AVN-944

Cat. No.: HY-13560

CAS No.: 297730-17-7

Molecular Formula: $C_{25}H_{27}N_5O_5$

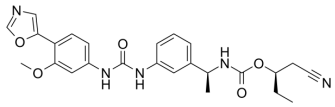
Molecular Weight: 477.51

Target: Arenavirus; DNA/RNA Synthesis; Apoptosis; Caspase; Bcl-2 Family

Pathway: Anti-infection; Cell Cycle/DNA Damage; Apoptosis

Storage:

Powder	-20°C	3 years
	4°C	2 years
In solvent	-80°C	2 years
	-20°C	1 year



SOLVENT & SOLUBILITY

In Vitro

DMSO : 100 mg/mL (209.42 mM; Need ultrasonic)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	2.0942 mL	10.4710 mL	20.9420 mL
	5 mM	0.4188 mL	2.0942 mL	4.1884 mL
	10 mM	0.2094 mL	1.0471 mL	2.0942 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 (5.24 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (5.24 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

AVN-944 (VX-944) is an orally active, potent, selective, noncompetitive and specific inhibitor of IMPDH (inosine monophosphate dehydrogenase). AVN-944 is an essential rate-limiting enzyme in de novo guanine nucleotide synthesis. AVN-944 is also an inhibitor of arenavirus RNA synthesis, and blocks arenavirus infection. AVN-944 has broad anti-cancer activities, and can be used for multiple myeloma (MM) and acute myeloid leukemia (AML) research[1][2][3].

In Vitro

AVN-944 (0-1 μM, 48 h) inhibits growth of human multiple myeloma (MM) cell lines in a dose-dependent manner[1].
AVN-944 (800 nM, 0-72 h) induces apoptosis in MM cell lines via a caspase-independent, Bax/AIF/Endo G pathway[1].
AVN-944 (0-200 nM) enhances the cytotoxicity of Doxorubicin (HY-15142A) and Melphalan (HY-17575)[1].
AVN-944 inhibits the proliferation of the human MV-4-11 and murine Ba/F3-Flt3-ITD-dependent cell lines with IC_{50} values of 26 and 30 nM, respectively[2].

AVN-944 (0-32 μM, 48 h) shows good activity against arenavirus infection at low doses (7.5 μM) with less cytotoxicity[3].
AVN-944 (0-6.4 μM, 48 h) does not reduce the viability of peripheral blood mononuclear cells (PBMNCs)[1].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Cell Proliferation Assay[1]

Cell Line:	RPMI8226, MM.1S, and U266 cells
Concentration:	0, 100, 200, 300, 400, 600, 1000 nM
Incubation Time:	48 h
Result:	Significantly inhibited the growth of RPMI8226, MM.1S, and U266 cells in a dose-dependent fashion, with 50% inhibition (IC_{50}) values at 48 h of 450, 450, and 600 nM, respectively. Inhibited growth of drug-resistant cell lines, including Doxorubicin (Dox)-resistant RPMI8226-Dox40, Melphalan (Mel) resistant RPMI8226-LR5, and Dex (Dexamethasone) resistant MM.1R cells, with IC_{50} values similar to the parental drug-sensitive cell lines.

Apoptosis Analysis[1]

Cell Line:	MM.1S and RPMI8226 cells
Concentration:	800 nM
Incubation Time:	48 and 72 h
Result:	Induced apoptosis in MM cell lines.

Western Blot Analysis[1]

Cell Line:	MM.1S and RPMI8226 cells
Concentration:	800 nM
Incubation Time:	12, 24, 48 h
Result:	Induced modest cleavage of caspase 3, 8 and 9 in MM.1S cells and RPMI8226 cells. Markedly upregulated Bax and Bak, without significant changes in Bcl-2, Mcl-1, XIAP, and Bad. Observed translocation of mitochondrial proapoptotic proteins, apoptosis-inducing factor (AIF) and endonuclease G (Endo G) to cytosolic fractions.

Cell Cytotoxicity Assay[1]

Cell Line:	MM.1S cells, MM.1S cells cultured with BMSCs
Concentration:	0, 50, 200 nM
Incubation Time:	24 h
Result:	Enhanced the cytotoxicity of of Doxorubicin and Melphalan in MM.1S cells. Additive effects were also observed in MM.1S cells cultured with BMSCs derived from MM patient.

In Vivo

AVN-944 (0-150 mg/kg, Orally, twice daily) significantly increases the median survival time of leukemia model mice[2].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Animal Model:	Balb/c mice (leukemia model, using Ba/F3 cells transduced with an activating human Flt-3 mutation injected into mice)[2]

Dosage:	75 or 150 mg/kg
Administration:	Orally, twice daily
Result:	Provided a significant increase in median survival time. Three of the 12 mice treated with 150 mg/kg AVN-944 were still alive on Day 35 when the study was terminated.

CUSTOMER VALIDATION

- Biomed Pharmacother. 2019 Oct;118:109305.
- Viruses. 2021 Jun 28;13(7):1255.
- Microbiol Spectr. 2023 Jul 6;e0056623.

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REFERENCES

[1]. Zimmermann AG, et al. Inosine-5'-monophosphate dehydrogenase: regulation of expression and role in cellular proliferation and T lymphocyte activation. Prog Nucleic Acid Res Mol Biol. 1998;61:181-209.

[2]. Huang M, et al. Guanine nucleotide depletion inhibits pre-ribosomal RNA synthesis and causes nucleolar disruption. Leuk Res. 2008 Jan;32(1):131-41.

[3]. Floryk D, et al. Antiproliferative effects of AVN944, a novel inosine 5-monophosphate dehydrogenase inhibitor, in prostate cancer cells. Int J Cancer. 2008 Nov 15;123(10):2294-302.

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