

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

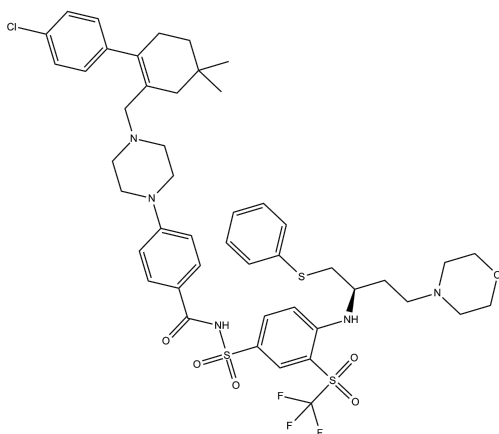
Formula $C_{47}H_{55}ClF_3N_5O_6S_3$ M.Wt 974.61

Solubility $\geq 48.7305\text{mg/mL}$ 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 K_i 1.5×10^{-5} nM, 1.5×10^{-5} nM and 1.5×10^{-5} 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 μ mol/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 1 μ M ;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. Nucleation 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 $K_i \leq 0.5$ 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,

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

ABT-263 (Navitoclax) exhibited modest (IC_{50} =3-8 μ M) single agent potency in 8 ovarian cancer cell lines. Navitoclax(0.4 μ M;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, Tchkonja 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/ace.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]. Mérimo 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.

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