

Global Effort to Evacuate Ukrainian Children with Cancer and Blood Disorders Affected by War

Asya Agulnik¹, Roman Kizyma², Marta Salek¹, Marcin W. Wlodarski¹, Mikhail Pogorelyy¹, Aleksandra Oszer³, Taisiya Yakimkova¹, Yuliya Nogovitsyna⁴, Malgorzata Dutkiewicz⁵, Jean-Hugues Dalle⁶, Uta Dirksen⁷, Angelika Eggert⁸, Ana Fernández-Teijeiro⁹, Jeanette Greiner¹⁰, Kathelijne Kraal¹¹, Alexandra Mueller¹², Lucie Sramkova¹³, Marco Zecca¹⁴, Paul H. Wise¹⁵, Wojciech Mlynarski³ on behalf of the SAFER Ukraine Collaborative

SAFER Ukraine Collaborative: See group authors on **Appendix pages 19-30**

Affiliations:

¹St Jude Children's Research Hospital, Memphis, TN, USA

²Western Ukrainian Specialized Children's Medical Center, Lviv, Ukraine

³Department of Pediatrics, Oncology & Hematology, Medical University of Lodz, Poland

⁴Tabletochki Charity Foundation, Kyiv, Ukraine

⁵Fundacja Herosi, Warsaw, Poland

⁶Gustave Roussy Cancer Campus, Villejuif, France

⁷University Hospital Essen, Essen, Germany

⁸Charité Medical School, Berlin, Germany

⁹Hospital Universitario Virgen Macarena, Seville, Spain

¹⁰Children's Hospital of Eastern Switzerland, St. Gallen, Switzerland

¹¹Princess Maxima Centre for Pediatric Oncology, Utrecht, Netherlands

¹²University Medical Center, Freiburg, Germany

¹³2nd Medical School and University Hospital Motol, Prague, Czech Republic

¹⁴Pediatric Hematology/Oncology, Fondazione IRCCS Policlinico San Matteo, Pavia, Italy

¹⁵Stanford University School of Medicine, Stanford, CA, USA

***Corresponding Authors:**

Asya Agulnik, MD, MPH

Department of Global Pediatric Medicine, Division of Critical Care

St. Jude Children's Research Hospital, Memphis, TN, USA

email: asya.agulnik@stjude.org

Wojciech Mlynarski, MD, PhD

Department of Pediatrics, Oncology & Hematology

Medical University of Lodz, Sporna 36/50, 91-738 Lodz, Poland

email: wojciech.mlynarski@umed.lodz.pl

Contributions:

Conceptualization: AA, RK, TY, YN and WM

Data Curation: AA, RK, MS, MWW, MP, AO, TY, YN, JHD, AE, AFT, JG, KK, AM, LS, MZ, and WM

Formal Analysis: AA, MP, AM

Funding Acquisition: AA, YN, MD

Investigation: AA, MS, MWW, MP, AO, AM, WM

Methodology: AA, RK, PHW, WM

Project Administration: MS, MWW, MP, AO, TY, YN, MD, AM, WM

Resources: AA, YN, MD, JHD, UD, AE, AFT, JG, KK, LS, MZ, WM

Supervision: PHW and WM

Validation: MS, MWW, WM

Visualization: AA, MP

Writing—original draft: AA, RK, MS, MWW, MP, AO, TY, YN, MD, PHW, WM

Writing—review and editing: All authors

Declaration of interests:

