Lenvatinib

Cat. No.: HY-10981

CAS No.: 417716-92-8

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

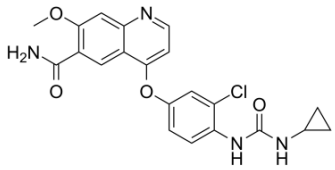
Molecular Weight: 426.85

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	6 months
	-20°C	1 month



SOLVENT & SOLUBILITY

In Vitro

DMSO : 12.78 mg/mL (29.94 mM; Need ultrasonic)

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	2.3427 mL	11.7137 mL	23.4274 mL
5 mM	0.4685 mL	2.3427 mL	4.6855 mL
10 mM	0.2343 mL	1.1714 mL	2.3427 mL

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

In Vivo

1. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: ≥ 2.5 mg/mL (5.86 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.5 mg/mL (5.86 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (5.86 mM); Clear solution
4. 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	VEGFR2	VEGFR3	FGFR1
22 nM (IC_{50})	4 nM (IC_{50})	5.2 nM (IC_{50})	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

- Sci Transl Med. 2018 Jul 18;10(450):eaaq1093.
- EMBO J. 2021 Apr 28;e106771.
- Acta Pharmacol Sin. 2021 Jan;42(1):108-114.
- J Cell Mol Med. 2020 Nov 18.
- Exp Cell Res. 2020 Aug 1;393(1):112054.

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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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