Lenvatinib

Cat. No.: HY-10981

CAS No.: 417716-92-8

Molecular Formula: $C_{21}H_{19}ClN_4O_4$

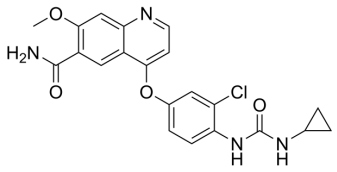
Molecular Weight: 427

Target: VEGFR; FGFR; PDGFR; c-Kit; RET

Pathway: Protein Tyrosine Kinase/RTK

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 : ≥ 12.78 mg/mL (29.93 mM)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	2.3419 mL	11.7096 mL	23.4192 mL
5 mM	0.4684 mL	2.3419 mL	4.6838 mL
10 mM	0.2342 mL	1.1710 mL	2.3419 mL

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

In Vivo

1. Add each solvent one by one: 0.5% Methylcellulose/saline water
   Solubility: 6.67 mg/mL (15.62 mM); Suspended solution; Need ultrasonic
2. Add each solvent one by one: 5% DMSO >> 95% (20% SBE-β-CD in saline)
   Solubility: ≥ 0.64 mg/mL (1.50 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

Lenvatinib (E7080) is an oral, multi-targeted tyrosine kinase inhibitor that inhibits VEGFR1-3, FGFR1-4, PDGFR, KIT, and RET, shows potent antitumor activities[1][2].

IC_{50} & Target

VEGFR1 22 nM (IC_{50})	VEGFR2 4 nM (IC_{50})	VEGFR3 5.2 nM (IC_{50})	FGFR1 46 nM (IC_{50})
FGFR2	FGFR3	FGFR4	PDGFRα 51 nM (IC_{50})

	PDGFRβ 39 nM (IC_{50})	c-Kit 100 nM (IC_{50})	RET

In Vitro	Lenvatinib (E7080) has IC_{50}s of 4, 5.2, 22 nM for VEGFR2 (KDR), VEGFR3 (Flt-4), and VEGFR1 (Flt-1), respectively. Lenvatinib inhibits PDGFRα, PDGFRβ, FGFR1, and KIT with IC_{50}s of 51, 39, 46, and 100 nM, respectively[3]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	Lenvatinib (E7080) (100 mg/kg, p.o.) significantly inhibits local tumor growth at the m.f.p., and at the end of treatment, Lenvatinib mesylate also significantly inhibits metastasis to both regional lymph nodes and distant lung[3]. Lenvatinib (E7080) inhibits the growth of H146 tumor at 30 and 100 mg/kg (BID, QDx21) in a dose-dependent manner and causes tumor regression at 100 mg/kg in H146 xenograft model. IHC analysis with anti-CD31 antibody shows that lenvatinib at 100 mg/kg decreases microvessel density more than anti-VEGF antibody and STI571 treatment[4]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Cell Assay [1]	H146 (1.2×10^3 cells/50 μL/well) in SFM containing 0.5% BSA are cultured in 96-well multi-plates. After overnight culture at 37°C, SFM (150 μL/well) containing 0.5% FBS and several concentrations of SCF are added with or without several concentrations of compound. After culture for 72 hr, the ratios of surviving cells are measured by WST-1. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Animal Administration [1]	Female BALB/c nude mice (8-12 weeks old, 20-25 g) are maintained under clean-room conditions. H146 tumor cells (6.5×10^6) are implanted subcutaneously (s.c.) into the flank region of mice. Twelve days after inoculation, mice are randomized into control (n=12) and treatment (n=6 or n=5) groups and this point in time is identified as day 1. Lenvatinib and STI571, and VEGF neutralization antibody are suspended in 0.5% methylcellulose and saline, respectively, and administered orally twice a day for lenvatinib and STI571 and twice a week for antibody from day 1 to day 21. Tumor volume is measured on the indicated days and calculated. Antitumor activity is shown as a relative tumor volume (RTV=calculated tumor volume at indicated days/volume on day 1). MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- Drug Resist Updat. 2023 Jul;69:100976.
- Sci Transl Med. 2018 Jul 18;10(450):eaaq1093.
- Mol Ther. 2023 May 4;S1525-0016(23)00253-8.
- EMBO J. 2021 Apr 28;e106771.
- MedComm. 26 August 2022.

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REFERENCES

[1]. Kudo M, et al. Lenvatinib versus Bay 43-9006 in first-line treatment of patients with unresectable hepatocellularcarcinoma: a randomised phase 3 non-inferiority trial. Lancet. 2018 Mar 24;391(10126):1163-1173.

[2]. Suyama K, et al. Lenvatinib: A Promising Molecular Targeted Agent for Multiple Cancers. Cancer Control. 2018 Jan-Dec;25(1):1073274818789361.

[3]. Matsui J, et al. E7080, a novel inhibitor that targets multiple kinases, has potent antitumor activities against stem cell factor producing human small cell lung cancer

H146, based on angiogenesis inhibition. Int J Cancer. 2008, 122(3), 664-671.

[4]. Matsui J, et al. Multi-kinase inhibitor E7080 suppresses lymph node and lung metastases of human mammary breast tumor MDA-MB-231 via inhibition of vascular endothelial growth factor-receptor (VEGF-R) 2 and VEGF-R3 kinase. Clin Cancer Res. 2008, 14(17),545.

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