IRAK4-IN-14

Cat. No.: HY-146112

CAS No.: 2667681-71-0

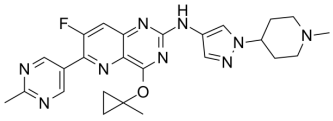
Molecular Formula: $C_{25}H_{28}FN_9O$

Molecular Weight: 489.55

Target: IRAK

Pathway: Immunology/Inflammation

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



BIOLOGICAL ACTIVITY

Description

IRAK4-IN-14 (compound 28) is a potent, selective and orally active IRAK4 inhibitor with an IC_{50} of 0.003 μM. IRAK4-IN-14 shows good PK parameters in rats and mouse. IRAK4-IN-14 shows synergistic in vitro activity against MyD88/CD79 double mutant ABC-DLBCL in combination with Acalabrutinib[1].

IC_{50} & Target

IRAK4
0.003 μM (IC_{50})

In Vitro

IRAK4-IN-14 (compound 28) shows cell pIRAK4 potencies with an IC_{50} of 0.11 μM[1].
IRAK4-IN-14 (compound 28) shows selectivity with IC_{50}s of 0.003,1.4, >8, >9, 0.053, 0.27, 0.76, 0.27 μM for IRAK4, IRAK1, BTK, Flt3, PI3Kδ, TRKa, TRKb, TRKc, respectively[1].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

In Vivo

IRAK4-IN-14 (i.v. or p.o.) shows good PK parameters with oral bioavailability of 66% for mouse[1].
Pharmacokinetic Parameters of IRAK4-IN-14 in Male Han Wistar rats, male CD1 mice, male Cynomolgus monkeys[1].

parameter	Value
A2B P_{app}	31
Efflux ratio	1.4
Solubility (μM)	800
Rat/mouse/monkey/human %free	21/16/33/21
Rat LM/H CL_{int}	16/5.6
Mouse LM/H CL_{int}	13/11
Minipig LM/H CL_{int}	18/8.2

Dog LM/H CL_{int}		21/4.5
Monkey LM/H CL_{int}		35/4.7
Rat	CL	15
	Vd_{ss}	4.3
	$t_{1/2}$	5.2
	F%	55%
Mouse	CL	17
	Vd_{ss}	4.1
	$t_{1/2}$	4.2
	F%	66%
Monkey	CL	68
	Vd_{ss}	8.6
	$t_{1/2}$	1.4

Male Han Wistar rats; 1 mg/kg i.v.; 2 mg/kg p.o.; Male CD1 mice; 0.5 mg/kg i.v.; 1 mg/kg p.o.; Male Cynomolgus monkeys; 1 mg/kg i.v.[1].

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

REFERENCES

[1]. Degorce SL, et al. Improving metabolic stability and removing aldehyde oxidase liability in a 5-azaquinazoline series of IRAK4 inhibitors. Bioorg Med Chem. 2020 Dec 1;28(23):115815.

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