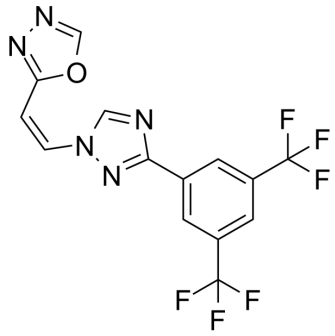
KPT-251

Cat. No.:	HY-117996
CAS No.:	1388841-50-6
Molecular Formula:	$C_{14}H_7F_6N_5O$
Molecular Weight:	375.23
Target:	CRM1; Apoptosis
Pathway:	Membrane Transporter/Ion Channel; Apoptosis
Storage:	4°C, protect from light * In solvent : -80°C, 6 months; -20°C, 1 month (protect from light)



BIOLOGICAL ACTIVITY

Description

KPT-251 is an orally active chromosome region maintenance 1 protein (CRM1) inhibitor. KPT-251 induces cancer cell apoptosis and shows antileukemic activity[1][2].

In Vitro

KPT-251 binds in the NES-binding groove, which is located on the central, convex side of the CRM1 ring[1].
KPT-251 (72 h) suppresses melanoma cell proliferation[2].
KPT-251 (1 μM; 0-48 h) modulates levels of p53, pRb, survivin, and ERK phosphorylation[2].
KPT-251 (0.1 and 1 μM; 0-72 h) induces cell-cycle arrest and apoptosis[2].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Western Blot Analysis[2]

Cell Line:	Melanoma BRAF WT (Mewo) and mutant cells (A375)
Concentration:	1 μM
Incubation Time:	4, 8, 24 and 48 h
Result:	Prevented cytoplasmic p53 degradation, decreased survivin levels, increased ERK phosphorylation in both BRAF WT and mutant and reduced pRb and p-pRb levels.

Cell Cycle Analysis[2]

Cell Line:	Mewo and A375 cells
Concentration:	1 μM
Incubation Time:	24, 48 and 72 h
Result:	Reduced S-phase, both G1 and/or G2 cell-cycle arrest can be observed.

Apoptosis Analysis[2]

Cell Line:	Mel-Juso, SK-MEL-28, SK-MEL-5 and A375 cells
Concentration:	0.1 and 1 μM
Incubation Time:	24, 48 and 72 h

Result:	Increased caspase-3 and -7 activity in the tested melanoma cell lines in a dose- and time-related manner.

In Vivo

KPT-251 (75 mg/kg/day; i.g.; three times per week for 5 weeks) effectively suppresses the growth of MV4-11 cells engrafted into NSG mice and provides a significant survival benefit[1].
KPT-251 (50 mg/kg; p.o.; every other day for 21 days) suppresses tumor growth in mice melanoma xenograft models[2].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Animal Model:	7-weekold female NOD-SCID-IL2Rc$_{\gamma}^{null}$ (NSG) mice, introduced 2 × 10^6 luciferase-expressing MV4-11 cells via tail-vein injections[1]
Dosage:	75 mg/kg/day
Administration:	Gavage, three times per week for 5 weeks
Result:	Exhibited significantly increased survival with leukemia progression occurring only after cessation of treatment, prevented infiltration of leukemia cells into mouse bone marrow and spleen, and spared normal hematopoietic cells.

Animal Model:	Athymic nude mice Nu/Nu, melanoma xenograft models[2]
Dosage:	50 mg/kg
Administration:	Oral, every other day for 21 days
Result:	Suppressed tumor growth, increased cleaved caspase-3 and decreased Ki67.

REFERENCES

[1]. Etchin J, et al. Antileukemic activity of nuclear export inhibitors that spare normal hematopoietic cells. Leukemia. 2013 Jan;27(1):66-74.

[2]. Salas Fragomeni RA, et al. CRM1 and BRAF inhibition synergize and induce tumor regression in BRAF-mutant melanoma. Mol Cancer Ther. 2013 Jul;12(7):1171-9.

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