Pan-FLT3/Pan-BTK Multi-kinase Inhibitor CG-806

National Cancer Institute

Source

National Cancer Institute. Pan-FLT3/Pan-BTK Multi-kinase Inhibitor CG-806. NCI Thesaurus. Code C162573.

An orally bioavailable reversible, pan-inhibitor of both FMS-like tyrosine kinase 3 (FLT3; CD135; STK1; FLK2) and Bruton's tyrosine kinase (BTK; Bruton agammaglobulinemia tyrosine kinase), with potential antineoplastic activity. Upon oral administration, the pan-FLT3/pan-BTK multi-kinase inhibitor CG-806 targets, non-covalently binds to and inhibits the activity of both FLT3, including both wild-type (WT) FLT3 and FLT3-ITD (internal tandem duplications), tyrosine kinase domain (FLT3-TKD), and gatekeeper (FLT3-F691L) mutant forms, and BTK, including both the WT and its C481S mutant (BTK-C481S) form. This inhibits both uncontrolled FLT3-mediated and B-cell antigen receptor (BCR)-mediated signaling, respectively. This results in the inhibition of proliferation in tumor cells overexpressing FLT3 and BTK. In addition, CG-806 also inhibits, to a lesser degree, other oncogenic kinases, such as MET, RET, discoidin domain-containing receptor 2 (DDR2), Aurora kinase A, and interleukin-2-inducible T-cell kinase (ITK). FLT3, a class III receptor tyrosine kinase (RTK), is overexpressed or mutated in most B-lineage neoplasms and in acute myeloid leukemias (AMLs), and plays a key role in tumor cell proliferation. BTK, a member of the Src-related BTK/Tec family of cytoplasmic tyrosine kinases essential to BCR signaling, is overexpressed or mutated in B-cell malignancies; it plays an important role in the development, activation, signaling, proliferation and survival of B-lymphocytes.