

Genz-644282

Chemical Properties

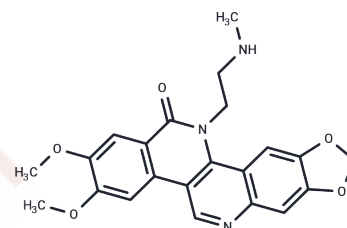
CAS No. : 529488-28-6

Formula: C₂₂H₂₁N₃O₅

Molecular Weight: 407.42

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	Genz-644282, a novel non-camptothecin topoisomerase I inhibitor for cancer treatment.
Targets(IC50)	Topoisomerase
In vitro	Human bone marrow CFU-GM was more sensitive to the Top1 inhibitors than was mouse bone marrow CFU-GM. The ratio of mouse to human IC(90) values was more than 10 for the camptothecins and less than 10 for Genz-644282, which had more potency as a cytotoxic agent toward human tumor cells in culture than the camptothecins in the colony-forming and 72-hour proliferation assays. Genz-644282 has superior or equal antitumor activity in the human tumor xenografts than the standard drug comparators [1].
In vivo	In vivo, Genz-644282 at its MTD (4 mg/kg) induced maintained complete responses (MCR) in 6/6 evaluable solid tumor models. At 2 mg/kg Genz-644282 induced CR or MCR in 3/3 tumor models relatively insensitive to topotecan, but there were no objective responses at 1 mg/kg. Further testing at 2 mg/kg showed that Genz-644282 induced objective regressions in 7 of 17 (41%) models. There was a significant correlation between predictive response scores based on Affymetrix U133Plus2 baseline tumor expression profiles and the observed in vivo responses to Genz-644282[2].
Cell Research	Colony-forming assays were conducted with mouse and human bone marrow and eight human tumor cell lines. In addition, 29 human tumor cell lines representing a range of histology and potential resistance mechanisms were assayed for sensitivity to Genz-644282 in a 72-hour exposure assay. The efficacy of Genz-644282 was compared with standard anticancer drugs (i.e., irinotecan, docetaxel, and dacarbazine) in human tumor xenografts of colon cancer, renal cell carcinoma, non-small cell lung cancer, and melanoma[1].
Animal Research	Genz-644282 was tested against the PPTP in vitro panel (0.1 nM to 1 μM), and in vivo using three times per week × 2 schedule repeated at day 21 at its maximum tolerated dose (MTD) of 4 mg/kg. Subsequently Genz-644282 was tested at 4, 3, 2, and 1 mg/kg in 3 models to assess the dose-response relationship. mRNA gene signatures predictive for Genz-644282 response in vitro were applied to select 15 tumor models that were evaluated prospectively[2].

Solubility Information

Solubility	DMSO: 2 mg/mL (4.91 mM), Sonication and heating are recommended. (< 1 mg/ml refers to the product slightly soluble or insoluble)
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Preparing Stock Solutions

	1mg	5mg	10mg
1 mM	2.4545 mL	12.2723 mL	24.5447 mL
5 mM	0.4909 mL	2.4545 mL	4.9089 mL
10 mM	0.2454 mL	1.2272 mL	2.4545 mL
50 mM	0.0491 mL	0.2454 mL	0.4909 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

Kurtzberg L S , Roth S , Krumbholz R , et al. Genz-644282, a Novel Non-Camptothecin Topoisomerase I Inhibitor for Cancer Treatment[J]. Clinical Cancer Research, 2011, 17(9):2777-2787.

Houghton P J , Lock R , Carol H , et al. Testing of the Topoisomerase 1 Inhibitor Genz644282 by the Pediatric Preclinical Testing Program[J]. Pediatric Blood & Cancer, 2012, 58(2):200-209.

Inhibitor · Natural Compounds · Compound Libraries · Recombinant Proteins

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