Clinical Utility of a Molecular Cancer Classifier for Primary Site Identification in Neuroendocrine Tumors
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Abstract
Neuroendocrine tumors (NETs) vary significantly in their clinical presentation and biological behavior based on primary site of origin. In patients with metastatic NETs, identification of the primary tumor site is essential for clinical management and to determine prognosis. We sought to determine the clinical utility of a 92-gene panel assay in patients with metastatic NET of unknown primary site.

Background
Neuroendocrine tumors (NETs) vary significantly in their clinical presentation and biological behavior based on primary site of origin. In patients with metastatic NETs, identification of the primary tumor site is essential for clinical management and to determine prognosis. We sought to determine the clinical utility of a 92-gene panel assay in patients with metastatic NET of unknown primary site.

Methods
In this study, we reviewed patients with a metastatic NET of unknown primary site who were evaluated with a 92-gene panel assay (CancerTYPE ID, BioTheranostics, Inc., San Diego, CA) as part of routine care. Demographics, pathology, and treatment data were collected. Based on the assay prediction, patients were further evaluated with surgical exploration, endoscopic procedures, and/or imaging. Predictions were classified as “correct” if confirmed on further evaluation or “incorrect” if the primary site was identified in a different location or could not be found where predicted.

Results
Results of the 92-gene panel assay were reported in 150 patients. The assay prediction of GI carcinoid was correct on further evaluation in 88% of patients. The assay was correct in less than half of patients when islet cell carcinoid (47%) and lung carcinoid (40%) were predicted (Table 1). In 50 patients (33%) with incorrect assay predictions, the primary tumor was identified in a different location on surgical exploration (14%), endoscopic procedure (6%), or imaging (4%). The remaining 38 patients (76%) underwent extensive evaluation in attempts to identify their primary tumor (Figure 1).

Conclusions
In this study, we determined that a 92-gene panel assay may be useful in patients with metastatic NETs of unknown primary site. A prediction of GI carcinoid may provide guidance for clinicians, especially surgeons, in identifying the primary tumor while predictions of islet cell and lung carcinoid require more extensive evaluation.
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Table 1. Results by Subtype Predicted by a 92-gene Panel Assay (N=150)

<table>
<thead>
<tr>
<th>Assay Prediction</th>
<th>N</th>
<th>Correct, N (%)</th>
<th>Incorrect, N (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>GI Carcinoid</td>
<td>85</td>
<td>75 (88)</td>
<td>10 (12)</td>
</tr>
<tr>
<td>Islet Cell</td>
<td>32</td>
<td>15 (47)</td>
<td>17 (53)</td>
</tr>
<tr>
<td>Lung Carcinoid</td>
<td>15</td>
<td>6 (40)</td>
<td>9 (60)</td>
</tr>
<tr>
<td>Other NET</td>
<td>9</td>
<td>3 (33)</td>
<td>6 (67)</td>
</tr>
<tr>
<td>Other Cancer</td>
<td>9</td>
<td>1 (11)</td>
<td>8 (89)</td>
</tr>
</tbody>
</table>

Abbreviations: NET, neuroendocrine tumor

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Results

Figure 1. Predicted primary tumor subtype using a 92-gene panel assay and its clinical utility in the identification of NETs of unknown primary

- GI Carcinoid N=85 (57%)
  - Correct N=75/85 (88%)
  - Incorrect N=10/85 (12%)
  - NET 1st found elsewhere N=1
  - No NET 1st found in GI tract or elsewhere N=9

- Islet Cell N=32 (21%)
  - Correct N=15/32 (47%)
  - Incorrect N=17/32 (53%)
  - NET 1st found elsewhere N=3
  - No NET 1st found in Pancreas, Stomach, or Duodenum or elsewhere N=14

- Lung Carcinoid N=15 (10%)
  - Correct N=6/15 (40%)
  - Incorrect N=9/15 (60%)
  - NET 1st found elsewhere N=1
  - No NET 1st found in Lung or elsewhere N=8

- Other NET N=9 (6%)
  - Correct N=3/9 (33%)
  - Incorrect N=6/9 (67%)
  - NET 1st found elsewhere N=3
  - No NET 1st found where predicted N=3

- Other Cancer N=9 (6%)
  - Correct N=1/9 (11%)
  - Incorrect N=8/9 (89%)
  - Follow up evaluation confirmed NET diagnosis N=8

Patients diagnosed with a metastatic NET of unknown primary site who were evaluated with CancerTYPE ID N=150

Click figure to enlarge.
CONCLUSIONS

• In this study, we determined that a 92-gene panel assay may be useful in patients with metastatic NETs of unknown primary site.

• A prediction of GI carcinoid may provide guidance for clinicians, especially surgeons, in identifying the primary tumor while predictions of islet cell and lung carcinoid require more extensive evaluation.