First-in-human evaluation of $^{68}$Ga-FAP-2286, a fibroblast activation protein targeted radioligand

Brad Kline

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No relevant disclosures

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FAP-2286

- Cyclic polypeptide linked to a DOTA chelator
  - Does not share the quinolone motif used in the FAPI family of molecules
- Is potent and selective for FAP, and is stable in plasma
Imaging of Solid Tumors Using $^{68}$Ga-FAP-2286

- Three cohorts:
  - Cohort 1 (n=10): Metastatic disease present on conventional imaging defined as having RECIST 1.1 measurable disease or multiple bone metastases.
    - Agnostic to tumor type.
  - Cohort 2 (n=40): Metastatic disease present on conventional imaging defined as having RECIST 1.1 measurable disease or multiple bone metastases.
    - Pathologically confirmed breast cancer, pancreatic adenocarcinoma, sarcoma, castrate resistant prostate cancer, bladder cancer, or colon cancer.
    - Basket subgroup (n=10)
  - Cohort 3 (n=30): No evidence of metastatic disease as defined as the absence of RECIST 1.1 measurable disease or bone metastases.

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Materials and Methods

• Inclusion criteria:
  • Age ≥18 years
  • Confirmed solid tumor as defined by one of the three cohorts
• 48 patients enrolled from December 2020 to June 2022

<table>
<thead>
<tr>
<th>Tumor type</th>
<th># Enrolled</th>
</tr>
</thead>
<tbody>
<tr>
<td>Breast</td>
<td>4</td>
</tr>
<tr>
<td>Bladder</td>
<td>17</td>
</tr>
<tr>
<td>Prostate</td>
<td>5</td>
</tr>
<tr>
<td>Colon</td>
<td>2</td>
</tr>
<tr>
<td>Head/neck</td>
<td>6</td>
</tr>
<tr>
<td>Pancreas</td>
<td>1</td>
</tr>
<tr>
<td>Sarcoma</td>
<td>7</td>
</tr>
<tr>
<td>Cholangio/HCC</td>
<td>5</td>
</tr>
<tr>
<td>Lung</td>
<td>1</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>48</strong></td>
</tr>
</tbody>
</table>
Materials and Methods

• On average, patients received 5.9±1.3 mCi of $^{68}$Ga-FAP-2286 and were imaged 64±7 minutes after injection.

• Reconstructed images were evaluated by a board-certified nuclear medicine physician.

• Tumor-to-background ratio (TBR): $\frac{SUV_{\text{max lesion}}}{SUV_{\text{mean blood pool}}}$

• Image quality:
  • Qualitative: 5-point Likert scale (1 – non-diagnostic to 5 – good image quality)
  • Quantitative: Noise = (SD of $\text{SUV}_{\text{mean}}$) / $\text{SUV}_{\text{mean}}$

• Biodistribution: Mean SUVs were recorded from VOIs placed on the right lobe of the liver, middle of the spleen, right and left kidneys, and mediastinum (blood pool).

• Scanners: Siemens Vision PET/CT and GE Signa PET/MRI.
Results: Image Quality and Noise

Dose did not significantly impact noise.

Image reconstruction did impact noise.
Results: Biodistribution

Biodistribution in 48 patients

Representative bladder cancer patient
Results: Tumor Uptake

- Pancreatic Ca (n=1)
- Prostate Ca (n=5)
- Bladder Ca (n=17)
- Colon Ca (n=2)
- Head/neck Ca (n=6)
- Lung Ca (n=1)
- Breast Ca (n=4)
- Sarcoma (n=7)
- Cholangio/HCC (n=5)

SUV\textsubscript{max-avg}

CRPC
- SUV\text{max} = 8.5

Sarcoma
- SUV\text{max} = 33.1
Case Example #1:
76-year-old male with bladder cancer

SUVmax = 16.1

SUVmax = 14.3

*No FDG PET comparison available
Case Example #2: 
72-year-old male with cholangiocarcinoma

<table>
<thead>
<tr>
<th></th>
<th>30 min</th>
<th>60 min</th>
<th>120 min</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kidney</td>
<td>3.42</td>
<td>3.53</td>
<td>3.76</td>
</tr>
<tr>
<td>Liver</td>
<td>3.73</td>
<td>3.16</td>
<td>2.49</td>
</tr>
<tr>
<td>Blood pool</td>
<td>1.98</td>
<td>1.44</td>
<td>1.43</td>
</tr>
</tbody>
</table>
Case Example #3: 72-year-old female with invasive lobular breast cancer

- Mediastinal nodes and thoracic spine lesions
  - FAP-2286
  - FDG
  - SULmax 5.0
  - (background 2.2)

- Peritoneal carcinomatosis
  - FAP-2286
  - FDG
  - SULmax 6.8 RI 7.1 LI
  - SULmax 2.1 RI 2.3 LI

FAP PET  FDG PET
Summary

• The dose of $^{68}$Ga-FAP-2286 did not have a significant impact on image quality.

• Biodistribution mimics FAPI compounds, with the highest activity in the kidneys consistent with renal excretion.

• $^{68}$Ga-FAP-2286 PET is a promising tool for staging patients across cancer types.
Thank you!

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