Six-month safety and efficacy outcomes from the WRAPSODY® Arteriovenous Access Efficacy (WAVE) trial

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Disclosures

- Consultancy for Merit Medical

General Background

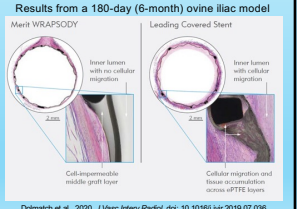
- Inability to maintain long-term vascular access in hemodialysis patients directly correlate to mortality and vascular access dysfunction[1]
- Venous outflow circuit stenosis is one of the most common causes of vascular access dysfunction in hemodialysis patients
- Percutaneous transluminal angioplasty (PTA) is a common initial intervention; however, treatment durability is poor
- Covered stents have improved target lesion primary patency (TLPP), but access circuit primary patency (ACPP) has not been significantly improved

[1]Lawson, et al. 2020. *Nat Rev Nephrol.* doi:10.1038/s41581-020-0333-2

The Unique Characteristics of the WRAPSODY Cell-Impermeable Endoprosthesis

Middle cell-impermeable layer engineered to prevent transmural cellular migration without the need for drug bonding

Results from a 180-day (6-month) ovine iliac model



Dolmatch et al., 2020. *J Vasc Interv Radiol.* doi: 10.1016/j.jvir.2019.07.036

WRAPSODY First-in-Human Study

- In 2021, clinical outcomes were published from a first-in-human study[2] of WRAPSODY to treat venous outflow stenosis in arteriovenous fistula/graft (AVF/AVG)
- Results demonstrated that WRAPSODY has an acceptable safety profile and is associated with high TLPP and ACPP
- The WAVE study is a pivotal trial designed to expand on the first-in-human results to confirm the clinical benefits for patients with stenosis in their venous outflow circuit

[2]Gilbert et al., 2021. *Cardiovasc Intervent Radiol.* doi:10.1007/s00270-021-02953-8

WAVE Study Design Overview

- Prospective, multicenter study conducted across 43 international centers
- Two arm study
  - **AVF Peripheral arm**: patients with AVF randomized 1:1 to treatment with WRAPSODY or PTA
  - **AVG Anastomosis arm**: single arm cohort, patients with AVG compared to safety and efficacy performance goals from prior published studies
- Patients could have up to one non-target outflow lesion requiring intervention if it was at least 10 cm from target lesion
- Non-target lesion could only be treated with standard PTA
- Study is on-going; follow-up data collected at 6, 12, 24 months following index procedure

Trial registration number: NCT04540302

Study Endpoints

Primary Safety Endpoint: Proportion of patients without a local or systemic safety event† 30 days post-intervention	†Affecting the access or venous outflow circuit and resulted in reintervention, hospitalization, or death (not including stenosis or thrombosis)
Primary Efficacy Endpoint: 6-month target lesion primary patency (TLPP)‡	TLPP: freedom from clinically-driven target lesion revascularization or thrombosis ‡Target lesion restenosis included the adjacent 5mm on either side of the treated vessel segment, as adjudicated by core laboratory[a,b]
Secondary Efficacy Endpoint of Interest: 6-month access circuit primary patency (ACPP)	Time to loss of primary patency of the entire access circuit, specifically, the time from the index procedure to any venous outflow circuit re-intervention, access thrombosis, or access abandonment

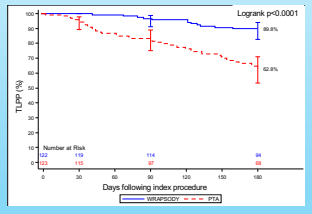
[a]Garcia-Garcia, et al. 2018. *Circulation*. doi:10.1161/CIRCULATIONAHA.117.029289
[b]Dolmatch et al., 2023. *Kidney Int*. doi:10.1016/j.kint.2023.03.015

AVF Peripheral Cohort: Patient Demographics

Characteristic	AVF Peripheral Cohort (N=245) WRAPSODY (N=122)	PTA (N=123)
Demographics		
Mean (±SD) age, years	61.6 ± 13.9	60.1 ± 14.5
Males, no./total no. (%)	70 (57.4)	69 (56.1)
Medication status,* no./total no. (%)		
No medications	52/ 122 (42.6)	56/ 123 (45.5)
Medications[b]	70/ 122 (57.4)	67/ 123 (54.5)
Lesion characteristics		
Arteriovenous fistula location, no./total no. (%)		
Radiocephalic	2 / 122 (1.6)	3 / 121 (2.5)
Brachiocephalic	89 / 122 (73.0)	83 / 121 (68.6)
Brachiobasilic	31 / 122 (25.4)	35 / 121 (28.9)
Target lesion type, no./total no. (%)		
De novo	46 / 122 (37.7)	53 / 123 (43.1)
Restenotic	76 / 122 (62.3)	70 / 123 (56.9)
Core Lab Angiographic data[c]		
Mean length (±SD)	39.8 (± 15.7)	33.8 (± 17.0)
Mean percent diameter stenosis (±SD)	63.6 (± 12.0)	61.5 (± 12.9)
Procedure characteristics		
Total number of non-target lesions	19	18

