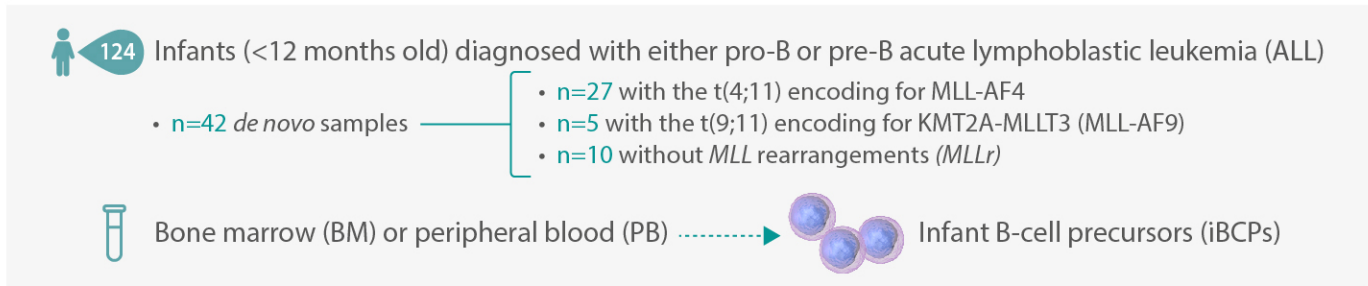


# A multi-layered genome-wide analysis to investigate the clinical relevance of subclonal mutations and gene expression signature in a large cohort of infant B-cell precursor acute lymphoblastic leukemia (iBCP-ALL)

## Interfant99 treatment study



## WES and WGS analyses

- A **silent mutation landscape** in 3 iBCP-ALL subtypes: MLL-AF4+, MLL-AF9+ and non-MLL (n=42)
  - 1 genomic rearrangement and 2.5 non-silent SNVs, **2-fold higher** than previously reported
  - 34% of the iBCP-ALL cases carry mutations in either *K-RAS* or *N-RAS*
  - 1/3 mutations showed a mutant allele frequency (**MAF**) <20%
- ➡ iBCP-ALL contains genetically different intratumoral subclones despite its genomic stability

## Deep sequencing analysis of B-Cell Receptor (BCR) repertoires

- Performed on t(4;11)/MLL-AF4+ iBCP-ALL PB samples using a PCR-based method
- BCR repertoires did not exhibit significantly expanded VDJ rearranged B-cell clones either in diagnosis and relapse
- t(4;11)/MLL-AF4+ iBCP-ALL malignant cells are developmentally stalled at pro-B stage, and the cellular origin of such genomic drivers has to be a **pre-VDJ stem/progenitor cell**