Olverembatinib

Cat. No.: HY-15666

CAS No.: 1257628-77-5

Molecular Formula: $C_{29}H_{27}F_3N_6O$

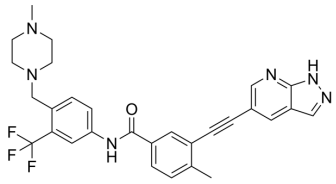
Molecular Weight: 532.56

Target: Bcr-Abl

Pathway: Protein Tyrosine Kinase/RTK

Storage:

Powder	-20°C	3 years
	4°C	2 years
In solvent	-80°C	2 years
	-20°C	1 year



SOLVENT & SOLUBILITY

In Vitro

DMSO : 41.67 mg/mL (78.24 mM; ultrasonic and warming and heat to 60°C)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	1.8777 mL	9.3886 mL	18.7772 mL
	5 mM	0.3755 mL	1.8777 mL	3.7554 mL
	10 mM	0.1878 mL	0.9389 mL	1.8777 mL

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

In Vivo

1. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: ≥ 2.75 mg/mL (5.16 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.75 mg/mL (5.16 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.75 mg/mL (5.16 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

Olverembatinib (GZD824) is a potent and orally active pan-Bcr-Abl inhibitor. Olverembatinib potently inhibits a broad spectrum of Bcr-Abl mutants. Olverembatinib strongly inhibits native Bcr-Abl and Bcr-Abl^{T315I} with IC_{50}s of 0.34 nM and 0.68 nM, respectively. Olverembatinib has antitumor activity[1]. Olverembatinib is a click chemistry reagent, it contains an Alkyne group and can undergo copper-catalyzed azide-alkyne cycloaddition (CuAAc) with molecules containing Azide groups.

IC_{50} & Target

IC50: 0.68 nM (Bcr-Abl^{T315I}), 0.27 nM (Bcr-Abl^{E255K}) , 0.71 nM (Bcr-Abl^{G250E}) , 0.15 nM (Bcr-Abl^{Q252H}), 0.35 nM (Bcr-Abl ^{H396P}), 0.29 nM (Bcr-Abl ^{M351T}), 0.35 nM (Bcr-Abl^{Y253F}), Bcr-Abl^{F317L}[1]

In Vitro

Olverembatinib shows antiproliferative activity in stably transformed Ba/F3 cells whose growth was driven by native Bcr-Abl or Bcr-Abl mutants[1].
Olverembatinib selectively and potently inhibits the proliferation of Bcr-Abl-positive leukemia cells[1].
Olverembatinib inhibits Bcr-Abl signaling in K562 (1-20 nM; 4.0 hours) and Ba/F3 stable cell lines expressing native Bcr-Abl (0.1-100 nM; 4.0 hours) or Bcr-Abl^{T315I}(0.1-100 nM; 4.0 hours)[1].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Western Blot Analysis[1]

Cell Line:	K562 cells
Concentration:	1 nM, 2 nM, 5 nM, 10 nM, 20nM
Incubation Time:	4.0 hours
Result:	Inhibited Bcr-Abl signaling in K562 cell lines.

In Vivo

Olverembatinib suppresses tumor growth in mice bearing allografted Ba/F3 cells expressing Bcr-Abl ^{WT}[1].
Olverembatinib (1-20 mg/kg; i.g.; daily; for 10 days) significantly increases the median survival of the mice bearing allografted Ba/F3 cells expressing Bcr-Abl^{T315I}[1].
Olverembatinib exhibits a good oral bioavailability (rat 48.7%) and C_{max} (rat 390.5 μg/L) following oral administration (rat; 25 mg/kg)[1].
Olverembatinib exhibits terminal elimination half-lives (rat 5.6 h) due to high plasma clearance (rat 1.7 L/h/kg) following intravenous administration (rat 5 mg/kg)[1].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Animal Model:	SCID nude mice, bearing allografted Ba/F3 cells expressing Bcr-Abl^{T315I}[1]
Dosage:	1 mg/kg, 2 mg/kg, 5.0 mg/kg, 10 mg/kg, 20 mg/kg
Administration:	Oral gavage, daily, for 10 days
Result:	Efficiently prolonged animal survival in an allograft leukemia tumor model.

Animal Model:	Rats[1]
Dosage:	5 mg/kg for i.v.; 25 mg/kg for oral (Pharmacokinetic Analysis)
Administration:	Intravenous injection and oral administration
Result:	Oral bioavailability (48.7%), C_{max} (390.5 μg/L), $T_{1/2}$ (5.6 h).

CUSTOMER VALIDATION

- Research Square Print. 2023 Mar 23.
- Research Square Preprint. 2021 Oct.
- Biochim Biophys Acta. 2018 May 25;1865(9):1173-1186.

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REFERENCES

[1]. Ren X, Pan X, Zhang Z, Identification of GZD824 as an orally bioavailable inhibitor that targets phosphorylated and nonphosphorylated breakpoint cluster region-Abelson (Bcr-Abl) kinase and overcomes clinically acquired mutation-induced resistance against imatinib. J Med Chem. 2013 Feb 14;56(3):879-94.

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