Roundtable Session 2 – Table 10 – Global Health in Cell and Gene Therapy

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Abstract:

The world is witnessing unprecedented advances in medical technology, including Cell and Gene Therapeutics, allowing treatments for conditions not previously envisioned. The cost of these therapeutics, sometimes exceeding 2 million dollars per treatment, is very high, precluding availability for most patients. This roundtable session will focus on a vision of increased accessibility to Cell and Gene Therapy products for more patients around the globe, including populations of lower socioeconomic status.

Questions for Discussion:

- What characteristics of cell and gene therapy products elevate their cost thus contributing global health inequity?
- What strategies could be employed to reduce health inequity with respect to cell and gene therapy products to increase access to these life-altering treatments?
- Are you aware of any initiatives that are aimed at addressing health equity challenges for cell and gene therapy products.
- What types of technological advances could ameliorate the financial costs of Cell and Gene Therapy products

Notes:

The discussion began with the group attempting to define what global health equity means. Some of the ideas included:

- Getting approved/approvable products into more countries/regions
- Eliminating cost as a barrier to receiving cell and gene therapy products
- Health insurance support of cell/gene therapies and moving these treatments to earlier line of therapies
- Inclusion of indications from less represented or less affluent regions/populations
- Ability to set up the logistics and cold chain applicable for cell and gene therapies

We clarified that while there are many things that have the ability to impact global health equity, there are certain things more outside of the control of the people in this conversation and therefore would be excluded from discussion. These include insurance brokers, pharmacy benefit managers, and more commercial oriented people/organizations/systems. This discussion is more focused on efficiencies that can be made within CMC, including lowering COGS, reducing development resource/timeline, and making the regulatory approval process more efficient.

The group discussed the experiences from the COVID vaccine, where there was WHO prequalification which allowed getting products into more countries. Are there learnings that we can take from times of health emergencies? Will the most extensive realization of global health equity ONLY happen in times of health emergencies? Are there things that we can learn from vaccines (e.g., polio)? The flu?

Regulatory sophistication and harmonization/alignment/information sharing as barriers and enablers, respectively, was a topic the group discussed quite a bit. In order to get a therapy into multiple jurisdictions, the amount of work (and associated time/cost) is high. The burden of sponsors to spend time and resources on Module 1 for each jurisdiction is high. Is Module 1 alignment between countries a goal we can strive towards? There may be barriers due to legislation within each jurisdiction. Could this be an area where artificial intelligence (AI) can support?

Regarding mutual recognition, as much efficiency and overlap that can be achieved will support the efforts of global health equity. We see some health authorities leaning more on their health authority colleagues, both for the efficiency standpoint (not enough people to do all the work needed) and the harmonization perspective. Any and all work on mutual recognition and harmonization would be helpful. Can we harmonize GMO applications between countries?

Regulatory requirements must be maintained to ensure safe and efficacious products are provided to patients. Regulatory authorities can work to accommodate but must follow laws and regulations. But the move to more harmonization and mutual recognition would lower barrier to access. Organizations like ICH and PIC/S are hugely beneficial.

Regulation modernization is needed to update for the complexities of cell and gene therapies, and it is in progress in some areas. For example, ensuring the physician has the ability to make the assessment to take and administer an OOS product.

The determination by health authorities of which programs and areas will be funded/supported is key to determine the successes in rare disease impact. The priority review voucher (PRV) program is one example. The START program, advanced manufacturing technology (AMT) designation, and platform technology designation are all programs that can help lower the time and cost burden to approved products.

Within a singular company, prior knowledge and platform technologies should be utilized to make additional therapies move through development quicker with less new data.

Transparency of sponsor interactions with agencies will help drive efficiencies. For profit sponsors may not want this to hurt intellectual property (IP) or competitive advantage. Would this be something health authorities can aim to share (e.g., if they keep having the same issues/questions/etc.)? There is value in work like PaVe-GT, the NCATS initiative that shares information publicly.

Regarding clinical trial diversity, the participants should match the prevalence of the disease. However, too often economics and for-profit business models exclude areas and populations based on the lack of return on investment. This was highlighted in the keynote address, with regions of Asia and the whole continent of Africa excluded. In reaching people in different geographies, flying them to other jurisdictions for treatment is not sustainable or a solution to the problem.

Not only does the population included for developmental purposes for a certain indication have a role here, but what indications are even evaluated in the first place are impacted. When the business case does not make sense, non-profit organizations are more likely to have efforts in that area. Can more be done to financially incentivize companies to reach wider populations and/or rare and ultrarare diseases?

From a cost perspective, it was noted that the cost of shipping products via liquid nitrogen can be quite costly. The possibility of distributed manufacturing or point of care manufacturing was discussed as a solution to the supply chain and logistics cost/burden. The use of academic institutions in this distributed fashion was evaluated. However, there are still burdens with this approach. The sites will need to be GMP certified. Instead of a sponsor managing one or a few manufacturing sites, there would need to be oversight and management of orders of magnitude more sites/people/locations.

Themes kept arising of the balancing act at play: when you deregulate to make things more efficient the risk of ensuring quality therapies increases.

Regarding innovations are going to enable greater equity, the predominant solutions the group came up with were implementation of AI, quicker processes, and modified release paradigms.

The following bullet points also came up in discussion:

- Some health regulators appreciate innovation and agility as long as it is appropriate
- Interaction and communication with health authorities is key
- Big pharma participation would be great to support smaller, non-profit groups
- If limiting manufacturing occurs (e.g., ≤ 1 batch per year), consistency challenges and regulatory burden for changes
- START discussion this morning – sponsors overinterpreting the guidance causes wasted time/resources, and it would be beneficial to share more broadly and publicly the most overinterpreted guidance
- Space for innovation in development – do not want hurdles or barriers, so the most detailed, resource intensive process is usually performed
- QTPP discussion – need to utilize risk-based approaches
- Having a clear path, but want to deviate but still fits with the spirit of guidelines, discuss with regulatory agencies
- Issues with CMC being the bottleneck – with the speed of clinical, may be pushed to be innovative to move along CMC timelines
- Need for development work post-approval. Is there more room for post approval commitment plans?
- Wide range of approaches in sponsor companies seen by regulatory agencies
- IP out licensing model may be mutually beneficial to jurisdiction and innovator company, similar to how classical biologics have been provided to other jurisdictions
- CGT biosimilar?
- Market drive versus altruism