the composite outcome of HF admissions and death in frail than in non-frail patients (HR 0.42 (CI 0.19-0.89) vs. HR 2.5 (CI 0.46-13.69)). Finally, one study investigated the effect of telemonitoring, which was comparable regarding the composite outcome of hospitalisations and death in frail and non-frail patients (HR 0.38 (CI 0.08-2.07) and HR 0.45 (CI 0.18-1.11), respectively). HF related complication rates (hospitalisations, death) were consistently higher in frail than in non-frail patients. The incidence of adverse events between the intervention and control groups did not differ among the frailty groups.
Conclusion: In frail patients, HF therapies are equally or more effective in improving outcomes and equally safe compared to non-frail patients. With higher complication rates in frail patients, the absolute benefit is even greater. Clinicians should therefore not withhold guideline-directed treatment from frail HF patients.

Heart Failure – Chronic Heart Failure, Treatment

First-in-human study of left ventricular remuscularization with induced pluripotent stem cell derived cardiomyocyte spheroids for severe ischemic heart failure patients: preliminary LAPiS study result

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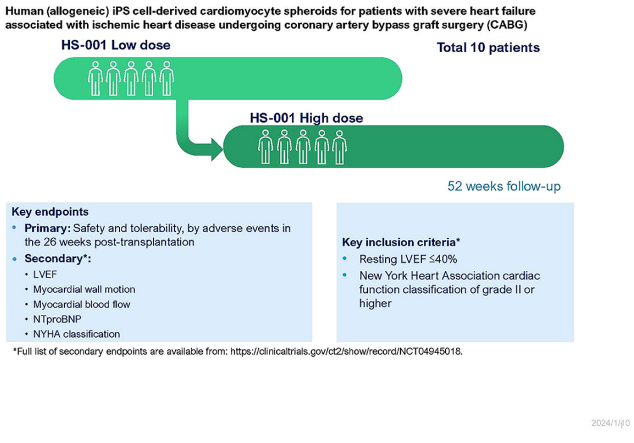
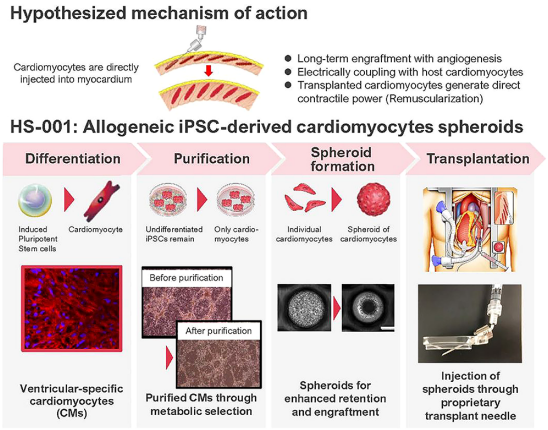
Funding Acknowledgements: Type of funding sources: Private company. Main funding source(s): Heartseed Inc.

