A2AR-antagonist-1

Cat. No.: HY-149916

CAS No.: 2922920-71-4

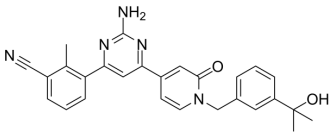
Molecular Formula: $C_{27}H_{25}N_5O_2$

Molecular Weight: 451.52

Target: Adenosine Receptor

Pathway: GPCR/G Protein

Storage: Please store the product under the recommended conditions in the Certificate of Analysis.



BIOLOGICAL ACTIVITY

Description

A2AR-antagonist-1 (compound 38) is an orally active adenosine A2A receptor (A2AR) antagonist (IC_{50}=29 nM). A2AR-antagonist-1 exhibits anti-tumor activity and mouse liver microsomal metabolic stability ($t_{1/2}$=86.1 min). A2AR-antagonist-1 is also a T cells activator, via inhibiting immunosuppressive molecules (LAG-3 and TIM-3) and enhancing effector molecules (GZMB, IFNG, and IL-2)[1].

IC_{50} & Target

A2AR
29 nM (IC_{50})

In Vitro

A2AR-antagonist-1 (0.001-10 μM; 30 min) decreases the level of phosphorylated ERK induced by NECA in HEK293-A2AR cells [1].

A2AR-antagonist-1 (0.1-10 μM; 5 h) inhibits NECA-induced immunological molecules expression and increases effector molecules expression in Jurkat T cells (human immortalized T lymphocyte cell line)[1].

A2AR-antagonist-1 (0.1-10 μM; 48 h) recovers impairment of cytotoxic function of OT-I mouse splenocyte (OT-I CTL) against MC38-OVA cells, enhances T cell's activation and effector function in vitro[1].

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

RT-PCR[1]

Cell Line:	Jurkat T cells
Concentration:	0.1 μM, 1 μM, and 10 μM
Incubation Time:	5 hours
Result:	Reversed NECA (1 μM)-induced up-regulation of immunosuppressive molecules (LAG-3 and TIM-3), and NECA-induced down-regulation of effector molecules (GZMB, IFNG, and IL-2).

Immunofluorescence[1]

Cell Line:	Cytotoxic T lymphocytes from OT-I mouse splenocyte (OT-I CTL)
Concentration:	0.1 μM, 1 μM, and 10 μM
Incubation Time:	48 hours

Result:	Increased relative killing ability of OT-I CTL according to image.

In Vivo

A2AR-antagonist-1 (100 mg/kg; p.o.; once daily for 23 days) exhibits excellent anti-tumor activity in vivo in C57BL/6 mice bearing colon cancer MC38 cells[1].

Pharmacokinetic Analysis in mouse[1]

Route	Dose (mg/kg)	C_{max} (ng/mL)	$AUC_{0\text{-last}}$ (ng·h/mL)	$AUC_{0\text{-t}}$ (ng·h/mL)	$t_{1/2}$ (h)	F (%)
i.v.	2	2584	5577	5565	0.93	/
p.o.	10	8823	24008	24003	2.35	86.1

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

Animal Model:	MC38 xenograft model in mouse[1]
Dosage:	100 mg/kg
Administration:	PO; once daily for 23 days
Result:	Promoted CD8+ T cell accumulation. Enhanced antitumor immunity, promoted tumor regression. Had insignificant effect on body weight of the mice.

REFERENCES

[1]. Zhu C, et al. Discovery of Pyridinone Derivatives as Potent, Selective, and Orally Bioavailable Adenosine A2A Receptor Antagonists for Cancer Immunotherapy. J Med Chem. 2023 Mar 23.

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