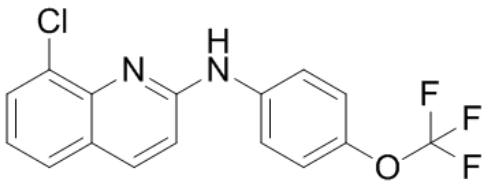
Product Data Sheet

Product Name: ABX464
Cat. No.: GC32145

Chemical Properties

Cas. No.	1258453-75-6		
SMILES	FC(F)(F)OC1=CC=C(NC2=NC3=C(Cl)C=CC=C3C=C2)C=C1		
Formula	$C_{16}H_{10}ClF_3N_2O$	M.Wt	338.71
Solubility	DMSO : ≥ 100 mg/mL (295.24 mM)	Storage	Store at -20°C
General tips	For obtaining a higher solubility , please warm the tube at 37 °C and shake it in the ultrasonic bath for a while.Stock solution can be stored below -20°C for several months.		
Shipping Condition	Evaluation sample solution : ship with blue ice All other available size: ship with RT , or blue ice upon request.		

Structure



Protocol

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Cell experiment: 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].

Animal experiment: 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].

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.

Background

ABX464 is a potent anti-HIV agent. ABX464 inhibits HIV-1 replication in stimulated peripheral blood mononuclear cells (PBMCs) with an IC50 ranging between 0.1 μM and 0.5 μM.

ABX464 inhibits HIV-1 production in PBMC- and macrophages-infected cells. ABX464 has a strong inhibitory effect for all HIV-1 subtypes tested including subtype B, C and recombinant viruses. ABX464 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 ABX464. To generalize the effect of ABX464 on HIV-1 replication in other primary cells, cells are treated with between 0.01 μM up to 30 μM concentrations of ABX464 and p24 antigen levels are monitored in culture supernatants over a 12 days period. ABX464 efficiently blocks virus replication in a dose-dependent manner with an IC50 ranging between 0.1 μM and 1 μM[1].

Humanized mice reconstituted with human lymphoid cells provide rapid, reliable, reproducible

experimental systems for testing the efficacy of ABX464 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 ABX464. Measures of viral RNA show that the oral treatment with ABX464 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 ABX464 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].

[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.