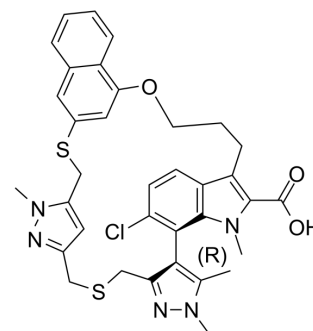


AZD-5991

Cat. No.:	HY-101533		
CAS No.:	2143061-81-6		
Molecular Formula:	$C_{35}H_{34}ClN_5O_3S_2$		
Molecular Weight:	672.26		
Target:	Bcl-2 Family		
Pathway:	Apoptosis		
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 : 250 mg/mL (371.88 mM; Need ultrasonic)

	Solvent Concentration	Mass	1 mg	5 mg	10 mg
Preparing Stock Solutions	1 mM		1.4875 mL	7.4376 mL	14.8752 mL
	5 mM		0.2975 mL	1.4875 mL	2.9750 mL
	10 mM		0.1488 mL	0.7438 mL	1.4875 mL

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

In Vivo

- Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
Solubility: ≥ 2.08 mg/mL (3.09 mM); Clear solution
- Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
Solubility: ≥ 2.08 mg/mL (3.09 mM); Clear solution
- Add each solvent one by one: 10% DMSO >> 90% (20% SBE- β -CD in saline)
Solubility: 2.08 mg/mL (3.09 mM); Suspended solution; Need ultrasonic
- Add each solvent one by one: 10% DMSO >> 90% (20% SBE- β -CD in saline)
Solubility: 2.08 mg/mL (3.09 mM); Suspended solution; Need ultrasonic
- Add each solvent one by one: 10% DMSO >> 90% corn oil
Solubility: ≥ 2.08 mg/mL (3.09 mM); Clear solution
- Add each solvent one by one: 10% DMSO >> 90% corn oil
Solubility: ≥ 2.08 mg/mL (3.09 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

AZD-5991 is a potent and selective Mcl-1 inhibitor with an IC_{50} of 0.7 nM in FRET assay and a K_d of 0.17 nM in surface plasmon

	resonance (SPR) assay ^[1] .	
IC ₅₀ & Target	Mcl-1 0.7 nM (IC ₅₀)	Mcl-1 0.17 nM (K _d)
In Vitro	The selectivity of AZD-5991 is evaluated against pro-survival Bcl-2 family members using FRET assays. AZD-5991 is selective for Mcl-1 (IC₅₀ 0.72 nM, K_i=200 pM) vs. Bcl-2 (IC₅₀=20 μM, K_i=6.8 μM), Bcl-xL (IC₅₀=36 μM, K_i=18 μM), Bcl-w (IC₅₀=49 μM, K_i=25 μM), and Bfl-1 (IC₅₀=24 μM, K_i=12 μM). MOLP-8, MV4-11, and NCI-H23 cells are treated with AZD5991 (EC₅₀=0.033, 0.024, 0.19 μM, respectively).AZD5991 binds directly to Mcl-1 and induces rapid apoptosis in cancer cells, most notably myeloma and acute myeloid leukemia, by activating the Bak-dependent mitochondrial apoptotic pathway. AZD5991 reduces the levels of Mcl-1 protein in AZD5991-sensitive but not in AZD5991-resistant MM cell lines further supporting the notion that activation of caspases by AZD5991 reduces Mcl-1 protein levels in AZD5991-sensitive cell lines^[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.	
In Vivo	A single intravenous (i.v.) dose of AZD5991 leads to a dose-dependent antitumor effect ranging from tumor growth inhibition (TGI) to tumor regression (TR). Ten days after treatment, AZD5991 shows 52% and 93% TGI (p<0.0001) at 10 and 30 mg/kg, respectively. At the same time point, AZD5991 at 60 mg/kg leads to 99% TR with no detectable tumors in 6 out of 7 mice, while complete TR is seen in 7 out of 7 mice in the 100 mg/kg dose group. AZD5991 also shows a dose-dependent duration of response with tumors in the 100 mg/kg group growing back later than those in the 60 mg/kg group. The magnitude of in vivo tumor efficacy is correlated with activation of caspase-3 in the tumor and concentration of AZD5991 in plasma. Treatment with AZD5991 was well tolerated at all dose levels with no significant body weight loss. A single dose of AZD5991 36 days after the first dose causes tumor regression in 4 out of 4 mice. In mice dosed with AZD5991 at 100 mg/kg on day 0 and day 1, tumors grow back later than those dosed with a single dose of AZD5991 at the same dose level^[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.	

PROTOCOL

Animal Administration ^[1]

Mice and Rats^[1]

In mice, drugs (e.g., AZD5991; 10-100 mg/kg) are dosed intravenously in a volume of 5 mL/kg except for Venetoclax that is dosed orally in a volume of 10 mL/kg. One million MV4-11, five million MOLP-8, ten million NCI-H929 or five million OCI-AML3 cells are injected subcutaneously in the right flank of mice in a volume of 0.1 mL. In rats, AZD5991 (10-100 mg/kg) is dosed intravenously in a volume of 10 mL/kg. Ten million MV4-11 cells are injected subcutaneously in the right flank of rats in a volume of 0.1 mL. Tumor volumes (measured by caliper), animal body weight, and tumor condition are recorded twice weekly for the duration of the study. The tumor volume is calculated^[1].

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

CUSTOMER VALIDATION

- Cell Death Dis. 2022 Apr 28;13(4):410.
- Cell Death Dis. 2021 Jul 27;12(8):741.
- Apoptosis. 2022 Aug 9.
- Int J Cancer. 2020 Oct 15;147(8):2176-2189.
- Cells. 2022 Sep 3;11(17):2752.

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REFERENCES

[1]. Tron AE, et al. Discovery of Mcl-1-specific inhibitor AZD5991 and preclinical activity in multiple myeloma and acute myeloid leukemia. Nat Commun. 2018 Dec 17;9(1):5341.

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

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