“First Look” at Data from the AVeVA Study

Prospective, Multi-Center Study of an **A**rterio**v**enous (AV) Covered Stent to Treat Stenos**e**s at the **V**enous **A**nastomosis of AV Graft Access Circuits

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Disclosure

Bart Dolmatch:

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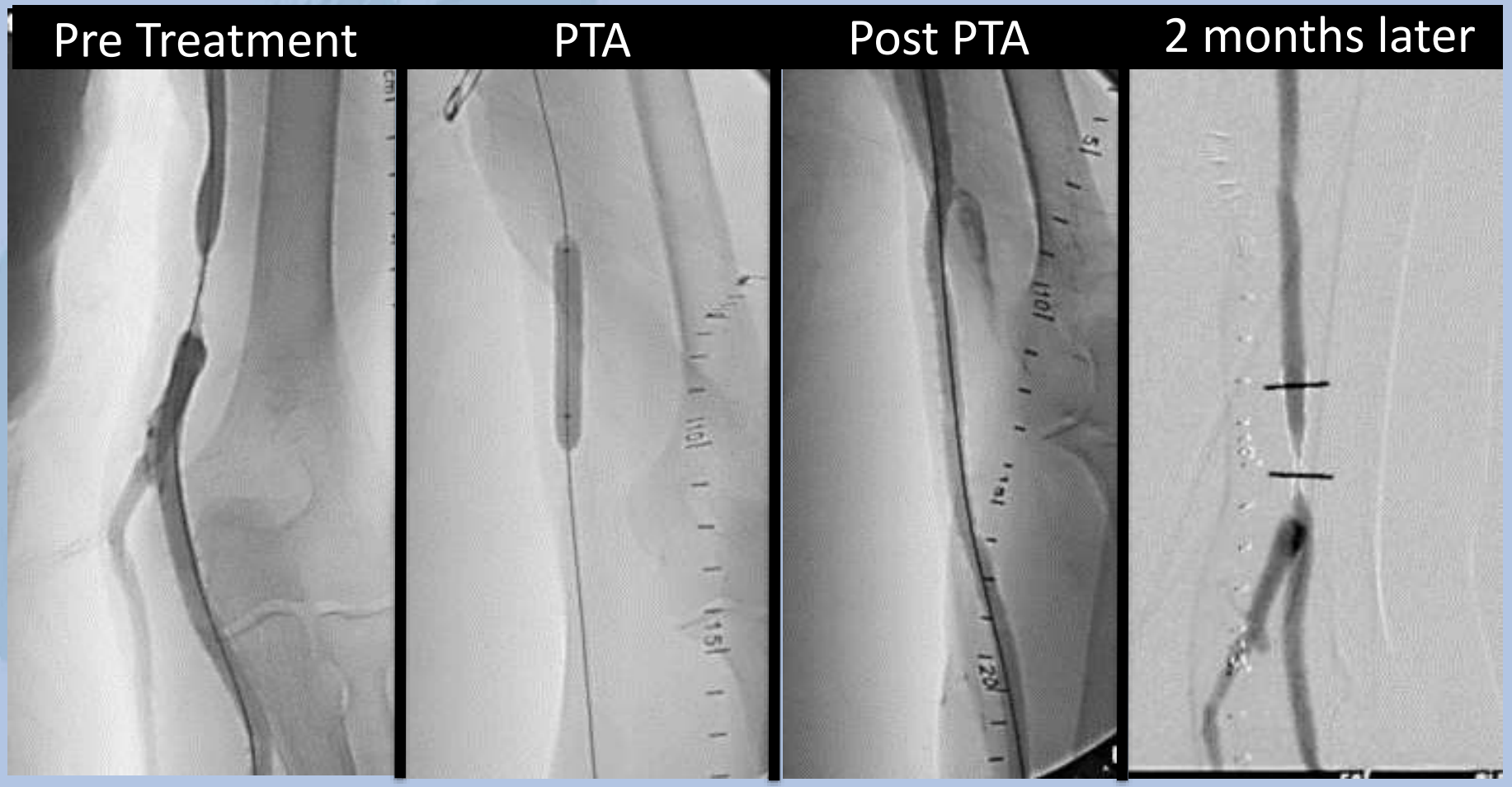
I have the following potential conflicts of interest to report:

