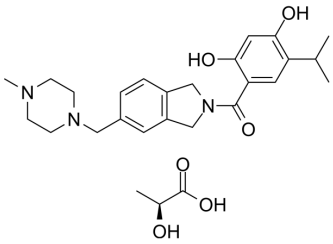
Onalespib lactate

Cat. No.:	HY-113916
CAS No.:	1019889-35-0
Molecular Formula:	$C_{27}H_{37}N_3O_6$
Molecular Weight:	499.6
Target:	HSP
Pathway:	Cell Cycle/DNA Damage; Metabolic Enzyme/Protease
Storage:	Please store the product under the recommended conditions in the Certificate of Analysis.



BIOLOGICAL ACTIVITY

Description

Onalespib lactate is a potent and cross the blood-brain barrier heat-shock-protein-90 (Hsp90) inhibitor with an K_d value of 0.71 nM. Onalespib lactate inhibits the proliferation, survival and migration. Onalespib lactate decreases the expression of EGFR, p-EGFR, AKT, P-AKT, ERK1/2, P-ERK1/2, S6, P-S6 protein. Onalespib lactate shows antitumor activity. Onalespib lactate has the potential for the research of non-small cell lung cancer (NSCLC)[1][2][3][4].

IC_{50} & Target

HSP90
0.71 nM (Kd)

In Vitro

Onalespib lactate (0-0.4 μM; 72 h, 48 h) inhibits the proliferation, survival and migration of glioma cells[2].
Onalespib lactate (0-0.4 μM; 48 h) decreases the expression of EGFR, p-EGFR, AKT, P-AKT, ERK1/2, P-ERK1/2, S6, P-S6 protein in a dose-dependent manner[2].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Cell Proliferation Assay[2]

Cell Line:	LN229, U251 and A172 cells
Concentration:	0.1, 0.2, 0.4 μM
Incubation Time:	72 h
Result:	Inhibited cell proliferation in a dose-dependent manner.

Western Blot Analysis[2]

Cell Line:	LN229, U251 and A172 cells
Concentration:	0.1, 0.2, 0.4 μM
Incubation Time:	48 h
Result:	Decreased the expression of EGFR, p-EGFR, AKT, P-AKT, ERK1/2, P-ERK1/2, S6, P-S6 protein in a dose-dependent manner.

In Vivo

Onalespib lactate (30 mg/kg; i.v.; once) crosses the blood-brain barrier (BBB) and causes sustained inhibition of HSP90 in 6-week-old ICR mice[2].

Onalespib lactate (0.5 μM; from 5 to 10 days post-transplant) and TMZ (10 μM) reduce tumor growth and extend survival in zebrafish embryos[2].

Onalespib lactate (5, 10 mg/kg for HCT116 xenografts, 20 mg/kg for A431 xenografts; i.p.; daily for 3 days) shows anti-tumor activity in HCT116 and A431 xenografts[3].

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

Animal Model:	Female nu/nu Balb/c mice (HCT116 and A431 xenografts)[3]
Dosage:	5, 10 mg/kg for HCT116 xenografts, 20 mg/kg for A431 xenografts
Administration:	I.p.; on day 1, 2, and 3 days
Result:	Inhibited tumor growth and had a median survival of 9.5 days and the maximum survival was 14 days in HCT116 xenografts, reduced the tumor size significantly by 32% in A431 xenografts.

REFERENCES

[1]. Riess JW, et al. Erlotinib and Onalespib Lactate Focused on EGFR Exon 20 Insertion Non-Small Cell Lung Cancer (NSCLC): A California Cancer Consortium Phase I/II Trial (NCI 9878). Clin Lung Cancer. 2021 Nov;22(6):541-548.

[2]. Canella A, et al. Efficacy of Onalespib, a Long-Acting Second-Generation HSP90 Inhibitor, as a Single Agent and in Combination with Temozolomide against Malignant Gliomas. Clin Cancer Res. 2017 Oct 15;23(20):6215-6226.

[3]. Woodhead AJ, et al. Discovery of (2,4-dihydroxy-5-isopropylphenyl)-[5-(4-methylpiperazin-1-ylmethyl)-1,3-dihydroisoindol-2-yl]methanone (AT13387), a novel inhibitor of the molecular chaperone Hsp90 by fragment based drug design. J Med Chem. 2010 Aug 26;53(16):5956-69.

[4]. Spiegelberg D, et al. The HSP90 inhibitor Onalespib exerts synergistic anti-cancer effects when combined with radiotherapy: an in vitro and in vivo approach. Sci Rep. 2020 Apr 3;10(1):5923.

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