard Ratio)



Freedom from Loss of ACPP (through 12 months)

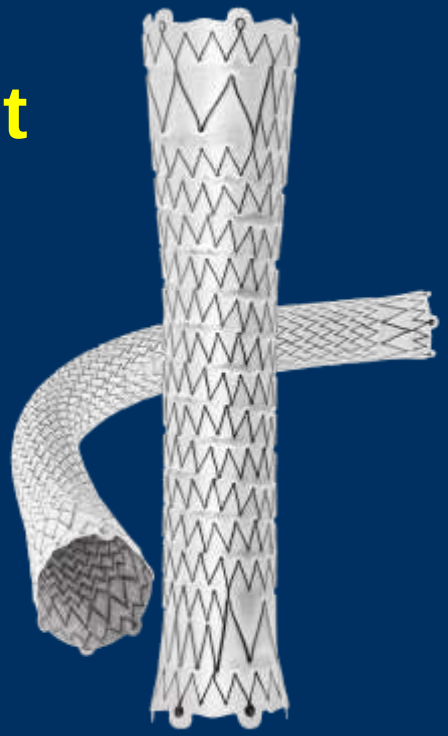


Rates are estimated using the Kaplan-Meier method, and the 95% confidence intervals are estimated using Greenwood's formula

AVeNEW Summary

This is the first study of its type and size that prospectively compared outcomes using a covered stent versus PTA to treat AV fistula stenosis.

At 12 months, target lesion and circuit patency were superior for the covered stent group.



AVeNEW Trial follow-up is ongoing through 3 years

AVeNEW Trial: 12-Month Update

Bart Dolmatch, MD FSIR
(on behalf of the AVeNEW Investigators)