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Circulating Tumor DNA Tumor Fraction as a Precision Biomarker for Radiotherapy in Oligometastatic NSCLC

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Pre-RT ctDNA maximum variant allele frequency is associated with worse outcomes

Oligometastatic NSCLC patients
n=1487

↓

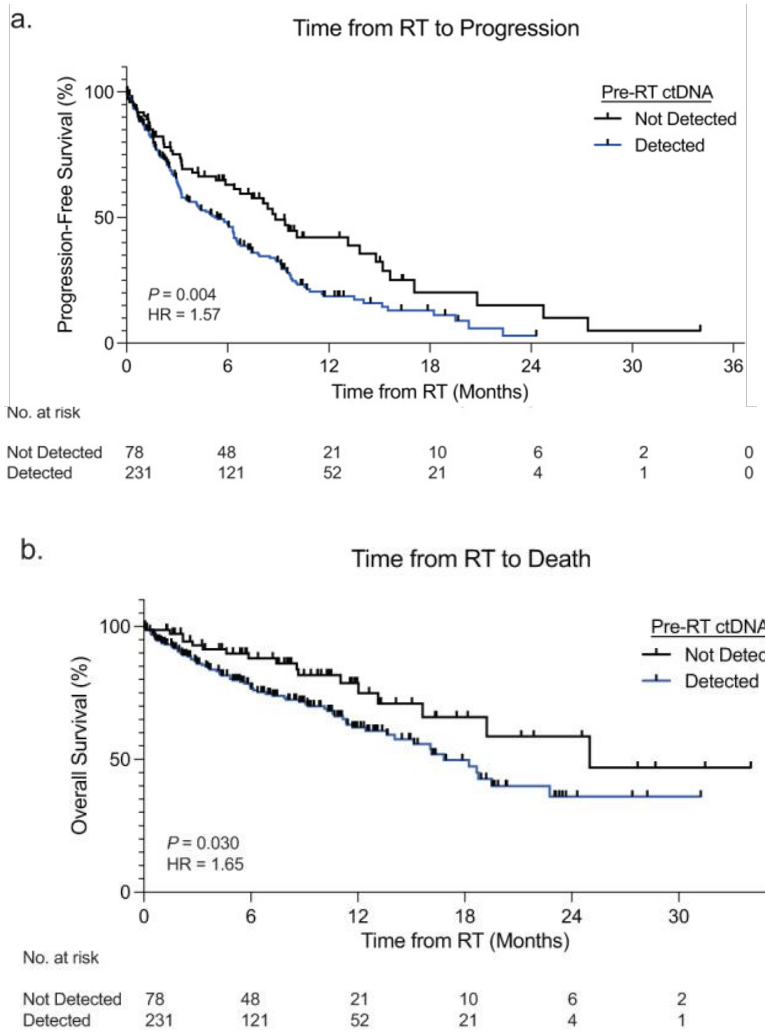
RT data available
n=918

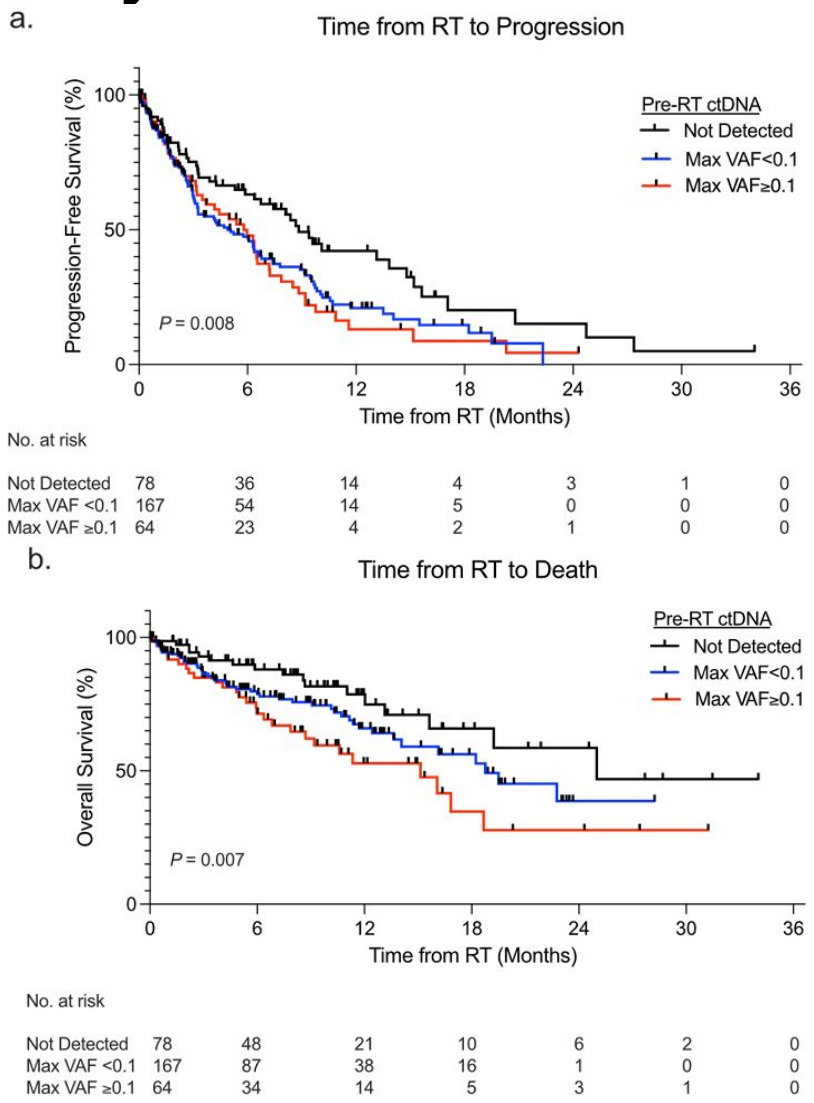
↓

Confirmed metastatic disease pre-RT
n=554

↓

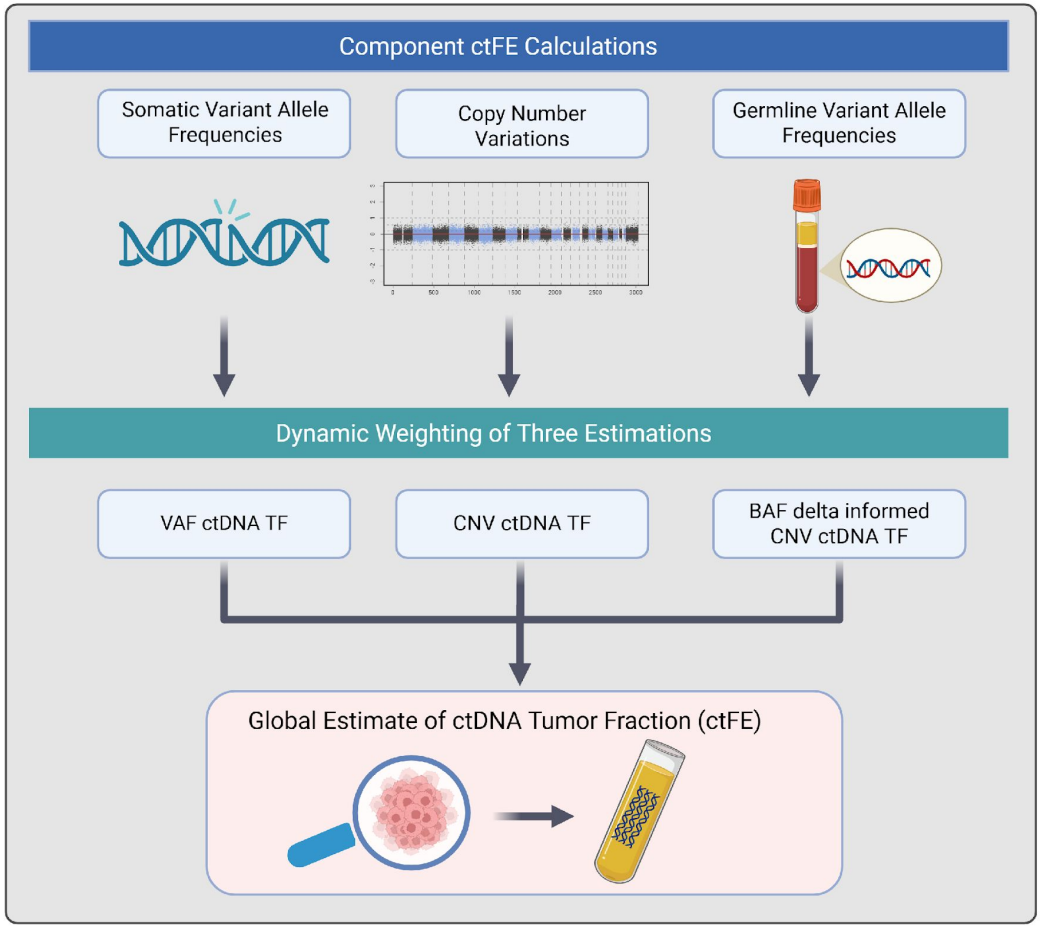
ctDNA sample drawn after OM diagnosis but before RT
n=309





