IN.PACT™ AV Access IDE Study Full Baseline Data

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On Behalf of the IN.PACT AV ACCESS Investigators

Disclosures

Speaker name: Robert Lookstein, MD

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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
- [x] Other(s)

- [ ] I do not have any potential conflict of interest

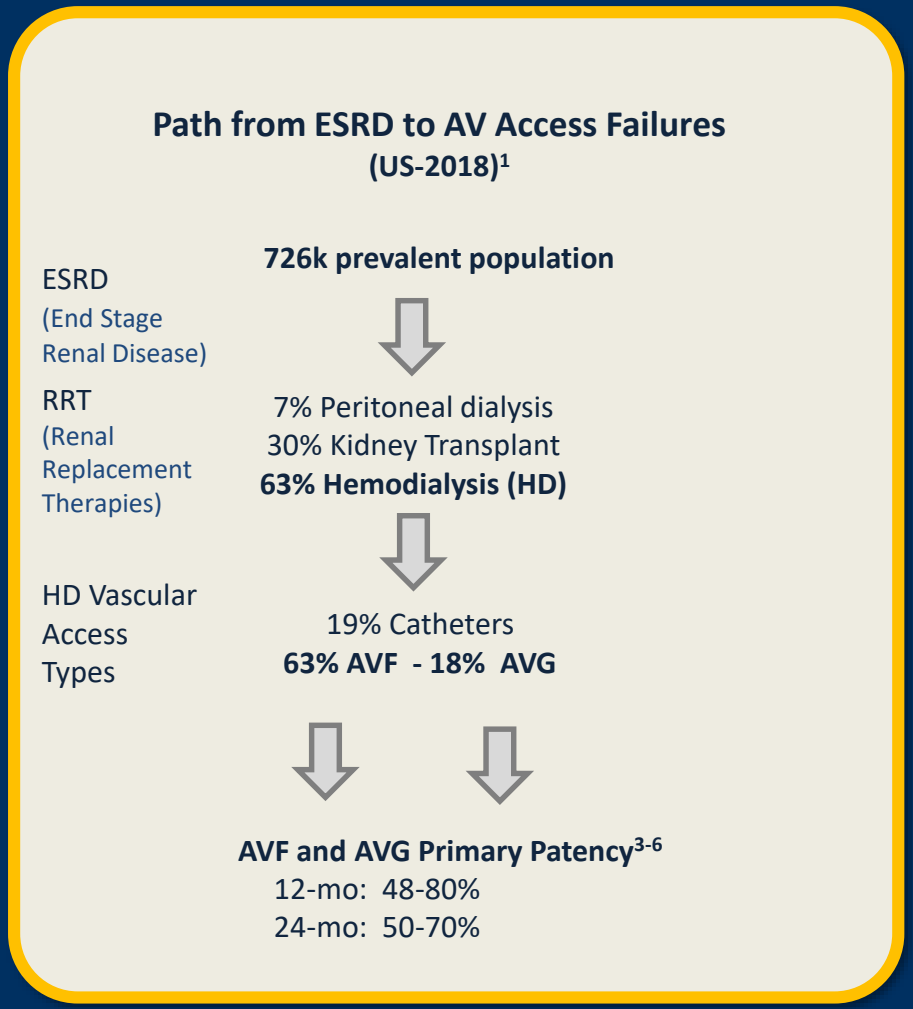
Conflicts:

- **Consultant:**
- Medtronic
- Boston Scientific
- Abbott
- BTG
- **Advisory Board**:
- Medtronic
- Boston Scientific

- **Research Support:**
- Boston Scientific
- Medtronic
- Bard
- Terumo
- Penumbra
- BTG
- **Clinical Events Committee:**
- INTACT Vascular
- Shockwave
- Boston Scientific

Hemodialysis Treatment for ESRD

- End-stage renal disease (ESRD) is treated in ~726k patients in the US[1]
  - ~125k new ESRD patients annually[1]
  - $35.4B cost to Medicare[1]
- Hemodialysis represents a significant burden to healthcare system
- Clinical practice guidelines recommend an autogenous arteriovenous (AV) fistula as the preferred vascular access for hemodialysis[7]
- Both AVF and AVG failures necessitate access revisions



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7. HD; National Kidney Foundation, 2006

Arteriovenous Access Failures

- While conventional therapies have prolonged access viability, primary patency rates leave much room for improvement
  - PTA: 23-72.8% at 6 mo[1-4]
  - Cutting balloon: 47.9% at 6 mo[1]
  - Bare-metal stents: 39.3% at 6 mo[2]
  - Stent-grafts: 51-53% at 6 mo[3-4]
- Drug-coated balloons (DCBs) have demonstrated success in treating femoropopliteal lesions associated with peripheral arterial disease (PAD)[5-6]
- Current clinical landscape is comprised of a single DCB randomized controlled trial (RCT) and several single-center reports

