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Guest Editorial

Humanitarian Program for Gaucher Disease and Other Lysosomal Storage Disorders

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Lysosomal storage disorders (LSDs) comprise more than 50 diseases, each of which is individually rare, although collectively their prevalence is 1 in 5000 people (Verma et al., 2022). Majority of them occur due to mutations in specific enzymes that degrade the respective substrate that enters the lysosome through autophagy (van der Ploeg, 2022). The logical treatment is to make the enzyme and administer it to the patients. The challenge lies in the fact that the patients with each specific lysosomal storage disorder are very few, and pharmaceutical companies are not willing to take up the manufacture of these enzymes, because such a project would not be financially viable. Henry Termeer who pioneered the programs for enzyme replacement therapy (ERT) in 1990s for Gaucher disease and set the ball rolling for the manufacture of ERTs for other lysosomal disorders had recognized this downside of the high cost of manufacture of therapies for rare disorders. He knew that the introduction of enzyme replacement therapy (ERT) for Gaucher disease in 1991 would transform the life of patents with this disease. However, he recognized that due to the high cost of treatment it may remain unavailable to the vast majority of patients, especially in poor-resource countries. He stated right at the beginning that "any patient with Gaucher disease who needed to be treated with ERT, would have access to it, regardless of whether the cost could be paid" (Hawkins, 2019). This led to sowing the seeds of the humanitarian program for supply of ERT, and we must applaud his magnanimity in initiating this program.

International Gaucher Day (IGD) was launched in 2014 and is celebrated annually on 1st October to raise awareness of this disease. During the 2nd South Asia Gaucher Summit held on 1st October 2022, a presentation was made to describe the humanitarian program for this disease and the transformative impact it has had on the lives of patients. However, the program was not about simply distributing the enzyme, but involved building the support systems for it, and developing local expertise to manage these patients.

For ensuring success of the humanitarian program a number of principles were recognized and accepted (Verma et al., 2022): (1) A charitable foundation was set up, obtaining tax exemption for its activities, and ensuring that all products and services would be channelized through it. (2) Core elements of governance were identified such as engagement of senior executives / management of the manufacturing company and complete separation between humanitarian and commercial activities, with decision regarding allocation of ERT to be taken by the local experts' committee using detailed and consistent disease-specific medical criteria. (3) A number of committees were set up such as the management committee, cross-functional steering committee, and operation committee, to oversee the functioning, ensure program compliance at local, regional and country level, and establish the vision, mission, goals and objectives for the program.

Vital elements of the program were formulated: (1) Development of local healthcare systems to improve patient outcomes; (2) Provision of help where it was needed, and where treatment access was limited; (3) Planning for sustainable and long-term access; (4) Treatment based on recommendation by local doctors on consistent criteria, using best practices in disease management. This was necessary due to unique phenotypes and genotypes in developing countries that may differ from those in the West; (5) Operational excellence following all international and local regulations; (6) Establishing an infrastructure to support patient care, with local governments, physicians and non-government organizations; (7) Provision of same treatment and attention as is given to those patients who pay; (8) Entry to registries was made available; and (9) Compliance with ethical standards, institutional policies, and external governmental requirements, and continued efforts to meet strategic goals. These guiding principles were to be followed at all times striving for global standards.

The first charitable program was started in USA in 1991, in China in 1999 and in India in 2007, followed by multiple regional initiatives rolled out, culminating in the first non-US collaboration with an NGO [the Gaucher Initiative/Project HOPE

(Health Opportunities for People Everywhere)]. In India the first therapy was provided in 1997, although the Indian humanitarian program was officially launched later in September 2007. It is managed by the India Medical Advisory Board (IMAB) comprising of 16 leading global and national consultants, who provide clinical support and coordinate treatment for all patients – all brought together by one common thread – HOPE!! The Indian experts prepared for a leadership role in the care for lysosomal storage disorders and developed operational protocols and published guidelines on management (Puri et al., 2018).

Prior to the initiation of the program, during the visits by the senior staff of the company (Genzyme), the local experts emphasized the need for early and correct diagnosis. They put forward the request for support of the local laboratory scientists for training in foreign diagnostic centers. Soon, diagnosis of lysosomal disorders on dried blood spots was established and provided free to all patients in India and neighbouring countries. The Biochemical Genetics Laboratory in Sir Ganga Ram Hospital was made the nodal laboratory for this exercise. From January 2016 to September 2022, 6,788 dried blood spots were assayed and 1504 (22.1 %) turned out to be positive. There were 2,503 samples for estimation of glucocerebrosidase, the enzyme for Gaucher Disease and 499 (19.9%) positive cases were identified (Verma et al., 2017; Unpublished data).

The interest generated in inborn errors of metabolism (IEMs) through the humanitarian program led to the formation of the parent support group called the Lysosomal Storage Disorders Support Society of India (LSDSS). It was formed in 2006 but got registered in 2010. It has played a critical role in creating awareness and organizing meetings for the benefit of the patients and their parents and advocating for the cause of the affected children.

More than 3,300 patients with four LSDs [Gaucher disease, Fabry disease, and mucopolysaccharidosis (MPS) I and II] have been enrolled in more than 100 countries in six continents, while some of these patients have received treatment for more than 20 years. Of these patients 63.7% had Gaucher disease. This care represents more than 50,000 patient-years of experience extending over 30 years. Since the introduction of the program in 1991, the number of patients with Gaucher disease served is 1,248, number of countries supported since inception is 75, the number of individuals receiving humanitarian treatment annually is 652, the number of countries supported today is 52, average number of new cases approved each year over past 5 years is 48, while the average time current individuals have received humanitarian treatment is 9.8 years. The number of patents of Gaucher disease getting treatment in India at present is 75.

The first boy provided ERT in India was in 1997. From a pot-bellied child he has now grown to be a handsome adult who has qualified as an engineer and works in an IT firm and is currently Regional Manager for South Asia for the International Gaucher Alliance (IGA). Similarly, there are other success stories of courage and hope, well described in the book 'Roar for Rare: The Unheard Voices' (Sanofi Genzyme, 2020). There are 10 stories of people with Gaucher disease, five with Pompe disease, five with Fabry disease and seven with MPS I: in this book.

Takeda also has a successful humanitarian program based on a similar operational model for three diseases –Gaucher disease, Fabry disease and MPS II. Takeda's humanitarian program is on a smaller scale, there being 36 patients with Gaucher disease (GD), 26 with MPS II, and 7 with Fabry disease. Majority of patients with GD have been enrolled for 4-5 years, while 95% of patients with GD are being followed up regularly.

In closing while one thanks the pharmaceutical companies for their generosity in supporting the humanitarian program, we must spare a thought for the many affected children who are not covered by this program. Many children whose parents are working in large corporate organizations in India such as the Employees' State Insurance Corporation (ESIC) of the Ministry of Labor and Employment, the Armed Forces, and Public Sector Undertakings (PSUs) are fortunately receiving ERT from these organizations. However, the other children have to cope with their disease and disability with despair, and a bleak future. Let us hope their prayers will be answered by understanding officials in the Ministry of Health and Family Welfare, Government of India, with additional help from different PSUs under their corporate social responsibility (CSR).

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