Nedisertib

Cat. No.: HY-101570

CAS No.: 1637542-33-6

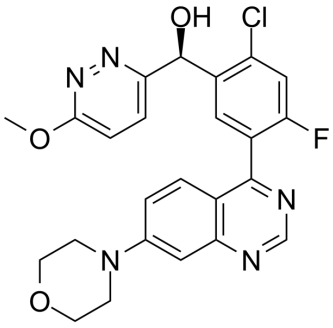
Molecular Formula: $C_{24}H_{21}ClFN_5O_3$

Molecular Weight: 481.91

Target: DNA-PK

Pathway: Cell Cycle/DNA Damage; PI3K/Akt/mTOR

Storage: -20°C, protect from light, stored under nitrogen
* In solvent : -80°C, 6 months; -20°C, 1 month (protect from light, stored under nitrogen)



SOLVENT & SOLUBILITY

In Vitro

DMSO : 50 mg/mL (103.75 mM; Need ultrasonic)

Preparing Stock Solutions	Mass / Solvent / Concentration	1 mg	5 mg	10 mg
	1 mM	2.0751 mL	10.3754 mL	20.7508 mL
	5 mM	0.4150 mL	2.0751 mL	4.1502 mL
	10 mM	0.2075 mL	1.0375 mL	2.0751 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 (5.19 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

Nedisertib (M3814) is a potent, orally available and selective inhibitor of DNA-PK, with an IC_{50} of <3 nM. Anti-tumor activity[1][2][3].

IC_{50} & Target

DNA-PK
<3 nM (IC_{50})

In Vitro

Nedisertib (Compound 136) is a potent and selective inhibitor of DNA-PK,? with an IC_{50} of <3 nM for DNA-PK and <0.5 μM for cellular pDNA-PK[3].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

In Vivo

In combination with IR, Nedisertib shows efficacy in all of the 6 mouse models of human cancer. In all models, a dose of 2 Gy administered daily for 1 week in combination with Nedisertib induces statically significant tumor growth inhibition compare to IR alone. Nedisertib, alone or in combination with IR, does not induce significant weight loss or visual signs of toxicity in

	the mice in any study[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Animal Administration [1]	The efficacy of Nedisertib in combination with IR is evaluated in 6 human xenograft models (HCT116, FaDu, NCI-H460, A549, Capan-1, BxPC3) in mice representing 4 different cancer types (colon, head and neck, lung, and pancreas). Tumor cells are injected s.c. into nude mice, and treatment starts when palpable tumors are established (~100 to 200 mm^3). Nedisertib is given orally at different doses (25 to 300 mg/kg) 10 min prior to IR. IR is applied using a radiation therapy device for small rodents calibrated to deliver 2 Gy. Autophosphorylation of DNA-PK (serine^{2056}) in FaDu tumor lysates is measured by immunoassay to assess pharmacological inhibition by Nedisertib[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- Nat Methods. 2023 Jul 20.
- Sci Immunol. 2024 Feb 2;9(92):eadi0042.
- Nat Commun. 2022 Sep 8;13(1):5295.
- Nat Commun. 2022 Jun 27;13(1):3662.
- Nat Commun. 2022 Jan 25;13(1):489.

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REFERENCES

[1]. L. Damstrup, et al. M3814, a DNA-dependent Protein Kinase Inhibitor (DNA-PKi), Potentiates the Effect of Ionizing Radiation (IR) in Xenotransplanted Tumors in Nude Mice. IJROBP. 2016; 94, 940-941.

[2]. Frank T. Zenke, et al. Abstract 1658: M3814, a novel investigational DNA-PK inhibitor: enhancing the effect of fractionated radiotherapy leading to complete regression of tumors in mice. AACR; Cancer Res 2016;76(14 Suppl):Abstract nr 1658.

[3]. Thomas Fuchss, et al. Arylchinazoline. WO2014183850A1.

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