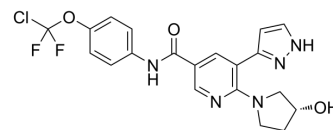


Asciminib

Cat. No.:	HY-104010		
CAS No.:	1492952-76-7		
Molecular Formula:	C ₂₀ H ₁₈ ClF ₂ N ₅ O ₃		
Molecular Weight:	449.84		
Target:	Bcr-Abl		
Pathway:	Protein Tyrosine Kinase/RTK		
Storage:	Powder	-20°C	3 years
		4°C	2 years
	In solvent	-80°C	6 months
		-20°C	1 month



SOLVENT & SOLUBILITY

In Vitro

DMSO : 100 mg/mL (222.30 mM; Need ultrasonic)

Concentration	Solvent	Mass		
		1 mg	5 mg	10 mg
Preparing Stock Solutions	1 mM	2.2230 mL	11.1151 mL	22.2301 mL
	5 mM	0.4446 mL	2.2230 mL	4.4460 mL
	10 mM	0.2223 mL	1.1115 mL	2.2230 mL

Please refer to the solubility information to select the appropriate solvent.

In Vivo

- Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
Solubility: ≥ 2.5 mg/mL (5.56 mM); Clear solution
- Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
Solubility: ≥ 2.5 mg/mL (5.56 mM); Clear solution
- Add each solvent one by one: 10% DMSO >> 90% corn oil
Solubility: ≥ 2.5 mg/mL (5.56 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

Asciminib (ABL001) is a potent and selective allosteric BCR-ABL1 inhibitor, which inhibits Ba/F3 cells grown with an IC₅₀ of 0.25 nM^[1].

In Vitro

Asciminib binds to the myristoyl pocket of ABL1 and induces the formation of an inactive kinase conformation. NMR and biophysical studies confirm that asciminib binds potently (dissociation constant=0.5-0.8nM) and selectively to the myristoyl pocket of ABL1 and induces the inactive C-terminal helix conformation. Asciminib binding mimics the structural consequences of myristate binding to the N terminus of ABL1. Consistent with this binding site, asciminib exhibits the same

non-ATP-competitive biochemical kinetics as the BCR-ABL inhibitor GNF-2 but with approximately 100-fold greater potency. Asciminib lacks activity against more than 60 kinases, including SRC, and is similarly inactive against G-protein-coupled receptors, ion channels, nuclear receptors and transporters. In BCR-ABL1-transformed Ba/F3 cells grown without IL-3, asciminib has an anti-proliferative with IC₅₀ value of 0.25nM. In the CML blast-phase cell line KCL-22, asciminib inhibits phosphorylation of both STAT5 (Tyr694; pSTAT5) and BCR-ABL1 (Tyr245; pBCR-ABL1) after 1h using concentrations that correlate with those required for inhibition of cell proliferation. Asciminib is selectively active against all BCR-ABL1 lines (IC₅₀ value of 1–20nM), irrespective of the presence of either the p210 or the p190 BCR-ABL1 isoform.^[1]
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

In Vivo

Asciminib is undergoing clinical development testing in patients with CML and Philadelphia chromosome-positive acute lymphoblastic leukaemia. Single doses of 7.5, 15 and 30 mg/kg ABL001, administered to mice bearing KCL- 22 xenografts, inhibits pSTAT5 (Tyr694), which return to baseline at 10, 12 and 16-20h after administration of the dose, respectively. In mice implanted with KCL-22 tumors, the minimum dose of asciminib required for complete regression is 7.5 mg/kg twice a day (BID) or 30 mg/kg once a day (QD), and is tolerated at doses up to 250 mg/kg BID. Similarly, in xenografts derived from patients, treatment with 7.5 and 30 mg/kg asciminib leads to regressions that are maintained during dosing^[1].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Cell Assay ^[1]

Ba/F3 cells are treated with a range concentration of asciminib (0-10000 nM) for 48 h. Cell proliferation is measured using the Britelite luciferase detection assay^[1].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Animal Administration ^[1]

Mice: 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].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- Cell Death Dis. 2021 Sep 25;12(10):875.
- Cancer Immunol Immunother. 2023 Jan 5.
- J Biol Chem. 2022 Aug;298(8):102238.
- BMC Cancer. 2020 May 7;20(1):397.

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REFERENCES

[1]. Wylie AA, et al. The allosteric inhibitor ABL001 enables dual targeting of BCR-ABL1. Nature. 2017 Mar 30;543(7647):733-737.

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

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