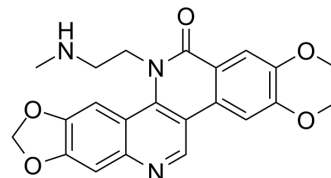


Genz-644282

Cat. No.:	HY-16228
CAS No.:	529488-28-6
Molecular Formula:	C ₂₂ H ₂₁ N ₃ O ₅
Molecular Weight:	407.42
Target:	Topoisomerase
Pathway:	Cell Cycle/DNA Damage
Storage:	4°C, protect from light * In solvent : -80°C, 6 months; -20°C, 1 month (protect from light)



SOLVENT & SOLUBILITY

In Vitro

DMSO : 3.64 mg/mL (8.93 mM; ultrasonic and warming and heat to 75°C)

Concentration	Solvent	Mass		
		1 mg	5 mg	10 mg
Preparing Stock Solutions	1 mM	2.4545 mL	12.2723 mL	24.5447 mL
	5 mM	0.4909 mL	2.4545 mL	4.9089 mL
	10 mM	---	---	---

Please refer to the solubility information to select the appropriate solvent.

BIOLOGICAL ACTIVITY

Description

Genz-644282 is a non-camptothecin topoisomerase I inhibitor, used for cancer research.

IC₅₀ & Target

Topoisomerase I

In Vitro

Genz-644282 is a topoisomerase I inhibitor. Genz-644282 shows potent activities against 29 human tumor cell lines with IC₅₀s ranging from 1.8 nM to 1.8 μM^[1]. Genz-644282 suppresses the PPTP cell lines, with IC₅₀s of 0.2-21.9 nM, and the mean IC₅₀ value is 1.2 nM^[2]. Genz-644282 is potent at trapping Top1-DNA covalent cleavage complexes. Genz-644282 (0.1 μM) induces γH2AX foci in human colon cancer HCT116 cells and breast cancer MCF7 cells. Genz-644282 is cytotoxic on the CPT-resistant human cancer cell lines^[3].

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

In Vivo

Genz-644282 (1-4 mg/kg) is active when administered intravenously to the mice. Genz-644282 (2.7 mg/kg, i.v.) causes tumor growth delay (TGD) of 34 days in the human HCT-116 colon cancer xenograft, 27 days in the human HT-29 colon carcinoma xenograft and mice bearing the NCI-H460 human non-small cell lung carcinoma. Genz-644282 (2 mg/kg, i.v.) results in a TGD of 33 days in the human HCT-15 colon carcinoma xenograft, and 28 days in mice bearing LOX-IMVI melanoma. Moreover, Genz-644282 (1 mg/kg, i.v.) leads to 14 days of TGD in mice bearing the DLD-1 human colon carcinoma xenograft. Genz-644282 (1.7 mg/kg, i.v.) also produces a TGD of 23 days in mice bearing 786-O tumors and 33 days in NCI-H1299 human non-

small cell lung carcinoma xenograft^[1]. Genz644282 at maximum tolerated dose (MTD, 4 mg/kg) results in maintained complete responses (MCR) in 6/6 evaluable solid tumor models. Genz644282 (2 mg/kg) induces CR or MCR in 3/3 tumor models and causes objective regressions in 7 of 17 (41%) models, but there are no objective responses at 1 mg/kg^[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Cell Assay ^[1]

Twenty-nine established human tumor cell lines are exposed to a concentration range of Genz-644282 in two-four independent experiments. Human tumor cell lines representing a range of histology and potential resistance mechanisms include MIA PaCa-2, AsPC-1, BxPC-3, CFPAC-1, Hs766T and Capan-1 pancreatic cancers, MEL624, C32, Hs695T and SK-MEL-3 melanomas, NCI-H1299, NCI-H292, NCI-H1915 and SW900 non-small cell lung cancers, HCC1395, HCC1937, HCC202, Hs578T, T-47D and ZR-75-1 breast cancer, ACHN, 769-P, A-498, A-704, SW156, Caki-2 and TK-10 renal cancers and OVCAR-4 and OVCAR-5 ovarian cancers. Cells are plated at 4×10^3 /well in 96-well tissue culture plates in 100 μ L RPMI medium supplemented with 5% FBS and 12 concentrations of Genz-644282 from 0.1 nM to 10 μ M, with each concentration tested in triplicate. Plates are incubated overnight at 37°C in humidified air with 5% CO₂. Plates are incubated with Genz-644282 at 37°C with humidified air/5% CO₂ for 72 hrs. After the incubation period, the test plates are read utilizing Cell Titer-Glo Luminescent Cell Viability Assay. Luminescence is measured with a Synergy HT plate reader utilizing the associated inetic software, Version #3.4. Luminescence data are converted to growth fraction by comparison to the luminescence for the untreated control for each cell line and IC₅₀ and IC₉₀ values determined from the graphical data. Each cell line is tested in at least two independent experiments^[1].

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Animal Administration ^[1]

Nu/nu mice are implanted subcutaneously with a 4 mm³ tumor fragment, and treatments are initiated when tumors reach 200 mm³. Compounds are prepared freshly prior to injection, with Genz-644282 is formulated in M/6 lactate, irinotecan in D5W (5% Dextrose, aqueous), gemcitabine in saline, and docetaxel in ethanol, Cremophor EL and saline. Genz-644282 is compared with irinotecan in experiments with the human HCT-116, HT-29, HCT-15 and DLD-1 colon carcinoma and 786-O renal cell carcinoma xenografts. Irinotecan is administered at 60 mg/kg/day by IV injection every fourth day for three injections. Genz-644282 is compared with docetaxel in the human CIH460 non-small cell lung carcinoma xenograft. Docetaxel is administered at 12, 16 or 20 mg/kg/day by IV injection on alternate days for three injections. Genz-644282 is compared with dacarbazine in the human LOX-IMVI melanoma xenograft. Dacarbazine is administered at 90 mg/kg/day by IP injection once daily for 5 days. Genz-644282 is administered at 1, 1.36, 1.7, 2.7 or 4.1 mg/kg/day by IV on alternate days 3-times per week for 2 weeks in all in vivo experiments^[1].

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- J Mol Med (Berl). 2019 Aug;97(8):1183-1193.

See more customer validations on www.MedChemExpress.com

REFERENCES

- [1]. Kurtzberg LS, et al. Genz-644282, a novel non-camptothecin topoisomerase I inhibitor for cancer treatment. Clin Cancer Res. 2011 May 1;17(9):2777-87.
- [2]. Houghton PJ, et al. Testing of the topoisomerase 1 inhibitor Genz-644282 by the pediatric preclinical testing program. Pediatr Blood Cancer. 2012 Feb;58(2):200-9.
- [3]. Sooryakumar D, et al. Molecular and cellular pharmacology of the novel noncamptothecin topoisomerase I inhibitor Genz-644282. Mol Cancer Ther. 2011 Aug;10(8):1490-9.

Caution: Product has not been fully validated for medical applications. For research use only.

Tel: 609-228-6898

Fax: 609-228-5909

E-mail: tech@MedChemExpress.com

Address: 1 Deer Park Dr, Suite Q, Monmouth Junction, NJ 08852, USA