Medtronic Satellite Symposium

Hemodialysis Access Creation and Maintenance: Implications of Long-term Data on Patient Outcomes

Leipzig Interventional Course 2023
Tuesday 06 June 2023
15:30-16:15 CEST; Main Arena 2
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Overview of Long-term Evidence in AVF Creation and Maintenance

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Director Vascular and Interventional Radiology Department
Careggi University Hospital
Florence, Italy

Case Discussion: EndoAVF Creation from Mapping to Cannulation

Robert Shahverdyan
Head of Vascular Access Center
Asklepios Clinic Barmbek
Hamburg, Germany

Treating Challenging Lesions: My Algorithm for Cephalic Arch Stenosis

Matteo Tozzi
Head of Vascular Surgery
University of Insubria
Varese, Italy
Guidelines-Vascular Access
Eur J Vasc Endovasc Surg (2018) 55, 757-818


Clinical practice guideline on peri- and postoperative care of arteriovenous fistulas and grafts for haemodialysis in adults

KDOQI
KIDNEY DISEASE OUTCOMES QUALITY INITIATIVE
National Kidney Foundation


Spanish Clinical Guidelines on Vascular Access for Haemodialysis
KDOQI and Evidence Timelines for AV Access Management

Guidelines are Helpful, but do not Keep Pace with Evidence

1997 - First set of guidelines
Established importance of placing fistulae in long-term hemodialysis patients

2006 - Second Update
Detailed approach to promoting AVF

2019 - Third Update
Introduction of ESKD “Life-Plan” new targets for AVF/AVG/CVC, management of specific complications

2016
Ellipsys™ vascular access system receives CE Mark

IN.PACT™ Admiral™ drug-coated balloon receives CE Mark\(^1\) for AV Access

2022
IN.PACT AV Access RCT
12-Month data published

IN.PACT AV RCT
3-year data presented

Percutaneous AVF (Ellipsys)
5-year data published

IN.PACT Admiral drug-coated balloon is approved for treatment of obstructive lesions of arteriovenous dialysis fistulae in the European Union. Please consult the approved product labeling and indications for use for your region or country as indicated within the respective product manual.
## Evidence with IN.PACT™ AV Drug-Coated Balloon

Robust Clinical Program with Strong Long-term Safety and Effectiveness Outcomes

### IN.PACT AV DCB - Evidence

<table>
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<th>Timeframe</th>
<th>Summary</th>
<th>Endpoints</th>
<th>Notes</th>
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<td><strong>6 Months</strong></td>
<td>Primary Endpoint Results&lt;sup&gt;a&lt;/sup&gt;</td>
<td>Outcomes by lesion subsets&lt;sup&gt;b&lt;/sup&gt;</td>
<td></td>
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<tr>
<td><strong>1 Year</strong></td>
<td>Primary outcomes&lt;sup&gt;c&lt;/sup&gt;</td>
<td>Outcomes by lesion subsets&lt;sup&gt;d&lt;/sup&gt;</td>
<td>Econmics – Japan/South Korea&lt;sup&gt;f&lt;/sup&gt;</td>
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<td></td>
<td>Outcomes in Japanese Participants&lt;sup&gt;f&lt;/sup&gt;</td>
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<td></td>
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<tr>
<td></td>
<td>Economic Analysis&lt;sup&gt;e&lt;/sup&gt;</td>
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</tr>
<tr>
<td><strong>2 Years</strong></td>
<td>Primary outcomes&lt;sup&gt;h&lt;/sup&gt;</td>
<td>Outcomes by lesion subsets&lt;sup&gt;i&lt;/sup&gt;</td>
<td>Outcomes in Japanese Participants&lt;sup&gt;k&lt;/sup&gt;</td>
</tr>
<tr>
<td></td>
<td>Demographic Subsets&lt;sup&gt;i&lt;/sup&gt;</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>3 Years</strong></td>
<td>Primary outcomes&lt;sup&gt;l&lt;/sup&gt;</td>
<td></td>
<td>Outcomes in Japanese Participants&lt;sup&gt;n&lt;/sup&gt;</td>
</tr>
<tr>
<td></td>
<td>Thrombosis outcomes&lt;sup&gt;m&lt;/sup&gt;</td>
<td>Outcomes by lesion subsets&lt;sup&gt;o&lt;/sup&gt;</td>
<td></td>
</tr>
<tr>
<td><strong>4 Years</strong></td>
<td>Vital Status Update only&lt;sup&gt;o&lt;/sup&gt;</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>5 Years</strong></td>
<td>Vital Status Update only (TBD)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>


<sup>b</sup> Presented by Lookstein R, VIVA 2019.


