AEE788

Cat. No.: HY-10045

CAS No.: 497839-62-0

Molecular Formula: $C_{27}H_{32}N_6$

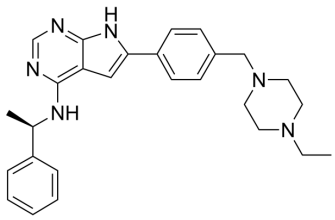
Molecular Weight: 440.58

Target: EGFR; Apoptosis

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

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 : 50 mg/mL (113.49 mM; Need ultrasonic)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	2.2697 mL	11.3487 mL	22.6974 mL
	5 mM	0.4539 mL	2.2697 mL	4.5395 mL
	10 mM	0.2270 mL	1.1349 mL	2.2697 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 (5.67 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: 2.5 mg/mL (5.67 mM); Suspended solution; Need ultrasonic
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (5.67 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

AEE788 is an inhibitor of the EGFR and ErbB2 with IC_{50} values of 2 and 6 nM, respectively.

IC_{50} & Target

EGFR	ErbB2
2 nM (IC_{50})	6 nM (IC_{50})

In Vitro

AEE788 inhibits EGFR and VEGF receptor tyrosine kinases in the nM range (IC_{50}:EGFR 2 nm, ErbB2 6 nm, KDR 77 nm, and Flt-1 59 nm). In cells, growth factor-induced EGFR and ErbB2 phosphorylation is also efficiently inhibited (IC_{50}:11 and 220 nm,

	respectively). AEE788 demonstrates antiproliferative activity against a range of EGFR and ErbB2-overexpressing cell lines (including EGFRvIII-dependent lines) and inhibits the proliferation of epidermal growth factor- and VEGF-stimulated human umbilical vein endothelial cells[1]. Treatment of cutaneous SCC cells with AEE788 leads to dose-dependent inhibition of EGFR and VEGFR-2 phosphorylation, growth inhibition, and induction of apoptosis[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	AEE788 efficiently inhibits growth factor-induced EGFR and ErbB2 phosphorylation in tumors for >72 h. AEE788 also inhibits VEGF-induced angiogenesis in a murine implant model[1]. In mice treated with AEE788, tumor growth is inhibited by 54% at 21 days after the start of treatment compared with control mice[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Kinase Assay [1]	The invitro kinase assays are performed in 96-well plates (30 μL) at ambient temperature for 15–45 min using the recombinant glutathione S-transferase-fused kinase domains (4–100 ng, depending on specific activity). [γ^{33}P]ATP is used as phosphate donor and polyGluTyr-(4:1) peptide as acceptor. Assays are optimized for each kinase using the following ATP concentrations: 1.0 μM (c-Kit, c-Met, c-Fms, c-Raf-1, and RET), 2.0 μM (EGFR, ErbB2, ErbB3, and ErbB4), 5.0 μM (c-Abl), 8.0 μM (Flt-1, Flt-3, Flt-4, Flk, KDR, FGFR-1, and Tek), 10.0 μM (PDGF receptor-β, protein kinase C-α, and cyclin-dependent kinase 1), and 20.0 μM (c-Src and protein kinase A). The reaction is terminated by the addition of 20 μL 125 mM EDTA. Thirty μL (c-Abl, c-Src, insulin-like growth factor-1R, RET-Men2A, and RET-Men2B) or 40 μL (all other kinases) of the reaction mixture is transferred onto Immobilon-polyvinylidene difluoride membrane, presoaked with 0.5% H3PO4 and mounted on a vacuum manifold. Vacuum is then applied and each well rinsed with 200 μL 0.5% H_3PO_4. Membranes are removed and washed four times. Dried membranes are counted. IC_{50} are calculated by linear regression analysis of the percentage inhibition and are averages of at least three determinations[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Cell Assay [2]	AEE788 is dissolved in 90% polyethylene glycol 300 plus 10% 1-methyl-2-pyrrolidinone to a concentration of 6.25 mg/mL. Tumor cells are seeded into 96-well plates in complete medium and allowed to attach for 24 hours. The cultures are re-fed with medium with 2% serum. After 24 hours, cells are treated with different concentrations (0-2 μM) of AEE788 (negative control with DMSO alone) for 72 hours. After a 2-hour incubation in medium containing 0.42 mg/mL MTT, the cells are lysed in 100 μL DMSO. The conversion of MTT to formazan is measured at an absorbance of 570 nm[2] MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Animal Administration [1]	Mice: AEE788 is diluted in DMSO and diluted in the optimal medium. BALB/c mice bearing s.c. A-431 squamous tumors (3 animals/group) or HC11-NeuT-driven breast tumors (2 animals/group) are dosed orally with 30 mg/kg of AEE788 or vehicle once daily for 5 days. At different time points after the end of compound treatment and before sacrificing the animals the mice are given i.v. 500 μg EGF/kg body weight or 0.2 ml 0.9% w/v NaCl as vehicle control. Five min after EGF administration, the mice are sacrificed, tumors are removed[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.
- Oncol Rep. 2018 Nov;40(5):2944-2954.
- Int J Clin Exp Med. 2016;9(8):15892-15899.

See more customer validations on www.MedChemExpress.com

REFERENCES

[1]. Traxler P, et al. AEE788: a dual family epidermal growth factor receptor/ErbB2 and vascular endothelial growth factor receptor tyrosine kinase inhibitor with antitumor and antiangiogenic activity. Cancer Res. 2004 Jul 15;64(14):4931-4941.

[2]. Park et al. AEE788, a dual tyrosine kinase receptor inhibitor, induces endothelial cell apoptosis in human cutaneous squamous cell carcinoma xenografts in nude mice. Clin Cancer Res. 2005 Mar 1;11(5):1963-1973.

Tel: 609-228-6898 Fax: 609-228-5909 E-mail: tech@MedChemExpress.com

Address: 1 Deer Park Dr, Suite Q, Monmouth Junction, NJ 08852, USA