

Ertugliflozin to Reduce Arrhythmic burden in ICD/CRT patients (ERASe-Trial) – a phase III Study

Dirk von Lewinski¹, Norbert J Tripolt², Harald Sourij², Abderrahim Oulhaj³, Hannes Alber⁴, Marianne Gwechenberger⁵, Martin Martinek⁶, Michael Nürnberg⁷, Franz Xavier Roithinger⁸, Clemens Steinwender⁹, Markus Stühlinger¹⁰, Ursula Rohrer¹, Martin Manninger-Wünscher¹, Daniel Scherr, MD¹ on behalf of the ERASe study group

¹Medical University of Graz, Department of Internal Medicine, Division of Cardiology, 8010 Graz, Austria. ²Medical University of Graz, Department of Internal Medicine, Division of Endocrinology and Diabetology, 8010 Graz, Austria. ³College of Medicine and Health Sciences, United Arab Emirates University, P.O.Box 17666, Al-Ain, United Arab Emirates. ⁴Klinikum Klagenfurt, Abteilung für Innere Medizin und Kardiologie ⁵Medical University of Vienna, Department of Cardiology, 1090 Vienna, Austria. ⁶Ordensklinikum Linz Elisabethinen, Innere Medizin 2 mit Kardiologie, Angiologie und Intensivmedizin ⁷Klinik Ottakring, Abteilung für Kardiologie, Wien ⁸Landesklinikum Wiener Neustadt, Abteilung für Innere Medizin, Kardiologie und Nephrologie, Wiener Neustadt ⁹Kepler University Hospital Linz, Department of Cardiology and Intensive Care Medicine, Linz, Austria. ¹⁰Medical University of Innsbruck, Univ. Clinic of Internal Medicine III / Cardiology and Angiology, 6020 Innsbruck, Austria

Hypothesis

- Treatment with the SGLT-2 inhibitor ertugliflozin will reduce sVT/VF episodes more effectively than placebo within 12 months

Background and intervention

Sodium glucose cotransporter 2 (SGLT2) have proven profound positive effects in heart failure with reduced ejection fraction (HFrEF). These effects are independent from the presence of diabetes. Since SGLT2 receptors are not expressed in human myocardium, these cardioprotective effects rather are indirect or pleiotropic. Besides metabolic effects anti-inflammatory anti-fibrotic properties are discussed.

Ventricular arrhythmias are a typical feature of advanced heart failure and account for a large proportion of cardiac death in this population. Implantation of an ICD is a class IA recommendation in the ESC heart failure guidelines both in secondary prevention and primary prevention. Despite a strong correlation of ventricular arrhythmias with heart failure, the impact of SGLT2 inhibitors on the arrhythmic burden has not been prospectively investigated, yet. The medical intervention will be orally administered Ertugliflozin, 5mg or placebo once daily