<sup>d</sup> Presented by Holden A, Charing Cross 2021.


<sup>f</sup> Haruguchi H, et al. Ther Apher Dial. 2023;doi:10.1111/1744-9987.13966


<sup>h</sup> Presented by Holden A, Charing Cross 2021.

<sup>i</sup> Presented by Holden A, CIRSE 2021.

<sup>j</sup> Presented by Lookstein R, VIVA 2021.

<sup>k</sup> Presented by Suemitsu K, JSDA 2021

<sup>l</sup> Presented by Holden A, Charing Cross 2022.

<sup>m</sup> Presented by Misra S on behalf of Lookstein R, SIR 2022

<sup>n</sup> Presented by Suemitsu K, VAIVT 2023.

<sup>o</sup> Presented by Holden A, Charing Cross 2023
Evidence with Ellipsys Vascular Access System

Robust Clinical Program with Strong Long-term Safety and Effectiveness Outcomes

<table>
<thead>
<tr>
<th>Ellipsys Vascular Access System – Evidence</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Feasibility and Pivotal Studies</strong></td>
</tr>
</tbody>
</table>
| Phase II Trial¹  
N= 26                                          |
| US Pivotal Study²  
N= 107                                          |
| **Post Market Studies**                      |
| Paris Registry                                 |
| Inclusion of PTA at T=0⁵  
N= 33                                          |
| 2-Year results⁶  
N= 234                                          |
| Surgical vs pAVF⁷  
pAVF N= 107  
sAVF N= 107                                     |
| Hamburg Registry                               |
| Ellipsys vs. WavelinQ⁸  
pAVF N= 100                                        |
| 2-Year Results³  
N= 105                                          |
| Ellipsys vs surgical (Gracz)⁹  
pAVF N= 89                                         |
| 5-Year Results⁴  
N= 107                                          |
| Eligibility for pAVF¹⁰  
N=524                                          |
| RVC Registry                                   |
| Maturation Study¹¹  
N= 60                                          |

Overview of Long-term Evidence in AVF Creation and Maintenance

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Director Vascular and Interventional Radiology
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Florence, Italy
I have the following potential conflicts of interest to report:

- **Consulting:** Abbott, Ivascular, Medtronic, Cook, WL Gore & Associates, Penumbra, Philips, Volcano, Merit, BD, Zylox Tonbridge

- **Employment in industry**

- **Stockholder of a healthcare company**

- **Owner of a healthcare company**

- **Other(s)**

I do not have any potential conflict of interest
Continuum of Care
End-stage Kidney Disease

Fistula/Circuit Maintenance

Access Creation

Endovascular Treatment
- PTA
- Thrombectomy
- DCB
- BMS
- Covered Stent-Grafts

Surgical Revision or Re-do Operation

Access Abandonment

Irreversible/decreased treatment options
## Comparing EndoAVF with Surgical AVF Creation

<table>
<thead>
<tr>
<th>Procedure Metrics</th>
<th>Surgical AVF</th>
<th>Ellipsys Vascular Access System</th>
</tr>
</thead>
<tbody>
<tr>
<td>Access type</td>
<td>Open surgical incision</td>
<td>Single puncture - venous only&lt;sup&gt;1&lt;/sup&gt;</td>
</tr>
<tr>
<td>AV creation method</td>
<td>Sutured anastomosis</td>
<td>Fused anastomosis by thermal energy&lt;sup&gt;1&lt;/sup&gt;</td>
</tr>
<tr>
<td>Patient eligibility</td>
<td>N/A</td>
<td>45 to 65%&lt;sup&gt;1, 2, 3, 4, 5, 6&lt;/sup&gt;</td>
</tr>
<tr>
<td>Procedure time</td>
<td>30-60 minutes</td>
<td>24 minutes&lt;sup&gt;1&lt;/sup&gt;</td>
</tr>
<tr>
<td>Maturation rate (used for dialysis)</td>
<td>Hemodialysis Fistula Maturation NIH Study: 58% (CKD); 76% (ESKD) at 12 months&lt;sup&gt;7&lt;/sup&gt;</td>
<td>Ellipsys IDE: 88% at 90 days&lt;sup&gt;1&lt;/sup&gt;</td>
</tr>
<tr>
<td>Image guidance required</td>
<td>Open surgery</td>
<td>Ultrasound (no ionizing radiation)&lt;sup&gt;8&lt;/sup&gt;</td>
</tr>
</tbody>
</table>

