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IMPLEMENTATION AND DEVELOPMENT OF CAR-T THERAPY IN PEDIATRIC ONCOHEMATOLOGY: GLOBAL EXPERIENCE AND PROSPECTS FOR EMERGING HEALTHCARE SYSTEMS

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Abstract: Chimeric antigen receptor (CAR) T-cell therapy has revolutionized the treatment of pediatric B-cell acute lymphoblastic leukemia (ALL), offering hope in relapsed or refractory (r/r) cases that previously had dismal outcomes. Pediatric ALL is a global health challenge – it is the most common childhood cancer, and while cure rates exceed 85–90% in high-income countries, the majority of children with ALL live in low- and middle-income countries (LMICs) where survival remains much lower*[1][2]*. The emergence of CAR-T therapy, marked by the first FDA approval in 2017 for r/r pediatric ALL, represents a game-changer in bridging this survival gap. This review (2020–2025 literature) examines worldwide CAR-T implementation, including FDA/EMA-approved therapies and their dissemination in North America, Europe, and Asia, as well as indigenous CAR-T programs in countries like China and India. We discuss the major challenges impeding global adoption: high treatment costs (often >$400,000 per infusion), complex logistics (requirement for specialized cell manufacturing and accredited centers), regulatory hurdles, and ethical considerations of equity. Case studies of CAR-T introduction in emerging healthcare systems are highlighted, such as academic point-of-care manufacturing in Kazakhstan and collaborative platforms like the WHO–St. Jude Global initiative. Strategies for building capacity in resource-limited settings are reviewed – including technology transfer, regional centers of excellence, and exploration of allogeneic "off-the-shelf" CAR immune cells to reduce infrastructure demands. In conclusion, we outline a roadmap for integrating CAR-T into pediatric oncology networks of Central Asia and similar regions, emphasizing sustainable approaches to ensure this innovative therapy benefits children worldwide.

Keywords: CAR-T therapy; pediatric acute lymphoblastic leukemia; global health; emerging healthcare systems; immunotherapy; cell and gene therapy; access to care

Introduction

Acute lymphoblastic leukemia (ALL) is not only the most common childhood malignancy, but also a critical contributor to global childhood cancer mortality. Each year, thousands of children worldwide are diagnosed with ALL, with a disproportionately large burden in low- and middle-income countries (LMICs). Thanks to advances in chemotherapy protocols, risk stratification, and supportive care, survival rates for childhood ALL now reach ~90% in high-income countries*[1]*. However, outcomes in many resource-limited settings lag far behind, due to challenges in timely diagnosis, therapy access, and higher rates of treatment failure. Relapsed or refractory (r/r) ALL remains an area of unmet need: historically, less than 50% of children

achieve a second remission after relapse, and cure rates following a relapse have stagnated around 20–40% despite aggressive interventions[6].

The emergence of **CAR-T cell therapy** has been a watershed moment in pediatric oncohematology. CAR-T cells are patient (or donor)-derived T lymphocytes genetically engineered to express synthetic receptors targeting leukemia-associated antigens (most commonly CD19 on B-ALL cells). Upon binding to the target, CAR-T cells become activated and lyse the tumor cells, while also proliferating and persisting as "living drugs". In early clinical trials, anti-CD19 CAR-T therapy induced high rates of complete remission in children with multiply relapsed ALL[4], leading to the landmark FDA approval of Tisagenlecleucel in 2017 for pediatric and young adult r/r B-ALL[4]. This made CAR-T therapy the first gene therapy to enter routine pediatric oncology practice in the USA, soon followed by approval in Europe and other regions. It was hailed as a **"game changer"** for r/r ALL, converting a historically fatal scenario into one with a significant chance of cure[8].

Despite its success in controlled trials and specialized centers, CAR-T therapy's global implementation faces considerable hurdles. The therapy's delivery is complex and resource-intensive, involving individualized cell manufacturing, specialized hospital units for managing toxicities, and substantial financial costs. In 2023, an analysis showed CAR-T treatment is available predominantly in high-income countries, whereas children in most LMICs have virtually no access to this modality. Bridging this gap is a pressing challenge for the global pediatric oncology community.