Semenkovich. npj Precision Onc. 2023

Circulating Tumor Fraction Estimate (ctFE)



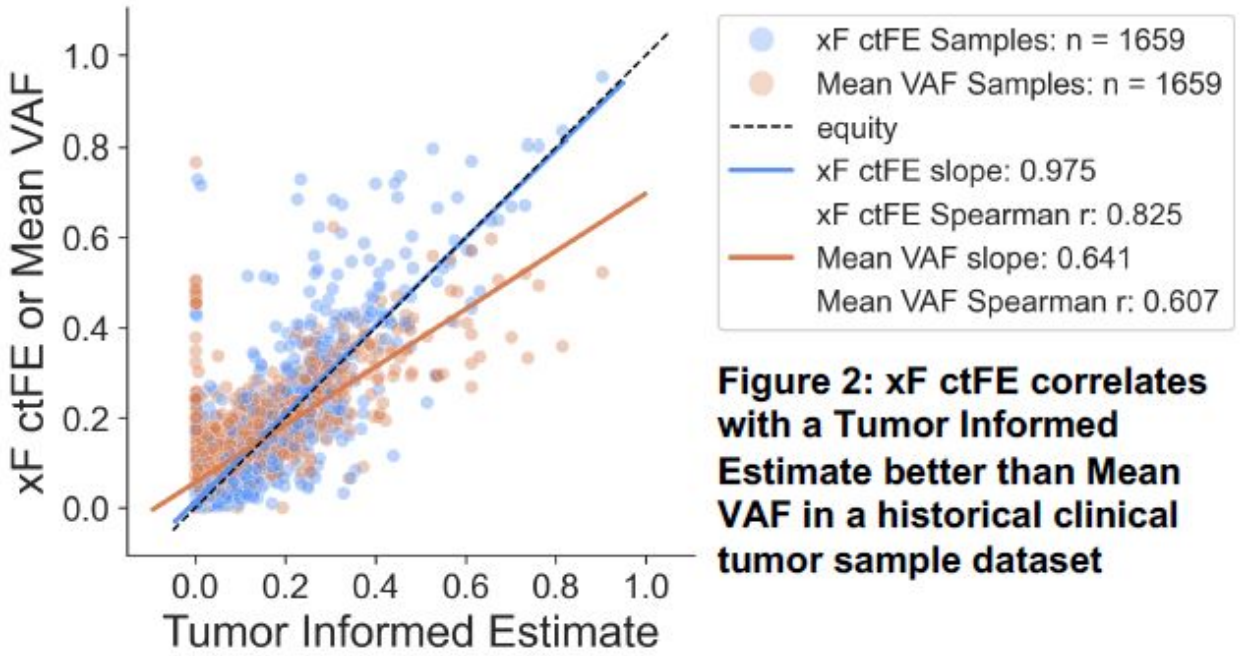


Figure 2: xF ctFE correlates with a Tumor Informed Estimate better than Mean VAF in a historical clinical tumor sample dataset

