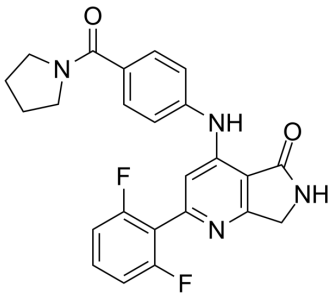
TYK2-IN-12

Cat. No.:	HY-150720
CAS No.:	2244061-66-1
Molecular Formula:	$C_{24}H_{20}F_2N_4O_2$
Molecular Weight:	434.44
Target:	JAK; IFNAR
Pathway:	Epigenetics; JAK/STAT Signaling; Stem Cell/Wnt; Immunology/Inflammation
Storage:	Please store the product under the recommended conditions in the Certificate of Analysis.



BIOLOGICAL ACTIVITY

Description

TYK2-IN-12 (compound 30) is an orally active, potent and selective TYK2 (tyrosine kinase 2) inhibitor, with a K_i of 0.51 nM. TYK2-IN-12 inhibits IL-12 induced IFNγ, with IC_{50} values of 2.7 and 7.0 μM in human and mouse whole blood, respectively. TYK2-IN-12 can be used for psoriasis research[1].

IC_{50} & Target

Tyk2	JAK3	JAK2	JAK1
0.51 nM (Ki)	6.63 nM (Ki)	21.93 nM (Ki)	45.9 nM (Ki)

In Vitro

TYK2-IN-12 (compound 30) shows 90, 43, and 13-fold selectivity over JAK1, JAK2, and JAK3, respectively[1].
TYK2-IN-12 exhibits excellent selectivity over hERG (IC50 > 30 μM) and over a panel of 10 cytochrome P450 enzymes (IC50s > 30 μM against CYP450s 3A4, 3D6, 2C9, 2C8, 1A2, 2A6, 2B6, 2C19, 2E1, and 3A5)[1].
TYK2-IN-12 shows cell-based potency and selectivity in human PBMC by blockade of IL-12 induced phospho-STAT4, GM-CSF induced phospho-STAT5, and IL-2 induced phospho-STAT5, with IC_{50} values of 0.10 μM, 4.1 μM and 0.25 μM, respectively[1].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

In Vivo

TYK2-IN-12 (compound 30) (0-100 mg/kg, PO, daily for 10 days) dose-dependently reduces immune responses[1].
TYK2-IN-12 (3 mg/kg (IV), 10 mg/kg (PO), once) shows moderate clearance and volumes of distribution, and exhibits moderate to good oral absorption[1].
Pharmacokinetic Parameters of TYK2-IN-12 in male C57Bl/6 mice and smale Sprague-Dawley rats[1].

Species	Mouse	Rat
PPB Fu_{max} (h)	0.061	0.10
CL (mL/min/kg)	28	27
$t_{1/2}$ (h)	1.8	1.6
Vd (L/kg)	1.2	1.9
F (%)	>90	32

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

Animal Model:	C57BL/6 mice (IL-23 induced inflammation model)[1]
Dosage:	0, 10, 30, and 100 mg/kg
Administration:	PO, daily for 10 days
Result:	Dose-dependently reduced immune responses, with up to 74 % inhibition of ear swelling and 96 % inhibition of tissue levels of IL-17A at 100 mg/kg, highlighting the crucial role of TYK2 in IL-23 induced IL-17 and tissue inflammation. Exhibited improved skin histology and a dose-dependent reduction of spleen weight.

Animal Model:	Male C57Bl/6 mice, male SD rats[1]
Dosage:	3 mg/kg (IV), 10 mg/kg (PO)
Administration:	IV or PO, once (Pharmacokinetic Analysis)
Result:	Showed moderate clearance and volumes of distribution of 1.2 L/Kg and 1.9 L/Kg, respectively in mouse and rat IV PK, and exhibited moderate to good oral absorption, with oral bioavailabilities of 32-100%.

REFERENCES

[1]. Leit S, et al. Potent and selective TYK2-JH1 inhibitors highly efficacious in rodent model of psoriasis. Bioorg Med Chem Lett. 2022 Jul 13;73:128891.

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