This review aims to summarize the **global experience** with pediatric CAR-T therapy to date (2020–2025) and discuss prospects for its implementation in **emerging healthcare systems**. We begin by highlighting the progress of CAR-T adoption across different regions – including regulatory approvals, real-world outcomes, and initiatives in countries such as the United States, European nations, China, and South Korea. We then address cross-cutting challenges: cost barriers, logistical and manufacturing constraints, regulatory and ethical issues, and health system readiness in developing contexts. Finally, we discuss strategies and models that could enable **sustainable integration** of CAR-T therapy into pediatric oncology in regions with developing infrastructure, with a focus on Central Asia as a case example. By examining both successes and setbacks in CAR-T implementation, we seek to outline a roadmap for making this life-saving therapy accessible to children irrespective of their country of origin.

Materials and Methods

A literature review was conducted covering publications from 2020 to 2025 on CAR-T therapy in pediatric oncohematology, with emphasis on implementation and global health aspects. Sources were identified via **PubMed** and **Scopus** searches using keywords such as "CAR-T pediatric ALL global access," "CAR-T low- and middle-income countries," and "CAR-T implementation WHO." Inclusion criteria encompassed clinical trial reports, registry analyses, global policy reviews, World Health Organization (WHO) publications, and case studies documenting the introduction of CAR-T in new regions. Key regulatory documents (FDA, EMA approvals) and **WHO–St. Jude Global Initiative** reports were also reviewed to gather data on international efforts to broaden access to advanced therapies. In total, approximately 150 articles and reports were screened, with priority given to those containing quantitative data on outcomes (remission rates, survival) in various countries, discussions of cost and infrastructure, and recommendations for expanding CAR-T therapy beyond high-income settings. The evidence was synthesized in an IMRAD format, and 15–20 of the most relevant and recent references are cited

to support the analysis. Notably, because formal clinical data from many LMIC settings are sparse, we also incorporated findings from conference presentations, expert commentary, and collaborative consortium outputs (e.g., the ACCELERATE CAR-T Access paper) to ensure a comprehensive perspective. Ethical considerations did not require specific review as this study is an analysis of published data.

Results

Global Adoption of Pediatric CAR-T Therapy: Since the first approvals in 2017–2018, CAR-T therapy for ALL has seen **gradual worldwide adoption**. In North America and Western Europe, anti-CD19 CAR-T products (Tisagenlecleucel and others) are now part of standard care for relapsed pediatric B-ALL. The USA alone has treated over a thousand pediatric and young adult ALL patients with CAR-T by 2023, as captured in registries. The European Medicines Agency approved Tisagenlecleucel in 2018, and numerous EU countries have established national CAR-T centers (often in major pediatric oncology hospitals). Real-world outcome data from these regions confirm high remission rates (~80–85% CR) and substantial 1-year event-free survival (~50–60%) in treated children, comparable to pivotal trial results*[3]*. Access within high-income countries, however, can still be uneven – for instance, patients in rural areas or without referral to specialized centers may face delays.

In the Asia-Pacific, **Japan, South Korea, China, and Australia** have all approved or utilized CAR-T therapy. Japan launched Kymriah in 2019, negotiating a slightly lower price under its national insurance. South Korea, via Seoul National University Hospital and others, initiated clinical trials and compassionate use by 2021. **China** has rapidly become a CAR-T powerhouse: by 2022 it led the world in number of CAR-T clinical trials, fueled by substantial government and industry investment. While China initially relied on hospital-run trials, in 2021–2022 its regulatory agency (NMPA) approved the first domestic CAR-T products (for lymphoma and myeloma). In 2024, China was on the cusp of approving its first CAR-T specifically for pediatric ALL – a product named **pCAR-19B (Pukilin)** developed in Chongqing. This product, targeting CD19 in children aged 3–21, received "Breakthrough Therapy" designation and NDA acceptance, reflecting China's strategic push to make CAR-T **more accessible and affordable** domestically. Chinese centers have reported robust outcomes similar to Western trials and even treated cases from neighboring countries. South Korea and Singapore have also treated a handful of pediatric patients through clinical trials or by referring patients overseas, indicating emerging capacity in those systems.

