

Product Data Sheet

Product Name: Ulixertinib (hydrochloride)

Cat. No.: GC11422

Chemical Properties

Cas. No. 1956366-10-1

Chemical Name 4-[5-chloro-2-[(1-methylethyl)amino]-4-pyridinyl]-N-[(1S)-1-(3-chlorophenyl)-2-hydroxyethyl]-1H-pyrrole-2-carboxamide, monohydrochloride

SMILES CC(C)NC1=CC(C2=CNC(C(N[C@H](CO)C3=CC(Cl)=CC=C3)=O)=C2)=C(Cl)C=N1.Cl

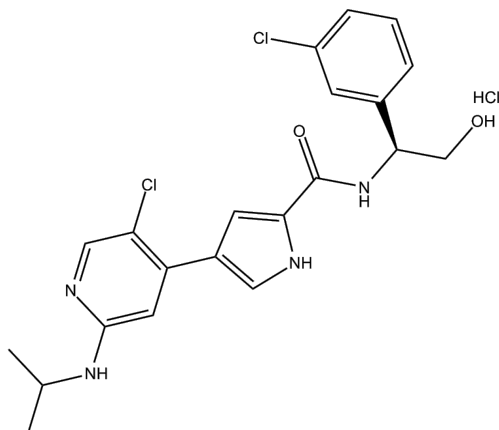
Formula $C_{21}H_{22}Cl_2N_4O_2 \cdot HCl$ M.Wt 469.8

Solubility ≤ 1 mg/ml in ethanol; 30mg/ml in DMSO; 30mg/ml in dimethyl formamide
Storage Store at $-20^{\circ}C$

General tips For obtaining a higher solubility, please warm the tube at $37^{\circ}C$ and shake it in the ultrasonic bath for a while. Stock solution can be stored below $-20^{\circ}C$ for several months.

Shipping Condition Evaluation sample solution: ship with blue ice. All other available size: ship with RT, or blue ice upon request.

Structure



Background

Ulixertinib, also named as BVD-523, is a novel and reversible inhibitor of ERK1/2. Ulixertinib potently and selectively inhibits the activity of ERK1 and ERK2 kinases in a reversible, ATP-competitive fashion [1].

Caution: Product has not been fully validated for medical applications. For research use only.

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The Ras-dependent extracellular signal-regulated kinase (ERK)1/2 mitogen-activated protein (MAP) kinase pathway plays a central role in cell proliferation control. In normal cells, sustained activation of ERK1/ERK2 is necessary for G1- to S-phase progression and is associated with induction of positive regulators of the cell cycle and inactivation of antiproliferative genes. The RAF-MEK-ERK1/2 signal pathway plays a dominant role in promoting cell survival [2].

In vitro: In two lymphoma cell lines (SUDHL-10 and Raji), treatment with ulixertinib significantly reduced the expression of ERK1/2 phosphorylation in a dose-dependent manner. Treatment with 0.4 nM ulixertinib decreased the percentage of G2-M phase cells in the SUDHL-10 cells. In the Raji cells, treated with ulixertinib at 0.4 and 1.0 nM increased the percentage of G0-G1 phase cells and decreased S phase cells [1]. Treatment of ulixertinib at the dose of 0.1, 0.4 and 1.0 nM for 48 h dose-dependently increased the number of early apoptotic SUDHL- 10 and Raji cells [1]. In SUDHL-10 and Raji cells, ulixertinib reduced mRNA and protein expression of VEGFR2 and Bcl-2 genes and increased the expression of Bax and caspase-3 genes [1].

In vivo: BVD-523 inhibited tumor growth in BRAF-mutant melanoma and colorectal xenografts as well as in KRAS-mutant colorectal and pancreatic models. BVD-523 treatment in combination with dabrafenib inhibited tumor growth in a BRAF-mutant melanoma model [3]. Single-agent BVD-523 inhibited the growth of a patient-derived tumor xenograft harboring cross-resistance to dabrafenib, trametinib, and the combination treatment following clinical progression on a MEK inhibitor [3].

Clinical trials: In patients (pts) with advanced solid tumors, BVD-523 (ulixertinib) achieved pharmacologically relevant exposure and manageable tolerability at its MTD of 600 mg twice a day [4].

References:

- [1] Ding W J, Tao W P, Zeng T, et al. Selective ERK inhibitor ulixertinib inhibits proliferation and induces apoptosis in lymphoma cell lines[J]. INTERNATIONAL JOURNAL OF CLINICAL AND EXPERIMENTAL MEDICINE, 2016, 9(6): 10955-10962.
- [2] Meloche S, Pouyssegur J. The ERK1/2 mitogen-activated protein kinase pathway as a master regulator of the G1-to S-phase transition[J]. Oncogene, 2007, 26(22): 3227-3239.
- [3] Germann U, Furey B, Roix J, et al. The selective ERK inhibitor BVD-523 is active in models of MAPK pathway-dependent cancers, including those with intrinsic and acquired drug resistance[J].

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2015.

[4] Infante J R, Janku F, Tolcher A W, et al. Dose escalation stage of a first-in-class phase I study of the novel oral ERK 1/2 kinase inhibitor BVD-523 (ulixertinib) in patients with advanced solid tumors[J]. 2015

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