FGFR-IN-9

Cat. No.: HY-152104

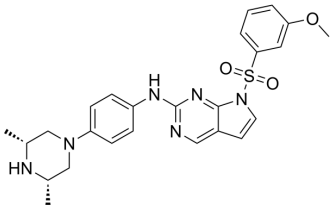
Molecular Formula: $C_{25}H_{28}N_6O_3S$

Molecular Weight: 492.59

Target: FGFR

Pathway: Protein Tyrosine Kinase/RTK

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



BIOLOGICAL ACTIVITY

Description

FGFR-IN-9 (Compound 19) is a potent, reversible and orally active FGFR inhibitor with an IC_{50} of 17.1, 29.6, 30.7, 46.7 and 64.3 nM against $FGFR4^{WT}$, FGFR3, $FGFR4^{V550L}$, FGFR2 and FGFR1, respectively[1].

IC_{50} & Target

$FGFR4^{WT}$ 17.1 nM (IC_{50})	FGFR3 29.6 nM (IC_{50})	$FGFR4^{V550L}$ 30.7 nM (IC_{50})	FGFR2 46.7 nM (IC_{50})
FGFR1 64.3 nM (IC_{50})			

In Vitro

FGFR-IN-9 (Compound 19) (0-2 mM; 72 h) inhibits HUH7 cells with an IC_{50} of 94.7 ± 28.6 nM, and inhibits proliferation with IC_{50}s of 82.5 ± 19.2 nM and 260.0 ± 50.2 nM against Ba/F3 $FGFR4^{WT}$ and Ba/F3 $FGFR4^{V550L}$ cells, respectively[1].

FGFR-IN-9 (0-400 nM; 4 h) inhibits FGFR signaling pathway[1].

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

Western Blot Analysis[1]

Cell Line:	Ba/F3-TEL-FGFR4 cells
Concentration:	0, 50, 100, 200 and 400 nM
Incubation Time:	4 h
Result:	Showed dose-dependent inhibition of the FGFR4 signal cassette, including the phosphorylation of FGFR4 and its downstream effectors FRS2 and PLCγ.

In Vivo

FGFR-IN-9 (Compound 19) (30 and 45 mg/kg; i.g.; daily for 3 weeks) shows antitumor activity in the HUH7 xenograft mouse model[1].

In Vivo Pharmacokinetic Profile Data for FGFR-IN-9 (Compound 19) [1]

FGFR-IN-9	i.v. 1 mg/kg	p.o. 10 mg/kg
$T_{1/2}$ (h)	1.3	2.37

T_{max} (h)	/	2
C_{max} (ng/mL)	/	202
AUC_{max} (h·ng/mL)	175	965
AUC_{INF} (h·ng/mL)	177	1087
MRT_{inf} (h)	1.13	3.87
F (%)	/	61.5
V_{SS} (L/kg)	6.37	/
CL (L/h/kg)	5.65	/

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

Animal Model:	Female BALB/c nude mice, HUH7 xenograft model[1]
Dosage:	30 and 45 mg/kg
Administration:	Intragastric gavage; daily for 3 weeks
Result:	Resulted in significant tumor growth inhibition with a TGI value of 81% and an IR value of 63% at a dose of 45 mg/kg. No significant body weight loss (<5%) was observed.

Animal Model:	Male CD-1 mice[1]
Dosage:	1 mg/kg and 10 mg/kg
Administration:	i.v. and p.o. (Pharmacokinetic Analysis)
Result:	Showed good in vivo pharmacokinetic profile.

REFERENCES

[1]. Xie W, et al. Discovery of 2-Amino-7-sulfonyl-7 H-pyrrolo [2, 3-d] pyrimidine Derivatives as Potent Reversible FGFR Inhibitors with Gatekeeper Mutation Tolerance: Design, Synthesis, and Biological Evaluation. Journal of Medicinal Chemistry, 2022.

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

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