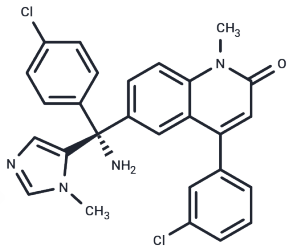
Data Sheet (Cat.No.T6271)

TargetMol

Tipifarnib

Chemical Properties



CAS No. : 192185-72-1

Formula: C27H22Cl2N4O

Molecular Weight: 489.4

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	Tipifarnib (IND 58359) is a nonpeptidomimetic quinolinone with potential antineoplastic activity. Tipifarnib binds to and inhibits the enzyme farnesyl protein transferase, an enzyme involved in protein processing (farnesylation) for signal transduction. By inhibiting the farnesylation of proteins, this agent prevents the activation of Ras oncogenes, inhibits cell growth, induces apoptosis, and inhibits angiogenesis.
Targets(IC50)	Transferase
In vitro	Using Tipifarnib 5 μM for 72 hours, the percentage of apoptotic cells is significantly higher in drug-treated compared to DMSO-treated LGL T-cells. Using T-cells from healthy donors, Tipifarnib reduces the percentage of IFNγ-positive cells in a time-dependent manner. Tipifarnib reduces the amount of activated Ras in precipitates compared to DMSO. [2] Tipifarnib exerts selective in vitro toxicity against clonal MDS hematopoiesis at concentrations less than 10 nM the effect being more prominent in white cell progenitors. This action is not due to apoptosis induction as both normal and MDS progenitors displays equivalent DiOC3 and annexin V expression up to 72 hours after exposure to Tipifarnib. [3] Combining Tipifarnib with 10 nM 4-OH-tamoxifen in the presence of E2 reduces the IC50 8-fold from 400 to 50 nM. [4] Tipifarnib induces apoptosis in U937 cells. [5] In addition, Tipifarnib inhibits isolated human farnesyltransferase for a lamin B peptide and for the K-RasB peptide with IC50 of 0.86 nM and 7.9 nM, respectively. [6]
In vivo	Ki-67 is lower in the tumors treated with E2 withdrawal plus Tipifarnib compared with E2 withdrawal alone. The combination of tamoxifen and Tipifarnib results in significantly lower Ki-67 compared with either tamoxifen or Tipifarnib alone (mean of 5% versus 16.9% and 67.3%, respectively). [4] In contrast, no significant difference in apoptotic scores is seen between the treatment groups. Tipifarnib alone also reduces the CTI compared with control. The combination of tamoxifen and Tipifarnib or Tipifarnib coupled with E2 withdrawal is most effective at lowering the CTI (0.8 and 0.7, respectively), which may account for the decrease in tumor volume. [4]
Cell Research	MACS-selected CD34+ cells are seeded in Methocult 4435 'complete' 1% bovine serum albumin, 3 U/mL recombinant human (rh) erythropoietin, 0.1 mM 2-mercaptoethanol, 2 mM L-glutamine and the following cytokines: 50 ng/mL rh stem cell factor, 20 ng/mL rh GM-CSF, 20 ng/mL rh IL-3, 20 ng/mL rh IL-6 and 20 ng/mL h G-CSF. DMSO or Tipifarnib is added at the concentrations of 2.5, 10, 25 and 50 nM at day 1. All cultures are performed in duplicates and the numbers of colonies are scored after 14 days of incubation at 37 °C

Cell Research	in a humidified incubator containing 5% CO2</sub(Only for Reference)

Solubility Information

Solubility	DMSO: 48.9 mg/mL (99.92 mM),Sonication is recommended. Ethanol: 9.8 mg/mL (20.02 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: 2 mg/mL (4.09 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	2.0433 mL	10.2166 mL	20.4332 mL
5 mM	0.4087 mL	2.0433 mL	4.0866 mL
10 mM	0.2043 mL	1.0217 mL	2.0433 mL
50 mM	0.0409 mL	0.2043 mL	0.4087 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

Margolin KA, et al. Clin Cancer Res. 2012, 18(4), 1129-1137.
Bai F, et al. Cancer Immunol Immunother. 2012, 61(4), 523-533.
Kotsianidis I, et al. Acta Haematol. 2008, 120(1), 51-56.
Martin LA, et al. Mol Cancer Ther. 2007, 6(9), 2458-2467.
Krzykowska-Petitjean K, et al. J Cancer Res Clin Oncol. 2012, 138(3), 537-544.

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