Circulating tumor DNA (ctDNA) clearance as a biomarker in patients with locally advanced NSCLC following chemoradiation

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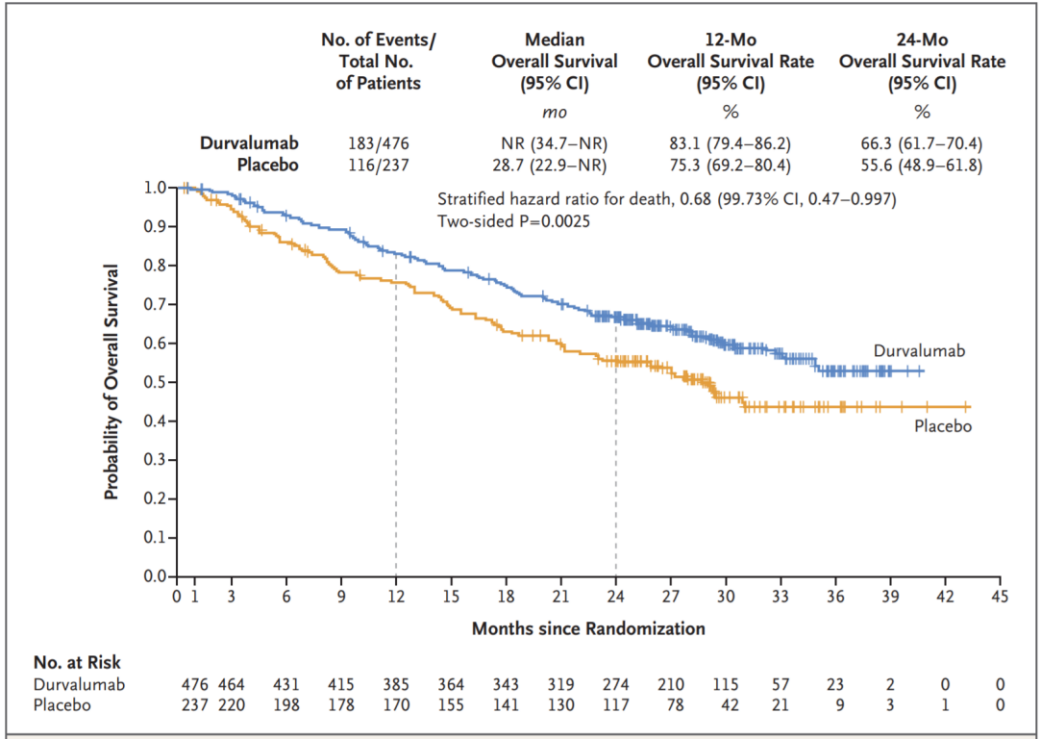
DISCLOSURES

I do not have any relevant financial relationships to disclose.

Introduction

- **Approximately 27% of patients with non-small cell lung cancer present with locally advanced disease (LANSCLC)[1]**
- **Consolidation therapy with Durvalumab is the current standard of care[2]**
- **Prognostic biomarkers can potentially identify patients likely to benefit from treatment intensification or de-escalation**