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4. Presented by Vesely T, American Society of Diagnostic and Interventional Nephrology (ASDIN) Phoenix, AZ, USA 2014.
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IN.PACT AV Access Product Specifications

DCB Components	IN.PACT AV Access
Balloon (Based on Admiral Extreme PTA)	4.0 – 12.0 mm diameters 40, 60, 80, 120, 150 mm lengths 40*/ 80 / 130 cm shaft
Paclitaxel	Proven anti-proliferative drug **3.5 µg/mm²**
Sheath Compatibility	5-7 French
Pressure Characteristics	Nominal pressure 6-8 ATM Rated burst pressure 9-14 ATM

- 40 cm shaft - unique feature of IN.PACT AV Access catheter

IN.PACT AV Access IDE Study

Objective:

Evaluate the safety and efficacy of the IN.PACT™ AV Access drug coated balloon (DCB) compared to percutaneous transluminal angioplasty (PTA) for treatment of *de-novo* or *restenotic* obstructive lesions of *native* arteriovenous fistulae (AVF) in the upper extremity

Principal Investigators:

- Robert Lookstein, MD *(USA)*
- Andrew Holden, MD *(New Zealand)*
- Hiroaki Haruguchi, MD *(Japan)*

IN.PACT AV Access IDE Study Design

- Prospective, global, multicenter, randomized, single-blinded study
- 330 patients
- 24 month follow-up
- 1:1 randomization
- Lesions up to 10 cm in length in the AV Access
- Independent and blinded Duplex Ultrasound Core Lab[1], Angiographic Core Lab[2], and Clinical Events Committee[3]
- 30 Global Sites (US, Japan and New Zealand)



1. VasCore DUS Core Laboratory
2. SYNTACTX Angiographic Core Laboratory
3. Clinical Events Committee and Data Safety Monitoring services provided by SYNTACTX

IN.PACT AV Access Key Inclusion Criteria

- Life expectancy of ≥ 12 months
- Native AV fistula created ≥ 60 days prior to the index procedure
- Target AV fistula has undergone dialysis for at least 8 of 12 sessions during a four week period
- Patient has a *de novo* and/or non-stented restenotic lesion located between the arteriovenous anastomosis and axillosubclavian junction with ≥ 50% stenosis
- Target lesion or a tandem lesion that is ≤ 100 mm in length

  Note: Tandem lesions may be enrolled provided they meet <u>all</u> of the following criteria:
  - Separated by a gap of ≤ 30mm (3 cm)
  - Total combined lesion length, including 30 mm gap, is less than 100 mm
  - Able to be treated as a single lesion
- Target vessel diameter of 4– 12 mm
- Patient underwent successful crossing of the target lesion with the guide wire and pre-dilatation with a HP balloon:
  - stenosis of ≤ 30% in the absence of a flow limiting dissection (Grade ≥ C) or perforation

IN.PACT AV Access Key Exclusion Criteria

- Undergone prior intervention of access site within 30 days of index procedure
- Target AVF previously had or currently has a thrombosis
- Planned surgical revision of access site
- Hemodynamically significant central venous stenosis that cannot be successfully treated prior to treatment of target lesion
- Presence of a stent located in the target AV access circuit
- Secondary non-target lesion requiring treatment within 30 days post index procedure
- Judged to have a lesion that prevents complete inflation of an angioplasty balloon or proper placement of the delivery system
- Significant arterial inflow lesion requiring treatment more than 2 cm upstream from the anastomosis in the AV access
- Presence of pseudoaneurysm or aneurysm requiring treatment at the lesion site

IN.PACT AV Access Primary Endpoints

Primary Safety Endpoint:

- ***Serious Adverse Event Rate within 30 Days***
  - Defined as the Serious Adverse Event (SAE) rate involving the AV access circuit through 30 days post-procedure

Primary Efficacy Endpoint:

- ***Primary Patency Rate through 6 Months***
  - Defined as freedom from clinically-driven target lesion revascularization (CD-TLR) or access circuit thrombosis measured through 6 months post-procedure
    - *Clinically-Driven Target Lesion Revascularization (CD-TLR)*: Any re-intervention involving the target lesion in which:
      - The subject has a ≥ 50% diameter stenosis (per angiographic core lab assessment) in the presence of clinical or physiologic abnormalities that indicate dialysis access dysfunction *OR*
      - ≥ 70% stenosis without the presence of clinical or physiologic abnormalities indicating dialysis access dysfunction
  - IN.PACT AV access primary patency is measured out to **210 days endpoint (rather than 180 days)**

