Product Data Sheet

Product Name: EGFR-IN-2
Cat. No.: GC33195

Chemical Properties

Cas. No.	1643497-70-4		
SMILES	O=S(N(N=C1)C=C1C2=NC=CC(NC3=NC=C(C(N4CC(C(C)(O)C)C4)=NN5[C@H](CC)C)C5=C3)=N2)(C6CC6)=O		
Formula	$C_{26}H_{33}N_9O_3S$	M.Wt	551.66
Solubility	Soluble in DMSO	Storage	Store at -20°C
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	EGFR-IN-2		

Protocol

Animal experiment:

Mice[1]Eight week old female SCID beige mice are inoculated subcutaneously with 5×106 NCI-H1975 cells. When tumors reach a mean volume of 300 to 500 mm3, mice with similarly sized tumors are randomized into treatment groups. EGFR-IN-2 at 50 mg/kg or 100 mg/kg is administered orally as a single dose. Tumor and plasma samples are collected at 2, 8 or 16 h post dose[1].

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References:

[1]. Chan BK, et al. Discovery of a Noncovalent, Mutant-Selective Epidermal Growth Factor Receptor Inhibitor. J Med Chem. 2016 Oct 13;59(19):9080-9093.

Background

EGFR-IN-2 is a a noncovalent, irreversible, mutant-selective second generation EGFR inhibitor.

EGFR-IN-2 (Compound 21) inhibits EGFR autophosphorylation with IC50s of 0.027 μM, 0.009 μM ,0.033 μM , and 0.218 μM in double mutant TMLR cell line H1975, double mutant TMdel cell line PC9-ER, activating mutant del70% when tested at 0.1 μM, 61-fold over the TMLR Ki and 63-fold over the TMdel Ki)[1].

To examine its inhibitory effect on pEGFR levels in vivo, EGFR-IN-2 (Compound 21) is studied in a mouse H1975 (TMLR) xenograft model. After a single oral dose of 21 at 50 mg/kg, free plasma concentrations of EGFR-IN-2 at or exceeding the in vitro p-EGFR IC50 of 0.027 μM are sustained over 8 h. When administered at 100 mg/kg, the coverage of p-EGFR IC50 is extended to the last measured time point of 16 h postdose. Corresponding knockdown of p-EGFR and the downstream effectors pERK1/2 and AKT levels are observed at those time points, suggesting target engagement in vivo. In mouse, after intravenous and oral administration, the plasma clearance of EGFR-IN-2 is determined to be 104 mL/kg per min with a bioavailability of 19%. In dogs, the plasma clearance is 13 mL/kg per min with an oral bioavailability of 30%[1].

[1]. Chan BK, et al. Discovery of a Noncovalent, Mutant-Selective Epidermal Growth Factor Receptor Inhibitor. J Med Chem. 2016 Oct 13;59(19):9080-9093.

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