**BIOLOGICAL ACTIVITY:**

BMS-911543 is a selective JAK2 inhibitor, with IC\textsubscript{50}s of 1.1 nM, less selective at JAK1, JAK3 and TYK2 (IC\textsubscript{50}, 75, 360, 66 nM, respectively). IC\textsubscript{50} & Target: IC\textsubscript{50}: 1.1 nM (JAK2), 75 nM (JAK1), 360 nM (JAK3), 66 nM (TYK2)\textsuperscript{[1]}

In Vitro: BMS-911543 is a selective JAK2 inhibitor, with IC\textsubscript{50}s of 1.1 nM, less selective at JAK1, JAK3 and TYK2 (IC\textsubscript{50}, 75, 360, 66 nM, respectively). BMS-911543 displays IC\textsubscript{50} of >25 μM for all targets except PDE4 (IC\textsubscript{50}, 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 IC\textsubscript{50}s 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 (IC\textsubscript{50}, 80 and 65 nM, respectively)\textsuperscript{[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\textsuperscript{[2]}.

In Vivo: BMS-911543 is well tolerated up to 100 mg/kg in rats (mean AUC\textsubscript{0-72 h}, 11300 μM.h) and dogs (AUC\textsubscript{0-24 h}, 610 μM.h). A 15 mg/kg/day dose (Day 14 AUC\textsubscript{0-24 h}, 3200 μM.h) is well tolerated\textsuperscript{[3]} 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\textsuperscript{+} T regulatory cells in mice administered BMS-911543\textsuperscript{[2]}.

**PROTOCOL (Extracted from published papers and Only for reference)**

**Cell Assay:** BMS-911543 is dissolved in DMSO, and diluted before use\textsuperscript{[2],[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\textsuperscript{[2]}.

**Animal Administration:** BMS-911543 is formulated in 20% citrate/80% PEG400\textsuperscript{[2],[2]}. Mice\textsuperscript{[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\textsuperscript{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\textsubscript{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\textsuperscript{[2]}.

**References:**


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

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