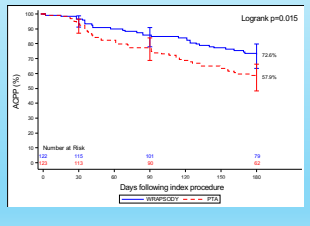
* In accordance with NKF KDOQI patients were administered medication(s) based on discretion of their treating physician, pharmacological intervention was not required for this study.
[b] Patients could be administered more than one medication from baseline throughout the follow-up period.
[c] Based on operator's visual estimate.

AVF Peripheral Cohort 6-Month TLPP



6-month TLPP was significantly higher in patients treated with WRAPSODY versus patients randomized to PTA

AVF Peripheral Cohort 6-Month ACPP



6-month ACPP was significantly higher in patients treated with WRAPSODY versus patients randomized to PTA

AVF Peripheral Cohort Safety Endpoint

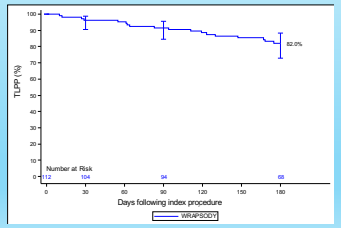
Cohort	Freedom from Localized or Systemic Safety Events	Non-inferiority p-value
WRAPSODY	**96.6%**	**<0.0001**
Standard PTA	**95.0%**	

AVG Anastomosis Cohort: Patient Demographics

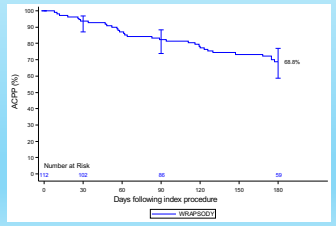
Characteristic	AVG Anastomosis Cohort (N=112)
Demographic	
Mean (±SD) age, years	64.1 ± 13.3
Males, no./total no. (%)	51 / 112 (45.5%)
Medication status,* no./total no. (%)	
No medications	43 / 112 (38.4%)
Medications[b]	69 / 112 (61.6%)
Location of Venous Anastomosis, no./total no. (%)	
Axillary	50 / 112 (44.6%)
Basilic	42 / 112 (37.5%)
Brachial	14 / 112 (12.5%)
Cephalic	4 / 112 (3.6%)
Other[c]	2 / 112 (1.8%)
Location of Arterial Anastomosis, no./total no. (%)	
Axillary	15 / 112 (13.4%)
Brachial	92 / 112 (82.1%)
Unknown	4 / 112 (3.6%)
Target lesion type, no./total no. (%)	
De novo	53 / 113 (46.9%)
Restenotic[d]	60 / 113 (53.1%)
Core Lab Angiographic data*	
Mean length (±SD)	36.5 ± 18.4
Mean percent diameter stenosis (±SD)	64.5 ± 13.8
Total number of non-target lesions	11

* In accordance with NKF KDOQI patients were administered medication(s) based on discretion of their treating physician, pharmacological intervention was not required for this study.
[b] Patients could be administered more than one medication from baseline throughout the follow-up period.
[c] Graft (n=1), HeRO® Graft (n=1)
[d] One patient had more than one target lesion.

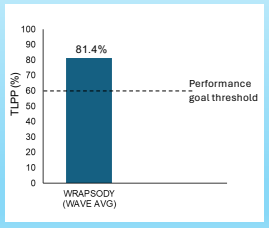
AVG Anastomosis Cohort 6-Month TLPP Kaplan Meier Estimate



AVG Anastomosis Cohort 6-Month ACPP Kaplan Meier Estimate



AVG Anastomosis Cohort 6-Month TLPP Rate



6-month TLPP was higher than the efficacy performance goal of 60% in AVG patients treated with WRAPSODY (p<0.0001)

AVG Anastomosis Cohort: Safety Endpoint

Cohort	Freedom from Localized or Systemic Safety Events	P-value*
WRAPSODY AVG Anastomosis Cohort	**95.4%**	**0.0162**
Safety Performance Goal	**89.0%**	

*One-sided p-value from the exact binomial test compared to the null hypothesis performance goal

Conclusions

- AVF Peripheral Cohort
  - WRAPSODY exhibits superior 6-month TLPP compared to PTA
  - WRAPSODY has significantly higher 6-month ACPP versus PTA
  - The safety profile of WRAPSODY was similar to PTA
- AVG Anastomosis Cohort
  - WRAPSODY demonstrated higher 6-month TLPP relative to the performance goal
  - WRAPSODY exhibited 68.8% ACPP through 6 months
  - Freedom from primary safety events was higher for WRAPSODY as compared to the performance goal
- This 6-month analysis provides insight regarding WRAPSODY's anticipated long-term performance