Evaluating a tumor-agnostic methylation-based mrd assay in a real-world setting: the lb-clear study

Abstract Submitter: Guy Froyen, Belgium*

Co-Authors: Sarah Deville, Pieter-Jan Volders, Sofie de Meulder, Elke Van Mieghem, Pascal Peeters, Brigitte Maes

*Jessa Hospital

Abstract

Background

Detecting minimal residual disease (MRD) through circulating tumor DNA (ctDNA) is transforming post-surgical risk assessment and personalized treatment decisions in solid tumors. Methylation-based approaches provide a promising avenue to detect ctDNA in liquid biopsies. It is a tumor-agnostic strategy that will expand the potential of MRD detection across multiple cancer types, enabling more accessible liquid biopsy applications in routine clinical practice.

Objective

The LB-CLEAR study aims to clinically validate the analytical performance of a tumor-agnostic methylation-based MRD assay, in a real-world setting. This prospective study evaluates the ability of a ctDNA-based test to detect tumor-associated methylation patterns in patients with early-stage colorectal cancer (CRC) to support post-surgical adjuvant chemotherapy decisions.

Methods

LB-CLEAR is a multicenter, observational study conducted in Belgium, designed to bring the power of MRD detection into real-world clinical practice. Liquid biopsies are collected from a cohort of healthy volunteers and early-stage CRC patients and assayed with the Avida Methyl kit (Agilent Technologies), interrogating 3400 cancer-related methylation sites. The analytical performance of this assay will first be assessed. Patients will be clinically followed for 2 years, with liquid biopsy sampling throughout their clinical trajectory for MRD analysis. The study aims to optimize the workflow and evaluate key clinical factors, ensuring the method is not only scientifically robust but also seamlessly applicable in a clinical setting.

Results

The Avida Methyl assay generates a methylation index (MI) as an output, which is used for MRD assessment. Our initial findings show that the MI is very low (mean 0.195) in 33 healthy volunteers and significantly elevated (mean 20.69) in ctDNA from 12 metastasized CRC patients. The performance of the assay in early stage CRC needs to be explored. Data from this validation cohort will be extended and discussed, as well as bioinformatic improvements in data analysis towards CRC.

Conclusion

Our study will provide critical real-world evidence on the performance of a tumor-agnostic methylation-based MRD assay for post-surgery treatment decision, thereby paving the way for a broader clinical implementation of MRD testing. These findings should support more personalized post-surgical risk assessment and adjuvant treatment strategies, ultimately improving the quality of life of cancer patients.

Do you have any conflicts of interest?

No, I do not have a conflict of interest.