Inclusion and exclusion criteria

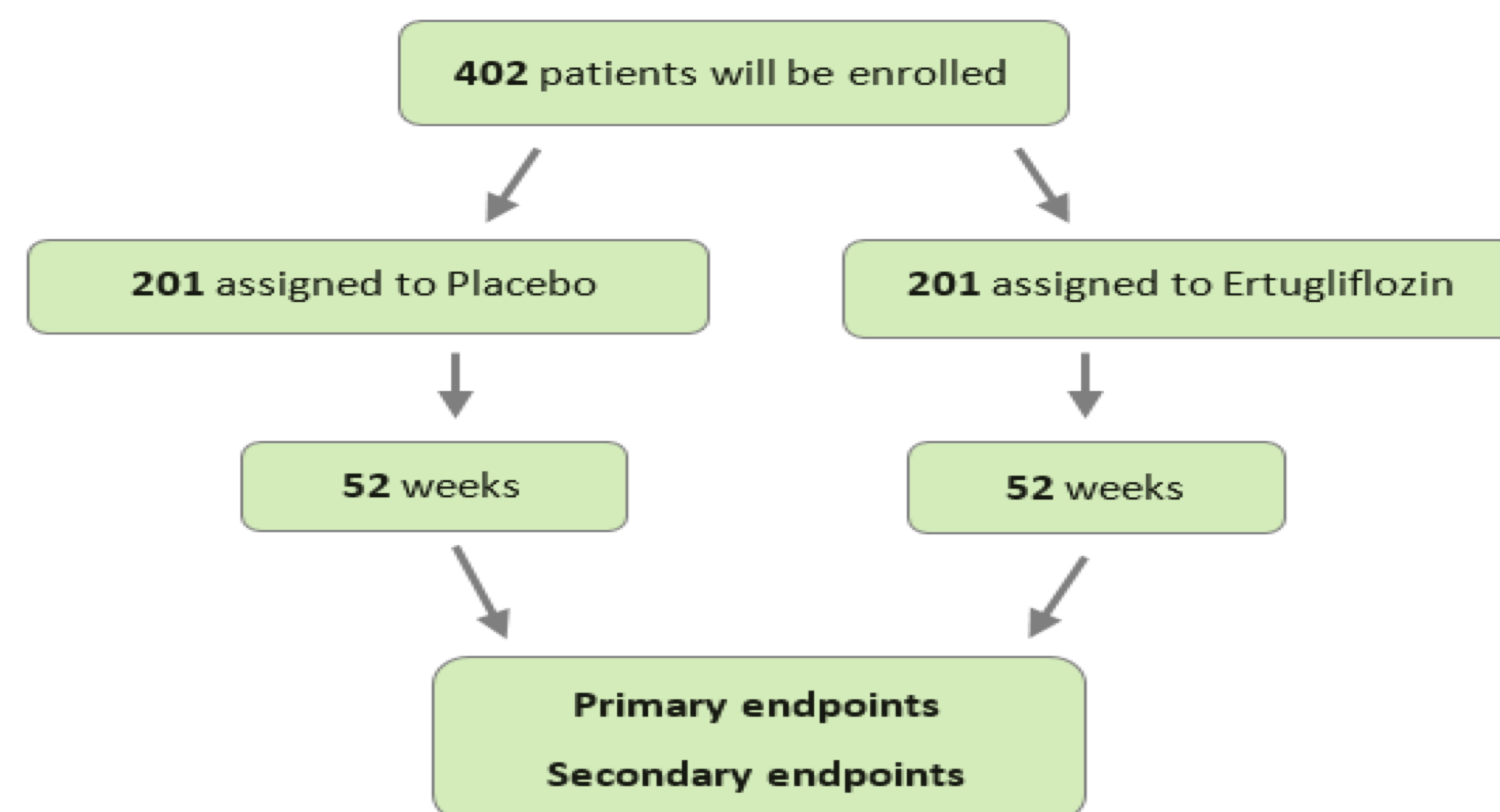
Inclusion criteria

- 1) HFrEF or HFmrEF and ICD±CRT therapy > 3 months
- 2) ≥ 10 documented non-sustained VTs within the last 12 months plus
 - nt-proBNP > 500pg/mL or
 - LV-EF < 35% or
 - hospitalization for heart failure within the last 12 months or
 - >100nsVTs within the last 12 mo.- > 1 sVT/VF within the last 12 mo.
- 3) Informed consent has to be given in written form.
- 4) eGFR > 30 ml/min/1.73m²
- 5) Blood pressure before first drug dosing: RR_{systolic} >100mmHg
- 6) Blood pressure before first drug dosing: RR_{diastolic} >60mmHg
- 7) 18 – 80 years of age

Exclusion criteria

- 1) Any other form of diabetes mellitus than type 2 diabetes mellitus, history of diabetic ketoacidosis
- 2) Ongoing ventricular arrhythmia
- 3) Known allergy to SGLT-2 inhibitors
- 4) Hemodynamic instability as defined by intravenous administration of catecholamine, calcium-sensitizers or phosphodiesterase inhibitors
- 5) >1 episode of severe hypoglycemia within the last 6 months under treatment with insulin or sulfonylurea
- 6) planned catheter ablation for ventricular arrhythmia
- 7) planned explantation of ICD, or planned up/downgrade to/from CRT-D device

Trial design



Outlook

The first center is initiated and randomisation starts June 2021. It is planned to complete recruitment within 18 months and the last visit is scheduled for end of 2023.

Prespecified safety objectives include all-cause mortality, SAEs, hypoglycemic and ketoacidotic events, genital infections, ventricular electric storm episodes and changes in liver and renal function. ICD interrogation data, echocardiography and blood samples will be available from baseline and follow-up visits.