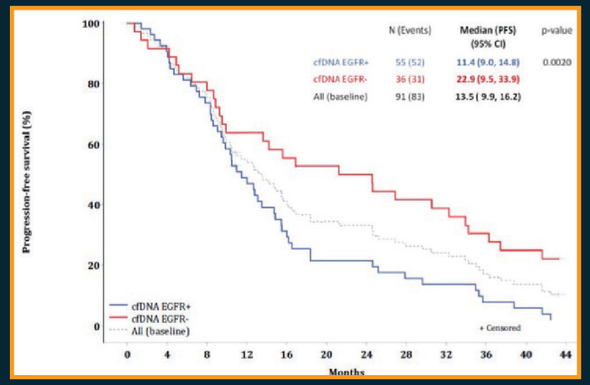
J Thorac Oncol.

(2020)
DOI: https://doi.org/10.1016/j.jtho.2019.11.023

Results from the European Thoracic Oncology Platform (ETOP) BELIEF trial, Evolution and Clinical Impact of EGFR Mutations in Circulating Free DNA in the BELIEF Trial

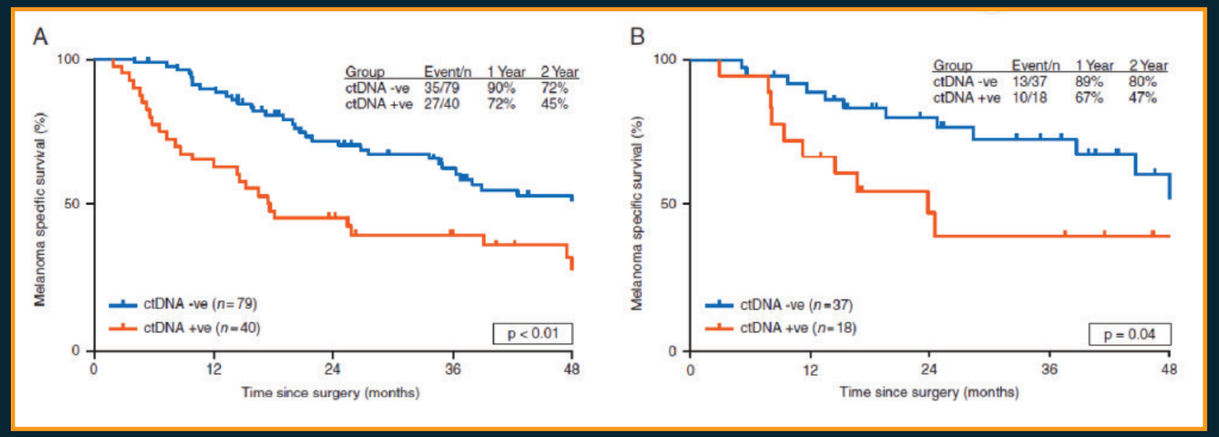


- PFS much longer in baseline EGFR non-shedders
- Overall survival poorer in EGFR shedders than non-shedders at progression

Ann Oncol.

2019 May 1;30(5):815-822, DOI:10.1093/annonc/mdz075

Pre-operative ctDNA predicts survival in high-risk stage III cutaneous melanoma patients



The detection of ctDNA in the discovery and validation cohort was 34% and 33%, respectively, and was associated with larger nodal melanoma deposit, higher number of melanoma-involved LNs, more advanced stage, and high lactate dehydrogenase (LDH) levels.

Detectable ctDNA was significantly associated with worse MSS in the discovery [hazard ratio (HR) 2.1 I P<O.OI] and validation cohort (HR 2.29, P=0.04) and remained significant in a multivariable analysis (HR 1.85, P=0.04). ctDNA further sub-stratified patients with AJCC stage III substage, with increasing significance observed in more advanced stage melanoma.

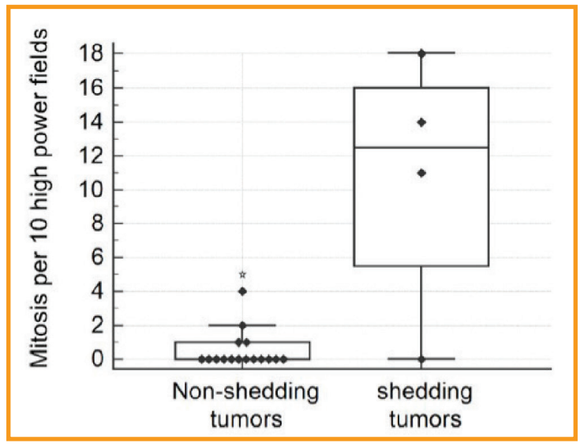
- Detectable pre-operative ctDNA was associated with a higher number of involved lymph nodes and extra-nodal extension
- Pre-operative ctDNA predicted a poor melanoma-specific survival in fully resected stage III melanoma

PLoS ONE

15(3):e0230622.
https://doi.org/10.1371 journal.pone.0230622

Clinicopathological parameters for circulating tumor DNA shedding in surgically resected non-small cell lung cancer with EGFR or KRAS mutation

- ctDNA associated with nodal metastasis, vascular invasion, tumor necrosis and high mitotic rate in resected lung adenocarcinomas



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Liquid Biopsy ctDNA Shedders and Non-Shedders

GETTING PATIENTS ON THE RIGHT TREATMENT, FASTER

LIQUID BIOPSY

With every new cancer technology comes new knowledge. Liquid biopsies provide a view of tumor biology never before known. It is not tissue and plasma discordancy. It is ctDNA shedders and non-shedders. Plasma NGS ctDNA can be very predictive when a targetable driver mutation is identified but it is also very prognostic. The shedding of somatic ctDNA in plasma by a cancer reflects a tumor biology aggressiveness. The 20-30% of advanced cancers not shedding ctDNA have a much better prognosis than cancers shedding ctDNA, with the simple number of ctDNA alterations strongly associated with a much poorer cancer survival.

