Evolution of left ventricular function after Wharton's jelly mesenchymal stem cells transcoronary administration: 5-year follow up in a pilot cohort of CIRCULATE-AMI Randomized Trial

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Introduction: CIRCULATE-Acute Myocardial Infarction is a double-blind controlled trial randomizing (RCT) in 105 consecutive patients with their first, large AMI (cMRI-LVEF $\leq$45% and/or cMRI-infarct size $\geq$10% of LV) with successful infarct-related artery (IRA) primary percutaneous coronary intervention (pPCI) to transcoronary administration of Wharton's Jelly Mesenchymal Stem Cells (WJMSCs) vs. placebo (2:1). The pilot study cohort (PSC) preceded the RCT.

Aim: To evaluate WJMSCs long-term safety, and evolution of left-ventricular (LV) function in CIRCULATE-AMI PSC.

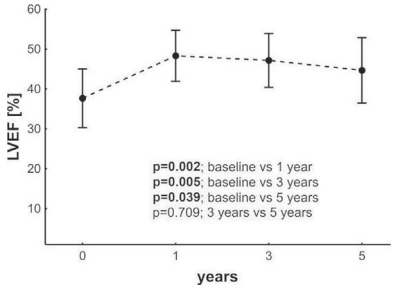
Material and methods: 30 000 000 WJMSCs (50% labelled with 99mTc-exametazime) were administered via IRA in a ten-patient PCS (age 32–65 years, peak hs-Troponin T 17.3±9.1ng/mL and peak CK-MB 533±89U/L, cMRI-LVEF 40.3±2.7% and infarct size 20.1±2.8%) at ≈5–7 days after AMI using a cell delivery-dedicated, coronary-non-occlusive method. Other treatments were per guidelines.

WJMSCs showed an unprecedented high myocardial uptake (30.2±5.3%; 95% CI 26.9–33.5%), corresponding to ≈9×10 000 000 cells retention in the infarct zone – in absence of epicardial flow or myocardial perfusion impairment (TIMI-3 in all; cTFC 45±8 vs. 44±9, p=0.51) or any hs-Troponin T elevation. Five-year follow up included cardiac Magnetic Resonance Imaging (cMRI) (at baseline, 1 year and 3 years) and detailed echocardiography (echo) at baseline, 1 year, 3 years and 5 years.

Results: By 5 years, one patient died from a new, non-index territory AMI. There were no other cardiovascular events and MACCE that might be related to WJMSCs transplantation.

On echo (Fig), there was an increase in left ventricular ejection fraction (LVEF) between WJMSCs administration point and 1 year (37.7±2.9% vs. 48.3±2.5%, p=0.002) that was sustained at 3 years (47.2±2.6%, p=0.005 vs. baseline) and at 5 years: (44.7±3.2%, p=0.039 vs. baseline). LVEF reached a peak at 1 year after the AMI and WJMSCs transfer (Fig). cMRI data (obtained up to 3 years; 1 year 41.9±2.6% vs. 51.0±3.3%, p<0.01; 3 years 52.2±4.0%, p<0.01 vs. baseline) were consistent with the echo LVEF assessment.

Conclusions: 5-year follow up in CIRCULATE-AMI PSC indicates that WJMSC transcoronary application is safe and may be associated with an LVEF improvement. The magnitude of LV increase appears to peak at 1 year, suggesting a potential role for repeated WJMSCs administration(s). Currently running double-blind RCT will provide placebo-controlled insights into the WJMSCs effect(s) on changes in LV function, remodelling, scar reduction and clinical outcomes.



Echo-LVEF evolution