ZD-4190

Cat. No.: HY-U00002

CAS No.: 413599-62-9

Molecular Formula: $C_{19}H_{16}BrFN_6O_2$

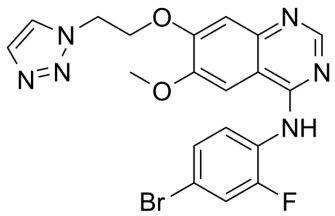
Molecular Weight: 459.27

Target: VEGFR; EGFR

Pathway: Protein Tyrosine Kinase/RTK; JAK/STAT Signaling

Storage:

Powder	-20°C	3 years
	4°C	2 years
In solvent	-80°C	2 years
	-20°C	1 year



SOLVENT & SOLUBILITY

In Vitro

DMSO : 20.83 mg/mL (45.35 mM; Need ultrasonic)

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	2.1774 mL	10.8868 mL	21.7737 mL
5 mM	0.4355 mL	2.1774 mL	4.3547 mL
10 mM	0.2177 mL	1.0887 mL	2.1774 mL

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

In Vivo

1. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.08 mg/mL (4.53 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

ZD-4190 is a potent, orally available inhibitor of the vascular endothelial cell growth factor receptor 2 (VEGFR2) and of epidermal growth factor receptor (EGFR) signalling, used for the treatment of cancer.

IC_{50} & Target

EGFR VEGFR2

In Vitro

ZD4190 exhibits cytotoxic activity against the tumor cells[2].

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

In Vivo

ZD4190 (100 mg/kg, p.o.) effectively delays MDA-MB-435 tumor growth in mice. In ZD4190-treated tumors, 18F-FPPRGD2 uptake has decreased significantly relative to baseline by 26.74±8.12% ($p<0.05$) on day 1 and by 41.19±6.63% ($p<0.01$) on day 3, then has returned to baseline on day 7. Tumor uptake of 18F-FLT has also decreased on both day 1 and day 3 after initiation of ZD4190 treatment. However, ZD4190 does not significantly change 18F-FDG uptake in tumors, compared with

	the control group[1]. ZD4190 (50 mg/kg, p.o.) prevents outgrowth of residual tumour in a muscle model of minimal residual carcinoma[2]. ZD4190 (12.5-100 mg/kg, p.o.) produces a dose-dependent reduction in K(trans) in PC-3 prostate tumors. At 100 mg/kg, ZD4190 reduces K(trans) in PC-3 tumors by 31% following 2 doses and by 53% following 8 doses[3]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Cell Assay [2]	The cytotoxicity of ZD4190 for PDVC57B cells is established when 10^4 cells are exposed to 1-10 μM ZD4190 for 96 h before MTS solution is added and the optical density measured at 490 nm. Cells are also grown to 40% confluence and treated with 1-100 μM ZD4190 for 7 days and the cytopathic effect examined by staining with crystal violet. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Animal Administration [3]	ZD4190 is suspended in a 1% (v/v) solution of polyoxyethylene sorbitan mono-oleate in deionized water and administered by oral gavage (0.1 mL/10 g body weight). In each experiment, mice are randomized to receive either vehicle or ZD4190, administered once daily using a 1 day (at 0 and 22 h) or 7 day (at 0, 24, 48, 72, 96, 120, 144, and 166 h) treatment regimen (i.e., daily administration of compound for 1 or 7 days with an additional dose given 2 h prior to the end of the treatment period) followed by DCEMRI under terminal anesthesia. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

REFERENCES

[1]. Yang M, et al. PET imaging of early response to the tyrosine kinase inhibitor ZD4190. Eur J Nucl Med Mol Imaging. 2011 Jul;38(7):1237-47. doi: 10.1007/s00259-011-1742-z. Epub 2011 Mar 1.

[2]. Gaballah K, et al. The antiangiogenic agent ZD4190 prevents tumour outgrowth in a model of minimal residual carcinoma in deep tissues. Br J Cancer. 2009 Aug 4;101(3):418-23. doi: 10.1038/sj.bjc.6605092. Epub 2009 Jul 21.

[3]. Checkley D, et al. Dynamic contrast-enhanced MRI of vascular changes induced by the VEGF-signalling inhibitor ZD4190 in human tumour xenografts. Magn Reson Imaging. 2003 Jun;21(5):475-82.

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