- [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

Most AVG Failures = Stenosis at graft-to-vein anastomosis
Post PTA recurrence of this stenosis is common



Study Device: COVERA™ Vascular Covered Stent

ePTFE covered, helical, nitinol stent:

Straight and **Flared** configurations

Flared

Flared: 3mm larger in diameter over the last 15mm of the distal end.

Straight

Study Device:

- Radiopaque tantalum markers on both ends
- Diameters: 6-10 mm
- Lengths: 30 (straight only), 40, 60, 80, and 100 mm

Triaxial Delivery System:

- 8-9 F compatible
- 0.035” over-the-wire
- 80 & 120 cm working lengths

Design:

- Prospective, Multicenter, Non-Randomized:
- 110 Patients enrolled and treated
- 14 Investigative centers (USA)

Objectives: Treat stenotic lesions at the graft-vein anastomosis of **AV grafts** with the COVERA™ Vascular Covered Stent and assess safety and patency

Analyses:

- Clinical Events Committee (CEC) adjudicated safety events
- Endpoints measured against Performance Goals
- 6 mo. Data presented today, ongoing through 2 yrs

Demographics & Lesion Characteristics

	Covered Stent Group
Number of Patients	110
Mean Age, years ± SD	64.3 ± 14.0
Male/Female, %	45.5/54.5
Mean BMI, kg/m^2 ± SD	28.7 ± 6.6
Risk Factor, % (n)	
Hypertension	98.2 (108)
Smoker	39.1 (43)
Diabetes (Type 2)	61.8 (68)
Lesion Type (Restenotic), % (n)	71.8 (79)
Mean Lesion Length, mm ± SD	24.1 ± 15.3
Mean Baseline Target Lesion Stenosis, % ± SD	71.5 ± 14.8
Thrombosis at Baseline, % (n)	25.5 (28)
Outflow Vein Diameter, mm ± SD	8.5 ± 2.0
Graft Diameter, mm ± SD	6.8 ± 0.7

Key Endpoints & Definitions

Safety through 30 days: Freedom from any protocol-defined safety event in the AV access circuit (not including stenosis or thrombosis)

✓ Control: Performance Goal (PG) of 88% derived from the literature

Target Lesion Primary Patency (TLPP) at 6 months: Time from the study procedure until the next clinically-driven re-intervention at the treatment site, thrombotic occlusion, surgery, or permanent access abandonment

✓ Control: PG of 40% derived from the literature & pivotal studies

Secondary Endpoints include:

- Technical Success & Procedural Successful
- Access Circuit Primary Patency: Time until the next access thrombosis or clinically-driven repeated intervention anywhere in the access circuit
- Index of Patency Function: Time to study completion or access abandonment divided by the number of reinterventions to maintain vascular access

Procedural Observations

	Covered Stent Group
Upper Arm Access Site, % (n)	98.2 (108)
Flared Stent Graft Configuration, % (n)	83.6 (92)
Most Used Covered Stent Diameters, % (n)	
8 mm	56.4 (62)
9 mm	30.0 (33)
Most Used Covered Stent Lengths, % (n)	
40 mm	49.1 (54)
60 mm	42.7 (47)
Mean Residual Stenosis after Stent Graft Post-Dilation, % $\pm$ SD	0.9 $\pm$ 2.8
Peri-procedural Complications, % (n)	7.3 (8)
Dialysis Resumed for $\geq$ 1 Session after Procedure, % (n)	98.2 (108)
Acute Technical Success, % (n)	100 (110)
Acute Procedural Success, % (n)	100 (110)

Primary Endpoint Analyses

Safety (30 Days): **Freedom from a Primary Safety Event**

Primary Safety Endpoint **(Proportional Analysis)**	Covered Stent Group (N= 110)	(90% CI) p-value
Freedom from a Primary Safety Event through 30 days, (n/N)	**96.4%** (106/110)	(91.9, 98.7) p=0.002