[1]Morgensztern et al, *JTO*, 2010; [2]Antonio et al, *NEJM*, 2018

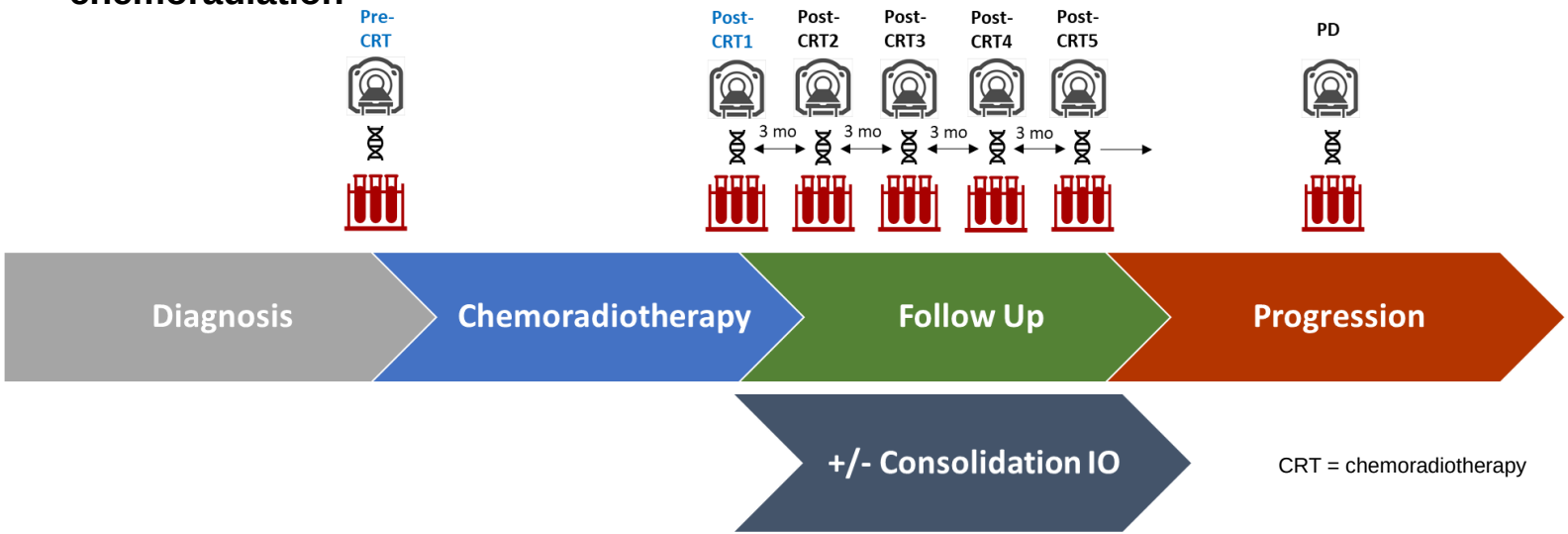
Introduction

- **Previous studies have shown the utility of ctDNA using large fixed hybrid capture panels in locally advanced non-small cell lung cancer[3,4].**
- **These hybrid capture panels use tumor informed analysis and require prior knowledge of genomic alterations in a tumor[3,4]**
- **InVisionFirst-Lung™ is a commercially available liquid biopsy panel of 37 genes[5]**
- **<u>Hypothesis:</u> ctDNA testing using a commercially available panel in patients with locally advanced non small lung cancer is feasible and may predict outcomes**

[3]Chaudhuri et al, *Can Disc,* 2017; [4]Moding et al, *Nat Can,* 2020; [5]Pritchett et al, *JCO Prec Onc,* 2019

Methods

- **Inclusion Criteria: Stage II or III NSCLC and had received definitive concurrent chemoradiation**

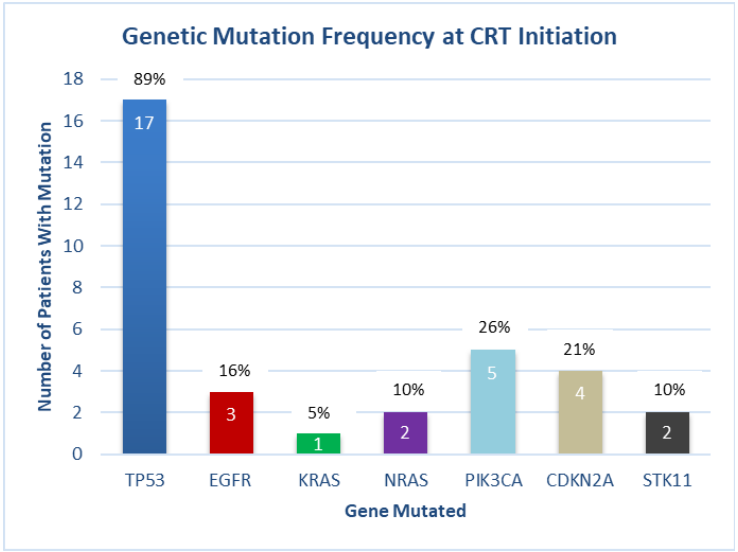


- **ctDNA clearance was defined as absence of Pre-CRT variants at Post-CRT1.**
- **Patients without detectable Pre-CRT variants or no Post-CRT1 samples were excluded from analysis**

Baseline Characteristics

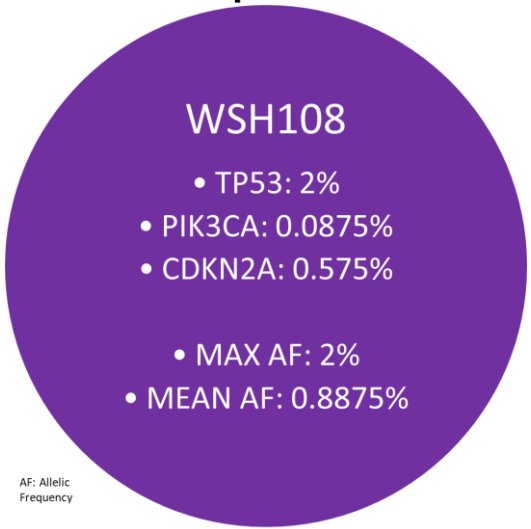
Characteristic	# of Patients
Patients Enrolled	43
Age at Diagnosis:	65 years (43 - 82)
Gender (male):	12/19 (63%)
Tobacco Use:	16/19 (84%)
Stage:	
IIA	1/19 (5%)
IIIA	7/19 (37%)
IIIB	10/19 (52%)
IIIC	1/19 (5%)
Histology:	
Squamous	9/19 (47%)
Adenocarcinoma	7/19 (37%)
NSCLC NOS	3/19 (16%)
Chemotherapy:	
Carboplatin + Paclitaxel	19/19 (100%)
Consolidation IO:	
None	10/19 (53%)
Atezolizumab	2/19 (10%)
Durvalumab	6/19 (32%)
Unknown	1/19 (5%)

