LETTER TO THE EDITOR

Betibeglogene Autotemcel; A new hope for transfusion dependent beta-thalassaemia

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Respected Editor, Beta thalassaemia is an autosomal recessive disorder that leads to abnormal production of functional adult haemoglobin because of either inadequate or absent production of the B globin chain (β+/β0).[1] Transfusion-dependent thalassemia (TDT) is a rare and most severe form requiring life-long blood transfusions. To mitigate the effects of TDT, life-long blood transfusions every 2-5 weeks are required, which can elicit transfusion-based reactions and lead to an iron overload state, which can further cause widespread organ damage despite the use of iron chelation therapy.[2]

Curative treatment for beta-thalassemia is by performing allogeneic *haematopoietic* stem cell (H.S.C.) transplantation with H.L.A matching donors.[1-3] Allogenic H.S.C. transplantation is associated with an increased risk of morbidity and mortality; therefore, autologous H.S.C. transplantation with genetic modification is considered a better option.[3] Betibeglogene autotemcel is a one-off administration gene addition treatment for TDT that offers the prospect of achieving transfusion independence.[1,2]

Recently, the US FDA approved the use of Beti-cel for both adult and paediatric populations with TDT in late August 2022 and hauled it as the first cell-based gene therapy for Beta Thalassemia.[4]

Betibeglogene autotemcel recruits a lentiviral vector to add a modified β A-T87Q globin gene into autologous CD34+ *haematopoietic* stem cells. Patients must undergo a complete myeloablative conditioning regimen with Busulfan before Beti-cel infusion.[5] Several phase 1 and 2 studies have concluded that Beti-cel increased Haemoglobin A levels and, therefore, achieved transfusion independence in over 90% of the patients who were given this gene therapy.[1,5] Patients who achieve transfusion independence with Beti-cel are reported to have normal levels of Hepcidin post a year and two.[1] Beti-cel is not recommended for lactating women. Cryopreservation of ova and semen is recommended prior to the treatment.[5]

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A study on the cost-effectiveness of Beti-cel has reported that it is much more cost-effective than the current standard of care (SoC) needed for TDT. Beti-cel also improved the quality of life (QoL) by a gain of 3.8 and 6.9 Life Years' (L.Y.s) and Quality Adjusted Life Years (QALYs), respectively.[2]

While Beti-cel possibly provides a promising cure for TDT, more extensive studies need to be conducted to establish the treatment's long-term safety and efficacy. Further research is required to identify the risk of insertional oncogenesis in patients receiving this therapy. Careful consideration must be made for the third-world countries as gene therapy is supremely expensive, and specialized treatment for its' implementation is scarce in such parts of the world.

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