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Lieferung & Zahlungsart

siehe unsere Liefer- und Versandbedingungen

Zuschläge

- Mindermengenzuschlag
- Trockeneiszuschlag
- Gefahrgutzuschlag
- Expressversand

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Alvespimycin

Cat. No.: HY-10389

CAS No.: 467214-20-6

Molecular Formula: $C_{32}H_{48}N_4O_8$

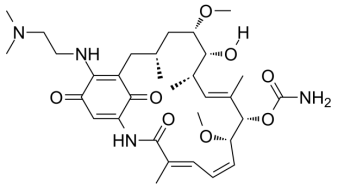
Molecular Weight: 616.75

Target: HSP

Pathway: Cell Cycle/DNA Damage; Metabolic Enzyme/Protease

Storage:

Powder	-20°C	3 years
	4°C	2 years
In solvent	-80°C	6 months
	-20°C	1 month



SOLVENT & SOLUBILITY

In Vitro

DMSO : 100 mg/mL (162.14 mM; Need ultrasonic)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	1.6214 mL	8.1070 mL	16.2140 mL
	5 mM	0.3243 mL	1.6214 mL	3.2428 mL
	10 mM	0.1621 mL	0.8107 mL	1.6214 mL

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

In Vivo

1. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: ≥ 2.5 mg/mL (4.05 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

Alvespimycin (17-DMAG) is a potent inhibitor of Hsp90, binding to Hsp90 with an EC_{50} of 62 ± 29 nM.

IC_{50} & Target

HSP90	GRP94
62 nM (EC50)	65 nM (EC50)

In Vitro

Alvespimycin (17-DMAG) is a potent inhibitor of Hsp90, binding to Hsp90 with an EC_{50} of 62 nM. Alvespimycin (17-DMAG) inhibits the growth of the human cancer cell lines SKBR3 and SKOV3, which overexpress Hsp90 client protein Her2, and causes down-regulation of Her2 as well as induction of Hsp70 consistent with Hsp90 inhibition, for Her2 degradation with EC_{50} of 8 ± 4 nM and 46 ± 24 nM in SKBR3 and SKOV3 cells, respectively; for Hsp70 induction with EC_{50} of 4 ± 2 nM and 14 ± 7 nM in SKBR3 and SKOV3 cells, respectively[1]. Compared with the vehicle control, Alvespimycin (17-DMAG) dose-dependent apoptosis (P<0.001 averaged across 24- and 48-hour time points) at concentrations of 50 nM to 500 nM, which represent pharmacologically attainable doses. Similar to many other agents, Alvespimycin (17-DMAG) also demonstrates time-

	dependent apoptosis (P <0.001, averaged across all doses) in chronic lymphocytic leukemia (CLL) cells with extended exposure from 24 to 48 hours. In addition,Alvespimycin (17-DMAG) is much more potent after 24 and 48 hours of treatment than 17-AAG[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	The tumors are grown for two months before the start of i.p. injections every four days over one month with 0, 50, 100 and 200 mg/kg dipalmitoyl-radicicol or 0, 5, 10 and 20 mg/kg Alvespimycin (17-DMAG). Despite sample heterogeneity, the HSP90 inhibitor-treated animals have significantly lower tumour volumes than the vehicle control-treated animals. HSP90 inhibitors have been shown to cause liver toxicity in an animal model of gastrointestinal cancer. Nevertheless, the reduction in tumor size using dipalmitoyl-radicicol is statistically significant at 100 mg/kg, while Alvespimycin (17-DMAG) at either 10 or 20 mg/kg elicits a significant reduction in tumor size[3]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Cell Assay [2]	MTT assays are performed to determine cytotoxicity. A total of 1×10^6 CD19-selected B cells from CLL patients are incubated for 24 or 48 hours in Alvespimycin, 17-AAG, or vehicle. MTT reagent is then added, and plates are incubated for an additional 24 hours before spectrophotometric measurement. Apoptosis is determined by staining with annexin V-fluorescein isothiocyanate and propidium iodide (PI). After exposure to drugs, cells are washed with phosphate-buffered saline and stained in 1 time binding buffer. Cell death is assessed by flow cytometry. Data are analyzed with the System II software package. A total of 10000 cells are counted for each sample. Mitochondrial membrane potential changes are assessed by staining with the lipophilic cationic dye JC-1 and analysis by flow cytometry[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Animal Administration [3]	Mice[3] Young male CB-17/IcrHsd-Prkdc-SCID mice are used. Recombinant xenografts are made by mixing 1×10^5 BPH1 cells and 2.5×10^5 CAF per graft in collagen solution, allowed to gel, covered with medium and cultured overnight. Tumors are allowed to form over eight weeks, and then treated for four weeks with three different doses of dipalmitoyl-radicicol (50, 100 and 200 mg/kg) and Alvespimycin (5, 10 and 20 mg/kg) via intraperitoneal injections of compounds in sesame oil every four days. After 12 weeks in total, the mice are sacrificed, their kidneys resected, grafts cut in half and photographed before processing for histology. Graft dimensions are measured and the resultant tumour volume is calculated using the formula; volume=width × length × depth × π/6. This formula represents a conservative approach to evaluate tumour volumes, as it understates the volume of large, invasive tumours compared with smaller, non-invasive tumours. Resected grafts are fixed in 10% formalin, embedded in paraffin and processed for immunohistochemistry. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- Nat Commun. 2021 Jul 22;12(1):4457.
- Theranostics. 2020 Jul 9;10(18):8415-8429.
- Theranostics. 2020 Jul 9;10(18):8415-8429.
- Pharmacol Res. 2020 Jan;151:104512.
- Cell Death Dis. 2022 Jan 21;13(1):73.

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REFERENCES

[1]. Ge J, et al. Design, synthesis, and biological evaluation of hydroquinone derivatives of 17-amino-17-demethoxygeldanamycin as potent, water-soluble inhibitors of Hsp90. J Med Chem. 2006 Jul 27;49(15):4606-15.

[2]. Hertlein E, et al. 17-DMAG targets the nuclear factor-kappaB family of proteins to induce apoptosis in chronic lymphocytic leukemia: clinical implications of HSP90 inhibition. Blood. 2010 Jul 8;116(1):45-53.

[3]. Henke A, et al. Reduced Contractility and Motility of Prostatic Cancer-Associated Fibroblasts after Inhibition of Heat Shock Protein 90. Cancers (Basel). 2016 Aug 24;8(9). pii: E77.

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