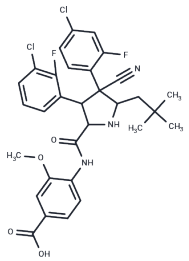
Data Sheet (Cat.No.T6254)

TargetMol

Idasanutlin

Chemical Properties



CAS No. : 1229705-06-9

Formula: C31H29Cl2F2N3O4

Molecular Weight: 616.48

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	Idasanutlin (Ro 5503781) is a potent, highly selective small-molecule MDM2 inhibitor with an IC_{50} value of 6 nM. Idasanutlin exerts its antitumor effects primarily by restoring the function of the p53 signaling pathway. Idasanutlin can be used in cancer treatment research.
Targets(IC50)	Mdm2,E1/E2/E3 Enzyme,MDM-2/p53
In vitro	**Methods**: MOLT-3 control and TP53 KO cells were treated with Idasanutlin at a concentration gradient (0.01–10 μM) for 72 hours. Cell viability was assessed using the CellTiter-Glo assay. **Results**: Idasanutlin exhibited dose-dependent inhibition in TP53 wild-type MOLT-3 cells but was ineffective in TP53 knockout cells, confirming p53-dependent activity. [1]
In vivo	**Methods**: Various T-ALL PDX cell lines (DFCI12, DFCI15, DFAT28537, CBAT27299) were intravenously injected or implanted into NSG mice to establish systemic leukemia models. Tumor burden was monitored by flow cytometry analysis of human $CD45^+$ cells. Once tumor establishment was confirmed, mice were randomly assigned to receive oral administration of Idasanutlin (40 mg/kg, administered for 5 consecutive days followed by a 2-day rest period) or Navitoclax (100 mg/kg, once daily) for 14 days. **Results**: Idasanutlin significantly inhibited leukemia progression and significantly prolonged survival in all four PDX models. [1] **Methods**: Human GBM10 cells were stereotaxically implanted into the brains of Rag2-null immunodeficient rats to establish an orthotopic tumor model. After tumor maturation (49 days post-implantation), multimodal imaging was performed, followed by oral administration of Idasanutlin (40 mg/kg, administered as 5 consecutive days of dosing followed by 2 days of rest) for a total of 14 days, and intraperitoneal injection of temozolomide (50 mg/m², once daily) for a total of 5 days, to assess overall survival. **Results**: Compared with the monotherapy group or the control group, the overall survival of rats in the Idasanutlin + temozolomide combination therapy group was significantly prolonged. [2]
Kinase Assay	Biochemical Binding Affinity - HTRF Assay: The p53-MDM2 HTRF assay is performed in buffer containing 50 mM Tris-HCl, pH 7.4, 100 mM NaCl, 1 mM DTT, 0.02 or 0.2 mg/ml BSA. Small-molecule inhibitors are stored in aliquots as 10 mM stock solutions in DMSO at 4°C in 96-deep-well plates. It is thawed and mixed immediately prior to testing. The compound is incubated with GST-MDM2 and a biotinylated p53 peptide for one hour at

Kinase Assay	37°C. Phycolink goat anti-GST (Type 1) allophycocyanin and Eu-8044-streptavidin are then added and followed by one hour incubation at room temperature. Plates are read using the Envision fluorescence reader. IC50 values are determined from inter-plate duplicate or triplicate sets of data. Data are analyzed by XLfit4 (Microsoft) using a 4 Parameter Logistic Model (Sigmoidal Dose-Response Model) and the equation Y= (A+ ((B-A)/ (1+ ((C/x)^D)))), where A and B are enzyme activity in the absence or presence of infinite inhibitor compound, respectively, C is the IC50 and D is the Hill coefficient.
Cell Research	Cell proliferation is evaluated by the tetrazolium dye assay. The concentration at which 50% inhibition (IC50) or 90% inhibition (IC90) of cell proliferation is determined from the linear regression of a plot of the logarithm of the concentration versus percent inhibition. (Only for Reference)

Solubility Information

Solubility	H2O: < 1 mg/mL (insoluble or slightly soluble), DMSO: 65 mg/mL (105.44 mM),Sonication is recommended. Ethanol: 8 mg/mL (12.98 mM),Heating is recommended. (< 1 mg/ml refers to the product slightly soluble or insoluble)
In vivo Formulation	20% Cremophor EL: 5 mg/mL (8.11 mM),Suspension. *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	1.6221 mL	8.1106 mL	16.2211 mL
5 mM	0.3244 mL	1.6221 mL	3.2442 mL
10 mM	0.1622 mL	0.8111 mL	1.6221 mL
50 mM	0.0324 mL	0.1622 mL	0.3244 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

Johansson KB, et al. Idasanutlin and navitoclax induce synergistic apoptotic cell death in T-cell acute lymphoblastic leukemia. Leukemia. 2023 Dec;37(12):2356-2366.
Vollmer J, Ecker J, Hielscher T, et al.Class I HDAC inhibition reduces DNA damage repair capacity of MYC-amplified medulloblastoma cells.Journal of Neuro-Oncology.2023: 1-16.
Jackson LR, et al. Use of multimodality imaging, histology, and treatment feasibility to characterize a transgenic Rag2-null rat model of glioblastoma. Front Oncol. 2022 Nov 22;12:939260.

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