Nilotinib is a second-generation phenylamino pyridine tyrosine kinase inhibitor that is clinically used to treat Bcr-Abl-positive chronic myelogenous leukemia (CML). Nilotinib is an ATP-competitive inhibitor of Abl, c-Kit, and PDGFR that exhibits anticancer chemotherapeutic, anti-fibrotic, anti-allergic, and anti-inflammatory activities. In cellular and animal models of hepatocellular carcinoma, nilotinib increases activation of AMPK and inhibits protein phosphatase 2A (PP2A), inducing autophagy in vitro and inhibiting tumor xenografts growth in vivo. In hepatic stellate cells, nilotinib decreases expression of histone deacetylases 1, 2, and 4 (HDAC1/2/4), increasing apoptotic cell death. In animal models of allergic reaction and inflammation, nilotinib inhibits expression of TNF-α and prevents mast cell histamine release, decreasing paw edema and preventing systemic anaphylaxis.

References