This prognostic aggressive tumor biology of ctDNA shedding holds true even for earlier-stage cancers. Tissue-only molecular testing only detects 67% of National Comprehensive Cancer Network (NCCN) guideline mutations, missing 33%. Liquid biopsy detects 87% of guideline mutations. Used together, liquid and tissue biopsy provides a more complete picture of the tumor's molecular makeup. Liquid biopsy has the advantage of detecting a multitude of biomarkers which may be an indication of metastasis away from the primary tumor.

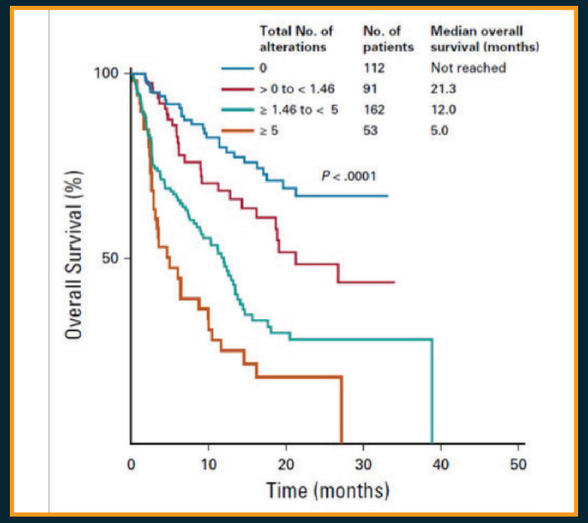
JCO Precis Oncol.

2020 4: 192-201

Total Number of Alterations in Liquid Biopsies Is an Independent Predictor of Survival in Patients With Advanced Cancers

We demonstrate that an increasing number of genomic alterations found on liquid biopsy correlates with progressively worse survival in patients with GI and other advanced cancers, independent of the percent ctDNA or allele fraction.

The total number of alterations found on a liquid biopsy may be a marker of more aggressive tumor biology and has the potential to become a clinically meaningful, tissue-agnostic biomarker for use in advanced cancers, and warrants additional testing in a prospective manner.

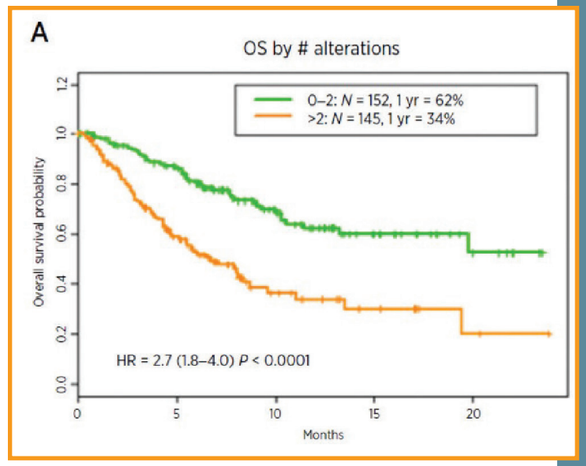


Clin Cancer Res.

2020; DOI: 10.1158/1078-0432.CCR-19-0306

Cell-free Circulating Tumor DNA Variant Allele Frequency Associates with Survival in Metastatic Cancer

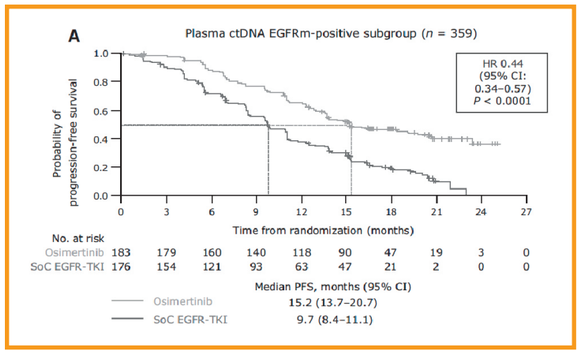
- 298 patients across all cancer types
- 20% non-shedders
- Number of ctDNA prognostic of poorer patient survival

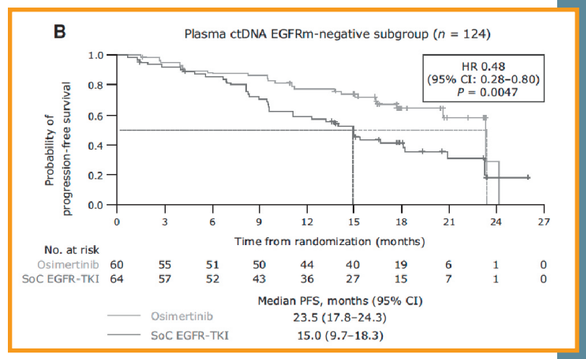


Clin Cancer Res.

2019 Nov 15;25(22):6644-6652, DOI: 10.1158/1078-0432.CCR-19-1126

Tissue and Plasma EGFR Mutation Analysis in the FLAURA Trial: Osimertinib versus Comparator EGFR Tyrosine Kinase Inhibitor as First-Line Treatment in Patients with EGFR-Mutated Advanced Non-Small Cell Lung Cancer





- EGFR ex19 del...21 % non-shedders EGFR ctDNA
- EGFR ex21 L858R...32% non-shedders EGFR ctDNA
- PFS 23 months in non-shedders compared to only 15 months in shedders

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