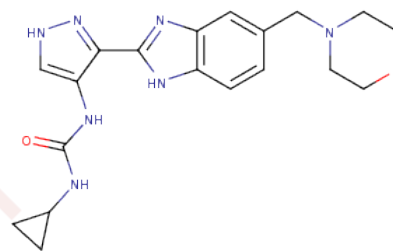


AT9283

Chemical Properties

CAS No. : 896466-04-9
Formula: C₁₉H₂₃N₇O₂
Molecular Weight: 381.43
Appearance: no data available
Storage: Powder: -20°C for 3 years | In solvent: -80°C for 1 year



Biological Description

Description	AT9283 (J-504568) is an effective multi-targeted inhibitor of JAK2 (IC ₅₀ =1.2 nM) and JAK3 (IC ₅₀ =1.1 nM), Aurora A, Aurora B and Abl (T315I).
Targets (IC ₅₀)	Apoptosis, FLT, JAK, Bcr-Abl, Aurora Kinase, Autophagy
In vitro	In mice bearing HCT116 human colorectal carcinoma xenografts, AT9283 (15-20 mg/kg) was capable of inhibiting tumor growth.
In vivo	In HCT116 cells, AT9283 inhibits Aurora B kinase activity with an IC ₅₀ value of 30 nM, leading to a polyploid phenotype and concurrently suppressing colony formation. Moreover, AT9283 significantly inhibits a range of kinases, including Aurora A (IC ₅₀ =3 nM), Aurora B (IC ₅₀ =3 nM), JAK3 (IC ₅₀ =1.1 nM), JAK2 (IC ₅₀ =1.2 nM), and Abl (IC ₅₀ =4 nM).
Kinase Assay	Aurora A and Aurora B Kinase Assays: Assays for Aurora A and B are performed in a DELFIA format. Aurora A enzyme is incubated with AT9283 and 3 μM cross-tide substrate (biotin-CGPKGPGRRRRTSSFAEG) in 10 mM MOPS, pH 7, 0.1 mg/mL BSA, 0.001% Brij-35, 0.5% glycerol, 0.2 mM EDTA, 10 mM MgCl ₂ , 0.01% β-mercaptoethanol, 15 μM ATP, and 2.5% DMSO. Aurora B enzyme is incubated with AT9283, 3 μM of the above substrate in 25 mM Tris, pH 8.5, 5 mM MgCl ₂ , 0.1 mg/mL BSA, 0.025% Tween-20, 1 mM DTT, 15 μM ATP, and 2.5% DMSO. Reactions are allowed to proceed for 60 minutes and 45-90 minutes for Aurora A and Aurora B, respectively, before quenching with EDTA. The reaction mixtures are then transferred to a neutravidin-coated plate, and phosphorylated peptide is quantified by means of a phospho-specific antibody and a europium labeled secondary antibody using time-resolved fluorescence (excitation, 337 nm; emission, 620 nm). IC ₅₀ values for the control compounds are 92 nM (Aurora A assay) and 17 nM (Aurora B).
Cell Research	HCT 116 cells are cultured in DMEM + 10% FBS + GLUTAMAX I. Black 96-well flat-bottomed (clear) tissue culture treated plates are seeded in 200 μL of medium and incubated for approximately 16 hours at 37°C in a humidified atmosphere of 5% CO ₂ in air. Cells are treated with test compound at nine different concentrations (spanning 1 nM to 10 μM, plus DMSO vehicle control) and then incubated for 72 hours. Polyploidy morphological observations of the cells are then noted. The concentration of AT9283 required to produce a distinct polyploid phenotype is reported. Cells are seeded at a concentration of 75-100 cells/mL relevant culture media onto 6- or 24-well tissue culture plates and allowed to recover for 16 hours. Test compound (11 concentrations spanning 0.1 nM to 10 μM) or vehicle control (DMSO)

is added to duplicate wells to give a final DMSO concentration of 0.1%. Following compound addition, colonies are allowed to grow between 10 and 14 days for optimum discrete colony counting. Colonies are fixed in 2 mL of Carnoy's fixative (25% acetic acid, 75% MeOH) and stained in 2 mL of 0.4% w/v crystal violet. The numbers of colonies in each well is counted. IC₅₀ values are calculated by sigmoidal dose-response (variable slope) IC₅₀ curves using Prism Graphpad software. (Only for Reference)

Solubility Information

Solubility	DMSO: 71 mg/mL (186.1 mM), Ethanol: 22 mg/mL(57.7 mM), H ₂ O: < 1 mg/mL (insoluble or slightly soluble), < 1 mg/ml refers to the product slightly soluble or insoluble)
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Preparing Stock Solutions

	1mg	5mg	10mg
1 mM	2.6217 mL	13.1086 mL	26.2171 mL
5 mM	0.5243 mL	2.6217 mL	5.2434 mL
10 mM	0.2622 mL	1.3109 mL	2.6217 mL
50 mM	0.0524 mL	0.2622 mL	0.5243 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.

Reference

Howard S, et al. J Med Chem, 2009, 52(2), 379-388.

Cheng S, Jin P, Li H, et al. Evaluation of CML TKI Induced Cardiovascular Toxicity and Development of Potential

Inhibitor · Natural Compounds · Compound Libraries · Recombinant Proteins

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