

Design and Rationale of DemonsTTRate: A Global, Long-Term Observational Study to Evaluate Vutrisiran in Patients with Transthyretin Amyloidosis with Cardiomyopathy



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Conclusions

- DemonsTTRate is a global, multi-centre, prospective, long-term, observational study that is enrolling patients with ATTR-CM who have initiated treatment either with vutrisiran or another approved ATTR-CM therapy in a real-world setting.
- Data will be extracted from patients' medical records and collected based on clinical and laboratory assessments during routine visits; direct patient data collection of PROs will occur at enrolment and every 6 months thereafter.
- This study will provide details on characteristics of patients receiving vutrisiran in real-world practice, impact of vutrisiran on health-related QoL and healthcare resource utilisation, and long-term comparative effectiveness data.



Key
takeaway

DemonsTTRate will generate robust real-world evidence on long-term outcomes with vutrisiran compared to other ATTR-CM treatments in routine clinical practice

Introduction

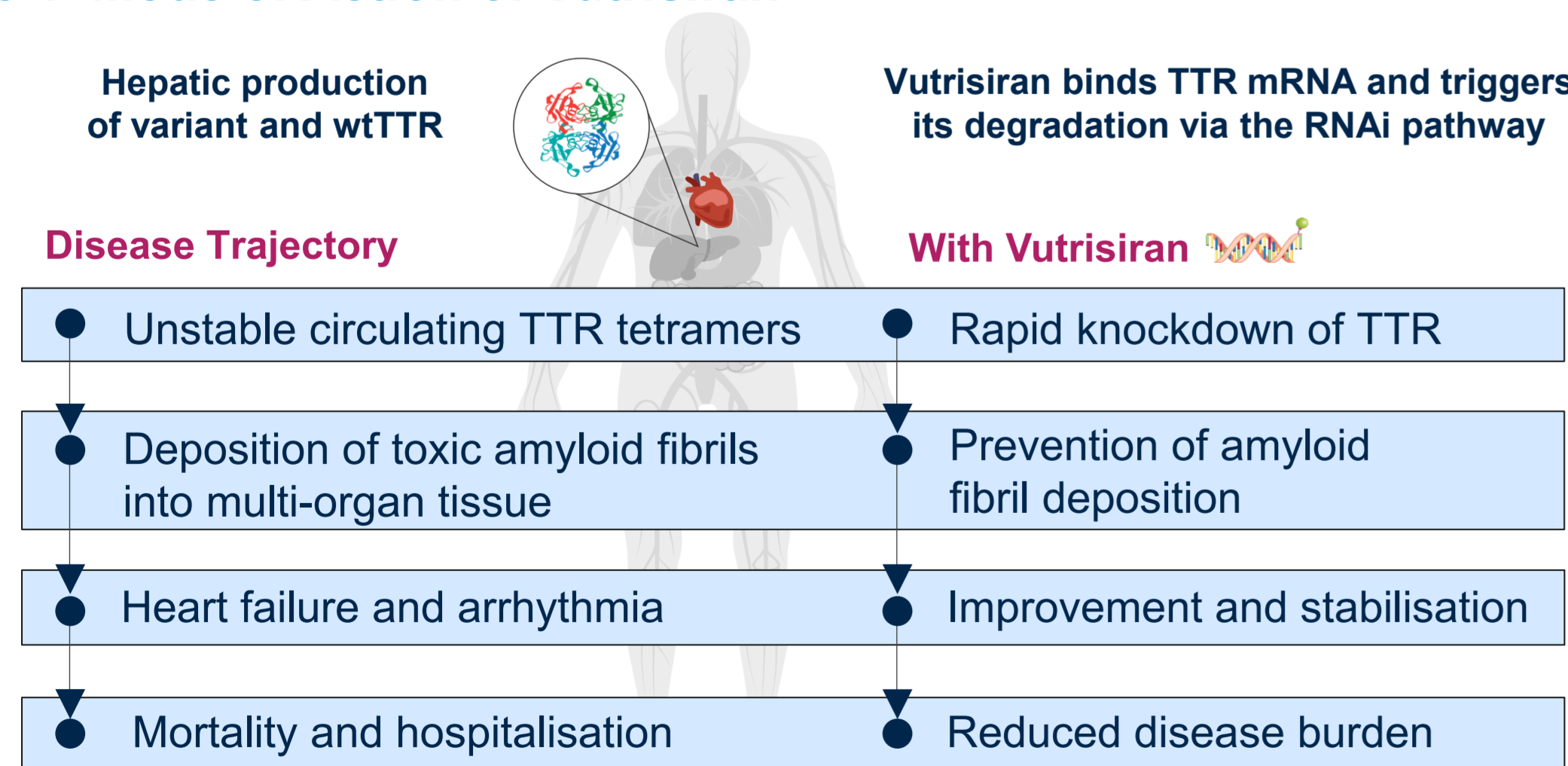
ATTR-CM

- ATTR is a progressive and fatal disease caused by the deposition of misfolded TTR as amyloid fibrils in multiple tissues¹⁻³
- In ATTR-CM, amyloid deposits accumulate in the cardiac tissue, ultimately causing restrictive heart failure, conduction disease and arrhythmias^{2,4}
