



## Press release

# Childhood Leukemia treatment 2022: where we are now and what it takes

(Vienna, 7.9.2022) The international FORUM study led by Prof. Christina Peters, MD, from St. Anna Children's Hospital and under the scientific coordination of St. Anna Children's Cancer Research Institute was so successful that the journal *Frontiers in Pediatrics* made a special kind of request: The experts in this field were invited to bring out an entire Research Topic on acute lymphoblastic leukemia in children. The result: 24 scientific articles by 105 authors addressing better-tolerable treatments with allogeneic stem cell transplantation and modern options for a cure without stem cell transplantation.

Acute lymphoblastic leukemia (ALL) is the most common cancer in children, generally curable with contemporary chemotherapy. However, if the disease is classified as high-risk ALL and a stem cell transplantation becomes inevitable, total body irradiation is still the treatment of choice prior to transplantation. This was the conclusion drawn from the FORUM study, including 35 countries on five continents (*Peters et al., Journal of Clinical Oncology 2020*).

"As the largest study on this topic to date, we published the results in the top-ranked *Journal of Clinical Oncology*. Soon after that, *Frontiers* invited us – the international transplant consortium for ALL – to publish a collection of reviews and scientific reports on ALL in children," recalls Christina Peters, Affiliated Clinician at St. Anna Children's Cancer Research Institute (St. Anna CCRI) and Senior Physician at St. Anna Children's Hospital. The editorial board of this Research Topic is formed by Christina Peters together with Assoc.-Prof. Adriana Balduzzi, MD (University of Milano Bicocca, Italy) and Prof. Peter Bader, MD (Goethe University Frankfurt am Main, Germany).

### Life at the price of long-term side effects?

Although total body irradiation and hematopoietic stem cell transplantation (HSCT) from healthy donors can be life-saving, long-term side effects sometimes have a massive impact on the quality of life of children and young adults. These include organ damage, growth retardation, and the development of secondary cancers. Hence, there was a dire need to clearly outline recent and previously published data, as well as to discuss potential new approaches, as did the aforementioned reviews.

"One of the most burning questions for me is whether we still need stem cell transplantation in the era of modern immunotherapies," Christina Peters points out. In the future, CAR-T cell or antibody therapies directly targeting leukemia cells could replace HSCT, which is addressed by three of the reviews mentioned. Jochen Büchner, MD, PhD, and colleagues are discussing the question of whether and when CAR-T cell therapy could be considered to bridge the time until transplantation and under what conditions it could replace transplantation. Another review, authored by Assoc.-Prof. Tony H. Truong, MD, and colleagues, is dedicated to the question which children should receive a stem cell transplantation at all. Of course, transplantation should only be considered for those patients who would not have a realistic chance of survival with 'milder' therapies. But it is exactly these boundaries that are currently shifting.

### 59,000 views of our work

So far, the review of Bianca A. W. Hoeben, MD, PhD, and colleagues, which deals with new methods of total body irradiation, has had the most views in this online collection. "In total, we have about 59,000 views of our Research Topic by now. Accordingly, it seems to be on many people's minds whether and



how we can improve transplantation methods to reduce side effects," says Christina Peters. For example, different radiotherapy centers have developed new methods of total body irradiation to achieve a lower irradiation dose in certain organs. There are, however, limitations to shield organs at risk without compromising the anti-leukemic and immunosuppressive effects – the latter to preserve a rejection of the transplanted cells.

In addition to the aforementioned long-term effects of irradiation and transplantation, acute side effects of transplantation also play a major role. These include infections during the period in which the immune system reconstitutes (*Olga Zajac-Spychala et al.*), or complications arising from a donor cells' attack against the patient's healthy tissue. The prevention and treatment of the so-called Graft-versus-Host Disease are addressed by six of the articles in this Research Topic (*Steven J. Keogh et al.*, *Anita Lawitschka et al.*, *Jacob Rozmus et al.*, *Agnieszka Sobkowiak-Sobierajska et al.*, *Matthias Wöfl et al.*, *Natalia Zubarovskaya et al.*).

"The publication of this Research Topic is a huge success for St. Anna CCRI. Together with the valuable contributions of a number of clinicians of St. Anna Children's Hospital, we have published highly topical and clinically relevant manuscripts that are of utmost importance for the treatment of children with high-risk ALL," highlights Christina Peters.

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### **About the FORUM Study**

The FORUM study demonstrated that patients over four years of age with high-risk ALL in need of a stem cell transplantation live longer and have a lower risk of relapse when they receive total body irradiation instead of chemotherapy in preparation for transplantation. After random assignment of 417 pediatric patients with high-risk ALL, a futility stopping rule was applied because it became apparent that patients receiving chemo-conditioning had a lower chance of cure and survival. FORUM is a randomized, international, multicenter phase III trial designed to investigate whether chemotherapy with fludarabine, thiotepa, and busulfan or treosulfan is non-inferior to total body irradiation plus etoposide as preparation prior to transplantation. The study, led by Christina Peters, is the result of a collaboration among international study groups (AIEOP-BFM-ALL-SG, IBFM-SG, INTREALL-SG, and EBMT-PD-WP).

