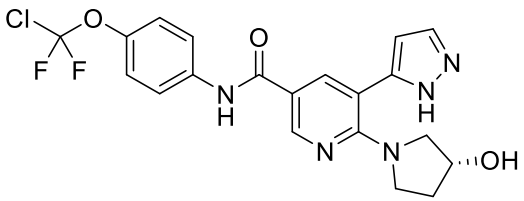
Product data sheet

MedKoo Cat#: 206490 Name: Asciminib free base CAS#: 1492952-76-7 (free base) Chemical Formula: $C_{20}H_{18}ClF_2N_5O_3$ Exact Mass: 449.1066 Molecular Weight: 449.8428	
Product supplied as:	Powder
Purity (by HPLC):	≥ 98%
Shipping conditions	Ambient temperature
Storage conditions:	Powder: -20°C 3 years; 4°C 2 years.
	In solvent: -80°C 3 months; -20°C 2 weeks.

1. Product description:
Asciminib, also known as ABL001, is a potent allosteric inhibitor of BCR-ABL. ABL001 prevents emergence of resistant disease when administered in combination with nilotinib in an in vivo murine model of chronic myeloid leukemia. Cell proliferation studies demonstrate that ABL001 selectively inhibited the growth of CML and Ph+ ALL cells with potencies ranging from 1-10nM range. ABL001 was tested for activity against clinically observed mutations and found to be active in the low nM range. In the KCL-22 mouse xenograft model, ABL001 displayed potent anti-tumor activity with complete tumor regression observed and a clear dose-dependent correlation with pSTAT5 inhibition.

2. CoA, QC data, SDS, and handling instruction
SDS and handling instruction, CoA with copies of QC data (NMR, HPLC and MS analytical spectra) can be downloaded from the product web page under "QC And Documents" section. Note: copies of analytical spectra may not be available if the product is being supplied by MedKoo partners. Whether the product was made by MedKoo or provided by its partners, the quality is 100% guaranteed.

3. Solubility data

Solvent	Max Conc. mg/mL	Max Conc. mM
DMSO	93.0	206.74
Ethanol	90.0	200.07

4. Stock solution preparation table:

Concentration / Solvent Volume / Mass	1 mg	5 mg	10 mg
1 mM	2.22 mL	11.11 mL	22.23 mL
5 mM	0.44 mL	2.22 mL	4.45 mL
10 mM	0.22 mL	1.11 mL	2.22 mL
50 mM	0.04 mL	0.22 mL	0.44 mL

5. Molarity Calculator, Reconstitution Calculator, Dilution Calculator
Please refer the product web page under section of "Calculator"

6. Recommended literature which reported protocols for in vitro and in vivo study
In vitro study

1. Mattiello L, Pucci G, Marchetti F, Diederich M, Gonfloni S. Asciminib Mitigates DNA Damage Stress Signaling Induced by Cyclophosphamide in the Ovary. Int J Mol Sci. 2021 Jan 30;22(3):1395. doi: 10.3390/ijms22031395. PMID: 33573271; PMCID: PMC7866503.
2. Eadie LN, Saunders VA, Branford S, White DL, Hughes TP. 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. doi: 10.18632/oncotarget.24393. PMID: 29568367; PMCID: PMC5862588.

In vivo study

1. Mattiello L, Pucci G, Marchetti F, Diederich M, Gonfloni S. Asciminib Mitigates DNA Damage Stress Signaling Induced by Cyclophosphamide in the Ovary. Int J Mol Sci. 2021 Jan 30;22(3):1395. doi: 10.3390/ijms22031395. PMID: 33573271; PMCID: PMC7866503.

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7. Bioactivity

Biological target:

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

In vitro activity

A clinically used ferto-protective drug should not interfere with the therapeutic effect of DNA-damaging chemotherapies. This assumption was validated by assessing the effect of Asciminib on 4-hydroperoxy-cyclophosphamide (4-OH-Cy)-treated MCF7 breast tumor cells. These results demonstrate that the co-treatment with Asciminib did not affect 4-OH-Cy-induced phosphorylation of DDR marker proteins like ATM, γH2AX, or p53 (Figure 4A). Additionally, single-cell gel electrophoresis (Comet) assays revealed that Asciminib did not interfere with the DNA-damaging effect of 4-OH-Cy (Figure 4B). Finally, the co-administration of Asciminib did not affect the cytotoxic effect of 4-OH-Cy (Figure 4C). Taken together, these data support the potential use of Asciminib as a ferto-protective drug without abrogating the cytotoxic effect of 4-OH-CY.

Reference: Int J Mol Sci. 2021 Feb; 22(3): 1395. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7866503/

In vivo activity

Next, P7 mice were injected with Cy alone (100 mg/kg) or in combination with increasing concentrations of Asciminib (0.1, 0.2, and 0.5 mg/kg, respectively). Co-treatment with Asciminib resulted in partial inhibition of TAp63 modification (commonly observed as a shift of TAp63 protein according to W.B. assay). In Figure 2A, a partial prevention of TAp63 shift (see yellow arrows) was observed 18 h after co-injection with Cy and Asciminib. The phosphorylation of histone H2AX was observed at Ser139 (γH2AX), an early marker of DDR in the ovarian lysates. To assess if Asciminib affects DDR activation in primordial/primary oocytes, the phosphorylation of DDR sentinel proteins were monitored using IF assays performed on ovarian sections. It was found that Asciminib attenuated DNA stress signaling induced by Cy in the ovarian reserve. Co-treated ovaries exhibited reduced staining for phospho-DNA-PK, γH2AX, and cleaved PARP in the nuclei of reserve oocytes (Figure 2B–D).Taken together, these data demonstrate that Asciminib can affect both of these signaling pathways activated by Cy in the ovary.

Reference: Int J Mol Sci. 2021 Feb; 22(3): 1395. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7866503/

Note: The information listed here was extracted from literature. MedKoo has not independently retested and confirmed the accuracy of these methods. Customer should use it just for a reference only.