Abstract: 1290

Repetitive levosimendan infusions for patients with advanced chronic heart failure in the vulnerable post-discharge period: the LeoDOR Trial

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Background

Readmission and mortality rates are high during the vulnerable period following an episode of acute heart failure. Experience in several clinical studies has indicated that administration of intravenous levosimendan in intermittent cycles may be effective in patients with advanced HF. We here describe the rationale and protocol of the LeoDOR study that will assess the efficacy and safety of intermittent levosimendan therapy during the vulnerable phase after a recent hospitalisation for acute HF in advanced HFrEF patients. The overarching hypothesis is that, compared with placebo, repetitive administration of levosimendan during the post-acute phase will be associated with greater clinical stability over a follow-up period of 14 weeks.

Methods

TheLeoDOR study is a randomised, double-blind, placebo-controlled, three-armed trial designed to evaluate the efficacy and safety of intermittent levosimendan therapy, administered in addition to standard therapy for a period of 12 weeks either as a 6-h continuous infusion at a rate of 0.2 µg/kg/min every 2 weeks or as a 24-h continuous infusion at a rate of 0.1 µg/kg/min every 3 weeks. The primary endpoint will be evaluated after 14 weeks. Information on safety events will be obtained after 6 months. The study that was started in March 2018 intends to include 264 patients in 30 centres in nine European countries.

The primary efficacy assessment will be made using a global rank endpoint in which all participants are ranked across three hierarchical groups: (i) time to death or urgent heart transplantation or implantation of a ventricular assist device (VAD); (ii) time to non-fatal HF requiring i.v. vasoactive therapy; and (iii) time-averaged proportional change in N-terminal pro-brain natriuretic peptide (NT-proBNP) from baseline to week 14 with (i) as the most important event. Secondary efficacy endpoints include individual components of the primary endpoint at short- (14 weeks) and intermediate-term (26 weeks) follow-up, as well as changes in functional status.
Conclusion

The LeoDOR trial will test efficacy and safety of intermittent levosimendan therapy in patients with "very" advanced but not acute heart failure with the highest short- and long-term mortality and rehospitalisation rates. The study is configured to examine evidence of efficacy of an intensified therapy using clinically relevant endpoints for severely ill patients managed on an outpatient basis.

Study schedule