Product Data Sheet

Product Name: Palifosfamide
Cat. No.: GC14762

Chemical Properties

Cas. No.	31645-39-3		
Chemical Name	bis(2-chloroethylamino)phosphinic acid		
SMILES	C(CCl)NP(=O)(NCCCl)O		
Formula	$C_4H_{11}Cl_2N_2O_2P$	M.Wt	221.02
Solubility	≥ 22.1 mg/mL in DMSO, ≥ 19.4 mg/mL in Water with ultrasonic and warming	Storage	Store at -20°C, protect from light, stored under nitrogen
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	Palifosfamide		

Protocol

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Cell experiment:

Palifosfamide is dissolved in phosphate buffered saline (PBS). Cells are plated in 96-well microtiter plates with approximately 500 cells per well in 100 µL of media. After 24 h of incubation at 37°C, cells are treated with increasing concentrations of palifosfamide lysine in separate plates either as a single-day treatment or three consecutive days of treatment, with fresh drug being added each day. The plates are incubated for 72 h at 37°C with 5% CO2. After 72 h, 250 µg of MTT is added to each well and incubated at 37°C for 6 h. MTT is converted to formazine crystals by mitochondria of viable cells, which are then dissolved in 100 µL of dimethyl sulfoxide. Optical density is measured at 595 nm[2].

Animal experiment:

Mice: CB17 female SCID mice are used in the study. Once the tumors reached 50–150 mm3, mice are randomized into control and treatment groups (5-8 mice/group) for each tumor line. Cyclophosphamide is administered at the dose of 150 mg/kg intraperitoneally once a week for 6 weeks. Palifosfamide lysine is administered intravenously at the maximum tolerated dose of 100 mg/kg for three consecutive days as a one-time treatment and serial tumor volumes are determined over the next 6 weeks. Mice are sacrificed at the end of the experiment[2].

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References:

[1]. Hingorani P, et al. Preclinical activity of palifosfamide lysine (ZIO-201) in pediatric sarcomas including oxazaphosphorine-resistant osteosarcoma. Cancer Chemother Pharmacol. 2009 Sep;64(4):733-40.
[2]. Jones B, et al. Anticancer activity of stabilized palifosfamide in vivo: schedule effects, oral bioavailability, and enhanced activity with docetaxel and doxorubicin. Anticancer Drugs. 2012 Feb;23(2):173-84.

Background

Palifosfamide is the active moiety of ifosfamide (IFA) [1].
IFA is alkylating agents which are active against a variety of pediatric sarcomas such as rhabdomyosarcoma (RMS), Ewing's sarcoma (ES), osteosarcoma (OS) and other undifferentiated soft tissue sarcomas [1].

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In human OS cell lines SaOS-2, OS229 and OS230, Palifosfamide lysine has broad activity with IC50 ranging from 2.25 to 6.75 μM. While OS222 had the IC50 of 31.5 μM [1].

In CB17 female SCID mice, palifosfamide lysine (100 mg/kg) administered intravenously for three consecutive days, the mean weight loss was less than 15% and complete recovery to baseline within 4 weeks of treatment. While, doses higher than 100 mg/kg for three consecutive days lead to either greater than 20% loss of body weight or death.

In NCr-nu/nu mice bearing established orthotopic mammary MX-1 tumor xenografts, palifosfamide suppressed MX-1 tumor growth by greater than 80% with 17% complete antitumor responses [2].

References:

[1]. Hingorani P, Zhang W, Piperdi S, et al. Preclinical activity of palifosfamide lysine (ZIO-201) in pediatric sarcomas including oxazaphosphorine-resistant osteosarcoma. Cancer Chemother Pharmacol, 2009, 64(4): 733-740.

[2]. Jones B, Komarnitsky P, Miller GT, et al. Anticancer activity of stabilized palifosfamide in vivo: schedule effects, oral bioavailability, and enhanced activity with docetaxel and doxorubicin. Anticancer Drugs, 2012, 23(2): 173-184.

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