Acute Lymphoblastic Leukemia (ALL) is a malignant clonal overgrowth of precursor lymphoid cells, B and T. Despite this hematologic tumor may occur at all ages, it is the most prevalent malignancy in childhood and has a propensity in males over females. Specifically, in Spain it comprised 28.5% of childhood malignancies between 1983 and 2002.

ALL is a multistep process associated with the acquisition of genetic and epigenetic alterations in the leukemic blast cells, that varies according to the age (Figure 1), and it is a heterogeneous disease composed of multiple biological subgroups. (Figure 2)

Proliferation and accumulation of blasts cells in the bone marrow results in a suppression of hematopoietic processes, causing symptoms that reflect bone marrow failure (pancytopenia), as anemia, thrombocytopenia and neutropenia.

It can be distinguished different methods of diagnosis. Firstly, the morphological diagnosis is made with an assessment of the bone marrow. Secondly, it is important flow cytometry, that is the standard procedure for ALL diagnosis and subclassification and also to detect minimal residual disease. In addition, cytogentic, FISH and karyotyping, are an important step in ALL classification because conventional karyotyping can be helpful in identification of recurrent translocations and gain and loss of chromosomal material. Next-generation sequencing approaches are important to comprehensively identify genetic alterations in the genome and transcriptome.

It is noteworthy that many of the involved genes are related with key roles in lymphoid development, cell cycle regulation and tumour suppression, apoptosis regulators, lymphoid signalling, transcriptual regulators, and chromatin structure and epigenetic regulators.

In B-ALL should be highlighted numerical abnormalities, that may involve ploidy changes or gain or loss of individual chromosomes (aneuploidy). It is important that ploidy is considered an imperative prognostic factor in childhood ALL. In this type of alterations, it can be distinguished high hypodiploidy, low hypodiploidy, hypodiploidy and near haploidy. (Table 2) Furthermore, there are recurrent translocations, such as ETV6-RUNX1 and MLL with different partners, and genomic alterations, such as iAMP21 or PAHX mutation. (Table 2)

T-ALL is characterized by a worse prognosis compared to B-ALL. In this subgroup there are also translocations involving T-receptor and chromosome 14q11 and subchromosomal alterations. Early-T precursor is a new subgroup in T-ALL that has 10% frequency and a poor outcome.

Finally, there are also important epigenetic alterations, as DNA methylation, histone modification and miRNA alterations. In this case the primary genetic sequence is normal but there are other factors that affect gene expression. It should be noted that are reversible events that could be targeted with therapeutic agents. (Figure 3)

In this kind of cancer predominante B-progenitor tumours, with genetic and epigenetic alterations. It is important to have in mind that with the analysis and the risk stratification in function of genetic alterations it can be made a prognosis approximation with the aim to administrate the best therapy.

As this kind of cancer is the most frequent in childhood, it will be successful to carry out studies to improve diagnostic and therapeutic approaches.

**References**