Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

With an array of novel therapies for non-Hodgkin lymphomas, anticipating responses is crucial before selecting the next line of therapy. One major drawback of CAR T-cell therapy is the need for individualised production from heavily pre-treated patients. In the JULIET study, the drop-off rate was substantial, and only 115 (69%) of the 165 patients who were apheresed for CAR T-cell production received tisagenlecleucel. The authors do not present an intention-to-treat analysis, which might have shown a lower complete response rate. Also, of the 115 patients treated, 70 died during the study period (with no treatment-related deaths), most likely of disease relapse or toxicity from further therapies, showing the highly resistant disease in the patients participating in the trial.

The findings reported by Schuster and colleagues[8] show the long-term benefit of CD19-directed CAR T cells as a standalone therapy for some patients with non-Hodgkin lymphomas. Moreover, emerging, not yet peer-reviewed, results showing the superiority of CD19-directed CAR T-cell therapies over standard-of-care autologous haematopoietic stem-cell transplantation in the second line will most likely change the treatment paradigm for patients with relapsed or refractory aggressive B-cell lymphomas in the near future. Still, the mechanisms of relapse and resistance to CAR T cells in non-Hodgkin lymphomas have not been completely elucidated, and some studies have suggested loss of the target antigen and insufficient co-stimulation of T cells as potential culprits.[10] Indeed, future studies should help to identify who are likely to benefit from CD19-directed CAR T cells, and help to design better CARs to overcome resistance. These data would aid clinicians in selecting the right therapy for the right patient at the right time.

For these **results** see https://bit.ly/2SBcMuj

EJ reports honorarium or participation on advisory boards for Amgen, Novartis, and Lonza. AA reports serving on advisory boards for Roche, Janssen, Sanofi, and Takeda.

*Elad Jacoby, Abraham Avigdor
elad.jacoby@sheba.health.gov.il

Center for Cell Therapy and Pediatric Hematology and Oncology (EJ) and Division of Hematology (AA), Sheba Medical Center, Tel Hashomer 5262000, Israel; Department of Pediatrics (EJ) and Department of Hematology (AA), Sackler School of Medicine, Tel Aviv University, Tel Aviv, Israel (EJ, AA)

1 Kochenderfer JN, Wilson WH, Janik JE, et al. Eradication of B-lineage cells and regression of lymphoma in a patient treated with autologous T cells genetically engineered to recognize CD19. *Blood* 2010; **116:** 4099–102.
2 Schuster SJ, Bishop MR, Tam CS, et al. Tisagenlecleucel in adult relapsed or refractory diffuse large B-cell lymphoma. *N Engl J Med* 2019; **380:** 45–56.
3 Locke FL, Ghobadi A, Jacobson CA, et al. Long-term safety and efficacy of axicabtagene ciloleucel in refractory large B-cell lymphoma (ZUMA-1): a single-arm, multicentre, phase 1–2 trial. *Lancet Oncol* 2019; **20:** 31–42.
4 Abramson JS, Palomba ML, Gordon LI, et al. Lisocabtagene maraleucel for patients with relapsed or refractory large B-cell lymphomas (TRANSCEND NHL 001): a multicentre seamless design study. *Lancet* 2020; **396:** 839–52.
5 Pasquini MC, Hu ZH, Curran K, et al. Real-world evidence of tisagenlecleucel for pediatric acute lymphoblastic leukemia and non-Hodgkin lymphoma. *Blood Adv* 2020; **4:** 5414–24.
6 Jacobson CA, Hunter BD, Redd R, et al. Axicabtagene ciloleucel in the non-trial setting: outcomes and correlates of response, resistance, and toxicity. *J Clin Oncol* 2020; **38:** 3095–106.
7 Jacobson C, Locke FL, Ghobadi A, et al. Long-term survival and gradual recovery of B cells in patients with refractory large B cell lymphoma treated with axicabtagene ciloleucel (axi-cel). *Blood* 2020; **136** (suppl 1)**:** 40–42.
8 Schuster SJ, Tam CS, Borchmann P, et al. Long-term clinical outcomes of tisagenlecleucel in patients with relapsed or refractory aggressive B-cell lymphomas (JULIET): a multicentre, open-label, single-arm, phase 2 study. *Lancet Oncol* 2021; published online Sept 10. https://doi.org/10.1016/S1470-2045(21)00375-2.
9 Hirayama AV, Gauthier J, Hay KA, et al. The response to lymphodepletion impacts PFS in patients with aggressive non-Hodgkin lymphoma treated with CD19 CAR T cells. *Blood* 2019; **133:** 1876–87.
10 Majzner RG, Mackall CL. Clinical lessons learned from the first leg of the CAR T cell journey. *Nat Med* 2019; **25:** 1341–55.

