

A Case of Stage II Hepatocellular Carcinoma Diagnosed Using A Multi-Cancer Early Detection Test

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INTRODUCTION

- Liver cancer is the third leading cause of cancer-related deaths in the world, with liver cancer incidence and related deaths increasing in the United States^{1,2}
- Although there is no guideline-recommended screening for liver cancer for the general population, the American Association for the Study of Liver Diseases (AASLD) recommends liver cancer surveillance in individuals with cirrhosis through ultrasound imaging, with or without alpha-fetoprotein (AFP) testing, every 6 months³
- A multi-cancer early detection (MCED) test (Galleri®, GRAIL, LLC, Menlo Park, CA) that analyzes methylation patterns of cell-free DNA in the blood using a sequencing assay and machine-learning classifiers is available as a complement to existing single-cancer screening tests⁴⁻⁶
- The MCED test reports either (1) 'cancer signal detected' with 1 or 2 cancer signal origin (CSO) prediction(s) or (2) 'cancer signal not detected'

OBJECTIVE

- Here, an early-stage liver cancer case is presented to review the diagnostic pathway guided by a positive MCED test result

SUPPORTING INFORMATION

Supporting Data

- In the third and final Circulating Cell-free Genome Atlas (CCGA) study (NCT02889978), this MCED test detected a shared cancer signal with a specificity of 99.5% and a sensitivity of 51.5% and predicted CSO with an accuracy of 88.7%⁶
- Sensitivity of cancer signal detection was 70% in stage II liver/bile duct cancer⁶ (Table S1)

Table S1. Sensitivity Of Cancer Signal Detection In Liver/Bile Duct Cancer By Stage

Cancer	Clinical stage	Total	Test positive	Sensitivity (95% CI)
Liver/Bile duct	All	46	43	93.5% (82.5%-97.8%)
	I	6	6	100.0% (61.0%-100.0%)
	II	10	7	70.0% (39.7%-89.2%)
	III	9	9	100.0% (70.1%-100.0%)
	IV	20	20	100.0% (83.9%-100.0%)
	Missing	1	1	100.0% (5.1%-100.0%)

KEY RESULTS: MCED TESTING DETECTED CANCER SIGNAL AND DIRECTED DOWNSTREAM DIAGNOSTIC EVALUATION OF A STAGE II HEPATOCELLULAR CARCINOMA

**White Male (BMI: 25 kg/m²)
62 Years With Chronic Hepatitis B**

- Low viral load since 9 years ago and no active therapy for hepatitis B
- Liver with confirmed marked (severe) steatosis but no fibrosis or cirrhosis

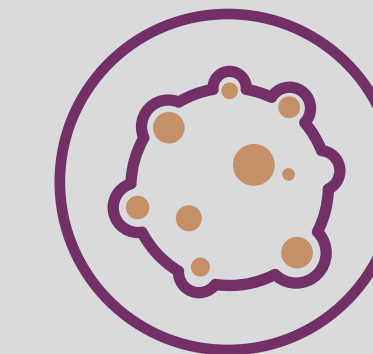
CSO1 = Liver/Bile duct
CSO2 = Lung



Male



62 Years



Prostatectomy for Prostate Cancer (2 years prior)



AFP 2.6 ng/mL (3 years prior)



Non-Smoker



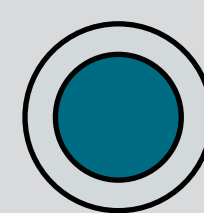
Alcohol Use (2-3/day)



No Genetic Cancer Predisposition



CSO Prediction was Correct



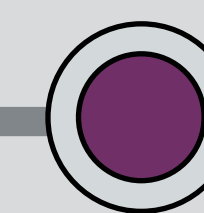
CT (Abdomen) Without Contrast

Clinical Notes

- CT of the abdomen without contrast (follow-up on a 1.7 cm indeterminate nodule without interval change for 1 year) showed a 1.9x1.9x1.9 cm left hepatic lobe nodule



10 DAYS

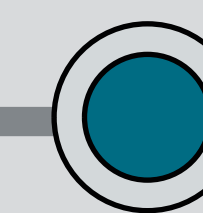


**DAY 1 AND 2
Cancer Signal Detected and Results Communicated**

CSO1 = Liver/Bile duct
CSO2 = Lung

Clinical Notes

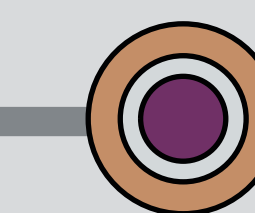
- The positive MCED test result resulted in aggressive evaluation of the mass



**DAY 10
Biopsy**

Clinical Notes

- Biopsy of the liver nodule revealed hepatocellular carcinoma, moderately differentiated
- The cancer was subsequently classified as **stage II hepatocellular carcinoma**



**DAY 10
Diagnosis**

Diagnosis

Hepatocellular Carcinoma, Stage II

Treatment and Status

- MRI with and without contrast showed no morphologic changes of cirrhosis or portal hypertension (Day 25)
- Mass completely resected (Day 52)
- Prior to surgery, AFP level was 29.3 ng/mL (Day 13); after surgery, AFP level was 5.7 ng/mL (Day 66)
- Patient currently has no clinical symptoms (normal appetite and no weight loss, pain, or jaundice; Day 234)

CONCLUSIONS

- The MCED test detected a cancer signal and predicted a liver CSO for an individual with stage II liver/bile duct cancer
- An indeterminate nodule was found in the patient 1 year prior to MCED test use with no resolution
 - Per the AASLD guidelines, based on the patient's medical history, he would not have been a candidate for hepatocellular carcinoma screening⁷
 - Thus, this cancer would potentially not have been detected unless the patient used the MCED test or the lesion was picked up incidentally based on imaging or labs
- In conjunction with a positive MCED test result with a top-CSO prediction of liver/bile duct, an aggressive workup took place resulting in diagnostic resolution within 2 weeks
- Early-stage hepatocellular carcinoma has better prognosis and outcomes than late-stage disease
- The use of the MCED test guided aggressive diagnostic workup and potentially improved outcomes for this patient

References

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CSO1, top-predicted CSO; AFP, alpha-fetoprotein; BMI, body mass index; CT, computerized tomography; MRI, magnetic resonance imaging