SAVER: Rationale and merits for an all-comers DCB e-Registry

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Disclosure

Speaker name:
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I have the following potential conflicts of interest to report:

- Consulting: Medtronic, Abbott Vascular, Terumo, Boston Scientific, Spectranetics

- Employment in industry

- Stockholder of a healthcare company

- Owner of a healthcare company

- Other(s)

- I do not have any potential conflicts of interest
Background: Clinical Evidence

• To inform clinical decision making
  • FIH: the right first step for safety and performance signals
  • RCTs: Level 1, necessary but too selective to properly answer all questions

“…although randomized trials remain the gold standard, they share with this precious metal limitations of cost and rarity…”

Ideally real world clinical decisions should be also informed by real world data

2. Go for the Silver? Using Simulated Randomized Trials - Mark S. Lesney 2010
Background: PAD Challenges

- PAD: involves many variables, calling for deep scrutiny regarding their implications on patient outcomes:

  1. **Clinical:** RCC, gender, age, diabetes + other comorbidities
  2. **Anatomic:** N / lesion locations, lesion length, calcium, occlusion, in-stent restenosis, etc....
  3. **Procedural:** pre- and post DCB treatment (POBA, scoring, debulking, stenting, ...)

- Concomitant variables may play as confounders if not properly tracked and accounted for (e.g. medical therapy)

- Trials frequently assess either SFA or BTK, rarely multi-level disease. Claudicant trials mainly focused on fem-pop, CLI trials mainly focused on BTK
Calls for standardization have been made

Efforts have been taken to standardize methods, endpoints and definitions
…and calls for standardization have been disregarded

“…lack of standardization across trials remains the rule in PAD therapies, particularly for percutaneous treatments…” [1]

And major differences in methods exist across trials making cross trial comparison difficult or misleading

• ≠ endpoint use and definition (i.e. ≠ PSVRs in restenosis)
• ≠ event reporting (exact rates vs. survival estimates)
• ≠ lesion length assessment (i.e. 20-20% vs. normal-to-normal)

What’s next?

After FIH and randomized trials, well conducted, sizable real world registries built on standard and uniform definitions remain a critical must-have to fully appreciate how a therapy is able to affect a disease across its multiple diversities and subsets.
Size matters

Sufficiently sized Registries offer potential for meaningful assessment on combined subsets beyond just their 1st-level

<table>
<thead>
<tr>
<th>Subsets and %</th>
<th>1st subset</th>
<th>2nd subset</th>
<th>3rd subset</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diabetics</td>
<td>N=800</td>
<td>N=320</td>
<td>N=34</td>
</tr>
<tr>
<td>Females</td>
<td>N=112</td>
<td>N=2000</td>
<td>N=700</td>
</tr>
<tr>
<td>CTOs</td>
<td>N=34</td>
<td>N=700</td>
<td>N=210</td>
</tr>
</tbody>
</table>

N=5000
Quality matters

Multi-center
Independent adjudication
Clinical Events Committee
Imaging Core lab
Monitoring
High Quality Real-World Assessment

ClinicalTrials.gov Identifier: NCT01855412

LIBERTY, non-Industry sponsored

N=1200 (US); RC 2-6

The LIBERTY study: Design of a prospective, observational, multicenter trial to evaluate the acute and long-term clinical and economic outcomes of real-world endovascular device interventions in treating peripheral artery disease

George L. Adams, MD, MHS, a Jihad Mustapha, MD, a William Gray, MD, c Nick J. Hargus, PhD, d Brad J. Martinsen, PhD, d Gary Ansel, MD, e and Michael R. Jaff, DO f Raleigh, NC; Wyoming, MI; New York, NY; St Paul, MN; Columbus, OH; and Boston, MA
High Quality Real-World Assessment

ClinicalTrials.gov Identifier: NCT01609296

IN.PACT Global, Medtronic sponsored

N=1500 (EU); RC 2-3-4

The IN.PACT Global Registry:
One-Year Outcomes Using the IN.PACT DCB in an Unrestricted, Real-World Environment

Gary Ansel, MD, FACC
System Medical Chief: Vascular
OhioHealth/Riverside Methodist Hospital
Columbus, OH

completed
SAVER: Stellarex Vascular e-Registry
ClinicalTrials.gov Identifier: NCT02769273

- Multi-center, international, real-world
- N = 5000 / up to 200 Sites
- Full PAD spectrum: clinical (IC / CLI) and anatomic (ATK/BTK)
- Patient treated as per center’s standard practice
- Independent Clinical Events Committee
- Duplex Core lab evaluation for Imaging cohort*
- Patient Follow up to 3 years
- Largest dataset ever studied within uniform definitions / endpoints

* specific subsets such as CTO, ISR, long lesions, Ca++
# SAVER: Organization

**Sponsor**  
Spectranetics

**Steering Committee**  
Prof. Dr. G. Torsello (Münster, Germany)  
Prof. Dr. F. Vermassen (Gent, Belgium)  
Prof. Dr. A. Cremonesi (Cotignola, Italy)  
Dr. A. Sauguet (Toulouse, France)

**Core Lab**  
Euroimaging Research (Roma, Italy)

**Clinical Events Committee**

**Monitoring**

**Electronic web-based CRF**
SAVER: Site participation

- Targeted site participation requirements
- Data analysis planned at global, country and site level
- Site’s own data access regulated by pre-defined conditions, for each site’s own awareness, review and analysis
Full PAD Assessment

- Claudication & Critical Limb Ischemia*
- Sharp separation in analysis and endpoints between Claudicants and CLI
- Primary Endpoints (Claudicant cohort)
  - **Efficacy:** Freedom from 12-month clinically-driven TLR, adjudicated by an independent CEC
  - **Safety:** Freedom from 30-day device and procedure related death and freedom from 12-month target limb major amputation and CD-TLR

* Protocol to be amended to include CLI when Stellarex .014 becomes commercially available
Full PAD Assessment

Real World – Real Practice

- RC 2-3-4-5-6*
- Single limb or bilateral
- Fem-pop and/or BTK [†]
- Single or multiple lesions
- De-novo / restenotic / ISR
- Stenosis or CTOs
- TASC A-B-C-D
- Calcium of any grade / severity
- With or w/out pre-dil
- Any lesion prep or post-treatment at operator’s discretion

* Protocol to be amended to include CLI when Stellarex .014 becomes commercially available
Conclusions

• SAVER: first effort to match “quantity and quality” within a real world, real practice registry of unprecedented size and quality

• Set to complement RCTs in informing medical community on DCB real-practice outcomes across multiple clinical, anatomical and procedural subsets

• Look into full PAD disease and (Stellarex) DCB treatment spectrum

• Offer individual sites a structured platform to assess and understand their own DCB practice
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