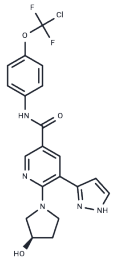
Data Sheet (Cat.No.T5177)

TargetMol

Asciminib

Chemical Properties



CAS No. : 1492952-76-7

Formula: C20H18ClF2N5O3

Molecular Weight: 449.84

Storage: Powder: -20°C for 3 years | In solvent: -80°C for 1 year
Actual storage temperature shall be subject to the COA.

Biological Description

Description	Asciminib (ABL001) (ABL001) is a potent and selective Bcr-Abl inhibitor (Kd: 0.5-0.8nM).
Targets(IC50)	Bcr-Abl
In vitro	In Asciminib-transformed Ba/F3 cells grown without IL-3, ABL001 had an anti-proliferative IC50 value of 0.25nM. By contrast, the addition of IL-3 to bypass Asciminib dependence renders these cells insensitive to ABL001. In the CML blast-phase cell line KCL-22, ABL001 inhibited phosphorylation of both STAT5 (Tyr694; pSTAT5) and Asciminib (Tyr245; pAsciminib) after 1h using concentrations that correlate with those required for inhibition of cell proliferation [1]. K562-Dox and K562-ABCG2 cells demonstrated increased LD50 (asciminib) vs K562 control cells: 256 and 299 nM respectively vs 24 nM. Sensitivity was completely restored with specific inhibitors cyclosporine (ABCB1) and Ko143 (ABCG2): K562-Dox LD50 (asciminib+cyclosporine) = 13 nM, K562-ABCG2 LD50 (asciminib+Ko143) = 15 nM [2].
In vivo	Single doses of 7.5, 15 and 30mg kg1 ABL001, administered to mice bearing KCL22 xenografts, inhibited pSTAT5 (Tyr694), which returned to baseline at 10, 12 and 16–20h after administration of the dose, respectively. In mice implanted with KCL-22 tumours, the minimum dose of ABL001 required for complete regression was 7.5mg/kg twice a day (BID) or 30mg/kg once a day (QD), and was tolerated at doses up to 250mg kg1 BID. Similarly, in xenografts derived from patients with Ph+ ALL, treatment with 7.5 and 30mg/kg ABL001 led to regressions that were maintained during dosing [1].
Cell Research	Cells were resuspended in fresh culture media before culture in 24-well plates in the presence of TKI or asciminib at a density of 2 × 105 cells/mL. Plates were seeded with 1 mL of cell suspension and incubated for 72 h before cell viability determination with 7-aminoactinomycin (7-AAD) and Phycoerythrin (PE)-conjugated Annexin V. Flow cytometric analysis was conducted with a BD LSRFortessa X-20 and FACSDiva software. The lethal dose of asciminib (LD50 asciminib), imatinib (LD50 IM), nilotinib (LD50 NIL) and dasatinib (LD50 DAS) required to cause 50% death of cells was calculated [2].
Animal Research	Asciminib efficacy in three patient-derived ALL systemic xenograft models (ALL-7015, AL-7119 and AL-7155) is assessed by FACS monitoring of the percentage of CD45+ cells per live cell in blood samples taken at varying time points after dosing with either 7.5 mg/kg BID (group 2) or 30 mg/kg BID (group 3) asciminib for 3 weeks [1].

Solubility Information

Solubility	H2O: Insoluble, DMSO: 245 mg/mL (544.64 mM),Sonication is recommended. (< 1 mg/ml refers to the product slightly soluble or insoluble)
In vivo Formulation	10% DMSO+40% PEG300+5% Tween 80+45% Saline: 2 mg/mL (4.45 mM),Sonication is recommended. *Please add the solvents sequentially, clarifying the solution as much as possible before adding the next one. Dissolve by heating and/or sonication if necessary. Working solution is recommended to be prepared and used immediately. The formulation provided above is for reference purposes only. In vivo formulations may vary and should be modified based on specific experimental conditions.*

Preparing Stock Solutions

	1mg	5mg	10mg
1 mM	2.223 mL	11.1151 mL	22.2301 mL
5 mM	0.4446 mL	2.223 mL	4.446 mL
10 mM	0.2223 mL	1.1115 mL	2.223 mL
50 mM	0.0445 mL	0.2223 mL	0.4446 mL

Please select the appropriate solvent to prepare the stock solution, according to the solubility of the product in different solvents. Please use it as soon as possible.

Note: The dilution table applies only to solid products. For liquid products, please calculate the stock solution based on the stated concentration and/or density.

Reference

Wylie AA, et al. The allosteric inhibitor ABL2001 enables dual targeting of BCR-ABL1. Nature. 2017 Mar 30;543 (7647):733-737.

Zhang C, Huang C, Xia H, et al. Autophagic sequestration of SQSTM1 disrupts the aggresome formation of ubiquitinated proteins during proteasome inhibition. Cell Death & Disease. 2022, 13(7): 1-15

Eadie LN, et al. The new allosteric inhibitor asciminib is susceptible to resistance mediated by ABCB1 and ABCG2 overexpression in vitro. Oncotarget. 2018 Feb 3;9(17):13423-13437.

Cheng S, Jin P, Li H, et al. Evaluation of CML TKI Induced Cardiovascular Toxicity and Development of Potential Rescue Strategies in a Zebrafish Model. Frontiers in Pharmacology. 2021: 2866.