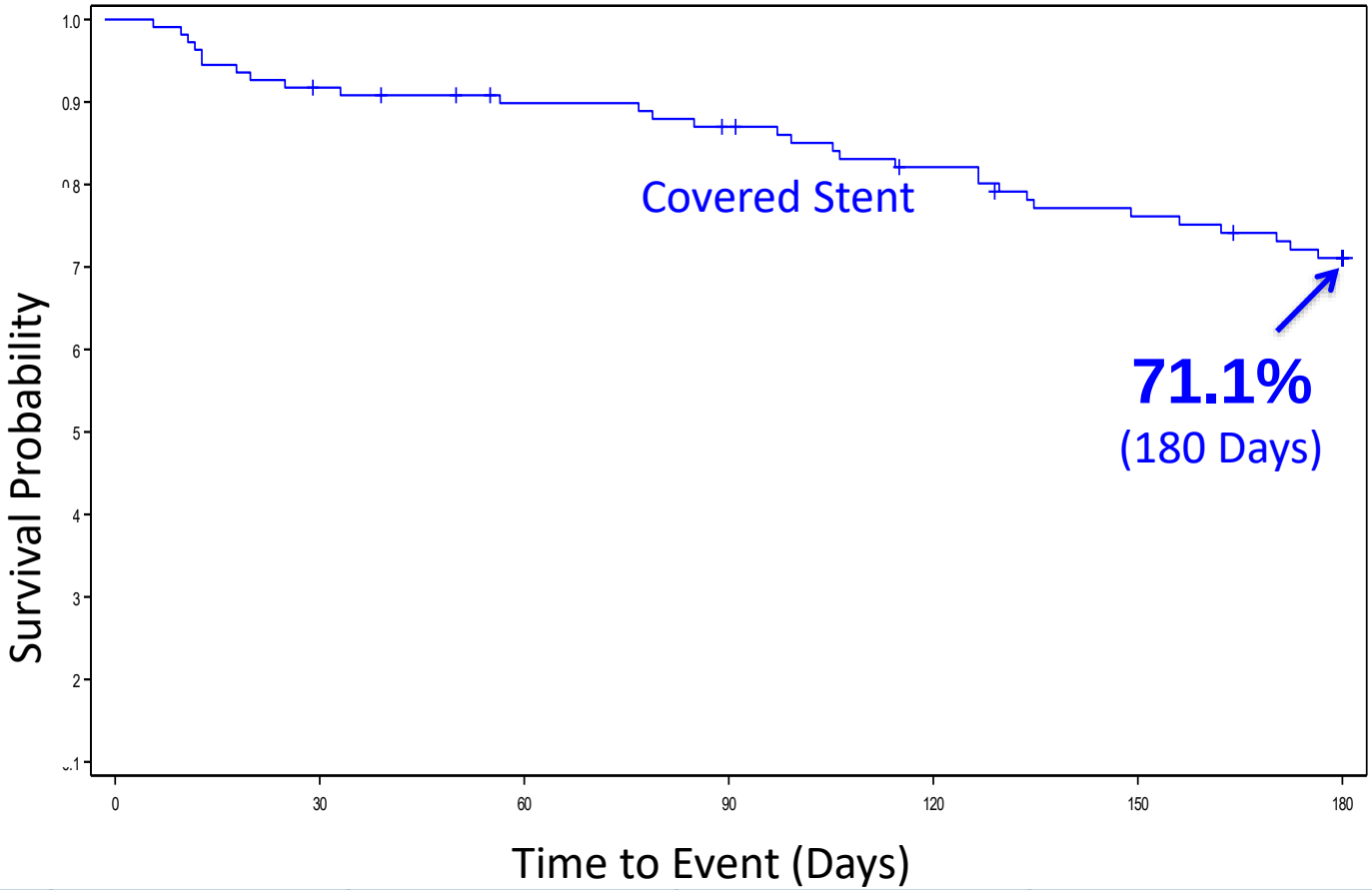
✓ Superior to the PG of 88% (p-value = 0.002)