Note: surgical AVF data from Hemodialysis Fistula Maturation NIH study (3)

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8. Ellipsys Vascular Access System Instructions for Use (IFU). UC202301639 EN
Ellipsys US Pivotal Study – Five-Year Outcomes
Most Fistulas are Being Cannulated; Once Cannulated, Most are Used Long Term

Kaplan-Meier Estimate of Time to First Cannulation

Kaplan-Meier Estimate of Functional Patency

Ellipsys Vascular Access System
Learnings from Post Market Registries

Paris Registry Balloon Dilatation of Anastomosis at T-0¹

• Eliminated 2-day follow up visit
• Decreased early thrombosis rate
• Reduced time to maturation


Maturation for Hemodialysis in RVC Registry²

<table>
<thead>
<tr>
<th>Brachial Artery Flow Volumes mL/min</th>
<th>323 ± 168 to 649 ± 246</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reduced Early Thrombosis</td>
<td>2%</td>
</tr>
<tr>
<td>Reduced Maturation Procedures</td>
<td>0.87 (52/60) per patient</td>
</tr>
</tbody>
</table>

Fistulas created with Ellipsys system show superior maturation rates and similar or better patency rates than surgically created fistulas³,⁴
IN.PACT AV Access Trial – Long-Term Outcomes

Only Randomized Pivotal Trial of a DCB Treating Dysfunctional Arteriovenous Fistulas to Demonstrate Consistent and Sustained Clinical Benefit Through 36 Months

Target Lesion Primary Patency

Access Circuit Primary Patency

Log-rank p < 0.001

IN.PACT AV DCB

PTA

IN.PACT AV Access IDE Study Outcomes Through 36 Months
Target Lesion Primary Patency by AVF Type

Radiocephalic (Forearm)

Brachiocephalic and Brachiobasilic (Upper Arm)

DCB, drug-coated balloon; PTA, percutaneous transluminal angioplasty
### IN.PACT AV Access IDE Study Outcomes Through 36 Months

**Target Lesion Primary Patency by AVF Type**

<table>
<thead>
<tr>
<th>Subgroups (N DCB/N PTA)</th>
<th>IN.PACT AV DCB*</th>
<th>Standard PTA*</th>
<th>Hazard Ratio [95% CI]</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>6 Months</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Forearm (86/80)</td>
<td>84.0% (13)</td>
<td>67.5% (24)</td>
<td>0.433 [0.220, 0.850]</td>
</tr>
<tr>
<td>Upper Arm (79/73)</td>
<td>88.6% (8)</td>
<td>70.8% (20)</td>
<td>0.351 [0.154, 0.796]</td>
</tr>
<tr>
<td><strong>12 Months</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Forearm (86/80)</td>
<td>65.4% (27)</td>
<td>48.9% (37)</td>
<td>0.538 [0.327, 0.884]</td>
</tr>
<tr>
<td>Upper Arm (79/73)</td>
<td>65.6% (22)</td>
<td>46.7% (35)</td>
<td>0.506 [0.297, 0.863]</td>
</tr>
<tr>
<td><strong>24 Months</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Forearm (86/80)</td>
<td>53.3% (35)</td>
<td>42.8% (41)</td>
<td>0.625 [0.398, 0.982]</td>
</tr>
<tr>
<td>Upper Arm (79/73)</td>
<td>49.8% (31)</td>
<td>29.8% (43)</td>
<td>0.548 [0.345, 0.871]</td>
</tr>
<tr>
<td><strong>36 Months</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Forearm (86/80)</td>
<td>44.5% (39)</td>
<td>33.8% (45)</td>
<td>0.639 [0.416, 0.982]</td>
</tr>
<tr>
<td>Upper Arm (79/73)</td>
<td>39.9% (35)</td>
<td>21.3% (45)</td>
<td>0.567 [0.363, 0.883]</td>
</tr>
</tbody>
</table>

DCB, drug-coated balloon; PTA, percutaneous transluminal angioplasty
Numbers are % with Kaplan-Meier estimate (number of patients with an event)
Forearm = radiocephalic fistulas; upper arm = brachiocephalic and brachio basilic fistulas
## IN.PACT AV Access IDE Study Outcomes Through 36 Months

