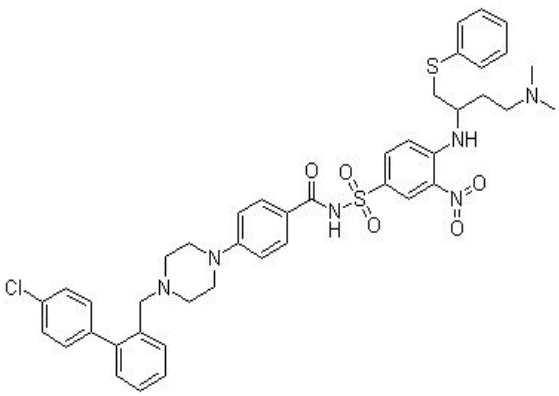
Biochempartner
瀚香生物科技

Product Introduction

ABT-737

ABT-737 is a BH3 mimetic inhibitor of **Bcl-xL**, **Bcl-2** and **Bcl-w** with **EC50** of 78.7 nM, 30.3 nM and 197.8 nM, respectively; no inhibition observed against Mcl-1, Bcl-B or Bfl-1. Phase 2.

Technical Data:

Molecular Weight (MW):	813.43	
Formula:	$C_{42}H_{45}ClN_6O_5S_2$	
Solubility (25°C) * <1 mg/ml means slightly soluble or insoluble:	DMSO 100 mg/mL	
	Water <1 mg/mL	
	Ethanol <1 mg/mL	
Purity:	>98%	
Storage:	3 years -20℃Powder	
	6 months-80℃in DMSO	
CAS No.:	852808-04-9	

Biological Activity

ABT-737 shows low activity to Bcl-B and no effects to Mcl-1 and BFL-1. ABT-737 is sensitive to HL60, KG1 and NB4 cells with IC50 of 50 nM, 80 nM and 80 nM, respectively. ABT-737 induces apoptosis in HL60 cells, which due to decreased Bcl-2/Bax heterodimerization and has no effect on cell cycle distribution. ABT-737 also induces cytochrome c release from purified mitochondria and promotes conformational changes in Bax that are associated with apoptosis. [1] Resistant cells (Hela and MCF-7) can be sensitized to ABT-737 by approaches that down-regulate, destabilize, or inactivate Mcl-1. ABT-737 also causes

Bax/BAK-dependent cytochrome c release only when Mcl-1 has been neutralized. [2] ABT-737 displaces Bim from Bcl2's BH3-binding pocket, allowing Bim to activate Bax, induce mitochondrial permeabilization, and rapidly commit the primary chronic lymphocytic leukemia (CLL) cells to death. [3] Knockdown of Mcl-1 with siRNA sensitizes two resistant SCLC cell lines H196 and DMS114 to ABT-737 by enhancing the induction of apoptosis. Likewise, up-regulation of Noxa sensitizes H196 cells to ABT-737. ABT-737 inhibits many SCLC cell lines including NCI-H889, NCI-H1963, NCI-H1417, NCI-H146 and etc. Bcl-2 and Noxa may contribute mechanistically to the cellular response to ABT-737 in NCI-H146 cells. [4] A recent study shows that ABT-737 significantly induces apoptosis in HTLV-1 infected T-cell lines as well as in fresh ATLL cells. [5]
In aggressive leukemia model, ABT-737 suppresses the leukemia burden by 53% at the 30 mg/kg, with significantly extended survival of mice. ABT-737 does not induce significantly abnormalities in blood cell counts or serum chemistries. [1] ABT-737 prolongs the survival of recipient mice transplanted with Bcl-2-transduced tumors. [2] ABT-737 shows great antitumor activity in an ATLL mouse model at a dose of 100 mg/kg. [5]
First-generation inhibitor of anti-apoptotic Bcl-2 proteins.

References

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[3] Del Gaizo Moore V, et al. J Clin Invest, 2007, 117(1), 112-121.
[4] Tahir SK, et al. Cancer Res, 2007, 67(3), 1176-1183.
[5] Ishitsuka K, et al. Cancer Lett, 2012, 317(2), 218-225.
[6] Konopleva M, et al. Cancer Res, 2008, 68(9), 3413-3420.
[7] Wade M, et al. Cell Cycle, 2008, 7(13), 1973-1982.
[8] Paoluzzi L, et al. Blood, 2008, 112(7), 2906-2916.
[9] Li R, et al. Mol Pharmacol, 2009, 75(5), 1231-1239.

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