The DANCE Trial (ATX and PTA groups)
2-year results

George Adams, MD, MHS, FACC, FSCAI
University of North Carolina – Rex Healthcare
Raleigh, North Carolina, USA
on behalf of the DANCE Investigators
and co-PI Mahmood Razavi, MD
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
Understanding the Need

• Approximately 27 million people in Europe and North America have PAD, with more than 1 million lower extremity endovascular interventions per year in U.S. and Europe

• Local luminal drug delivery with DCB and DES have improved patency rates

• Paucity of long-term data in large populations: women, diabetics, long lesions, heavy calcification, and atherectomy therapy

• Adventitial drug delivery of dexamethasone (ADD-DEX) is proposed as a baseline therapy to treat the chronic underlying and acute inflammation and improve patency
Dexamethasone Administration via the Bullfrog® Micro-Infusion Device

1.5 mm long "Painting" the vessel with 0.5 mL per cm of lesion:

20% contrast : 80% drug (4 mg/mL dexamethasone) is mixed and co-administered to provide immediate feedback.
The DANCE Trial Tested the Hypothesis that Treating Inflammation Reduces Restenosis

Restenosis results from the inflammatory cascade:

- **Hours**: Injury
  - Endovascular Procedure
  - Dexamethasone

- **Days**: Transcription
  - Signaling

- **Weeks**: Recruitment
  - Migration
  - Proliferation

- **Months**: Hyperplasia/Narrowing

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

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The DANCE Trial
Dexamethasone to the Adventitia to eNhance Clinical Efficacy in fem/pop disease

- Multicenter, open-label trial
- SFA and Popliteal
- Primary atherectomy (ATX) or primary angioplasty (PTA) based on investigator decision
- Adventitial drug delivery of dexamethasone (ADD-DEX) in all subjects
- National co-PIs:
  - Mahmood Razavi, MD
  - George Adams, MD
- Primary Endpoints:
  - Safety: MALE+POD within 30 days from the procedure
  - Efficacy: Primary patency at 12 months
    - Freedom from angiographic or duplex ultrasound binary restenosis (PSVR ≤ 2.4)
    - Freedom from clinically-driven target lesion revascularization (CD-TLR)

Baseline angiogram and biomarker blood draw

159 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

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## Patient and Lesion Characteristics

<table>
<thead>
<tr>
<th>CHARACTERISTIC</th>
<th>DANCE-ATX</th>
<th>DANCE-PTA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of Limbs</td>
<td>159</td>
<td>124</td>
</tr>
<tr>
<td>Age (years)</td>
<td>68.3 ± 9.9</td>
<td>68.8 ± 9.1</td>
</tr>
<tr>
<td>Male Gender</td>
<td>56.6%</td>
<td>64.5%</td>
</tr>
<tr>
<td>Black or African American</td>
<td>17.0%</td>
<td>20.2%</td>
</tr>
<tr>
<td>Caucasian</td>
<td>79.9%</td>
<td>77.4%</td>
</tr>
<tr>
<td>Obesity (BMI ≥ 30 kg/m²)</td>
<td>34.6%</td>
<td>33.9%</td>
</tr>
<tr>
<td>Coronary Artery Disease</td>
<td>67.3%</td>
<td>54.8%</td>
</tr>
<tr>
<td>Diabetes Mellitus</td>
<td>50.3%</td>
<td>52.4%</td>
</tr>
<tr>
<td>Hyperlipidemia</td>
<td>80.5%</td>
<td>83.1%</td>
</tr>
<tr>
<td>Hypertension</td>
<td>92.5%</td>
<td>89.5%</td>
</tr>
<tr>
<td>Tobacco Use (Current)</td>
<td>32.7%</td>
<td>39.3%</td>
</tr>
<tr>
<td>Baseline C-Reactive Protein (mg/dL)</td>
<td>5.0 ± 9.4</td>
<td>5.8 ± 7.3</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>CHARACTERISTIC</th>
<th>DANCE-ATX</th>
<th>DANCE-PTA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rutherford 2</td>
<td>22.6%</td>
<td>36.3%</td>
</tr>
<tr>
<td>Rutherford 3</td>
<td>60.4%</td>
<td>60.5%</td>
</tr>
<tr>
<td>Rutherford 4</td>
<td>17.0%</td>
<td>3.2%</td>
</tr>
<tr>
<td>Ankle (or Toe) Brachial Index</td>
<td>0.80 ± 0.26</td>
<td>0.74 ± 0.22</td>
</tr>
<tr>
<td>Lesion Length (cm)</td>
<td>8.9 ± 5.2</td>
<td>7.5 ± 4.0</td>
</tr>
<tr>
<td>TASCII A</td>
<td>29.9%</td>
<td>53.2%</td>
</tr>
<tr>
<td>TASCII B</td>
<td>62.4%</td>
<td>40.3%</td>
</tr>
<tr>
<td>TASCII C</td>
<td>6.4%</td>
<td>5.6%</td>
</tr>
<tr>
<td>TASCII D</td>
<td>1.3%</td>
<td>0.8%</td>
</tr>
<tr>
<td>Severe Calcification</td>
<td>29.7%</td>
<td>21.3%</td>
</tr>
<tr>
<td>Popliteal Involvement</td>
<td>16.4%</td>
<td>18.5%</td>
</tr>
<tr>
<td>Stent Utilization</td>
<td>34.6%</td>
<td>51.6%</td>
</tr>
</tbody>
</table>