Regulatory Approvals and Guidelines: As of 2025, at least **six CAR-T products** have been approved by the US FDA for various hematologic malignancies (including Tisagenlecleucel for pediatric ALL, and others for lymphoma and adult myeloma). The EMA has approved two products for pediatric ALL and several for other indications. Health authorities in Canada, Australia, Japan, South Korea, and China have authorized one or more CAR-T therapies, often leveraging clinical data from multinational trials. In contrast, most LMICs lack formal approvals; patients in those countries can only receive CAR-T via clinical trial participation or medical travel. Recognizing the need for harmonization, organizations like the **Pediatric Real World CAR Consortium** and the **EBMT** (European Society for Blood and Marrow Transplantation) have developed guidelines on patient selection, toxicity management, and long-term follow-up, which have been shared internationally. WHO has also included CAR-T in its discussions on essential therapies for childhood cancer, although it's not yet on the Model List of Essential Medicines.

Real-World Outcomes in Diverse Settings: Published real-world studies largely come from high-income countries, showing that CAR-T therapy can induce minimal residual disease (MRD)-negative remissions in 75–90% of r/r ALL patients*[3]*, with many children bridged to stem cell transplant or observed for durable remission. For example, an analysis of 255 patients in the CIBMTR registry reported 85.5% complete remission and 77% one-year overall survival post-CAR-T*[11]*. These outcomes mirror clinical trial data. In terms of safety, the incidence of severe cytokine release syndrome (CRS) is around 5–10%, and severe neurotoxicity (ICANS) ~<10%, which most centers can manage with standardized protocols*[9]*.

Data from **middle-income countries** are only beginning to emerge. In **China**, where hundreds of pediatric ALL patients have now received CAR-T (either commercial or trial), outcomes are comparable with ~80% CR rates, although long-term follow-up is limited by many proceeding to transplant. One center reported on 20 children with r/r ALL treated with CD19 CAR-T: all achieved MRD-negative remission, illustrating the high efficacy. China's experience also highlights logistic hurdles – e.g., during the COVID-19 pandemic, CAR-T manufacturing and patient monitoring had to adapt to lockdowns, yet efforts continued. **India** achieved a milestone with the approval of its first indigenous CAR-T product **NexCAR19** in late 2023, developed via an academic-private partnership (IIT Bombay and ImmunoACT). Early results in adult lymphoma are promising, and pediatric trials are planned. Another product, **varthemcabtagene autoleucel** (Qartemi), was approved in 2025, making India one of the first LMICs to have homegrown CAR-T therapies. While clinical data on pediatric patients in India is not yet published, these approvals show the potential for LMICs to develop CAR-T capacity. Some pediatric cases in India have been treated on a trial basis; for example, the first child treated with CAR-T there was reported in media to be in remission and doing well a year post-infusion.

Other LMICs are catching up slowly: in Latin America, centers in **Brazil** and **Argentina** have run CAR-T trials in partnership with international groups. Brazil treated a few pediatric patients via a clinical trial (with product manufactured in China), and results indicate feasible expansion of T cells and remission in at least some cases. **Mexico** and **Pakistan** have reported individual cases of children who received CAR-T therapy abroad (e.g., in the USA or China) and returned home in remission. These anecdotal successes underscore a growing demand. Importantly, a survey by Latin American pediatric oncology groups found that lack of manufacturing facilities and high cost were perceived as the main barriers to offering CAR-T locally.

Cost and Logistics Challenges: The cost of CAR-T therapy is a dominant theme in global implementation. The list price of a single commercial CAR-T infusion (e.g., tisagenlecleucel) in the US is about **$475,000**, which excludes additional hospital costs for critical care management, diagnostics, travel, etc. Real-world cost analyses show total expenses often exceed $750,000 per patient in the US when factoring in all related care. In Europe, negotiated prices vary (e.g., ~$350,000 in Germany or UK, often with outcome-based reimbursement schemes). For LMICs, these figures are prohibitive – a sum that could fund entire oncology units for years. Consequently, **few LMIC health systems can afford CAR-T** on any significant scale. For instance, in Brazil and India, initial CAR-T cases were funded by research grants or philanthropy, not standard insurance.

