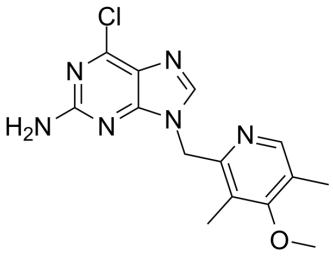
BIIB021

Cat. No.:	HY-10212
CAS No.:	848695-25-0
Molecular Formula:	$C_{14}H_{15}ClN_6O$
Molecular Weight:	318.76
Target:	HSP; Autophagy
Pathway:	Cell Cycle/DNA Damage; Metabolic Enzyme/Protease; Autophagy
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 : ≥ 45 mg/mL (141.17 mM)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	3.1372 mL	15.6858 mL	31.3716 mL
	5 mM	0.6274 mL	3.1372 mL	6.2743 mL
	10 mM	0.3137 mL	1.5686 mL	3.1372 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 (7.84 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (7.84 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

BIIB021 (CNF2024) is an orally active, fully synthetic inhibitor of HSP90 with a K_i and an EC_{50} of 1.7 nM and 38 nM, respectively[1].

IC_{50} & Target		
	HSP90 1.7 nM (Ki)	HSP90 38 nM (EC50)

In Vitro

BIIB021 binds in the ATP-binding pocket of Hsp90, interferes with Hsp90 chaperone function, and results in client protein degradation and tumor growth inhibition. BIIB021 inhibits tumor cell (BT474, MCF-7, N87, HT29, H1650, H1299, H69 and H82) proliferation with IC_{50} from 0.06-0.31 μM. BIIB021 induces the degradation of Hsp90 client proteins including HER-2, Akt, and

Raf-1 and up-regulated expression of the heat shock proteins Hsp70 and Hsp27[1].
BIIB021 inhibits Hodgkin's lymphoma cells (KM-H2, L428, L540, L540cy, L591, L1236 and DEV) with IC_{50} from 0.24-0.8 μM. BIIB021 shows low activity in lymphocytes from healthy individuals. BIIB021 inhibits the constitutive activity of NF-κB despite defective IκB. BIIB021 induces the expression of ligands for the activating NK cell receptor NKG2D on Hodgkin's lymphoma cells resulting in an increased susceptibility to NK cell-mediated killing[2].
BIIB021 enhances the in vitro radiosensitivity of HNSCCA cell lines (UM11B and JHU12) with a corresponding reduction in the expression of key radioresponsive proteins, increases apoptotic cells and enhances G2 arrest[3].
BIIB021 is considerably more active than 17-AAG against adrenocortical carcinoma H295R. The cytotoxic activity of BIIB021 is not influenced by loss of NQO1 or Bcl-2 overexpression, molecular lesions that do not prevent client loss but are nonetheless associated with reduced cell killing by 17-AAG. BIIB021 is also active in 17-AAG resistant cell lines (NIH-H69, MES SA Dx5, NCI-ADR-RES, Nalm6)[4].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

In Vivo

Oral administration of BIIB021 leads to tumor growth inhibition in many tumor xenograft models including N87, BT474, CWR22, U87, SKOV3 and Panc-1[1].
BIIB021 effectively inhibits growth of L540cy tumor at a dose of 120 mg/kg[2]. BIIB021 significantly enhances antitumor growth effect of radiation in JHU12 xenograft[3].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Kinase Assay [1]

For fluorescence polarization competition measurements, the FITC-geldanamycin probe (20 nM) is reduced with 2 mM TCEP at room temperature for 3 hours, after which the solution is aliquoted and stored at -80°C until used. Recombinant human Hsp90α (0.8 nM) and reduced FITC-geldanamycin (2 nM) are incubated in a 96-well microplate at room temperature for 3 hours in the presence of assay buffer containing 20 mM HEPES (pH 7.4), 50 mM KCl, 5 mM $MgCl_2$, 20 mM Na_2MoO_4, 2 mM DTT, 0.1 mg/mL BGG, and 0.1% (v/v) CHAPS. Following this preincubation, BIIB021 in 100% DMSO is then added to final concentrations of 0.2 nM to 10 μM (final volume 100 μL, 2% DMSO). The reaction is incubated for 16 hours at room temperature and fluorescence is then measured in an Analyst plate reader, excitation=485 nm, emission=535 nm. High and low controls contain no BIIB021 or no Hsp90, respectively. The data are fit to a four-parameter curve and IC_{50} is generated.
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Cell Assay [1]

