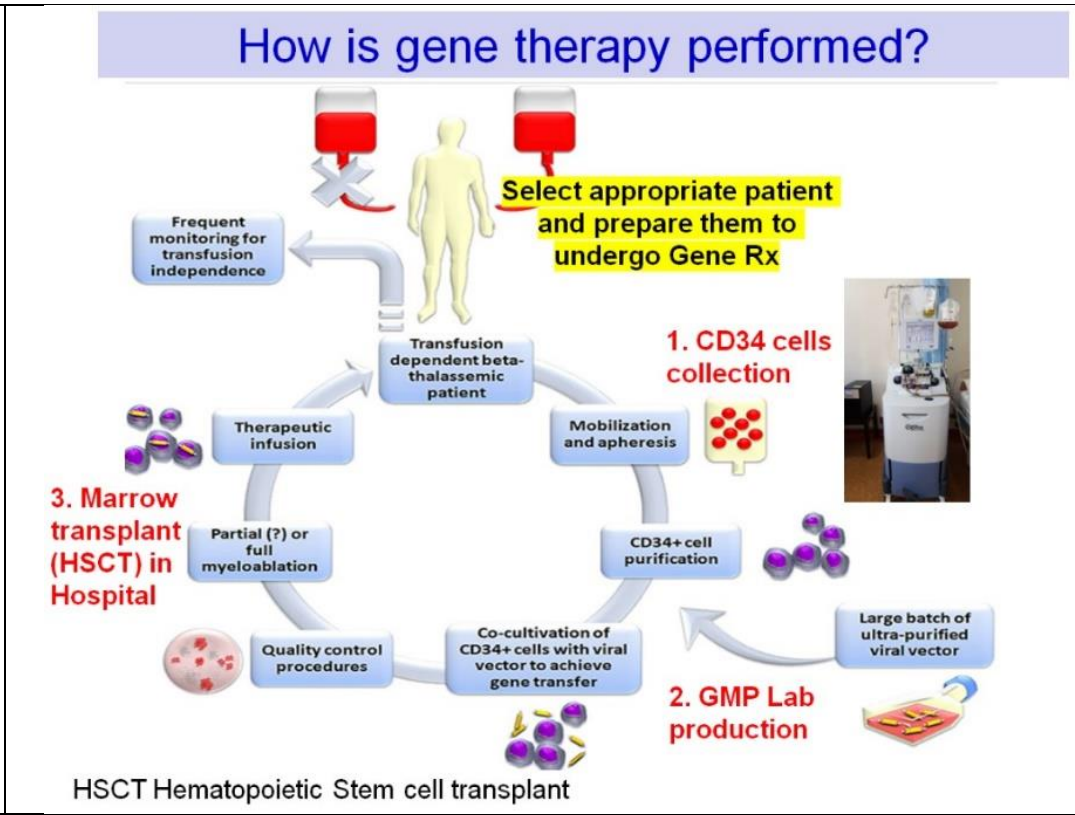
FREQUENTLY ASKED QUESTIONS (FAQ)

Vebeglogene autotemcel, an LV-HSC gene therapy for Transfusion dependent Beta-Thalassemia (TDT)

