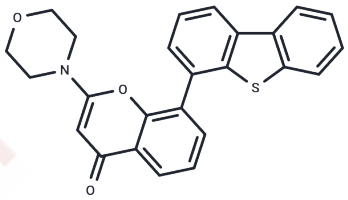
Data Sheet (Cat.No.T6276)

TargetMol

KU-57788

Chemical Properties



CAS No. : 503468-95-9

Formula: C25H19NO3S

Molecular Weight: 413.49

Storage: Powder: -20°C for 3 years | In solvent: -80°C for 1 year
Actual storage temperature shall be subject to the COA.

Biological Description

Description	NU7441 (KU-57788 (NU7441)) is a highly effective and specific DNA-PK inhibitor (IC50: 14 nM).
Targets(IC50)	CRISPR/Cas9,DNA-PK
In vitro	0.3 μM of KU-57788 (NU7441), nontoxic to both normal and tumor cells, caused a significant radio-sensitization in tumor cells exposed to X-rays and carbon ions. This concentration did not seem to cause inhibition of DNA DSB repair but induced a significant G2/M arrest [1]. The addition of NU7441 to cells following introduction of the Cas9/sgGFP editing system and the ΔGFP repair template caused a decrease of approximately 40 % in NHEJ events which was accompanied by an approximately two-fold stimulation in HDR. This effect was dose-dependent and reached a maximum at approximately 2.0 μM for NU7441 [2]. NU7441 reduced the CCK-8 counts in the HepG2 culture, further enhanced 60Cox03B3; radiation injury to HepG2 cells, which was manifested by decreasing the DNA-PKcs (S2056) protein expression, increasing x03B3 [3]. Even though RPA p34 is still localized into foci following UV-irradiation and inhibitor treatment, treatment of cells with NU7441 eliminates staining for hyperphosphorylated RPA p34 [4].
In vivo	Tumors in control mice reached four times their starting volume (RTV4) at a median time of 5.6 days. Treatment with etoposide phosphate alone caused a tumor growth delay of 2.7 days, which was extended to 5.4 days by coadministration of NU7441 [5].
Cell Research	Cells were irradiated with 290 MeV/n carbon ions (LET: 50 keV/μm) at the Heavy Ion Medical Accelerator in Chiba. The dose rate for carbon ions was 1 Gy/min. X-ray irradiation was performed using a TITAN-320 (200 kV, 20 mA) at a dose rate of 1 Gy/min. NU7441 was dissolved in DMSO and stored at ?20°C in a freezer. Cells were pretreated with NU7441 1 h before irradiation, and the drug was kept throughout the experiment [1].
Animal Research	All in vivo experiments were reviewed and approved by the relevant institutional animal welfare committees and done according to national law. We determined the plasma pharmacokinetics after administering NU7441 i.v. at 5 mg/kg in 10% DMSO/10% cyclodextrin in saline or i.p. or orally at 10 mg/kg (dissolved at 1 mg/mL in 40% PEG400/saline) to female BALB/c mice. These were the maximum administrable doses by the route used due to the limit of solubility of NU7441. Mice were killed at intervals up to 360 minutes after NU7441 administration; blood was taken and immediately

Animal Research	centrifuged, and the plasma fraction was removed and stored at ?20°C [5].

Solubility Information

Solubility	DMSO: 8 mg/mL (19.35 mM),Sonication is recommended. (< 1 mg/ml refers to the product slightly soluble or insoluble)
In vivo Formulation	10% DMSO+40% PEG300+5% Tween-80+45% Saline: 0.5 mg/mL (1.21 mM),Sonication is recommended. *Please add the solvents sequentially, clarifying the solution as much as possible before adding the next one. Dissolve by heating and/or sonication if necessary. Working solution is recommended to be prepared and used immediately. The formulation provided above is for reference purposes only. In vivo formulations may vary and should be modified based on specific experimental conditions.*

Preparing Stock Solutions

	1mg	5mg	10mg
1 mM	2.4184 mL	12.0922 mL	24.1844 mL
5 mM	0.4837 mL	2.4184 mL	4.8369 mL
10 mM	0.2418 mL	1.2092 mL	2.4184 mL
50 mM	0.0484 mL	0.2418 mL	0.4837 mL

Please select the appropriate solvent to prepare the stock solution, according to the solubility of the product in different solvents. Please use it as soon as possible.

Note: The dilution table applies only to solid products. For liquid products, please calculate the stock solution based on the stated concentration and/or density.

Reference

Sunada S, et al. Nontoxic concentration of DNA-PK inhibitor NU7441 radio-sensitizes lung tumor cells with little effect on double strand break repair. Cancer Sci. 2016 Sep;107(9):1250-5.
Zhang B, Wu H, Hao J, et al. Inhibition of DNA-PKcs activity re-sensitizes uveal melanoma cells to radio-and chemotherapy. Biochemical and Biophysical Research Communications. 2019
Feng Y L, Liu S C, Chen R D, et al.Proximal binding of dCas9 at a DNA double strand break stimulates homology-directed repair as a local inhibitor of classical non-homologous end joining.Nucleic Acids Research.2023: gkad116.
Robert F, et al. Pharmacological inhibition of DNA-PK stimulates Cas9-mediated genome editing. Genome Med. 2015 Aug 27;7:93.
Yang C, et al. NU7441 Enhances the Radiosensitivity of Liver Cancer Cells. Cell Physiol Biochem. 2016;38(5):1897-905.
Cruet-Hennequart S, et al. UV-induced RPA phosphorylation is increased in the absence of DNA polymerase eta and requires DNA-PK. DNA Repair (Amst). 2006 Apr 8;5(4):491-504.
Zhao Y, et al. Preclinical evaluation of a potent novel DNA-dependent protein kinase inhibitor NU7441. Cancer Res. 2006 May 15;66(10):5354-62.
Zhang B, Wu H, Hao J, et al. Inhibition of DNA-PKcs activity re-sensitizes uveal melanoma cells to radio-and chemotherapy[J]. Biochemical and Biophysical Research Communications. 2019

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