Comparison of tumor marker cancer antigen 72-4 (CA 72-4) to other tumor markers in the monitoring of metastatic or recurrent tumors of the gastrointestinal tract, lung, breast, and ovaries

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INTRODUCTION
In the treatment of metastatic and recurrent cancers, measuring response to anti-tumor is a constant challenge. The tumor-associated glycoprotein 72 (TAG-72) has been identified with the monoclonal antibody as a potential TM for the monitoring of various cancers. The DRG TM-CA72.4 is a solid phase enzyme-linked immunosorbent assay based on the sandwich principle using the monoclonal mouse antibody (Clone CC49) directed towards an antigenic site on a CA 72-4.

OBJECTIVE
The current study aimed to 1) quantify the abnormality rate of the tumor marker CA72-4 in each cancer type compared to the abnormality rate of current FDA approved tumor biomarkers and 2) correlate levels of CA72-4 to clinical outcomes in patients with measurable disease.

METHODS
We conducted a prospective, single center study at Winthrop-University Hospital, Mineola, New York involving 96 patients between March 2013 and August 2016 with various histologically confirmed, locally advanced, non-surgically resectable and/or metastatic carcinoma with measurable disease that were known to express CA72-4 (Figure 1). Quantification of CA72-4 was performed according to manufacturer’s instructions using the DRG TM-CA 72-4 ELISA kit (Developed by DRG International, Germany). Spectrophotometer measurements of 450nm with cut-off of 1) 0.8U/mL or 2) 4.0U/mL were used. The study was reviewed approved by the Institutional IRB.

RESULTS
➢ Total of 96 patients were enrolled. Median age of patients with positive and negative CA72-4 were 65.5 vs 65.0 years respectively (p=0.34). Of the positive patients, 33% were male compared to 67% females and of the negative patients 40% were males compared to 60% females (p=0.53).
➢ Using 0.8U/mL as the level of detection for CA72-4 in our assay, we found 55.2% (53/96) of the patients were positive and 44.8% (43/96) were negative for the study tumor marker at the time of enrollment. Using the previously reported 4U/mL as the detection level decreased positivity rate to 33.3% (32/96) and increased negativity to 66.7% (64/96) at enrollment (Table 1).
➢ Using 0.8U/mL cut-off, 30.2% (13/43) of the negative patients developed detectable levels of CA72-4 in their serum vs 18.0% (2.50) in 4U/mL analysis. Using 0.8U/mL cut-off, highest positivity of 72-4 was found in pancreatic cancer 82% (27/33) while currently established FDA markers such as CA19-9 were positive 84.8% (28/33) of patients while using 4U/mL, this rate dropped to 58% (19/33).
➢ Lowest rates of positivity remained unchanged between 0.8U/mL and 4U/mL: gastric/gastroesophageal junction tumors -50% (1/2), gall bladder/Biliary tract-20% (2/5) while lung cancer decreased from 50% (2/4) positivity for 0.8U/mL to 0% (0/4) for 4U/mL, although very few patients were enrolled in these types.
➢ Other sites of high positivity included ovarian- 64.3% (18/28) for 0.8U/mL vs. 57% (16/28) for 4U/mL cut-offs however this included both mucinous and non-mucinous subtypes.
➢ Total positivity for CA72-4 amongst all patients across all categories was 68% (66/96) at 0.8U/mL and 50% (48/96) for 4U/mL.

CONCLUSIONS
➢ Positivity rates of CA72-4 varied based on different assay cut-off levels with the highest positivity noted in the pancreatic, ovarian and colorectal carcinomas.
➢ CA72-4 showed concordance with existing tumor markers which correlated with clinical course of patients.
➢ Levels of CA72-4 were found to be transiently elevated in some patients with biliary dysfunction.
➢ This study demonstrates that the DRG TM-CA 72-4 ELISA assay can be readily performed in a hospital laboratory and may serve as a useful adjunct to conventional tumor markers in the follow-up of a variety of metastatic cancers.

Table 1: Positivity rates according to disease site.

<table>
<thead>
<tr>
<th>Disease Site</th>
<th>CA72-4 (0.8 U/mL)</th>
<th>CA72-4 (4 U/mL)</th>
<th>CA19-9 (&gt;38.6 U/mL)</th>
<th>CA27-29 (&gt;38.6 U/mL)</th>
<th>CEA (&gt;5 ng/mL)</th>
<th>CA-125 (&gt;34.9 U/mL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Breast</td>
<td>8/12 (67%)</td>
<td>5/12 (42%)</td>
<td>12/12 (100%)</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Lung (Adenocarcinoma)</td>
<td>2/4 (50%)</td>
<td>0/4 (0%)</td>
<td>4/4 (100%)</td>
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<tr>
<td>Colorectal, Small Bowel</td>
<td>8/12 (67%)</td>
<td>5/12 (42%)</td>
<td>10/12 (83%)</td>
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<tr>
<td>Ovarian</td>
<td>18/28 (64%)</td>
<td>16/28 (57%)</td>
<td>22/28 (78%)</td>
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<tr>
<td>Pancreatic</td>
<td>27/33 (82%)</td>
<td>19/33 (58%)</td>
<td>28/33 (85%)</td>
<td>9/33 (27%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gallbladder/Biliary/Ampullary</td>
<td>2/5 (40%)</td>
<td>2/5 (40%)</td>
<td>3/5 (60%)</td>
<td>2/5 (40%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gastric/Adeno GE junction/Adeno Esophagel</td>
<td>1/2 (50%)</td>
<td>1/2 (50%)</td>
<td>1/2 (50%)</td>
<td>1/2 (50%)</td>
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</tr>
<tr>
<td>Total Positive</td>
<td>66/96 (68%)</td>
<td>48/96 (50%)</td>
<td>31/28 (82%)</td>
<td>12/12 (100%)</td>
<td>26/56 (46%)</td>
<td>23/28 (78%)</td>
</tr>
<tr>
<td>Total Negative</td>
<td>30/96 (31%)</td>
<td>48/96 (50%)</td>
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</table>

REFERENCES

ACKNOWLEDGEMENTS
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