Monitoring response to targeted treatment in children with ALK-driven neuroblastoma using a novel assay for detection of circulating tumor DNA

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Background & objectives

Neuroblastoma is a cancer derived from neuroblasts of the sympathetic nervous system and accounts for 6 % of pediatric cancers. Activating somatic mutations in the anaplastic lymphoma kinase (ALK) gene is detected in approximately 10% of neuroblastomas and is associated with worse prognosis. Preliminary data suggest that children with relapsed or refractory ALK-driven neuroblastoma may respond to treatment with the ALK inhibitor lorlatinib. However, current methods for evaluation of the treatment have limited sensitivity and may increase the risk of long-term complications.

This study aims to design a sequencing panel covering all neuroblastoma-associated activating and treatment resistance mutations in the ALK gene, and evaluate its potential for monitoring of circulating tumor DNA (ctDNA) during lorlatinib treatment in 5 children with ALK-driven neuroblastoma.

Methods

To allow quantification at low levels of ctDNA and filter out sequencing errors, we use the highly sensitive next generation sequencing technique named SiMSenSeq.

Results

All 5 patients responded well to lorlatinib treatment. The levels of circulating ALK-mutated DNA increased at time of initial disease relapse and decreased gradually during effective treatment. In some cases, ctDNA was detected while no other clinical marker or imaging modality showed signs of disease. No novel mutations associated with ALK inhibitor resistance were found throughout the treatment.

Conclusion

In conclusion, analysis of ctDNA using the novel ALK panel shows promise as a biomarker during ALK inhibitor treatment in children with ALK-driven neuroblastoma. More data is needed to assess its potential to detect resistance mutations during treatment.