AZD1152

Cat. No.: HY-10127
CAS No.: 722543-31-9
Molecular Formula: C₂₆H₃₁FN₇O₆P
Molecular Weight: 587.54
Target: Aurora Kinase
Pathway: Cell Cycle/DNA Damage; Epigenetics
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: ≥ 33 mg/mL (56.17 mM)
* “≥” means soluble, but saturation unknown.

<table>
<thead>
<tr>
<th>Preparing Stock Solutions</th>
<th>Solvent Mass Concentration</th>
<th>1 mg</th>
<th>5 mg</th>
<th>10 mg</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>1 mM</td>
<td>1.7020 mL</td>
<td>8.5101 mL</td>
<td>17.0201 mL</td>
</tr>
<tr>
<td></td>
<td>5 mM</td>
<td>0.3404 mL</td>
<td>1.7020 mL</td>
<td>3.4040 mL</td>
</tr>
<tr>
<td></td>
<td>10 mM</td>
<td>0.1702 mL</td>
<td>0.8510 mL</td>
<td>1.7020 mL</td>
</tr>
</tbody>
</table>

Please refer to the 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: ≥ 2.17 mg/mL (3.69 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.17 mg/mL (3.69 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.17 mg/mL (3.69 mM); Clear solution

BIOLOGICAL ACTIVITY

Description
AZD1152 is a pro-drug of Barasertib-hQPA, which is a highly selective Aurora B inhibitor with IC₅₀ of 0.37 nM in a cell-free assay.

IC₅₀ & Target
IC₅₀: 0.37 nM (Aurora B)
AZD1152 displays >3000-fold selectivity for Aurora B as compared with Aurora A which has an IC\textsubscript{50} of 1.368 μM. AZD1152 has even less activity against 50 other serine-threonine and tyrosine kinases including FLT3, JAK2, and Abl. AZD1152 inhibits the proliferation of hematopoietic malignant cells such as HL-60, NB4, MOLM13, PALL-1, PALL-2, MV4-11, EOL-1, THP-1, and K562 cells with IC\textsubscript{50} of 3-40 nM, displaying appr 100-fold potency than another Aurora kinase inhibitor ZM334739 which has IC\textsubscript{50} of 3-30 μM. AZD1152 inhibits the clonogenic growth of MOLM13 and MV4-11 cells with IC\textsubscript{50} of 1 nM and 2.8 nM, respectively, as well as the freshly isolated imatinib-resistant leukemia cells with IC\textsubscript{50} values of 1-3 nM, more significantly compared with bone marrow mononuclear cells with IC\textsubscript{50} values of >10 nM. AZD1152 induces accumulation of cells with 4N/8N DNA content, followed by apoptosis in a dose- and time-dependent manner\textsuperscript{[1]}. AZD1152 causes significant accumulation of cells with 4N/8N DNA content in KMS12 and U266 and induces apoptosis in KMS18 and U266. AZD1152 in combination with DEX, has negative effects on cell viability in comparison with single agent in PMI8226, KMS11 and U266\textsuperscript{[3]}.

Administration of AZD1152 (25 mg/kg) alone markedly suppresses the growth of MOLM13 xenografts, confirmed by the observation of necrotic tissue with infiltration of phagocytic cells\textsuperscript{[1]}. In addition, AZD1152 (10-150 mg/kg/day) significantly inhibits the growth of a variety of human solid tumor xenografts, including colon, breast, and lung cancers, in a dose-dependent manner\textsuperscript{[2]}. AZD1152 (25 mg/kg/day) treatment reduces xenograft levels such that they are slightly lower levels than after the first round of treatment, but this is not statistically significant indicating that residual cells might be more resistant to a second cycle of AZD1152\textsuperscript{[4]}.

**In Vivo**

**Cell Assay**\textsuperscript{[3]}

Approximately 1×10\textsuperscript{5} cells in RPMI media with 10% FBS media are plated per well in a treated 96-well plate at 24-h intervals for up to 120 h (in triplicate for each time-point). For each timepoint, 20 μL of MTS reagent [3-(4,5-dimethylthiazol-2-yl)-5- (3-carboxymethoxyphenyl)-2-(4-sulfophenyl)-2Htetrazolium, inner salt] solution is added to each well and incubated at 37°C for 4 h. The plate absorbance is read at 490 nm on a 96-well spectra max 190 Plate Reader using Softmax Pro 4.8 Software. MTS solution is added to media-only wells to correct for background. Setting the control cells at 100% viability, the viability of cells treated with various concentrations of siRNA or drug is determined and graphed using MS Excel.

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

**Animal Administration**\textsuperscript{[1]}

Female immune-deficient BALB/c nude mice at 4 weeks of age are purchased from JAPAN SLC and are maintained in pathogen-free conditions with irradiated chow. Animals are bilaterally, subcutaneously injected with 2×10\textsuperscript{6} MOLM13 cells/tumor in 0.1 mL Matrigel. When MOLM13 cells formed palpable tumors, mice are divided randomly into control (n=5) and treatment groups (n=5), and treatment is begun. AZD1152 (5 or 25 mg/kg) with or without vincristine (0.2 mg/kg) is given to mice by intraperitoneal injection 4 times a week or every another day, respectively. Daunorubicin (1 mg/kg) is given to mice by intraperitoneal injection 6 times during 2 weeks of treatment either alone or in combination with AZD1152 (5 mg/kg). The dose of these agents is determined by our preliminary studies. Control diluent is given to the untreated control mice. Body weight and tumors are measured twice a week. Tumor sizes are calculated. At the end of the experiment, animals are killed by CO\textsubscript{2} asphyxiation and tumor weights are measured after their careful resection. Tumor tissue is collected for analysis.

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

**CUSTOMER VALIDATION**

REFERENCES


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

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