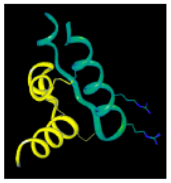

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Relaxera

The development of Synthetic Human Relaxin-2 for Heart Failure with preserved Ejection Fraction

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Relaxin-2 for HFpEF: rationale

- Fifty % (and rising) of patients with Chronic Heart Failure (CHF) have Heart Failure with preserved Ejection Fraction (HFpEF).
  - ✓ Germany: ~750,000 - EU: ~ 3.7 million – USA: ~2.8 million patients
- CHF most common cause of hospital admission, third most common cause of death in Germany.
- HFpEF prognosis comparable to HF with reduced EF (HFrEF) (~50 % mortality over 5 years). However, there is **no mortality-lowering pharmacological treatment** for this entity of CHF.

ESC 2016: Guidelines on HF; https://www.cdc.gov/dhdsp/data_statistics/fact_sheets/fs_heart_failure.htm; Stoerk et al., Clin Res Cardiol 2017

Relaxin-2

Insulin Superfamily

- **Discovered as pregnancy hormone**
- **Relaxin**-1, **-2**, -3
  - ✓ Human1, H2, H3
- **Receptor: RXFP1**
  - ✓ G protein-coupled receptor

Summary 1: Relaxin-2 for HFpEF

- HFpEF - still the biggest unanswered question in contemporary cardiology.
- Relaxin's unique receptor and signaling characteristics render it an exceptionally strong drug candidate. A multi-faceted syndrome like HFpEF needs a pleiotropic approach.
- At pre-clinical level, the relaxin-2 concept is effective in all 3 phenogroups of HFpEF models. Relaxin-2 delivery reverses diastolic dysfunction, arrhythmia susceptibility, inflammation, and excess fibrosis.
- The atrial and ventricular antiarrhythmic properties of relaxin-2 are clinically important: afib heralds worsening of HFpEF, SCD poses the most frequent cause of cardio-vascular death in phase-III HFpEF trials.

Summary 2: Relaxin-2 for HFpEF

- With Bolus Therapy, signaling can be achieved with periodic pulses of the peptide, irrespective of its short half-life in circulation. This enables excellent therapy control and compliance in highly susceptible patients.
- The entire signalling portfolio of the native peptide (e. g., Wnt1-related myocardial rejuvenation, GR-mediated anti-inflammation free of steroid-related adverse effects) is of the essence. This pleiotropic signalling is most likely trimmed down by relaxin-modifying approaches.

Relaxera are preparing a
phase IIa/b clinical trial in HFpEF