Rigosertib sodium

Cat. No.: HY-12037

CAS No.: 592542-60-4

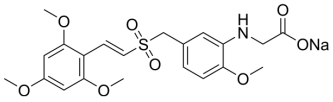
Molecular Formula: $C_{21}H_{24}NNaO_8S$

Molecular Weight: 473.47

Target: Polo-like Kinase (PLK); PI3K; Apoptosis

Pathway: Cell Cycle/DNA Damage; PI3K/Akt/mTOR; Apoptosis

Storage: 4°C, stored under nitrogen
* In solvent : -80°C, 6 months; -20°C, 1 month (stored under nitrogen)



SOLVENT & SOLUBILITY

In Vitro

DMSO : 150 mg/mL (316.81 mM; Need ultrasonic)
H_2O : ≥ 52 mg/mL (109.83 mM)
* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	2.1121 mL	10.5603 mL	21.1207 mL
5 mM	0.4224 mL	2.1121 mL	4.2241 mL
10 mM	0.2112 mL	1.0560 mL	2.1121 mL

Please refer to the solubility information to select the appropriate solvent.

In Vivo

1. Add each solvent one by one: PBS
   Solubility: 50 mg/mL (105.60 mM); Clear solution; Need ultrasonic
2. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: ≥ 5.25 mg/mL (11.09 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 5.25 mg/mL (11.09 mM); Clear solution
4. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 5.25 mg/mL (11.09 mM); Clear solution
5. Add each solvent one by one: 5% DMSO >> 40% PEG300 >> 5% Tween-80 >> 50% saline
   Solubility: ≥ 2.5 mg/mL (5.28 mM); Suspended solution
6. Add each solvent one by one: 5% DMSO >> 95% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.5 mg/mL (5.28 mM); Clear solution

BIOLOGICAL ACTIVITY

Description	Rigosertib sodium (ON-01910 sodium) is a multi-kinase inhibitor and a selective anti-cancer agent, which induces apoptosis by inhibition the PI3K/Akt pathway, promotes the phosphorylation of histone H2AX and induces G2/M arrest in cell cycle[1][2]. Rigosertib sodium is a selective and non-ATP-competitive inhibitor of PLK1 with an IC_{50} of 9 nM[3].

IC_{50} & Target			
PLK1 9 nM (IC_{50})	PLK2 260 nM (IC_{50})	PDGFR 18 nM (IC_{50})	Src 155 nM (IC_{50})
BCR-ABL 32 nM (IC_{50})	Cdk1 260 nM (IC_{50})	Flt1 42 nM (IC_{50})	Fyn 182 nM (IC_{50})

In Vitro

Rigosertib is non-ATP-competitive inhibitor of PLK1 with IC_{50} of 9 nM. Rigosertib also exhibits inhibition of PLK2, PDGFR, Flt1, BCR-ABL, Fyn, Src, and CDK1, with IC_{50} of 18-260 nM. Rigosertib shows cell killing activity against 94 different tumor cell lines with IC_{50} of 50-250 nM, including BT27, MCF-7, DU145, PC3, U87, A549, H187, RF1, HCT15, SW480, and KB cells. While in normal cells, such as HFL, PrEC, HMEC, and HUVEC, Rigosertib has little or no effect unless its concentration is greater than 5-10 μM. In HeLa cells, Rigosertib (100-250 nM) induces spindle abnormalities and apoptosis[3]. Rigosertib also inhibits several multidrug resistant tumor cell lines, including MES-SA, MES-SA/DX5a, CEM, and CEM/C2a, with IC_{50} of 50-100 nM. In DU145 cells, Rigosertib (0.25-5 μM) blocks cell cycle progression in G2/M phase, results in an accumulation of cells containing subG1 content of DNA, and activates apoptotic pathways. In A549 cells, Rigosertib (50 nM-0.5 μM) induces loss of viability and caspase 3/7 activation[4]. Rigosertib sodium (2 μM) induces apoptosis in chronic lymphocytic leukemia (CLL) cells without toxicity against T-cells or normal B-cells. Rigosertib sodium (2 μM) also abrogates the pro-survival effect of follicular dendritic cells on CLL cells and reduces SDF-1-induced migration of leukemic cells[5].

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

In Vivo

Rigosertib (250 mg/kg, i.p.) markedly inhibits tumor growth in mouse xenograft models of Bel-7402, MCF-7, and MIA-PaCa cells[3]. Rigosertib (200 mg/kg, i.p.) shows inhibition on tumor growth in a mouse xengraft model of BT20 cells[4].

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Cell Assay [2]

Tumor cells are plated into six-well dishes at a density of 1×10^5 cells/mL/well, and Rigosertib is added 24 hours later at various concentrations. Cell counts are determined from duplicate wells after 96-hour of treatment. The total number of viable cells is determined by trypan blue exclusion.

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Animal Administration [1]

Bel-7402 tumor models: twenty female athymic (NCR-nu/nu) nude mice are injected with 1×10^7 Bel-7402 tumor cells subcutaneously, and 10-14 days later, when the tumor volumes reach 200-250 mm, the mice are divided into four groups such that each group harbors tumors of the same volume. Rigosertib (ON01910, 250 mg/kg) dissolved in PBS is administered alone or in combination with NSC 266046 (100 mg/kg) intraperitonially on alternate days. Tumor measurements are done two times/week using traceable digital vernier calipers. Body weight is determined during each measurement. The animals are observed for signs of toxicity[1].

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- Sci Transl Med. 2018 Jul 18;10(450):eaaq1093.
- Int J Biol Sci. 2020 Jun 27;16(13):2382-2391.
- Sci Rep. 2017 Aug 17;7(1):8629.
- Oncol Res. 2021 Feb 11.

- Harvard Medical School LINCS LIBRARY

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REFERENCES

[1]. Xu F, et al. Rigosertib as a selective anti-tumor agent can ameliorate multiple dysregulated signalingtransduction pathways in high-grade myelodysplastic syndrome. Sci Rep. 2014 Dec 4;4:7310.

[2]. Hyoda T, et al. Rigosertib induces cell death of a myelodysplastic syndrome-derived cell line by DNA damage-induced G2/M arrest. Cancer Sci. 2015 Mar;106(3):287-93.

[3]. Gumireddy K, et al. ON01910, a non-ATP-competitive small molecule inhibitor of Plk1, is a potent anticancer agent. Cancer Cell. 2005 Mar;7(3):275-86.

[4]. Reddy MV, et al. Discovery of a clinical stage multi-kinase inhibitor sodium (E)-2-{2-methoxy-5-[(2',4',6'-trimethoxystyrylsulfonyl)methyl]phenylamino}acetate (ON 01910.Na): synthesis, structure-activity relationship, and biological activity. J Med Chem.

[5]. Chapman CM, et al. ON 01910.Na is selectively cytotoxic for chronic lymphocytic leukemia cells through a dual mechanism of action involving PI3K/AKT inhibition and induction of oxidative stress. Clin Cancer Res. 2012 Apr 1;18(7):1979-91

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