How Reliable is Circulating Tumor DNA in Detecting Disease Progression and Regression of Non-colorectal Gastrointestinal Cancers?

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Introduction

- Circulating tumor DNA is short DNA sequence shed by tumor cells to the circulation [1]
- CtDNA has a vast possible applications: tumor molecular profiling, tracking treatment response, detection of resistance, and detection of minimal residual disease [1]
- Literature is limited for non-colorectal GI cancers, with a few studies available for pancreatic, hepato-biliary and gastric cancers [2-6]
- Dynamic ctDNA changes during treatment and detection of progression or regression has not been well described in studies [2-6]

Methodology

- **Study design and setting:**
  - Retrospective observational study of 18 patients with non-colorectal GI cancers at William Beaumont Hospital, MI
- **Inclusion/Exclusion criteria:**
  - Included patients ≥ 18 years of age. Excluded patients without corresponding imaging to compare
- **Variables:**
  - Baseline characteristics: Demographics, BMI, tobacco/alcohol use, family history, stage of disease, treatment received
  - Variables of interest:
    - Disease progression: increased size of known cancerous lesion or development of new lesion, noted in imaging
    - Disease regression: decreased or resolution size of known lesion
    - Presence of disease: Significant burden of disease noted on imaging
    - Absence of disease: no cancerous lesions on imaging

Methodology

- **Statistical Analysis:**
- **With single ctDNA**: Correlation of single ctDNA results with imaging to predict presence of disease
- **With serial ctDNA**: Analysis of pairs of consecutive ctDNA trend (either up-trending or down- trending or negative persistently) and correlation with imaging to predict disease progression/regression
- Calculation of sensitivity, specificity, PPV, NPV for analyses of both single and serial ctDNA

Results

Baseline characteristics of participants

Characteristics	Frequency
Age	64 (31, 80)
Sex	Male 50% (9/18)
Patients' Race:	Caucasian 66.7% (12/18) AA 16.7% (3/18) Others 16.7% (3/18)
BMI	27 (20, 35)
Tobacco Use	77.8% (14/18)
Alcohol Use	16.7% (3/18)
Family History	0% (0/19)
Type of Cancer:	Hepato-biliary carcinoma - 33.3% (6/18) Pancreatic adenocarcinoma - 27.8% (5/18) Anal squamous cell carcinoma - 11.1% (2/18) Neuroendocrine tumor - 11.1% (2/18) Gastric adenocarcinoma - 5.6% (1/18) Small bowel adenocarcinoma - 5.6% (1/18) GI cancer of unknown origin - 5.6% (1/18)
Stage at Diagnosis:	Stage I - 5.6% (1/18) Stage II - 22.2% (4/18) Stage III - 33.3% (6/18) Stage IV - 38.9% (7/18)
Treatment received	Chemotherapy - 83.3% (15/18) Surgery - 55.5% (10/18) Targeted therapy - 44.4% (8/18) Immunotherapy - 33.3% (6/18) Radiation - 16.7% (3/18)

Results

- **Analysis with single ctDNA: predicts presence of disease**

CtDNA results (Single values)	Imaging finding		
	Presence of disease	**Absence of disease**	**Total**
Positive	12	0	12
Negative	8	13	21
Total	20	13	33

✓ **Finding: Sensitivity - 60% ; Specificity - 100%; PPV - 100%; NPV – 61.9%**

- **Analysis with serial ctDNA**

❑ **All ctDNA values and disease trend**

CtDNA trend (Pairs)	Imaging finding				
	Disease progression	**Disease regression**	**Stable disease**	**Absence of disease**	**Total**
Up trending	4	0	1	0	5
Down trending	0	4	0	0	4
Persistent Negative	0	0	1	5	6
Total	4	4	2	5	15

❑ **Up-trending ctDNA analysis: predicts disease progression**

CtDNA trend	Imaging finding		
	Disease progression	**Other than progression**	**Total**
Up-trending	4	1	5
Non up-trending	0	10	10
Total	4	11	15

✓ **Finding: Sensitivity – 100%; Specificity – 90.9%, PPV – 80%; NPV – 100%**

Results

❑ **Down trending ctDNA analysis: predicts disease regression**

CtDNA trend	Imaging finding		
	Disease regression	**Other than regression**	**Total**
Down-trending	4	0	14
Non down-trending	0	11	11
Total	4	11	15

✓ **Finding: Sensitivity- 100%; Specificity – 100%; PPV – 100%; NPV – 100%**

- **Median Lead time:** Earlier detection of progression by ctDNA compared to imaging: **44 days**

Discussion and Conclusion

- We describe good sensitivity, specificity, PPV and NPV of serial ctDNA to detect either disease progression or regression. But lower than our separate analysis of colorectal cancers.
- Above test results, and lead time of 44 days can assist physicians to make/change treatment plans prior to the imaging, and can reduce radiation exposure
- Our sample size was small and we recommend larger prospective studies are required to describe impact of ctDNA – guided surveillance in clinical outcomes

References

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