Childhood cancer control during the COVID-19 pandemic

See **Articles** page 1416

In early 2020, the COVID-19 pandemic set the research community on a new path to understand the virus, how it affects different populations, and how it influences access to essential services. The ensuing research could have been done in isolation or with a competitive spirit. In childhood cancer, the opposite occurred; the research community united in solidarity, offering another opportunity to use investments in data systems and collaborative networks, which have defined childhood cancer research for the past half century. It is in this context that the value of the publication in *The Lancet Oncology* by Sheena Mukkada and colleagues[1] can be understood. This prospective cohort study of the characteristics and outcomes of children and adolescents (<19 years) with cancer and COVID-19 around the world, reports data from 1500 patients from 131 institutions in 45 countries. 259 (19·9%) of 1301 patients had a severe or critical infection, with 50 (3·8%) of 1319 cases resulting in death. In adults with cancer, the death rate is higher (28%) than that for children and correlates with age.[2] Mukkada and colleagues found a high percentage (35·0%) of

asymptomatic children with cancer. Furthermore, patients from low-income and lower-middle-income countries had a higher proportion of severe or critical outcomes (41·7%) than patients from upper-middle-income countries (16·5%), and high-income countries (7·4%). Deaths from COVID-19 were also higher in patients from low-income and lower-middle-income countries than patients from upper-middle-income countries, and high-income countries, despite the under-representation of low-income countries (African, South-East Asian, and Western Pacific Regions), probably secondary to the scarcity of SARS-CoV-2 testing or overwhelmed services that were unable to report cases.

The strength and merits of the Article's conclusions were achieved because of the legacy of global collaborative networks that have driven innovation, advanced research priorities, and, ultimately, improved childhood cancer care. Unfortunately, the results from Mukkada and colleagues also show a known tragic reality, that inequities in health systems globally have been exacerbated by the COVID-19 pandemic. Children living in low-income and middle-income countries have the greatest burden of childhood cancer and experience the greatest inequities.[3,4]

The pandemic has exposed weaknesses in health systems and capacities to control childhood cancer. As described by Vasquez and colleagues[5] and summarised by Moreira and colleagues[6] on the early and overall effect of the pandemic on childhood cancer care globally, there have been reductions in access to diagnostic and therapeutic services, worsened access to essential medicines, postponement of chemotherapy administration, delay and even indefinite postponement of radiotherapy, and lower rates of follow-up and surveillance. Disruptions to childhood cancer services have not been as severe in high-income countries. Therein lies the problem: resilient health systems can absorb shocks during times of crisis (such as the pandemic, conflict, and climate change). Although childhood cancer functions to some extent in its own health ecosystem, services still rely on investments in health systems and prioritisation of the broader cancer and non-communicable disease agenda, as part of universal health coverage. Such investments continue to lag in low-income and middle-income countries.

