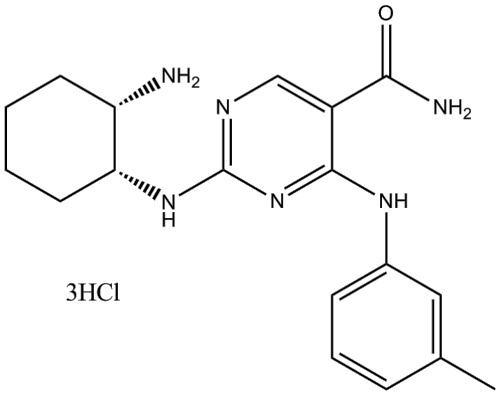
Product Data Sheet

Product Name: PRT-060318
Cat. No.: GC11321

Chemical Properties

Cas. No.	1194961-19-7		
Chemical Name	2-(((1R,2S)-2-aminocyclohexyl)amino)-4-(m-tolylamino)pyrimidine-5-carboxamide		
SMILES	O=C(C1=CN=C(N[C@H]2[C@@H](N)CCCC2)N=C1NC3=CC=CC(C)=C3)N		
Formula	$C_{18}H_{27}Cl_3N_6O$	M.Wt	449.81
Solubility	DMF: 3 mg/ml,DMF:PBS (pH7.2) (1:30): 0.03 mg/ml,DMSO: Insouble,Ethanol: Insouble,PBS (pH 7.2): Insouble	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: PRT318 is dissolved in DMSO. Cells are incubated for 14 days in 24-well plates. CLL cells are cultured under standardized conditions on NLC or in suspension, in the presence or absence of PRT318 and P505-15. At 24, 48, 72 h, CLL cells are collected and assayed for cell viability[2].

Animal experiment: Mice: Heparin-induced thrombocytopenia (HIT) model mice are treated with KKO (20 mg/kg body weight, intraperitoneally) on day 0. The mice are divided into sex- and weight-matched experimental and control groups. On days 1 to 7, experimental mice (n=6) receives PRT318 (30 mg/kg body weight) orally via gavage twice a day, whereas control mice (n=6) receives vehicle only (sterile water). Both groups receives heparin (1600 U/kg body weight, subcutaneously) once daily. Mice are anesthetized by isoflurane inhalation for injections and blood collections[1].

References:

[1]. Reilly MP, et al. PRT-060318, a novel Syk inhibitor, prevents heparin-induced thrombocytopenia and thrombosis in a transgenic mouse model. Blood. 2011 Feb 17;117(7):2241-6.
[2]. Hoellenriegel J, et al. Selective, novel spleen tyrosine kinase (Syk) inhibitors suppress chronic lymphocytic leukemia B-cell activation and migration. Leukemia. 2012 Jul;26(7):1576-83.

Background

IC50: 4 nM

PRT-060318 is a novel Syk inhibitor.

Heparin-induced thrombocytopenia is a heparin therapy complication in which IgG antibodies against the platelet factor 4-heparin complex activate platelets. The FcγRIIA clustering initiates signaling cascades involving tyrosine kinases, such as spleen tyrosine kinase (Syk).

In vitro: PRT-060318 was identified as a potent inhibitor of purified Syk kinase. Syk kinase was inhibited by 92%, while the activities all other kinases retained more than 70% when PRT-060318

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were evaluated at a concentration of 50 nM in a broad panel of kinase enzyme assays. In addition, PRT-060318 could dose-responsively inhibited convulxin-induced human PRP aggregation. Moreover, it was found that PRT-060318 was able to dose-responsively inhibit the increases in intracellular calcium in convulxin-treated platelets [1].

In vivo: Animal study showed that in contrast to vehicle-treated mice developed the expected thrombocytopenia, PRT-060318-treated mice had no significant change in platelet counts after injection of heparin. Moreover, the nadir platelet counts of PRT-060318-treated mice were found to be significantly higher than control mice. The PRT-060318-treated mice showed no bleeding diathesis or other adverse effects. In addition, PRT-060318 treatment in crush thrombosis model resulted in significant inhibition of platelet deposition without changing bleeding time [1].

Clinical trial: Up to now, PRT-060318 is still in the preclinical development stage.

Reference:
[1] Reilly MP,Sinha U,André P,Taylor SM,Pak Y,Deguzman FR,Nanda N,Pandey A,Stolla M,Bergmeier W,McKenzie SE. PRT-060318, a novel Syk inhibitor, prevents heparin-induced thrombocytopenia and thrombosis in a transgenic mouse model. Blood.2011 Feb 17;117(7):2241-6.