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EXHIBIT DATES: MAY 7-9, 2023

NOVEL PLASMA BIOMARKER (SENTINEL 10™) CAN DETECT SMALL HCC WITH ALL OTHER MARKERS NEGATIVE

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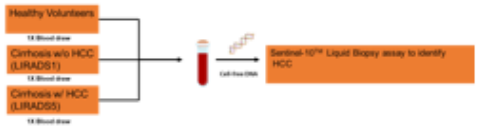
INTRODUCTION

Hepatocellular carcinoma (HCC) is the 5th most common cancer and 3rd leading cause of cancer death worldwide, with significant health disparities. Cirrhosis is a 'pre-malignant' disease, and even with poor quality screening tools, screening for HCC is standard-of-care. Expected rates of HCC in cirrhosis is 2-8%/year. Discovery of a cost-effective biomarker with high specificity and sensitivity for early detection of HCC and minimally invasive confirmatory diagnosis could markedly improve outcomes for this deadly disease.

AIM

We have developed a liquid biopsy for early cancer detection called Sentinel 10™. Our bioinformatics analysis suggest that Sentinel-10 could detect HCC with high sensitivity and specificity (Figures 1 and 2). In this pilot study we investigate if Sentinel 10™ liquid biopsy assay could detect HCC in the setting of cirrhosis and other chronic liver diseases (CLD).

STUDY DESIGN



Healthy volunteers are self described as having no liver disease or other chronic illnesses.

Liver disease patients undergoing screening dynamic MRI where defined as without HCC by meeting LI-RADS 1 criteria, and with HCC by meeting LI-RADS 5 criteria.

HCC patients determined by imaging criteria as above.

Cirrhosis or non-cirrhosis was determined by imaging, endoscopy, labs, VTCE and/or biopsy

Sentinel-10™ liquid biopsy assay is described in detail in Vrba et al 2020.

RESULTS

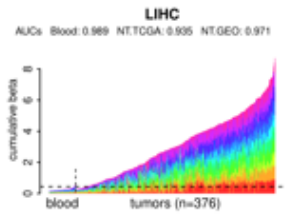


Figure 1. Bioinformatic analysis of Sentinel -10 ™ biomarkers for HCC detection using TCGA data bases.

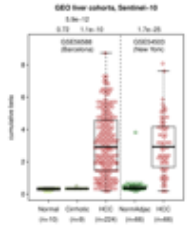


Figure 2. In Silico validation of Sentinel -10 ™ biomarkers for HCC detection using Barcelona GEO HCC tissue, and New York GEO HCC tissue data bases.

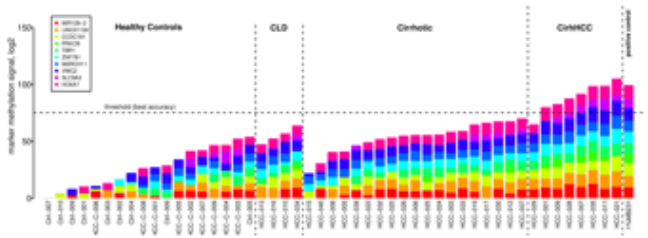


Figure 4. Rainbow plot of the methylation signal from the biomarker set on the different study cohorts – Healthy volunteers, chronic liver disease without cirrhosis (CLD), cirrhosis without HCC (Cirrhotic), hepatocellular carcinoma with cirrhosis(CirhHCC). The threshold for the cut off value is represented by the dashed horizonal line. The y axis is the $\log_2$ scale and the x-axis is the degree of methylation for each individual DNA methylation marker and each subject in the study. The MDA-MB-231 DNA was used as positive control since all the markers are methylated in this cell line.

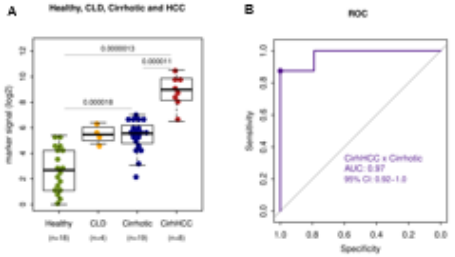


Figure 3. The Sentinel-10™ DNA methylation biomarker set differentiates between healthy volunteers (healthy), patients with chronic liver diseases without advanced fibrosis (CLD), patients with cirrhosis (Cirrhotic), and patients with HCC (CirhHCC). A) Mean methylation signal per marker for healthy group, CLD, Cirrhosis cases, and HCC cases. The y-axis is log 2 scale. B) Receiver operating characteristic (ROC) analysis of the biomarker set signal from controls, cirrhosis cases, and HCC cases

Results Summary

The methylation signal was markedly higher in subjects with HCC compared to healthy volunteers (Figure 3A & Figure 4)

Cirrhotic and non-cirrhotic Subjects with HCC had AFP (and AFP-L3 and DCP , and GALAD scores) levels less than 20 ng/ml (2-<20); <10% AFP-L3, in 7 of 8 cases and all 8 were staged as HCC by Barcelona 0-B, PS-0 and within Milan criteria.

We also observed a significant difference between HCC and subjects with cirrhosis or chronic liver disease (Figure 3A)

Subjects with cirrhosis and chronic liver disease has a higher signal than healthy volunteers (Figure 3A)

The performance characteristics of the Sentinel-10 assay for detecting HCC in the setting of cirrhosis was sensitivity 88%, specificity 100%, and accuracy 97% (Figure 3B)

CONCLUSIONS

- The Sentinel-10™ liquid biopsy assay can detect HCC in the setting of cirrhosis and other chronic liver diseases.
- Although the AFP values were not suggestive of HCC, the increased DNA methylation signal (Sentinel 10™) identifies those cirrhotic subjects who had HCC by Dynamic MRI imaging criteria.
- Expansion of this pilot study to a larger biomarker phase 2 and phase 3 study are warranted.

REFERENCES

Vrba L, Oshiro MM, Kim SS, Garland LL, Placencia C, Mahadevan D, Nelson MA, Futscher BW. DNA methylation biomarkers discovered *in silico* detect cancer in liquid biopsies from non-small cell lung cancer patients. Epigenetics. 2020 Apr;15(4):419-430. doi: 10.1080/15592294.2019.1695333. Epub 2019 Nov 27. PMID: 31775567; PMCID: PMC7153541.

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