The DANCE Trial
12 month results

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on behalf of the DANCE Investigators
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Disclosure

Speaker name: George Adams

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
# DANCE Trial Organization

(Dexamethasone to the Adventitia to eNhance Clinical Efficacy in Fem-Pop Lesions)

| National Co-PIs | George Adams, MD, UNC-Rex Healthcare, Raleigh, NC  
Mahmood Razavi, MD, St. Joseph’s, Orange, CA |
|-----------------|---------------------------------------------------|
| Ultrasound Core Laboratory | Vascore, Boston, MA  
Director: Michael Jaff, DO |
| Angiographic Core Laboratory | CRF, New York, NY  
Director: Philippe Genereux, MD |
| Biomarker Laboratory | Quest Diagnostics Clinical Trials |

| Sites:  
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Guarav Aggarwala, MD (Palestine, TX)  
Sam Ahn, MD (Dallas, TX)  
Vaquar Ali, MD (Jacksonville, FL)  
Gary Ansel, MD (Columbus, OH)  
Ehrin Armstrong, MD (Denver, CO)  
Nelson Bernardo, MD (Washington, DC)  
Ian Cawich, MD (Little Rock, AR)  
Michael Curi, MD (Newark, NJ)  
Tom Davis, MD (Detroit, MI)  
Suhail Dohad, MD (Beverly Hills, CA)  
W. Britton Eaves, MD (Bossier City, LA) | Andrey Espinoza, MD (Flemington, NJ)  
Robert Feldman, MD (Ocala, FL)  
Warren Gasper, MD (San Francisco, CA)  
Stuart Harlan, MD (Pensacola, FL)  
Donald Jacobs, MD (St. Louis MO)  
Richard Kovach, MD (Browns Mills, NJ)  
Louis Lopez, MD (Ft. Wayne, IN)  
Amir Malik, MD (Ft. Worth, TX)  
Luke Marone, MD (Pittsburgh, PA)  
Christopher Metzger, MD (Kingsport, TN)  
Christopher Owens, MD (San Francisco, CA)  
John Papanowski, MD (Tucson, AZ)  
Richard Powell, MD (Lebanon, NH) | Anthony Pucillo, MD (New York, NY)  
Venkatesh Ramaiah, MD (Phoenix, AZ)  
Mahmood Razavi, MD (Orange, CA)  
Bhavanada Reddy, MD (Salt Lake City, UT)  
Andrez Shanzer, MD (Worcester, MA)  
Immad Sadiq, MD (Hartford CT)  
Peter Soukas, MD (Providence RI)  
Cezar Staniloae, MD (New York, NY)  
John Taggart, MD (Albany, NY)  
Robert Wilkins, MD (Hattiesburg, MS)  
John Winscott, MD (Jackson, MS)  
Jason Yoho, MD (Seguin, TX) |
Understanding the Need

• Approximately 27 million people in Europe and North America have PAD resulting in more than 1 million lower extremity endovascular interventions per year
• Local luminal drug delivery with DCB and DES have improved patency rates above the knee
• Paucity of data in large populations: women, diabetics, long lesions, heavy calcification, chronic total occlusions, and atherectomy therapy
• Adventitial drug delivery of dexamethasone (ADD-DEX) is proposed as a baseline therapy to treat inflammation and improve patency
Treating Inflammation with a Potent Anti-Inflammatory

Restenosis results from the inflammatory cascade:

- **Hours**: Inflammation
- **Days**: Transcription
- **Weeks**: Migration
- **Months**: Proliferation

Upstream targeting of the early inflammatory process limits or eliminates downstream restenosis, but allows healing and resolution.

Adams, LINC 2017
Adventitial and Perivascular Targeting with Bullfrog® Micro-Infusion Device

20% contrast: 80% drug is mixed and co-administered to provide immediate feedback

“Painting” the vessel

Compliant balloon treats broad range of vessel diameters

1.5 mm long Microneedle (34 Ga) penetrates artery for drug delivery

Adams, LINC 2017
DANCE Trial Design

- Multicenter, open-label trial in two populations: primary atherectomy (ATX) and primary angioplasty (PTA)
- Key eligibility criteria
  - ≥18 years of age
  - Rutherford 2-4
  - De novo or non-stented restenotic SFA or popliteal lesions (>70% stenosis, ≤15 cm length)
  - Reference diameter 3-8mm
  - No prior bypass, stenting or DCB of target lesion
  - No acute thrombus or acute limb ischemia
  - No concurrent use of drug-eluting products in target limb