Background: Heart failure is a devastating disease causing significant morbidity and mortality despite new treatment options approved in the past 10 years. There is a strong impetus to develop alternative treatment strategies because therapeutic options for severe heart failure (sHF) are essentially limited to mechanical circulatory support and heart transplantation. The LAPiS study is a first-in-human, phase I/II clinical trial of allogeneic iPSCs-derived cardiomyocyte spheroids (HS-001), for the treatment of patients with sHF.
Purpose: The LAPiS study evaluates the safety and efficacy after HS-001 transplantation.
Methods: LAPiS is a single-arm phase I/II, open-label, multi-centre clinical trial of HS-001 transplantation. A total of 10 patients with sHF due to ischemic heart disease will be given HS-001 by multiple intramyocardial injections during coronary artery bypass grafting (CABG) using a specially designed needle. The first 5 patients will receive a total of 50 million cells and the second cohort of 5 patients will receive a total of 150 million cells. HS-001 is manufactured from human-iPSCs under GMP, which are differentiated into ventricular-specific cardiomyocytes and purified (>98% cardiomyocyte identity) via metabolic selection, before formulation to generate ~150-μm cardiomyocyte spheroids to improve retention. The hypothesized mode of action is remuscularization of the left ventricle wall, intending to trigger reverse remodeling, improvement of cardiac function, and ultimately a survival benefit for sHF patients. Immunosuppression is provided during the study. The study protocol duration is 12 months.
Results: Our institute has enrolled 3 sHF patients into the low-dose cohort of the LAPiS study. Baseline patient characteristics were: NYHA class 3, LVEF 17-26%, and NT-proBNP 3935-9157 pg/ml. Two of the patients have follow-up beyond the planned interim 6-month analysis after HS-001 transplantation. At the 6-month visit, both patients had improved wall motion by longitudinal strain, especially for segments where HS-001 was transplanted. All patients improved symptomatically by NYHA score (1-2 class improvement), and on objective testing by echocardiography (LVEF: 4-20% improvement) or biochemically (NT-proBNP: 37-80% reduction). Serious adverse event (SAE) related to the surgical procedure was atrial fibrillation (1 patient). No life-threatening arrhythmia was observed, although asymptomatic short-duration accelerated idioventricular rhythm 1-2 weeks after transplantation was detected.
Conclusion: The LAPiS study introduces the first and only iPSC-derived cardiomyocyte spheroid therapy for sHF. The early results demonstrate the potential to deliver functional improvement in patients with advanced heart failure where improvements due to CABG alone are limited. The managed risks of immunosuppression and graft-related arrhythmia pave the way for this direct myocardial therapy to become a practical and effective approach.



Picure 1



Picure 2

Heart Failure – Chronic Heart Failure, Treatment

Cardiac rhythm management devices in patients with heart failure - preliminary results of the DIRECT HF international survey on healthcare professionals' educational needs

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On behalf of: DIRECT HF Working Group
Funding Acknowledgements: Type of funding sources: Private company. Main funding source(s): MedtronicA. Bayes-Genis, B. Bozkurt, L. Hill, A. Mebazaa, G. Rosano, A.M. Russo, N. Sato (working group members).

Background: Guidelines for the management of heart failure (HF) recommend cardiac rhythm management (CRM) devices - implantable cardioverter-defibrillators (ICDs) and cardiac resynchronization therapy (CRT) - for selected patients with HF with reduced ejection fraction (HFrEF). However, CRM devices are underutilized in clinical practice and their appropriate use is debated.
Purpose: DIRECT HF (DevIce Rhythm managEment for Cardiac Therapy in Heart Failure) is an educational programme aimed at reemphasizing the role of CRM devices and providing practical guidance for their optimal use. We aimed to assess healthcare professionals' educational needs by conducting an international survey.
Methods: A working group of 16 heart rhythm specialists, HF cardiologists and HF nurses developed a questionnaire encompassing 32 questions on eligibility criteria and main barriers to the provision of guideline-recommended device therapy. The link to the online, anonymous survey was disseminated via email and social media.
Results: Between Nov 8 and Dec 8, 2023, the survey was completed by 335 respondents (of whom 35% were females) in 64 countries. Geographic representation was as follows: Americas, 10%; Asia-Pacific, 42%; Europe & Central Asia, 42%; Middle East & Africa, 6%. The majority (76%) of respondents were cardiologists. For

54% of participants, discussing treatment options with their patients and involving them in a shared decision-making process was fairly or very challenging. Among the respondents' institutions, 66% had a multidisciplinary HF team. 85% of respondents prioritized initiating all foundational HF drugs, whereas 15% focused on uptitrating some of them. Most participants (79%) were fairly or very confident in identifying patients with HFrEF who are eligible for CRT or for an ICD. Among the criteria considered important for CRT eligibility, the two most frequently cited were QRS duration (83%) and LVEF (78%) (Figure 1). The most frequently cited criteria for ICD eligibility were LVEF (74%) and a history of ventricular arrhythmia (70%) (Figure 2). The main perceived barriers to the provision of guideline-recommended device therapy were uncertainties about the appropriate timing of device therapy, uncertainties about appropriate patient selection, and lack of awareness about devices. The tools considered most helpful in helping implement guideline-directed device therapy were expert consensus documents with practical guidance and algorithms, user-friendly guideline summaries, and institutional protocols for patient selection and enhanced referrals.

