

Product Data Sheet

Product Name: ABL 127
Cat. No.: GC18687

Chemical Properties

Cas. No. 1073529-41-5

Chemical Name (3R)-3-cyclopentyl-4-oxo-3-phenyl-1,2-diazetidine-1,2-dicarboxylic acid 1,2-dimethyl ester

SMILES COC(N(N(C(OC)=O)[C@@]1(C2=CC=CC=C2)C3CCCC3)C1=O)=O

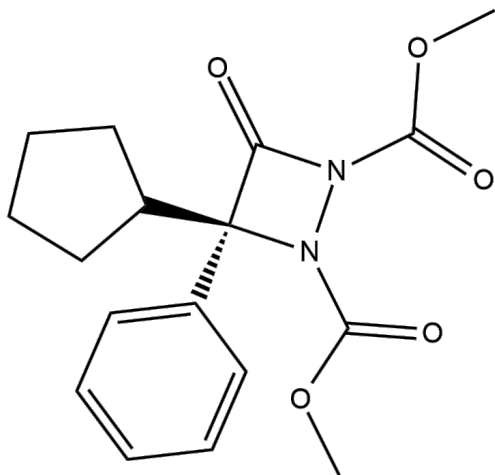
Formula $C_{17}H_{20}N_2O_5$ M.Wt 332.4

Solubility DMSO: ≥ 5 mg/mL; Ethanol: ≥ 1 mg/mL 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.

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

Structure



Protocol

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

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- Kinase experiment:** Human PME-1 protein lacking the last three amino acids (PME-1des3) is purified from Sf9 cells. The assay is completed by first conducting a 10 min pre-incubation of 1 μ M PME-1des3 with 100 μ M ABL127, 100 μ M AMZ-30, 100 μ M EHT, or vehicle (0.05 % DMSO) in the presence of SYBR Orange (1:1000, v/v) at 37°C in 1 $\times$ NEB buffer 2 (50 mM NaCl, 10 mM Tris-HCl, 10 mM MgCl₂, 1 mM DTT, pH 7.9 at 25 °C); a thermal gradient is performed increasing temperature by 2°C per minute increments from 37 to 95°C, and fluorescence (492 to 610 nm) is acquired on a thermal cycler[1].
- Cell experiment:** Cells are subjected to 5 μ g/mL puromycin selection for 10 to 14 days and are clonally expanded. Validated clones are incubated with media and compounds (including ABL127) for the indicated times for phenotypic assays[1].
- Animal experiment:** ECC-1 cells are subcutaneously inoculated into the flanks of female SCID mice and are allowed to grow until tumors reached ~400 mm³. A single intratumoral dose of ABL127 diluted in 10% DMSO/PBS is administered. The highest concentration tested is 5 mg/kg of ABL127 due to poor solubility of the compound[1].

References:

- [1]. Pusey M, et al. Inhibition of protein methylesterase 1 decreased cancerous phenotypes in endometrial adenocarcinoma cell lines and xenograft tumor models. *Tumour Biol.* 2016 Sep;37(9):11835-11842.
- [2]. Bachovchin DA, et al. Academic cross-fertilization by public screening yields a remarkable class of protein phosphatase methylesterase-1 inhibitors. *Proc Natl Acad Sci U S A.* 2011 Apr 26;108(17):6811-6.

Background

ABL127 is a selective and covalent inhibitor of protein methylesterase 1 (PME-1) with IC₅₀s of 6.4

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nM and 4.2 nM in HEK293T and MDA-MB-231 cells, respectively.

Three described PME-1 inhibitors are tested in this assay and a thermal shift with 100 μ M ABL127 is detected. Using 25 or 50 μ M ABL127 also shows a shift in protein melting temperature. It is found that treatment of Ishikawa cells with ABL127 and AMZ-30 significantly decreases cell proliferation similarly to depletion of PME-1 with shRNA. It is also found that treatment of ECC-1 cells with ABL127 or AMZ-30 affects cell invasion in a dose-dependent manner. The treatment of EC cells with ABL127 leads to a significant ~45 % increase in protein phosphatase 2A (PP2A) activity, while treatment with AMZ-30 leads to a modest ~10 % increase in PP2A activity[1].

No significant decrease in tumor burden can be assessed in these pilot studies[1]. Gel-based profiles indicate that brain PME-1 is inactivated by ABL127, but overlapping serine hydrolase activities preclude a confident assessment of the extent of inactivation[2].

References:

- [1]. Pusey M, et al. Inhibition of protein methylesterase 1 decreased cancerous phenotypes in endometrial adenocarcinoma cell lines and xenograft tumor models. *Tumour Biol.* 2016 Sep;37(9):11835-11842.
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