- Without treatment, patients with ATTR-CM experience significant morbidity, mortality and marked decline in physical function and QoL³⁻⁷
- Vutrisiran was approved for ATTR-CM by the FDA (March 2025) and EMA (June 2025), adding to existing approved therapies including tafamidis and acoramidis⁸⁻¹¹

Vutrisiran and HELIOS-B

- Vutrisiran is an RNAi therapeutic that achieves rapid knockdown of TTR to reduce the formation of misfolded TTR (**Figure 1**)^{12,13}
- In HELIOS-B (NCT04153149), vutrisiran significantly reduced the risk of ACM and recurrent CV events while preserving functional capacity and QoL vs placebo with no safety concerns, in patients with ATTR-CM¹²
- The significant clinical benefits and tolerability of vutrisiran were maintained through the first year of the HELIOS-B open-label extension¹⁴
- Real-world data can enhance understanding of treatment patterns and demonstrate the effectiveness of vutrisiran in clinical practice

Figure 1. Mode of Action of Vutrisiran



Methods

DemonsTTRate

- DemonsTTRate (NCT07358078) is a global, multi-centre, prospective, long-term, observational study, designed to assess vutrisiran use in the real-world healthcare management of patients with ATTR-CM
- Patients enrolled in DemonsTTRate are being treated as per standard of care; the study protocol does not recommend the use of any specific treatments, and no assessments are required for the study

