

INTRODUCTION

- Rapid genomic profiling is critical in non-metastatic NSCLC to guide selection of the optimal perioperative or consolidative systemic therapy strategy
- ctDNA offers a readily accessible sample for molecular testing
- The ability to detect genomic alterations using ctDNA in the non-metastatic setting is unclear

AIMS

1. To characterize the proportion of actionable genomic alterations (AGAs) detected by ctDNA relative to tissue-based molecular testing
2. To estimate the turnaround time of ctDNA testing compared to tissue-based testing

METHODS

- Single-center retrospective cohort study at the University of Colorado Anschutz School of Medicine.
- Patients evaluated at the Thoracic Multidisciplinary Clinic (MDC) with non-metastatic NSCLC and paired pretreatment ctDNA and tissue-based testing from January 2020 to December 2024 were included.
- AGAs (Tier 1) and pathogenic variants (Tier 2) were defined per the AMP/ASCO/CAP consensus interpretation system.
- ctDNA detection was defined relative to alterations identified by tissue-based molecular testing.
- Turnaround time (TAT) was defined as the interval from molecular laboratory specimen receipt to final report.

CONCLUSIONS

1. Commercially available pretreatment ctDNA testing detected 42% of actionable genomic alterations and 30% of pathogenic non-actionable alterations.
2. The turnaround time of ctDNA testing was nearly 2-weeks less than tissue-based molecular testing (7 vs 20 days).
3. These findings suggest ctDNA may have a role in accelerating genomic profiling in patients with potentially curable, non-metastatic NSCLC.

BASELINE CHARACTERISTICS

Characteristic	Classification	Frequency (%)
Total	-	55
Age	Median (Q1-Q3)	68 (64-75)
Sex	Female	25 (46)
	Male	30 (54)
Tobacco Exposure	None	27 (49)
	≤ 10 pack years	7 (13)
	>10 pack years	21 (38)
PD-L1	<1%	10 (20)
	1-49%	25 (51)
	≥50	14 (29)
	Missing	6
Stage	I-II	13 (24)
	III	36 (66)
	Locally recurrent	6 (11)
Baseline PET imaging	Performed	55 (100)

Table 1: Baseline patient characteristics

AGA DETECTION

- Tissue-based molecular testing identified AGAs in 31 cases.
- The ctDNA detection rate was 42 % (13 of 31)
- No AGAs were detected exclusively by ctDNA testing

Gene	Alteration	ctDNA detection (%)
Overall	All AGAs	13 / 31 (42)
EGFR	Total	3 / 11 (27)
	Exon 19 deletion	2 / 6 (33)
	p.L858R	1 / 2 (50)
	Atypical mutations	0 / 3 (0)
ALK	EML4::ALK	2 / 6 (33)
KRAS	p.G12C	2 / 4 (50)
RET	Total	2 / 3 (66)
	KIF5B::RET	2 / 2 (100)
	ZMIZ1::RET	0 / 1 (0)
MET	Exon 14 skipping	1 / 3 (33)
ERBB2	Exon 20 insertion	2 / 2 (100)
ROS1	EZR::ROS1	0 / 1 (0)
BRAF	p.V600E	1 / 1 (100)

Table 2: Detection of AGAs by ctDNA testing. Percentages were calculated based on the total number of AGAs identified on tissue-based testing (n=31).

ASSOCIATED FACTORS

The associations between clinical and radiographic factors with ctDNA AGA detection were evaluated:

- No AGAs were detected in ctDNA in patients with stage I-II disease.
- Higher PD-L1 TPS was associated with higher odds of AGA detection by ctDNA (odds ratio: 1.02, p=0.04)

NON-AGA DETECTION

- ctDNA detected 30% (17 of 56) non-actionable pathogenic alterations identified by ctDNA
- There were 22 non-actionable pathogenic alteration detected exclusively by ctDNA

