PRT-060318

Cat. No.: HY-12974
CAS No.: 1194961-19-7
Molecular Formula: C₁₈H₂₄N₆O
Molecular Weight: 340.42
Target: Syk
Pathway: Protein Tyrosine Kinase/RTK
Storage: Powder
-20°C: 3 years
4°C: 2 years
In solvent
-80°C: 6 months
-20°C: 1 month

SOLVENT & SOLUBILITY

In Vitro
H₂O: 5.6 mg/mL (16.45 mM; Need ultrasonic and warming)

Preparation of Stock Solutions

<table>
<thead>
<tr>
<th>Solvent Concentration</th>
<th>Mass (mL)</th>
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</thead>
<tbody>
<tr>
<td>1 mM</td>
<td>2.9375 mL</td>
</tr>
<tr>
<td>5 mM</td>
<td>0.5875 mL</td>
</tr>
<tr>
<td>10 mM</td>
<td>0.2938 mL</td>
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</tbody>
</table>

Please refer to the solubility information to select the appropriate solvent.

BIOLOGICAL ACTIVITY

Description
PRT-060318 (PRT318) is a novel selective inhibitor of the tyrosine kinase Syk with an IC₅₀ of 4 nM.

IC₅₀ & Target
IC₅₀: 4 nM (Syk)[1]

In Vitro
PRT318 is a potent inhibitor of purified Syk kinase with an IC₅₀ of 4 nM. Syk kinase is inhibited by 92%, whereas all other kinases retains more than 70% at a concentration of 50 nM of PRT318[1]. PRT318 and PS05-15 effectively antagonize CLL cell survival after B-cell receptor (BCR) triggering and in nurse-like cell-co-cultures. They inhibit BCR-dependent secretion of the chemokines CCL3 and CCL4 by CLL cells, and leukemia cell migration toward the tissue homing chemokines CXCL12, CXCL13, and beneath stromal cells. PRT318 and PS05-15 inhibit Syk and extracellular signal-regulated kinase phosphorylation after BCR triggering[2].

In Vivo
PRT318 completely inhibits HIT immune complex-induced aggregation of both human and transgenic HIT mouse platelets. Pretreatment of mice with PRT318 markedly reduces HIT IC-induced thrombosis in the lungs. The Thrombosis Score is significantly lower for PRT318-treated mice compared with control[1].
PROTOCOL

Cell Assay [2]

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]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Animal Administration [1]

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) receive PRT318 (30 mg/kg body weight) orally via gavage twice a day, whereas control mice (n=6) receive vehicle only (sterile water). Both groups receive heparin (1600 U/kg body weight, subcutaneously) once daily. Mice are anesthetized by isoflurane inhalation for injections and blood collections [1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

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REFERENCES
