Product Data Sheet

Product Name: AVG-233
Cat. No.: GC67960

Chemical Properties

Cas. No.	2151937-80-1		
Formula	$C_{26}H_{22}ClN_5O_3$	M.Wt	487.94
Solubility	DMSO : 50 mg/mL (102.47 mM; ultrasonic and warming and heat to 60°C)	Storage	4°C, away from moisture and light
General tips	For obtaining a higher solubility , please warm the tube at 37 ℃ and shake it in the ultrasonic bath for a while.Stock solution can be stored below -20℃ 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	AVG-233		

Background

AVG-233 is a potent, orally active **RNA dependent RNA polymerase (RdRp)** inhibitor. AVG-233 prevents initiation of the viral polymerase complex at the promoter. AVG-233 binding site is present in the L_{1-1749} fragment. AVG-233 has nanomolar activity against both RSV strains and clinical RSV isolates (**EC_{50}**=0.14-0.31 μM). AVG-233 can be used for research of respiratory syncytial virus (RSV)[1][2].

AVG-233 (1-100 μM) blocks 3´RNA extension elongation but does not interfere with 3´RNA extension by up to three nucleotides after de novo initiation from the promoter or back-priming[1].
AVG-233 (20 μM) reduces virus yield of RSV A2-L19F (EC_{50}=0.31 μM), RSV strain 2-20 (EC_{50}=0.14 μM) and RSV clinical isolate 718 (EC_{50}=0.2 μM) [1].
AVG-233 (1.25-40 μM; 0-300 s) suppresses RNA synthesis by the L1-1749 fragment in a dose-dependent manner with an IC_{50} value of 13.7 μM. AVG-233 bounds L and the L_{1-1749} fragment with similar affinities (dissociation constants (KD's) are 38.3 μM and 53.1 μM, respectively)[2].

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AVG-233 (50-100 mg/kg; i.g.; once) decreases lung viral load in the RSV mouse model[2].

AVG-233 (2-20 mg/kg; i.v. and p.o.; once; male CD-1 mice) has good orally bioavailable and the maximum plasma concentration about 2 μM[1].

Animal Model:	Female Balb/cJ mice with recRSV-mKate xenograft[2]
Dosage:	50 and 100 mg/kg
Administration:	Oral gavage; once
Result:	Reduced in lung viral load of 0.89 log_{10} $TCID_{50}$ (median tissue culture infectious dose)/mL.
Animal Model:	Male CD-1 mice (27-29 g)[1]
Dosage:	2 mg/kg (i.v.) and 20 mg/kg (p.o.)
Administration:	Intravenous injection and oral administration; once, obtains blood samples at pre-dose and 0.083, 0.25, 0.5, 1, 2, 4, 8, and 24 h post-dosing

Result:

Route	Dose	T_{max}	C_{max}	$AUC_{0-\infty}$	CL/F	$T_{1/2}$	Bioavailability
	mg/kg	h	nmol/ml	h×nmol/ml	liters/h/kg	h	%
Oral	20	1	2.17	5.95	6.98	5.28	33.8

[1]. Cox RM, et, al. Development of an allosteric inhibitor class blocking RNA elongation by the respiratory syncytial virus polymerase complex. J Biol Chem. 2018 Oct 26;293(43):16761-16777.
[2]. Sourimant J, et, al. Orally efficacious lead of the AVG inhibitor series targeting a dynamic interface in the respiratory syncytial virus polymerase. Sci Adv. 2022 Jun 24;8(25):eabo2236.

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