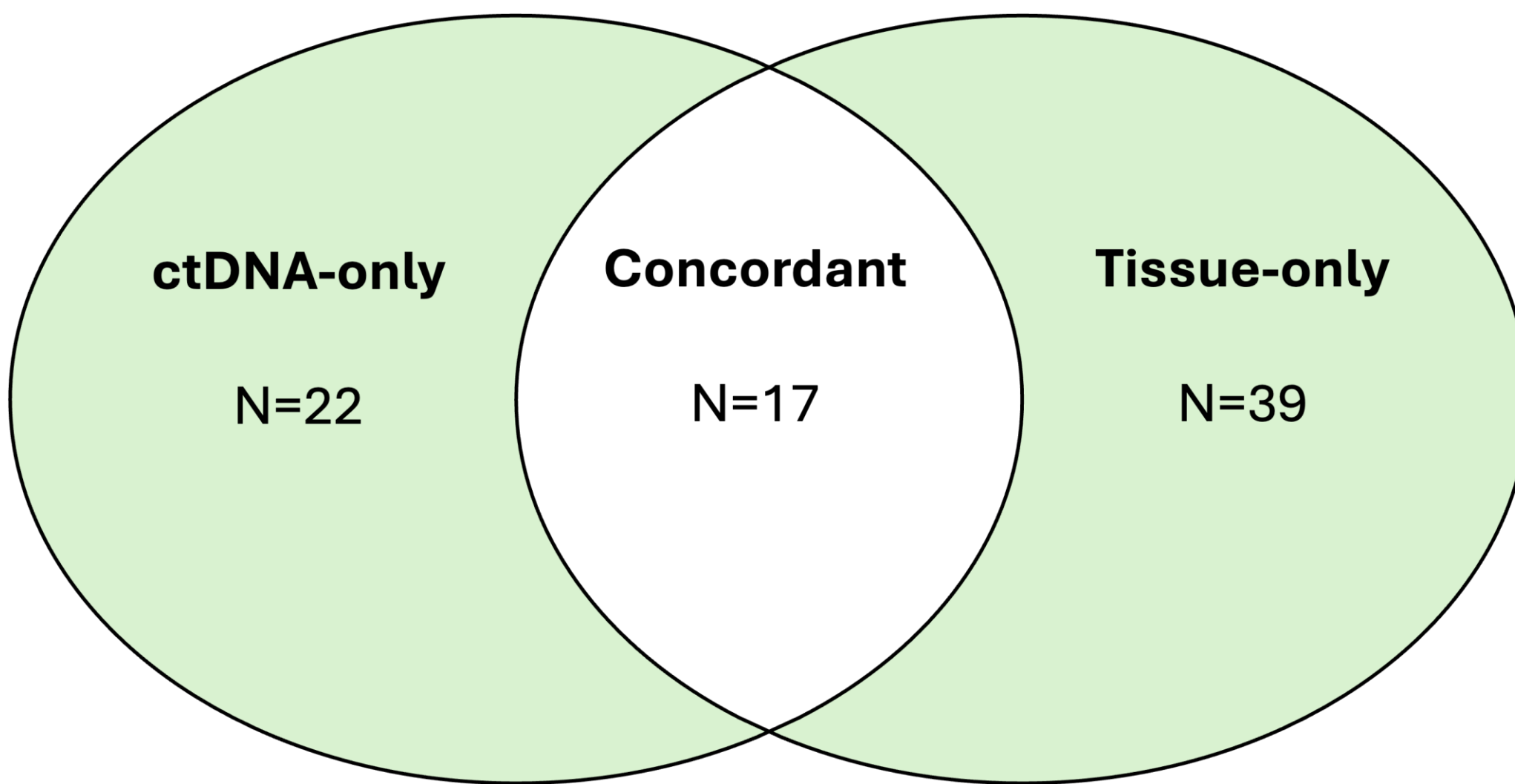


Figure 1: Venn diagram illustrating the concordance of tissue-based and ctDNA testing for detection of non-actionable pathogenic alterations

TURNAROUND TIME

- The median TAT was 20 days for tissue-based testing vs 7 days for ctDNA.
- Represents a 13-day difference in result TAT (p<0.001)