Efficacy (6 Months): Target Lesion Primary Patency (TLPP)

Primary Efficacy Endpoint **(Proportional Analysis)**	Covered Stent Group	(90% CI) p-value
TLPP through 6 Months, (n/N)	**70.3%** (71/101)	(61.9, 77.7) P<0.0001

✓ Superior to the PG of 40% (p-value <0.0001)

Freedom from Loss of TLPP (K-M Analysis*)



Time	Subjects at Risk	Subjects Censored	Subjects with Primary Safety Event	Estimated Primary Safety Survival Rate (95% CI)
30 Days	99	1	9	**91.7%** (84.7%, 95.6%)
90 Days	90	5	14	**87.0%** (79.0%, 92.1%)
180 Days	0	79	30	**71.1%** (61.3%, 78.8%)

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

Secondary Outcomes

6-Month Outcomes	Covered Stent Group	(95% CI)
Access Circuit Primary Patency (ACPP), (n/N)[+]	39.2% (40/102)	(29.7%, 49.4%)
Kaplan-Meier Estimate of ACPP[~]	40.4%	(30.9%, 49.8%)
# of Access Circuit Reinterventions, $\mu \pm SD$	1.05 ± 1.14	
# of Target Lesion Reinterventions, $\mu \pm SD$	0.41 ± 0.73	
Secondary Patency, (n/N)[^]	91.1% (92/101)	

[+] Time until the next access thrombosis or clinically-driven repeat intervention in the access circuit

[~] Survival analysis of ACPP – rates are estimated using the Kaplan-Meier method, and the 95% confidence intervals are estimated using Greenwood's formula

[^] Time until the access is abandoned. Multiple repetitive treatments can be included in secondary patency

Exploratory Subgroup Analysis

Observation: Patients with **thrombosis** had lower TLPP rates than patients without thrombosis

Subgroup	TLPP n/N (%)	95% CI (%)	Exploratory p-value[+]
Presence of Thrombus at Index Procedure?			
Yes	11/23 (47.8)	(26.8, 69.4)	0.0093
No	60/78 (76.9)	(66.0, 85.7)	
Presence of Thrombus at and /or within 30 days of Index Procedure?			
Yes	15/28 (53.6)	(33.9, 72.5)	0.0254
No	56/73 (76.7)	(65.4, 85.8)	

[+]The p-value is exploratory only, and calculated using the chi-squared test

AVeVA "First-Look" Summary

Primary Outcomes:

94.6% Freedom from a Primary Safety Event (30 days): (PG of 88%)

70.3% 6- Month TLPP rate (primary efficacy endpoint): (PG of 40%)

Secondary Outcomes through 6 Months

100% Acute technical and procedural success rates

39.2% : (40.2% K-M Analysis) 6-Month ACPP rate

Target Lesion Intervention Rate: 0.41 (6 months)

Access Circuit Intervention Rate: 1.05 (6 months)

91.1% Secondary Acess Circuit Patency (6 months)

Follow up in the AVeVA Trial is ongoing through 2 years

AVeNEW Study Overview: **A**rterio**ven**ous (AV) Stent Graft vs. PTA alone in the Treatment of Stenoses in the V**e**nous Outflo**w** of AV Fistula Access Circuits

AVeNEW Study Design

Design:

- Prospective, International Multicenter, Randomized Study
- 280 AVF patients at 35 Investigative Sites: USA, Europe, Australia, and New Zealand

Objective: Compare the COVERA™ Vascular Covered Stent to PTA (1:1 randomization) for the treatment of stenotic lesions in the venous outflow tract of upper extremity, autogenous fistula access circuits.

Primary Endpoints:

- 30-Day Freedom from Safety Events
- 6-Month Target-Lesion Primary Patency (TLPP) and

Secondary Endpoints: 12-month TLPP & 6-month Access Circuit Primary Patency (ACPP)

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