The 13th Biennial Childhood Leukemia and Lymphoma Symposium (CLLS 2023)

6–7 May 2023,
Hotel Sercotel Sorolla Palace,
Valencia, Spain

www.clls2023.org

The 13th Biennial Childhood Leukemia and Lymphoma Symposium

6 May

Scientific Programme at a Glance

13:00 - 13:45
Opening lecture
Susana Rives (ES)

11:00 - 18:40
Registration open

14:00 - 16:10 Acute myeloid leukemia & JMML & MDS

14:00 **Michel Zwaan (NL)**
IL 1 *- Options in the future therapy of childhood MDS and JMML*

14:30 **Jolien Vanhooren (BE)**
O 01 *- Deciphering the role of Nidogen-1 in pediatric acute myeloid leukemia*

14:55 **Maddalena Benetton (IT)**
O 02 *- Tracking ROS Levels to Hunt Leukemia Stem Cells in Pediatric Acute Myeloid Leukemia*

15:20 **Ambra Da Ros (IT)**
O 03 *- Patient-derived Xenograft Models Are The Leading Strategy To Identify New Agents For Pediatric Acute Myeloid Leukemia*

15:45 **Bianca-Andreea David (BE)**
O 04 *- Challenges in CBL-mutated juvenile myelomonocytic leukaemia: to treat or not to treat?*

16:10 *Coffee Break*

16:30 - 18:40 Acute lymphoblastic leukemia (clinical topics)

16:30 **Kjeld Schmiegelow (DK)**
IL 2 *- How to envision next-generation childhood ALL trials in 2030*

17:00 **Rob Pieters (NL)**
O 05 *- Improved outcome for acute lymphoblastic leukemia by prolonging therapy for IKZF1 deletion and decreasing therapy for ALL in children with ETV6::RUNX1, Down syndrome or prednisone poor response*

17:25 **Julian Schliehe-Diecks (DE)**
O 06 *- HDAC6 ablation represses in vivo growth of BCR-ABL1 + leukemia cells by innate-immune response inducing RNase T2 expression*

17:50 **Dagmar Schinnerl (AT)**
O 07 *- Prognostic relevance of DUX4 childhood and adolescent B-cell acute lymphoblastic leukemia – results from Austrian ALL-BFM-studies*

18:15 **Lea Spory (DE)**
O 08 *- AP-1 transcription factor complex members FOSB and FOS are linked with central nervous system (CNS) infiltration and inferior prognosis in childhood T-cell Acute Lymphoblastic Leukemia (T-ALL)*

20:30 **Symposium Dinner**

7 May

08:30 - 10:40 Acute lymphoblastic leukemia (genetics / predisposition)

08:30 **Oskar Haas (AT)**
IL 3 *- Diagnostic stratification of childhood ALL: What we want to know and what we need to know*

09:00 **Britt Vervoort (NL)**
O 09 *- IKZF1 deletions cause targetable resistance to cytarabine in acute lymphoblastic leukemia*

09:25 **Eline Bertrums (NL)**
O 10 *- The role of TP53 mutations in mutagenesis and selection dynamics under exposure of platinum-based compounds*

09:50 **Elena García Sánchez (ES)**
O 11 *- Description Of Global Cytogenomics Features In Childhood Acute Lymphoblastic Leukemia By Optical Genome Mapping*

10:15 **Stefanie Verena Junk (DE)**
O 12 *- Constitutional variants in patients developing second malignant neoplasms after therapy for pediatric acute lymphoblastic leukemia – a case-control study*

10:40 *Coffee Break*

11:00 - 12:40 Non-Hodgkin's lymphoma

11:00 **Amos Burke (GB)**
IL 4 *- How to approach r/r mature B-cell neoplasms*

11:25 **Dilys Weijers (NL)**
O 13 *- Molecular characterization of hematological malignancies in children with CMMRD*

11:50 **Emma Kroeze (NL)**
O 14 *- The genomic landscape of pediatric T-cell lymphoblastic lymphoma*

