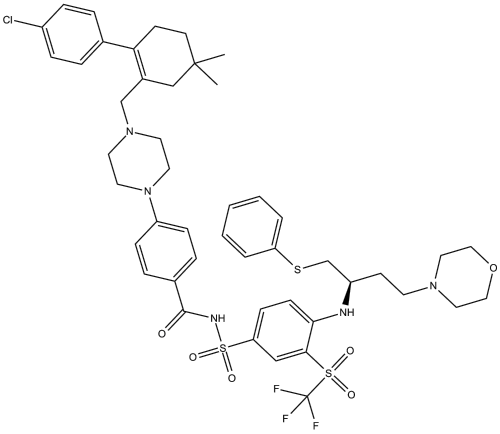
Product Data Sheet

Product Name: ABT-263 (Navitoclax)
Cat. No.: GC12405

Chemical Properties

Cas. No.	923564-51-6		
Chemical Name	(R)-4-(4-((4'-chloro-4,4-dimethyl-3,4,5,6-tetrahydro-[1,1'-biphenyl]-2-yl)methyl)piperazin-1-yl)-N-((4-((4-morpholino-1-(phenylthio)butan-2-yl)amino)-3-((trifluoromethyl)sulfonyl)phenyl)sulfonyl)benzamide		
SMILES	CC(CC1)(C)CC(CN2CCN(C3=CC=C(C(NS(C4=CC=C(N[C@@H](CSC5=CC=CC=C5)CCN6CCOCC6)C(S(C(F)(F)F)(=O)=O)=C4)(=O)=O)=O)C=C3)CC2)=C1C7=CC=C(Cl)C=C7		
Formula	$C_{47}H_{55}ClF_3N_5O_6S_3$	M.Wt	974.61
Solubility	≥ 48.7305mg/mL in DMSO	Storage	Desiccate at -20°C
General tips	For obtaining a higher solubility , please warm the tube at 37 °C and shake it in the ultrasonic bath for a while.Stock solution can be stored below -20°C for several months.		
Shipping Condition	Evaluation sample solution : ship with blue ice All other available size: ship with RT , or blue ice upon request.		
Structure			

Protocol

Kinase experiment [1]:

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Preparation Method	K_i or IC_{50} values of ABT-263 (Navitoclax) on different subtypes of the Bcl-2 family were determined by competitive fluorescence polarization assay using the following peptide probe pairs or protein pairs :f-bad (1 nM) and Bcl-xL (6 nM), f-Bax (1 nM) and Bcl-2 (10 nM),f-Bax (1 nM) and Bcl-w (40 nM), f-Noxa (2 nM) and Mcl-1 (40 nM),and f-Bax (1 nM) and Bcl-2-A1 (15 nM) were used to determine the binding tightness of ABT-263 and Bcl-xL by time-resolved fluorescence resonance energy transfer method. Bcl-xL with His label was used for 1 nM and 200 nM f-Bak and 1 nMTb-labeled His antibodies were mixed and then treated at room temperature for 30 minutes.
Applications	ABT-263 (Navitoclax) is a inhibitor of Bcl-xL, Bcl-2 and Bcl-w, with Ki ¡■■5 nM, ¡■ nM and ¡■ nM respectively.

Cell experiment [2]:

Cell lines	HeLa, U2OS, OVCAR-5, and A549 cell
Preparation Method	In four cancer cell lines, nvitokera (ABT-263) was treated with 1 μmol/L alone or in combination with other agents. Individual cells were monitored by phase-contrast and fluorescence time-lapse microscopy, and time from mitotic entry to morphologic death was measured and plotted as cumulative survival curves.
Reaction Conditions	1μM ;60 hours
Applications	Navitoclax accelerates apoptosis mainly by inhibiting Bcl-xL.

Animal experiment [3]:

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Animal models	H345 transplanted tumor model(C.B.-17 scid-bg (scid-bg) or C.B.-17 scid (scid) mice)
Preparation Method	Mice were implanted with H345 cells maintained by in vivo propagation. Noculation volume was 0.2 mL consisting of 50% Matrigel. When tumors reached the appropriate tumor volume, mice were size matched (day 0) into treatment(ABT-263 (Navitoclax)) and control groups.
Dosage form	100 mg/kg/day ABT-263 (Navitoclax);p.o. ;once daily for 21 days
Applications	ABT-263 (Navitoclax) treated a mouse model inoculated with H345 cells, and significant antitumor efficacy was observed.

References:
[1]. Tse C, Shoemaker AR, et,al. ABT-263: a potent and orally bioavailable Bcl-2 family inhibitor. Cancer Res. 2008 May 1;68(9):3421-8. doi: 10.1158/0008-5472.CAN-07-5836. PMID: 18451170.
[2].Shi J, Zhou Y, Huang HC, Mitchison TJ. Navitoclax (ABT-263) accelerates apoptosis during drug-induced mitotic arrest by antagonizing Bcl-xL. Cancer Res. 2011 Jul 1;71(13):4518-26. doi: 10.1158/0008-5472.CAN-10-4336. Epub 2011 May 5. PMID: 21546570; PMCID: PMC3129452.
[3]. Shoemaker AR, Mitten MJ, et,al.Activity of the Bcl-2 family inhibitor ABT-263 in a panel of small cell lung cancer xenograft models. Clin Cancer Res. 2008 Jun 1;14(11):3268-77. doi: 10.1158/1078-0432.CCR-07-4622. PMID: 18519752.

