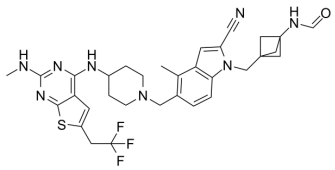
# MI-3454

| | |
|---|---|
| **Cat. No.:** | HY-136360 |
| **CAS No.:** | 2134169-43-8 |
| **Molecular Formula:** | $C_{32}H_{35}F_3N_8OS$ |
| **Molecular Weight:** | 637 |
| **Target:** | Epigenetic Reader Domain |
| **Pathway:** | Epigenetics |
| **Storage:** | 4°C, stored under nitrogen<br>* In solvent : -80°C, 2 years; -20°C, 1 year (stored under nitrogen) |



## SOLVENT & SOLUBILITY

**In Vitro**

DMSO : 31.25 mg/mL (49.06 mM; Need ultrasonic)

| Preparing Stock Solutions | Solvent / Mass / Concentration | 1 mg | 5 mg | 10 mg |
|---|---|---|---|---|
| | 1 mM | 1.5699 mL | 7.8493 mL | 15.6986 mL |
| | 5 mM | 0.3140 mL | 1.5699 mL | 3.1397 mL |
| | 10 mM | 0.1570 mL | 0.7849 mL | 1.5699 mL |

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

**In Vivo**

1. Add each solvent one by one: 20% HP-β-CD >> 5% Cremophor EL
   Solubility: 5 mg/mL (7.85 mM); Suspended solution; Need ultrasonic

## BIOLOGICAL ACTIVITY

**Description**

MI-3454 is an orally active, highly potent and selective menin-MLL1 interaction inhibitor with an $IC_{50}$ 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].

**$IC_{50}$ & Target**

IC50: 0.51 nM (menin-MLL1 interaction)[1]

**In Vitro**

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 $GI_{50}$ values ranging from 7 to 27 nM. MI-3454 blocks the interaction of menin with an $MLL1_{4-43}$ fragment encompassing the entire menin binding motif[1].

MI-3454 does not potently inhibit cytochromes P450 (<50% inhibition at 10 μM)[1].

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

Cell Proliferation Assay[1]

| | |
|---|---|
| Cell Line: | Murine bone marrow cells transformed with MLL-AF9 or Hoxa9/Meis1 |
| Concentration: | 0.001, 0.01, 0.1, 1, 10 μM |
| Incubation Time: | 7 days |
| Result: | Demonstrated strong reduction of cell proliferation. |

RT-PCR[1]

| | |
|---|---|
| Cell Line: | Human leukemic cell lines MV-4-11 cells or MOLM13 |
| Concentration: | 50 nM |
| Incubation Time: | 6 days |
| Result: | Led to downregulated expression of HOXA9 and MEIS1 and expression level of other MLL fusion target genes, including MEF2C, DLX2, HOXA10, PBX3, and FLT3. |

**In Vivo**

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 $T_{1/2}$ of 3.2 hours, a $C_{max}$ of 4698 mg/mL for PO[1].

MI-3454 exhibits favorable stability in murine and human liver microsomes ($t_{1/2}$=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].

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

| | |
|---|---|
| Animal Model: | 8- to 10-week-old female NSG mice (MV-4-11 xenotransplantation model of MLL leukemia) [1] |
| Dosage: | 120 mg/kg |
| Administration: | Orally; one or twice daily for 7 consecutive days |
| Result: | A once-daily treatment was sufficient to block leukemia progression. |

| | |
|---|---|
| Animal Model: | Female CD-1 mice[1] |
| Dosage: | 100 mg/kg (PO) or 15 mg/kg (IV) (Pharmacokinetic Analysis) |
| Administration: | PO or IV |
| Result: | Had a $T_{1/2}$ of 3.2 hours, a $C_{max}$ of 4698 mg/mL for PO.<br>Had a $T_{1/2}$ of 2.4 hours, a CL of 2375 mL/hours•kg, and a $V_{ss}$ of 5358 mL/kg for IV. |

## CUSTOMER VALIDATION

- iScience. 2021 Dec 25;25(1):103679.

See more customer validations on www.MedChemExpress.com

## REFERENCES

[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.



Tel: 609-228-6898 Fax: 609-228-5909 E-mail: tech@MedChemExpress.com
Address: 1 Deer Park Dr, Suite Q, Monmouth Junction, NJ 08852, USA