cytogenetic risks according to National Cancer Institute (NCI) and BFM risk classifications, early response to treatment, among others. Cohort was divided into two 11-year periods for analysis purposes. We calculated event-free survival and overall survival rates at 5 and 10 years. Finally, we performed a multivariate analysis using Cox proportional hazards models. Results: At 5 years, in the 1st decade, the event-free survival was 50.7% (±3.0) and the overall survival was 61.5% (±2.9). This rates for low-risk patients (n = 26) were 84% and 87.8% respectively, for medium-risk (n = 111), 66.5% and 74.8% and for high-risk (n = 144), 33.4% and 47.7%. In the 2nd decade, the event-free survival was 61.6% (±2.8) and the overall survival was 70.5% (±10.6). This rates for low-risk patients (n = 32) were 84.5% and 92.6%, for medium-risk (n = 166), 63.1% and 75.2% and for high-risk (n = 208), 57.9% and 63.8%. Immunophenotypic classification showed 81.15% B and 18.85% T cells cases. The percentages of high-risk patients based on BFM risk (51.2%), high-risk NCI (54.7%), leukocyte count greater than 50,000 (27.1%) and age less than one or greater than 10 years (28.6%) were higher than the ones found in other ALL studies from developed countries. When it comes to quality of treatment across different periods (before 2008 vs. after 2008), the number of deaths before complete remission (inducted death) was 10 vs. 11 (3.5% vs. 2.7%, p = 0.545), during the first complete remission, 33 vs. 24 (11.6% vs. 5.9%, p = 0.007) and abandonment cases were 12 vs. 5 (4% vs. 1.2%, p = 0.017). **Discussion:** Our cohort presented a higher leukocyte count at the time of diagnosis and an increased prevalence of high-risk classification compared to cohorts of other BFM studies, mainly composed by Caucasians. Those results lead us to consider that this higher high-risk proportion may be caused by 3 factors: delays in treatment, the use of an overestimate risk classification on the 8th day of treatment and/or unique genetic features of our population, which has Indigenous, Black and European ancestries. In the latest period, our results were similar to those of AllIC-BFM 2009. **Conclusions:** Over the past 2 decades, the overall and event-free survivals of children and adolescents with ALL have improved significantly in Rio de Janeiro, Brazil. We also observed a significant reduction in deaths in the first complete remission. Further investigations are needed to define the factors associated with the elevated proportion of high-risk cases. This study marks the beginning of Rio de Janeiro-based multicenter survival analysis, focusing on pediatric ALL using BFM-modified protocols.

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TROMBOCITOSE GRAVE DURANTE TRATAMENTO DE TROMBOCITOPENIA IMUNE COM ELTROMBOPAGUE EM PACIENTE PEDIÁTRICO

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Introdução/objetivos: O Eltrombopague é um agonista do receptor da trombopoetina, indicado para Pacientes com Trombocitopenia Imune (PTI) com resposta insuficiente a corticosteroides, imunoglobulinas ou esplenectomia. O objetivo deste caso é relatar um efeito adverso grave em paciente pediátrico em uso de agonista do receptor da Trombopoetina. **Material e métodos:** As informações foram obtidas por meio de revisão do prontuário e revisão da literatura. **Resultados:** Paciente feminina, 6 anos, com PTI crônica, iniciou uso de Eltrombopague em 04/07/2021, aproximadamente, 1 ano e 10 meses após o diagnóstico. Foi ajustada dose em 15/02/2023 para 75 mg/dia por apresentar plaquetas abaixo de 40.000, além de sangramentos orais eventuais. Após 1 mês do ajuste de dose foi evidenciado trombocitose grave de 2.953.000. Medicação foi suspensa e mantida rigorosa observação e controle até plaquetas reduzirem a menos que 100.000, fato que ocorreu em 14 dias. **Discussão:** A PTI é uma doença autoimune adquirida caracteriza pela baixa contagem plaquetária e o Eltrombopague é uma medicação considerada de segunda linha no tratamento para PTI, porém seu uso resultou em redução ou descontinuação dos corticosteroides. Os efeitos adversos relacionados ao seu uso ainda são pouco relatados. Há relatos de aumento de eventos trombóticos em pacientes em tratamento com agonistas do receptor da trombopoetina comparados com uma população não exposta a eles. Porém esses eventos trombóticos podem ocorrer com níveis de plaquetas baixos, normais ou alto. No caso relatado foi optado por não iniciar terapia com antiagregantes e a paciente evoluiu bem sem eventos trombóticos. **Conclusão:** Por fim, deve-se considerar os riscos trombóticos potenciais de cada paciente, além de garantir monitorização e acompanhamento contínuos ao tratar pacientes com PTI com agonista do receptor da Trombopoetina.

