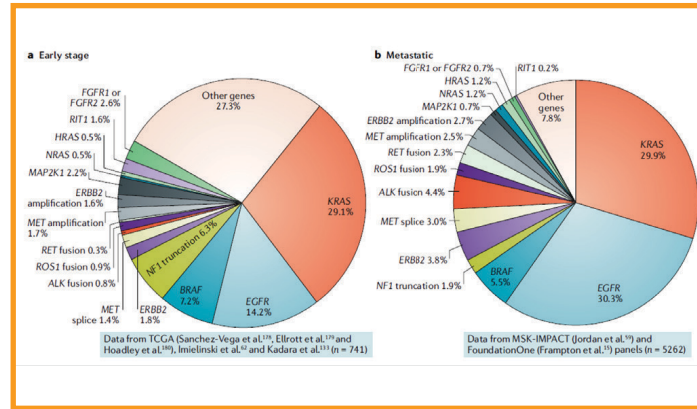


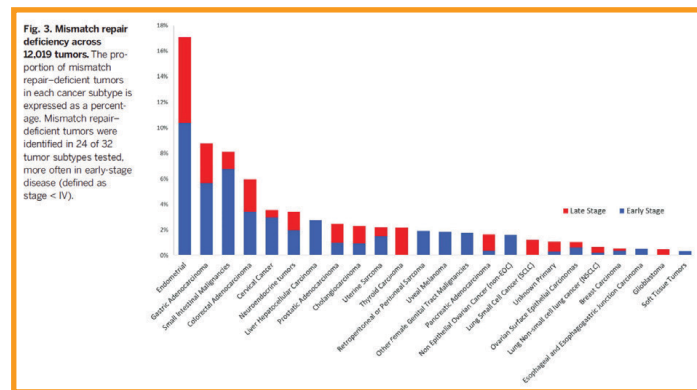
Mutations, Fusions, and MSI-H are **Present** in Early-Stage Cancers

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

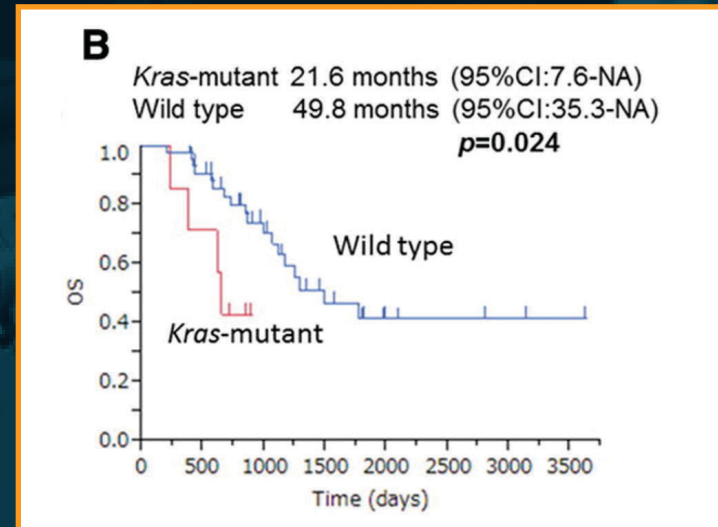
Microsatellite Instability-High/MSI-H is more prevalent in early-stage cancers than in late-stage cancers



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-1 blockade

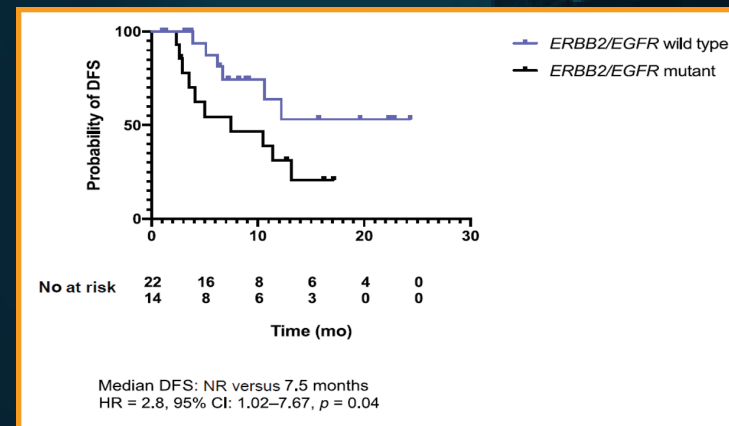
Molecular Findings in Early-Stage Cancers **Matter**