A modified tetrazolium salt assay is used to measure the IC_{50}. Tumor cells are added to 96-well plates and propagated for 24 hours before BIIB021 addition. BIIB021 is added to the plated cells. DMSO (0.03-0.003%) is included as a vehicle control. After incubation phenazine methosulfate (stock concentration 1 mg/mL) and 3-(4,5-dimethylthiazol-2-yl)-5-(3-carboxymethoxyphenyl)-2-(4-sulfophenyl)-2H-tetrazolium, inner salt (stock concentration 2 mg/mL) are mixed at a ratio of 1:20 and added to each well of a 96-well plate. Reduction of 3-(4,5-dimethylthiazol-2-yl)-5-(3-carboxymethoxyphenyl)-2-(4-sulfophenyl)-2H-tetrazolium, inner salt gives rise to a soluble formazan product that is secreted into the culture medium. After 4 hours incubation, the formazan product is quantitated spectrophotometrically at a wavelength of 490 nm. Data are acquired using SOFTmaxPRO software, and 100% viability is defined as the A490 of DMSO-treated cells stained with 3-(4,5-dimethylthiazol-2-yl)-5-(3-carboxymethoxyphenyl)-2-(4-sulfophenyl)-2H-tetrazolium, inner salt (the mean A490 of cells treated with DMSO at a range of 0.03-0.003%). Percent viability of each sample is calculated from the A490 values as follows: % viability=(A490 nm sample/A490 nm DMSO-treated cells × 100). The IC_{50} is defined as the concentration that gives rise to 50% inhibition of cell viability.
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Animal Administration [1]

BALB/c and athymic mice are obtained from Harlan Sprague-Dawley at age 6 to 8 weeks. The mice are maintained in sterilized cages in a ventilated caging system with a 12 h light/12 h dark photoperiod at temperature of 21°C to 23°C and a relative humidity of 50±5%. Irradiated pelleted food and autoclaved deionized water are provided ad libitum. Animals are identified by the use of individually numbered ear tags. N87 tumor fragments (appr 2 mm^3) are implanted s.c. in the right flank of the animal. BIIB021 is administered to animals bearing N87 stomach carcinoma tumors at doses of 31, 62.5, and 125 mg/kg, once daily, from Monday to Friday, for 5 weeks. Tumor dimensions are measured using calipers and tumor volumes are calculated using the equation for an ellipsoid sphere $(l \times w^2)/2=mm^3$, where l and w refer to the larger and smaller

dimensions collected at each measurement, respectively. Tumor volumes are measured and animals are weighed and monitored for toxicity at least twice weekly. P values are calculated using the two-tailed Student's t test to assess the difference in tumor volumes between control and treated groups. $P<0.05$ is considered significant.

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

CUSTOMER VALIDATION

- Nat Commun. 2017 Sep 4;8(1):422.
- Viruses. 2021, 13(4), 610.

See more customer validations on www.MedChemExpress.com

REFERENCES

[1]. Lundgren, Karen., et al. BIIB021, an orally available, fully synthetic small-molecule inhibitor of the heat shock protein Hsp90. Molecular Cancer Therapeutics (2009), 8(4), 921-929.

[2]. B?ll B, et al. Heat shock protein 90 inhibitor BIIB021 (CNF2024) depletes NF-kappaB and sensitizes Hodgkin's lymphoma cells for natural killer cell-mediated cytotoxicity. Clin Cancer Res. 2009 Aug 15;15(16):5108-16.

[3]. Yin X, et al. BIIB021, a novel Hsp90 inhibitor, sensitizes head and neck squamous cell carcinoma to radiotherapy. Int J Cancer. 2010 Mar 1;126(5):1216-25

[4]. Zhang H, et al. BIIB021, a synthetic Hsp90 inhibitor, has broad application against tumors with acquired multidrug resistance. Int J Cancer. 2010 Mar 1;126(5):1226-34

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