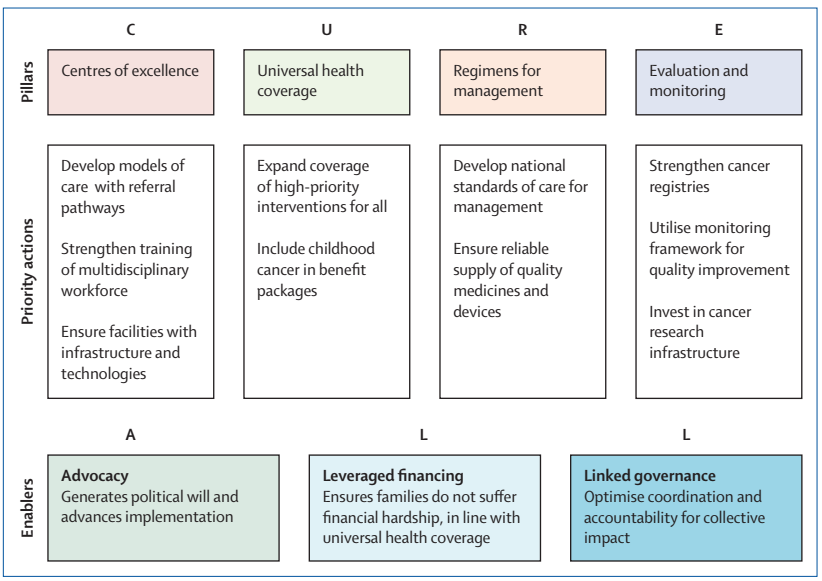

Figure: **CureAll framework**
Reproduced with permission from WHO.[10]

Childhood cancer should be a strategic priority. It is among the most curable group of cancers, with an 80% overall survival in high-income countries.[7] This probability of cure is feasible and sustainable in all countries with appropriate resources.[7] Yet, in low-income and middle-income countries, which have about three-quarters of the global burden of childhood cancer, only 20–30% of individuals have long-term survival. Delays in early detection; poor access to diagnostic services and technologies; absence of full access to required anticancer drugs (as defined on the WHO list of essential medicines); higher rates of comorbidities (eg, malnutrition, infection, and poverty); and refusal and abandonment of therapy are common, resulting in increased morbidity and treatment-related mortality.[8] All these factors result in lower survival rates and higher amounts of morbidity than in high-income countries.

Added to the disadvantages of children with cancer in low-income and middle-income countries, the COVID-19 pandemic is worsening inequalities. The past 4 years have seen improved positioning of childhood cancer in the global health agenda. With the mandate given by governments in the World Health Assembly resolution on cancer (WHA 70.12), in 2018, WHO, alongside St Jude Children's Research Hospital (Memphis, TN, USA) and other key strategic partners like the International Society of Pediatric Oncology,

both of whom are leading the Global Registry of COVID-19 in Childhood Cancer,[1] launched the Global Initiative for Childhood Cancer with the overall target to cure 60% of all children with cancer globally and decrease suffering for all.[9]

The Cure*All* Framework for childhood cancer outlines the steps necessary to improve access to care and reduce inequalities as part of building more resilient health systems and achieving universal health coverage (figure).[10] This framework is feasible for all countries and in all contexts.

The data from Mukkada and colleagues' study[1] provide us with a new understanding of childhood cancer during the pandemic. When combined with the legacy of global collaboration in childhood cancer and political prioritisation through the WHO Global Initiative for Childhood Cancer, there is a unique opportunity to develop and implement mitigation strategies, tailored to the current threats encountered in specific health systems, and to reduce globally inequalities. Collaboration and solidarity drive progress in childhood cancer care. This approach has been shared among the childhood cancer community for decades and is needed now more than ever.

SL-F declares support from St Jude Children's Research Hospital and WHO, Unit of Management of Noncommunicable diseases. SL-F, AI, and RO are staff members or consultants of WHO. The authors alone are responsible for the views expressed in this Comment and they do not necessarily represent the decisions, policy, or views of WHO.

