Product Data Sheet

Product Name: Atuveciclib (BAY-1143572)
Cat. No.: GC34422

Chemical Properties

Cas. No.			
SMILES	N=[S@](CC1=CC(NC2=NC(C3=CC=C(F)C=C3OC)=NC=N2)=CC=C1)(C)=O		
Formula	$C_{18}H_{18}FN_5O_2S$	M.Wt	387.43
Solubility	DMSO : ≥ 128.5 mg/mL (331.67 mM)	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	Atuveciclib (BAY-1143572)		

Protocol

Cell experiment:

HeLa human cervical tumor cells (CCL-2) and MOLM-13 human acute myeloid leukemia cells (ACC 554) are propagated under the suggested growth conditions in a humidified 37°C incubator. Proliferation assays are conducted in 96-well plates at densities of 3000 (HeLa) and 5000 (MOLM-13) cells per well in the growth medium containing 10 % fetal calf serum (FCS). Cells are treated in quadruplicate with serial dilutions of test compounds (e.g., Atuveciclib (BAY-1143572)) for 96 h. Relative cell numbers are quantified by crystal violet staining (HeLa) or CellTitre-Glo Luminescent Cell Viability Assay (MOLM-13). IC50 values are determined by means of a four-parameter fit on measurement data which are normalized to vehicle (DMSO) treated cells (=100 %) and measurement readings taken immediately before compound exposure (=0 %)[1].

Tel: (909) 407-4943 Fax: (626) 353-8530 E-mail: tech@glpbio.com
Address: 10292 Central Ave. #205, Montclair, CA, USA

Product Data Sheet

Animal experiment:

Mice and Rats[1]For the acute myeloid leukemia (AML) mouse model, 2×106 MOLM-13 human AML cells are inoculated subcutaneously to the left flank of female NMRI nu/nu mice (18-21 g, 5-6 weeks). For the AML model in rats, 2×106 MV4-11 human AML cells are inoculated subcutaneously to the left flank of female athymic nude rats (160-200 g, 5-6 weeks). Animals are stratified into treatment and control groups (n=8-13/group for mice, n=12/group for rats) based on primary tumor size. Treatments are started 3-13 days after tumor cell inoculation when the average tumor sizes are 23-38 mm2 and 43 mm2 for mice and rats, respectively. The 20 and 25 mg/kg once daily dose is for nude mice. Furthermore, Atuveciclib (BAY-1143572) administered at 25 or 35 mg/kg, three days on/two days off. BAY-1143572 is administered daily oral administration of Atuveciclib (BAY-1143572) at 12 mg/kg for rats. Unless otherwise indicated, all treatments are administered orally (p.o.) and are continued until the end of the experiment. Body weight and tumor areas (longest diameter multiplied by its perpendicular) measured by caliper are determined at least twice weekly. T/C ratios are calculated by dividing the mean tumor area of the treatment group by the mean tumor area of the vehicle group at the time point when the vehicle group is sacrificed[1].

Tel: (909) 407-4943 Fax: (626) 353-8530 E-mail: tech@glpbio.com
Address: 10292 Central Ave. #205, Montclair, CA, USA

References:

[1]. Lücking U, et al. Identification of Atuveciclib (BAY 1143572), the First Highly Selective, Clinical PTEFb/CDK9 Inhibitor for the Treatment of Cancer. ChemMedChem. 2017 Nov 8;12(21):1776-1793.

Background

Atuveciclib (BAY-1143572) is a potent and highly selective, oral PTEFb/CDK9 inhibitor. Atuveciclib (BAY-1143572) inhibits CDK9/CycT1 with an IC50 of 13 nM.

Positive transcription elongation factor b (PTEFb) is a heterodimer of CDK9 and one of four cyclin partners, cyclin T1, cyclin K, cyclin T2a or cyclin T2b. Atuveciclib (BAY-1143572) demonstrates potent antiproliferative activity against HeLa cells (IC50=920 nM) and MOLM-13 cells (IC50=310 nM)[1].

In vivo efficacy studies in the MOLM-13 xenograft model in mice, Atuveciclib (BAY-1143572) demonstrates great potency and high antitumor efficacy. Daily administration of Atuveciclib (BAY-1143572) at 6.25 or 12.5 mg/kg results in a dose-dependent antitumor efficacy with a treatment-to-control (T/C) ratio of 0.64 and 0.49, respectively ($p<0.001$). In a separate experiment with a higher daily dose of 20 or 25 mg/kg Atuveciclib (BAY-1143572), antitumor efficacy with a T/C ratio of 0.41 and 0.31,

respectively, is observed ($p<0.001$). The 25 mg/kg once daily dose is the maximum tolerated dose in nude mice. Furthermore, Atuveciclib (BAY-1143572) administered at 25 or 35 mg/kg, three days on / two days off, results in a T/C ratio of 0.33 and 0.20, respectively ($p<0.001$). Treatment with Atuveciclib (BAY-1143572) is well-tolerated, as demonstrated by less than 10 % mean body weight reduction throughout the study. In an in vivo pharmacokinetic study in rats, Atuveciclib (BAY-1143572) shows low blood clearance (CLb 1.1 L/kg per hour)[1].

[1]. Lücking U, et al. Identification of Atuveciclib (BAY 1143572), the First Highly Selective, Clinical PTEFb/CDK9 Inhibitor for the Treatment of Cancer. ChemMedChem. 2017 Nov 8;12(21):1776-1793.

Tel: (909) 407-4943 Fax: (626) 353-8530 E-mail: tech@glpbio.com
Address: 10292 Central Ave. #205, Montclair, CA, USA