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Equitable access: How can we make cell and gene therapies a reality or possibility for all mankind?

Cell and gene therapies (CGT) are promising to transform medical care, but product development is only one part of the equation. Without equitable access to these ground-breaking agents, unmet medical need will continue to impact patient's lives, and the gap will continue to grow.

Since the first gene therapies were approved around six years ago, we have already seen inequities in access to licensed products and clinical trials, both within and between regions and countries. With a slew of new CGT products expected in the coming years, the time is approaching to meet this challenge head on.

The current state of play

Growing understanding of the human genome and underlying mechanisms of disease has given rise to a revolution in healthcare. Advanced cell and genetically-engineered products are part of that charge, offering an opportunity to treat, and in some cases even cure, serious, rare, and often previously unaddressed conditions.

Chimeric antigen receptors (CAR) T cells, for example, are now an established approach in a number of haematological cancers,[1] while Zolgensma (onasemnogene abeparvovec-xio), a one-time gene therapy, has finally offered children with spinal muscular atrophy (SMA) a therapeutic option.[2]

These are just two of the growing number of CGT approved worldwide, and many more are in the pipeline. According to the American Society of Gene and Cell Therapy (ASGCT), 3,726 products were in development in 2022, with oncology and rare diseases being the most investigated indications.[3]

By 2030, up to 60 new products are expected to be ready for routine practice.[4] But unless the issue of equitable access is addressed, they stand little chance of reaching all of 350,000-plus people worldwide[4] who stand to benefit.

Table 1: FDA-approved CGTs as of October 2023[5]

Product	Approved indication	FDA approval date
Cell therapies		
Kymriah (tisagenlecleucel)	Relapsed or refractory acute lymphoblastic leukemia	2017
	Large B cell lymphoma	2018
	Refractory follicular lymphoma	2022
Yescarta (axicabtagene ciloleucel)	Large B cell lymphoma	2017
	Follicular lymphoma	2021
Tecartus (brexucabtageneciloleucel)	Relapsed or refractory mantle cell lymphoma	2020
	Relapsed or refractory adult B cell lymphoblastic leukaemia	2021
Breyanzi (lisocabtagene maraleucel)	Relapsed or refractory large B cell lymphoma	2021
Abecma (Idecabtagene vicleucel)	Relapsed or refractory multiple myeloma	2021
Carvykti (ciltacabtagene autoleucel)	Relapsed or refractory multiple myeloma	2022
Gene therapies		
Luxturna (voretigene neparvovec-rzyl)	Leber's congenital amaurosis	2017
	Retinitis pigmentosa	2017
Zolgensma (onasemnogene abeparvovedxiol)	Spinal muscular atrophy (SMA) Type 1	2019
Zynteglo (betibeglogene autotemcel)	Beta-thalassemia	2022
Skysona (elivaldogene autotemcel)	Cerebral adrenoleukodystrophy (CALD)	2022
Hemgenix (etranacogene dezaparvovecdrib)	Haemophilia B	2022
Elevidys (delandistrogene moxeparvovec-rokl)	Duchenne muscular dystrophy	2023
Roctavian (valoctocogene roxaparvovec)	Haemophilia A	2023

ACCESS TO APPROVED CGTS

In the United States (US) the FDA has cleared 11 products for use in 16 indications[5] (**see table 1**), while 10 were available in the European Union (EU) as of January 2022.[6] However, as of 2021, only three were approved in low and middle income countries (LMICs).[4] But there have been early access programmes for some of these innovative products.

For example, in 2020, Novartis launched a global Managed Access program for Zolgensma[7]. In France, both Kymriah® and Yescarta® were available prior to marketing authorisation through the early access programme 'Temporary Authorisation for Use' (Autorisation Temporaire d'Utilisation).[8]

Regulations differ for expanded access mechanisms from country to country. There is a spectrum of mechanisms, including allowing an individual patient access to groups of patients, free of charge access or charged for access. The mechanism in France for example, allows for charged for access which is reimbursed by the authorities. In Russia there is the Circle of Kindness which helps patients afford treatment to unlicensed medicines.[9] There is no one size fits all approach to expanded access with specific considerations required for each asset and company.

> "For LMICs, some might see the hurdles to implementing gene therapy as too high and therefore not worth pursuing. We must remember this argument was made about HIV treatment, and those critics have been proven wrong."
>
> **Equitable Access to Gene Therapy: A Call to Action for the American Society of Gene and Cell Therapy, 2018[10]**

ACCESS TO CLINICAL TRIALS

Clinical trials are an important part of drug development globally and participation offers patients the potential of positive health outcomes, increased quality of life years or even hope when faced with a life-limiting condition.

