Product Name: S63845

Revision Date: 6/30/2016

Product Data Sheet

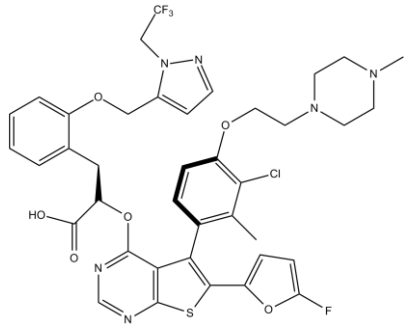
Chemical Properties

Product Name: S63845

Cas No.: 1799633-27-4

M.Wt: 829.26

Formula: C39H37ClF4N6O6S



Chemical Name: (S)-2-(((S)-5-(3-chloro-2-methyl-4-(2-(4-methylpiperazin-1-yl)ethoxy)phenyl)-6-(5-fluorofuran-2-yl)thieno[2,3-d]pyrimidin-4-yl)oxy)-3-(2-((1-(2,2,2-trifluoroethyl)-1H-pyrazol-5-yl)methoxy)phenyl)propanoic acid

Canonical SMILES: OC([C@@H](OC1=NC=NC2=C1[C@]([C@]3=C(C)C(Cl)=C(C=C3)OCCN4CCN(C)CC4)=C(C5=CC=C(F)O5)S2)CC6=CC=CC=C6OCC7=CC=NN7CC(F)(F)F)=O

Solubility: ≥41.45mg/mL in DMSO

Storage: Store 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.

Shopping Condition: Evaluation sample solution : ship with blue ice
All other available size: ship with RT , or blue ice upon request

Biological Activity

Targets : Apoptosis

Pathways: Bcl-2 Family

Description:

S63845 is a small molecule MCL1 inhibitor with Ki < 1.2 nM [1].
Myeloid cell leukemia 1 (MCL1) is a pro-survival protein and belongs to BCL-2 family proteins.

BCL-2 family proteins are key regulators of the mitochondrial apoptotic pathway. MCL1 is overexpressed in many cancers, so inhibitors targeting this protein may kills MCL1-dependent cancer cells [1].
S63845 is a highly selective and potent MCL1 inhibitor. S63845 bound human MCL1 with KD value of 0.19 nM. S63845 was approximately 1,000-fold more potent in killing MCL1-dependent H929 multiple myeloma cells than MCL1 inhibitor A-1210477. S63845 also induced caspase-dependent phosphatidyl-serine exposure, PARP cleavage and cytochrome c release from mitochondria. In HeLa cells, S63845 disrupted binding of BAK and BAX to MCL1. S63845 killed cancer cells through activation of the BAX/BAK-dependent mitochondrial apoptotic pathway by direct inhibition of MCL1 [1].
In immunocompromised mice with human multiple myeloma (H929 and AMO1) xenografts, intravenously injected (i.v.) S63845 showed dose-dependent anti-tumour activity with maximal tumour growth inhibition (TGImax) of 103% and 114% in the H929 and AMO1 model, respectively [1].

***Reference**:*

1.Kotschy A, Szlavik Z, Murray J, et al. The MCL1 inhibitor S63845 is tolerable and effective in diverse cancer models. Nature. 2016 Oct 19;538(7626):477-482.

Protocol

Cell experiment:

Cell lines	Haematological cancer-derived cell lines, Myeloma cell lines, Human lymphomas and chronic myeloid leukaemia cell lines
Preparation method	This compound is soluble in DMSO. General tips for obtaining a higher concentration: Please warm the tube at 37 ℃ for 10 minutes and/or shake it in the ultrasonic bath for a while. Stock solution can be stored below -20℃ for several months.
Reacting conditions	1-10 μM, 48 h, 37°C
Applications	S63845 is a small molecule MCL1 inhibitor with Ki 1 μM). In a panel of human lymphomas and chronic myeloid leukaemia 11 cell lines: five lines were highly sensitive to S63845 (IC50 1 μM). In a panel of eight AML cell lines: all lines were sensitive to S63845 (IC50 4–233 nM) [1].

Animal experiment [3]:

Animal models	Human multiple myeloma (H929 and AMO1) xenografted mice
Dosage form	Intravenously injected (i.v.), 25 mg/kg

Applications	Intravenously injected (i.v.) S63845 exerted dose-dependent anti-tumour activity in human multiple myeloma (H929 and AMO1) xenografts in immunocompromised mice, with maximal tumour growth inhibition (TGImax) of 114% in the AMO1 model and 103% in the H929 model. S63845 (25 mg/kg) induced complete regression in 7 out of 8 of the mice at 100 days after treatment in the AMO1 model. S63845 (i.v., 25 mg/kg, 5 days) cured 70% of immuno-competent C57BL/6 mice bearing Eμ-Myc mouse lymphomas, with no side-effects evident in normal tissues. S63845 (12.5 mg/kg) showed potent activity in the MV4-11 human AML xenograft model, with a TGImax of 86%. S63845 (25 mg/kg) resulted in completeremission in 6 out of 8 mice after 80 days.
Other notes	Please test the solubility of all compounds indoor, and the actual solubility may slightly differ with the theoretical value. This is caused by an experimental system error and it is normal.

Reference:
[1]. Kotschy A, Szlavik Z, Murray J, et al. The MCL1 inhibitor S63845 is tolerable and effective in diverse cancer models. Nature. 2016 Oct 19;538(7626):477-482.

Caution

FOR RESEARCH PURPOSES ONLY.

NOT FOR HUMAN, VETERINARY DIAGNOSTIC OR THERAPEUTIC USE.

Specific storage and handling information for each product is indicated on the product datasheet. Most ApexBio products are stable under the recommended conditions. Products are sometimes shipped at a temperature that differs from the recommended storage temperature. Shortterm storage of many products are stable in the short-term at temperatures that differ from that required for long-term storage. We ensure that the product is shipped under conditions that will maintain the quality of the reagents. Upon receipt of the product, follow the storage recommendations on the product data sheet.

7505 Fannin street, Suite 410, Houston, TX 77054.

Tel: +1-832-696-8203 | Fax: +1-832-641-3177 | Email: info@apexbt.com