Wharton’s jelly mesenchymal stem/stromal cells in no-option critical limb ischemia – the CIRCULATE N-O CLI pilot study

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Disclosure

Speaker name:

*Tomasz Kwiatkowski*

I have the following potential conflicts of interest to report:

- [ ] 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
Results:

Stem cell therapy (SCT) improved ulcer healing

Significant improvement in ABI, TcO2 and PFWD

No significant improvement in major limb salvage

SCT could reduce the amputation rate and improve the ulcer healing rate in DM subgroup

8 RCTs reported the side effects of SCT, no serious side effects related to stem cells were reported.
Stem Cell Exhaustion – acceleration of cellular aging and senescence of stem cells

Circulating endothelial progenitor cells, vascular function, and cardiovascular risk

Jonathan M Hill, Gloria Zalos, Julian P J Halcox, William H Schenke, Myron A Waclawiw, Arshed A Quyyumi, Toren Finkel

Strong correlation between the number of EPC and Framingham risk factor score.

Trials transplanting autologous cells to treat CLI may have transferred cells with compromised function.

Wharton’s jelly Mesenchymal Stem Cells (WJMSCs)

• Easily reached allogenic stem cells source

• Spontaneous secretion of pro-angiogenic factors (VEGF, angiopoetin-1, HGF, TGFβ1)

• Modest expression of pluripotency genes (Oct-4, Nanog, SOX-2)- lack of tumorogenic potential

• Inhibition of alloreactive T-lymphocytes and lack of MHC II type antigens expression – no transplant ejection.
Combined intra-arterial and intra-muscular transfer of Wharton’s jelly mesenchymal stem/stromal cells in no-option critical limb ischemia – the CIRCULATE N-O CLI Pilot Study

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5 patients (age 61-71, 60% male)

N-O CLI, Rutherford 4-6

30x10⁶ WJMSCs administered intra-arterially and intra-muscularly (50%/50%) over 3-6 weeks intervals.
WJMSCs administered per protocol in all patients

No administration technique-related adverse events
This pilot study demonstrated safety and feasibility of WJMSCs use in N-O CLI patients and suggested efficacy.

<table>
<thead>
<tr>
<th>No.</th>
<th>Sex</th>
<th>Age</th>
<th>CLI etiology</th>
<th>Level of no-option occlusion</th>
<th>Initial Rutherford stage</th>
<th>Number of WJMSCs administrations</th>
<th>Interval between WJMSCs injections (weeks)</th>
<th>12-month FU (±2 months) Rutherford stage</th>
<th>12-month FU (±4 months) Rutherford stage, claudication distance (if no rest pain)</th>
<th>48-month FU (±4 months) Rutherford stage, claudication distance (if no rest pain)</th>
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<tbody>
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<td>SFA, trifurcation</td>
<td>Rutherford 5</td>
<td>3</td>
<td>6</td>
<td>Rutherford 4</td>
<td>Rutherford 3</td>
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<tr>
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<td>M</td>
<td>61</td>
<td>LEAD</td>
<td>SFA, Fem-Pop bypass</td>
<td>Rutherford 6</td>
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<td>3</td>
<td>Amputation</td>
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<tr>
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<td>PA, trifurcation, Fem-Pop bypass, Co-existing PA aneurysm</td>
<td>Rutherford 5</td>
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<td>6</td>
<td>Rutherford 2 Claudication 400 m</td>
<td>Rutherford 2 Claudication 200 m</td>
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<td>SFA, Fem-Pop bypass</td>
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<td>3</td>
<td>Rutherford 3 Claudication 80 m</td>
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<td>LEAD</td>
<td>SFA, Fem-Pop bypass, trifurcation, BTK arteries</td>
<td>Rutherford 5</td>
<td>6</td>
<td>6</td>
<td>Rutherford 3 Claudication 90 m</td>
<td>Rutherford 3 Claudication 60 m</td>
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</table>

Clinical signs of hyperemia after WJMSCs administration.
USE OF INNOVATIVE CARDIOCELL DRUG

IN PATIENTS WITH CRITICAL LIMB ISCHEMIA

Randomized, double blinded, placebo- controlled, multi-center clinical trial.

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Jerzy Krzywoń

Paweł Maga
Łukasz Drelicharz

Wacław Kuczmik
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