Cardiac Stem Cells in Patients with Ischaemic Cardiomyopathy

Bolli R. et al.

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“Ischemic Cardiomyopathy refers to a state of severe LV dysfunction caused by chronic coronary artery disease (CAD).”

Previous Studies

- 10 years ago: first success in infusion of bone marrow stem cells in mice and a patient
- rather modest successes
- application mostly in AMI
- encouraging results of application of CSCs in animal models

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2 HEUSCH G.. SCIPIO brings new momentum to cardiac cell therapy. (2011)
Methods

- phase 1, open-label trial
- inclusion criteria
  - CABG
  - LVEF ≤ 40%
  - myocardial infarction with evidence of a scar
  - < 75 years

<table>
<thead>
<tr>
<th>Phase</th>
<th>Treated Patients</th>
<th>Control Group Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Phase A</td>
<td>9</td>
<td>4</td>
</tr>
<tr>
<td>Phase B</td>
<td>7</td>
<td>3</td>
</tr>
</tbody>
</table>
Methods

- right atrial appendage
- Ham’s F12 medium containing Collagenase NB 6
- isolation of c-kit-positive CSCs
- FISH
- PCR
- $p16^{INK4a}$
- FACS

Figure 1&2: BOLLI, R. et al.. Cardiac stem cells in patients with ischaemic cardiomyopathy (SCIPIO): initial results of a randomised phase 1 trial (2011)
Methods

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Figure 1&2: BOLLI, R. et al.. Cardiac stem cells in patients with ischaemic cardiomyopathy (SCIPIO): initial results of a randomised phase 1 trial (2011)
c-kit-positive cells: 88%
lineage-positive cells: 1,1%

Figure 3: BOLLI, R. et al.. Cardiac stem cells in patients with ischaemic cardiomyopathy (SCIPIO): initial results of a randomised phase 1 trial (2011)
Methods

- intracoronary infusion at a mean of 113d after CABG
- 1 million CSCs into anterior wall infarcts
- 500 000 CSCs into LCX or RCA
### Methods

<table>
<thead>
<tr>
<th></th>
<th>2D/3D transthoracic echocardiogram</th>
<th>Routine laboratory tests</th>
<th>Physical examination</th>
<th>NYHA class assessment</th>
<th>MLHFQ</th>
<th>cMRI</th>
<th>24h ECG</th>
</tr>
</thead>
<tbody>
<tr>
<td>Before CSC infusion</td>
<td>×</td>
<td>×</td>
<td>×</td>
<td>×</td>
<td>×</td>
<td>×</td>
<td>×</td>
</tr>
<tr>
<td>24h</td>
<td></td>
<td>×</td>
<td>×</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1 week</td>
<td></td>
<td>×</td>
<td>×</td>
<td></td>
<td></td>
<td></td>
<td>×</td>
</tr>
<tr>
<td>2 weeks</td>
<td></td>
<td>×</td>
<td>×</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1 month</td>
<td>×</td>
<td>×</td>
<td>×</td>
<td></td>
<td></td>
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<td></td>
</tr>
<tr>
<td>4 months</td>
<td>×</td>
<td>×</td>
<td>×</td>
<td>×</td>
<td>×</td>
<td></td>
<td>×</td>
</tr>
<tr>
<td>8 months</td>
<td>×</td>
<td>×</td>
<td>×</td>
<td></td>
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<td></td>
</tr>
<tr>
<td>12 months</td>
<td>×</td>
<td>×</td>
<td>×</td>
<td>×</td>
<td>×</td>
<td></td>
<td>×</td>
</tr>
</tbody>
</table>
Results

Ejection Fraction

Figure 5: BOLLI, R. et al.. Cardiac stem cells in patients with ischaemic cardiomyopathy (SCIPIO): initial results of a randomised phase 1 trial (2011)
Results

Wall Motion Score Index

Figure 6: BOLLI, R. et al.. Cardiac stem cells in patients with ischaemic cardiomyopathy (SCIPIO): initial results of a randomised phase 1 trial (2011)
Results

Infarct Size

Figure 7&8: BOLLI, R. et al.. Cardiac stem cells in patients with ischaemic cardiomyopathy (SCIPIO): initial results of a randomised phase 1 trial (2011)
Results

NYHA Functional Class

Figure 9: BOLLI, R. et al. Cardiac stem cells in patients with ischaemic cardiomyopathy (SCIPIO): initial results of a randomised phase 1 trial (2011)
Results

MLHFQ

Figure 10: BOLLI, R. et al. Cardiac stem cells in patients with ischaemic cardiomyopathy (SCIPIO): initial results of a randomised phase 1 trial (2011)
### Results

#### Adverse Events

<table>
<thead>
<tr>
<th>Event</th>
<th>Treatment group (n=16)</th>
<th>Control group (n=7)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Death</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Myocardial infarction (peri-procedural or post-procedural)</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>New tumour</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Ventricular arrhythmia</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Systemic infection (within 1 year)</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Stroke</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Allergic reaction</td>
<td>0</td>
<td>NA</td>
</tr>
<tr>
<td>Procedure-related event*</td>
<td>1 (6%)</td>
<td>NA</td>
</tr>
<tr>
<td>Revascularisation</td>
<td>0</td>
<td>1 (14%)</td>
</tr>
<tr>
<td>Hospital admission for heart failure†</td>
<td>1 (6%)</td>
<td>0</td>
</tr>
<tr>
<td>Hospital admission for angina</td>
<td>1 (6%)</td>
<td>2 (29%)</td>
</tr>
</tbody>
</table>

NA = not applicable. *Tortuous left internal mammary artery engaged for cardiac-stem-cell infusion had intimal dissection after balloon deflation; drug-eluting stent was placed without complication. †Secondary to worsening valvular disease.

Table 2: Adverse events in cardiac-stem-cell-treated and control patients

Table 1: BOLLI, R. et al.. Cardiac stem cells in patients with ischaemic cardiomyopathy (SCIPIO): initial results of a randomised phase 1 trial (2011)
Conclusion

- congruent with preclinical studies
- 2 theories concerning mechanism
  - CSCs differentiate
  - activation of resident CSCs
- positive and no adverse effects, but only a small number of patients and no masking