Product Data Sheet

Product Name: HLI 373
Cat. No.: GC10650

Chemical Properties

Cas. No.	502137-98-6		
Chemical Name	5-((3-(dimethylamino)propyl)amino)-3,10-dimethylpyrimido[4,5-b]quinoline-2,4(3H,10H)-dione dihydrochloride		
SMILES	O=C(C1=C(NCCCN(C)C)C2=C(N(C)C1=N3)C=CC=C2)N(C)C3=O.Cl.Cl		
Formula	$C_{18}H_{23}N_5O_2.2HCl$	M.Wt	414.33
Solubility	<37.79mg/ml in Water	Storage	Desiccate at RT
General tips	For obtaining a higher solubility , please warm the tube at 37 ℃ and shake it in the ultrasonic bath for a while.Stock solution can be stored below -20℃ 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	HLI 373		

Background

IC50: N/A

HLI 373 is an inhibitor of Hdm2 ubiquitin ligase (E3).

Hdm2 ubiquitin ligase(E3) is a major regulator of p53 by promoting its ubiquitylation and proteasomal degradation. Therefore, blocking Hdm2-mediated activities may be a therapeutic approach for cancers expressing wild-type p53 [1].

In vitro: HLI373 effectively induces apoptosis of several tumor cells that are sensitive to DNA-damaging agents. HLI373-treated cells showed significantly more DNA retained on the filter, indicating that it does not induce single-strand break in U2OS cells. Having no discernable effect on gp78 or AO7, HLI373 seems prefer to inhibit the ubiquitin ligase activity of Hdm2. Treatment of U2OS cells with HLI373 at 10 Amol/L also leaded to a marked decrease in ubiquitylated species immunoprecipitated with anti-Hdm2, whereas the level of immunoprecipitated Hdm2 increased. Inhibition of Hdm2-mediated

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ubiquitylation in cells can trigger stabilization of both p53 and Hdm2 and preferential killing of tumor cells expressing wild-type p53. HLI373 increased p53 through inhibiting Hdm2-mediated ubiquitylation and not by inducing a DNA damage response in U2OS cells. HLI373 has high potency in stabilizing Hdm2 and p53. HLI373 inhibits the ubiquitin ligase activity of Hdm2 and induces a wild-type p53-dependent apoptosis in several tumor cells that are sensitive to DNA-damaging agents [1,2].

In vivo: So far, no study in vivo has been conducted.

Clinical trial: So far, no clinical study has been conducted.

References:
[1]. Kitagaki J, Agama KK, Pommier Y, et al. Targeting Tumor Cells Expressing p53 with a Water-soluble Inhibitor of Hdm2. Molecular Cancer Therapeutics, 2008; 7(8): 2445-1454.
[2]. Yang Y, Kitagaki J, Wang H, Hou DX, Perantoni AO. Targeting the Ubiquitin-proteasome System for Cancer Therapy. Cancer Science, 2009, 100(1): 24-28.