### Target Lesion Primary Patency by Lesion Type

<table>
<thead>
<tr>
<th>Subgroups (N DCB/N PTA)</th>
<th>IN.PACT AV DCB*</th>
<th>Standard PTA*</th>
<th>Hazard Ratio [95% CI]</th>
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</thead>
<tbody>
<tr>
<td><strong>6 Months</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>De Novo (51/49)</td>
<td>93.3% (3)</td>
<td>82.2% (8)</td>
<td>0.367 [0.097, 1.382]</td>
</tr>
<tr>
<td>Restenotic (119/111)</td>
<td>83.8% (18)</td>
<td>63.3% (38)</td>
<td>0.379 [0.216, 0.664]</td>
</tr>
<tr>
<td><strong>12 Months</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>De Novo (51/49)</td>
<td>78.4% (9)</td>
<td>63.2% (16)</td>
<td>0.519 [0.229, 1.176]</td>
</tr>
<tr>
<td>Restenotic (119/111)</td>
<td>59.9% (42)</td>
<td>39.3% (61)</td>
<td>0.485 [0.327, 0.720]</td>
</tr>
<tr>
<td><strong>24 Months</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>De Novo (51/49)</td>
<td>67.5% (13)</td>
<td>50.7% (21)</td>
<td>0.538 [0.269, 1.075]</td>
</tr>
<tr>
<td>Restenotic (119/111)</td>
<td>45.8% (55)</td>
<td>30.7% (68)</td>
<td>0.560 [0.392, 0.800]</td>
</tr>
<tr>
<td><strong>36 Months</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>De Novo (51/49)</td>
<td>50.6% (18)</td>
<td>42.2% (23)</td>
<td>0.654 [0.353, 1.215]</td>
</tr>
<tr>
<td>Restenotic (119/111)</td>
<td>40.5% (58)</td>
<td>22.7% (72)</td>
<td>0.552 [0.390, 0.781]</td>
</tr>
</tbody>
</table>

DCB, drug-coated balloon; PTA, percutaneous transluminal angioplasty

* numbers are % with Kaplan-Meier estimate (number of patients with an event)
Background: Lack of Long-Term Evidence for Treatment of Dysfunctional AVF
Very Few Large Studies; Very Few Studies in Devices Other Than PTA


CEC, Clinical Events Committee; DCB, drug-coated balloon; FDA, United States Food and Drug Administration; PTA, percutaneous transluminal angioplasty. For inclusion on this chart, studies were required to report target lesion primary patency outcomes of endovascular treatment of dysfunctional AVF; they did not include AVG, ISR, CV, and all enrolled over 100 patients. Results are not directly comparable. Primary patency rates may be defined differently. Information provided is for illustration purposes only, and may differ in head-to-head comparison.
Case Discussion: EndoAVF Creation from Mapping to Cannulation

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Hamburg, Germany
I have the following potential conflicts of interest to report:

- **Consulting:** Becton Dickinson, Medtronic, Laminate medical, Xeltis, Bluegrass Vascular

- **Employment in industry**

- **Stockholder of a healthcare company**

- **Owner of a healthcare company**

- **Other(s):** Speaking/Teaching: W.L. GORE, BrosMed medical; Scientific Advisory Board Member: VENOVA medical

I do not have any potential conflict of interest
Considerations for Success

Mapping

Consider:
- Outflow vein anatomy
- Arterial requirements
- Perforator requirements

45-65% of patients qualify for the Ellipsys device in peer-reviewed literature1-6

Outflow Vein Anatomy
- Verify patency
- Check for thrombosis
- Diameter (> 2 mm)

Arterial Requirements
- PRA Diameter (> 2 mm)
- No inflow restrictions
- Calcification (non-occlusive)
- Patent Palmar Arch

Perforator Requirements
- Diameter (> 2 mm)
- Proximity to artery (< 1.5 mm)
- Must be straight enough to allow 21 Ga needle to be directed inside the lumen

References:
Mapping

Cephalic Brachii

Courtesy of Dr. Robert Shahverdyan
Mapping

Basilic Brachii

Left Basilic Brachii Prox

Courtesy of Dr. Robert Shahverdyan
Mapping Perforator

Courtesy of Dr. Robert Shahverdyan
Mapping
Perforator

Left Perforant Radial

Courtesy of Dr. Robert Shahverdyan
Considerations for Success:

Assessing Procedural Outcomes

Brachial Artery Doppler Waveform:

