Archives of Medicine©
15 (2) 2023 : 001-002 • OPINION

New therapies for beta-thalassemia and laws governing orphan drugs

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INTRODUCTION

Mutations that affect the synthesis of the adult hemoglobin subunits (or chains) are the root cause of the serious autosomal recessive diseases known as -THAL. Red blood cells become abnormally small (microcytic) as a result of the absence of chains; The precipitation of -globin–heme complexes as a result of the /non-chain imbalance hinders the maturation of erythroid cells (ineffective erythropoiesis). In a vicious cycle, severe anemia brought on by a combination of hemolysis and ineffective erythropoiesis encourages hemopoietic expansion. The primary feature of this pathology is ineffective erythropoiesis, which in turn causes iron overload, anemia, increased thrombosis risk, organ damage, and increased mortality. More than 350 -THAL mutations, ranging from silent mutations (silent) to mutations that cause a quantitative reduction in -globin chains (+) to the most severe mutations, which result in the complete absence of -globin chain synthesis (0), have been identified since the first molecular cloning and characterization of the human -globin gene cluster in 1980 [1].

DESCRIPTION

Patients are classified clinically as having either transfusion-dependent thalassemia (TDT), in which regular blood transfusions (BTs) are required since childhood; or non-transfusion-dependent thalassemia (NTDT), in which BTs are not required at all or only occasionally.4 In TDT, the additional iron provided by BT would unavoidably result in iron overload, necessitating iron chelation therapy (ICT). Because ineffective erythropoiesis suppresses hepcidin, resulting in excessive iron absorption, it has also become increasingly apparent that ICT may be recommended even in NTDT [2].

Cooley and Lee were the first to describe THAL in the medical literature more than 90 years ago. Allogeneic hematopoietic stem cell transplantation (HSCT) is the only proven and conclusive treatment for -THAL at this time. Sadly, it is constrained by clinical conditions and the availability of a matched donor; Acute and chronic graft-versus-host disease (GVHD) are also potential outcomes. In patients with -THAL, a new treatment option called gene therapy (GT) is being tested to prevent risks associated with GVHD [3].

Thalassemia heterozygotes or carriers make up about 1.5% of the global population. The evolutionary explanation for their high prevalence in the region encompassing the Mediterranean basin, Middle East, Indian subcontinent, and Southeast Asia is their relative resistance to malaria.

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Word count: 983 **Tables:** 00 **Figures:** 00 **References:** 05

Received: 01.02.2023, Manuscript No. ipaom-23-13551; **Editor assigned:** 03.02.2023, PreQC No. P-13551; **Reviewed:** 15.02.2023, QC No. Q-13551; **Revised:** 20.02.2023, Manuscript No. R-13551; **Published:** 27. 02.2023

-THAL has also spread to northern Europe and North America as a result of recent migrations, where it is recognized as a rare disease by US and EU legislation. Any medicinal product (a "drug") designed to treat a rare disease may be eligible for ODD in accordance with the Orphan Drug Act, which was enacted in the United States in 1983, and EU Regulation (EC) [4].

When a new drug, previously unlicensed drug, or new use of an already licensed drug is used to treat a rare and severe disease, ODD is granted by the FDA in the United States and the EMA in Europe. Despite some minor differences, the goals of the US and EU laws are similar: They want to give investors incentives to invest in disease areas that might not be profitable otherwise. There are two types of incentives: On the one hand, there are "push" incentives like tax credits and protocol assistance that make R&D less expensive and less uncertain. On the other hand, so-called "pull" incentives (such as a predetermined additional period of market exclusivity) increase the likelihood of profitability once a product is marketed.

In this paper, we examine every drug that has received ODD from the FDA or EMA to date. We have provided a window into the evolution of therapeutic approaches for -THAL over time through this set of drugs, allowing us to evaluate factors that have attracted investors as well as factors that may have been determinants of successful drug development.

Allogeneic bone marrow transplantation or gene therapy as potential treatments for -THAL have recently gained attention. These possibilities should not diminish the significance of continuing unrelenting efforts to improve treatment protocols for the vast majority of patients who do not currently have access to gene therapy or bone marrow transplantation for a variety of reasons. In order to achieve the best possible long-term management for -THAL, it is imperative that drug combination CTs be designed and carried out. In addition, this strategy has the potential to help bridge the gap between the standard of care that is currently in place and the potential future widespread use of gene therapy [5].

CONCLUSION

Blood transfusion has been the mainstay of treatment for nearly a century since THAL was identified as a disease. Despite the obvious significance of iron chelation, new medications to combat iron overload and deliberately address other aspects of the disease have only become available in the past 30 years, following the passage of orphan drug legislation. Our investigation shows that little medium endeavors and public establishments enjoy not generally taken benefit of the motivations given by vagrant medication regulations to the degree that one could have anticipated. It has not been demonstrated that the type of molecule and the pathophysiological target in and of themselves can predict drug development success.

ACKNOWLEDGEMENT

None.

CONFLICT OF INTEREST

None.

REFERENCES

1. **Kattamis A, Forni GL, Aydinok Y, et al.** Changing patterns in the epidemiology of β-thalassemia. *Eur Oncol Haematol*. 2020;105(6):692-703.
2. **Giannuzzi V, Landi A, Bosone E, et al.** Failures to further developing orphan medicinal products after designation granted in Europe: An analysis of marketing authorisation failures and abandoned drugs. *BMJ open*. 2017;7(9):e017358.
3. **Nemeth E, Tuttle MS, Powelson J, et al.** Hepcidin regulates cellular iron efflux by binding to ferroportin and inducing its internalization. *Sci*. 2004;306(5704):2090-2093.
4. **Nicolas G, Bennoun M, Devaux I, et al.** Lack of hepcidin gene expression and severe tissue iron overload in upstream stimulatory factor 2 (USF2) knockout mice. Proc Natl Acad Sci. 2001;98(15):8780-5.
5. **Pasricha SR, Frazer DM, Bowden DK, et al.** Transfusion suppresses erythropoiesis and increases hepcidin in adult patients with β-thalassemia major: A longitudinal study. *Am J Hematol*. 2013;122(1):124-33.