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



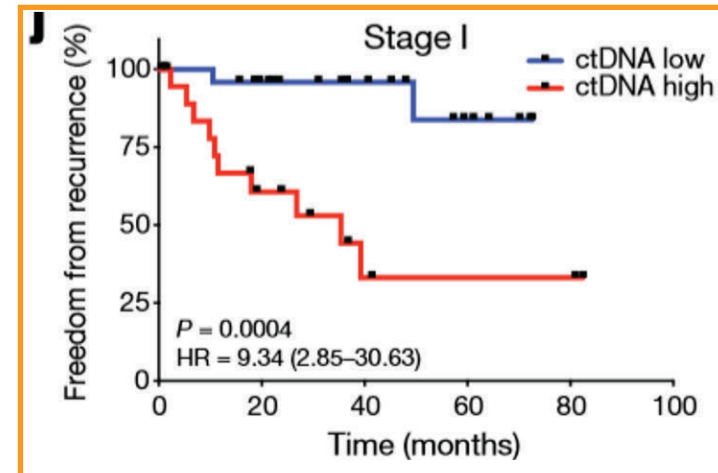
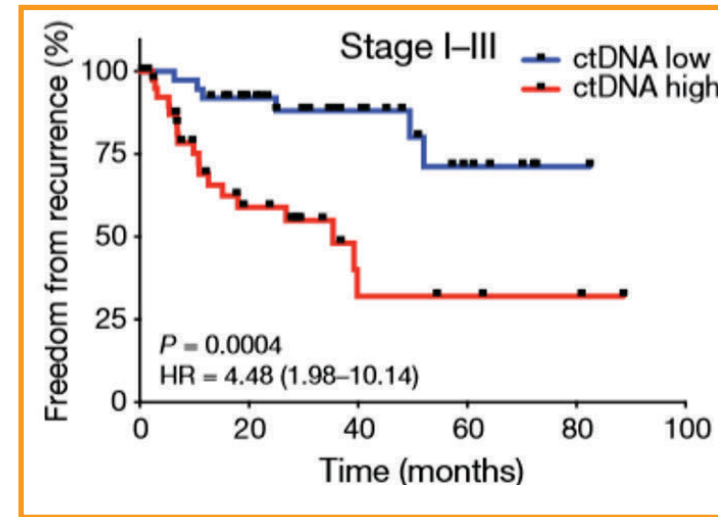
J Thorac Oncol.
 2015 Dec;10(12):1720-5. doi: 10.1097/JTO.0000000000000675.
 Kosuke Tanaka, Toyooki Hida, Yuko Oya, et. al.
 EGFR Mutation Impact on Definitive Chemoradiation Therapy for Inoperable Stage III Adenocarcinoma

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



J Thorac Oncol.
 February 01, 2021 DOI:<https://doi.org/10.1016/j.tho.2020.12.020>
 Jessica A. Hellyer et. al.
 Role of Consolidation Durvalumab in Patients with EGFR- and HER2-Mutant Unresectable Stage III NSCLC

Pre-Surgical ctDNA is Very **Prognostic** in Early-Stage Lung Cancers



Nature March 2020
<https://doi.org/10.1038/s41586-020-2140-0>
 Received: 30 July 2019
 Integrating genomic features for non-invasive early lung cancer detection



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Plasma NGS
 Testing Impact in
 Early-Stage Cancers

