Elimusertib hydrochloride

Cat. No.: HY-101566A

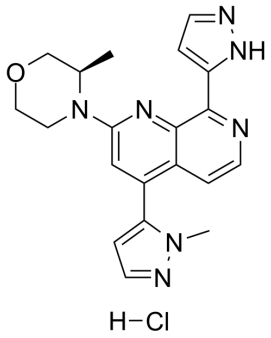
Molecular Formula: $C_{20}H_{22}ClN_7O$

Molecular Weight: 411.89

Target: ATM/ATR

Pathway: Cell Cycle/DNA Damage; PI3K/Akt/mTOR

Storage: 4°C, sealed storage, away from moisture
* In solvent : -80°C, 2 years; -20°C, 1 year (sealed storage, away from moisture)



SOLVENT & SOLUBILITY

In Vitro

DMSO : 50 mg/mL (121.39 mM; Need ultrasonic)
H_2O : 50 mg/mL (121.39 mM; Need ultrasonic)

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	2.4278 mL	12.1392 mL	24.2783 mL
5 mM	0.4856 mL	2.4278 mL	4.8557 mL
10 mM	0.2428 mL	1.2139 mL	2.4278 mL

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

In Vivo

1. Add each solvent one by one: PBS
   Solubility: 100 mg/mL (242.78 mM); Clear solution; Need ultrasonic
2. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: ≥ 2.08 mg/mL (5.05 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.08 mg/mL (5.05 mM); Clear solution
4. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.08 mg/mL (5.05 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

Elimusertib (BAY 1895344) hydrochloride is a potent, orally active and selective ATR inhibitor with an IC_{50} of 7 nM. Elimusertib hydrochloride has anti-tumor activity[1][2]. Elimusertib hydrochloride can be used for the research of solid tumors and lymphomas[3].

IC_{50} & Target

ATR
7 nM (IC_{50})

In Vitro

Elimusertib hydrochloride potently inhibits the proliferation of a broad spectrum of human tumor cell lines with a median IC_{50} of 78 nM[1].
Elimusertib hydrochloride potently suppresses hydroxyurea-induced H2AX phosphorylation (IC_{50}: 36 nM)[1].
Elimusertib hydrochloride shows good selectivity against mTOR (ratio of IC_{50} values: mTOR/ATR 61)[3].
Elimusertib hydrochloride reveals high selectivity against other related kinases, such as DNA-PK (IC_{50}: 332 nM), ATM (IC_{50}: 1420 nM), and PI3K (IC_{50}: 3270 nM)[3].
Elimusertib hydrochloride has potent antiproliferative activity against various cancer cell lines in vitro, 25 for example in the CRC cell lines HT-29 (IC_{50}: 160 nM) and LoVo (IC_{50}: 71 nM), and in the B-cell lymphoma cell line SU-DHL-8 (IC_{50}: 9 nM)[3].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

In Vivo

Elimusertib hydrochloride shows potent anti-tumor efficacy in monotherapy in a variety of xenograft models of ovarian and colorectal cancer, and causes complete tumor remission in mantle cell lymphoma models[2].
Elimusertib hydrochloride (50 mg/kg; p.o.; b.i.d.; 3 days on/4 days off; for 11 days) exhibits strong antitumor efficacy in the ATM-mutated SU-DHL-8 (ATM K1964E) human GCB-DLBCL cell line derived xenograft model in mice[3].
Elimusertib hydrochloride (20 mg/kg, and 10 mg/kg from day 14; p.o.; daily; 2 days on/5 days off; for 42 days) in combination with Carboplatin (40 mg/kg; i.p.; daily; 1 day on/6 days off) results in synergistic antitumor activity in the platinum-resistant ATM protein low expressing CR5038 human CRC PDX model in NOD/SCID mice[3].
Elimusertib hydrochloride exhibits moderate oral bioavailability (rat 87%, dog 51%) following oral administration (rat and dog 0.6-1 mg/kg)[3].
Elimusertib hydrochloride exhibits terminal elimination half-lives (mouse 0.17 h, rat 1.3 and, dog 1.0 h) due to plasma clearance (3.5, 1.2, and 0.79 L/h/kg respectively) following intravenous administration (mouse, rat and dog 0.3-0.5 mg/kg)[3].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Animal Model:	Female C.B-17 SCID mice, SU-DHL-8 GCB-DLBCL xenograft model[3]
Dosage:	50 mg/kg
Administration:	Oral administration, b.i.d., 3 days on/4 days off, for 11 days
Result:	Inhibited tumor area.

Animal Model:	Male Wistar rats[3]
Dosage:	0.3-0.5 mg/kg for i.v.; 0.6-1 mg/kg for oral (Pharmacokinetic Analysis)
Administration:	Intravenous injection and oral administration
Result:	Oral bioavailability (87%), $T_{1/2}$ (1.3 h).

Animal Model:	Female beagle dogs[3]
Dosage:	0.3-0.5 mg/kg for i.v.; 0.6-1 mg/kg for oral (Pharmacokinetic Analysis)
Administration:	Intravenous injection and oral administration
Result:	Oral bioavailability (51%), $T_{1/2}$ (1.0 h).

CUSTOMER VALIDATION

- Cancer Res. 2022 Jan 12;canres.1707.2021.
- Biochem Pharmacol. 2023 Mar 14;115494.

- Research Square Preprint. 2023 Jun 9.
- Research Square Preprint. 2023 May 17.

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REFERENCES

[1]. Ulrich T. Luecking, et al. Abstract 983: Identification of potent, highly selective and orally available ATR inhibitor BAY 1895344 with favorable PK properties and promising efficacy in monotherapy and combination in preclinical tumor models. Cancer Resea

[2]. Antje Margret Wengner, et al. Abstract 836: ATR inhibitor BAY 1895344 shows potent anti-tumor efficacy in monotherapy and strong combination potential with the targeted alpha therapy Radium-223 dichloride in preclinical tumor models. Cancer Research. July

[3]. Ulrich Lücking, et al. Damage Incorporated: Discovery of the Potent, Highly Selective, Orally Available ATR Inhibitor BAY 1895344 with Favorable Pharmacokinetic Properties and Promising Efficacy in Monotherapy and in Combination Treatments in Preclinical

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