Epidermal growth factor receptor tyrosine kinase inhibitor

- Metabolic Profiling of Canertinib: A Comprehensive Cross-Species Investigation Using Advanced UPLC-MS/MS and LC-Orbitrap-HRMS Techniques
- Challenges and resistance mechanisms to EGFR targeted therapies in head and neck cancers and breast cancer: Insights into RTK dependent and independent mechanisms
- Correlation between treatments and outcomes of patients with EGFR-mutated non-small-cell lung cancer that transitioned into small-cell lung cancer: an international retrospective study
- EGFR TKIs suppress MUC1 glycosylation through the PI3K/AKT/SP1/C1GALT1 pathway to enhance TnMUC1 CAR-T efficacy in EGFR-mutant NSCLC
- Targeting both wild-type EGFR and its drug-resistant mutants with erlotinib-aptamer conjugates
- Prevalence of osimertinib-induced cardiotoxicity in non-small cell lung cancer patients: a systematic review and meta-analysis
- Design, synthesis, and evaluation of 1,3,4-oxadiazole-based EGFR inhibitors
- Molecular dynamics simulations reveal a strong binding capacity of colossolactone H to the EGFR inactive conformation

A substance that blocks the activity of a protein called epidermal growth factor receptor (EGFR).

A tyrosine kinase inhibitor (TKI) is a pharmaceutical drug that inhibits tyrosine kinases.

The discovery of Epidermal Growth Factor Receptor (EGFR)-activating mutations and Anaplastic Lymphoma Kinase (ALK) rearrangements in patients with non-Small-cell lung cancer has allowed for the introduction of small-molecule tyrosine kinase inhibitors to the treatment of advanced-stage patients.

EGFR is found on the surface of some normal cells and is involved in cell growth. It may also be found at high levels on some types of cancer cells, which causes these cells to grow and divide. Blocking EGFR may keep cancer cells from growing. Some EGFR inhibitors are used to treat cancer. Also called EGFR tyrosine kinase inhibitor, epidermal growth factor receptor inhibitor, and epidermal growth factor receptor tyrosine kinase inhibitor.

Tyrosine kinases are enzymes responsible for the activation of many proteins by signal transduction cascades. The proteins are activated by adding a phosphate group to the protein (phosphorylation), a step that TKIs inhibit. TKIs are typically used as anticancer drugs. For example, they have substantially improved outcomes in chronic myelogenous leukemia.

They are also called tyrphostins, the short name for “tyrosine phosphorylation inhibitor”, originally coined in a 1988 publication,which was the first description of compounds inhibiting the catalytic activity of the epidermal growth factor receptor (EGFR).

The 1988 study was the first demonstration of a systematic search and discovery of small-molecular-weight inhibitors of tyrosine phosphorylation, which do not inhibit protein kinases that phosphorylate serine or threonine residues and can discriminate between the kinase domains of the EGFR and that of the insulin receptor. It was further shown that in spite of the conservation of the tyrosine-kinase domains one can design and synthesize tyrphostins that discriminate between even closely related protein tyrosine kinases such as EGFR and its close relative HER2.

Brain-to-tumor interface (BTI) features and volume of peritumoral edema (VPE) were associated with the EGFR mutation status, response to EGFR-TKI and T790M mutation status in NSCLC patients with BM [1].

EGFR and ALK tyrosine kinase inhibitors (TKIs) provide significantly superior systemic response rates and progression-free survival compared to standard chemotherapy in the molecularly defined NSCLC subpopulations. An apparent intracranial activity of new generation TKIs triggered the discussion on their role in brain metastases in lieu of local therapies. The aim of a review of Wrona et al. was to summarize the current therapeutic landscape of brain metastases management in NSCLC, with a particular focus on EGFR-mutated and ALK-rearranged NSCLC subtypes [2].

Tyrosine kinase inhibitor for non-Small-cell lung cancer intracranial metastases treatment

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Case reports

A 57-year-old man presented with seizures. Until the seizure onset, he had been treated for thyroid cancer and its metastases to the thoracic vertebral body with the multi-receptor tyrosine kinase inhibitor (RTK) lenvatinib for 4 years. MRI revealed a slightly high intensity lesion in the left frontal base area on T2-weighted or fluid-attenuated inversion recovery (FLAIR) images, and the lesion showed only faint enhancement on T1-weighted images after gadolinium administration. Total resection was performed and the histopathological diagnosis was glioblastoma. However, grade IV histology was observed in only a limited area, and the majority of the specimen showed lower grade histology with moderate vascularization that lacked microvascular proliferation.

Lenvatinib, which is antiangiogenic, might have affected the radiological characteristics, as well as the pathology of the tumor. Brain tumors arising during treatment with RTKs for other cancers could show atypical imaging findings [3].

1)
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2)
Wrona A, Dziadziuszko R, Jassem J. Management of brain metastases in non-small cell lung cancer in the era of tyrosine kinase inhibitors. Cancer Treat Rev. 2018 Oct 21;71:59-67. doi: 10.1016/j.ctrv.2018.10.011. [Epub ahead of print] Review. PubMed PMID: 30366200.
3)
Arai N, Sasaki H, Tamura R, Obara K, Yoshida K. Unusual magnetic resonance imaging findings of a glioblastoma arising during treatment with lenvatinib for thyroid cancer. World Neurosurg. 2017 Aug

10. pii: S1878-8750(17)31314-1. doi: 10.1016/j.wneu.2017.08.017. [Epub ahead of print] PubMed PMID: 28804045.