Innovative Approaches To Cell Therapy For CLI

Bijan Modarai PhD FRCS
READER/CONSULTANT IN VASCULAR SURGERY
BRITISH HEART FOUNDATION FELLOW
Academic Department of Vascular Surgery
Guy’s & St Thomas’ NHS Foundation Trust, King’s College London

Consultancy to Cook Medical
Grant Support Cook Medical, Medtronic Inc

Disclosures

Qureshi et al. Neurosurgery 2002
Fung et al. Frontiers Physiol 2012

Neovascularisation and Collateralisation

Qureshi et al. Neurosurgery 2002
Fung et al. Frontiers Physiol 2012

Clinical Studies of Cell therapy

<table>
<thead>
<tr>
<th>Trial</th>
<th>Treatment</th>
<th>Patients</th>
<th>n</th>
<th>Design</th>
<th>Adjuvants</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>TACT</td>
<td>BM-MNC BM MNC</td>
<td>21</td>
<td>50</td>
<td>randomised</td>
<td></td>
<td>Safety, feasibility</td>
</tr>
<tr>
<td></td>
<td>BM-MNC MicroBead CSF</td>
<td>22</td>
<td>50</td>
<td>randomised</td>
<td></td>
<td>ABPI tCpO2, pain</td>
</tr>
<tr>
<td></td>
<td>BM-MNC BM MNC</td>
<td>22</td>
<td>50</td>
<td>randomised</td>
<td></td>
<td>ABPI: NS, tCpO2: NS</td>
</tr>
<tr>
<td></td>
<td>BM-MNC BM MNC BM MNC</td>
<td>22</td>
<td>50</td>
<td>randomised</td>
<td></td>
<td>Ulcer: Imp, AFS: NS</td>
</tr>
<tr>
<td></td>
<td>BM-MNC BM MNC BM MNC</td>
<td>22</td>
<td>50</td>
<td>randomised</td>
<td></td>
<td>Time to Rx, sig</td>
</tr>
<tr>
<td></td>
<td>BM-MNC BM MNC BM MNC</td>
<td>22</td>
<td>50</td>
<td>randomised</td>
<td></td>
<td>Major Amp: NS</td>
</tr>
<tr>
<td></td>
<td>BM-MNC BM MNC BM MNC</td>
<td>22</td>
<td>50</td>
<td>randomised</td>
<td></td>
<td>AFS: sig, time to Rx: sig, Major Amp: NS</td>
</tr>
<tr>
<td></td>
<td>BM-MNC BM MNC BM MNC</td>
<td>22</td>
<td>50</td>
<td>randomised</td>
<td></td>
<td>Safety, feasibility</td>
</tr>
<tr>
<td></td>
<td>BM-MNC BM MNC BM MNC</td>
<td>22</td>
<td>50</td>
<td>randomised</td>
<td></td>
<td>ABPI, tCpO2, pain</td>
</tr>
<tr>
<td></td>
<td>BM-MNC BM MNC BM MNC</td>
<td>22</td>
<td>50</td>
<td>randomised</td>
<td></td>
<td>ABPI, AFS, Ulcer: Imp</td>
</tr>
<tr>
<td></td>
<td>BM-MNC BM MNC BM MNC</td>
<td>22</td>
<td>50</td>
<td>randomised</td>
<td></td>
<td>AFS: sig, time to Rx: sig, Major Amp: NS</td>
</tr>
<tr>
<td></td>
<td>BM-MNC BM MNC BM MNC</td>
<td>22</td>
<td>50</td>
<td>randomised</td>
<td></td>
<td>Safety, feasibility</td>
</tr>
<tr>
<td></td>
<td>BM-MNC BM MNC BM MNC</td>
<td>22</td>
<td>50</td>
<td>randomised</td>
<td></td>
<td>ABPI, tCpO2, pain</td>
</tr>
<tr>
<td></td>
<td>BM-MNC BM MNC BM MNC</td>
<td>22</td>
<td>50</td>
<td>randomised</td>
<td></td>
<td>ABPI, AFS, Ulcer: Imp</td>
</tr>
<tr>
<td></td>
<td>BM-MNC BM MNC BM MNC</td>
<td>22</td>
<td>50</td>
<td>randomised</td>
<td></td>
<td>AFS: sig, time to Rx: sig, Major Amp: NS</td>
</tr>
<tr>
<td></td>
<td>BM-MNC BM MNC BM MNC</td>
<td>22</td>
<td>50</td>
<td>randomised</td>
<td></td>
<td>Safety, feasibility</td>
</tr>
<tr>
<td></td>
<td>BM-MNC BM MNC BM MNC</td>
<td>22</td>
<td>50</td>
<td>randomised</td>
<td></td>
<td>ABPI, tCpO2, pain</td>
</tr>
<tr>
<td></td>
<td>BM-MNC BM MNC BM MNC</td>
<td>22</td>
<td>50</td>
<td>randomised</td>
<td></td>
<td>ABPI, AFS, Ulcer: Imp</td>
</tr>
<tr>
<td></td>
<td>BM-MNC BM MNC BM MNC</td>
<td>22</td>
<td>50</td>
<td>randomised</td>
<td></td>
<td>AFS: sig, time to Rx: sig, Major Amp: NS</td>
</tr>
<tr>
<td></td>
<td>BM-MNC BM MNC BM MNC</td>
<td>22</td>
<td>50</td>
<td>randomised</td>
<td></td>
<td>Safety, feasibility</td>
</tr>
<tr>
<td></td>
<td>BM-MNC BM MNC BM MNC</td>
<td>22</td>
<td>50</td>
<td>randomised</td>
<td></td>
<td>ABPI, tCpO2, pain</td>
</tr>
<tr>
<td></td>
<td>BM-MNC BM MNC BM MNC</td>
<td>22</td>
<td>50</td>
<td>randomised</td>
<td></td>
<td>ABPI, AFS, Ulcer: Imp</td>
</tr>
<tr>
<td></td>
<td>BM-MNC BM MNC BM MNC</td>
<td>22</td>
<td>50</td>
<td>randomised</td>
<td></td>
<td>AFS: sig, time to Rx: sig, Major Amp: NS</td>
</tr>
</tbody>
</table>
**Poor cell retention**

