Olverembatinib dimesylate

Cat. No.: HY-15666A

CAS No.: 1421783-64-3

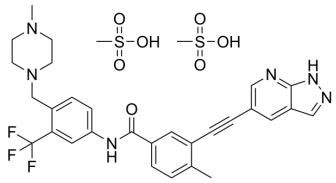
Molecular Formula: $C_{31}H_{35}F_3N_6O_7S_2$

Molecular Weight: 724.77

Target: Bcr-Abl

Pathway: Protein Tyrosine Kinase/RTK

Storage: 4°C, sealed storage, away from moisture and light
* In solvent : -80°C, 6 months; -20°C, 1 month (sealed storage, away from moisture and light)



SOLVENT & SOLUBILITY

In Vitro

DMSO : 125 mg/mL (172.47 mM; Need ultrasonic)
H_2O : ≥ 50 mg/mL (68.99 mM)
* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	1.3797 mL	6.8987 mL	13.7975 mL
5 mM	0.2759 mL	1.3797 mL	2.7595 mL
10 mM	0.1380 mL	0.6899 mL	1.3797 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: ≥ 2.08 mg/mL (2.87 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.08 mg/mL (2.87 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.08 mg/mL (2.87 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

Olverembatinib (GZD824) dimesylate is a potent and orally active pan-Bcr-Abl inhibitor. Olverembatinib dimesylate potently inhibits a broad spectrum of Bcr-Abl mutants. Olverembatinib dimesylate strongly inhibits native Bcr-Abl and Bcr-Abl^{T315I} with IC_{50}s of 0.34 nM and 0.68 nM, respectively. Olverembatinib dimesylate has antitumor activity[1]. Olverembatinib (dimesylate) 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 dimesylate shows antiproliferative activity in stably transformed Ba/F3 cells whose growth was driven by native Bcr-Abl or Bcr-Abl mutants[1].
Olverembatinib dimesylate selectively and potently inhibits the proliferation of Bcr-Abl-positive leukemia cells[1].
Olverembatinib dimesylate 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 dimesylate suppresses tumor growth in mice bearing allografted Ba/F3 cells expressing Bcr-Abl ^{WT}[1].
Olverembatinib dimesylate (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 dimesylate 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 dimesylate 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.

Tel: 609-228-6898 Fax: 609-228-5909 E-mail: tech@MedChemExpress.com

Address: 1 Deer Park Dr, Suite Q, Monmouth Junction, NJ 08852, USA