# Plasma NGS Testing Impact in Early-Stage Cancers

Getting patients on the right treatment, faster



Liquid biopsy plasma next-generation sequencing (NGS) testing continues to be a transformative advance in cancer medicine. Initial clinical utility was in identifying targetable driver oncogenes guiding treatment in advanced cancers. Evolving clinical utility has now demonstrated benefit in early response monitoring with a change in ctDNA/RNA alterations and mutant allele fractions, as well as upon recurrent or progressing disease, to identify treatment-resistant pathways and progressed targetable sub-clonal evolution.

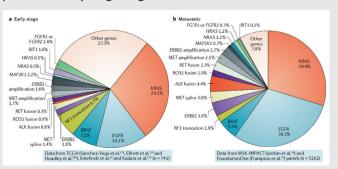
Plasma NGS is now showing impactful clinical utility in early-stage cancers. The dramatic disease-free survival benefit in the ADAURA trial of targeting EGFR mutations in resectable early-stage NSCLC is a powerful proof of principle of the benefit of molecular testing in early-stage cancers. Knowing oncogene mutation and fusion targets, MSI status, and immune therapy resistance mutations is demonstrating therapeutic and clinical outcome impact across the spectrum of early-stage cancers.

# MUTATIONS, FUSIONS, AND MSI-H ARE PRESENT IN EARLY-STAGE CANCERS

Nat Rev Cancer 19, 495-509 (2019)

https://doi.org/10.1038/s41568-019-0179-8 Skoulidis, F., Heymach, J.V. Co-occurring genomic alterations in non-small-cell lung cancer biology and therapy

Mutations and fusions that are both targetable and actionable are present in early-stage lung cancers



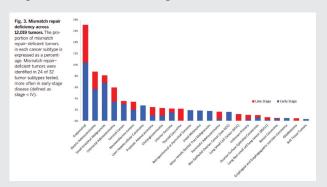
## Science. 2017

Jul 28;357(6349):409-413.

doi: 10.1126/science.aan6733. Epub 2017 Jun 8. PMID: 28596308; PMCID: PMC5576142. Le et al.

Mismatch repair deficiency predicts response of solid tumors to PD-I blockade

Microsatellite Instability-High/MSI-H is more prevalent in earlystage cancers than in late-stage cancers



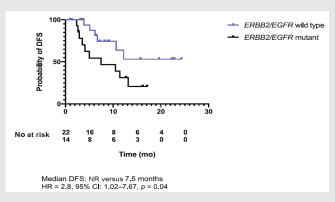
## MOLECULAR FINDINGS IN EARLY-STAGE CANCERS MATTER

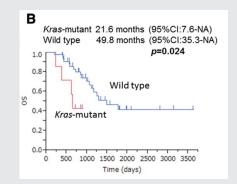
### J Thorac Oncol.

2015 Dec;10(12):1720-5. doi: 10.1097/JTO.00000000000000675. Kosuke Tanaka, Toyoaki Hida, Yuko Oya, et. al.

EGFR Mutation Impact on Definitive Concurrent Chemoradiation Therapy for Inoperable Stage III Adenocarcinoma

KRAS mutations are predictive of very poor overall survival in stage III NSCLC treated with standard CRT





## J Thorac Oncol.

February 01, 2021DOI:https://doi.org/10.1016/j.jtho.2020.12.020 Jessica A. Hellyer et al

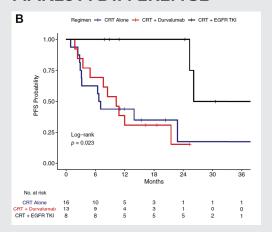
Role of Consolidation Durvalumab in Patients With EGFR- and HER2-Mutant Unresectable Stage III NSCLC

EGFR and ERBB2 mutations are predictive of a lack of benefit from immune therapy consolidation after CRT

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# TREATMENT GUIDED BY MOLECULAR FINDINGS IN EARLY-STAGE CANCERS MAKES A DIFFERENCE

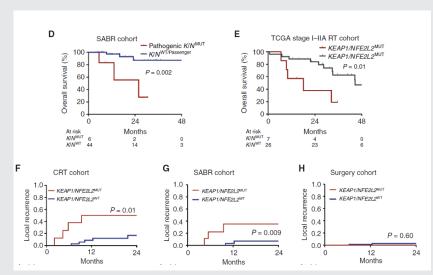


#### J Thorac Oncol. 2021

DOI: https://doi.org/10.1016/j.jtho.2021.01.1628 V.Aredo et al

Durvalumab for Stage III EGFR-Mutated NSCLC After Definitive Chemoradiotherapy

Significant progression-free survival benefit by targeting EGFR after CRT in stage III EGFR mutated NSCLC



### **Cancer Discov**

2020 Dec;10(12):1826-1841. doi: 10.1158/2159-8290.CD-20-0282. Epub 2020 Oct 18. Binkley et al

KEAP1/NFE2L2 Mutations Predict Lung Cancer Radiation Resistance That Can Be Targeted by Glutaminase Inhibition

KEAPI mutations are predictive of very poor local control and OVERALL SURVIVAL when treated with a radiation modality

KEAPI mutations do not impact local control impact in patients treated with surgery

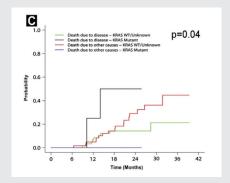
## Clin Transl Radiat Oncol. 2017 Dec; 7: 91-93.

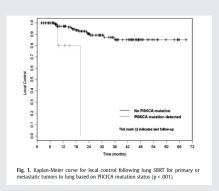
Published online 2017 Nov 4. doi: 10.1016/j.ctro.2017.11.002 Lockney et al

PIK3CA mutation is associated with increased local failure in lung stereotactic body radiation therapy (SBRT)

SBRT in NSCLC with KRAS mutations is predictive of very poor local control and survival

SBRT in NSCLC with PIK3CA mutations has very poor local control





## PRE-SURGICAL ctDNA IS VERY PROGNOSTIC IN EARLY-STAGE LUNG CANCERS

## Nature March 2020

https://doi.org/0.1038/s41586-020-2140-0 Received: 30 July 2019 Integrating genomic features for non-invasive early lung cancer detection