### **Frontiers Research Topic**

The *Frontiers in Pediatrics* "Research Topic" *Allogeneic Hematopoietic Stem Cell Transplantation for Children with Acute Lymphoblastic Leukemia in the Era of Immunotherapy* is available for download here: <https://www.frontiersin.org/research-topics/19704/allogeneic-hematopoietic-stem-cell-transplantation-for-children-with-acute-lymphoblastic-leukemia-in#overview>

The specific thematic areas envisaged to be addressed in this article collection are the following:

- Are HLA-identical siblings still the best available donor for ALL?
- The challenge of treating "older children": what is the best transplant strategy for Adolescents and Young Adults (AYAs)?
- Tyrosine Kinase Inhibitors (TKIs) for Philadelphia Chromosome positive (Ph+) and Ph-like ALL: could we omit Hematopoietic Stem Cell Transplantation (HSCT)?
- Bispecific Antibodies before HSCT: less toxicity for better transplant outcome?
- CAR-T cell therapy: only bridge to transplant?
- T-cell depletion: Cyclophosphamide after transplantation versus in vitro T-cell depletion
- Why is Total Body Irradiation so effective in high-risk ALL?
- Total Body Irradiation forever? New chemotherapeutic options for irradiation-free conditioning
- Minimal Residual Disease (MRD): Which level of negativity is relevant?



- Current treatment options for acute Graft-versus-Host-Disease (GVHD) in children
- Current treatment options for chronic GVHD in children
- Immunoreconstitution and chimerism: a different story compared to adults?
- Non-relapse mortality after HSCT: where are we now?
- High-risk ALL: Transplant indications in 2021
- COVID-Infection after allogeneic stem cell transplantation
- Transplantation for the youngest: better than chemotherapy?

### **About Christina Peters**

Christina Peters, MD, is Professor of Pediatrics at the Department of Stem Cell Transplantation of St. Anna Children's Hospital and Affiliated Clinician at St. Anna Children's Cancer Research Institute in Vienna. She is principal investigator of active studies within the European Society for Blood and Marrow Transplantation (EBMT) and the International Berlin Frankfurt Münster Study Group (IBFM) for the treatment of pediatric leukemia. Her research interests include allogeneic hematopoietic transplantation in children and adolescents with malignant and non-malignant diseases from related and unrelated donors, infectious and toxic complications after stem cell transplantation, adoptive therapies for hematological malignancies and family oriented rehabilitation for children with life threatening diseases. Christina Peters chaired the EBMT Pediatric Diseases Working Party between 2008 and 2014. She has authored and co-authored numerous papers in peer-review journals such as *The Lancet*, *The New England Journal of Medicine*, or *The Journal of Clinical Oncology*. Christina Peters acts as a regular reviewer of publications for hematology, pediatric and leukemia journals. She is a member of many professional societies including IBFM, the Center for International Blood and Marrow Transplant Research (CIBMTR), the German and Austrian Society of Pediatric Hematology and the Austrian Gene Therapy Commission. Furthermore, Christina Peters is a member of the Advisory Board of the Austrian Ministry of Health, the Bioethical committee of the Austrian Prime Minister and member of the European Network Pediatric Research at the European Medicines Agency EMA (ENPREMA).

### **Photo**

Prof. Christina Peters, MD

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### **About St. Anna Children's Cancer Research Institute, St. Anna CCRI**

St. Anna CCRI is an internationally renowned multidisciplinary research institution with the aim to develop and optimize diagnostic, prognostic, and therapeutic strategies for the treatment of children and adolescents with cancer. To achieve this goal, it combines basic research with translational and clinical research and focus on the specific characteristics of childhood tumor diseases in order to provide young patients with the best possible and most innovative therapies. Dedicated research groups in the fields of tumor genomics and epigenomics, immunology, molecular biology, cell biology, bioinformatics and clinical research are working together to harmonize scientific findings with the clinical needs of physicians to ultimately improve the wellbeing of our patients.

[www.ccri.at](http://www.ccri.at) [www.kinderkrebsforschung.at](http://www.kinderkrebsforschung.at)

### **About St. Anna Children's Hospital**

Established in 1837 in the former suburb of Schottenfeld, St. Anna was the first children's hospital in Austria and the third independent hospital in Europe dedicated exclusively to the health of children. St. Anna Children's Hospital has evolved into an institution that provides state-of-the-art medical care. Thus, in addition to its performance as a general children's hospital, the Center for Pediatrics and Adolescent Medicine has also been able to establish an excellent reputation throughout Austria and internationally over the past 40 years as a center for the treatment of pediatric hematologic disorders and tumor diseases (cancer).

[www.stanna.at](http://www.stanna.at)



St. Anna Kinderkrebsforschung  
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