The number of registered clinical trials has increased significantly in recent years. As of 29 May 2023, there were nearly 454,000 clinical studies registered globally. This has increased significantly from just 2119 registered in 2000.[11]

When the authors of an ASGCT paper searched clinicaltrials.gov in September 2018, they found 179 recruiting gene therapy studies. However, just two were open in Africa, three in South America, and one in South East Asia.[7]

Yet many of these therapies would have a much higher positive impact in LMICs than high income countries (HICs). Of the 179 trials, 41% matched to the search term "cancer", widely regarded as the next major health threat in LMICs.[7] Four percent related to sickle cell disease (SCD), but, despite 75.5% of those with the condition living in sub-Saharan Africa, Africa had no open SCD trials.[7]

THE RIGHT TO HEALTH

Access to medicines is a fundamental part of the right to health, first articulated in the 1946 Constitution of the World Health Organization (WHO), and enshrined in the Universal Declaration of Human Rights two years later.[12]

Part of that is ensuring everyone, regardless of who they are or where they live, has access to the CGTs that could improve, or even save, their lives. The alternative is a two-tier healthcare system in which those already in disadvantaged groups are left behind.

BARRIERS TO ACCESS

Although cell and gene therapies have the potential to treat or even cure life-limiting diseases and infections, the full impact can only be realised if they are delivered for the benefit of everyone, as opposed to widening the existing gap in health inequalities between different countries.

Aside from cost, there are other barriers to the access of cell and gene therapies in LMICs, including manufacturing technologies, research and development, and policy and regulation.[13]

CGTs tend to require expensive individualised manufacturing and single-dose administration, and as such provide long-term benefits at high, front-loaded costs. One-time treatment with Zolgensma, for example, has a list price of $2.123 million in the US.[8] Traditional health technology assessment (HTA) calculations were not built to accommodate such pricing structures.

These products, based on biologic materials, also require special logistical considerations in terms of their manufacture and delivery. They have shorter shelf lives, greater temperature sensitivities, and incredibly complex supply chains. Simply getting the right product to the right patient at the right time can be a logistical nightmare.

With dozens more CGTs expected to break through in the coming years, there is a growing debate around how healthcare systems will evaluate, pay for, and deliver them. Such challenges, already acute in HICs are compounded significantly in LMICs.

> "While patients in HICs may find access to gene therapy challenging, the outlook for access for individuals in LMICs can only be described as bleak."
>
> **Equitable Access to Gene Therapy: A Call to Action for the American Society of Gene and Cell Therapy, 2018[10]**

Towards a solution

There is no hard or fast solution, but the first steps are already being taken.

The ASCGT has issued a “call to action”, in which it renewed its commitment to working with advocacy groups and policy makers to insist that access “be distributed fairly to all those in need”.[10] The paper also recommends fostering CGT research in LMICs, through grants and mentorships.[10]

WHO has encouraged global regulators and policy makers to share knowledge and expertise when building CGT regulatory frameworks.[14] This, it said, would strengthen oversight capacity in all regions, and ease the implementation of clinical trials and manufacturing processes.

Work is also ongoing at the regional and national levels, with innovative payment models, such as risk-sharing schemes and outcomes-based pricing, being discussed as potential solutions to the challenges of high up-front costs.[15] The European Federation of Pharmaceutical Industries and Associations (EFPIA) has also recommended that cost-effectiveness frameworks be adapted to account for the rarity and severity of the target indication.[15]

THE TIME IS NOW

There may be a lot of work to be done, but the issue cannot be ignored. Because even the most innovative, efficacious products are worthless if the people who need them cannot access them.

No one part of the healthcare ecosystem alone can provide the solution. Rather everyone, from regulators and policy makers to industry, advocacy groups, patients and clinicians, will need to work together to identify – and implement – solutions.

Expanded Access Programs (EAPs) have demonstrated that they are able to offer a solution to access which meet the requirements of these stakeholders.

EAPs offer ethical, compliant, and controlled mechanisms of access to investigational drugs outside of the clinical trial space, and before the commercial launch. They also develop positive relationships with key opinion leaders, patients, advocacy groups and regulators, and the data captured from the implementation of EAPs supports in the formulation of global commercialisation strategies.[16]

Within our first white paper we explored a number of the complexities with supplying cell and gene therapies through an expanded access program. Uniphar holds an in depth understanding of the underlying regulations, supply chain requirements, order management processes and value-added services such as patient support programs, real world data collection and advanced treatment site support. This makes us well placed to support you to understand Expanded Access Programs.

Be part of that discussion. Be part of the solution.

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