GETTING PATIENTS ON THE
 RIGHT TREATMENT, FASTER



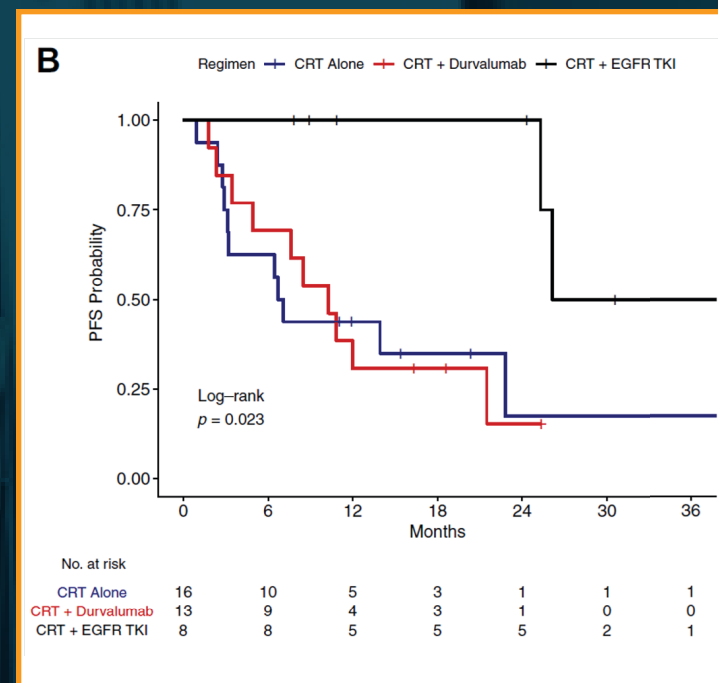
PLASMA NGS

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.

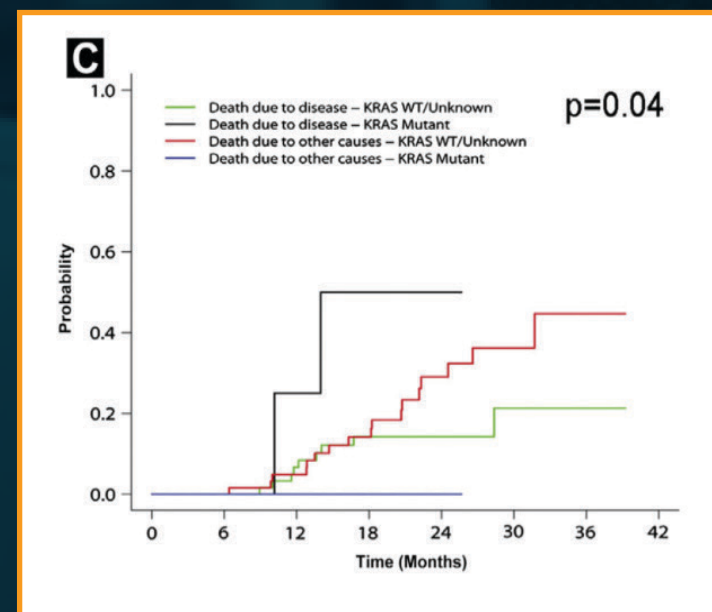
Treatment Guided by Molecular Findings in Early-Stage Cancers Makes a Difference

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



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

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



Clin Trans Radiat Oncol. 2017 Dec; 7: 91-93.
Published online 2017 Nov. 4. doi: [10.1016/j.ctro.2017.11.002](https://doi.org/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 PIK3CA mutations has very poor local control