Baseline angiogram and biomarker blood draw

157 ATX
124 PTA

ADD-DEX Treatment

Blood draws for change in biomarkers (~1/3 of patients) at 24 hours and 4 weeks

Clinical, hemodynamic and duplex U/S follow-up at 6, 12, 18, 24 months

Adams, LINC 2017
DANCE Trial Design (cont’d)

• Primary Endpoints

  Safety
  – Composite of freedom from all cause peri-operative (30 day) death and freedom at 1 year in the index limb from major amputation (ATK or BTK), bypass surgery or thrombolysis

  Efficacy
  – Primary patency of the target lesion at 1 year: Core lab adjudicated absence of binary restenosis (DUS PSVR > 2.4 or angiographic narrowing >50%) & freedom from clinically-driven target lesion revascularization (CD-TLR)

• Comparator Analysis
  – Per-protocol group was selected based on matched eligibility to DCB studies, for comparison purposes:
    • No residual stenosis ≥ 35% at end of procedure (N=13 in ATX group, N=16 in PTA group)
    • No concurrent use of DES in lesion (N=2 in ATX group)
    • No lesions that extended beyond the popliteal segment (N=1 in ATX group)
## DANCE Demographics

<table>
<thead>
<tr>
<th></th>
<th>PTA</th>
<th>ATX</th>
</tr>
</thead>
<tbody>
<tr>
<td>N (legs)</td>
<td>124</td>
<td>157</td>
</tr>
<tr>
<td>Age (years)</td>
<td>68.9±9.1</td>
<td>68.4±9.6</td>
</tr>
<tr>
<td>Male</td>
<td>65%</td>
<td>57%</td>
</tr>
<tr>
<td>Caucasian</td>
<td>77%</td>
<td>80%</td>
</tr>
<tr>
<td><strong>African American</strong></td>
<td><strong>20%</strong></td>
<td><strong>17%</strong></td>
</tr>
<tr>
<td>Diabetes</td>
<td>52%</td>
<td>50%</td>
</tr>
<tr>
<td>CAD</td>
<td>55%</td>
<td>67%</td>
</tr>
<tr>
<td>Hypertension</td>
<td>90%</td>
<td>92%</td>
</tr>
<tr>
<td>Hyperlipidemia</td>
<td>83%</td>
<td>80%</td>
</tr>
<tr>
<td>Obesity (BMI≥30 kg/m²)</td>
<td>34%</td>
<td>34%</td>
</tr>
<tr>
<td>Creatinine (mg/dL)</td>
<td>1.02±0.28</td>
<td>1.10±0.51</td>
</tr>
<tr>
<td>CRP, pre-procedure (mg/dL)</td>
<td>5.01±9.37</td>
<td>5.78±7.25</td>
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</tbody>
</table>

Typically 5-15%
DANCE Baseline Characteristics

<table>
<thead>
<tr>
<th></th>
<th>PTA</th>
<th>ATX</th>
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<tbody>
<tr>
<td><strong>Rutherford Category</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>36.3%</td>
<td>60.5%</td>
<td>3.2%</td>
</tr>
<tr>
<td>3</td>
<td></td>
<td></td>
</tr>
<tr>
<td>22.9%</td>
<td>59.9%</td>
<td>17.2%</td>
</tr>
<tr>
<td>4</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2</td>
<td></td>
<td>4</td>
</tr>
<tr>
<td>36.3%</td>
<td></td>
<td>17.2%</td>
</tr>
<tr>
<td><strong>TASC II Classification</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>A</td>
<td>40%</td>
<td>62%</td>
</tr>
<tr>
<td>53%</td>
<td>6%</td>
<td>6%</td>
</tr>
<tr>
<td>B</td>
<td>4%</td>
<td>1%</td>
</tr>
<tr>
<td>30%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>C</td>
<td></td>
<td></td>
</tr>
<tr>
<td>6%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>D</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1%</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Severe Calcification</strong></td>
<td>21.3%</td>
<td>29.4%</td>
</tr>
<tr>
<td><strong>Popliteal Involvement</strong></td>
<td>15.3%</td>
<td>17.2%</td>
</tr>
<tr>
<td><strong>Mean Lesion Length (cm)</strong></td>
<td>7.4 ± 4.0</td>
<td>8.8 ± 5.2</td>
</tr>
<tr>
<td>[range: 1.5 – 19.6]</td>
<td>[range: 1.7 – 31.0]</td>
<td></td>
</tr>
<tr>
<td><strong>Mean % Diameter Stenosis (Pre)</strong></td>
<td>73% ± 16%</td>
<td>70% ± 17%</td>
</tr>
<tr>
<td><strong>Total Occlusions</strong></td>
<td>17%</td>
<td>15%</td>
</tr>
<tr>
<td><strong>Grade B-D Dissection</strong></td>
<td>44%</td>
<td>26%</td>
</tr>
<tr>
<td><strong>Stent Utilization</strong></td>
<td>52%</td>
<td>35%</td>
</tr>
<tr>
<td><strong>Mean % Diameter Stenosis (Post)</strong></td>
<td>24%±12%</td>
<td>23%±9%</td>
</tr>
</tbody>
</table>
DANCE 12-Month Safety Endpoints

