PreSERVE-AMI:  
A randomized double blind placebo controlled trial of intracoronary infusion of CD34+ cells for LVSD s/p STEMI

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Disclosures

• None
Cochrane Summaries
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**Stem Cell therapy for chronic ischemic heart disease and heart failure**

- 23 RCTs
- 1,255 patients
- Autologous bone marrow stem cell treatment
- > 12 months
- Mortality: RR 0.28, 95% CI 0.14 - 0.53; p = 0.0001 (8 studies, 494 patients with low quality of evidence)
- Rehospitalization: RR 0.26, 95% CI 0.07 - 0.94, p = 0.04
- < 12 month data
- - no benefit on mortality or morbidity
- LVEF: improved in 6 studies, n = 254 patients; p = 0.02

- Conclusions: moderate quality evidence supporting an improvement in LVEF after ABMC administration; lesser quality evidence suggesting longer term benefit
STEM CELL TREATMENTS FOR ACUTE MYOCARDIAL INFARCTION

- 38 RCTs
- 1,765 patients
- Mortality

**OR**

- Morbidity (defined as re-infarction, hospital re-admission, restenosis and TVR)
  - RR 0.70; (95% CI 0.4 – 1.21)

- LVEF: increased (weighted mean difference 2.87; (95% CI 2.57 – 3.73); and sustained over 12 -61 months  WMD 3.75; (95% CI 2.57 – 4.93)

- Positive correlation between dose of cells administered and timing
- BUT significant heterogeneity in the mortality results related mostly to impact of contemporary ACS care. A definitive mortality trial will require a large population
PreSERVE-AMI

• **Strengths:**
  - encouraging phase II data
  - sufficient data, RE: change in LVEF, to adequately power a phase III trial
  - additional data to support CD34+ cells as a target regenerative therapy to restore LV function
  - SAFETY

• **Concerns**
  - underpowered to use mortality as a valid endpoint
  - failure to demonstrate a reduction in the extent of scar/ischemia
  - absence of mechanistic insight RE: engraftment vs. paracrine effect

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Conclusions

• Tread cautiously – approximately 4,000 patients with LV dysfunction, acute or chronic, have been treated with stem cells with modest to minimal signals of meaningful benefit

• Is it time to pause – feasibility and safety are now well-established
  – Pursue more mechanistic data
  – Re-assess endpoints: is LVEF only a surrogate marker of responsiveness?
  – Consider issues of scale and broader applicability
  – Be aware of concerns RE: relationship of reported successes and likelihood of research discrepancies (Imperial College, London, 2014)