Obefazimod

Cat. No.: HY-100870

CAS No.: 1258453-75-6

Molecular Formula: $C_{16}H_{10}ClF_3N_2O$

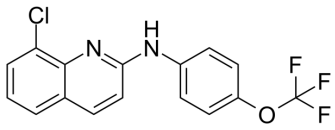
Molecular Weight: 338.71

Target: HIV

Pathway: Anti-infection

Storage:

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



SOLVENT & SOLUBILITY

In Vitro

DMSO : ≥ 100 mg/mL (295.24 mM)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	2.9524 mL	14.7619 mL	29.5238 mL
5 mM	0.5905 mL	2.9524 mL	5.9048 mL
10 mM	0.2952 mL	1.4762 mL	2.9524 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: ≥ 3.75 mg/mL (11.07 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 3.75 mg/mL (11.07 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

Obefazimod (ABX464) is a potent anti-HIV agent. Obefazimod inhibits HIV-1 replication in stimulated peripheral blood mononuclear cells (PBMCs) with an IC_{50} ranging between 0.1 μM and 0.5 μM.

IC_{50} & Target

HIV-1

0.1-0.5 μM (IC_{50}, in PBMCs)

In Vitro

Obefazimod inhibits HIV-1 production in PBMC- and macrophages-infected cells. Obefazimod has a strong inhibitory effect for all HIV-1 subtypes tested including subtype B, C and recombinant viruses. Obefazimod also very efficiently inhibits the replication of viral strains harbouring mutations that confer resistance to different therapeutic agents in vitro. While the antiviral drug 3TC is not highly active on K65R and M184V mutant strains, both strains are inhibited by Obefazimod. To

	generalize the effect of Obefazimod on HIV-1 replication in other primary cells, cells are treated with between 0.01 μM up to 30 μM concentrations of Obefazimod and p24 antigen levels are monitored in culture supernatants over a 12 days period. Obefazimod efficiently blocks virus replication in a dose-dependent manner with an IC_{50} ranging between 0.1 μM and 1 μM [1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	Humanized mice reconstituted with human lymphoid cells provide rapid, reliable, reproducible experimental systems for testing the efficacy of Obefazimod in vivo. In the initial setting, SCID mice are reconstituted with PBMCs and then infected with the HIV-1 strain JR-CSF. Mice are treated twice a day (b.i.d) for 15 days by oral gavage with 20 mg/kg of Obefazimod. Measures of viral RNA show that the oral treatment with Obefazimod is able to significantly reduce the viral load over a period of 15 days of treatment. FACS analysis of blood samples show that treatment with Obefazimod prevents depletion of $CD4^+$ cells following infection of reconstituted mice and thereby restores the $CD8^+/CD4^+$ ratio back to that of non-infected mice[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Cell Assay [1]	The concentration of ABX464 with minimal side effects on cell viability is determined using an MTS test. PBMCs are treated with ABX464 (2, 4, 8, 16, 31, 63, 125, and 250 μM). Cell viability is measured by MTS assay after 6 days of incubation and cytotoxicity is indicated as percentage as compared with untreated cells[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Animal Administration [1]	Mice[1] SCID mice are reconstituted with fresh human PBMCs for two weeks and the reconstitution rates are estimated by human IgG titration. Reconstituted SCID mice are infected with JRCSF HIV-1 strain by intraperitoneal injection. Control group receive labrafil and 5% DMSO by gavage (n=15) and the treated group receive 20 mg/kg b.i.d of ABX464 (n=14) for 15 days[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

REFERENCES

[1]. Campos N, et al. Long lasting control of viral rebound with a new drug ABX464 targeting Rev-mediated viral RNA biogenesis. Retrovirology. 2015 Apr 9;12:30.

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