Latest innovations in NSCLC management: Introduction

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Gefitinib or Carboplatin–Paclitaxel in Pulmonary Adenocarcinoma

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CONCLUSIONS
Gefitinib is superior to carboplatin–paclitaxel as an initial treatment for pulmonary adenocarcinoma among nonsmokers or former light smokers in East Asia. The presence in the tumor of a mutation of the EGFR gene is a strong predictor of a better outcome with gefitinib. (ClinicalTrials.gov number, NCT00322452.)

EGFR M+: Post-progression treatment after EGFR TKI’s

**Treatment of sensitive clones with activating EGFR mutation**
- Reversible EGFR-TKI

**Treatment of resistant clones (T790M, c-met amplification, other)**
- Chemotherapy

**Treatment of re-emerging sensitive clones with activating EGFR mutation**
- Same Reversible EGFR-TKI Comb or Seq
  - ICARUS (Gefitinib)

**Reversible EGFR-TKI**

**Chemotherapy**

**Different Reversible EGFR-TKI Comb or Seq**

**Irreversible EGFR-TKI**
MET Pathways

HGF/SF

α

β

Met

Plasma membrane

Grb2

Sos

Gab1

Shp2

Crk

C3G

Rap1

PI3K

Akt/PKB

ERK/MAPK

N-WASP

Arp2/3

Cdc42

Cadherins

pRB

Cdk6

p27

uPA

MMPs

Fibronectin

Paxillin

FAK

Integrins

Bad

Caspase-9

N-WASP

Arp2/3

Cdc42

Cadherins

pRB

Cdk6

p27

uPA

MMPs

Fibronectin

Paxillin

FAK

Integrins

Bad

Caspase-9

- Cell polarity
- Actin cytoskeleton
- Motility

- Proliferation
- Cell-cycle progression

- Cell junction
- Migration
- Invasion

- Survival

- Pak

- Ets1

- AP1
The PI3K/AKT/mTOR Pathway Plays a Key Role in Cellular Metabolism, Proliferation, and Survival

PI3Ks activated by RTKs, GPCR, or RAS

PI3K signaling negatively regulated by PTEN

AKT activates downstream effectors, including mTORC1, FOXO, GSK3 and BAD

Key role in multiple cellular processes

FOXO, forkhead transcription factors; GPCR, G protein-coupled receptor; GSK3, glycogen synthase kinase-3; mTOR, mammalian target of rapamycin; mTORC1, mTOR complex 1; PI3K, phosphatidylinositol 3-kinase; PIP_2, phosphatidylinositol-3,4-bisphosphate; PIP_3, phosphatidylinositol-3,4,5-trisphosphate; mTORC2, phosphatidylinositol-3,4,5-trisphosphate; RTK, receptor tyrosine kinase.

VEGF signaling

Ligand binding

Dimeric VEGF ligand

Receptor dimerization
Phosphorylation

Adapter molecule binding

Downstream signaling events

Nucleus
clinical practice guidelines

Metastatic non-small-cell lung cancer (NSCLC): ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up†

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