Figure 2. DemonsTTRate Study Objectives

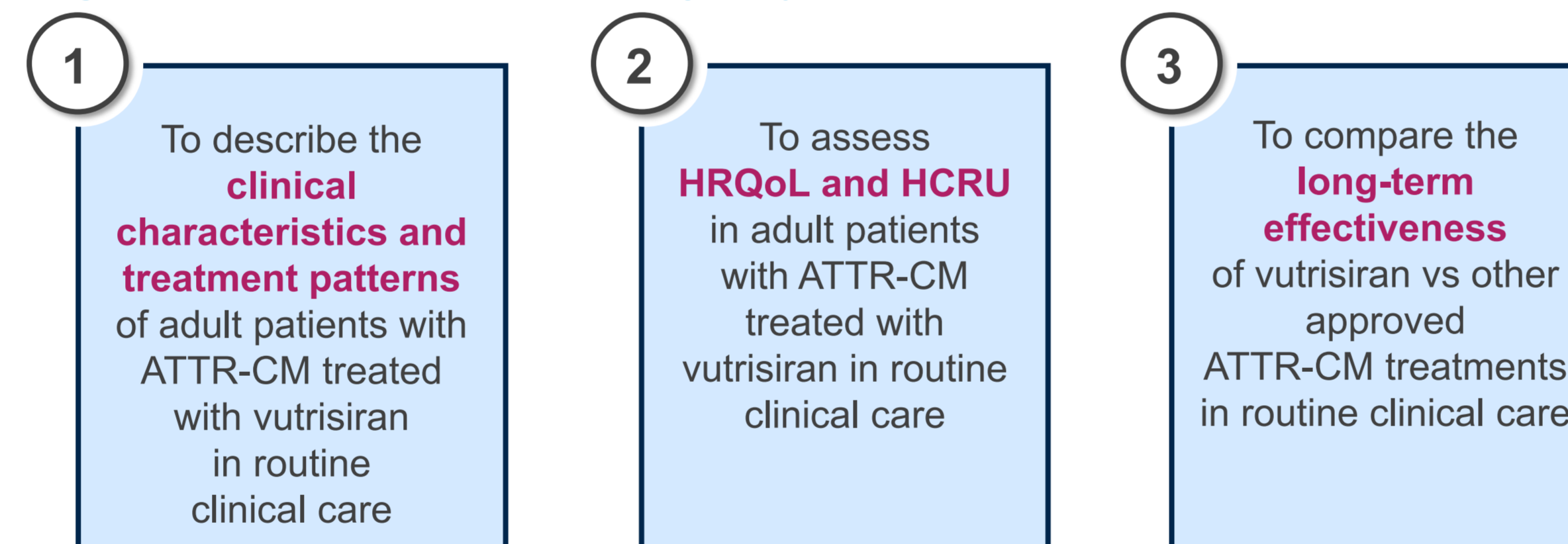


Figure 3. Key Patient Enrolment Criteria

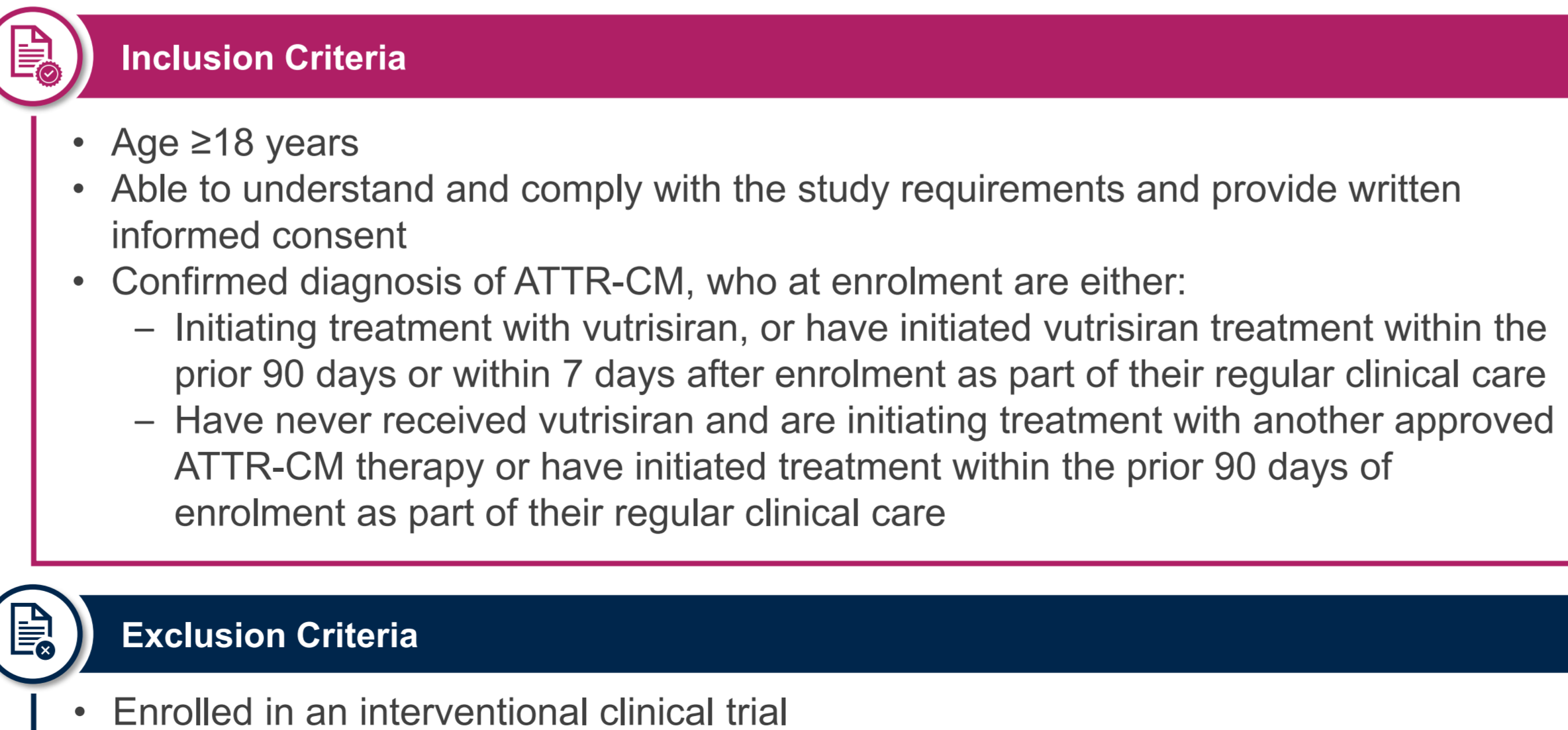


Figure 4. Study Design and Data Collection

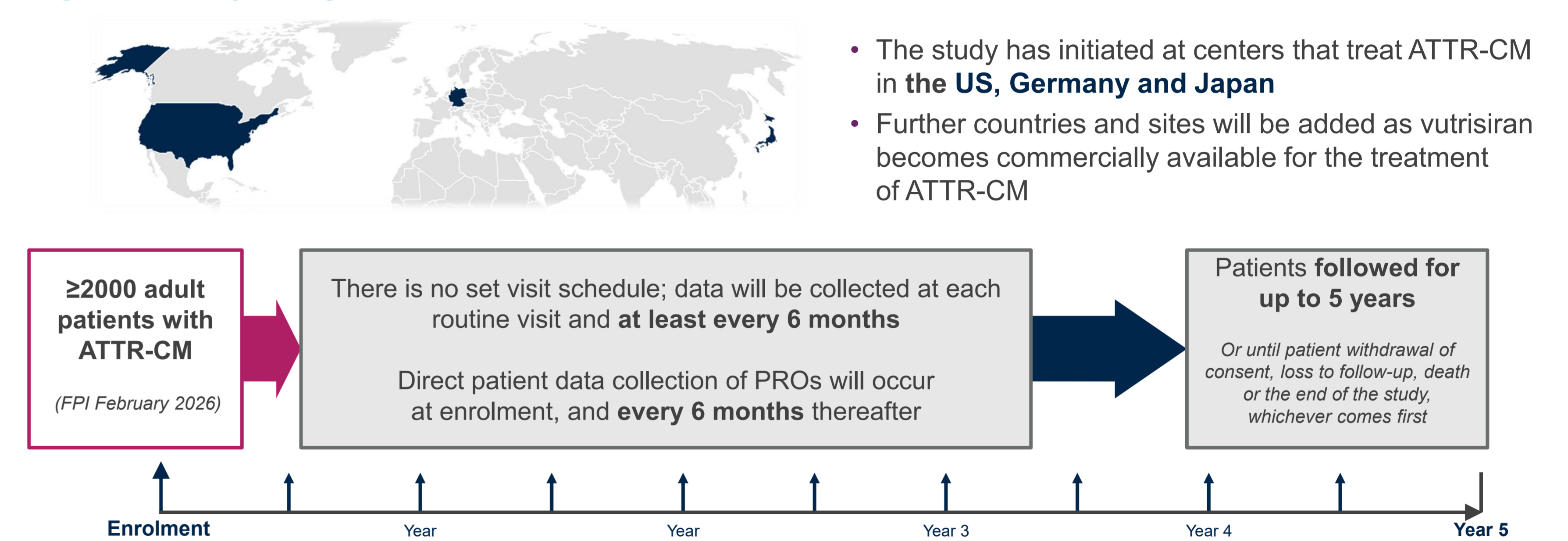
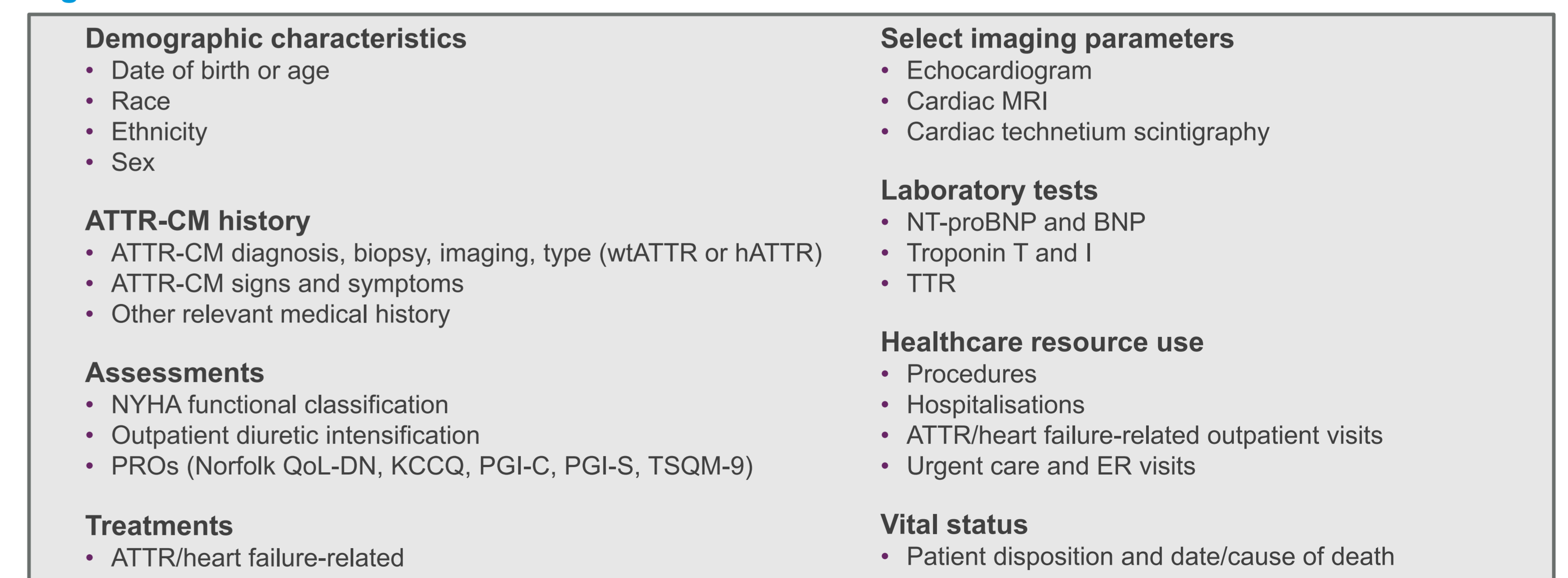


Figure 5. Data Collection



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Abbreviations: ACM, all-cause mortality; ATTR, transthyretin amyloidosis; ATTR-CM, ATTR with cardiomyopathy; BNP, B-type natriuretic peptide; CV, cardiovascular; EMA, European Medicines Agency; ER, emergency room; FDA, US Food and Drug Administration; FPI, first patient in; hATTR, hereditary ATTR; HCRU, healthcare resource utilisation; HRQoL, health-related quality of life; KCCQ, Kansas City Cardiomyopathy Questionnaire; MRI, magnetic resonance imaging; mRNA, messenger RNA; NT-proBNP, N-terminal pro-B-type natriuretic peptide; NYHA, New York Heart Association; PGI-C, Patient Global Impressions - Change; PGI-S, Patient Global Impressions - Severity; PRO, patient-reported outcome; QoL, quality of life; QoL-DN, Quality of Life - Diabetic Neuropathy; RNAi, RNA interference; TSQM-9, Treatment Satisfaction Questionnaire for Medication version 9; TTR, transthyretin; wtATTR, wild-type ATTR.