The IMR-SCD-301 study

Short title: A Phase 2b/3 Study to Evaluate the Safety and Efficacy of IMR-687 in Subjects with Sickle Cell Disease

Principal investigator: J.L.H. Kerkhoffs

Sponsor: IMARA Inc.

EudraCT nr. (if applicable): 2019-004471-39

Patient population: Patients with sickle cell disease

Required no. of patients (if applicable): 426

Type of study: A Phase 2b/3 Study to Evaluate the Safety and Efficacy of IMR-687 in Subjects with Sickle Cell Disease

Study objectives:

Primary objectives:

- To evaluate the fetal hemoglobin (HbF) response to IMR-687 versus placebo
- To evaluate the safety of IMR-687 versus placebo

Secondary objectives:

- To evaluate the effect of IMR-687 versus placebo on HbF-associated biomarkers
- To evaluate the effect of IMR-687 versus placebo on reticulocytes
- To evaluate the effect of IMR-687 versus placebo on the incidence of VOCs
- To evaluate the effect of IMR-687 versus placebo on quality of life

Subject eligibility criteria:

Inclusion criteria:

1. Male or female aged ≥18 to ≤65 years at the time of informed consent form (ICF) signing.

2. Confirmed diagnosis of SCD (HbSS, HbSB0 thalassemia, or HbSB+ thalassemia) in the medical record; if not available, the diagnosis must be confirmed at the site's local laboratory instead.

3. Subjects must have had at least 1 and no more than 12 documented episodes of VOC in the past 12 months at the time of ICF signing and at randomization (Day 1). For study eligibility, VOC is defined as a documented episode of an acute painful crisis (for which there was not an explanation other than VOC) that involved moderate to severe pain lasting for at least 2 hours and at least one of the following:

• Use of escalated analgesia (including healthcare professional-instructed use of an analgesic prescription)

• A hospital, emergency department, or clinic visit and/or healthcare telephone consultation at the time of occurrence

• Diagnosis of ACS (defined as an acute illness characterized by fever and/or respiratory symptoms, accompanied by a new pulmonary infiltrate on a chest X-ray), hepatic sequestration, or splenic sequestration

Exclusion criteria:

1. Hospital discharge for sickle cell crisis or other vaso-occlusive event within the 7 days prior to randomization (Day 1).

2. Red blood cell transfusion within 60 days of signing the ICF or on chronic transfusion therapy regimen. Transfusion status must be reassessed at randomization (Day 1).

Note: A subject who has a transfusion during the screening period may be rescreened once as specified in the protocol.

3. Subjects with hereditary persistence of HbF (i.e., HbF >25% at screening).

Status: recruiting

Participating sites: HagaZiekenhuis, Den Haag

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Summary (optional): This is a phase 2b, randomized, double-blind, placebo-controlled, multicenter study of subjects aged 18 to 65 years with SCD (HbSS, HbSB0 thalassemia, or HbSB+ thalassemia) to evaluate the safety and efficacy of the PDE9 inhibitor, IMR-687, administered qd for 52 weeks. This study will provide data on IMR-687 doses of ≥3.0 to ≤4.5 mg/kg and >4.5 to ≤6.7 mg/kg.