Product Data Sheet

Product Name: KPT-276
Cat. No.: GC12142

Chemical Properties

Cas. No.	1421919-75-6		
Chemical Name	(Z)-3-[3-[3,5-bis(trifluoromethyl)phenyl]-1,2,4-triazol-1-yl]-1-(3,3-difluoroazetidin-1-yl)prop-2-en-1-one		
SMILES	C1C(CN1C(=O)C=CN2C=NC(=N2)C3=CC(=CC(=C3)C(F)(F)F)C(F)(F)F)(F)F		
Formula	$C_{16}H_{10}F_8N_4O$	M.Wt	426.26
Solubility	≥ 19.85mg/mL in DMSO	Storage	Store at -20°C
General tips	For obtaining a higher solubility , please warm the tube at 37 ℃ and shake it in the ultrasonic bath for a while.Stock solution can be stored below -20℃ for several months.		
Shipping Condition	Evaluation sample solution : ship with blue ice All other available size: ship with RT , or blue ice upon request.		
Structure	KPT-276		

Protocol

Cell experiment [1]:

Cell lines	Twelve human myeloma cell lines
Preparation method	The solubility of this compound in DMSO is >19.85 mg/mL. General tips for obtaining a higher concentration: Please warm the tube at 37 ℃ for 10 minutes and/or shake it in the ultrasonic bath for a while. Stock solution can be stored below -20℃ for several months.

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Reacting condition	24 h
Applications	In twelve HMCLs, treatment with KPT-276 (≤ 1 μM) for 72 h reduced cell viability with a median IC50 value of approximately 160 nM. KPT-276 treatment reduced c-Myc, CDC25A and BRD4 levels in both MM1.S and OCI-MY5. Treatment with KPT-276 for 24 h induced cell cycle arrest in MM1.S cells.

Animal experiment [1]:

Animal models	Athymic NCr-nu/nu mice bearing MM1.S cells, Vk*MYC mouse model
Dosage form	Oral gavage, 150 mg/kg, 3 days/week for 3 weeks;
Application	In a xenograft MM1.S MM model, the tumor volume significantly decreased after treatment with KPT-276 (12 days). KPT-276 reduced monoclonal spikes in the Vk*MYC transgenic MM mouse model, and inhibited tumor growth in a xenograft MM mouse model.
Other notes	Please test the solubility of all compounds indoor, and the actual solubility may slightly differ with the theoretical value. This is caused by an experimental system error and it is normal.

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References:

[1]. Schmidt J, Braggio E, Kortuem K M, et al. Genome-wide studies in multiple myeloma identify XPO1/CRM1 as a critical target validated using the selective nuclear export inhibitor KPT-276[J]. Leukemia, 2013, 27(12): 2357.

Background

KPT-276, analog of KPT-185, is a selective inhibitor of nuclear export (SINE) and CRM1 [1].

Chromosomemaintenance protein 1 (CRM1) is a nuclear export receptor involved in the active transport of transcription factors, cell-cycle regulators, tumor suppressors and RNA molecules. In cancer, CRM1 is overexpression and overactive transport [1].

KPT-276 is an orally bioavailable and selective CRM1 inhibitor that irreversibly binds to CRM1 and blocks CRM1-mediated nuclear export [1]. In human multiple myeloma (MM) cell lines (HMCLs), KPT-276 irreversibly and specifically inhibited the nuclear export of XPO1, which encoded CRM1 and significantly reduced the viability of HMCLs. In bone marrow cells isolated from MM patients, KPT-276 induced apoptosis. Also, KPT-276 downregulated the expression of c-MYC, CDC25A and BRD4, which caused G1/S phase arrest [2].

In a xenograft human acute myeloid leukemia (AML) murine model, KPT-276 significantly increased the survival of mice and reduced the amount of white blood cells. Also, KPT-276 significantly reduced spleen weight and FLT3 protein expression [1]. In a xenograft MM mouse model, KPT-276 inhibited tumor growth [2].

References:
[1]. Ranganathan P, Yu X, Na C, et al. Preclinical activity of a novel CRM1 inhibitor in acute myeloid leukemia. Blood, 2012, 120(9): 1765-1773.
[2]. Schmidt J, Braggio E, Kortuem KM, et al. Genome-wide studies in multiple myeloma

identify XPO1/CRM1 as a critical target validated using the selective nuclear export inhibitor KPT-276. Leukemia, 2013, 27(12): 2357-2365.

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