Product Data Sheet

Product Name: MI-3454
Cat. No.: GC60246

Chemical Properties

Cas. No.	2134169-43-8		
SMILES	O=CNC1(C2)CC2(CN3C(C#N)=CC4=C3C=CC(CN5CCC(NC6=C(C=C(CC(F)(F)F)S7)C7=NC(NC)=N6)CC5)=C4C)C1		
Formula	$C_{32}H_{35}F_3N_8OS$	M.Wt	636.73
Solubility		Storage	
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.		

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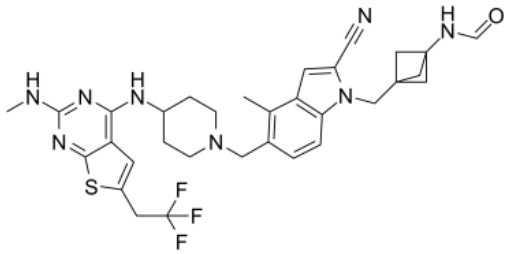
Structure



Background

MI-3454 is an orally active, highly potent and selective menin-MLL1 interaction inhibitor with an IC50 of 0.51 nM. MI-3454 inhibits proliferation, induces differentiation and complete remission or regression of leukemia in mouse models of MLL1-rearranged or NPM1-mutated leukemia through downregulation of key genes involved in leukemogenesis[1].

MI-3454 (0.001-10 μM; 7 days) strongly reduces murine bone marrow cells transformed with MLL-AF9 or Hoxa9/Meis1 proliferation[1]. MI-3454 (50 nM; 6 days) leads to downregulated expression of HOXA9 and MEIS1 in Human leukemic cell lines MV-4-11 cells or MOLM13[1]. MI-3454 markedly reduces the viability of leukemic cells harboring various MLL fusion proteins (MLL-AF9, MLL-AF4, MLL-ENL), with GI50 values ranging from 7 to 27 nM. MI-3454 blocks the interaction of menin with an MLL14-43 fragment encompassing the entire menin binding motif[1]. MI-3454 does not potently

inhibit cytochromes P450 (<50% inhibition at 10 μM)[1]. Cell Proliferation Assay[1] Cell Line: Murine bone marrow cells transformed with MLL-AF9 or Hoxa9/Meis1

MI-3454 induces complete remission or regression of leukemia in mouse models of mixed lineage leukemia 1 (MLL1)-rearranged or nucleophosmin 1 (NPM1)-mutated leukemia[1]. MI-3454 (p.o.; 120 mg/kg; one or twice daily for 7 consecutive days) sufficiently blocks leukemia progression by a once-daily treatment[1]. MI-3454 (p.o.; 100 mg/kg; b.i.d.; for 19 consecutive days) effectively blocks leukemia progression during the treatment period and markedly prolongs survival of MOLM13 xenotransplantation model mice. MI-3454 induces complete remission or blocks leukemia progression in patient-derived xenograft (PDX) models of MLL leukemia[1]. MI-3454 (100 mg/kg of PO or 15 mg/kg of IV) has a T1/2 of 3.2 hours, a Cmax of 4698 mg/mL for PO[1]. MI-3454 exhibits favorable stability in murine and human liver microsomes (t1/2=20.4 minutes and 37.1 minutes, respectively)[1]. MI-3454 demonstrates lower levels in brain and cerebrospinal fluid, suggesting limited ability to cross the blood-brain barrier[1]. Animal Model: 8- to 10-week-old female NSG mice (MV-4-11 xenotransplantation model of MLL leukemia)[1]

[1]. Szymon Klossowski, et al. Menin Inhibitor MI-3454 Induces Remission in MLL1-rearranged and NPM1-mutated Models of Leukemia. J Clin Invest. 2020 Feb 3;130(2):981-997.