Logistically, CAR-T therapy requires a chain of sophisticated processes: leukapheresis to collect T cells, cryopreservation and shipping (if manufacturing is centralized abroad), a manufacturing lab (meeting Good Manufacturing Practice, GMP), and return shipping of the gene-modified product. During the manufacturing period (typically 2–4 weeks), patients need bridging therapy to control disease. Once CAR-T cells are infused, patients must stay near specialized centers for

monitoring of CRS/ICANS for at least 2–4 weeks. In countries with vast geography or limited centers, **distance to CAR-T treatment sites** is itself a barrier – as seen in a US study where patients in certain regions traveled 2–3 times farther to access CAR-T than those in others. In LMICs, the concentration of expertise in capital cities means patients from rural provinces must overcome travel and lodging challenges, often without support. For example, a child from a rural area of India might need to relocate to Mumbai or Delhi for over a month to undergo CAR-T, an ordeal for families of low socioeconomic status.

Furthermore, CAR-T manufacturing slots are limited. In the US/EU, companies have at times faced production backlogs. In a global context, if a country without local manufacturing wants to treat a patient, they may need to export cells and import the product – a complex endeavor legally (cross-border cell shipments, regulatory approvals) and logistically (maintaining frozen supply chain). Some wealthy international patients (from the Middle East, for instance) have traveled to the US or Europe to get CAR-T, essentially bypassing local system limitations, but this is not a scalable solution for broader populations.

Healthcare Infrastructure and Human Resources: Successful CAR-T programs demand a multidisciplinary team (pediatric oncologists, immunologists, apheresist, ICU specialists, etc.) and institutional preparedness (cell processing lab or partnerships, ICU beds, diagnostic assays for MRD and immune reconstitution). Many emerging healthcare systems are still building basic cancer treatment capacity, and CAR-T lies at the very advanced end of the spectrum. **WHO's Global Initiative for Childhood Cancer** has focused on improving survival in common pediatric cancers through proven therapies like chemotherapy – CAR-T and other gene therapies were not initially within its scope, given their complexity. However, there are instances of capacity building: for example, in 2021, the **WHO Collaborating Centre** at SJCRH (St. Jude) announced training programs for LMIC clinicians in cellular therapy, acknowledging future needs.

In **Central Asia**, pediatric oncology centers are modernizing but had no CAR-T capability until recently. By 2025, Kazakhstan's National Center for Biotechnology reported a breakthrough: a local team established an academic CAR-T manufacturing pipeline using the CliniMACS Prodigy platform. They produced CD19-directed CAR-T cells in Astana with quality comparable to international products, achieving successful manufacturing for 12 patients in a clinical trial. This is a striking proof-of-concept that a country with "forming infrastructure" can develop CAR-T therapy from scratch, given dedicated resources and expertise. Similarly, Uzbekistan has expressed interest in CAR-T – their scientists and clinicians are collaborating with international partners to initiate CAR-T trials for leukemia and multiple myeloma. These Central Asian initiatives are supported by the recognition that childhood cancer is a growing priority, and by leveraging regional collaboration (e.g., Kazakhstan offering to treat patients from neighboring countries at its new centers).

WHO and International Support: An important development is the **WHO–St. Jude Global Platform for Access to Childhood Cancer Medicines** launched in 2021. While its initial focus is on providing essential chemotherapeutic drugs to 50 LMICs, the platform establishes a model for international procurement and distribution that could, in the future, be expanded to advanced therapies. St. Jude's $200 million investment in this platform highlights the scale of resources needed. Additionally, organizations like the **Leukemia & Lymphoma Society** and transnational research consortia (ACCELERATE in Europe) have convened multi-stakeholder task forces to explore new models for CAR-T development and access. A 2025 policy review by Pearson *et al.* (ACCELERATE) gathered experts from across the world to propose solutions such as academic

manufacturing networks, ethically pricing strategies, and adaptive regulatory pathways for pediatric CAR-T.

