cec oncology

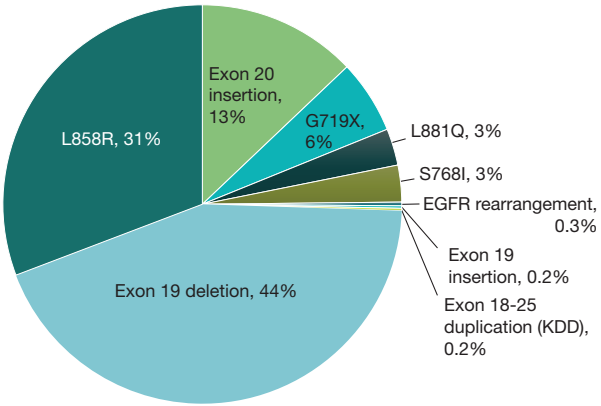
EGFR TESTING IN ADVANCED NSCLC

Strategies for the Oncology Clinician

Disclaimer: The information in this pocket guide is intended as reference material and should not replace clinical judgment or updated recommendations that may supersede those provided here.

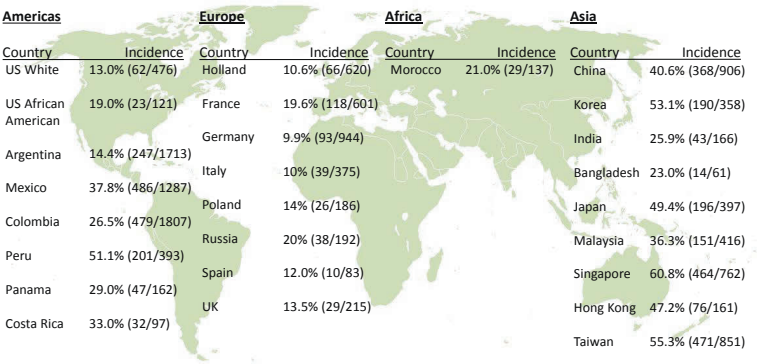
EGFR MUTATION-POSITIVE NSCLC

Mutation Frequencies



Adapted from Costa DB. *Transl Lung Cancer Res*. 2016.

Worldwide Incidence of EGFR Mutations



Americas		Europe		Africa		Asia	
Country	Incidence	Country	Incidence	Country	Incidence	Country	Incidence
US White	13.0% (62/476)	Holland	10.6% (66/620)	Morocco	21.0% (29/137)	China	40.6% (368/906)
US African American	19.0% (23/121)	France	19.6% (118/601)			Korea	53.1% (190/358)
Argentina	14.4% (247/1713)	Germany	9.9% (93/944)			India	25.9% (43/166)
Mexico	37.8% (486/1287)	Italy	10% (39/375)			Bangladesh	23.0% (14/61)
Colombia	26.5% (479/1807)	Poland	14% (26/186)			Japan	49.4% (196/397)
Peru	51.1% (201/393)	Russia	20% (38/192)			Malaysia	36.3% (151/416)
Panama	29.0% (47/162)	Spain	12.0% (10/83)			Singapore	60.8% (464/762)
Costa Rica	33.0% (32/97)	UK	13.5% (29/215)			Hong Kong	47.2% (76/161)
						Taiwan	55.3% (471/851)
						Thailand	53.8% (63/117)
						Vietnam	64.2% (77/120)

Tan DS, et al. *J Clin Oncol.* 2016.

EGFR MUTATION TESTING

Summary of Current Guidelines

Why test?	• To select patients who are likely to benefit from EGFR TKIs
Which tumors to test?	• Adenocarcinoma • Large Cell • NSCLC not otherwise specified (NOS) *Consider EGFR mutation testing for squamous cell carcinoma in never smokers or small biopsy specimens, or mixed histology**
When to test?	• At diagnosis: TNM stage IV disease (consider TNM stage I-III disease) • At recurrence/progression: TNM stage I-III disease, not previously tested; and prior to changing therapy, to determine mechanism of acquired resistance
What to test?	• Primary tumors or metastatic lesions • T790M testing: if tissue biopsy is not feasible, plasma biopsy should be considered. Consider reflex to tissue-based testing if plasma test is negative for T790M mutation.* • Formalin-fixed, paraffin-embedded; or fresh, frozen or alcohol-fixed specimens (decalcifying solutions should be avoided) • Cytologic specimens are acceptable
How fast should test results be available?	• Test results should be made available within 10 business days of receiving the specimen in the laboratory
How to test?	• Must be able to detect mutations in specimens with ≥50% cancer cell content • Testing assay should be able to detect all individual mutations that have been reported with a frequency of >1% of *EGFR*-mutated adenocarcinomas • IHC, FISH, and CISH are not recommended

Sheikine Y, et al. *Clin Lung Cancer.* 2016; *NCCN Guidelines Version 5.2017.

Implementing Guidelines

- Staying current with rapidly evolving practice standards
  - Consider promoting a local physician “champion” to educate colleagues in their region or community
  - Establish formal venues for the communication of biomarker education
- Managing resources and communication between stakeholders
  - Every patient suspected of having advanced-stage disease should, ideally, be evaluated by a multidisciplinary team
  - Each institution should establish a molecular testing policy that covers reflex testing
  - Nurse “navigators” may help streamline patient care and facilitate consistent communication among multidisciplinary teams
  - Electronic health records should be maintained and shared among the multidisciplinary teams
- Optimizing tissue acquisition and processing
  - Tissue acquirers and pathologists should communicate effectively to ensure that tissue obtained for molecular testing is of sufficient quantity and quality
  - Decision on the optimal diagnostic procedure for molecular testing should be individualized and include risk-benefit analysis
  - Ensure timely identification of actionable biomarkers
  - Efficient use of pleural fluid may facilitate molecular testing

Levy BP, et al. *Oncologist*. 2015.

EGFR TKI RESISTANCE

IASLC Definitions

Primary

- Stable disease as best response after EGFR TKI monotherapy

Secondary

- Partial response or stable disease for more than 6 months with an enlarging extracranial target lesion(s)
- Documented resistance mechanism (eg, T790M mutation, MET amplification, or other emerging mechanism relevant to the TKI)

Tan DS, et al. *J Thorac Oncol.* 2016.

LIQUID BIOPSY

Genotyping Circulating Tumor DNA

- Tumor cells release small fragments of cell-free plasma DNA (cfDNA) into circulation by multiple mechanisms:
  - Secretion
  - Apoptosis
  - Necrosis
- cfDNA includes normal and circulating tumor DNA (ctDNA)
  - ctDNA size: Average of 180-200 base pairs
  - Half-life: ~2 hours

Applications

- Early disease detection
- Assessment of molecular heterogeneity of overall disease
- Monitoring of tumor dynamics
- Identification of genetic determinants for targeted therapy
- Evaluation of early treatment response
- Monitoring of minimal residual disease
- Assessment of evolution of resistance in real time

Diaz LA Jr., Bardelli A. *J Clin Oncol*. 2014.

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