"Real-World" Enrollment Characteristics
# DANCE Safety Endpoints

<table>
<thead>
<tr>
<th>Time Period</th>
<th>Event Description</th>
<th>DANCE-ATX, ITT</th>
<th>DANCE-PTA, ITT</th>
</tr>
</thead>
<tbody>
<tr>
<td>30-Day Major Adverse Limb Events (MALE)</td>
<td>0/159 limbs (0.0%)</td>
<td>0/124 limbs (0.0%)</td>
<td></td>
</tr>
<tr>
<td>30-Day Post-Operative Death (POD)</td>
<td>0/159 limbs (0.0%)</td>
<td>0/124 limbs (0.0%)</td>
<td></td>
</tr>
<tr>
<td>30-Day Device or Procedure-Related Death</td>
<td>0/159 limbs (0.0%)</td>
<td>0/124 limbs (0.0%)</td>
<td></td>
</tr>
<tr>
<td>365-Day Device or Drug-Related SAE</td>
<td>0/159 limbs (0.0%)</td>
<td>0/124 limbs (0.0%)</td>
<td></td>
</tr>
<tr>
<td>365-Day MALE: Target lesion bypass</td>
<td>1/159 limbs (0.6%)</td>
<td>1/124 limbs (0.8%)</td>
<td></td>
</tr>
<tr>
<td>Major amputation</td>
<td>0/159 limbs (0.0%)</td>
<td>0/124 limbs (0.0%)</td>
<td></td>
</tr>
<tr>
<td>Thrombolysis</td>
<td>0/159 limbs (0.0%)</td>
<td>0/124 limbs (0.0%)</td>
<td></td>
</tr>
<tr>
<td>365-Day All-Cause Death</td>
<td>8*/127 subjects (5.3%)</td>
<td>2*/111 subjects (1.8%)</td>
<td></td>
</tr>
<tr>
<td>365-Day Cardiovascular (or unknown) Death</td>
<td>6*/127 subjects (4.7%)</td>
<td>2*/111 subjects (1.8%)</td>
<td></td>
</tr>
<tr>
<td>24-Month All-Cause Death</td>
<td>14**/106 subjects (13.2%)</td>
<td>8**/102 subjects (7.8%)</td>
<td></td>
</tr>
<tr>
<td>24-Month Cardiovascular (or unknown) Death</td>
<td>9**/106 subjects (8.5%)</td>
<td>5**/102 subjects (4.9%)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>1/26 Rutherford 2 (3.8%)</td>
<td>1/39 Rutherford 2 (2.6%)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>4/60 Rutherford 3 (6.7%)</td>
<td>3/59 Rutherford 3 (5.1%)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>4/20 Rutherford 4 (20.0%)</td>
<td>1/4 Rutherford 4 (25.0%)</td>
<td></td>
</tr>
</tbody>
</table>

*One subject counted in both ATX and PTA; **Two subjects counted in both ATX and PTA
DANCE Preliminary 2-Year Primary Patency
Kaplan-Meier Estimates (per protocol)

DANCE-ATX Primary Patency (PP)

DANCE-PTA Primary Patency (PP)

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DANCE Preliminary 2-Year Freedom from CD-TLR
Kaplan Meier Estimates (per protocol)
24-Month Primary Patency (K-M, per protocol) Preliminary Comparison Among Subgroups

- At 2 years after adventitial dexamethasone treatment:
  - Stents did not appear to have a large effect on patency, particularly in the DANCE-PTA study.
  - There was no significant gender disparity in patency rates.
  - Diabetics tended to do as well or better than non-diabetics, particularly in DANCE-PTA.
  - The popliteal region, where patency is not typically as durable, appears to benefit, especially with DANCE-ATX.
  - Severe calcification appears to have particular benefit with the addition of dexamethasone.
Summary and Conclusion

• The ADD-DEX procedure in DANCE has produced positive long-term 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
Current Clinical Trials of Adventitial-Perivascular Therapy with Bullfrog Delivery

Trauma → Recoil → Signaling → Recruitment → Proliferation → Migration → Obstruction

- **Vonapanitase**
  - SFA
  - Enrolling

- **Dexamethasone**
  - DANCE
    - 283 limbs
    - Open-label
    - COMPLETED
  - LIMBO-ATX
    - 120 total subjects
    - 1:1 RCT
    - Enrollment COMPLETE
  - LIMBO-PTA
    - 120 total subjects
    - 1:1 RCT
    - Enrolling

- **Temsirolimus**
  - TANGO
    - 60 total subjects
    - Dose-escalaion RCT
    - Enrolling

- **PRT201-115**
  - 40 subjects
  - Dose-escalation RCT
  - Enrolling

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