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

GASTROINTESTINAL ONCOLOGY

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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 Inc, 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.

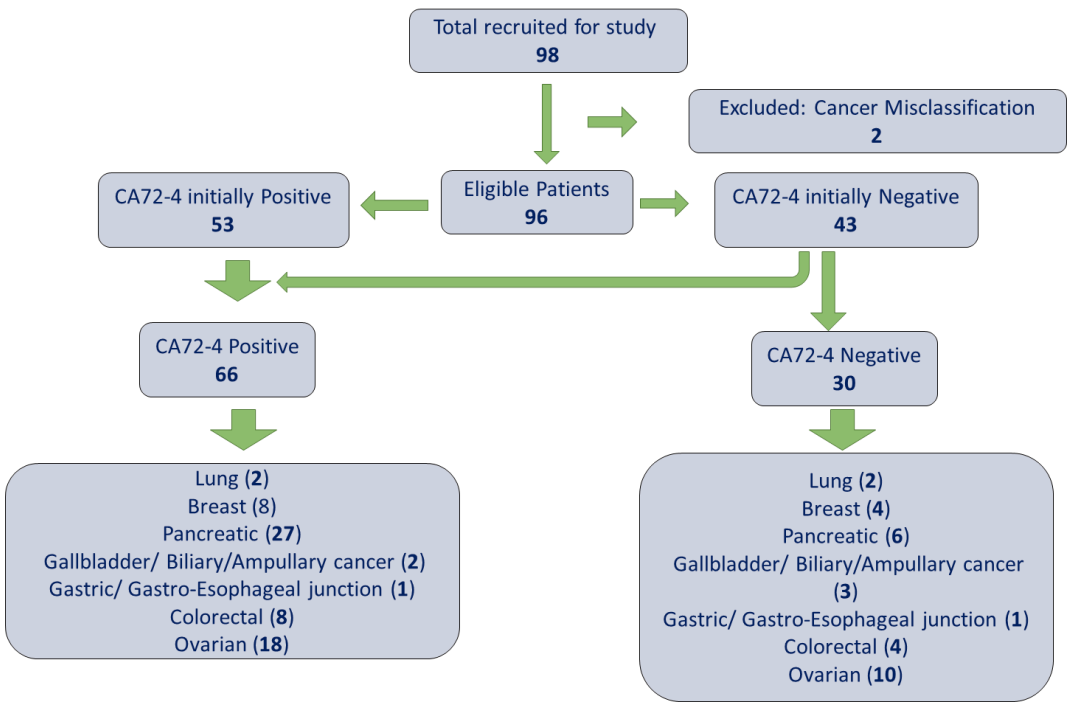

Figure 1: Study design based on 0.8U/mL as detection cut-off for assay.

Disease Site						
Tumor Marker (Assay-cut off)	**CA72-4** *(> 0.8U/mL)*	**CA72-4** *(> 4.0U/mL)*	**CA19-9** *(>35U/mL)*	**CA27-29** *(>38.6U/mL)*	**CEA** *(>5ng/mL)*	**CA-125** *(> 34U/mL)*
Breast	8/12 (67%)	5/12 (42%)		12/12 (100%)		
Lung (Adenocarcinoma)	2/4 (50%)	0/4 (0%)			4/4 (100%)	
Colorectal, Small Bowel	8/12 (67%)	5/12 (42%)			10/12 (83%)	
Ovarian	18/28 (64%)	16/28 (57%)				22/28 (78%)
Pancreatic	27/33 (82%)	19/33 (58%)	28/33 (85%)		9/33 (27%)	
Gallbladder/Biliary/Ampullary	2/5 (40%)	2/5 (40%)	3/5 (60%)		2/5 (40%)	
Gastric/Adeno GE junction /Adeno Esophageal	1/2 (50%)	1/2 (50%)			1/2 (50%)	
Total Positive	**66/96 (68%)**	**48/96 (50%)**	**31/38 (82%)**	**12/12 (100%)**	**26/56 (46%)**	**22/28 (78%)**
Total Negative	**30/96 (31%)**	**48/96 (50%)**				

Table 1: Positivity rates according to disease site.

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 **16/64 (25.0%)** 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/gasteroesophageal 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 patents 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.

References

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