ALK Inhibitors

Tyrosine kinases such as anaplastic lymphoma kinase (ALK) are becoming major targets in the development of new chemotherapeutics and anti-inflammatories. ALK plays an important role in the development of the brain; it also drives the progression of several cancers, including anaplastic large-cell lymphoma, neuroblastoma, and non-small cell lung cancer.

When the ALK gene is mutated or fused with other genes, it often produces extra or abberent proteins. Overactive ALK stimulates JAK/STAT, PI3K/Akt, and ERK, promoting unregulated cell cycle progression, survival, and proliferation[1]. Targeting ALK prevents these downstream effects, limiting cancer cell signaling and tumor growth.

Several ALK inhibitors also inhibit IGF-1R, an additional target in preventing growth of cancer cells[2-4]. Products that target both of these kinases include **LDK378 (L1340)**, **AZD3463 (A9600)**, and **GSK-1838705A (G7540)**.

References:
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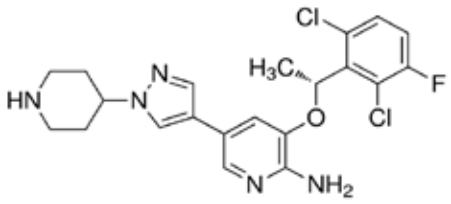

Crizotinib (C6935) is a well-characterized ALK inhibitor that also suppresses activity of ROS1 and c-MET. In cancer cells, this compound upregulates expression of pro-apoptotic BIM and downregulates expression of anti-apoptotic survivin to induce apoptosis[5].

CH5424802 (C2900) targets both wild-type and mutant L1196M ALK, inducing regression of non-small cell lung cancer metastasis in the brain[6].

Doramapimod (D5868) is an inhibitor of ALK, JNK, and p38 MAPK that suppresses pulmonary inflammation in vivo and in vitro[7].

ASP-3026 (A7400) is an inhibitor of ALK that lowers tumor burden in lung and intrapleural tumor models[8].