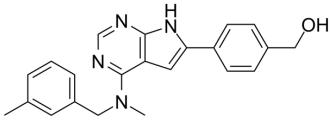
CSF1R-IN-15

Cat. No.:	HY-155001
CAS No.:	2925744-43-8
Molecular Formula:	$C_{22}H_{22}N_4O$
Molecular Weight:	358.44
Target:	c-Fms
Pathway:	Protein Tyrosine Kinase/RTK
Storage:	Please store the product under the recommended conditions in the Certificate of Analysis.



BIOLOGICAL ACTIVITY

Description

CSF1R-IN-15 (compound 23) is an inhibitor targeting CSF1R. The colony-stimulating factor-1 receptor (CSF1R) is a tyrosine kinase embedded in the cell membrane of macrophages. The receptor is activated by colony-stimulating factor-1 (CSF-1) and interleukin-34, and signaling via CSF1R is crucial for the differentiation, proliferation, and survival of macrophages[1].

In Vitro

CSF1R-IN-15 (0.007-10 μM, 72 h) is inactive to Ba/F3 cell viability, while Pex significantly (HY-16749) showed superior activity [1].

CSF1R-IN-15 assessment of plasma protein binding is measured by equilibrium dialysis. CSF1R-IN-15 (5 μM, 6 h, 37 °C) was incubated with plasma and showed 69% binding to mouse plasma proteins[1].

Pharmacokinetic Analysis for CSF1R-IN-15 (compound 23) in vitro[1]

CSF1R-IN-15 (compound 23) [illegible][1]

HLM CL_{int}(μL/min/mg)	HLM CL_{int}(μL/min/mg)	HLM CL_{int}(μL/min/mg)	Plasmastab.	PPB
15.5	40	86	69	94

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

Cell Viability Assay[1]

Cell Line:	Ba/F3-hCSF1R Cells
Concentration:	0.007-10 μM
Incubation Time:	72 h
Result:	Exhibited no activity while pexidartinib (HY-16749) has superior activity.

In Vivo

In vivo pharmacokinetic indices were derived from cassette dosing studies. The $t_{1/2}$, C_0, $AUC_{0-\infty}$, CL_{obs}, and $V_{ss,obs}$ of CSF1R-IN-15 were 0.5 h, 37 ng/mL, 18 h*ng/mL, 54 L/h/kg, and 32 L/kg in C57BLKS mice[1].

Pharmacokinetic Analysis in CSF1R-IN-15 (compound 23) for a cassette dosing study in C57BLKS mice[1]

CSF1R-IN-15 (compound 23) [illegible] C57BLKS [illegible][1]

$t_{1/2}$ (h)	C_0 (ng/mL)	$AUC_{0-\infty}$ (h*ng/mL)	CL_{obs} (L/h/kg)	$V_{ss,obs}$ (L/kg)
0.5	37	18	54	32

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

Animal Model:	In Vivo Pharmacokinetic Study
Dosage:	1mg/kg
Administration:	Intravenous injection (i.v.) single dosing of drugs (1 mg/kg each) in a 20% DMSO, 80% PEG400 formulation. Blood sampling was done after 10, 30, 60, 120, 240, and 480 min.
Result:	In vivo pharmacokinetic indexes were $t_{1/2}$ (0.5 h), C_0 (37 ng/mL), $AUC_{0-\infty}$ (18 h*ng/mL), CL_{obs} (54 L/h/kg), and $V_{ss,obs}$ (32 L/kg), respectively.

REFERENCES

[1]. Aarhus TI, et al. Synthesis and Development of Highly Selective Pyrrolo[2,3-d]pyrimidine CSF1R Inhibitors Targeting the Autoinhibited Form. J Med Chem. 2023 May 25;66(10):6959-6980.

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