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NGS STUDIES REVEAL GENOMIC VARIANTS IN 6 PEDIATRIC PATIENTS DIAGNOSED WITH ACUTE LEUKEMIA PRESENTING RARE CYTOGENETIC ABNORMALITIES

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Objectives: Leukemia is the most common childhood malignancy, with an incidence of 4.7 per 100,000 in pediatric

patients (< 20 years of age). Acute Leukemias (AL) represent a heterogeneous group of diseases that originate from the interaction between genetic and epigenetic alterations in hematopoietic progenitors, leading to the dysregulation of multiple crucial signal transduction pathways, resulting in hematopoietic insufficiency due to a clonal proliferation of immature precursors. Clonal heterogeneity has been implicated as a driving mechanism of leukemogenesis since a high degree of genetic variability is associated with an increased risk of particular subclones having a proliferative advantage leading to clonal expansion. In this context, cytogenetics is still considered one of the most valuable tools for understanding the mechanisms which lead to AL transformation since chromosomal abnormalities are found in 80% of children affected by the disease. In this regard, due to the relative rarity and aggressive potential of childhood AL, the prognostic impact of these abnormalities remains to be elucidated. Thus, by combining cytogenetics and genomic high throughput sequencing (NGS), it may be possible to characterize the genomic profile of pediatric patients with AL, identifying putative genes/gene fusions and genomic variants to help determine the risk stratification and provide appropriate treatment to patients, including adaptations in therapeutic protocols. Herein we describe the cytogenetic and genomic profile of six children with acute leukemia. Firstly, using banding cytogenetics and FISH, patients were sorted for further genomic investigations by NGS. **Material and methods:** We performed G-banding and FISH experiments. NGS was performed on a targeted approach. **Results:** We characterized six (6) pediatric patients diagnosed with acute leukemias presenting with rare cytogenetic abnormalities. The cytogenetic abnormalities studied were associated with genomic pathogenic variants by NGS analysis. We observed variants in IDH1 (2 cases); multi-hit TP53, Li-Fraumei related (1); novel RUNX1 (1); KIT (1); WT1 (1), besides a CBFA2T3-GLIS2 fusion associated with a Philadelphia chromosome. **Discussion:** The prognostic evaluation of acute leukemias at diagnosis is a critical step for proper clinical management. According to the WHO classification, risk stratification is based on cytogenetic and molecular data, morphological characteristics, and mutational screening. In this regard, NGS can be a powerful tool, allowing the parallel sequencing of multiple targets and detecting variants with prognostic impact. NGS became relevant in discovering genes/variants and characterizing the clonal architecture. Thus, due to its capability to screen a high number of genes and detect different types of molecular aberrations, targeted NGS has been increasingly incorporated into the clinical routine for the management of AL patients. **Conclusion:** We highlight the importance of cytogenetic studies combined with NGS in identifying leukemic putative genes and selecting pediatric patients with AL as possible candidates for future targeted therapies. Cytogenetic, molecular, and genomic technologies combined have been shown to help understand the AL mutational landscape and impact clinical practice.

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RELIABLE FLOW CYTOMETRY METHOD FOR MONITORING OF MINIMAL RESIDUAL DISEASE IN PATIENTS WITH B-CELL PRECURSOR ACUTE LYMPHOBLASTIC LEUKEMIA AFTER BLINATUMOMAB THERAPY

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Introduction: The recent active use of immunotherapy based on CD19/CD3 bispecific T-cell engager (blinatumomab), brings significant problems on monitoring Minimal Residual Disease (MRD) based on Multiparameter Flow Cytometry (MFC), due to possible CD19 downregulation by tumor cells. This phenomenon breaks the well-established approach of MFC strategy analysis, based gating on CD19 positivity. Also, the selective pressure of the CD19-directed immunotherapy increases the incidence of the so-called lineage switch, which has become one of the possible mechanisms of BCP-ALL resistance to immunotherapy. At present, there is no consensus approach to MFC-MRD monitoring after blinatumomab therapy for BCP-ALL. There are several described changes in MRD methodology, including the addition of other early B-lineage antigens (e.g., CD22, CD24 and CD79a) or only the modification of the gating strategy using conventional sets of antibodies. **Aim:** Evaluated two different antibody panels to monitor MFC-MRD in patients Relapsed/Refractory (R/R) B-cell ALL after blinatumomab therapy. **Materials and methods:** All Bone Marrow (BM) samples the MRD detection was performed with panel EuroFlow BCPALL MRD protocol standardized and added two more tubes (8 colors) with early B-lineage antigens according to previously described in literature (e.g., Tube 1: CD66b/CD22/CD34/CD19/CD24/CD38/CD10/CD45; Tube 2: CD20/CD22/CD34/CD19/CD79a/CD38/CD10/CD45). All BM samples were studied following the EuroFlow SOPs with the acquisition at least $\geq 5 \times 10^6$ events per samples and in both panels. The cytometer FACSCanto 8-color and Infinicyt software was used for acquisition and analyzed data files. The study enrolled real-world children in public health care systems and was approved by the local ethics committees. **Results:** A total of 54 BM samples obtained from 11 children -48% M and 52% F with a median age of 10-years (0–19) with R/R B-cell ALL were studied at different time points after treatment with blinatumomab, including: pré-transplant (n = 24) and post-transplant (n = 30). As controls without use of blinatumomab were include 04 BM from children with B-cell ALL at D15 of treatment with standard chemotherapy protocol. MRD were detected in 35% (19/54) of BM studied and of these 2/11 relapsed. We found 100% agreement between the two panels used. Only one sample was discordant at first time, but upon review it was noted that this CD19 negative population were very early CD19- normal B cell progenitors. **Discussion:** The wide implementation of CD19-directed therapy in the treatment in protocol for R/R BCP-ALL significantly complicated the rather routine procedure of MRD monitoring. Despite the