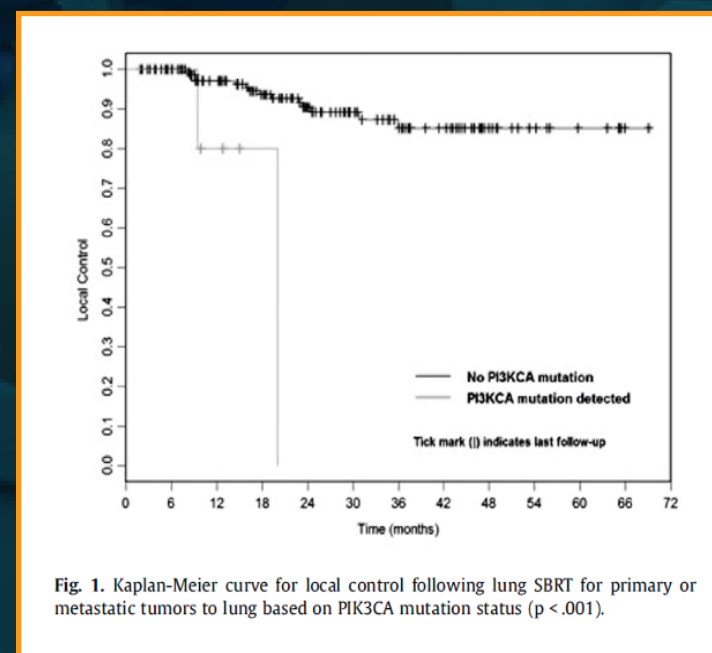
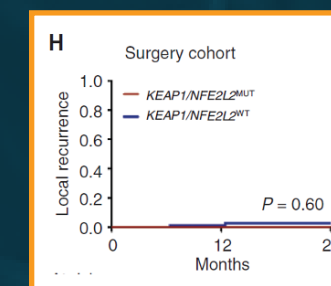
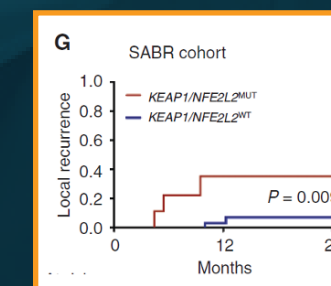
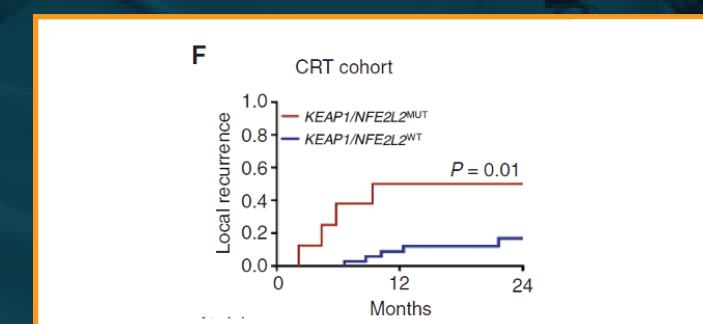
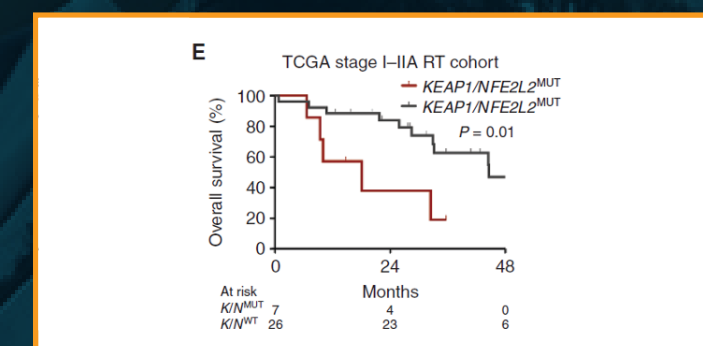
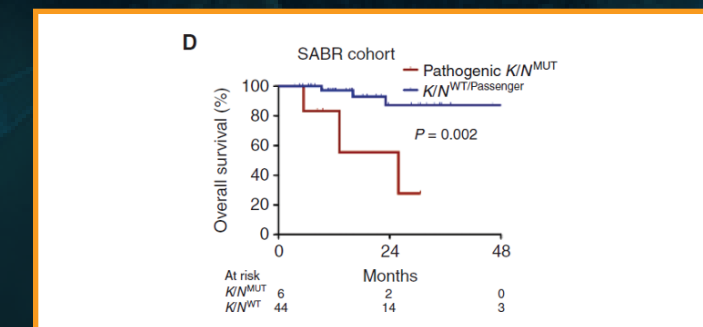


Fig. 1. Kaplan-Meier curve for local control following lung SBRT for primary or metastatic tumors to lung based on PIK3CA mutation status ($p < .001$).

Clin Trans Radiat Oncol. 2017 Dec; 7: 91-93.
Published online 2017 Nov. 4. doi: [10.1016/j.ctro.2017.11.002](https://doi.org/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)

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



Cancer Discov
2020 Dec; 10(12):1826-1841. doi: [10.1158/2159-8290.CD-20-0282](https://doi.org/10.1158/2159-8290.CD-20-0282). Epub 2020 Oct 18.
Binkley et al
KEAPI/NFE2L2 Mutations Predict Lung Cancer Radiation Resistance That Can Be Targeted by Glutaminase Inhibition

