A Practical Approach for the Adoption of the Hub and Spoke Model for Cell and Gene Therapies in Low- and Middle-Income Countries: Framework and Simulation Case Studies

HSD88

Scan QR code to access the poster

Shadi Saleh[1]; Omar Dabbous[2]; Sean D. Sullivan[3]; Dipen Ankleshwaria[4]; Daiane Trombini[5]; Mondher Toumi[6]; Mahmoud Diaa[7]; Anish Patel[2]; Burcu Kazazoglu Taylor[8]; Sean Tunis[9]

[1]American University of Beirut, Beirut, Lebanon; [2]Novartis Gene Therapies, Inc., Bannockburn, IL, USA; [3]CHOICE Institute, School of Pharmacy, University of Washington, Seattle, WA, USA; [4]Novartis, Dubai, United Arab Emirates; [5]Novartis, Miami, FL, USA; [6]Aix-Marseille University, Marseille, France; [7]Novartis, Singapore, Singapore; [8]Novartis Gene Therapies, Washington, DC, USA; [9]Rubix Health, Baltimore, MD, USA

Introduction

- CGTs are being developed and adopted at an increasing pace[1–4]
- Advancements in CGTs are accompanied by a multitude of challenges, and the stakeholders, processes, and outputs involved in CGTs differ from traditional pharmaceuticals. Approaches for planning, manufacturing, and delivering CGTs are urgently needed[5]
- CGTs are associated with infrastructural and therapeutic costs in terms of both supply and demand. The conventional approach of concentrating clinical, logistical, and infrastructural expertise and capacities in few large centers of care is not conducive for optimized delivery of CGTs.[1,3]
  - Currently, the manufacturing, utilization, and access of CGTs is concentrated in high-income countries[6–8]
  - LMICs bear an estimated 90% of the global burden of disease.[6,9] However, delivery and access to CGTs in LMICs face multiple barriers, including inequitable health care access, lack of resources, funding shortages, prohibitive therapeutic costs, and complex regulatory systems.[6–8]
- One novel approach for delivering CGTs to LMICs is the adoption of the hub and spoke model for health care delivery[10]
  - A main health facility (hub) receives the most resources and delivers the most intensive service. Another less complex health facility (spoke) complements the hub by offering a limited array of services.[10,11]
  - This model is scalable, efficient, and adaptable based on needs and context[11]

Objectives

- We proposed a hub and spoke model for CGT delivery in LMICs and developed a framework for the identities and roles of core CGT stakeholders
- We simulated the model in two distinct scenarios in LMICs: a within-country scenario in Brazil and a cross-country scenario in the MENA region.

Methods

- Extensive mapping was undertaken to develop the core CGT stakeholder framework (e.g., cell processing facilities, clinical trials sites, accredited health facilities)
- We used academic articles and other sources including grey literature, social media, and relevant web pages to inform the proposed delivery model
- Model simulations were undertaken for Brazil and the MENA region, informed by publicly available data sets and articles
- All mapping was done using QGIS (qgis.org), a free and open-source cross-platform desktop geographic information system application that supports viewing, editing, printing, and analysis of geospatial data

Results

- The proposed framework includes four direct (beneficiaries, therapeutic center, treatment coordinators, manufacturers) and two non-direct (payers, regulators) CGT delivery stakeholders (**Figure 1**)

