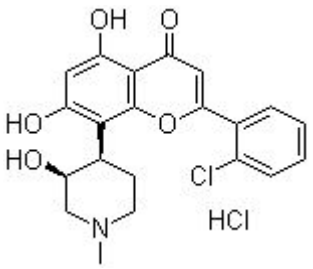
Product Introduction

Flavopiridol HCl

Flavopiridol competes with ATP to inhibit CDKs including **CDK1**, **CDK2**, **CDK4** and **CDK6** with **IC50** of ~ 40 nM. It is 7.5-fold more selective for CDK1/2/4/6 than CDK7. Flavopiridol is initially found to inhibit EGFR and PKA. Phase 1/2.

Technical Data:

Molecular Weight (MW):	438.3	
Formula:	$C_{21}H_{20}ClNO_5.HCl$	
Solubility (25°C) * <1 mg/ml means slightly soluble or insoluble:	DMSO 88 mg/mL	
	Water <1 mg/mL	
	Ethanol <1 mg/mL	
Purity:	>98%	
Storage:	3 years -20℃Powder	
	6 months-80℃in DMSO	
CAS No.:	131740-09-5	

Biological Activity

Flavopiridol is initially found to inhibit the epidermal growth factor receptor and protein kinase A (IC50 = 21 and 122 μM). Flavopiridol is later shown to inhibit cell proliferation, at more physiologically relevant concentrations (IC50 = 66 nM) when Flavopiridol is tested in the National Cancer Institute Development Therapeutics Program panel of 60 human tumor cell lines. [1] Flavopiridol induces G1 arrest with inhibition of CDK2 and CDK4 in human breast carcinoma cells in a time and concentration dependent manner. [2]

Short time treatment of Flavopiridol (~12 hours) induce apoptosis in hematopoietic cell lines including SUDHL4, SUDHL6 (B-cell lines), Jurkat and MOLT4 (T-cell lines), and HL60 (myeloid). [3] In the clonogenic assay, Flavopiridol functions as a highly potent cytotoxic compound with a mean IC70 with 8 ng/mL in 23 human tumor models. [4] A recent study shows Flavopiridol treatment induces a substantial AKT-Ser473 phosphorylation in human glioblastoma T98G cell line. [5]

At the maximal tolerated dose of 10 mg/kg/day administered p.o. on days 1-4 and 7-11, Flavopiridol effects tumor regression in PRXF1337 and tumor stasis lasting for 4 weeks in PRXF1369. [4] After treatment with 7.5 mg/kg Flavopiridol bolus intravenous (IV) or intraperitoneal on each of 5 consecutive days, 11 out of 12 advanced stage subcutaneous (s.c.) human HL-60 xenografts undergo complete regressions, and animals remain disease-free several months after one course of Flavopiridol treatment. SUDHL-4 s.c. lymphomas treated with flavopiridol at 7.5 mg/kg bolus IV for 5 days undergo either major (two out of eight mice) or complete (four out of eight mice) regression, with two animals remaining disease-free for more than 60 days. The overall growth delay is 73.2%. Daily IV or IP administration of flavopiridol results in peak plasma levels of about 7 μM, followed by a progressive decline to approximately 100 nM in 8 hours.[6]

References

[1] Senderowicz AM, Oncologist, 2002, 7 Suppl 3:12-9.

[2] Carlson BA, et al, Cancer Res, 1996, 56(13), 2973-2978.

[3] Parker BW, et al, Blood, 1998, 91(2), 458-465.

[4] Drees M, et al, Clin Cancer Res, 1997, 3(2), 273-279.

[5] Caracciolo V, et al, Cell Cycle, 2012, 11(6), 1202-1216.

[6] Arguello F,et al, Blood, 1998, 91(7), 2482-2490.