Evaluation of treatment response in paediatric leukaemia using patient specific circulating tumour DNA analysis.

Fani Pujol Calderón[1]
Raghda Ibrahim[1], Elisabeth Mellström[2], Linda Fogelstrand[3], Ida Rahmqvist[1], Robert Khashan[1], Moe Xylander[1], Christin Karlsson[1], Tobias Österlund[4], Anders Ståhlberg[4] and Martin Dalin[2]
[1] Sahlgrenska Center for Cancer Research, Department of Paediatrics, Institute of Clinical Sciences, Sahlgrenska Academy at University of Gothenburg, Gothenburg, Sweden. Wallenberg Centre for Molecular and Translational Medicine, University of Gothenburg, Gothenburg, Sweden.
[2] Sahlgrenska Center for Cancer Research, Department of Paediatrics, Institute of Clinical Sciences, Sahlgrenska Academy at University of Gothenburg, Gothenburg, Sweden. Wallenberg Centre for Molecular and Translational Medicine, University of Gothenburg, Gothenburg, Sweden. Childhood Cancer Centre, Queen Silvia Children's Hospital, Sahlgrenska University Hospital, Gothenburg, Sweden.
[3] Department of Clinical Chemistry, Sahlgrenska University Hospital, Gothenburg, Sweden. Department of Laboratory Medicine, Institute of Biomedicine, Clinical Genomics Gothenburg, Science for Life Laboratory, University of Gothenburg, Gothenburg, Sweden.
[4] Sahlgrenska Center for Cancer Research, Department of Laboratory Medicine, Institute of Biomedicine, Sahlgrenska Academy at University of Gothenburg, Gothenburg, Sweden. Wallenberg Centre for Molecular and Translational Medicine, University of Gothenburg, Gothenburg, Sweden. Department of Clinical Genetics and Genomics, Sahlgrenska University Hospital, Region Västra Götaland, Gothenburg, Sweden.

Background & objectives

Leukaemia is the most common paediatric cancer, accounting for almost 1 out of 3 childhood malignancies. As per gold standard, to diagnose and evaluate treatment response a bone marrow aspirate is required. Bone marrow aspiration is an invasive procedure that when done in children requires general anaesthesia, which is associated with a significant risk of complications. In contrast, blood samples are less invasive and entail less risks than bone marrow aspirates.

Methods

In this study, circulating tumour DNA (ctDNA) analysis using SimSenSeq is presented as a candidate for minimal residual disease (MRD) evaluations during treatment, where personalised multiplex assays are used for tracking multiple patient specific single nucleotide variants (SNVs) over the course of treatment in children with acute lymphoblastic leukaemia. The analysed SNVs are selected from those present in the diagnostic bone marrow aspirate and followed up in longitudinal paired bone marrow aspirates, plasma samples and peripheral blood cells samples.

Results

Preliminary results for 9 patients show that the targeted SNVs levels in ctDNA are comparable to those in bone marrow. In addition, the total amount of ctDNA follows a similar trend as the percentage of cells with leukaemia-associated immunophenotype in the bone marrow measured by flow cytometry as part of the clinical MRD evaluation. Similar results are observed when qPCR is used to evaluate the treatment response in T-ALL patients.

Conclusion

Further analyses are needed to determine a ctDNA cut-off value for MRD classification to be able to influence treatment strategy. However, these results show the potential use of patient-specific ctDNA analysis in peripheral blood as a marker for treatment response in childhood ALL.