Background

ABT-263 (Navitoclax) is a inhibitor of Bcl-xL, Bcl-2 and Bcl-w, with Ki ≤0.5 nM, ≤1 nM and ≤1 nM respectively[1].

ABT-263 (Navitoclax) is senolytic in some, but not all types of senescent cells: Navitoclax reduced viability of senescent human umbilical vein epithelial cells (HUVECs), IMR90 human lung fibroblasts,

and murine embryonic fibroblasts (MEFs)[2]. Navitoclax (1μM ; 60 hours) accelerates apoptosis mainly by inhibiting Bcl-xL[8].

ABT-263 (Navitoclax)exhibited modest (IC_{50}=3-8 μM) single agent potency in 8 ovarian cancer cell lines. Navitoclax(0.4μM;30h) enhanced the activation of caspase 3/7 induced by carboplatin and/or paclitaxel in Igrov-1 cells [3]. Multiple lymphoid subpopulations isolated from the thymi or BM of vavP-Bcl-2 transgenic mice were markedly more sensitive to ABT-263 (Navitoclax)[4].

ABT-263 (Navitoclax) (100 mg/kg/d;p.o;once daily for 21 days) treated a mouse model inoculated with H345 cells, and significant antitumor efficacy was observed [6]. Navitoclax with venetoclax and chemotherapy was well tolerated and had promising efficacy in patients with relapsed/refractory acute lymphoblastic leukemia or lymphoblastic lymphoma[5]. In 44 xenograft models representing 9 different histologies, ABT-263 (Navitoclax) (100 mg/kg/d;i.g; 21 days)demonstrated limited single agent in vivo activity against the PPTP's(pediatric preclinical testing program)solid tumor panels but showed significant activity against xenografts in the ALL panel [7].

References:References:
[1]. Tse C, Shoemaker AR, et,al. ABT-263: a potent and orally bioavailable Bcl-2 family inhibitor. Cancer Res. 2008 May 1;68(9):3421-8. doi: 10.1158/0008-5472.CAN-07-5836. PMID: 18451170.
[2]. Zhu Y, Tchkonia T, et,al.Identification of a novel senolytic agent, navitoclax, targeting the Bcl-2 family of anti-apoptotic factors. Aging Cell. 2016 Jun;15(3):428-35. doi: 10.1111/acel.12445. Epub 2016 Mar 18. PMID: 26711051; PMCID: PMC4854923.
[3]. Stamelos VA, Robinson E, et,al. Navitoclax augments the activity of carboplatin and paclitaxel combinations in ovarian cancer cells. Gynecol Oncol. 2013 Feb;128(2):377-82. doi: 10.1016/j.ygyno.2012.11.019. Epub 2012 Nov 17. PMID: 23168176.
[4]. Mérino D, Khaw SL, et,al. Bcl-2, Bcl-x(L), and Bcl-w are not equivalent targets of ABT-737 and navitoclax (ABT-263) in lymphoid and leukemic cells. Blood. 2012 Jun 14;119(24):5807-16. doi: 10.1182/blood-2011-12-400929. Epub 2012 Apr 26. PMID: 22538851; PMCID: PMC3382939.
[5]. Pullarkat VA, Lacayo NJ, et,al.Venetoclax and Navitoclax in Combination with Chemotherapy in Patients with Relapsed or Refractory Acute Lymphoblastic Leukemia and Lymphoblastic Lymphoma. Cancer Discov. 2021 Jun;11(6):1440-1453. doi: 10.1158/2159-8290.CD-20-1465. Epub 2021 Feb 16. PMID: 33593877; PMCID: PMC9533326.
[6]. Shoemaker AR, Mitten MJ, et,al. Activity of the Bcl-2 family inhibitor ABT-263 in a panel of small

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cell lung cancer xenograft models. Clin Cancer Res. 2008 Jun 1;14(11):3268-77. doi: 10.1158/1078-0432.CCR-07-4622. PMID: 18519752.
[7]. Lock R, Carol H, et,al. Initial testing (stage 1) of the BH3 mimetic ABT-263 by the pediatric preclinical testing program. Pediatr Blood Cancer. 2008 Jun;50(6):1181-9. doi: 10.1002/pbc.21433. PMID: 18085673.
[8].Shi J, Zhou Y, Huang HC, Mitchison TJ. Navitoclax (ABT-263) accelerates apoptosis during drug-induced mitotic arrest by antagonizing Bcl-xL. Cancer Res. 2011 Jul 1;71(13):4518-26. doi: 10.1158/0008-5472.CAN-10-4336. Epub 2011 May 5. PMID: 21546570; PMCID: PMC3129452.

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