Figure 1. Core stakeholders in CGT delivery

KEY ROLE	TYPE	STAKEHOLDERS
Cells are collected from patient or donor(s), or patient receives treatment	Beneficiary	Patient or donor(s)
Location for cell collection and/or infusion	Therapeutic Center	May include community or regional hospitals, specialist disease centers, centers of excellence, academic medical centers, independent or private practices. Also included health care professional or therapeutic coordinator.
Facilities, departments, or employees that coordinate fulfillment of batches across supply chain, move products under controlled conditions, track orders and payments, coordinate patient orders	Treatment Coordination	May include case manager, supply chain planner, patient operations professional, orchestration platform, accounting department, courier services, patient operations
Facilities that prepare cells for manufacturing, or manufacture the plasmids, genetic vector (viral or mRNA), cell product (CAR-T or CAR-NK), or analyze specimens from patient or genetic data	Manufacturing	May include cell preprocessing facility, plasmid manufacturing facility, genetic vector manufacturing facility, cell manufacturing facility, sequencing laboratory
Multiple payers are usually involved	Payers	May include health insurance companies, private individuals or organizations, or health agencies. Also includes payer/insurance coordinators.
Regulations are implemented based on the country/location of CGT delivery	Regulatory Agencies	May include health or non-health authorities.

CAR-NK, chimeric antigen receptor natural killer cells; CAR-T, chimeric antigen receptor T cells; CGT, cell and gene therapy.

- Our proposed CGT delivery model is composed of three interconnected components: hub, spoke, and partner spoke (**Figure 2**)
  - The hub is a leading academic medical center that is experienced in both comprehensive care and delivering CGTs
  - A spoke is a health care center with minimal CGT experience but serves as the home center for patients
  - A partner spoke is a supporting facility that is not necessarily a health center but facilitates the function of spokes within the system

Figure 2. Core capacities of a CGT hub (A), spoke (B), and partner spoke (C)

A. Core Capacities of a CGT Hub

- An academic medical center located in a major city
- Previous experience delivering CGTs/leading clinical trials
- High number of intensive care unit (ICU) beds
- In-house apheresis and cryopreservation capacity
- Existing and established logistics and supply chain, and storage capacity (e.g., refrigeration, deep cold storage, reconstitution)
- Ability to screen, diagnose, order, store, prepare, and administer CGTs
- Accredited by international organizations for delivering CGTs
- Capacity to perform longitudinal data collection and evaluation in collaboration with spokes
- Immunosuppression protocols in place

Clinical and Research Capacities

Human Resources

- Qualified health care professionals that can order, store, prepare, and administer various types of CGTs
- Ability to train spokes on proper treatment, collection, and shipping
- Employs a treatment coordinator, supply chain planner, patient operations professional, CGT registrar, visibility and monitoring unit, information technology harmonization unit, E2E delivery accountable, E2E quality accountable, logistics coordinator, accountant, payer/insurance coordinator

Manufacturing Services

Other Services

- Share space with or be physically close to CGT manufacturer. Facilities include sequencing laboratory, preprocessing, plasmid manufacturing, gene vector manufacturing, or cell manufacturing facilities
- Ability to establish a manufacturing network that can provide cell/tissue processing service or automated CGT manufacturing services
- The manufacturing services require a cell preprocessing production coordinator, cell preprocessing production planner, plasmid production coordinator, plasmid production planner, genetic manufacturing production coordinator, genetic manufacturing production planner, cell production coordinator, cell production planner, and quality responsible
- Houses an orchestration platform, with developed information technology infrastructure for proper monitoring and evaluation, as well as data sharing and analysis
- Ability to establish or having an existing CGT registry
- Houses an information technology harmonization
- Houses, or is associated with, a well-developed shipping service
- Regulatory services department to ensure proper regulatory oversight and compliance assistance for spokes

B. Core Capacities of a CGT Spoke

- Medical center with minimal or no experience in CGTs
- Clinical capacity to administer at least one type of CGT therapy
- Capacity to screen for and perform clinical trials
- Houses an apheresis center and a cell/gene therapy processing facility
- Performs regular follow-up (3–6 months) with patients undergoing CGT
- Capacity to perform longitudinal data collection and evaluation, in collaboration with hubs and partner spokes

Clinical and Research Capacities

Human Resources

- Qualified health care professionals that can order, store, prepare, and administer at least one type of CGT
- Ability to train partner spokes on proper collection and shipping
- Employs a treatment coordinator, with limited roles compared with hub
- Employs a patient operations professional, accountant, logistics coordinator, and payer/insurance coordinator