- Systolic velocity is typically **above 80 cm/sec**
  - If not, the ultrasound is likely set up incorrectly (gate, steer, angle-adjust)
- Diastolic velocity is typically **greater than 40%** of the systolic
  - If not, there is likely still spasm or stenosis present
- Volume flow rate should ideally be **greater than 500 ml/min**
  - If not, identify cause: occluded outflow, arterial disease

Thrill and Bruit:

- A palpable thrill should be detected near the anastomosis
- Bruit should be audible and indicate consistent diastolic murmur

---

Ellipsys Creation Case
Ellipsys Creation Case
Ellipsys Creation Case
Considerations for Success:

Prepare for Dialysis at 4 Weeks

Ensure path from anastomosis to cannulation zone is patent, devoid of blockages and has adequate flow

Goal: Achieve a palpable vein through the cannulation zone

---

Balloon Dilation 62%¹

Deep Embolization 32%¹

Cubital Banding 30%¹

Transposition or Superficialize 33%¹

---

Considerations for Success:

**Mapping**
- Outflow vein anatomy
- Arterial requirements
- Perforator requirements

**Procedure**
- Cannulating perforating vein
- Puncturing radial artery
  - Proficiency with ultrasound-guided puncture
  - Sharp understanding of 3D anatomy
- Phantom practice

**Maturation**
- Establish Brachial inflow >500 mL/min
- Angioplasty anastomosis and fistula as needed
- Direct flow to target cannulation vein(s)
- Determine best outflow
- Perform percutaneous maturations

**Cannulation**
- Establish Brachial inflow >500 mL/min
- Angioplasty anastomosis and fistula as needed
- Direct flow to target cannulation vein(s)
- Determine best outflow
- Perform percutaneous maturations
Cannulation Case
Thank you
Treating Challenging Lesions: My Algorithm for Cephalic Arch Stenosis

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Head of Vascular Surgery
University Teaching Hospital, University of Insubria
Varese, Italy
Disclosures
Matteo Tozzi, MD

I have the following potential conflicts of interest to report:

- Consulting – BD, Cardionovum Medtronic, Merit, WL Gore

  Employment in industry

  Stockholder of a healthcare company

  Owner of a healthcare company

  Other(s)

I do not have any potential conflict of interest
KDOQI Guidelines
What Do They Recommend?

• KDOQI considers it reasonable to use balloon angioplasty (with high pressure as needed) as primary treatment of AVF and AVG stenotic lesions that are both clinically and angiographically significant. (Expert Opinion)

• There is inadequate evidence for KDOQI to make a recommendation regarding the use of specialized balloons (drug-coated or cutting) versus standard high-pressure balloons in the primary treatment of AVF and AVG stenosis.

Future Research

• Study is needed in AVFs for multiple modalities of treatment (e.g., stent-grafts, drug-eluting balloons, etc.).
Past Experiences
Stent-grafts in AVF

Two RCTs have compared treatments for cephalic arch stenosis\textsuperscript{1,2}

$\rightarrow$ Stent grafts were statistically superior to control group in both studies

1) Shemesh et al. $\rightarrow$ PTA + stent graft vs. PTA + BMS

2) Rajan et al. $\rightarrow$ PTA + stent graft vs. PTA alone

Cephalic Arch Stenosis
Pathophysiology of Cephalic Arch Stenosis is Still Poorly Understood

Possible etiologies include:

- Altered flow in the vein leading to intimal hyperplasia as a compensatory mechanism;
- Extrinsic compression by fascia and the pectoralis major muscle preventing the fistulized cephalic vein from dilating in response to increased shear stress;
- Turbulence from increased flow rate, venous valves and cephalic arch morphology causing endothelial damage and intimal hyperplasia; and
- Renal failure causing intimal hyperplasia
Upstream Events

• Extrinsic compression by fascia and the pectoralis major muscle
• Turbulence from increased flow rate
• Venous valves and cephalic arch morphology
Downstream Events

High blood flow in AVF $\rightarrow$ high wall shear stress (WSS)

Results in:

1. Endothelial dysfunction, damage, and deendothelialization and exposing the subendothelial extracellular matrix (ECM) directly to flow
2. Exposed subendothelial layer $\rightarrow$ thrombus formation, adhesion and activation of platelets and monocytes and release of proinflammatory cytokines
3. Vascular smooth muscle cell (VSMC) migration and proliferation are promoted by platelet-derived growth factor (PDGF) and TNF-$\alpha$
4. Driven by cytokines such as transforming growth factor (TGF)-$\beta$, TNF-$\alpha$, and PDGF, fibroblasts differentiate to myofibroblasts, which proliferate and excrete ECM components
Downstream Events

