Trilaciclib hydrochloride

Cat. No.: HY-101467A

CAS No.: 1977495-97-8

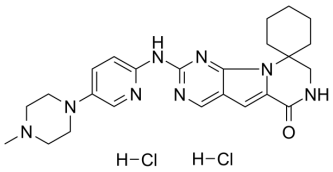
Molecular Formula: $C_{24}H_{32}Cl_2N_8O$

Molecular Weight: 519.47

Target: CDK

Pathway: Cell Cycle/DNA Damage

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



SOLVENT & SOLUBILITY

In Vitro

H_2O : 25.64 mg/mL (49.36 mM; ultrasonic and adjust pH to 2 with HCl)
DMSO : 1.1 mg/mL (2.12 mM; Need ultrasonic)

Preparing Stock Solutions

Concentration \ Solvent \ Mass	1 mg	5 mg	10 mg
1 mM	1.9250 mL	9.6252 mL	19.2504 mL
5 mM	0.3850 mL	1.9250 mL	3.8501 mL
10 mM	0.1925 mL	0.9625 mL	1.9250 mL

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

BIOLOGICAL ACTIVITY

Description

Trilaciclib hydrochloride (G1T28 hydrochloride) is a CDK4/6 inhibitor with IC_{50}s of 1 nM and 4 nM for CDK4 and CDK6, respectively[1].

IC_{50} & Target

Cdk4/cyclin D1	cdk6/cyclin D3
1 nM (IC_{50})	4 nM (IC_{50})

In Vitro

Incubation with Trilaciclib hydrochloride (G1T28) for 24 hours induces a robust G_1 cell-cycle arrest (time=0). By 16 hours after Trilaciclib hydrochloride washout, cells have reentered the cell cycle and demonstrate cell-cycle kinetics similar to untreated control cells. These results demonstrate that Trilaciclib hydrochloride causes a transient, and reversible G_1 arrest. A transient Trilaciclib hydrochloride-mediated G_1 cell-cycle arrest in CDK4/6-sensitive cells decreases the in vitro toxicity of a variety of commonly used cytotoxic chemotherapy agents associated with myelosuppression[1].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

In Vivo

Trilaciclib hydrochloride (G1T28) treatment results in a robust and dose-dependent suppression of proliferation in HSPCs at 12 hours, with 5-ethynyl-2′-deoxyuridine (EdU) incorporation returning near baseline levels in a dose-dependent manner by 24 hours after administration. These data demonstrate that a single oral dose of Trilaciclib hydrochloride can produce

reversible cell-cycle arrest in HSPCs in a dose-dependent manner in vivo. Mice given 100 mg/kg Trilaciclib hydrochloride 30 minutes prior to etoposide treatment, exhibits only background levels of caspase-3/7 activity. These data demonstrate that Trilaciclib hydrochloride can protect the bone marrow from chemotherapy-induced apoptosis in vivo. The data demonstrate that treatment with Trilaciclib hydrochloride prior to 5-fluorouracil (5-FU) likely decreases 5-FU-induced damage by chemotherapy in HSPCs, thus accelerating blood count recovery after chemotherapy[1].

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PROTOCOL

Kinase Assay [1]

HS68, WM2664, and A2058 cells are treated with 300 nM Trilaciclib hydrochloride (G1T28) or DMSO (0.1%), for 4, 8, 16, or 24 hours. Whole cell extracts are prepared using 1× radioimmunoprecipitation assay buffer containing 1× HALT protease and phosphatase inhibitors. Total protein concentration is determined by using the kit, according to the manufacturer's instructions. For Western blot analysis, protein is processed as described previously. Antibodies to total RB and β-tubulin run as a loading control are assessed[1].

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Cell Assay [1]

HS68 cells are treated for 24 hours with Trilaciclib hydrochloride (G1T28) at 10, 30, 100, 300, 1,000, or 3,000 nM final concentration. Cells are harvested and fixed in ice-cold methanol. Fixed cells are stained with 20 µg propidium iodide, 50 µg RNAse A in PBS-CMF (calcium magnesium free) +1% BSA, Fraction V. Samples are processed on Cyan ADP Analyzer, and cell-cycle analysis is completed using software[1].

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Animal Administration [1]

Female athymic nude mice are implanted with H69 cells and monitored until treatment initiation. Once tumors reach an acceptable size (150 mm^3), mice are dosed in various combinations of Trilaciclib hydrochloride (G1T28) and topotecan for 5 days per week for 4 weeks. Tumors are measured for up to 60 days after treatment. All mice that reach excessive tumor burden before 60 days are humanely euthanized. Topotecan and Trilaciclib hydrochloride levels in blood plasma from the mice treated with Trilaciclib hydrochloride and/or topotecan are processed and analyzed using established methods[1].

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

CUSTOMER VALIDATION

- Department of Biochemistry. 2020 Oct.

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REFERENCES

[1]. Bisi JE, et al. Preclinical Characterization of G1T28: A Novel CDK4/6 Inhibitor for Reduction of Chemotherapy-Induced Myelosuppression. Mol Cancer Ther. 2016 May;15(5):783-93.

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