# New childhood B-ALL subtypes and their challenges in the NGS era

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**Introdução**: B-ALL is heterogeneous disease and its classification can be defined by recurrent genetic abnormalities as WHO 5th. Recent gene expression studies have identified genetic drivers that confer distinct prognostic impact, as B-ALL ZNF384-r. Here, we report a case of TAF15::ZNF384 B-ALL recurring 6 years after the 1th diagnosis.

**Caso clínico**: 3-year-old boy admitted in 2014 with fever and petechiae. CBC HB 7.9 g/dL WBC 2.9×109/L Platelets 30×109/L. BMA showed 87% blasts and by flow cytometry (FC) with B-ALL. Cytogenetic analyses (CA):46,XY,t(17;17)(p12;q11)[3]/46,XY[17]. RT-PCR negative for BCR::ABL1 p190 and ETV6::RUNX1. It's collected biospecimens from BMA for further analysis. He's treated as HR-ALL according to "Brazilian Childhood Acute Lymphoblastic Leukemia Treatment Group 2009" protocol and achieved remission by the end of induction. He's out of therapy for 6 years when he presented with 2 weeks of fever. CBC HB 14.9 g/dL WBC 5440×109/L Platelet 335×109/L with 22% blasts. BMA was performed and through FC was confirmed B-cell ALL and CA was 47,XY,t(17;17)(p12;q11),+21[15]/46,XY[5].The same translocation from the 1th diagnosis. FISH reveal (ETV6 x 2, RUNX1 x 3)[112/200], (3'IGH × 2, 5'IGH x 1) [109/200], without other changes.

He received ALL-REZ BFM 2002 reinduction and as he failure the 1th therapy, he underwent to 2th reinduction with Mini-CVAD and Blinatumomab as bridge for HSCT. By the end of the 1th cycle MRD was up to 5%. Due to the refractory of the disease, we run NGS using the Oncomine Childhood Cancer Research Assay Panel. He's submitted to a 3th salvage plan with bortezomib plus chemotherapy. By the end of the 1th cycle MRD was 1%. NGS result showed TAF15::ZNF384 in the biospecimens from the diagnosis and relapse. With this information and in attempt to improve response to reach HSCT, it's proposed hybrid therapeutic with cytarabine, azacytidine and venetoclax. After 1th cycle, BMA demonstrated MRD of 0,02%, achieving better response as he could got to undergo to HSCT.

**Conclusão:** WHO 5th recognizes the importance of genetic information in the evaluation of lymphoid neoplasia, and this harbored spot to incorporate new entities whose recognition is increasing as molecular diagnostic become more available. TAF15::ZNF384 occurs in early common progenitor which may discern into myeloid or lymphoid. Considering the ZNF384-r lineaging plasticity and the highly chemorefractory in our case, it's proposed hybrid treatment associating myeloid scheme as salvage regimen.