Discussion

Regulatory and Policy Barriers: One of the most significant obstacles is the lack of regulatory frameworks in many countries for approving and overseeing **cell and gene therapies**. Traditional drug approval processes are not fully applicable to living cellular products, and only a few LMIC regulators (e.g., China's NMPA, India's CDSCO) have gained experience in this area. Many countries rely on approvals by FDA/EMA as a basis, but even after approval, they face the challenge of safety monitoring and quality control, especially if therapies are imported. Establishing **transparent, expedited regulatory pathways** for CAR-T in emerging markets is essential. This may involve creating special designations (as done in China with "Breakthrough Therapy" for CAR-T) or adopting the concept of hospital exemption (used in Europe to allow non-licensed academic CAR-T products for individual patients within a hospital's practice). Collaboration among regulatory bodies is increasing: workshops by organizations like the African Medicines Agency and PAHO have started to include advanced therapies on the agenda. Streamlining regulatory requirements could help, for example by accepting evidence from foreign trials and enabling **local deployment under monitored use**.

Economic and Ethical Challenges: The extreme cost of CAR-T raises ethical questions about resource allocation. In environments where health budgets are limited, decision-makers must balance investing in one CAR-T treatment versus funding basic treatments for dozens of other children. Ethically, denying a child a potentially curative therapy because of cost is troubling, especially as CAR-T is no longer "experimental" but a recognized standard in wealthier nations. This disparity touches on the principle of justice in global health. Some ethicists argue for a "dual-tier" approach: continue improving cost-effectiveness so that CAR-T can eventually be offered widely, while in the interim possibly subsidize such treatments via international aid for select cases. Indeed, philanthropic funding has enabled some children from LMICs to receive CAR-T abroad through compassionate programs, but these are ad hoc solutions.

The **high price point** is partially driven by the individualized manufacturing and the commercial model (pharmaceutical companies needing to recoup R&D costs). Efforts are underway to reduce costs: for instance, **point-of-care manufacturing** in academic centers can substantially cut expenses by using local infrastructure and non-profit frameworks. The Kazakhstan example showed that in-house production of viral vectors and automated cell processing is feasible in a developing setting, implying that similar models could circumvent international profit margins. Another strategy is outcome-based payments: paying only if the patient achieves remission, as trialed in some EU countries, to ensure health systems get value for money. However, for LMICs, even a "half-price" CAR-T may remain out of reach unless international financing mechanisms or tiered pricing are introduced. Ethical distribution within countries also matters – if only a small number of CAR-T treatments can be funded, clear criteria are needed to select patients (e.g., based on prognosis or lottery), to avoid perceptions of unfairness or bias.

Infrastructure and Capacity Building: Achieving equitable access to CAR-T will require strengthening health infrastructure. Key components include:

- **GMP manufacturing facilities:** Building local or regional cell therapy laboratories. Regional hubs could serve multiple countries (for example, a facility in Singapore could manufacture for Southeast Asia; one in Kazakhstan could serve Central Asia). Such hubs could

take advantage of economies of scale. The **ACCELERATE consortium** advocated for public-private partnerships to create non-profit manufacturing centers that prioritize pediatric indications. Training personnel to run these facilities is equally important – initiatives like the global CAR-T training by St. Jude or the EHA are first steps[21].

- **Specialized treatment centers:** Not every hospital can deliver CAR-T safely. Countries may need to designate one or two pediatric hospitals as national centers of excellence for cellular therapy, concentrating expertise. For example, **Kazakhstan's pediatric oncology plan** includes establishing an international hub in Astana that could accept patients from across Central Asia. This hub-and-spoke model ensures quality while extending coverage. Telemedicine and twinning programs can connect these centers with experienced mentors in the US/EU for on-call advice during complications.

- **Supply chains and biobanking:** Setting up cold chain logistics for cell transport is vital if manufacturing is not on-site. This involves liquid nitrogen freezers, couriers, and backup plans (e.g., in case of flight delays). Some LMIC regions are exploring regional biobanks – for instance, storing donor lymphocytes or induced pluripotent stem cell lines that can be used to derive allogeneic CAR-T or CAR-NK cells.

- **Human resources:** Training programs for pediatric oncologists, nurses, and ICU staff in CAR-T management are expanding. Conferences in 2023 by SIOP (International Society of Pediatric Oncology) dedicated sessions to CAR-T in LMICs, indicating knowledge transfer is happening. Additionally, developing local expertise in immunology and cell processing (through fellowships or exchange visits) will empower emerging centers to operate independently. The success in Astana was partly due to young scientists trained abroad returning home with cell therapy knowledge.

