Personalized circulating tumor DNA (ctDNA) monitoring for recurrence detection and treatment response assessment in hepatocellular carcinoma (HCC)

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Background

- HCC is an aggressive malignancy, accounting for ~90% of primary hepatic cancers1.
- While surgical resection and liver transplantation can be curative, 8-20% of post-transplantation and 40-70% of post-resection patients recur2,3,4.
- Here we sought to analyze the utility of longitudinal ctDNA testing for disease monitoring in patients with HCC.

Methods

- This multicenter study retrospectively analyzed 227 plasma samples from 68 patients with HCC.
- The curative-intent surgeries included liver transplantation (41/66, 62%) and hepatectomy (23/66, 35%); two patients (3%) who were inoperable received liver-directed and systemic targeted therapy. Five (15.2%) patients had stable disease and consistently low levels of ctDNA. In both these patients, AFP levels remained in the normal range even after ~120 months post-surgery.
- Patient-specific changes in ctDNA levels in response to treatment were depicted using the Signatera™ bespoke mPCR NGS assay.

Table 1. Patient characteristics (N=66)

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value (range) or # Patients (%)</th>
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<tbody>
<tr>
<td>Median age at diagnosis</td>
<td>67 years (21-84)</td>
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<tr>
<td>Sex</td>
<td>Male: 35 (51.5%), Female: 31 (48.5%)</td>
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<td>Stage</td>
<td>I: 24 (36.4%), II: 24 (36.4%), III: 10 (15.2%), IV: 8 (12%)</td>
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<td>Treatment</td>
<td>Curative transplantation: 41 (62%), Curative resection: 23 (35%), Other (liver-directed/surgical targeted therapy): 2 (3%)</td>
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Figure 1. Patient overview plots (Cohort A, B, and C)

Figure 2. Patient-specific changes in ctDNA levels in response to treatment

Figure 3. Scatter plots depicting treatment regimens, disease status by imaging, and changes in disease status by imaging, chemotherapy, and systemic therapy, as well as liver-directed therapies.

Conclusions

- In the setting of post-curative therapy for HCC (surgery and transplant), ctDNA positivity can detect recurrences ahead of radiological imaging.
- In the palliative setting, ctDNA dynamics are indicative of treatment response to systemic therapy, as well as liver-directed therapies.

References


Acknowledgments: Poster development support was provided by Chitra C. Patel, PhD, and Pursat Duta, PhD from Natera, Inc.