*Sandra Luna-Fineman, Roberta Ortiz, Andre Ilbawi
sandra.luna-fineman@childrenscolorado.org

University of Colorado School of Medicine, Aurora, CO 80045, USA (SL-F); Department for the Management of Noncommunicable Diseases, Disability, Violence and Injury Prevention, World Health Organization, Geneva, Switzerland (SL-F, RO, AI)

1 Mukkada S, Bhakta N, Chantada GL, et al. Global characteristics and outcomes of SARS-CoV-2 infection in children and adolescents with cancer (GRCCC): a cohort study. *Lancet Oncol* 2021; **22:** 1416–26.
2 Lee LYW, Cazier JB, Angelis V, et al. COVID-19 mortality in patients with cancer on chemotherapy or other anticancer treatments: a prospective cohort study. *Lancet* 2020; **395:** 1919–26.
3 Ward ZJ, Yeh JM, Bhakta N, Frazier AL, Atun R. Estimating the total incidence of global childhood cancer: a simulation-based analysis. *Lancet Oncol* 2019; **20:** 483–93.
4 Bhakta N, Force LM, Allemani C, et al. Childhood cancer burden: a review of global estimates. *Lancet Oncol* 2019; **20:** e42–53.
5 Vasquez L, Sampor C, Villanueva G, et al. Early impact of the COVID-19 pandemic on paediatric cancer care in Latin America. *Lancet Oncol* 2020; **21:** 753–55.
6 Moreira DC, Millen GC, Sands S, Kearns PR, Hawkins DS. The care of children with cancer during the COVID-19 pandemic. *Am Soc Clin Oncol Educ Book* 2021; **41:** 1–10.
7 Atun R, Bhakta N, Denburg A, et al. Sustainable care for children with cancer: a *Lancet Oncology* Commission. *Lancet Oncol* 2020; **21:** e185–224.
8 Lam CG, Howard SC, Bouffet E, Pritchard-Jones K. Science and health for all children with cancer. *Science* 2019; **363:** 1182–86.
9 WHO Global Initiative for Childhood Cancer. An overview. World Health Organization, 2020. https://www.who.int/docs/default-source/documents/health-topics/cancer/who-childhood-cancer-overview-booklet.pdf (accessed Aug 24, 2021).
10 WHO CureAll Framework: WHO Global Initiative for Childhood Cancer Pamphlet, 2021. https://cdn.who.int/media/docs/default-source/documents/health-topics/cancer/cureall-framework-who-global-initiative-for-childhood-cancer-pamphlet.pdf?sfvrsn=6e9c5b1b_8 (accessed Aug 24, 2021).

Anticipating the COVID-19-related surge in cancer care demand is urgent in Latin America and the Caribbean

Staraldo/Shutterstock.com

Published **Online** September 3, 2021 https://doi.org/10.1016/S1470-2045(21)00484-8

See **Articles** page 1427

The COVID-19 pandemic has disrupted regular health services in every health system worldwide, and cancer care is no exception. In Latin America and the Caribbean, cancer services have been reported to be foregone or delayed, including first-time visits to oncology services, pathology, cancer surgery, chemotherapy, and screening tests,[1] with similar findings in the paediatric cancer field.[2] The study by Zachary J Ward and colleagues[3] published in *The Lancet Oncology* goes a step further; using data from five cancer sites in Chile, their study assesses the future effects of delayed diagnosis on cancer outcomes. The study[3] estimates that an overburden of 14% of cancer diagnoses is already starting in 2021, with worse cancer stage distribution, predicting an excess in cancer deaths of 10·8% in 2022–24 compared with a counterfactual scenario with no COVID-19. This analysis does not consider eventual treatment delays or issues with quality of care that might further increase these projected negative trends for Chilean patients with cancer. Further, the trends might be worse for marginalised and minority population groups, such as those from indigenous communities.

Since other countries in Latin American and the Caribbean are showing similar trends of foregone or delayed cancer services, the findings of this study[3] serve as a warning sign for governments and other