- Lack of objective endpoint measures
- Soup of cells not specific angiogenic cell type(s)

**Angiogenic factors**
- e.g. VEGF, bFGF
- TIE2
- CD16

**The Angiogenic Monocyte**

**ROAM-CLI study**

**Retention Of Angiogenic Monocytes in Critical Limb Ischaemia**

- Production Scientist Training
- Scale Up & Engineering
- Radiolabelling
- Authorisation

**From bench to bedside**

**Enhancing Cell Retention: Encapsulation**

**Cell Encapsulation**

- 2% 2.50% 3.00% 3.50% 4.00% 4.50%
- Microsphere diameter

- 200μm
Summary

- Global drive for regenerative medicine
- Translational studies: Clinicians, scientists, industry
- Potent cells
- Improve retention
- Objective outcome measures
- Well designed clinical trials

Acknowledgements

Academic Dept Vascular Surgery
Leeds University
Prof Alberto Smith
Prof Stuart Egginton
Mr Ashish Patel
Mr Adnan Bajwa

Universita Vita-Salute San Raffaele, Milan
Dr Francesca Ludwinski
Prof Michele De Palma
Dr Gopinath Damadoran
Miss Joanna Furmston

University College London
Mr Prakash Saha
Dr Suwan Jayasinghe
Mr Hany Zayed
Mr Oliver Lyons

Leicester University
Ms Susan Clark
Prof David Cousins
Ms Laura Harley

Dr Mohammed Ikram

KCL Cardiovascular Division
Prof Quingbo Xu
Dr Aleksandar Ivetic
Dr Richard Siow
Dr Emanuele De Rinaldis,
KCL Division of Imaging Sciences
Prof Eike Nagel
Dr Greg Mullen