GSK2334470

Cat. No.: HY-14981
CAS No.: 1227911-45-6
Molecular Formula: C₂₅H₃₄N₈O
Molecular Weight: 462.59
Target: PDK-1
Pathway: PI3K/Akt/mTOR
Storage: Powder
-20°C 3 years
4°C 2 years
In solvent
-80°C 6 months
-20°C 1 month

SOLVENT & SOLUBILITY

In Vitro

DMSO: ≥ 50 mg/mL (108.09 mM)
* "≥" means soluble, but saturation unknown.

<table>
<thead>
<tr>
<th>Preparing Stock Solutions</th>
<th>Solvent</th>
<th>Concentration</th>
<th>Mass</th>
<th>1 mg</th>
<th>5 mg</th>
<th>10 mg</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 mM</td>
<td></td>
<td></td>
<td></td>
<td>2.1617 mL</td>
<td>10.8087 mL</td>
<td>21.6174 mL</td>
</tr>
<tr>
<td>5 mM</td>
<td></td>
<td></td>
<td>0.4323 mL</td>
<td>2.1617 mL</td>
<td>4.3235 mL</td>
<td></td>
</tr>
<tr>
<td>10 mM</td>
<td></td>
<td></td>
<td>0.2162 mL</td>
<td>1.0809 mL</td>
<td>2.1617 mL</td>
<td></td>
</tr>
</tbody>
</table>

Please refer to solubility information to select the appropriate solvent.

In Vivo

1. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: ≥ 2.5 mg/mL (5.40 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.5 mg/mL (5.40 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (5.40 mM); Clear solution

BIOLOGICAL ACTIVITY

Description
GSK2334470 is a highly specific and potent inhibitor of PDK1 with an IC₅₀ of 10 nM.

IC₅₀ & Target
IC₅₀: 10 nM(PDK1) [1]

In Vitro
Small molecule GSK2334470 inhibits PDK1 with an IC₅₀ of ~10 nM, but does not suppress the activity of other
protein kinases including 13 AGC-kinases most related to PDK1 at 500-fold higher concentrations. Addition of GSK2334470 ablates T-loop residue phosphorylation and activation of SGK isoforms and S6K1 induced by serum or IGF-1 (insulin-like growth factor 1). GSK2334470 and AZD8055 effectively inhibit phosphorylation of PDK1 and mTOR, respectively, and induce higher G0–G1 ratio in LAN-1-MK than that in LAN-1 as well. PDK1 and mTOR inhibitors effecte on phosphorylation of GSK3β in some of resistant sublines[2].

In Vivo

The efficacy of the PDK1 inhibitor (PDKi) GSK2334470 is tested in newborn Brafv600E::Pten−/− mice subjected to systemic administration of 4-HT. Twice weekly administration of PDK1 results in marked inhibition of pigmented lesions and concomitant melanomagenesis, as well as significant inhibition of lung metastases, seen by H&E staining-based quantification (~80%), and lymph node metastases as by S100 immunostaining, similar to the phenotype seen upon genetic ablation of Pdk1[3].

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

PROTOCOL

Cell Assay [2]

GSK2334470 is dissolved in DMSO and diluted with appropriate medium before use. To study the inhibitory effect of GSK2334470 on mTOR-S6K pathway, non-resistant cells and the resistant sublines are treated with GSK2334470 at 5 μM for 1.5 and 12 h in 10 % FBS medium with/without MK-2206 (5 μM)[2].

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Animal Administration [3]

Mice is dissolved in DMSO and then diluted with PBS or saline. Brafv600E::Pten−/− are generated as previously described. Cohorts of six animals per group are used in each experimental group. GSK2334470 is administered through IP injection (100 mg/kg) 3 times per week starting the same day of topical administration of 4-hydroxytamoxifen and ending at the time of mouse collection, based on earlier studies[3].

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CUSTOMER VALIDATION

- Br J Cancer. 2020 May 22.

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REFERENCES


Caution: Product has not been fully validated for medical applications. For research use only.

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