ABT-737

Cat. No.: HY-50907

CAS No.: 852808-04-9

Molecular Formula: $C_{42}H_{45}ClN_6O_5S_2$

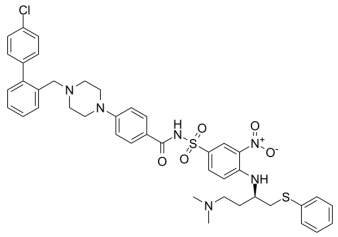
Molecular Weight: 813.43

Target: Bcl-2 Family; Autophagy; Mitophagy; Apoptosis

Pathway: Apoptosis; Autophagy

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 : 50 mg/mL (61.47 mM; Need ultrasonic)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	1.2294 mL	6.1468 mL	12.2936 mL
	5 mM	0.2459 mL	1.2294 mL	2.4587 mL
	10 mM	0.1229 mL	0.6147 mL	1.2294 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 (3.07 mM); Suspended solution; Need ultrasonic
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: 2.5 mg/mL (3.07 mM); Suspended solution; Need ultrasonic
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (3.07 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

ABT-737, a BH3 mimetic, is a potent Bcl-2, Bcl-x_L and Bcl-w inhibitor with EC_{50}s of 30.3 nM, 78.7 nM, and 197.8 nM, respectively. ABT-737 induces the disruption of the BCL-2/BAX complex and BAK-dependent but BIM-independent activation of the intrinsic apoptotic pathway. ABT-737 induces autophagy and has the potential for acute myeloid leukemia (AML) research[1][2][3].

IC_{50} & Target

Bcl-2	Bcl-xL	Bcl-W	Bcl-B
30.3 nM (EC50)	78.7 nM (EC50)	197.8 nM (EC50)	1820 nM (EC50)

	Bfl-1 >10 μM (EC50)	Mcl-1 >10 μM (EC50)

In Vitro

ABT-737 binds BCL-2, BCL-X_L, and BCL-W with high affinity (K_i<1 nM) but binds weakly (K_i>460 nM) to other antiapoptotic BCL-2 family members, including MCL-1 and BFL-1. ABT-737 binds the BH3-binding groove of BCL-X_L and BCL-2[1].
ABT-737 (100 nM; 1-72 hours) induces apoptosis and synergizes with chemotherapy in HL-60 cells[1].
ABT-737 (5, 7.5, 10 μM; 72 hours) causes approximately 80% HCT116 cell death. The BAX knockout variant is completely resistant to ABT-737[1].
ABT-737 has no effect on cell cycle distribution. ABT-737 disrupts BCL-2/BAX heterodimerization and induces BAX conformational change in HL-60 leukemic cells[1].
ABT-737 induces a BAX/BAK-dependent impairment of maximal O_2 consumption rate in sensitive cells. Stable BCL-2 overexpression in MCF10A cells induces an ABT-737-sensitive primed for death state. ABT-737 induces dose-dependent impairment of maximal O_2 consumption rate in B-cell lymphoma cells[3].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

In Vivo

ABT-737 (20, 30 mg/kg/day; i.p.; for 21 days) suppresses the leukemia burden by 48% and 53% at the 20 and 30 mg/kg dose levels, respectively, in four- to six-week-old CB.17 Scid mice with human leukemia KG-1 cells[1].
ABT-737 significantly extends survival of mice in this aggressive leukemia model[1].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Kinase Assay [1]

To determine the binding affinity of GST-BCL-2 family proteins to the FITC-conjugated BH3 domain of BIM (FITC-Ahx-DMRPEIWIAQELRRIGDEFNAYYAR), FPAs are performed as follows. Briefly, 100 nM of GST-BCL-2 family fusion proteins are incubated with serial dilutions of ABT-737 in PBS for 2 min. Then, 20 nM of FITC-BIM BH3 peptide (FITC-Ahx-DMRPEIWIAQELRRIGDEFNAYYAR) is added. Fluorescence polarization is measured using an Analyst TM AD Assay Detection System after 10 min using the 96-well black plate. IC_{50}s are determined using GraphPad Prism software.
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Cell Assay [3]

Cells are treated with ABT-737, ABT-263, or vehicle (DMSO) for 4 h in XF24 assay medium (6×10^4 MCF10A cells, see medium composition below) or RPMI 1640 medium (1×10^6 B-cell lymphoma cells) and apoptosis is analyzed by Annexin-V-binding/PI exclusion or by sub-diploid nuclei determination. FACS analysis is performed on Becton Dickinson FACScan or FACScalibur instruments. Data analysis is performed with CellQuest software.
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Animal Administration [1]

For intraperitoneal (i.p.) administration, 1 g/mL stock solution of ABT-737 in DMSO is added to a mixture of 30% propylene glycol, 5% Tween 80, 65% D5W (5% dextrose in water) (pH 4–5; final concentration of DMSO ≤ 1%). Mice injected with FD/ΔRaf-1:ER cells are treated with either ABT-737 (20 and 30 mg/kg/mouse every day i.p. for 21 days starting on day 1 post-cell injection (n=9-10 mice per group) or vehicle or left untreated (control); mice injected with human KG-1 cells are treated with 30 mg/kg ABT-737 starting on day 18 post-cell injection. For noninvasive imaging of FD/ΔRaf-1:ER-luc cells, anesthetized mice are injected with 150 mg/kg of D-luciferin and placed for imaging in the In Vivo Imaging System with total imaging time of 2 min.
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- Cell. 2022 Sep 1;185(18):3356-3374.e22.
- Cancer Cell. 2023 Jul 10;41(7):1242-1260.e6.
- Cell Mol Immunol. 2021 May;18(5):1186-1196.

- Nat Commun. 2023 Sep 19;14(1):5709.
- Adv Sci (Weinh). 2023 Jul 19;e2207108.

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[1]. Ahamed Saleem, et al. Effect of dual inhibition of apoptosis and autophagy in prostate cancer. Prostate. 2012 Sep 1;72(12):1374-81.

[2]. Clerc P, et al. Polster BM.Rapid Detection of an ABT-737-Sensitive Primed for Death State in Cells Using Microplate-Based Respirometry.PLoS One. 2012;7(8):e42487. Epub 2012 Aug 3.

[3]. Konopleva M, et al. Mechanisms of apoptosis sensitivity and resistance to the BH3 mimetic ABT-737 in acute myeloid leukemia. Cancer Cell. 2006 Nov;10(5):375-88.

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