Manufacturing Services

Other Services

- Share space with or be physically close to sequencing laboratories
- Sequencing and quality responsible
- Houses, or is associated with, a well-developed shipping service
- Secure information technology infrastructure to share patient data with hub and receive patient data from partner spokes

C. Core Capacities of a CGT Partner Spoke

- May include outpatient centers, clinics, apheresis, or blood collection centers
- Capacity to perform apheresis when necessary
- Houses the facilities to screen participants for clinical trials and referral to affiliated spokes
- Partner spoke is embedded within communities, especially in remote locations
- Secure information technology infrastructure to share patient data with affiliated spokes
- Qualified health care professionals that screen patients, potentially collect blood/apheresis, and refer patients to affiliated spokes
- Employs a treatment coordinator, patient operations professional, and a logistics coordinator, with limited roles

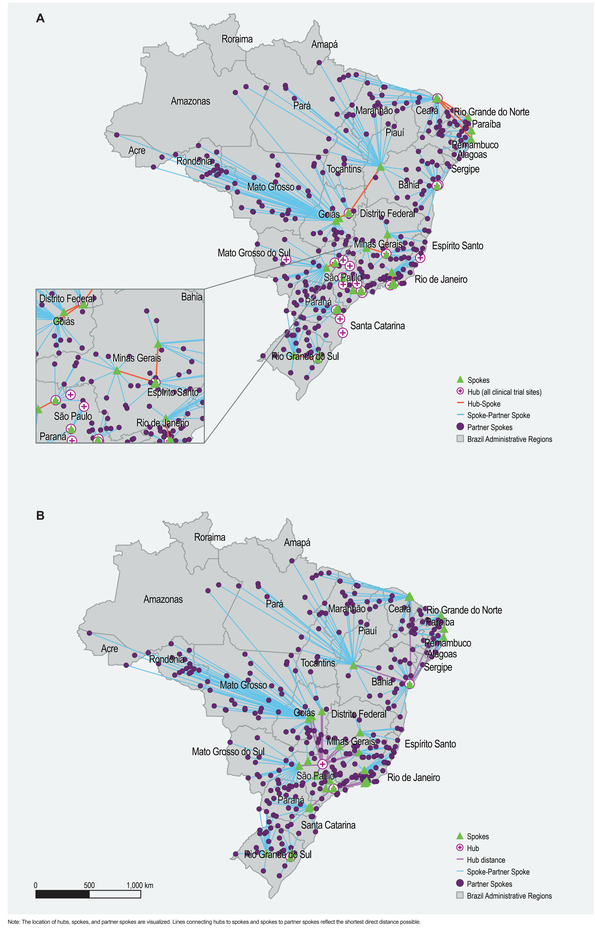
CGT, cell and gene therapy; E2E, end-to-end testing.

- In the model simulation for Brazil, hubs, spokes, and partner spokes were concentrated in the southeast region of the country, where health access and development are most advanced. Facilities were concentrated in major Brazilian cities, particularly São Paulo, reflecting the nation's health inequality (**Figures 3** and **4**).

Figure 3. Geographical distribution of facilities involved in CGT clinical trials, cell processing centers, and potential manufacturers in Brazil

CGT, cell and gene therapy; CPC, cell processing center.

Figure 4. Hub and spoke simulation in Brazil, including all clinical trial sites as hubs (A) or only those sites that performed both cell and gene therapies (B)



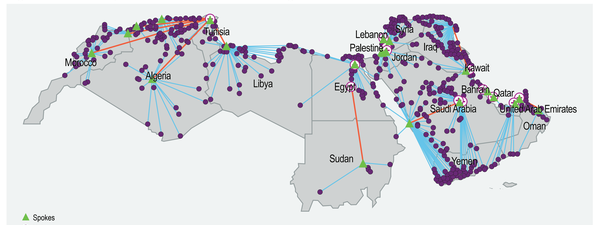
Note: The location of hubs, spokes, and partner spokes are visualized. Lines connecting hubs to spokes and spokes to partner spokes reflect the shortest direct distance possible.