Conclusions: The preliminary results of this international survey provide valuable insight into healthcare professionals' educational needs and knowledge gaps with respect to the management of patients with HFrEF and the use of CRM devices.

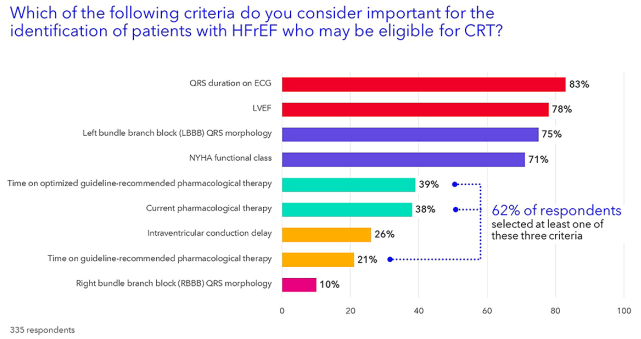


Figure 1

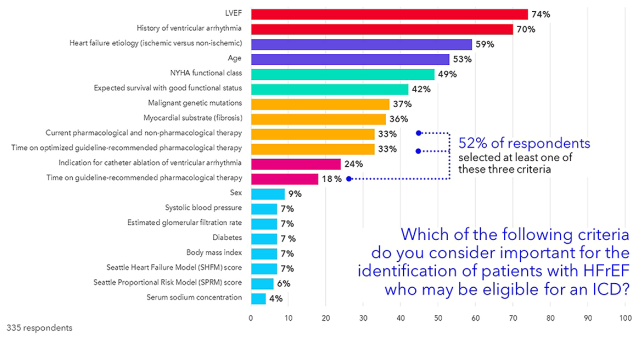


Figure 2

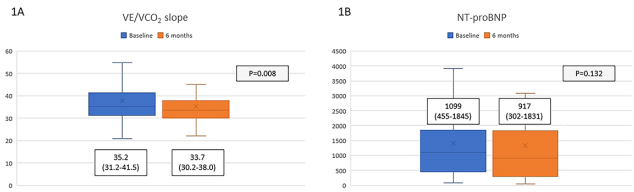
Heart Failure – Chronic Heart Failure, Treatment

Dapagliflozin effect on cardiopulmonary function, reverse cardiac remodelling and biomarkers in a cohort of HFrEF patients

NCT05770167M Mapelli[1]; I Mattavelli[1]; E Salvioni[1]; A Nepitella[1]; J Campodonico[1]; C Vignati[1]; V Mantegazza[1]; A Garlasche'[1]; A Nava[1]; A Piotti[1]; P Gugliandolo[1]; R Caputo[1]; C Paganin[1]; P Agostoni[1]; [1]*Monzino Cardiology Centre, Milan, Italy*;

Funding Acknowledgements: Type of funding sources: None.