Guittar. SITC 2023

Using ctFE as a precision biomarker

Oligometastatic NSCLC (1-5 mets) patients n=1487

↓

RT data available n=918

↓

Confirmed metastatic disease pre-RT n=554

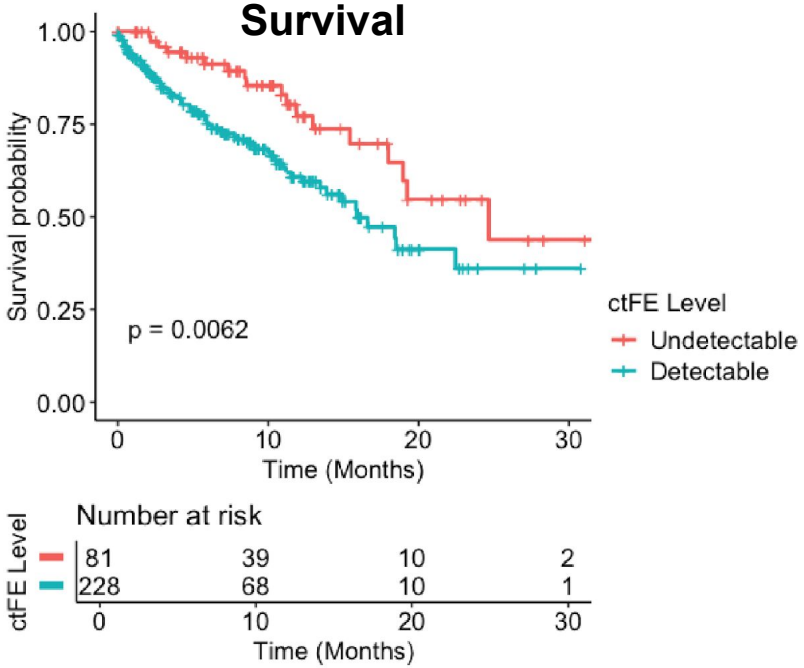
↓

ctDNA sample drawn after OM diagnosis but before RT n=309

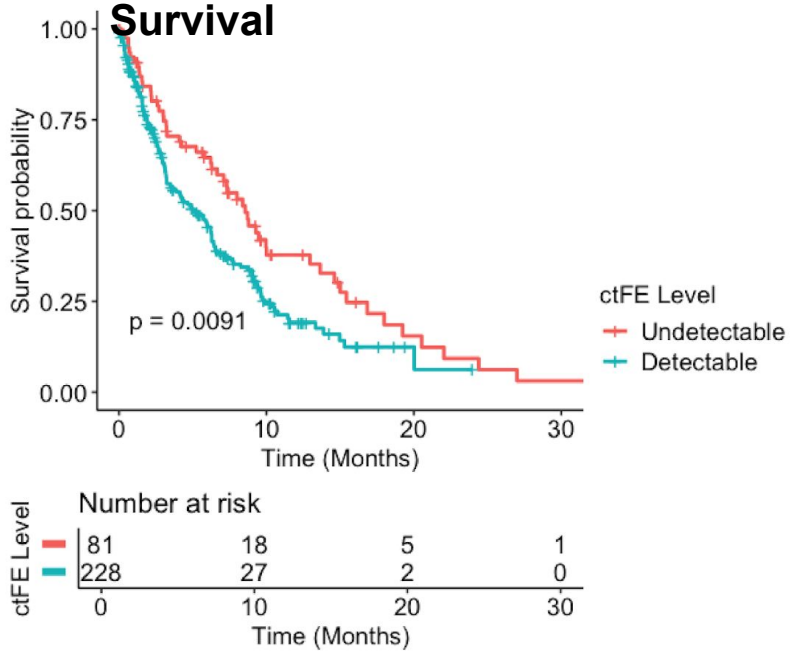
↓

Outcomes Prediction by maxVAF and ctFE

Overall Survival



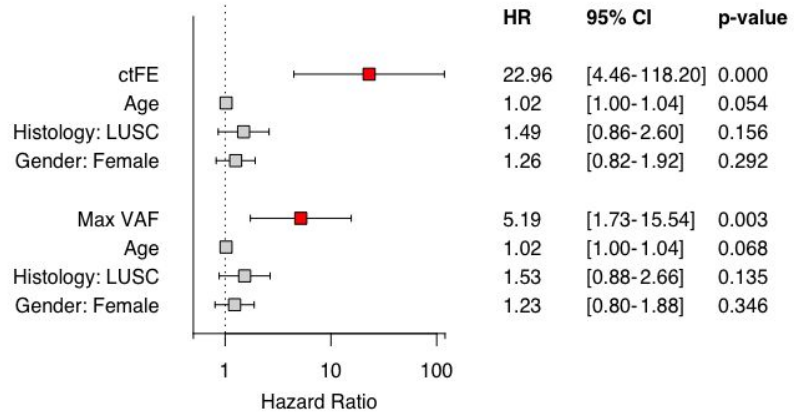
Progression Free Survival



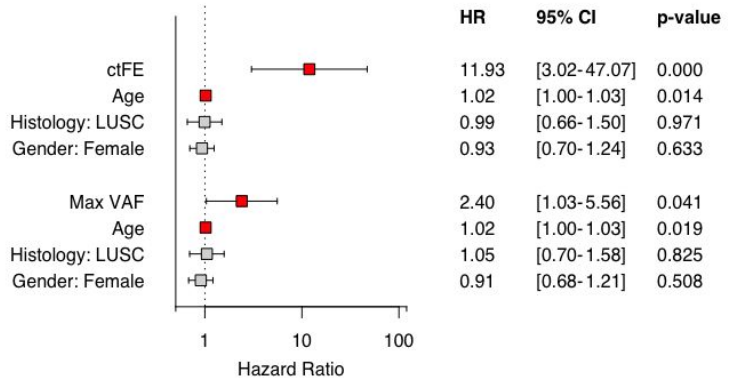
	Undetectable	Detectable	P
OS (m)	25	16.8	0.006
PFS (m)	8.7	5.2	0.009

Pre-RT ctFE is a stronger predictor than maxVAF

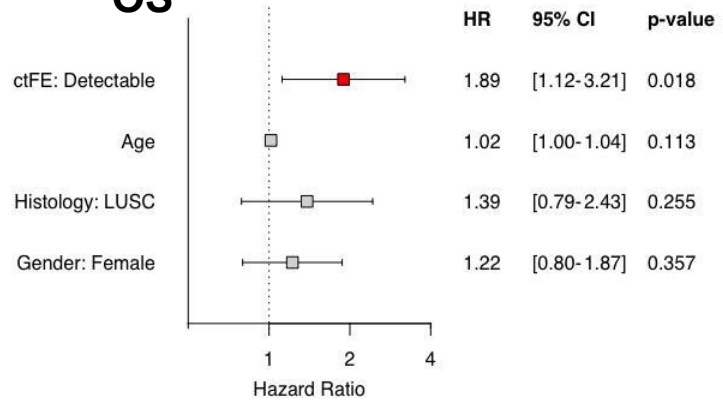
Multivariate Cox Regression: OS by ctFE and Max VAF



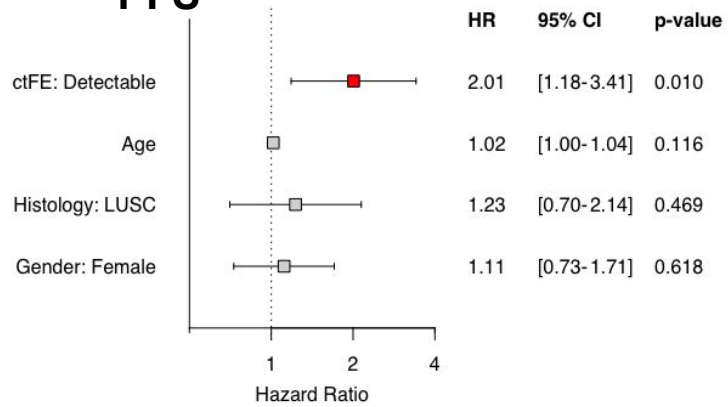
Multivariate Cox Regression: PFS by ctFE and Max VAF



ctFE as a binary variable: OS



ctFE as a binary variable: PFS



Conclusions and Next Steps

- Pre-radiation therapy ctDNA testing predicts outcomes in oligometastatic NSCLC
  - Pre-RT ctDNA Tumor Fraction Estimate (ctFE) is a stronger predictor of survival (OS HR 22.96) than pre-RT ctDNA maximum variant allele frequency (maxVAF; OS HR 5.19)
- Undetectable ctFE preRT was associated with improved OS and PFS, likely reflective of minimal micrometastatic disease burden
- Pre-RT ctFE can be utilized to risk-stratify patients who are likely to benefit from consolidative RT in oligometastatic NSCLC
- Can pre- and on-treatment ctFE guide systemic therapy escalation or de-escalation in metastatic NSCLC?
- Can mid-chemoradiation ctFE assessment guide treatment escalation in locally advanced NSCLC?

Thank You

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