<table>
<thead>
<tr>
<th>Safety Outcomes (ITT population)</th>
<th>DANCE-PTA</th>
<th>DANCE-ATX</th>
</tr>
</thead>
<tbody>
<tr>
<td>Device-related SAE 0-365 Days</td>
<td>0/124 (0.0%)</td>
<td>0/157 (0.0%)</td>
</tr>
<tr>
<td>Drug-related SAE 0-365 Days</td>
<td>0/124 (0.0%)</td>
<td>0/157 (0.0%)</td>
</tr>
<tr>
<td>Major Adverse Limb Events 0-365 Days</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Amputation</td>
<td>0/114 (0.0%)</td>
<td>1/126 (0.8%)</td>
</tr>
<tr>
<td>Bypass</td>
<td>1/114 (0.9%)</td>
<td>1/126 (0.8%)</td>
</tr>
<tr>
<td>Thrombolysis</td>
<td>0/114 (0.0%)</td>
<td>0/126 (0.0%)</td>
</tr>
<tr>
<td>Death 0-30 Days</td>
<td></td>
<td>0/244 (0.0%)</td>
</tr>
<tr>
<td>Death 0-365 Days</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Non-Cardiovascular</td>
<td></td>
<td>2/231 (0.9%)</td>
</tr>
<tr>
<td>Cardiovascular or Unknown</td>
<td></td>
<td>7/231 (3.0%)</td>
</tr>
</tbody>
</table>
DANCE 12-Month Efficacy Endpoint (13-Month K-M Primary Patency)

**DANCE-ATX**

- Kaplan-Meier Survival Estimate (PP)
  - Freedom from TLR
  - Primary Patency

**DANCE-PTA**

- Kaplan-Meier Survival Estimate (PP)
  - Freedom from TLR
  - Primary Patency

Adams, LINC 2017
DANCE Subgroup Analyses
(13-Month K-M Primary Patency)

DANCE Kaplan-Meier Survival Estimate of Primary Patency (PP)

- Male, N=148: 79.3%
- Female, N=100: 77.9%
- Diabetic, N=122: 79.5%
- Non-Diabetic, N=125: 78.8%

Adams, LINC 2017
DANCE Subgroup Analyses (13-Month K-M Primary Patency)

- Stented vs. unstented in angioplasty, the difference in patency outcomes appeared minor.
- Overall, ADD-DEX may enhance unstented patency and stented patency alike.
Summary and Conclusion

- The ADD-DEX procedure in DANCE has produced positive results in both primary atherectomy (in a challenging patient population) and primary angioplasty intervention.

- The paradigm shift:
  - Direct targeting (of the adventitia) with
  - Efficient delivery (Bullfrog Micro-Infusion) of an
  - Anti-inflammatory drug (dexamethasone) quells inflammation to
  - Improve patency after revascularization
Adventitial Drug Delivery: What the Future Holds for PAD

- **LIMBO-PTA**
  - ADD-DEX in BTK with PTA (N=120)
  - European Trial, enrolling (PI: Dierk Scheinert)

- **LIMBO-ATX**
  - ADD-DEX in BTK with Atherectomy (N=120)
  - U.S. Trial, enrolling (PIs: George Adams, Don Jacobs)

- **PRT-201-115 (Proteon)**
  - ADD-Vonapanitase (elastase) in BTK (N=40)
  - Phase 1 U.S. Trial, enrolling (PI: Jihad Mustapha)

- **TANGO**
  - ADD-LIMUS in BTK (N=60)
  - U.S. Trial planned for Q1 2017 start (PI: Ian Cawich)

- **TWIST**
  - ADD-COMBO
  - In planning stages
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12 month results

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on behalf of the DANCE Investigators
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