AA has a prior grant from the Conquer Cancer Foundation (Global Oncology Young Investigator Award). MS reports grant funding from the Conquer Cancer Foundation (Global Oncology Young Investigator Award). YN reports support from the Tabletochki Charity Foundation, St. Jude Children's Research Hospital (St. Jude Global), and Conquer Cancer International-Europe. . JH reports past grant funding from the French Ministry of Health, consulting fees and/or honoraria from Jazz Pharmaceuticals, Novartis, Vertex, Sanofi, and Orchard, participation in a data safety monitoring board for Vertex and Medac, and receipt of donated equipment from Orchard to his institution. AE reports honoraria from EUSA Pharma and participation on a data safety monitoring and/or scientific advisory board for LINES neuroblastoma low-risk trial (IIT), the Institute CURIE, and Fraunhofer Immunology. AFT reports grant funding from Asociacion Espanola Contra el Cancer, honoraria from Amgen and Novartis, support for conference attendance from Servier, Gilead, Novartis, Takeda, and Amgen, and leadership roles on the National Cancer Strategy working Group (Ministry of Health of Spain), Sociedad Espanola de Hematologia y Oncologia Pediatricas, Euronet Clinical Board, RedC, and OncoLabs. LS reports funding from the MH CX-DRO University Hospital Motol. MZ reports grant funding from Ricerca Corrente and Policlinico San Mateo, consulting fees from Vertex, Novartis, Amgen, MEDAC, and honoraria from Clinigen. PW reports consulting fees and travel funding from St. Jude Children's Research Hospital (St. Jude Global). The remaining authors declare no competing interests

Data sharing: De-identified data will be made available upon reasonable request to the communicating author (Dr. Agulnik).

Keywords: Pediatric Oncology, Pediatric Hematology, Cancer, War, Ukraine, Global Child Health

On February 24, 2022, Russian Federation military forces began a coordinated invasion of Ukraine. Russian assaults resulted in widespread damage to densely populated residential areas and critical civilian infrastructure including power stations, transportation hubs, schools, and health care facilities.¹ As a result, more than 10 million refugees have fled Ukraine, with approximately 50% to Poland.² Attacks on Ukraine's health system and pharmaceutical supply chains created challenges providing critical services for the injured and chronically ill.³ Among the most vulnerable patients are children with cancer and blood disorders who require timely access to diagnostic, therapeutic, and supportive care for survival. The war has resulted in acute interruption of medical care, threatening the lives of thousands of Ukrainian children.

In response to the urgent needs of Ukrainian children with cancer and blood disorders, the St. Jude Children's Research Hospital (St Jude) and American Lebanese Syrian Associated Charities (ALSAC) Global programs joined non-governmental organizations (NGO), the Polish Society of Pediatric Oncology and Hematology (PSPOH), the International Society for Pediatric Oncology-Europe (SIOP-E), the Childhood Cancer International-Europe (CCI-E), and government agencies to form Supporting Action for Emergency Response in Ukraine (SAFER Ukraine), an initiative to facilitate the safe evacuation of patients and families to reestablish medical care abroad (See **Appendix pages 2-6** for SAFER Ukraine collaborators). A timeline of the response during the first 12 weeks of war is presented in **Figure 1**.

Ukrainian patients and families needing evacuation were identified through the Ukrainian Tabletochki Foundation or the PSPOH hotline. Patients were transported to the Western Ukrainian Specialized Children's Medical Center (WUSCMC) in Lviv where they were stabilized for transfer abroad. The WUSCMC team worked with the Ukrainian and Polish governments and NGOs, including the Polish Center for International Aid and the Herosi Foundation, to coordinate medical evacuation of patients and their families to Poland (see **Appendix pages 7-13** for an overview of the SAFER Ukraine process).

Within the first week, an increasing number of patients requiring evacuation triggered concerns that the Polish medical system would become overwhelmed, jeopardizing medical care for both Ukrainian and Polish children. To mitigate this risk, SAFER Ukraine established the "Unicorn Marian Wilemski Clinic", a patient triage center in South-Eastern Poland. To evacuate increasingly larger groups of patients efficiently and safely, convoys leaving Ukraine were organized through humanitarian corridors to Poland. After arrival to Unicorn, patients were evaluated by the PSPOH medical team; high-risk or acutely ill patients were transferred to local hospitals; stable patients remained at Unicorn for definitive referral abroad. Unicorn also provided interpreters, volunteers, and patient liaisons to support the psychosocial needs of patients and families.