#	Questions	Answer
1.	What is this new gene therapy Vebeglogene autotemcel for TDT? Is it the same as Zyntelglo?	Vebeglogene autotemcel consists of a patient's own (autologous) blood stem cells (hematopoietic stem cell HSC) which is genetically modified (using lentivirus LV vector) in the lab by having a normal copy of beta-globin ($\beta^{A\text{-}T87Q}$) gene inserted into the patient's HSC. This newly inserted gene enable the production of a modified functional $\beta^{A\text{-}T87Q}$-globin, which has a nearly identical structure and similar oxygen carrying capacity to naturally occurring β-globin in our blood Hemoglobin. Just like viral vectored Covid19 vaccine (AstraZeneca, CanSino, J&J etc), various manufacturers can produce the same therapy (or vaccine) using the same technology, which is NOT exclusive to any company. Zyntelglo was the first approved $\beta^{A\text{-}T87Q}$-globin based gene therapy. Vebeglogene autotemcel is similar to Zyntelglo; it is currently undergoing clinical trial in China.
2.	How is the treatment carried out?	**This is 3 step procedure (see figure below):** 1. ***Apheresis***: Vebeglogene is made from your own blood stem cells (genetically modified HSC). Your healthcare provider will first collect some of your blood cells (CD34 cells) through a procedure using a machine (this is called "apheresis"). A tube (intravenous catheter) will be placed in your vein to collect your blood. The collection takes several days, each time for 3 to 6 hours. 2. ***GMP production***: The CD34 cells are frozen and sent to the GMP lab, where your HSC cells will be isolated and genetically modified by having a normal copy of beta-globin ($\beta^{A\text{-}T87Q}$) gene inserted into your HSC to make Vebeglogene. It takes about 4-6 weeks to make Vebeglogene. 3. ***Bone marrow transplant***: Before you can receive Vebeglogene, your healthcare provider will give you chemotherapy (myeloablation) over 3-4 days to prepare your bone marrow for grafting by the genetically modified HSC. This will wipe-out all the blood cells in your marrow. When your body is ready, your healthcare provider will give you Vebeglogene through a tube (intravenous catheter) in your vein. This usually takes less than one hour. After Vebeglogene infusion, you will be cared in an isolation tent or chamber until your bone marrow has recovered and start producing blood cells (platelet & white cells) and the genetically modified HSC has started producing normal red blood cells. This takes about 1-2 weeks.

		
3	How safe is it? Is its safety profile the same as Zyntelglo?	Vebeglogene is similar to Zyntelglo, so the safety profile is expected to be the same as Zyntelglo. As shown in the scientific data provided to your doctor, the vector design and construction of Vebeglogene is very similar to Zyntelglo. Zyntelglo has been given to human patients since 2010s (> 10 years), its safety record is pretty good though the number who have been treated is still limited (several hundreds). The most important side effect is related to marrow transplant rather than the gene therapy, that is graft failure after transplant. This means the marrow takes a long time or fail to recover after it has initially been wiped out (myeloablation); this is a rare (<1%) but potentially life-threatening. So far, all patients who had this side effect have recovered, nobody has ever died because of this side effect. It important to conduct the bone marrow transplant in an experienced medical centre.
4	How effective is it? Does it work as well as Zyntelglo?	Vebeglogene is similar to Zyntelglo, so the efficacy is expected to be the same. The LV vector is a platform technology (like AdV vector) for the transfer of gene into cells for therapeutic purpose (or AdV is used for vaccination purpose). We have completed pre-clinical studies in mice which showed that the treatment works. We have also commenced testing in human patients with TDT. So far, all patients treated have responded as expected with improved

		production of normal red blood cells and achieved normal blood Hemoglobin levels without the need for blood transfusion.
5	What about the long-term result?	We have just commenced the trial of Vebeglogene for the treatment of TDT. No long-term data is available yet. Vebeglogene is similar to Zyntelglo, so the longer-term efficacy is also expected to be the same. Zyntelglo has reported 9 years post-treatment data for patients treated in its trials. The data showed the gene therapy resulted in sustained transfusion independence and in improved quality of life; 90% of patients in the Phase 3 study achieved and maintained transfusion independence through to last follow-up (up to 6 years) [https://doi.org/10.1182/blood-2023-174068].
6	Can one get HIV after this treatment?	Vebeglogene uses a retrovirus (HIV belongs to the same family) as a vector to transfer normal copy of beta-globin (βA-T87Q) gene into the patient's cells. One cannot get HIV from gene therapy for Thalassemia; this has never happened.
7	What happens when there is serious adverse reaction?	The healthcare provider who administers the treatment will manage all adverse reactions and other health related issues. For patients treated under the clinical trial, the manufacturer will agree to support the cost of healthcare required to manage any adverse reactions.
8	Who is eligible to receive treatment?	All patients who have TDT are *potentially* eligible. However, we say *potentially* because some patients will be too ill, while others will have too much iron overload (especially in the heart and liver) to undergo bone marrow transplant treatment, which can be hazardous in unfit patients.
9	What is the cost?	Vebeglogene is undergoing clinical trial. The treatment is therefore free for patients enrolled in the trial. For patients who receive the treatment under early access use, your healthcare providers who administer the therapy and care for you will charge for their professional services.
1	Where can I find information about Vebeglogene ?	Vebeglogene is undergoing clinical trial. You can find out more about the trials below https://clinicaltrials.gov/study/NCT06308159