Product Data Sheet

Product Name: AZD-5991 Racemate
Cat. No.: GC33283

Chemical Properties

Cas. No.	2143010-83-5		
SMILES	O=C(O)C1=C(CCCOC2=C(C=CC=C3)C3=CC4=C2)C5=C(N1C)C(C6=C(C)N(C)N=C6CSCC7=NN(C)C(CS4)=C7)=C(Cl)C=C5		
Formula	$C_{35}H_{34}ClN_5O_3S_2$	M.Wt	672.26
Solubility	Soluble in DMSO	Storage	Store at -20°C
General tips	For obtaining a higher solubility , please warm the tube at 37 ℃ and shake it in the ultrasonic bath for a while.Stock solution can be stored below -20℃ 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	AZD-5991 Racemate		

Background

AZD5991 is a macrocyclic MCL-1 inhibitor with sub-nanomolar affinity for MCL-1 (Ki = 0.13 nM). The binding affinity of AZD5991 is about 25-fold lower for mouse Mcl-1 vs. human Mcl-1 but only four-fold lower for rat Mcl-1.

AZD5991 is a potent and direct inhibitor of Mcl-1 with high selectivity versus other Bcl-2 family proteins. AZD5991 binds directly to Mcl-1 and induces rapid apoptosis in cancer cells, most notably myeloma and acute myeloid leukemia (GI50 < 100nM), by activating the Bak-dependent mitochondrial apoptotic pathway. In a panel of cancer-derived cell lines of hematological or solid tumor origin, AZD5991 preferentially kills hematological cells[1][3].

AZD5991 shows potent antitumor activity in vivo with complete tumor regression in several models of multiple myeloma and acute myeloid leukemia after a single tolerated dose as monotherapy or in combination with bortezomib or venetoclax. In these in vivo studies, the cytotoxic activity of AZD5991 tightly correlates with induction of the mitochondrial apoptotic pathway as evidenced by cleavage of caspase-3 and PARP[1].

[1] Tron AE, et al. Nat Commun. 2018, 9(1):5341. [2] Garner TP, et al. Curr Opin Chem Biol. 2017, 39:133-142. [3] Adriana E. Tron, et al. AACR Cancer Res. 2018, 78(13 Suppl):Abstract nr 302.

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