Background: Sodium-glucose co-transporter-2 inhibitors (SGLT2i) represent a standard therapy for heart failure with reduced ejection fraction (HFrEF) patients. We aim to assess the effects of Dapagliflozin on exercise capacity, cardiac biomarkers, fluid retention, renal and pulmonary function.
Methods: We prospectively enrolled a cohort of stable HFrEF outpatients (LVEF<40%, NYHA, class II or III) eligible for SGLT2i therapy and performed serial cardiopulmonary exercise tests (CPET), pulmonary function tests (spirometry and diffusing capacity of the lungs for carbon monoxide, DLCO), laboratory and echocardiographic assessments at baseline and after 6 months of therapy.
Results: 75 patients (85% males, age 65 ± 13 years) on optimal medical therapy (80% sacubitril/valsartan; 96% β-blockers, 80% MRAs) were evaluated. We observed an increase in LVEF (34.7 ± 8.2 vs. 37.4 ± 9.1%; $p < 0.001$) and a reduction in left ventricular end-diastolic (EDV) and end-systolic (ESV) volumes (EDV: 193 ± 77 vs. 188± 75 mL, $p < 0.001$; ESV: 129 ± 67 vs. 123± 65 mL, $p < 0.001$). There were no significant changes in peak oxygen uptake, while ventilatory efficiency during exercise (VE/VCO2 slope) showed a significant improvement (fig.1A). Hemoglobin (Hb) and hematocrit levels improved, while renal function sodium and potassium levels remained stable, as did blood urea nitrogen, while BNP, NT-proBNP (fig. 1B), glycated Hb, ST2, and hs-TNI did not reach statistical significance in this sub-population. NYHA functional class improved, together with a significant decrease of MECKI (Metabolic Exercise test data combined with Cardiac and Kidney Indexes) score, from 3.6% [2.2-8.7] to 2.9% [1.2-5.2] ($p < 0.001$) with a positive impact on 2-year prognosis.
Conclusion: Medium-term treatment with Dapagliflozin demonstrated beneficial effects on LV remodelling, exercise ventilatory efficiency and functional status. In particular, an improvement in VE/VCO2 slope and MECKI score paralleled with an enhancement in echocardiographic parameters and NYHA functional class was observed. However, our study did not detect medium-term effects of Dapagliflozin on spirometry values, DLCO, fluid retention and NT-proBNP. These results suggest that some favourable effects could unfold over a longer period of time. Further studies with longer follow up are desirable to assess Dapagliflozin effects even in such a well-treated HF population.



Figure

	Baseline (mean ± SD)	6 months (mean ± SD)	p
BMI (kg/m²)	26.5± 3.6	26.4± 3.4	0.133
Peak VO_2 (mL/min/kg)	16.5± 5.1	16.5± 4.6	0.365
Peak workload (Watt)	111.3± 44.9	113.5± 46.9	0.710
VE/VCO_2	37.9± 10.7	35.4± 7.9	0.006
Hemoglobin (g/dL)	13.8± 1.5	14.6± 1.7	0.000
Hematocrit (%)	40.8± 5.5	45.0± 13.1	0.009
Creatinine (mg/dL)	1.1± 0.3	1.2± 0.3	0.108
Blood urea nitrogen (mg/dL)	51.3± 19.1	49.5± 19.2	0.330
Sodium (mmol/L)	140.3± 2.0	140.6± 2.2	0.378
Potassium (mmol/L)	4.4± 0.4	4.4± 0.4	0.478

Table

Heart Failure – Chronic Heart Failure, Treatment

A real-world population with HFrEF treated with dapagliflozin or empagliflozin: a comparative analysis with DAPA-HF and EMPEROR REDUCED studies

M Mapelli[1]; I Irene Mattavelli[1]; E Salvioni[1]; R Caputo[1]; C Paganin[1]; A Nepitella[1]; J Campodonico[1]; C Vignati[1]; V Mantegazza[1]; A Garlasche'[1]; A Nava[1]; A Piotti[1]; P Gugliandolo[1]; P Agostoni[1]; [1]*Monzino Cardiology Centre, Milan, Italy*;

Funding Acknowledgements: Type of funding sources: None.

Introduction: SGLT2 inhibitors (dapagliflozin and empagliflozin) have demonstrated cardiovascular benefits in landmark trials, becoming pivotal in treating HFrEF, as confirmed by the EMPEROR-Reduced and DAPA-HF. We aimed to compare the characteristics of a real-world population assigned to treatment with either empagliflozin or dapagliflozin against the respective registrative trials.
Methods: We retrospectively compared the baseline characteristics of consecutive stable HFrEF patients at the time of treatment prescription against the respective clinical trials. The analysis focused on demographic and clinical parameters to explore potential differences.
Results: We analysed data from 278 patients treated with dapagliflozin and 98 patients treated with empagliflozin, comparing them with DAPA-HF (n = 2373) and EMPEROR-Reduced (n = 1863) trials, respectively. As for Dapagliflozin, in our population there was an equal sex distribution, and patients had a similar LVEF compared to the DAPA-HF trial. Notably, a significantly higher percentage of patients were in