To facilitate international patient referral, SAFER Ukraine partnered with hospitals and foundations organized through SIOP-E and CCI-E. Hospitals volunteering to take Ukrainian patients were asked to organize centrally through a national coordinator (a senior clinician familiar with national capacity and expertise) and provide medical transportation, financing of medical care, and full psychosocial services for evacuated Ukrainian patients and families. To

support logistics of patient evacuation, SAFER Ukraine created a 24-hour/7-days-per-week virtual command center staffed by St. Jude and ALSAC Global employees and more than 400 international volunteers. The command center maintained a secure electronic patient registry, translated medical records, coordinated transportation logistics, distributed medical records to referral hospitals, and facilitated communication to assure continuity of patient care.

On February 27, 2022, the first three Ukrainian patients arrived in Poland. During the following 12 weeks, SAFER Ukraine registered 1031 Ukrainian children with cancer or blood disorders from all regions of Ukraine requesting evacuation for medical care (**Figure 2a and Appendix page 14**). The first convoy of 37 patients arrived in Poland on March 1st; in the following 12 weeks, SAFER Ukraine organized 15 convoys ranging from 6 to 73 patients (**Figure 1**). **Appendix pages 15-16** demonstrates changes in patient volume during this time.

As of May 19th, 2022, 949 patients had arrived at referral hospitals abroad; the rest (n=82) either remained in Ukraine, were pending referral, or had an unknown final destination (n=33) (**Figure 2b and Appendix page 17**). Two patients, one with acute myeloid leukemia and one with relapse of acute lymphoblastic leukemia, died within 24 hours of transport (see **Appendix page 18** for clinical details). These “transport-related deaths” correspond to 0.21% of all evacuated patients and 0.49% of patients transported via convoy (n=405). The remaining patients arrived safely to their accepting hospitals abroad.

After the first 12 weeks of war, the volume of patients requesting evacuation decreased significantly; however, we continue to support an average of 1 to 2 evacuation requests per week. In July, evacuation requests increased again due to escalating attacks in central and eastern Ukraine. While the future needs of Ukrainian children with cancer and blood disorders remain uncertain, SAFER Ukraine remains committed to supporting access to high-quality medical care for these patients both in Ukraine and abroad.

SAFER Ukraine leveraged collaborations between multiple medical, NGO, and government stakeholders to develop an adaptive infrastructure that successfully met the security and medical needs of a highly vulnerable group of seriously ill children during a war. The need for this large-scale, urgent, coordinated response was the result of the destruction of food and water supplies, shelter, and health care due to war.⁴

The SAFER Ukraine initiative represents a unique humanitarian response to the indirect effects of war, and its’ strategic and operational elements may not be generalizable to all conflict settings or patient populations. These unique features, however, can inform future emergency responses for complex, high-risk patients. Notable elements of SAFER Ukraine include characteristics of the patient population, geopolitical context, and well-established pre-war collaborations.

Children with cancer and blood disorders are especially vulnerable to the indirect effects of war. With modern treatment and supportive care, survival in children with cancer is over 80%;⁵ however, interruptions in treatment and lack of supportive care can result in significantly higher

mortality. The juxtaposition of the high therapeutic efficacy of childhood cancer treatment with precise timing requirements for its administration underscores the substantial survival benefit expected from rapid evacuation of patients whose care has been disrupted to resume medical treatment abroad. The long-term medical and psychological outcomes of evacuation on patients and families, however, will need to be assessed in future work.