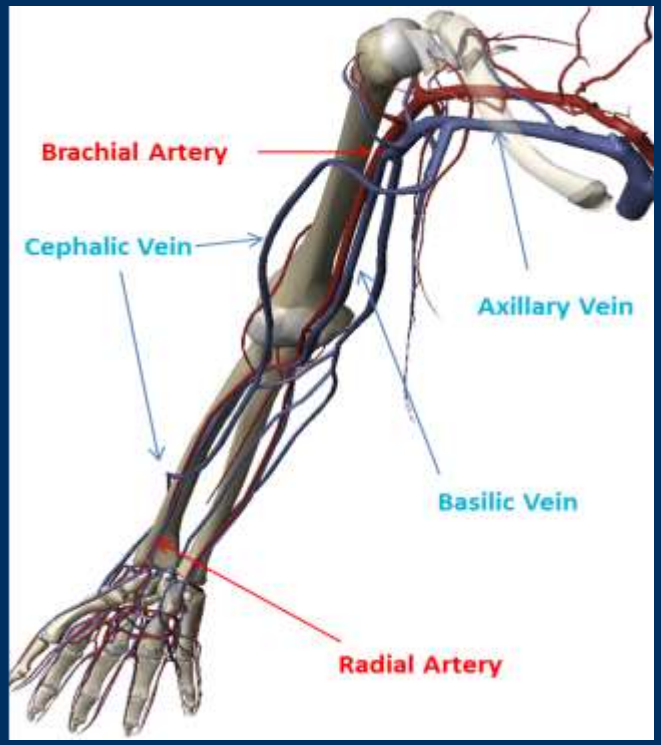
IN.PACT AV Access Baseline Characteristics

Baseline Demographics	ITT Analysis Set (N=330)*
Age (yrs) (mean ± SD)	65.6 ± 13.3
Male	64.5% (213/330)
Hypertension	92.7% (306/330)
Hyperlipidemia	53.3% (176/330)
Diabetes Mellitus Type 1 Type 2	65.8% (217/330) 3.0% (10/330) 62.7% (207/330)
Renal Insufficiency	100.0% (330/330)
Carotid Artery Disease	6.4% (21/330)
Congestive Heart Failure	23.6% (78/330)
Coronary Heart Disease	37.3% (123/330)
Peripheral Artery Disease	17.3% (57/329)
Smoker Current Former	 13.6% (45/330) 33.0% (109/330)
Previous AV Access Endovascular Procedure	74.5% (246/330)

*Baseline data includes all subjects randomized to PTA and DCB; ITT, intent-to-treat

IN.PACT AV Access- Clinical Characteristics

Clinical Characteristics	ITT Analysis Set (N=330)**
AVF Type*	
Radiocephalic	50.3% (166/330)
Brachiocephalic	36.4% (120/330)
Brachiobasilic	9.7% (32/330)
Other	3.6% (12/330)
Target Arm	
Right	25.5% (84/330)
Left	74.5% (246/330)
Dominant Arm	23.6% (78/330)
Presenting Clinical Symptoms Indicating AV Access Dysfunction	
Decreased Blood Flow	59.4% (196/330)
Elevated Venous Pressures	17.9% (59/330)
Unexplained Reduction in Hemodialysis Dose (Kt/V)	3.0% (10/330)
Abnormal Recirculation Values	2.1% (7/330)
Swollen Extremity or Aneurysm Formation	6.1% (20/330)
Elevated Negative Arterial Prepump Pressures	8.8% (29/330)
Unexplained Reduction of Dialysis Efficiency	4.2% (14/330)
Abnormal Physical Findings (thrill, murmur, arm swelling, etc)	43.9% (145/330)
Abnormally High BUN	0.6% (2/330)
Other	3.6% (12/330)
Age of AVF (yrs)	3.3 ± 3.4
Years of Hemodialysis (mean ± SD)	4.3 ± 5.1



*AVF type locations are site-reported
**Baseline data includes all subjects randomized to PTA and DCB
AVF, arteriovenous fistula; BUN, blood-urea-nitrogen; ITT, intent-to-treat

IN.PACT AV Access Lesion Characteristics*

Lesion Characteristics	ITT Analysis Set (N=330)**
Lesion Type	
De Novo	30.3% (100/330)
Restenotic	69.7% (230/330)
Target Lesion Location	
Anastomosis	25.5% (84/330)
Arterial Inflow	3.3% (11/330)
Cephalic Arch	20.0% (66/330)
In Cannulation Zone	11.2% (37/330)
Swing Point	7.9% (26/330)
Venous Outflow	32.1% (106/330)

*Target lesion locations are site reported
**Baseline data includes all subjects randomized to PTA and DCB
ITT, intent-to-treat

IN.PACT AV Access Conclusions

- IN.PACT AV Access IDE Study is evaluating the safety and efficacy of the IN.PACT™ AV Access DCB compared to percutaneous transluminal angioplasty (PTA) for treatment of de-novo or restenotic obstructive lesions of native arteriovenous fistulae (AVF) in the upper extremity

- Subjects from 3 geographies (USA, Japan, NZ) are included

- Anticipating 6-Month Primary results presented in Fall 2019

Thank You