Juggling between the Cost and Value of New Therapies:

Does Science Still Serve Patient Needs?

**By Dr Androulla Eleftheriou*

Decades of hope for a cure vanished into thin air when cost outweighed the value of the first gene therapy for thalassaemia and obliged the manufacturing company to withdraw it from Europe. This may indeed create a precedent for other curative therapies that currently are in the pipeline after many decades of research, raising questions over their future acceptance by payers and the fulfilment of their purpose: to cure as many patients as possible, providing them with increased life expectancy and better quality of life.

We, the Thalassaemia International Federation (TIF), representing the united voice of people with thalassaemia and their families globally, wonder what happened to our long lost dream of finding a cure for our children. We have been striving for more than three decades to empower the research and academic communities, and the industry, to focus on and develop a safe and effective curative approach for Thalassaemia. When gene therapy marked a historical milestone in the history of thalassaemia, thanks to the efforts of US-based Biotech Company, bluebird bio, we expected a more humane approach by both the governments and the industry and not a series of financial studies that have shattered the dreams of hundreds of thousands of patients globally. If the developed countries of Europe cannot afford an innovative therapy, what will happen to low- and middle-income countries, where the 80% of the global thalassaemia population lives? And more importantly, how can we prevent a detrimental domino effect from ensuing?

In the 1960s and 1970s, treating physicians started using haematopoietic stem cell transplantation (HSCT) to cure patients with genetic disorders, including thalassaemia. Despite the successful implementation of this approach in both developed and developing countries, and the long and ongoing efforts for further improvements, the limitations for successful outcomes are still to-date the same, i.e. HLA identical sibling matching and young age. Therefore, the global patient

community has been promoting for years the development of another option, another therapeutic approach that could overpass the challenges of HSCT, covering more patients and of a larger age span. Gene-based approaches were those promising to make the dream for a final cure come true. It is very well remembered, by all of us involved in the care of this disorder that all reports, conferences and work of every national patient association in every country across the world and especially of TIF, focused on this topic that reflected one of the most important expectations of patients: better health and quality of life. All patients have been living with this dream and have grown with this hope.

Research on genome-based therapies has been undertaken by many eminent researchers for decades now. The journey to find an effective and safe cure was difficult and immensely challenging, with a number of failures on the way, which disheartened and disappointed both the patient and the scientific communities, until there was finally light at the end of the tunnel a few years ago. This light raised hopes and expectations amongst patients and led TIF to work very committedly with every single scientist, academic, research group and industry expert that focused on such innovative approaches, including the team of bluebird bio that undertook the improvement of the vector produced by Leboulch in 1994. This small company succeeded in what predecessors failed, because it paid attention to the patients' perspective and their everyday journey with this debilitating disease, which costs them their quality of life. Frequent transfusions, chronic pain, inability to concentrate, absence from school and work, discrimination, mental health issues are just a few of the daily challenges of patients. Standard care that includes lifelong regular blood transfusions, iron chelation therapy and multidisciplinary care has achieved an increase in life expectancy. But what about those other unmet needs?

With a view to provide patients with accurate and reliable information regarding the safety and effectiveness of this novel therapeutic approach, TIF produced a wealth of educational material on gene therapy and organised a series of events across all regions of the world, paving the way for patients to claim their inalienable human rights to life, health, education and work.

The gene therapy product of bluebird bio, called Zynteglo™, was finally authorised in May 2019 by the European Medicinal Agency. **In the eyes, hearts, minds, activities and work of the global patient community, after decades of fighting for a curative approach, there has never been any discussion or focus on the cost effectiveness of such approaches versus the standard of care ones. In the minds and souls of patients, the only focus and wish was to reach a day when science could provide a safe cure for their disease and serve its purpose, i.e. to serve human needs**. Such a cure would lead a new life with equal opportunities and challenges, as every other person not suffering from a chronic disease. Coming out of their life-long dependency on medications, transfusions and medical treatment has always been and still is each and every patient's dream.

Our deep concern is that all stakeholders always knew that an innovative and complex therapy for beta thalassaemia would be expensive but always supported and fought for its development. Governments and academia provided research grants, the industry invested in the product's improvement, healthcare professionals and patients monitored the pipeline and hoped for access to Zynteglo™. When the European Medicines Agency granted Zynteglo™ a conditional market authorisation, everyone focused on numbers and opted for cost of illness and cost effectiveness studies, inadmissibly ignoring the patients' voice and needs. This is because no study and no health economist would ever capture, truly and accurately, the real cost of thalassaemia in terms of pain, uncertainty, fear and quality of life.

As patients, we strongly condemn this shift of focus that does not reflect decades of discussions and efforts and our willing and struggle to have access to any treatment that would improve our quality of life. We condemn this discriminatory behaviour against us, given that patients in other disease areas already receive experimental therapies bearing a hefty price tag. The withdrawal of an authorised gene therapy from Europe will most probably slow down or even halt the access of people with thalassaemia to curative approaches, rendering the future of thalassaemia treatment gloomy at the very least.. Depriving patients from a chance to be cured is at the minimum unethical and everyone has a share in the blame.

Moreover, if governments want novel therapies to remain on the shelf, why invest in them? Why encourage researchers to focus on their discovery and improvement? We are fully aware of the fact that countries do not have unlimited funds and financial resources. That is why a number of countries, in the European Union for example, opted for joint procurements in the context of regional alliances, such as the Valletta Declaration or the BeneluxA initiative. Such alliances would increase their negotiating powers for the purchase of expensive medicines and therapies, making them available to every patient in need.

Therefore, what is of utmost important is for all interested stakeholders, and especially the industry and any other academic teams engaged in the development of medicines, to seek and be engaged in early and transparent dialogue, from early drug discovery to preclinical studies, clinical development, regulatory review and finally post-market monitoring, with the aim to identify safety and cost hurdles early on and render costly therapies affordable and accessible to payers and patients, respectively.

The developers of medicines, after having invested considerable amounts of money in developing and commercialising a product, should not be left exposed to failure but be given the necessary space, time and adequate motivation to mitigate problems, whether regulatory or with regard to market access, and eventually make their product available to as many patients as possible. Additionally, a central, special fund on innovative therapies should be created and managed by the European Commission. Such a fund could be a viable solution, or part of a solution to support and compliment national funds and allow Member States to provide their patients with novel therapies.

Governments need to take action, develop synergies and discuss pricing early on, taking into account the lessons of the past and the challenges to come. Treating physicians, along with patients, should become actively and meaningfully involved in the development process from the very early stages in order to be proactive and ready to provide concrete information to their national competent authorities on the potential number of patients that could benefit from the different authorised innovative therapies based on inclusion, exclusion

criteria, on the medical and other priorities and short, medium and long term plans for the access of eligible patients to such therapies towards, thus facilitating the national efforts of decision makers.

We should bear in mind that everyone has a role to play and that we all share the same responsibility for the sad decision of bluebird bio to withdraw its services (even temporarily) from Europe. No Government, industry or academic/regulatory body has the right to deprive the patients' from their choice to have access to an innovative curative therapy. This is a huge and unacceptable violation of human and patients' rights endorsed for decades now by relevant EU and international bodies.

Life cannot be measured using mathematical models. We thus strongly believe that Science needs to be available, accessible and most importantly, **at the service of patient needs**.

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