HG-7-85-01

Cat. No.: HY-15814

CAS No.: 1258391-13-7

Molecular Formula: $C_{31}H_{31}F_3N_6O_2S$

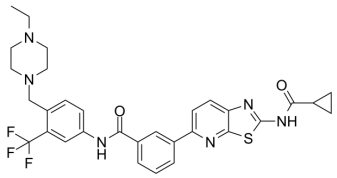
Molecular Weight: 608.68

Target: Bcr-Abl; PDGFR; c-Kit; Src; Apoptosis; JAK

Pathway: Protein Tyrosine Kinase/RTK; Apoptosis; Epigenetics; JAK/STAT Signaling; Stem Cell/Wnt

Storage:

Powder	-20°C	3 years
	4°C	2 years
In solvent	-80°C	6 months
	-20°C	1 month



SOLVENT & SOLUBILITY

In Vitro

DMSO : 125 mg/mL (205.36 mM; Need ultrasonic)

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	1.6429 mL	8.2145 mL	16.4290 mL
5 mM	0.3286 mL	1.6429 mL	3.2858 mL
10 mM	0.1643 mL	0.8214 mL	1.6429 mL

Please refer to the solubility information to select the appropriate solvent.

BIOLOGICAL ACTIVITY

Description

HG-7-85-01 is a type II ATP competitive inhibitor of wild-type and gatekeeper mutations forms of Bcr-Abl, PDGFRα, Kit, and Src kinases. HG-7-85-01 inhibits T315I mutant Bcr-Abl kinase, KDR and RET with IC_{50}s of 3 nM, 20 nM and 30 nM, and is only weak or no inhibition of other kinases (IC_{50}>2 μM). HG-7-85-01 inhibits the cell proliferation, which is mediated by the induction of apoptosis, and inhibition of cell-cycle progression[1].

IC_{50} & Target

$Bcr\text{-}Abl^{T315I}$ 3 nM (IC_{50})	PDGFRα 440 nM (IC_{50})	KDR 20 nM (IC_{50})	RET 30 nM (IC_{50})
JAK1 120 nM (IC_{50})	MK5 560 nM (IC_{50})		

In Vitro

HG-7-85-01 (0-1 μM; 24 hours; BCR-ABL-, BCR-ABL-T315I-, Kit-T670I-, PDGFRα-T674M-, and PDGFRα-T674I-expressing cells) treatment leads to G0G1 arrest of BCR-ABL-expressing cells[1].

HG-7-85-01 (0-1 μM; 72 hours; BCR-ABL-, BCR-ABL-T315I-, Kit-T670I-, PDGFRα-T674M-, and PDGFRα-T674I-expressing cells)

treatment also leads to induction of apoptosis of BCR-ABL-expressing cells[1].
HG-7-85-01 treatment potently and selectively inhibits the proliferation of 32D- and Ba/F3 cells expressing nonmutant BCR-ABL and the BCR-ABL-T315I gatekeeper mutant. HG-7-85-01 shows higher potency against nonmutant BCR-ABL and BCR-ABL-T315I (IC_{50} = 0.06-0.14 μM)[1].
HG-7-85-01 inhibits BCR-ABL kinase activity in a concentration-dependent manner, suggesting selective targeting of the BCR-ABL kinase as the mechanism of action of HG-7-85-01[1].
HG-7-85-01 potently inhibits the proliferation of Ba/F3 cells expressing the Kit-T670I gatekeeper mutation (Ba/F3- Kit-T670I) and Ba/F3 cells expressing TEL/PDGFRβ and no effect on parental Ba/F3 cells. HG-7-85-01 inhibits Kit, PDGFR phosphorylation in a concentration-dependent manner[1].
The PDGFRα-T674M and PDGFRα-T674I gatekeeper mutant variants are highly responsive to HG-7-85-01 and significant IL-3 rescue[1].
HG-7-85-01 inhibits the proliferation of Ba/F3 cells transformed with human c-Src (EC_{50} = 190 nM), T338I Src (EC_{50} = 290 nM), and T338M Src (EC_{50} = 150 nM; chicken c-Src numbering). And potently inhibits the proliferation of exon 11 Kit mutant-expressing cells, exon 9 kit mutant-expressing cells are significantly less responsive[1].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Cell Cycle Analysis[1]

Cell Line:	BCR-ABL-, BCR-ABL-T315I-, Kit-T670I-, PDGFRα-T674M-, and PDGFRα-T674I-expressing cells
Concentration:	0 μM, 0.01 μM, 0.1 μM and 1 μM
Incubation Time:	24 hours
Result:	Led to G0G1 arrest of BCR-ABL-expressing cells.

Apoptosis Analysis[1]

Cell Line:	BCR-ABL-, BCR-ABL-T315I-, Kit-T670I-, PDGFRα-T674M-, and PDGFRα-T674I-expressing cells
Concentration:	0 μM, 0.01 μM, 0.1 μM and 1 μM
Incubation Time:	72 hours
Result:	Led to induction of apoptosis of BCR-ABL-expressing cells.

In Vivo

HG-7-85-01 has limited oral bioavailability (BAV % F mouse = 5 %, rat = 19 %), a moderate half life ($T_{1/2}$ mouse =1.1 h rat = 5.8 hours), a relative low maximal serum concentration (C_{max} mouse = 106 ng/mL at 10 mg/kg , rat = 292 ng/mL and 2 mg/kg) and a relatively high clearance (Cl mouse = 23 ml/min/kg, rat = 13 ml/min/kg) [1].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

REFERENCES

[1]. Ellen Weisberg, et al. Discovery of a Small-Molecule Type II Inhibitor of Wild-Type and Gatekeeper Mutants of BCR-ABL, PDGFRalpha, Kit, and Src Kinases: Novel Type II Inhibitor of Gatekeeper Mutants. Blood. 2010 May 27;115(21):4206-16.

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