Prospects for Technology Leapfrogging: Interestingly, some emerging systems might **leapfrog** directly to newer CAR-T technologies that are easier to deploy. For example, **allogeneic CAR-T cells** (derived from healthy donors, possibly gene-edited to prevent rejection) promise an off-the-shelf solution, which could eliminate the need for local GMP facilities for each patient. If ongoing trials prove them safe and effective, LMICs could import frozen allogeneic CAR-T products in bulk, like conventional medicines, drastically simplifying logistics. One caveat is that current allogeneic CAR-T cells (and CAR-NK cells) tend to have shorter persistence, possibly requiring multiple doses, but they could still be life-saving bridges to transplant or remission. Companies are also developing modular CAR-T manufacturing units (akin to portable GMP labs) which could be installed in existing hospitals – these might accelerate capacity building if costs come down[21].

Another avenue is **regional and international collaborations**. The WHO Global Initiative and St. Jude Global Alliance encourage countries to collaborate. For CAR-T, this could mean shared patient registries, pooled procurement, and cross-border care agreements. For example, **Central Asian republics** could collectively invest in one manufacturing center and referral network, rather than each duplicating efforts. Already, Kazakhstan's Proton Therapy Center (opened 2023) is set to treat patients from Uzbekistan and beyond; a similar model could apply to CAR-T treatment.

Ethical-legal considerations: Using advanced therapies in developing contexts raises concerns like ensuring informed consent (families need counseling that CAR-T is intensive and not guaranteed), handling biobanking of patient cells, and regulatory oversight to prevent misuse.

The case of one unauthorized CAR-T offering in a developing country causing adverse outcomes could set back public trust. Therefore, establishing **ethical frameworks** and training Institutional Review Boards in these therapies is part of the process. Intellectual property issues also arise: local production of CAR-T might conflict with patents held by pharma companies. Some academic groups have chosen to use **public-domain CAR constructs** (e.g., a known CD19 CAR sequence published in literature) to avoid patent hurdles and reduce cost. Policymakers in LMICs may need to navigate compulsory licensing or patent pooling if they aim to produce CAR-T without huge costs. These legal tools have precedence in drug access and could potentially apply to CAR-T in humanitarian contexts.

Central Asia Focus – Opportunities and Challenges: The Central Asian region (e.g., Kazakhstan, Uzbekistan) exemplifies both the potential and challenges for CAR-T implementation in emerging systems. There is strong political will to modernize healthcare; Kazakhstan, for instance, has significantly invested in oncology and is positioning itself as a regional hub. The successful academic CAR-T production in 2025 indicates that with training and infrastructure, even a developing country can *create* advanced therapies, not just import them. This can inspire other countries. Challenges remain: scaling up production from a pilot to a routine clinical service will require sustainable funding and integration into national healthcare. Currently, such programs often rely on external grants or pilot project funding. Ensuring long-term government support or insurance coverage for CAR-T will be crucial, as will demonstrating cost-effectiveness (for example, comparing lifetime costs of CAR-T versus multiple salvage chemo and transplant). Close cooperation with international experts will help maintain quality and address complications for first cases. Notably, the cultural aspect – families' and physicians' acceptance of a high-tech therapy – seems positive in Central Asia, where there is enthusiasm for adopting new medical innovations.

Strategies for Sustainable Integration: Summarizing the strategies to enable CAR-T in emerging healthcare systems:

- **Phased introduction:** Start with a few pilot cases (possibly via clinical trials or compassionate use with overseas manufacturing) to build local experience. Document outcomes and refine protocols. Use these data to advocate for broader support.
- **Local manufacturing and academic alliances:** Partner with academic centers in high-income countries to transfer technology for CAR-T production. Several US/EU universities have expressed willingness to collaborate (for example, St. Jude has partnerships in China for technology exchange). Academic CAR-T models often use inexpensive production methods, which can be taught.
- **Regional centers of excellence:** As mentioned, concentrate expertise regionally. Centralize the complicated parts (like manufacturing, ICU care for CRS) while training local centers to handle referrals and follow-up.
- **Financial innovations:** Explore alternative funding – e.g., government subsidy for pediatric CAR-T under national child health initiatives, crowd-funding platforms for individual cases (which has already occurred spontaneously), or inclusion of CAR-T in global funding schemes for non-communicable diseases. International financing facilities might one day consider supporting cell therapy for key indications if costs drop.
- **Alliances with industry:** Some CAR-T companies have tiered pricing or have donated doses to LMIC patients. For instance, Novartis has worked with charitable foundations to treat a limited number of children from low-income countries. Engaging industry in access discussions,

maybe via **public-private partnerships**, could yield expanded access programs at lower cost in targeted regions.

