The IMR-BTL-201 study

Short title: A Phase 2 Study to Evaluate the Safety and Tolerability of IMR-687 in Subjects with Beta Thalassemia

Principal investigator: J.L.H. Kerkhoffs

Sponsor: IMARA Inc.

EudraCT nr. (if applicable): 2019-002989-12

Patient population: *Patients with transfusion dependent as well as independent Beta-thalassemia*

Required no. of patients (if applicable): 120

Type of study: A Phase 2 Study to Evaluate the Safety and Tolerability of IMR-687 in Subjects with Beta Thalassemia

Study objectives:

Primary objectives:

The primary objective of this study in both Population 1 (TDT) and Population 2 (NTDT) is to assess the safety and tolerability of IMR-687 in adult subjects with β-thalassemia.

Secondary objectives:

• To evaluate the effect of IMR-687 versus placebo on reduction in red blood cell (RBC) transfusion burden.

• To evaluate the change in transfusional iron load rate of IMR-687 versus placebo.

• To characterize the pharmacokinetic (PK) profile of IMR-687.

• To evaluate the effect of IMR-687 versus placebo on fetal hemoglobin (HbF).

• To evaluate the effect of IMR-687 versus placebo on anemia.

Subject eligibility criteria:

Inclusion criteria:

1. Subjects must understand and voluntarily provide informed consent and sign an informed consent form (ICF) prior to any study-related assessments/procedures being conducted. Although RBC transfusions and associated Hb laboratory measurements 12 weeks prior to the Screening visit are not study related, the ICF will specifically request subject consent to collect these data.

2. Subjects must be ≥18 to ≤65 years of age at the time of signing the ICF.

3. Subjects must have documented diagnosis of β-thalassemia or HbE/β-thalassemia. Concomitant single alpha gene deletion, duplication, or triplication is allowed.

4. For TDT subjects only: Subjects must be regularly transfused, defined as >3 to 10 RBC units1 in the 12 weeks prior to screening and no transfusion-free period for ≥35 days during that period.

For NTDT subjects only: Subjects must be transfusion independent, defined as 0 to ≤3 units1 of RBCs received during the 12-week period prior to randomization, must not be on a regular transfusion program, must be RBC transfusion-free for at least ≥ 4 weeks prior to randomization, and must not be scheduled to start a regular hematopoietic stem cell transplantation within 9 months.

Exclusion criteria:

1. Any significant medical condition, laboratory abnormality, or psychiatric illness that would prevent the subject from participating in the study, including the presence of laboratory abnormalities that may place the subject at unacceptable risk if he/she were to participate in the study.

2. Any situation or condition that confounds the ability to interpret data from the study (e.g., subjects also receiving RBC transfusions at centers not able to obtain laboratory samples for central processing).

3. Diagnosis of α-thalassemia (e.g., hemoglobin H [HbH]) or hemoglobin S (HbS)/ β-thalassemia.

4. Body mass index (BMI) <17.0 kg/m2 or a total body weight <45 kg; or BMI >35 kg/m2.

Status: recruiting

Participating sites: HagaZiekenhuis, Den Haag

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Summary (optional): This is a phase 2 study intended to explore the potential use of IMR-687 to treat subjects with β-thalassemia. This is the first study of IMR-687 in a β-thalassemia population, and, as such, is designed to examine the safety, tolerability, and PK, as well as the potential PD effects, of IMR-687 administered qd for 36 weeks in adult subjects with β-thalassemia.