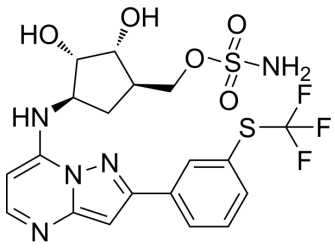
TAK-243

Cat. No.:	HY-100487
CAS No.:	1450833-55-2
Molecular Formula:	$C_{19}H_{20}F_3N_5O_5S_2$
Molecular Weight:	520
Target:	E1/E2/E3 Enzyme; NF-κB; Apoptosis
Pathway:	Metabolic Enzyme/Protease; NF-κB; Apoptosis
Storage:	Powder -20°C 3 years 4°C 2 years In solvent -80°C 1 year -20°C 6 months



SOLVENT & SOLUBILITY

In Vitro

DMSO : 50 mg/mL (96.15 mM; Need ultrasonic)

H_2O : < 0.1 mg/mL (ultrasonic) (insoluble)

Preparing Stock Solutions	Mass / Solvent / Concentration	1 mg	5 mg	10 mg
	1 mM	1.9231 mL	9.6154 mL	19.2308 mL
	5 mM	0.3846 mL	1.9231 mL	3.8462 mL
	10 mM	0.1923 mL	0.9615 mL	1.9231 mL

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

In Vivo

1. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: ≥ 2.08 mg/mL (4.00 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.08 mg/mL (4.00 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.08 mg/mL (4.00 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

TAK-243 (MLN7243) is a first-in-class, selective ubiquitin activating enzyme, UAE (UBA1) inhibitor (IC_{50}=1 nM), which blocks ubiquitin conjugation, disrupting monoubiquitin signaling as well as global protein ubiquitination. TAK-243 (MLN7243) induces endoplasmic reticulum (ER) stress, abrogates NF-κB pathway activation and promotes apoptosis[1][2].

IC_{50} & Target

IC50: 1 nM (UBA1)[1]

In Vitro	TAK-243 shows anti-proliferative effect on a panel of cell lines derived from hematologic and solid tumors with variable EC_{50} values that ranged from 0.006 μM to 1.31 μM[1]. ?TAK-243 reduces growth and viability of human AML cell lines (OCI-AML2, TEX, U937 and NB4) in a concentration- and time-dependent manner with IC_{50}s ranging from 15-40 nM after treatment for 48 hours[3]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	TAK-243 significantly delays tumor growth in mice (T/C=0.02) with no toxicity as evidenced by no changes in mouse body weight, serum chemistry, or organ histology. TAK-243 reduces primary AML tumor burden in both tested samples without toxicity[3]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Cell Assay [1]	Normal keratinocytes (normal human keratinocytes (NHK) and recessive dystrophic epidermolysis bullosa keratinocytes (RDEBK)) and cSCC cell lines are seeded into 96 well plates and live cell number and cell death are analysed with an IncuCyte ZOOM real-time imager using the CellTox Green Cytotoxicity Assay. Relative EC50 values are determined using GraphPad Prism. For clonogenic assays cells are seeded into six well plates. Inhibitors (e.g., TAK-243; 0.01, 0.1, 1, and 10 μM) are added for the indicated times and then cells are maintained in drug-free medium for up to 2 weeks to allow colony formation. Colonies are fixed in 10% methanol, 10% acetic acid and stained with crystal violet[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Animal Administration [2]	Mice[2] The preclinical efficacy and toxicity of TAK-243 are assessed in mouse models of AML. OCI-AML2 cells are injected subcutaneously (sc) into SCID mice, and when tumors are palpable, mice are treated with TAK-243 (20 mg/kg sc twice weekly). As an additional model, primary AML cells from 2 patients are injected into the femurs of NOD-SCID mice. Two weeks after injection, mice are treated with TAK-243 (20 mg/kg sc twice weekly). After 3 weeks of treatment, mice ae sacrificed, and AML engraftment in the non-injected femur is measured by flow cytometry[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- Nature. 2023 Jun;618(7964):394-401.
- Nat Commun. 2023 Jul 15;14(1):4227.
- Mol Cell. 2022 Aug 10;S1097-2765(22)00663-3.
- Mol Cell. 2020 Jul 16;79(2):320-331.e9.
- Mol Cell. 2019 Aug 22;75(4):849-858.e8.

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REFERENCES

[1]. Hyer ML, et al. A small-molecule inhibitor of the ubiquitin activating enzyme for cancer treatment. Nat Med. 2018 Feb;24(2):186-193.

[2]. Best SR, et al. TAK-243, a small molecule inhibitor of ubiquitin-activating enzyme (UAE), induces ER stress and apoptosis in diffuse large B-cell lymphoma (DLBCL) cells. Blood 2017 130:1533.

[3]. Samir H. Barghout, et al. TAK-243 Is a Selective UBA1 Inhibitor That Displays Preclinical Activity in Acute Myeloid Leukemia (AML). Blood 2017, 130:814.

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

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