Non-invasive circulating tumor dna analyses for diagnosis and monitoring of treatment response in hodgkin lymphoma.

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Abstract

Background: Genetic profiling of Hodgkin lymphoma (HL) is challenging due to the rarity of Hodgkin cells in biopsies. Analyzing plasma circulating cell-free DNA (cfDNA) is a promising, non-invasive approach for characterizing somatic aberrations and monitoring measurable residual disease (MRD).

Objectives:

1. Evaluate the clinical feasibility of using panel sequencing on cfDNA for comprehensive genomic profiling of HL at diagnosis.

2. Assess the additional value of longitudinal cfDNA analysis to FDG-PET/CT for MRD determination.

Methods: This study is part of the BioLymph study (ISRCTN12948913). Plasma samples were collected before primary treatment, at interim evaluation after two chemotherapy cycles (IE), end of primary treatment (EOT), during follow-up, and during relapse treatment for refractory patients (≥5 timepoints/patient). Diagnostic plasma cfDNA was analyzed using the Genomic Medicine Sweden (GMS) Lymphoid Gene panel. Follow-up cfDNA samples were analyzed using a custom-designed targeted sequencing panel tracking 7 to 107 targets per patient. FDG-PET/CT was performed according to clinical routines, with Tumour Metabolic Volume (MTV) and Total Lesion Glycolysis (TLG) calculated at treatment start, IE, and EOT.

Results: 36 HL patients were included, median age 42 years (19–84). Most had advanced stage disease (IIB-IV, n=23), and 10/26 informative samples were EBV-positive. Treatment included AVD/ABVD +/- radiotherapy (n=25) and escBEACOPP (n=11). Five patients had progression (3 relapse, 2 primary refractory disease at PET-CT EOT evaluation).

Total cfDNA burden at diagnosis correlated significantly with FDG-PET-CT MTV ($R=0.38$, $p<0.05$) and TLG ($R=0.37$, $p=0.05$). 1498 somatic SNV/Indels were detected in baseline plasma (7–157 variants/case), with 532 non-synonymous, protein-coding variants (median 14.5 variants/patient, range 1-57) and a median VAF range of 0.35 to 8%. Mutations were found in genes implicated in HL, including SOCS1, TNFAIP3, GNA13, B2M, ARID5B, and STAT6. CNV profiling revealed clinically relevant gains in 9p and 2p arms. Paired tumor tissue and plasma analyses for eight patients showed higher variant allele frequency (VAF) in plasma than in tissue ($p<0.001$).

Analysis of the longitudinal samples and correlation to PET-CT is ongoing.

Conclusions: Preliminary results demonstrate the potential and feasibility of targeted deep sequencing of ctDNA for comprehensive genomic profiling in HL at diagnosis.

Do you have any conflicts of interest?

No, I do not have a conflict of interest.