Gene therapy

Clinical trials for adults only

Drug: AG-348

Age: Adult Participants with Non-transfusion-dependent Thalassaemia

Primary Purpose: Treatment

Trial Phase: 2

Official Title: A Phase 2, Study to determine the efficacy, safety, pharmacokinetics, and pharmacodynamics of AG-348 in adult subjects with non-transfusion-dependent thalassaemia.

Description:

This study is to evaluate the efficacy, and safety of treatment with AG-348 in adult participants with non-transfusion-dependent thalassaemia (NTDT). Mitapivat (AG-348) is an oral, small-molecule, allosteric activator of the RBC-specific form of pyruvate kinase (PK-R). PK-R is a key enzyme for maintaining energy homeostasis in RBCs, as they rely almost exclusively on the process of glycolysis to generate ATP. In healthy adults, mitapivat activates wild-type PK-R and increases ATP levels in RBCs.

Participants with alpha or beta thalassaemia received AG-348 50 mg twice daily (BID), orally up to Week 6. Following Week 6, depending on the participants' safety and haemoglobin (Hb) concentrations, they could undergo one potential dose-level increase from 50 to 100 mg BID. After completion of the Core Period of 24 weeks, participants were eligible to continue to receive AG-348 in the Extension Period which is up to 10 years.

For more details click below:

https://clinicaltrials.gov/ct2/show/NCT03692052?cond=thalassaemia&map_cntry=GB&draw=2&rank=1

Drug: IMR-687

Age: 18 Years to 65 Years (Adult, Older Adult)

Primary Purpose: Treatment

" This clinical trial has been terminated."

Trial Phase: 2

Official Title: A Phase 2 Study to Evaluate the Safety and Tolerability of IMR-687 in Subjects with Beta Thalassaemia

Description:

This study is to evaluate the efficacy, safety and Tolerability of treatment with IMR-687 in adult participants with transfusion dependent thalassaemia (TDT) and non-transfusion-dependent thalassaemia (NTDT).

For more details click below:

https://clinicaltrials.gov/ct2/show/NCT04411082?cond=thalassaemia&map_cntry=GB&draw=2&rank=3

Drug: ST-400

Age: 18 years to 40 years

Primary Purpose: Treatment

Trial Phase: 1/2

Official Title: A Phase 1/2, study to assess the safety, tolerability, and efficacy of ST-400 autologous hematopoietic stem cell transplant for treatment of transfusion-dependent beta-thalassaemia (TDT).

Description:

ST-400 is composed of the patient's own blood stem cells which are genetically modified in the laboratory using Sangamo's zinc finger nuclease (ZFN) technology to disrupt a precise and specific sequence of the enhancer of the BCL11A gene (which normally suppresses fetal haemoglobin production in erythrocytes). This process is intended to boost fetal haemoglobin (HbF), which can substitute for reduced or absent adult (defective) haemoglobin. ST-400 is then infused back into the patient after receiving conditioning chemotherapy to make room for the new cells in the bone marrow, with the aim of producing new erythrocytes with increased amounts of HbF. The primary objective is to

understand safety and tolerability of ST-400, and secondary objectives are to assess the effects on HbF levels and transfusion requirements.

For more details click below:

https://clinicaltrials.ucsf.edu/trial/NCT03432364

Gene Editing

Clinical trials for children and adults

Drug: SLN124

Age: 18 Years and older (Adult, Older Adult)

Primary Purpose: Treatment

Trial Phase: 1

Official Title: A Phase 1 Study to Evaluate the Safety and Tolerability of SLN124 in Subjects with alpha or beta thalassaemia

Description:

This study is to evaluate the efficacy, safety and Tolerability of treatment with SLN124 in adult participants with alpha or beta non-transfusion-dependent thalassaemia (NTDT).

SLN124 aims to temporarily 'silence' TMPRSS6, a gene that prevents the liver from producing hepcidin. Which is a protein made in the liver, in human is encoded by the *HAMP* gene. As hepcidin increases, iron levels in the blood are expected to decrease, which may increase the production of healthy red blood cells, thereby reducing anaemia.

Hepcidin is a key regulator of the entry of iron into the circulation in mammals. It controls the delivery of iron to blood plasma from intestinal cells absorbing iron, from erythrocyte-recycling macrophages, and from iron-storing hepatocytes. Hepcidin acts by binding to and inactivating the cellular iron exporter, ferroportin, which delivers iron to plasma from all iron-transporting cells.

Erythropoiesis is the process which produces red blood cells (erythrocytes), which is the development from erythropoietic stem cell for mature red blood cell. In mammals (including humans), this usually occurs within the red bone marrow. In the early foetus, erythropoiesis takes place in the mesodermal cells of the yolk sac. By the third or fourth month,

erythropoiesis moves to the liver. After seven months, erythropoiesis occurs in the bone marrow. Increased level of physical activity can cause an increase in erythropoiesis.

Decreased O2 in circulation is stimulating erythropoiesis. This decrease is detected by the kidneys, which then secrete the hormone erythropoietin. This hormone stimulates proliferation and differentiation of red cell precursors, which leads to producing red blood cells (erythrocytes).

Increased erythropoietic activity suppresses hepcidin, which leads to increased iron absorption and release of iron from stores.

For more details click below:

https://clinicaltrials.gov/ct2/show/NCT04718844?cond=thalassaemia&map_cntry=GB&draw=2&rank=10

Drug: CTX001

Age: 12 Years to 35 Years (Child, Adult)

Primary Purpose: Treatment

Trial Phase: 3

Official Title: A Phase 3 Study to Evaluate the Safety and Tolerability of CTX001 in Subjects with beta thalassaemia

Description:

The study will evaluate the safety and efficacy of CTX001, an experimental gene-editing cell therapy. CTX001 involves the engineering of a patient's haematopoietic stem cells to generate high fetal haemoglobin levels in red blood cells.

HbF is a form of the oxygen-carrying haemoglobin that is naturally present at birth, which then switches to the adult form of haemoglobin. The aim here is to use the body's own machinery to switch back to producing fetal haemoglobin.

For more details click below:

https://clinicaltrials.gov/ct2/show/NCT03655678?cond=thalassaemia&map_cntry=GB&draw=3&rank=12

Drug: LentiGlobin BB305

Age: up to 50 Years (Child, Adult)

Primary Purpose: Treatment

Trial Phase: 3

Official Title: A Phase 3 Study to Evaluate the efficacy and safety of autologous hematopoietic stem cell transplantation (HSCT) using LentiGlobin BB305 drug product in subjects with transfusion-dependent β-thalassaemia (TDT)

Description:

It is delivered as a single dose straight into the blood following a course of chemotherapy. If LentiGlobin BB305 is licenced for use in the UK, it could be the first treatment option for beta-thalassaemia major that has the potential to add a working copy of the beta-globin gene to patients' stem cells. It may improve survival and quality of life by reducing or eliminating the need for blood transfusions and iron-chelation therapy.

For more details click below:

https://clinicaltrials.gov/ct2/show/NCT03207009?cond=thalassaemia&map_cntry=GB&draw=3&rank=14

https://clinicaltrials.gov/ct2/show/NCT02633943?cond=thalassaemia&map_cntry=GB&draw=3&rank=15