Product Datasheet

Voxtalisib

Catalog No. **BP-02151** · CAS **934493-76-2** · Form **free base** · Physical state **other** · Color **Light brown to brown** · Version **1.0** · Revision **2026-09-03**

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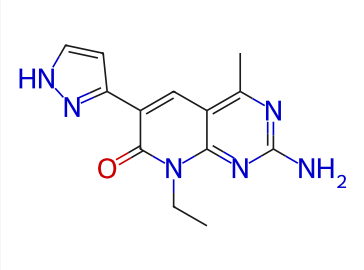
Target	Research area
PI3K; mTOR	**Cancer**

Molecular formula	$C_{13}H_{14}N_6O$
Molecular weight	**270.2899**

STRUCTURE



DESCRIPTION

Voxtalisib (XL765) is a potent PI3K inhibitor, which has a similar activity toward class I PI3K (IC50s=39, 113, 9 and 43?nM for p110α, p110β, p110γ and p110δ, respectively), also inhibits DNA-PK (IC50=150?nM) and mTOR (IC50=157?nM). Voxtalisib (XL765) inhibits mTORC1 and mTORC2 with IC50s of 160 and 910 nM, respectively.

BIOLOGICAL ACTIVITY

In Vitro

Voxtalisib (XL765) displays potent inhibitory activity against class I PI3K isoforms p110α, p110β, p110δ, and p120γ, with IC50s of 39, 110, 43, and 9 nM, respectively. The IC50 value for inhibition of PI3Kα by Voxtalisib is determined at various concentrations of ATP, revealing Voxtalisib be an ATP-competitive inhibitor with an equilibrium inhibition constant (Ki) value of 13 nM. Voxtalisib also inhibits mTOR (IC50s of 160 and 910 nM for mTORC1 and mTORC2, respectively) in an immune-complex kinase assay and the PI3K-related kinase DNA-PK (IC50 value of 150 nM). In contrast, Voxtalisib (XL765) has relatively weak inhibitory activity toward the class III PI3K vacuolar sorting protein 34 (VPS34; IC50 value of ~9.1 μM). Consistent with its inhibitory activity against purified PI3K proteins, SAR245409 inhibits EGF-induced PIP3 production in PC-3 and MCF7 cells with IC50s of 290 and 170 nM, respectively. The ability of Voxtalisib to inhibit phosphorylation of key signaling proteins downstream of PI3K is examined by assessing its effects on EGF-stimulated phosphorylation of AKT and on nonstimulated phosphorylation of S6 in PC-3 cells by cell-based ELISA. Voxtalisib inhibits these activities with IC50s of 250 and 120 nM, respectively. In MCF7 and PC-3 cells, Voxtalisib inhibits proliferation (monitored by BrdUrd incorporation) with IC50s of 1,070 and 1,840 nM, respectively. To further characterize the effects of Voxtalisib on tumor cell growth, an assay monitoring the anchorage-independent growth of PC-3 and MCF7 cells in soft agar over a 14-day period is used. SAR245409 inhibits colony growth with an IC50 value of 270 nM in PC-3 cells and 230 nM in MCF7 cells.

In Vivo

Oral administration of Voxtalisib (XL765) causes a dose-dependent decrease of phosphorylation of AKT, p70S6K, and S6 in the tumors, reaching a maximum of 84% inhibition of S6 phosphorylation at 30 mg/kg at 4 hours. The

dose-response relationships derive from the 4 hours time point predict 50% inhibition of AKT, p70S6K, and S6 phosphorylation to occur at doses of 19 mg/kg (pAKTT308 and pAKTS473), 51 mg/kg (p-p70S6K), and 18 mg/kg (pS6). Inhibition of AKT, p70S6K, and S6 phosphorylation in MCF7 tumors following a 30 mg/kg dose of Voxtalisib is maximal at 4 hours, reaching 61% to 84%; however, the level of inhibition decreases to 0% to 42% by 24 hours, and minimal or no inhibition is evident by 48 hours. Following a 100 mg/kg dose of Voxtalisib, inhibition is also maximal at 4 hours (52%-75%).

SOLUBILITY

Soluble in DMSO

REFERENCES

[1].Garcia-Echeverria C, et al. Drug discovery approaches targeting the PI3K/Akt pathway in cancer. Oncogene. 2008 Sep 18;27(41):5511-26.

[2]. Yu P, et al. Characterization of the activity of the PI3K/mTOR inhibitor XL765 (SAR245409) in tumor models with diverse genetic alterations affecting the PI3K pathway. Mol Cancer Ther. 2014 May;13(5):1078-91.