- Vascular Anatomy
- Age
- Life Expectancy
- Quality of Life

Patient Selection

Optimizing Vascular Access Outcomes

Biological Therapies

- Peripheral Vascular Therapies
- Tissue Engineered Vessels
- Systemic Therapies
- Endovascular-Delivered Drugs

Optimizing Vascular Access Outcomes

Optimizing Vascular Access Outcomes

Arteriovenous conduits for hemodialysis: how to better modulate the pathophysiological vascular response to optimize vascular access durability, Yan-Ting Shiu,1 * Joris I. Rotmans,2 * Wouter Jan Geelhoed,2 Daniel B. Pike,1 and Timmy Lee3,4 - Am J Physiol Renal Physiol

New Evidence
IN.PACT AV Access IDE Study

Lesion Location Groups for Long-term Data

<table>
<thead>
<tr>
<th>Target Lesion Location†</th>
<th>IN.PACT AV DCB (n=170)</th>
<th>Standard PTA (n=160)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Peri-anastomotic</td>
<td>36.5% (62/170)</td>
<td>36.9% (59/160)</td>
</tr>
<tr>
<td>Arterial Inflow</td>
<td>2.4 (4/170)</td>
<td>4.4 (7/160)</td>
</tr>
<tr>
<td>Anastomosis</td>
<td>25.9 (44/170)</td>
<td>25.0 (40/160)</td>
</tr>
<tr>
<td>Swing Point</td>
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<td>14.7 (25/170)</td>
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<tr>
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<td>17.6% (30/170)</td>
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DCB, drug-coated balloon; PTA, percutaneous transluminal angioplasty
Table values are % (n/N)
†Target lesion location was site-reported

Arterial Inflow: treated segment is isolated to the arterial side
Anastomosis: treated segment crosses or meets the AV anastomosis
Swing Point: treated segment includes the curved segment of mobilized vessel
In Cannulation Zone: treated segment is isolated to straight segment of vessel where cannulation is performed
Venous Outflow: treated segment is in basilic vein (non-mobilized) or distal to the cephalo-axillary junction
Cephalic Arch: treated segment includes curved segment of cephalic vein as the vein crosses between the pectoralis major and deltoid muscles
## IN.PACT AV Access IDE Study Outcomes Through 36 Months

### Target Lesion Primary Patency by Lesion Location

<table>
<thead>
<tr>
<th>Subgroups (N DCB/N PTA)</th>
<th>IN.PACT AV DCB*</th>
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<td>Cephalic Arch (30/36)</td>
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Cephalic Arch Case Example

2 DCBs within 21 Months of Follow-up

Images courtesy of Dr. Matteo Tozzi
Case Example

17 Months Later

Images courtesy of Dr. Matteo Tozzi
Insubria Experience
More than 600 DCB PTA from 2014-2022

Cephalic Arch Stenosis
N=124

De Novo
N=78

DCB Angioplasty

Provisional Stent Graft
11 (14%)  

12 Month Primary Patency: 76%
Stent graft after 720 days: 43%

Recurrent
N=26

Stent Graft

12 Month Primary Patency: 64%
DCB PTA after 720 days: 71.5%
KDOQI Goals and Targets

ESKD Patient on HD Life Plan Target

Life-Plan goal: establish and document the patients P-L-A-N short term (1-2 years) and long-term (5 years) and access needs

AV Access (Fistula or Graft) Target

Intervention goals: ≤ 2, ≤ 3 interventions to maintain AV access use per year

IN.PACT Admiral DCB and IN.PACT AV DCB are not intended for treatment of AV grafts, inside stents, and central veins
Maintenance Goal

If the goal is to prolong life of vascular access it is not important which method has the best primary patency

Combine the right sequence of methods for the best results

DCB first, stent graft second

IN.PACT Admiral DCB and IN.PACT AV DCB are not intended for treatment of AV grafts, inside stents, and central veins
Thank you
IN.PACT™ AV Paclitaxel-coated PTA balloon catheter

Brief Statement

Indications for Use:
The IN.PACT™ AV Paclitaxel-coated PTA Balloon Catheter is indicated for percutaneous transluminal angioplasty, after appropriate vessel preparation, for the treatment of obstructive lesions up to 100 mm in length in the native arteriovenous dialysis fistulae with reference vessel diameters of 4 to 12 mm.

