Regorafenib Hydrochloride

Cat. No.: HY-13308

CAS No.: 835621-07-3

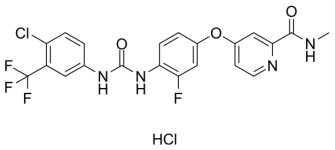
Molecular Formula: $C_{21}H_{16}Cl_2F_4N_4O_3$

Molecular Weight: 519

Target: VEGFR; Autophagy; PDGFR; Raf; RET

Pathway: Protein Tyrosine Kinase/RTK; Autophagy; MAPK/ERK Pathway

Storage: 4°C, sealed storage, away from moisture
* In solvent : -80°C, 6 months; -20°C, 1 month (sealed storage, away from moisture)



SOLVENT & SOLUBILITY

In Vitro

DMSO : ≥ 5.6 mg/mL (10.79 mM)
H_2O : < 0.1 mg/mL (insoluble)
* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions	Concentration / Solvent / Mass	1 mg	5 mg	10 mg
	1 mM	1.9268 mL	9.6339 mL	19.2678 mL
	5 mM	0.3854 mL	1.9268 mL	3.8536 mL
	10 mM	0.1927 mL	0.9634 mL	1.9268 mL

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

In Vivo

1. Add each solvent one by one: 50% PEG300 >> 50% saline
Solubility: 2 mg/mL (3.85 mM); Suspended solution; Need ultrasonic

BIOLOGICAL ACTIVITY

Description

Regorafenib Hydrochloride (BAY 73-4506 hydrochloride) is a multi-target inhibitor for VEGFR1/2/3, PDGFRβ, Kit, RET and Raf-1 with IC_{50}s of 13/4.2/46, 22, 7, 1.5 and 2.5 nM, respectively[1].

IC_{50} & Target

VEGFR1 13 nM (IC_{50})	VEGFR2 4.2 nM (IC_{50})	VEGFR3 46 nM (IC_{50})	PDGFRβ 22 nM (IC_{50})
Braf 28 nM (IC_{50})	$BRaf^{V600E}$ 19 nM (IC_{50})	Raf-1 2.5 nM (IC_{50})	

In Vitro

Regorafenib potently inhibits VEGFR2 autophosphorylation in NIH-3T3/VEGFR2 cells with an IC_{50} of 3 nM. In HAoSMCs, regorafenib inhibits PDGFR-β autophosphorylation after stimulation with PDGF-BB, with an IC_{50} of 90 nM. Regorafenib inhibits the proliferation of VEGF165-stimulated HUVECs, with an IC_{50} of 3 nM[1]. Regorafenib causes a concentration-

	dependent decrease in Hep3B cell growth, having an IC_{50} of 5 μM. Regorafenib subsequently increases the levels of phospho-c-Jun, a JNK target, but not total c-Jun in Hep3B cells[3]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	Regorafenib effectively inhibits growth of the Colo-205 xenografts in the dose range of 10-100 mg/kg reaching a TGI of 75% at day 14 at the 10 mg/kg dose. In the MDA-MB-231 model, regorafenib is highly efficacious at a dose as low as 3 mg/kg, resulting in a significant TGI of 81%, which increases to 93% at doses of 10 and 30 mg/kg, where tumor stasis is reached[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Cell Assay [1]	For proliferation assays, GIST 882 and TT cells are grown in RPMI medium containing L-glutamine, and MDA-MB-231, HepG2 and A375 cells in DMEM always containing 10% hiFBS. Cells are trypsinized, plated at 5×10^4 cells/well in 96-well plates in complete media containing 10% FBS and grown overnight at 37°C. The next day, vehicle or regorafenib serially diluted in complete growth media to between 10 μM and 5 nM final concentrations, and 0.2% DMSO, is added and incubation is continued for 96 hr. Cell proliferation is quantified using CellTitre-Glo™. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Animal Administration [1]	Female athymic NCr nu/nu mice, kept in accordance with Federal guidelines, are subcutaneously inoculated with 5×10^6 Colo-205 or MDA-MB-231 cells or implanted with 1 mm^3 786-O tumor fragments. When tumors reach a volume of 100 mm^3, regorafenib or vehicle control is administered orally qd×21 in the 786-O model, and qd×9 in the Colo-205 and MDA-MB-231 models, respectively, at doses of 100, 30, 10, and 3 mg/kg. Paclitaxel is administered intravenously at 10 mg/kg in ethanol/Cremophor EL®/saline (12.5%/12.5%/75%) every 2 days×5. Tumor size (volume) is estimated twice weekly $(l\times w^2)/2$, and the percentage of tumor growth inhibition (TGI) is obtained from terminal tumor weights (1-T/C×100). Mice are weighed every other day starting from the first day of treatment. The general health status of the mice is monitored daily. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- Cell Res. 2020 Sep;30(9):779-793.
- Cancer Discov. 2021 Jul;11(7):1716-1735.
- Cancer Discov. 2019 Dec;9(12):1686-1695.
- Sci Transl Med. 2018 Jul 18;10(450):eaaq1093.
- Adv Sci (Weinh). 2023 Jun 17;e2206798.

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REFERENCES

[1]. Wilhelm SM, et al. Regorafenib (BAY 73-4506): a new oral multikinase inhibitor of angiogenic, stromal and oncogenic receptor tyrosine kinases with potent preclinical antitumor activity. Int J Cancer, 2011, 129(1), 245-255.

[2]. Heng DY, et al. Targeted therapy for metastatic renal cell carcinoma: current treatment and future directions. Ther Adv Med Oncol, 2010, 2(1), 39-49.

[3]. Carr BI, et al. Fluoro-Sorafenib (Regorafenib) effects on hepatoma cells: growth inhibition, quiescence, and recovery. J Cell Physiol, 2013, 228(2), 292-297.

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

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