T790M

T790M, also known as Thr790Met, is a gatekeeper mutation of the epidermal growth factor receptor (EGFR). The mutation substitutes a threonine (T) with a methionine (M) at position 790 of exon 20, affecting the ATP binding pocket of the EGFR kinase domain. Threonine is a small polar amino acid; methionine is a more considerable nonpolar amino acid.

Over 50% of acquired resistance to EGFR tyrosine kinase inhibitors (TKI) is caused by a mutation in the ATP binding pocket of the EGFR kinase domain involving the substitution of a slight polar threonine residue with a sizeable nonpolar methionine residue, T790M.

In November 2015, the US FDA granted accelerated approval to osimertinib (Tagrisso) for the treatment of patients with metastatic epidermal growth factor receptor (EGFR) T790M mutation-positive non-Small-cell lung cancer (NSCLC), as detected by an FDA-approved test, which progressed on or after EGFR TKI therapy.

T790M as a common mutation to cause drug-resistance in EGFR-TKIs treated non-Small-cell lung cancer (NSCLC) patients may be a favorable prognostic factor on OS and PFS both. Further studies are necessary to demonstrate the prognostic role of secondary T790M in NSCLC patients [1)].

1)
Ma G, Zhang J, Jiang H, Zhang N, Yin L, Li W, Zhou Q. Epidermal growth factor receptor T790M mutation as a prognostic factor in EGFR-mutant non-small cell lung cancer patients that acquired resistance to EGFR tyrosine kinase inhibitors. Oncotarget. 2017 Jul 29. doi: 10.18632/oncotarget.19681. [Epub ahead of print] PubMed PMID: 28778092.