In addition to unique patient characteristics, the effectiveness of SAFER Ukraine depended on a geopolitical environment that supported evacuation of Ukrainian citizens abroad. Russia's attacks against civilians and infrastructure galvanized support for Ukraine, including unprecedented international sanctions.⁶ Within a week, the European Union announced immediate protection and legal status for Ukrainian refugees, creating the legal and financial framework for patient referral to hospitals in Europe.⁷ This supportive response stands in contrast to the more complex and less welcoming immigration policies impacting other populations fleeing conflict settings.⁸⁻¹¹

Finally, SAFER Ukraine was possible due to the rapid repurposing of existing collaborative networks to meet the urgent challenge of evacuating patients and families from an area of violent conflict. Patient convoys began within a week of the onset of fighting, evacuating hundreds of patients within the first few weeks of war. This achievement would not have been possible without pre-existing individual, national, and international collaborations through the PSPOH, SIOP-E, CCI-E, and the St. Jude and ALSAC Global network of hospitals, NGOs, and governments. In its essence, SAFER Ukraine provides a proof-of-concept for an innovative global health model of multilevel stakeholder engagement and collaboration that can be leveraged in future international emergency responses for a variety of high-risk, medically complex patients.

The health and well-being of all Ukrainians depend fundamentally on the cessation of the war. Until fighting ends, humanitarian law and norms require protection of civilians from direct and indirect harm. When this protection fails, there exists an imperative to assist refugees requiring evacuation and medical care. The initiative described in this report represents a successful global collaborative to mitigate the effects of a profoundly weakened health care system on one group of highly vulnerable children exposed to the horrors of war.

Figure Legends:

Figure 1: SAFER Ukraine Timeline. Timeline of Supporting Action for Emergency Response in Ukraine (SAFER Ukraine) activities and relevant geopolitical events in the first 12 weeks following the invasion of Ukraine by the Russian Federation.

Figure 2: Patient Origin and Referral Destination. Maps showing SAFER Ukraine patient region of origin in Ukraine (a) and country of referral destination (b). These maps don't include 286 patients without a registered region of origin (a) and 82 patients pending or missing a referral final destination (b).

References:

1. United Nations Office for the Coordination of Humanitarian Affairs. Ukraine Situation Report: May 6 2022. <https://reports.unocha.org/en/country/ukraine>.
2. OCHA. Ukraine Data Explorer. <https://data.humdata.org/visualization/ukraine-humanitarian-operations/> (accessed 8/2/22 2022).
3. Piccoli GB, Brunori G, Gesualdo L, Kalantar-Zadeh K. The impact of the Russian-Ukrainian war for people with chronic diseases. *Nat Rev Nephrol* 2022.
4. Wise PH. The Epidemiologic Challenge to the Conduct of Just War: Confronting Indirect Civilian Casualties of War. *Daedalus* 2017; **146**(1): 139-54.
5. Rodriguez-Galindo C, Friedrich P, Alcasabas P, et al. Toward the Cure of All Children With Cancer Through Collaborative Efforts: Pediatric Oncology As a Global Challenge. *Journal of clinical oncology : official journal of the American Society of Clinical Oncology* 2015; **33**(27): 3065-73.
6. Congress Lo. Russia's Invasion of Ukraine: Overview of U.S. Sanctions and Other Responses. In: Congress Lo, editor.; 2022.
7. Ukraine: Commission proposes temporary protection for people fleeing war in Ukraine and guidelines for border checks. 2022. https://ec.europa.eu/commission/presscorner/detail/en/ip_22_1469.
8. Salman Z, Shbair M, Zeineddin M, Balousha T, Qaddoumi I, Rodriguez-Galindo C. Cancer care for children in the Gaza Strip. *Lancet Oncol* 2021; **22**(12): 1667-8.
9. Saab R, Ghanem K, Jeha S. Cancer care for displaced children in Lebanon. *Lancet Oncol* 2021; **22**(12): 1663-4.
10. Metzger ML, Pereira A, Loggetto P, Rodriguez-Galindo C. Cancer care for displaced children from Venezuela. *Lancet Oncol* 2021; **22**(12): 1665-6.
11. Mansour A, Al-Omari A, Sultan I. Burden of Cancer Among Syrian Refugees in Jordan. *J Glob Oncol* 2018; **4**: 1-6.