

Product Data Sheet

Product Name: Rupintrivir

Cat. No.: GC50441

Chemical Properties

Cas. No. 223537-30-2

SMILES O=C(C1=NOC(C)=C1)N[C@@H](C(C)C)C(C[C@@H](CC2=CC=C(F)C=C2)C(N[C@H](/C=C/C(OCC)=O)C[C@@H]3CCNC3=O)=O)=O

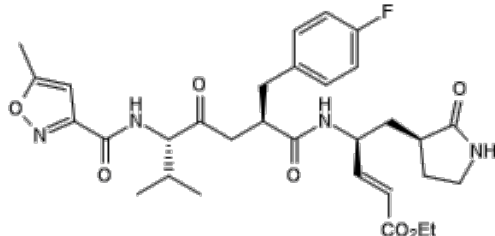
Formula C₃₁H₃₉FN₄O₇ M.Wt 598.66

Solubility DMSO : 50 mg/mL (83.52 mM; Need ultrasonic) Storage Store at -20°C

General tips For obtaining a higher solubility , please warm the tube at 37 °C and shake it in the ultrasonic bath for a while. Stock solution can be stored below -20°C for several months.

Shipping Condition Evaluation sample solution : ship with blue ice All other available size: ship with RT , or blue ice upon request.

Structure



Protocol

Cell experiment [1]:

Cell lines HG23 cells

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

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Preparation Method HG23 cells (Norwalk virus replicon-bearing Huh-7 origin) were grown in RPMI-1640 medium with 10% (v/v) fetal bovine serum (FBS), 2mM l-glutamine, 20mM HEPES, 0.075g/l sodium bicarbonate, 100U penicillin/ml, and 100µg/ml streptomycin at 37°C and 1.25mg/ml of Geneticin (G418) in a humidified atmosphere of 5% CO₂. Cells were seeded in 96-well plates at a density of 5×10^3 cells and cultured overnight. A serial dilution of Rupintrivir (0.1, 0.2, 0.4, 0.8, 1.6, 3.1, and 6.3µM) was added to the cultures. After 72h of incubation, cell monolayers were washed with phosphate-buffered saline (PBS) and collected for quantification of RNA load by qRT-PCR.

Reaction Conditions 0.1, 0.2, 0.4, 0.8, 1.6, 3.1, and 6.3µM; 72h

Applications Rupintrivir treatment significantly reduced the levels of Norovirus RNA in HG23 cells in a dose-dependent manner.

Animal experiment [2]:

Animal models Suckling ICR mice

Preparation Method Two-day-old suckling ICR mice (2.0-2.3g) were injected with 10^6 pfu EV71 (strain 695F) and subsequently underwent intraperitoneal (i.p.) injection with 5-15µl of Rupintrivir or ribavirin dissolved in DMSO to achieve a dosage of 0.1mg/kg (n=13) for Rupintrivir or 100mg/kg (n=10) for ribavirin; an equivalent volume of DMSO was injected in the control group (n=14). The Rupintrivir was injected every day for 10 days. Infected mice were monitored daily for signs of morbidity and mortality. The sickness of mice was evaluated using a graded score (0, healthy; 1, slow movement; 2, weakness in hind limbs; 3, paralysis in single limb; 4, paralysis in two limbs; and 5, death).

Dosage form 0.1mg/kg/day for 10 days; i.p.

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Applications Rupintrivir treatment effectively rescued EV71-induced paralysis and death in a suckling mouse model.

References:

- [1] Rocha-Pereira J, Nascimento M S J, Ma Q, et al. The enterovirus protease inhibitor rupintrivir exerts cross-genotypic anti-norovirus activity and clears cells from the norovirus replicon[J]. Antimicrobial agents and chemotherapy, 2014, 58(8): 4675-4681.
- [2] Zhang X, Song Z, Qin B, et al. Rupintrivir is a promising candidate for treating severe cases of enterovirus-71 infection: evaluation of antiviral efficacy in a murine infection model[J]. Antiviral research, 2013, 97(3): 264-269.

Background

Rupintrivir is a potent, irreversible inhibitor of human rhinovirus (HRV) 3C protease with a mean EC₅₀ value of 0.023μM for inhibiting the replication of all HRV serotypes [1]. Rupintrivir binds in a unique conformation to the active site of SARS-CoV-2 M^{pro}, splitting the catalytic cysteine and histidine residues and inhibiting the activity of SARS-CoV-2 [2]. Rupintrivir has been widely used to inhibit the replication of enterovirus 71 (EV 71), and is combined with IFN-α to develop combination therapies that efficiently eliminate the virus [3].

In vitro, Rupintrivir treatment for 72 hours significantly reduced the levels of Norovirus RNA in HG23 cells, with an EC₅₀ value of 0.3μM[4]. Treatment with 100nM Rupintrivir for 48 hours suppressed the HRV-induced hypersecretion of cytokines IL-6 and IL-4 in precision-cut lung slices (PCLS) from house dust mite (HDM)-sensitized mice [5].

In vivo, Rupintrivir treatment via daily intraperitoneal injection at a dose of 0.1mg/kg for 10 days can alleviate EV 71 virus-induced necrotizing myositis in suckling mice and increase the survival rate[6].

References:

- [1] Patick A K, Binford S L, Brothers M A, et al. In vitro antiviral activity of AG7088, a potent inhibitor of human rhinovirus 3C protease[J]. Antimicrobial agents and chemotherapy, 1999, 43(10): 2444-2450.
- [2] Lockbaum G J, Henes M, Lee J M, et al. Pan-3C protease inhibitor rupintrivir binds SARS-CoV-2

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main protease in a unique binding mode[J]. Biochemistry, 2021, 60(39): 2925-2931.

[3] Hung H C, Wang H C, Shih S R, et al. Synergistic inhibition of enterovirus 71 replication by interferon and rupintrivir[J]. Journal of Infectious Diseases, 2011, 203(12): 1784-1790.

[4] Rocha-Pereira J, Nascimento M S J, Ma Q, et al. The enterovirus protease inhibitor rupintrivir exerts cross-genotypic anti-norovirus activity and clears cells from the norovirus replicon[J]. Antimicrobial agents and chemotherapy, 2014, 58(8): 4675-4681.

[5] Danov O, Lasswitz L, Obernolte H, et al. Rupintrivir reduces RV-induced TH-2 cytokine IL-4 in precision-cut lung slices (PCLS) of HDM-sensitized mice ex vivo[J]. Respiratory research, 2019, 20(1): 228.

[6] Zhang X, Song Z, Qin B, et al. Rupintrivir is a promising candidate for treating severe cases of enterovirus-71 infection: evaluation of antiviral efficacy in a murine infection model[J]. Antiviral research, 2013, 97(3): 264-269.

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