12:15 **Agata Pastorczak (PL)**
O 15 *- Germline aberrations of DNA repair genes are frequently observed in selected children diagnosed with lymphomas*

12:40 *Lunch break* 13:30 **Poster Session** 16:00 *Coffee Break*

16:30 - 18:10 Cellular therapies in leukemia and lymphoma

16:30 **Claudia Rössig (DE)**
IL 5 *- How to envision CAR-T cell therapies in primary and first relapse of ALL*

16:55 **Eva Fronkova (CZ)**
O 16 *- Clinical significance of low minimal residual disease (MRD) positivity in post-transplant acute lymphoblastic leukemia (ALL) monitoring*

17:20 **Anna Alonso - Saladrigues (ES)**
O 17 *- Options in the future therapy of childhood MDS and JMML*

17:45 **Susana Rives (ES)**
O 18 *- Identification of Biomarkers Predictive of Relapse In Pediatric and Young Adults (Ya) Patients With Relapsed/refractory B-cell Acute Lymphoblastic Leukemia (R/r Pb-all) after Cd19-car T-cell Therapy*

18:10 - 18:30 **Adjourn**

O 04 - Challenges in CBL-mutated juvenile myelomonocytic leukaemia: To treat or not to treat?

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Background:

Patients with germline *CBL* pathogenic variants have syndromic features like growth and neurodevelopmental delays, facial dysmorphia, autoimmune manifestations, and a predisposition to develop juvenile myelomonocytic leukaemia (JMML) because of the loss of heterogeneity for the *CBL* gene in the leukemic cells. Due to its rarity and lack of markers that predict spontaneous resolution or progression to aggressive disease, the best follow-up and therapy approach is unknown at the time of diagnosis. The options could vary between *watch-and-wait* strategy to haematopoietic stem cell transplantation (HSCT).

Objective:

We describe the case of a child with a newly diagnosed *CBL*-mutated JMML and the therapeutic challenges encountered by the clinicians and the family.

Clinical case: A term born girl was referred to our hospital at the age of 17 months after multiple hospitalisations for recurrent infections and failure to thrive requiring tube feeding since the age of 6 months. Physical examination revealed two xanthogranulomas and two small *café-au-lait* spots and mild splenomegaly. The presence of leucocytosis, monocytosis, and mild thrombocytopenia prompted us to perform RASopathy panel for JMML and the c.1111T>C pathogenic variant (Class 4) (p.Tyr371His) on exon 8 of the *CBL* gene was identified both on somatic (bone marrow) and germinal level (fibroblast culture) confirming the diagnosis of *CBL*-mutated JMML.

Foetal Haemoglobin levels were normal for age and no other genetic anomalies were detected on somatic or germinal level. Exome sequencing for secondary mutations and genome-wide methylation profiling is pending. After multidisciplinary discussion, experts' opinion, and family approval, we chose the *watch-and-wait* approach. A follow-up schedule was made with monthly clinical evaluation and blood tests, and bone marrow aspirates every 6 months to look for secondary mutations or additional chromosomal alterations. No transfusion was required, and no severe complication was observed to date.

Discussion:

The milder manifestations encountered in some clinical presentations of *CBL*-mutated JMML could lead to diagnostic delays. Some patients with *CBL*-mutated JMML may have stable disease and even achieve spontaneous remission without treatment. Standard of care in most JMML patients relies on HSCT but in this case, hasty decision could lead to significant medical burden. The uncertainty regarding clinical evolution could be a trigger of anxiety both for physicians and family and alter the quality of life. Follow-up schedules, although largely dependent on the severity of the disease, could provide some reassurance and assure timely intervention if disease progression occurs.

Application to practice:

The *watch-and-wait* approach will spare some patients from unnecessary treatment and potential treatment-related toxicities. Further follow-up data and validation of the new classification of JMML based on the whole-exome sequencing and methylation profile is needed to identify which patients are the most appropriate candidates for *watch-and-wait* approach, and to better define the management schedule and the follow-up guidelines.

Keywords: JMML, c.1111T>C pathogenic variant, CBL gene, CBL syndrome, *watch-and-wait* strategy