ANALYSIS OF CIRCULATING TUMOR DNA FOR MALIGNANCIES SENT AT THE TIME OF ENDOSCOPIC VISUALIZATION: AN OPTIMAL STRATEGY FOR DIAGNOSIS AND SELECTION OF TARGETED THERAPIES

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Introductions

- Advances in genomic sequencing technology currently allow for noninvasive detection and molecular profiling of malignancies for targeted therapies.
- In particular, circulating tumor DNA (ctDNA) which is obtained from a blood sample has shown to be clinically relevant in many ways such as monitoring for recurrence of malignancy, monitoring for the presence of minimal residual disease after resection, and determining prognosis/treatment response.
- ctDNA are genetic fragments which are released into the bloodstream from tumor cells undergoing apoptosis or necrosis. These unique tumor markers may be used to tailor genome-specific chemotherapies and immunotherapies.
- This study made use of a blood based 88 gene panel (Circulogene, Pensacola, FL) for the detection of ctDNA fragments. This study evaluated overall results of ctDNA detection when performed at the time of endoscopy.

Methods

- Over a period of 2 years, blood samples for ctDNA were obtained from 231 patients at the time of endoscopic visualization when there was a high suspicion for malignancy. Pancreatic, colorectal, gastric, esophageal, and biliary lesions were all assessed for this study. Biopsies with immunohistochemical staining of the suspected lesions were used to confirm malignant pathology.

Results

Table 1

Tissue Site	Detected	Not Detected	Positive Detection Rate
Pancreatic	64	26	71.11%
Colorectal	24	18	57.14%
Gastric	14	14	50%
Biliary	10	5	66.67%
Other	6	3	66.67%
Esophageal	6	10	37.50%

Table 1: Number of cases in which ctDNA was detected at suspected malignancy site.

Table 2

Tissue Site	Frequently Identified Gene	Gene Count	Percent of ctDNA Positive Samples	Percent of Total Samples
Pancreatic	TP53	27	42.00%	30.00%
	BRCA2	12	18.75%	13.33%
	BRCA1	10	15.63%	11.11%
	KIT	9	14.06%	10.00%
	FBXW7	7	10.94%	7.78%
	KRAS	6	9.38%	6.67%
Colorectal	TP53	6	25.00%	14.29%
	KIT	5	20.83%	11.90%
	CHEK2	4	16.67%	9.52%
	ATM	3	12.50%	7.14%
Gastric	CHEK2	5	35.71%	17.89%
	TP53	4	28.57%	14.29%
	GNAS	3	21.43%	10.71%
	FGFR2	3	21.43%	10.71%
Biliary	TP53	5	50.00%	33.33%
	BRCA1	3	30.00%	20.00%
	PIK3CA	2	20.00%	13.33%
	PD-L1	1	10.00%	6.67%
Esophageal	PD-L1	2	33.33%	12.50%
	TP53	1	16.67%	6.25%
	CHEK2	1	16.67%	6.25%

Table 2: Most frequent genes identified for given tissue site. Percentages shown are what proportion of the gene is present in cases where ctDNA is detected vs. all samples for the given tissue site.

- ctDNA was found in 71.11% of patients for which pancreatic malignancy was suspected, compared to 66% of biliary, 57.14% of colorectal, 50% of gastric, and 37.5% of esophageal lesions (Table 1).
- For cases where biopsy results were positive for malignancy (74.68% of cases), ctDNA was positive in 56.78% of cases.
- In cases where biopsy results were negative, ctDNA was positive in 60.0% of cases.
- There were various genes that were found to be more prevalent in certain malignancies (Table 2).
- Average turnaround time for ctDNA reports was 12.75 days, and the average time for the patient to be seen by an oncologist was 19.78 days from the date of endoscopy.

Discussion

- ctDNA, which is obtained via blood sample, can be used as an detection tool for gastrointestinal malignancies. Genomic detection tools such as the ctDNA panel can be used by oncologists for targeted therapies.
- When sent at the time of endoscopic suspicion for malignancy, the ctDNA panel was usually available for the oncologist to aid in first line chemotherapy decision making.
- In cases where pathologic findings were negative for malignancy, but clinical suspicion for malignancy was high, ctDNA was found to be positive in 60.0% of cases.
- When ctDNA analysis was sent at the time of endoscopy, the oncologist usually was able to use this genomic information to aid in decision making for first-line therapy.
- Based on these findings, we feel it may be the responsibility of the endoscopist to send ctDNA analysis at the time of endoscopic visualization of a malignancy.

References

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