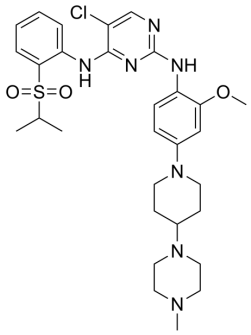
NVP-TAE 684



Cat. No.: HY-10192

CAS No.: 761439-42-3

Molecular Formula: $C_{30}H_{40}ClN_7O_3S$

Molecular Weight: 614.2

Target: Anaplastic lymphoma kinase (ALK); Apoptosis

Pathway: 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 : 7.69 mg/mL (12.52 mM; Need ultrasonic)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	1.6281 mL	8.1407 mL	16.2813 mL
	5 mM	0.3256 mL	1.6281 mL	3.2563 mL
	10 mM	0.1628 mL	0.8141 mL	1.6281 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: ≥ 0.77 mg/mL (1.25 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 0.77 mg/mL (1.25 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

NVP-TAE 684 (TAE 684) is a highly potent and selective ALK inhibitor, which blocks the growth of ALCL-derived and ALK-dependent cell lines with IC_{50} values between 2 and 10 nM[1].

IC_{50} & Target

IC50: 2-10 nM (ALK-dependent cell lines)[1]

In Vitro

TAE684 inhibits the proliferation of Ba/F3 NPM-ALK cells with an IC_{50} of 3 nM, without affecting the survival of parental Ba/F3 cells at concentrations up to 1 μM. TAE684 inhibits STAT3 and STAT5 phosphorylation in a dose-dependent manner in both Ba/F3 NPM-ALK and Karpas-299 cells. TAE684 induces apoptosis and G1 phase arrest in NPM-ALK-expressing Ba/F3 cells and ALCL patient cell lines[1].

NVP-TAE684 markedly reduces cell survival in both sensitive H3122 and H3122 CR cells, but has little to no effect on the

	viability of other, non-ALK-dependent cancer cell lines. NVP-TAE684 treatment of H3122 CR cells suppresses phosphorylation of ALK, AKT, and ERK and induces marked apoptosis. TAE684 potently suppresses the survival of Ba/F3 cells expressing the EML4-ALK L1196M mutant[2]. Neurite outgrowth induced by expression of the mALKR1279Q mutant is completely inhibited at 30 nM NVP-TAE684, which is comparable with the response seen with activated wt mALK[3]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	NVP-TAE684 suppresses lymphomagenesis in two independent models of ALK-positive ALCL and induces regression of established Karpas-299 lymphomas. TAE684 displays appreciable bioavailability and half-life in vivo. TAE684 (1, 3, and 10 mg/kg. p.o.) significantly delays in lymphoma development and shows 100- to 1,000-fold reduction in luminescence signal. The TAE684- (10 mg/kg) treated group appeares healthy and does not display any signs of compound- or disease-related toxicity[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Cell Assay [1]	Luciferase-expressing Karpas-299, SU-DHL-1, and Ba/F3 cells and transformed Ba/F3 stably expressing NPM-ALK, BCR-ABL, or TEL-kinase fusion constructs are plated in 384-well plates (25,000 cells per well) and incubated with serial dilutions of TAE684 or DMSO for 2-3 days. Luciferase expression is used as a measure of cell proliferation/survival and is evaluated with the Bright-Glo Luciferase Assay System. ICsub>50 values are generated by using XLFit software. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Animal Administration [1]	For in vivo compound efficacy studies, treatment is initiated 72 h after tail vein injection of 1×10^6 Karpas-299-, Ba/F3 NPM-ALK- or BCR-ABL-expressing cells into female Fox Chase SCIDBeige mice. Mice (n=10 per group) are administered either TAE684 resuspended in 10% 1-methyl-2-pyrrolidinone/90% PEG 300 solution at 1, 3, and 10 mg/kg once daily for 3 weeks or the vehicle solution at the same dosing schedule. Disease progression and compound efficacy is monitored weekly with bioluminescence imaging. To determine the efficacy of TAE684 on established disease, dosing is initiated on day 12, at which time the disease confirmed to be widespread by bioluminescence imaging. For analysis of downstream molecular effects in vivo, mice with established lymphomas are administered vehicle solution or TAE684 (10 mg/kg) for 3 days. At the end of treatment, mice are killed, and lymph nodes are extracted for immunoblotting and histological analysis. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- Theranostics. 2020 Apr 6;10(11):5120-5136.
- Cell Chem Biol. 2022 Aug 29;S2451-9456(22)00311-7.
- Cell Chem Biol. 2018 Feb 15;25(2):224-229.e2.
- BMC Biol. 2018 Sep 5;16(1):90.
- Mol Cancer Res. 2022 Mar.

See more customer validations on www.MedChemExpress.com

REFERENCES

[1]. Galkin AV, et al. Identification of NVP-TAE684, a potent, selective, and efficacious inhibitor of NPM-ALK. Proc Natl Acad Sci U S A. 2007 Jan 2;104(1):270-5.

[2]. Katayama R, et al. Therapeutic strategies to overcome PF-02341066 resistance in non-small cell lung cancers harboring the fusion oncogene EML4-ALK. Proc Natl Acad Sci U S A. 2011 May 3;108(18):7535-40.

[3]. Schonherr C, Activating ALK mutations found in neuroblastoma are inhibited by PF-02341066 and NVP-TAE684. Biochem J. 2011 Dec 15;440(3):405-13.

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