BMS-911543

Cat. No.: HY-15270
CAS No.: 1271022-90-2
Molecular Formula: C₂₃H₂₈N₈O
Molecular Weight: 432.52
Target: JAK
Pathway: Epigenetics; JAK/STAT Signaling; Stem Cell/Wnt
Storage:
- Powder: -20°C, 3 years; 4°C, 2 years
- In solvent: -80°C, 6 months; -20°C, 1 month

Solvent & Solubility

In Vitro

<table>
<thead>
<tr>
<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>2.312 mL</td>
<td>11.5602 mL</td>
<td>23.1203 mL</td>
<td></td>
</tr>
<tr>
<td>5 mM</td>
<td>0.4624 mL</td>
<td>2.3120 mL</td>
<td>4.6241 mL</td>
<td></td>
</tr>
<tr>
<td>10 mM</td>
<td>0.2312 mL</td>
<td>1.1560 mL</td>
<td>2.3120 mL</td>
<td></td>
</tr>
</tbody>
</table>

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

BIOLOGICAL ACTIVITY

Description
BMS-911543 is a selective JAK2 inhibitor, with IC₅₀ of 1.1 nM, less selective at JAK1, JAK3 and TYK2 (IC₅₀, 75, 360, 66 nM, respectively).

IC₅₀ & Target
JAK2, IC₅₀: 1.1 nM; Tyk2, IC₅₀: 66 nM; JAK1, IC₅₀: 75 nM; JAK3, IC₅₀: 360 nM

In Vitro
BMS-911543 is a selective JAK2 inhibitor, with IC₅₀ of 1.1 nM, less selective at JAK1, JAK3 and TYK2 (IC₅₀, 75, 360, 66 nM, respectively). BMS-911543 displays IC₅₀ of >25 μM for all targets except PDE4 (IC₅₀, 5.6 μM). BMS-911543 exhibits potent antiproliferative effect on the SET-2 and BaF3-V617F engineered cell lines (both dependent upon JAK2 pathway), with IC₅₀ of 60 and 70 nM, respectively, and such an effect on SET-2 and BaF3-V617F cells is correlated with similar activity on constitutively active pSTAT5 (IC₅₀, 80 and 65 nM, respectively)[1]. BMS-911543 (>20 μM) is cytotoxic to murine or human pancreatic ductal adenocarcinoma (PDAC) cell lines. BMS-911543 (5 and 10 μM) also blocks T regulatory cell differentiation in vitro[2].

In Vivo
BMS-911543 is well tolerated up to 100 mg/kg in rats (mean AUC₀-72 h, 11300 μM·h) and dogs (AUC₀-24 h, 610 μM·h).
A 15 mg/kg/day dose (Day 14 AUC$_{0-24\text{ h}}$ 3200 μM·h) is well tolerated$^{[1]}$ in two-week repeat dose studies in rats. BMS-911543 (30 mg/kg, p.o.) suppresses the growth of tumor and prolongs the median survival in KPC-Brca1 mice. BMS-911543 also selectively reduces pSTAT5 expression in pancreatic tumors and decreases levels of intratumoral FoxP3$^+$ T regulatory cells in mice administered BMS-911543$^{[2]}$.

**PROTOCOL**

**Cell Assay**$^{[2]}$

Human and murine pancreatic ductal adenocarcinoma (PDAC) tumor cells or PSC are cultured in 96 well plates and the following day treated with BMS-911543 or DMSO vehicle control for 48 hours. After 48 hours, MTT reagent (ATCC) is added for 2 hours at 37°C. Samples are analyzed on a plate reader testing for absorbance at 450 nM$^{[2]}$.

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

**Animal Administration**$^{[2]}$

Pancreatic tumors are confirmed in KPC-Brca1 mice by bioluminescent imaging (BLI) at 5-6 weeks of age. Briefly, mice are maintained on isofluorane anesthesia and imaged 10-15 minutes following intraperitoneal injection of Luciferin on a heated platform. Animals with a pancreatic mass of approximately 50-100 mm$^3$ are randomized, and treatment is initiated the day following imaging. Mice are then treated for 2 weeks by daily oral gavage at a dose of 30 mg/kg BMS-911543. Following 2 weeks of treatment, animals are euthanized via CO$_2$ asphyxiation followed by cardiac puncture. Plasma, splenocytes and tumor tissue are collected for further analysis. Pathology is assessed by H&E to determine differentiation state of the tissue as PanIN, papillary carcinoma or PDAC. For long term in vivo experiments, 8 week old KPC-Brca1 mice with advanced disease are continuously treated by oral gavage at 30 mg/kg of BMS-911543 until mice meet specified early removal criteria$^{[2]}$.

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**REFERENCES**
