Vecabrutinib

National Cancer Institute

Source

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An orally available second-generation, reversible inhibitor of Bruton's tyrosine kinase (BTK; Bruton agammaglobulinemia tyrosine kinase), with potential antineoplastic activity. Upon administration, vecabrutinib non-covalently binds to and inhibits the activity of both wild-type and the C481S mutated form of BTK, a resistance mutation in the BTK active site in which cysteine is substituted for serine at residue 481. This prevents the activation of the B-cell antigen receptor (BCR) signaling pathway and BTK-mediated activation of downstream survival pathways. This leads to an inhibition of the growth of malignant B-cells that overexpress BTK. Compared to other BTK inhibitors, SNS-062 does not require interaction with the BTK C481 site and inhibits the proliferation of cells harboring the BTK C481S mutation. Other irreversible BTK inhibitors covalently bind to the C481 site to inhibit BTK's activity; the C481S mutation prevents that binding. BTK, a member of the Src-related BTK/Tec family of cytoplasmic tyrosine kinases, is overexpressed in B-cell malignancies; it plays an important role in the development, activation, signaling, proliferation and survival of B-lymphocytes.