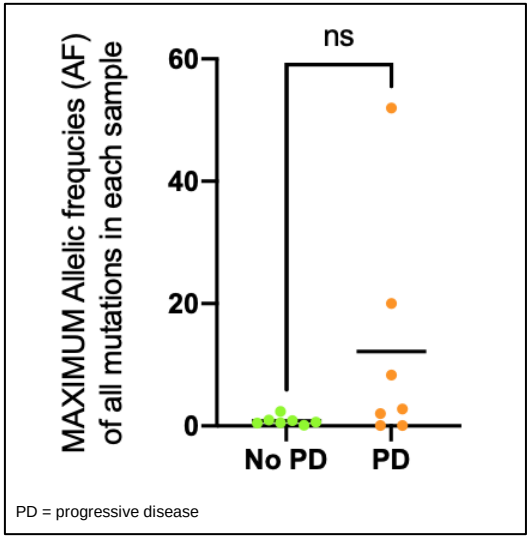
66% (28/43) patients had detectable variants at Pre-CRT
44% (19/43) had detectable variants Pre-CRT + Post-CRT samples collected (Median = 2 mutations per sample [range:1-5])

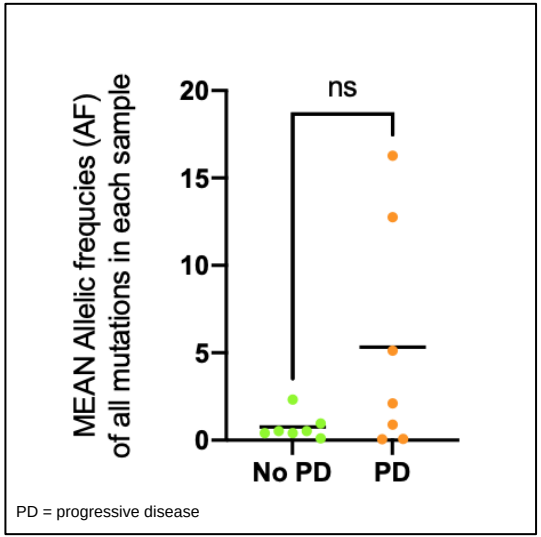


Pre-CRT Allelic Frequency and Outcomes

Example Patient







- **New variants after initiation of CRT were observed in 8/19 patients, 6 of whom had PD**

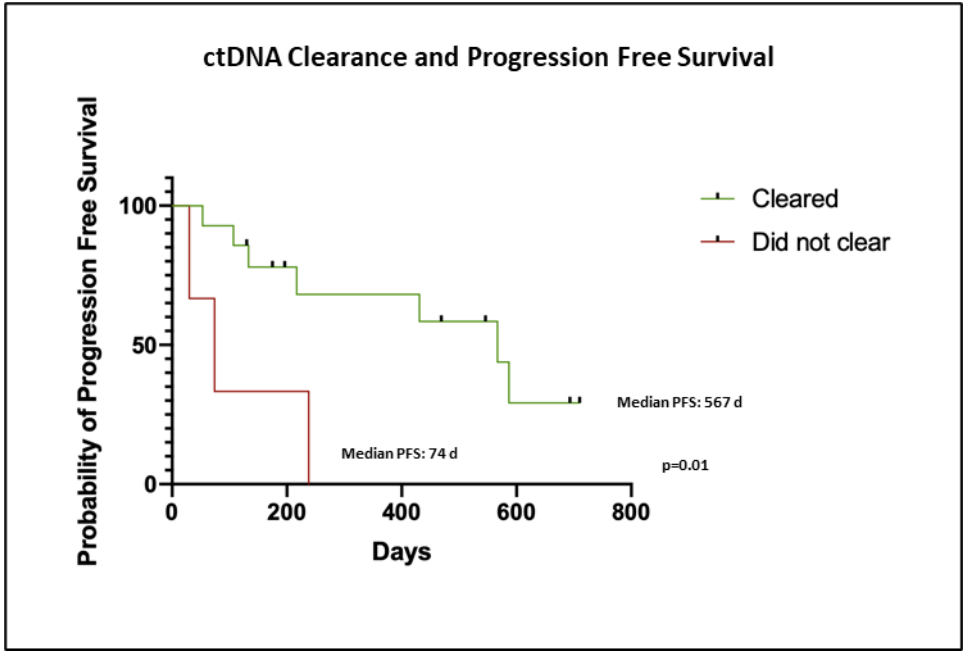
ctDNA Clearance and Outcomes

Two patients died from non-cancer related causes before post-CRT2 and were excluded from analysis on PD (1 cleared ctDNA, another did not)

ctDNA Clearance	PD	No PD	Total
Cleared ctDNA	7 (50%)	7 (50%)*	14
Did Not Clear ctDNA	3 (100%)	0	3

*Median Follow Up: 469 d, 130-710

PD = progressive disease



Conclusions

- 66% of patients had identifiable mutations at initiation of CRT
- Failure to clear ctDNA after CRT is a poor prognostic factor with 100% of patients recurring within 8 months
- ctDNA allelic frequency prior to CRT did not predict outcomes in this limited set of samples.
- Prospective validation in a larger data set and comparisons between tumor informed fixed panels and higher sensitivity personalized panels are needed

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