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ETV6/RUNX1-POSITIVE CHILDHOOD ACUTE LYMPHOBLASTIC LEUKEMIA (ALL); THE SPECTRUM OF CLONAL HETEROGENEITY AND ITS IMPACT ON PROGNOSIS

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## Highlights

- The prognostic implications of the ETV6/RUNX1 fusion, as well as the ones of the secondary aberrations, have been debated for more than a decade.
- ETV6/RUNX1 positive ALL is characterized by extreme clonal heterogeneity and presence of subclones upon diagnosis.
- In our cohort, the most common additional abnormalities detected were del12p13(37%), 3-6x21q22(22.2%), del9p21(18.5%) and 2-3xETV6/RUNX1(18.5%).
- Showing the correlation between the presence of clonal diversity and MRD clearance, we have indicated that the presence of subclones is associated with high levels of MRD during induction treatment.
- Common features of all ETV6/RUNX1-positive relapses were sub-clonal diversity at diagnosis, FCM-MRDd15 positivity at a high level( $10^{-3}$  or  $10^{-2}$ ), trisomy 21 and deletion of the 9p21 chromosomal region.
- Clonal diversity upon diagnosis and high levels of FC-MRD d15, may serve as a surrogate markers, distinguishing a subgroup of patients with heterogeneous outcome.
- A possible ongoing clonal evolution may further be associated with a greater genetic instability of the ancestral clone. Thus, we support that clonal heterogeneity may well be driving disparate outcomes, possibly coinciding with other underlying mechanisms.

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