Contraindications
• The IN.PACT AV DCB is contraindicated for use in the following anatomy and patient types:
  • Coronary arteries, renal arteries, and supra-aortic/cerebrovascular arteries
  • Patients who cannot receive recommended antiplatelet and/or anticoagulant therapy
  • Patients judged to have a lesion that prevents complete inflation of an angioplasty balloon or proper placement of the delivery system
  • Patients with known allergies or sensitivities to paclitaxel
  • Women who are breastfeeding, pregnant, or are intending to become pregnant, or men intending to father children. It is unknown whether paclitaxel will be excreted in human milk and whether there is a potential for adverse reaction in nursing infants from paclitaxel exposure

Warnings
• A signal for increased risk of late mortality has been identified following the use of paclitaxel-coated balloons and paclitaxel-eluting stents for femoropopliteal arterial disease beginning approximately 2-3 years post-treatment compared with the use of non-drug coated devices. There is uncertainty regarding the magnitude and mechanism for the increased late mortality risk, including the impact of repeat paclitaxel-coated device exposure. Inadequate information is available to evaluate the potential mortality risk associated with the use of paclitaxel-coated devices for the treatment of other diseases/conditions, including this device indicated for use in arteriovenous dialysis fistulae. Physicians should discuss this late mortality signal and the benefits and risks of available treatment options for their specific disease/condition with their patients.
• Use the product prior to the Use-by date specified on the package.
• Contents are supplied sterile. Do not use the product if the inner packaging is damaged or opened.
• Do not use air or any gaseous medium to inflate the balloon. Use only the recommended inflation medium (equal parts contrast medium and saline solution).
• Do not move the guidewire during inflation of the IN.PACT AV DCB.
• Do not exceed the rated burst pressure (RBP). The RBP is based on the results of in vitro testing. Use of pressures higher than RBP may result in a ruptured balloon with possible intimal damage and dissection.
• The safety of using multiple IN.PACT AV DCBs with a total drug dosage exceeding 15,105 μg paclitaxel has not been evaluated clinically.
IN.PACT™ AV Paclitaxel-coated PTA balloon catheter

Brief Statement

Precautions

- This product should only be used by physicians trained in percutaneous transluminal angioplasty (PTA).
- Assess risks and benefits before treating patients with a history of severe reaction to contrast agents. Identify allergic reactions to contrast media and antiplatelet therapy before treatment and consider alternatives for appropriate management prior to the procedure.
- This product is not intended for the expansion or delivery of a stent.
- Do not use the IN.PACT AV DCB for pre-dilatation or for post-dilatation.
- This product is designed for single patient use only. Do not reuse, reprocess, or resterilize this product. Reuse, reprocessing, or resterilization may compromise the structural integrity of the device and/or create a risk of contamination of the device, which could result in patient injury, illness, or death.
- The use of this product carries the risks associated with percutaneous transluminal angioplasty, including thrombosis, vascular complications, and/or bleeding events.
- The safety and effectiveness of the IN.PACT AV DCB used in conjunction with other drug-eluting stents or drug-coated balloons in the same procedure has not been evaluated.
- The extent of the patient’s exposure to the drug coating is directly related to the number of balloons used. Refer to the Instructions for Use (IFU) for details regarding the use of multiple balloons and paclitaxel content.
- Appropriate vessel preparation, as determined by the physician to achieve residual stenosis of ≤ 30%, is required prior to use of the IN.PACT AV DCB. Vessel preparation of the target lesion using high-pressure PTA for pre-dilatation was studied in the IN.PACT AV Access clinical study. Other methods of vessel preparation, such as atherectomy, have not been studied clinically with IN.PACT AV DCB.

Potential Adverse Effects

- Potential adverse effects which may be associated with balloon catheterization may include, but are not limited to, the following: abrupt vessel closure, allergic reaction, arrhythmias, arterial or venous aneurysm, arterial or venous thrombosis, death, dissection, embolization, hematoma, hemorrhage, hypotension/hypertension, infection, ischemia or infarction of tissue/organ, loss of permanent access, pain, perforation or rupture of the artery or vein, pseudoaneurysm, restenosis of the dilated vessel, shock, stroke, vessel spasms or recoil.
- Potential complications of peripheral balloon catheterization include, but are not limited to, the following: balloon rupture, detachment of a component of the balloon and/or catheter system, failure of the balloon to perform as intended, failure to cross the lesion. These complications may result in adverse effects.
- Although systemic effects are not anticipated, potential adverse effects not captured above that may be unique to the paclitaxel drug coating include, but are not limited to, the following: allergic/immunologic reaction, alopecia, anemia, gastrointestinal symptoms, hematologic dyscrasia (including leukopenia, neutropenia, thrombocytopenia), hepatic enzyme changes, histologic changes in vessel wall, including inflammation, cellular damage, or necrosis, myalgia/arthritis, myelosuppression, peripheral neuropathy.
- Refer to the Physician’s Desk Reference for more information on the potential adverse effects observed with paclitaxel. There may be other potential adverse effects that are unforeseen at this time.
- Please reference appropriate product Instructions for Use for a detailed list of indications, warnings, precautions and potential adverse effects. This content is available electronically at www.manuals.medtronic.com.