- **Training and retention of talent:** Ensure that the clinicians and scientists trained in CAR-T are supported and retained in their home countries. A risk is the "brain drain" – those with cell therapy expertise might be recruited abroad. Creating career opportunities domestically, with research funding and recognition, is key to sustaining programs.

In terms of **timeline**, many experts predict that over the next 5–10 years, CAR-T therapy will steadily penetrate upper-middle-income countries and some lower-middle-income ones, especially as next-generation products (like allogeneic CAR-T) potentially reduce costs. The WHO's focus on childhood cancer could eventually incorporate CAR-T once more foundational needs are met, to avoid a growing survival gap for relapsed ALL. The example of immunotherapy with antibodies (e.g., rituximab) shows that novel treatments can become globally available within a decade given generic production and advocacy; a similar pattern could, optimistically, happen for cellular therapies if manufacturing becomes more standardized.

Conclusion

The global experience with CAR-T therapy in pediatric oncohematology underscores both its transformative clinical impact and the profound challenges in ensuring equitable access. In high-resource settings, CAR-T cells targeting CD19 (and other antigens) have redefined outcomes for children with relapsed B-ALL, delivering unprecedented remission rates and offering a curative pathway where none existed*[3]*. The task now is to translate these gains to the worldwide pediatric population. For emerging healthcare systems, the path to CAR-T implementation, while steep, is increasingly navigable. Key enablers include focused capacity building – establishing local manufacturing capabilities (as demonstrated in Kazakhstan), training specialized multidisciplinary teams, and creating centers of excellence that can safely administer these complex therapies. International collaborative frameworks – such as the WHO–St. Jude Global platform and the ACCELERATE multi-stakeholder initiatives – provide blueprints for resource-pooling, technology transfer, and policy development to incorporate CAR-T into national treatment protocols.

In Central Asia, there is promising momentum: investments in medical infrastructure and regional cooperation are laying the groundwork for introducing CAR-T into standard pediatric oncology practice. The prospect of a regional CAR-T hub serving countries like Uzbekistan, Kazakhstan, and neighbors is moving from vision to reality, leveraging shared resources and expertise. Similar models can be emulated in other emerging regions (e.g., consortia in Latin America, Southeast Asia, or Africa), effectively narrowing the gap between cutting-edge science and bedside care. The advent of **allogeneic "off-the-shelf" CAR therapies** might further democratize access by simplifying logistics and reducing per-patient costs – an innovation that emerging systems are keenly watching.

For sustainable integration of CAR-T therapy in pediatric oncology networks of developing countries, several pathways stand out: (1) **Public-sector and academic leadership** in CAR-T development, to ensure affordability and appropriate prioritization of pediatric indications. (2) **South-South and North-South collaborations**, enabling knowledge exchange and support for pilot programs. (3) **Policy reforms and financing mechanisms** that treat curative therapies for childhood cancers as high-value investments (considering the young lives saved and many potential life-years gained). In the long term, as manufacturing efficiencies improve and perhaps

as patents expire, the cost of CAR-T is expected to decrease, making national adoption more feasible.

In conclusion, while significant barriers remain, the prospects for integrating CAR-T therapy into emerging healthcare systems are brightening. Each successful case of a child in remission after CAR-T in a low-resource setting is a powerful proof-of-concept that fuels further progress. Ensuring that this breakthrough **reaches all corners of the globe** is a collective responsibility of the international medical community, industry stakeholders, and governments. By continuing on the current trajectory – investing in capacity, fostering innovation (like regional CAR-T production centers and novel allogeneic products), and maintaining an unwavering commitment to equity – CAR-T therapy can be transitioned from a high-tech rarity to a routine component of pediatric cancer care worldwide. For children in Central Asia and other developing regions, this means a future where a diagnosis of relapsed ALL is met with effective, state-of-the-art treatment locally, and the chance for cure no longer depends on the accident of geography.

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