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EORTC study suggests detecting ERG gene deletion useful for risk stratification in childhood ALL

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Results of EORTC trial 58951 suggest that detecting ERG gene deletion at diagnosis of childhood B-cell precursor (BCP) acute lymphoblastic leukemia (ALL) would be useful for risk stratification. The study, published in *Leukemia* showed that patients with the ERG gene deletion had a very good outcome with an 8-year event-free survival of 86.4% and an overall survival of 95.6%.

ALL is the most common childhood malignancy, but it is characterized by a number of recurring genetic alterations. These alterations, each with a specific gene expression profile, can influence response to treatment. For example, high hyperdiploidy and the chromosomal translocation t(12;21)/ETV6–RUNX1 are the most prevalent alterations in young children and are associated with good treatment response and outcome. On the other hand, t(9;22)/BCR–ABL1, rearrangements of the MLL gene, low hypodiploidy, intrachromosomal amplification of chromosome 21 (iAMP21) are all associated with a high risk of relapse. In addition, IKZF1 gene deletion has been recently described as a strong marker of poor outcome.

Dr. Emmanuelle Clappier of the Hematology University Institute, St-Louis and Robert Debré Hospitals in Paris and lead author of this EORTC publication says, "The genetic basis of BCP-ALL is still unknown for a significant proportion of cases, and consequently outcome is unpredictable at the time of diagnosis. This is especially true

for older children and adolescents, more than half of whom display no classifying genetic alteration. There is a clear need for new biological markers to assist in making treatment decisions and improve outcome for these patients."

A genomic deletion in the ERG gene was identified by array-CGH analysis in selected patients. Then an independent non-selected cohort of 897 children aged 1-17 years and treated for BCP-ALL in the EORTC 58951 trial between December 1998 and July 2008 was screened for ERG gene deletions. ERG gene deletion was found in 3.2% of the patients (29 out of the 897 patients) and was associated with higher age (median age 7.0 years versus 4.0 years, P=0.004) and frequent IKZF1 Δ4-7 deletions (37.9% versus 5.3% in the remaining patients, P