CAUTION: Federal law (USA) restricts this device to sale by or on the order of a physician.
Ellipsys™ vascular access system

Brief Statement

**Indications**
The Ellipsys™ system is indicated for the creation of a proximal radial artery to perforating vein anastomosis via a retrograde venous access approach in patients with a minimum vessel diameter of 2.0 mm and less than 1.5 mm of separation between the artery and vein at the fistula creation site who have chronic kidney disease requiring dialysis.

**Contraindications**
The Ellipsys™ system is contraindicated for use in patients with target vessels that are <2 mm in diameter. The Ellipsys™ System is contraindicated for use in patients who have a distance between the target artery and vein > 1.5 mm

**Warnings**
- The Ellipsys™ system has only been studied for the creation of an AV fistula using the proximal radial artery and the adjacent perforating vein. It has not been studied in subjects who are candidates for surgical fistula creation at other locations, including sites distal to this location.
- The Ellipsys™ system is not intended to treat patients with significant vascular disease or calcification in the target vessels.
- The Ellipsys™ system has only been studied in subjects who had a patent palmar arch and no evidence of ulnar artery insufficiency.
- Use only with the Ellipsys™ Power Controller, Model No. AMI-1001.
- The Ellipsys™ Catheter has been designed to be used with the 6 F Terumo Glidesheath Slender™*. If using a different sheath, verify the catheter can be advanced through the sheath without resistant prior to use.
- Use ultrasound imaging to ensure proper placement of the catheter tip in the artery before retracting the sheath, since once the distal tip of the catheter has been advanced into the artery, it cannot be easily removed without creation of the anastomosis. If the distal tip is advanced into the artery at an improper location, complete the procedure and remove the catheter as indicated in the directions for use. It is recommended that a follow-up evaluation of the patient is performed using appropriate clinical standards of care for surgical fistulae to determine if any clinically significant flow develops that require further clinical action.
Precautions

• This product is sterilized by ethylene oxide gas.
• Additional procedures are expected to be required to increase and direct blood flow into the AVF target outflow vein and to maintain patency of the AVF. Care should be taken to proactively plan for any fistula maturation procedures when using the device.
• In the Ellipsys™ study, 99% of subjects required balloon dilatation (PTA) to increase flow to the optimal access vessel and 62% of subjects required embolization coil placement in competing veins to direct blood flow to the optimal access vessel. Prior to the procedure, care should be taken to assess the optimal access vessel for maturation, and appropriate patient follow-up. Please refer to the “Arteriovenous Fistula (AVF) Maturation” section of the labeling for guidance about fistula flow, embolization coil placement, and other procedures to assist fistula maturation and maintenance.
• The Ellipsys™ System is intended to only be used by physicians trained in ultrasound guided percutaneous endovascular interventional techniques using appropriate clinical standards for care for fistula maintenance and maturation including balloon dilatation and coil embolization.
• Precautions to prevent or reduce acute or longer-term clotting potential should be considered. Physician experience and discretion will determine the appropriate anticoagulant/antiplatelet therapy for each patient using appropriate clinical standards of care.

Potential Adverse Events

Potential complications that may be associated with creation and maintenance of an arteriovenous fistula include, but may not be limited to, the following:
• Total occlusion, partial occlusion or stenosis of the anastomosis or adjacent outflow vein
• Stenosis of the central AVF outflow requiring treatment per the treatment center’s standard of care
• Failure to achieve fistula maturation
• Incomplete vessel ligation when using embolization coil to direct flow
• Steal Syndrome
• Hematoma
• Infection or other complications
• Need for vessel superficialization or other maturation assistance procedures.

CAUTION: Federal (USA) law restricts this device to sale by or on the order of a physician.

Important Information: Indications, contraindications, warnings, and instructions for use can be found in the product labelling supplied with each device.
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Worldwide: +1 763.514.4000

medtronic.com