Diabetic Cardiomyopathy:
Baseline Characteristics of patients enrolled into the ARISE-HF trial

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BACKGROUND

Diabetic Cardiomyopathy (DbCM) is a severe complication of diabetes and a cause of HF in the absence of other causes of cardiac dysfunction such as coronary artery disease (CAD), clinically relevant arrhythmias, severe valvular heart disease, and uncontrolled blood pressure. Hyperactivation of the polyol pathway is one of the primary mechanisms contributing to the development of DbCM, which evolves over time into overt HF. Aldose reductase (AR) catalyzes the first and rate-limiting step in the polyol pathway, and AR inhibition has been shown to reduce diabetic complications including DbCM.

PURPOSE

The objective of this analysis was to describe a unique cohort of patients with DbCM at high risk of progression to overt HF enrolled in the ARISE-HF study.

METHODS

ARISE-HF trial is a global phase 3 randomized study evaluating the safety and efficacy of two doses a novel aldose reductase inhibitor (AT-001) versus placebo to improve or prevent decline in cardiac functional capacity in individuals with DbCM. DbCM was defined by elevated cardiac biomarkers and/or the presence of cardiac structural/functional abnormalities along with impaired cardiac functional capacity defined as peak VO2 uptake below 75% of predicted normal on a cardiopulmonary exercise test.

RESULTS

684 study participants with DbCM are described in Table 1. 50% of patients were female, with a mean age 67.5 years. Patients enrolled had a duration of diabetes of 14 years, with excellent glycemic control at baseline (HbA1c of 6.99%). The median NT-proBNP was 71 ng/L and hs-cTnT was 9 ng/L. Among echocardiographic abnormalities evaluated at enrollment, the most common were abnormal global longitudinal strain and impaired diastolic relaxation.

	n= 684
Age, yrs	67.5 (7.2)
Female, n, %	341 (50%)
Race, n, %	
White	562 (82%)
Black or African American	47 (7%)
Others	74 (11%)
Height, cm	167.5 (10.0)
Weight, kg	85.9 (17.4)
BMI, kg/m²	30.5 (4.5)
SBP, mmHg	129.8 (12.8)
DBP, mmHg	75.8 (9.1)
Medical History	
Hypertension, n, %	467 (68%)
Dyslipidemia, n, %	108 (16%)
Duration of T2DM, yrs	14.0 (9.2)
Concomitant medications, n, %	
Statins	490 (72%)
ACE inhibitors or ARBs	458 (67%)
B-blockers	139 (20%)
MRAs	12 (2%)
HCTZ	119 (17%)
SGLT2 inhibitors	184 (27%)
GLP1RA	140 (21%)
Metformin	462 (68%)
Insulin	163 (24%)

RESULTS

Laboratory tests	
NTproBNP, ng/L	71 (35-134)
Hs-Tnt, ng/L	9 (6-12)
HbA1c, %	6.99 (0.79)
Hgb, g/L	13.4 (1.4)
eGFR, mL/min/1.73	80.4 (16.3)
UACR, mg/g	8 (15-42)
Abnormal Echocardiogram, n, %	
GLS < -16%	167 (25%)
E/e' ≥ 13	163 (24%)
LAVI > 34 mL/m2	84 (12%)
LVMI ≥95 g/m² in men and ≥115 g/m² in women	77 (11%)
RVSP > 35 mmHg	26 (4%)
Questionnaires	
mKCCQ	90.3 (14.6)
PASE score	154.3 (89.6)
CPET	
PeakVO_2, ml/kg/min	15.7 (3.8)
VE/VCO_2 slope	31.2 (5.4)

CONCLUSIONS

- The ARISE-HF study is an ongoing placebo-controlled phase 3 clinic trial evaluating the safety and efficacy of a novel highly selective aldose reductase inhibitor (AT-001) on cardiac functional capacity in individuals with DbCM.
- The baseline analysis of patients enrolled into the ARISE-HF trial describes a cohort of persons with DbCM at high risk of progression to overt HF.
- Individuals with DbCM frequently have significant reduction in cardiac functional capacity and detectable cardiac changes despite good glucose control.