- In the model simulation for the MENA region, potential CGT facilities were concentrated in Gulf Cooperation Council countries (e.g., United Arab Emirates, Saudi Arabia), where large health infrastructure investments have recently been made (**Figures 5** and **6**)

Figure 5. Geographical distribution of facilities involved in CGT clinical trials, cell processing centers, and potential manufacturers in the MENA region

CPC, cell processing center; CGT, cell and gene therapy; MENA, Middle East and North Africa.

Figure 6. Hub and spoke simulation in the MENA region



MENA, Middle East and North Africa.
Note: The location of hubs, spokes, and partner spokes are visualized. Lines connecting hubs to spokes and spokes to partner spokes reflect the shortest direct distance possible.

Limitations

- We used an inclusive approach to gather information and we did not assess the quality of the sources in a systematic way
- The geographic areas in which we simulated our model may not represent health care systems in other countries or regions

Conclusions

- Our hub and spoke model provides a framework for the roles of core CGT stakeholders in the delivery of CGTs in LMICs. The model requires an existing infrastructure that is conducive to expanded CGT services.
- For any model of the planning, development, and expansion of CGT services, pharmaceutical, clinical, and policy stakeholders from LMICs must be included
- Further investigation into the practical adoption and implications of a hub and spoke model is needed and may serve to expand access to CGTs in LMICs

References

1. Abou-el-Enein M, et al. *Mol Ther Methods Clin Dev*. 2021;22:11–4.
2. Quinn C, et al. *Value Health*. 2019;22:621–6.
3. Sharpe M, et al. *J Pharm Sci*. 2021;110:1877–84.
4. Wirth T, et al. *Gene*. 2013;525:162–9.
5. Elverum K, Whitman M. *Gene Ther*. 2020;27:537–44.
6. Adair JE, et al. *Gene Ther*. 2021; doi: 10.1038/s41434-021-00284-4. Online ahead of print.
7. Cornetta K, et al. *Mol Ther*. 2022;30:2122–29.
8. Mehler M, et al. Operationalizing Cell & Gene Therapy: Challenges and Solutions. September 22, 2020. Available at: https://www.cellandgene.com/doc/operationalizing-cell-gene-therapy-challenges-and-solutions-0001. Accessed March 17, 2023.
9. Murray CJ, Lopez AD. *Lancet*. 1997;349:1436–42.
10. Elrod JK, Fortenberry JL, Jr. *BMC Health Serv Res*. 2017;17(Suppl 4):795.
11. Devarakonda S. *Rural Remote Health*. 2016;16:3476.

Abbreviations

CGT, cell and gene therapy; CAR-NK, chimeric antigen receptor natural killer cells; CAR-T, chimeric antigen receptor T cells; CPC, cell processing center; E2E, end-to-end testing; ICU, intensive care unit; IT, information technology; LMICs, low- and middle-income countries; MENA, Middle East and North Africa region

Acknowledgments and Disclosures

This study was funded by Novartis Gene Therapies, Inc. Editorial support was provided by Jennifer Gibson, PharmD, of Kay Square Scientific, Newtown Square, PA, USA. This support was funded by Novartis Gene Therapies, Inc.

Disclosures: OD, **DA**, **DT**, **MD**, **AP**, and **BKT** are employees of Novartis and own stock/other equities. **SS** and **MT** have received consulting fees from Novartis Gene Therapies, Inc., for this research. **SDS** has received research grants and consulting fees from Novartis Gene Therapies, Inc., and served as consultant/on an advisory board for Bayer US. **ST** has received honoraria from Novartis Gene Therapies, Inc., for conduct of this study and participation in the ForGHE advisory board. He has also received payment for participation on a BioMarin advisory board and participated in a scientific advisory board meeting for UCB Pharma.