Congestive Heart Failure Cardiopoietic Regenerative Therapy (CHART-1): Clinical Trial Primary Outcomes

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Disclosures

Jozef Bartunek is member of an institution which has been a co-founder of Cardio3Biosciences (now Celyad)

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Cardiopoietic cells: a unique approach for advanced ischemic heart failure patients

- **Ischemic heart failure** with extensive cardiac enlargement yields poor outcome, a still unmet clinical need
- Cell therapy is a paradigm-shifting intervention that targets **organ restoration**
- Cardiopoietic cells derived by **cardiogenic specification of patient's own mesenchymal stem cells** showed clinical promise as next generation therapy

Trial Objective

To validate the efficacy and safety of cardiopoietic cells delivered endomyocardially via a retention-enhanced injection catheter in advanced ischemic heart failure

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CHART-1: the largest cell therapy trial in ischemic heart failure

- Prospective, multicenter, randomized, sham-controlled, patient/evaluator-blinded clinical trial in 39 hospitals (Europe and Israel)

- Patients with ischemic heart failure on standard-of-care:
  - *Active* group: cardiopoietic cell therapy (C3BS-CQR-1, Celyad, Mont St Guibert, BE)
  - *Control* group: sham procedure

- Endomyocardial delivery: **retention-enhanced** delivery C-Cath$_{ez}$ catheter (Celyad, Mont St. Guibert, BE)

- Primary end point: **Finkelstein Schoenfeld hierarchical composite**
  - Each patient compared to every other patient with respect to all cause mortality, number of worsening HF events, changes in MLWHQ, 6MWD, LV ESV and LV EF
  - Statistical power: 120 patients per group to provide 87% power for Mann-Whitney estimator of 0.61 (values > 0.5 favors the treatment)

CHART-1: Key Findings

In the overall study patients:

- The primary composite end-points **neutral** (Mann-Whitney estimator g=0.54, 95% CI 0.47-0.61, p=0.27)
- Cardiopoietic cell treatment was **safe**
- **Lower incidence of sudden death and aborted sudden death** in the active group (HR 0.16, 95%CI 0.02-1.23, p=0.04)

CHART-1: Key Findings

Exploratory analysis by markers of baseline HF severity:

- In patients with baseline LV end-diastolic volume (EDV) 200-370 mL (60% of patients), **probability of a better outcom**e, Mann-Whitney favored the cardiopoietic cell therapy (g=0.61, 95% CI 0.52-0.70, p=0.015)

- **Benefit related to consistent trends:**
  - **Mortality** (4.5 vs 6.2%) **and worsening heart failure events** (12.2% vs 17.7%) in active vs control group
  - **Quality of life:** significant improvement for 68% active vs 49% control group
  - **6 Min walk distance:** improvement for 43% active vs 25% control group
  - In parallel, higher degree of **LV ESV improvement or stabilization** in active

Exploratory analysis by treatment intensity:

- In patients with ≤19 injections, **probability of a better outcome**, Mann-Whitney favored the cardiopoietic cell therapy (g=0.59, 95% CI 0.51-0.67, p=0.034)
- In patients with LVEDV 200-370 mL and ≤19 injections, Mann-Whitney corroborated favorable treatment effect therapy (g=0.70, 95% CI 0.59-0.81, p<0.001)

CHART-1 Key Learnings

- The CHART-1 trial identified a clinically relevant patient population with elevated baseline LV end-diastolic volume that benefited from cardiopoietic cell treatment

- Optimized treatment intensity together with disease severity-targeted patient selection should be considered for future trials and/or potential cell therapy application in heart failure

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