产品名称：**BMS 911543**
产品别名：**BMS-911543**

生物活性：

Description

BMS-911543 is a selective **JAK2** inhibitor, with **IC_{50}**s of 1.1 nM, less selective at JAK1, JAK3 and TYK2 (**IC_{50}**, 75, 360, 66 nM, respectively).

IC_{50} & Target

JAK2	Tyk2	JAK1	JAK3
1.1 nM (IC_{50})	66 nM (IC_{50})	75 nM (IC_{50})	360 nM (IC_{50})

In Vitro

BMS-911543 is a selective JAK2 inhibitor, with IC50s 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 IC50s 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 AUC0-24 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].

Solvent&Solubility

In Vitro:

DMSO : 25 mg/mL (**57.80 mM;** Need ultrasonic)

H_2O : < 0.1 mg/mL (insoluble)

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	2.3120 mL	11.5602 mL	23.1203 mL
5 mM	0.4624 mL	2.3120 mL	4.6241 mL
10 mM	0.2312 mL	1.1560 mL	2.3120 mL

*请根据产品在不同溶剂中的溶解度选择合适的溶剂配制储备液；一旦配成溶液，请分装保存，避免反复冻融造成的产品失效。

储备液的保存方式和期限：-80°C, 6 months; -20°C, 1 month。-80°C 储存时，请在 6 个月内使用，-20°C 储存时，请在 1 个月内使用。

In Vivo:

请根据您的实验动物和给药方式选择适当的溶解方案。以下溶解方案都请先按照 **In Vitro** 方式配制澄清的储备液，再依次添加助溶剂：

——为保证实验结果的可靠性，澄清的储备液可以根据储存条件，适当保存；体内实验的工作液，建议您现用现配，当天使用； 以下溶剂前显示的百分比是指该溶剂在您配制终溶液中的体积占比；如在配制过程中出现沉淀、析出现象，可以通过加热和/或超声的方式助溶

1.请依序添加每种溶剂： 10% DMSO→40% PEG300 →5% Tween-80 → 45% saline

Solubility: ≥ 2.5 mg/mL (5.78 mM); Clear solution

此方案可获得 ≥ 2.5 mg/mL (5.78 mM，饱和度未知) 的澄清溶液。

	以 1 mL 工作液为例，取 100 μL 25.0 mg/mL 的澄清 DMSO 储备液加到 400 μL PEG300 中，混合均匀向上述体系中加入 50 μL Tween-80，混合均匀；然后继续加入 450 μL 生理盐水定容至 1 mL。 2.请依序添加每种溶剂： 10% DMSO →90% corn oil Solubility: ≥ 2.5 mg/mL (5.78 mM); Clear solution 此方案可获得 ≥ 2.5 mg/mL (5.78 mM，饱和度未知) 的澄清溶液，此方案不适用于实验周期在半个月以上的实验。 以 1 mL 工作液为例，取 100 μL 25.0 mg/mL 的澄清 DMSO 储备液加到 900 μL 玉米油中，混合均匀。
References	[1]. Wan H, et al. Discovery of a Highly Selective JAK2 Inhibitor, BMS-911543, for the Treatment of Myeloproliferative Neoplasms. ACS Med Chem Lett. 2015 Jul 12;6(8):850-5. [2]. Mace TA, et al. Single agent BMS-911543 Jak2 inhibitor has distinct inhibitory effects on STAT5 signaling in genetically engineered mice with pancreatic cancer. Oncotarget. 2015 Dec 29;6(42):44509-22.

实验参考：

Cell Assay	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].
Animal Administration	Mice[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 mm3 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 CO2 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 carcincoma 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].
References	[1]. Wan H, et al. Discovery of a Highly Selective JAK2 Inhibitor, BMS-911543, for the Treatment of Myeloproliferative Neoplasms. ACS Med Chem Lett. 2015 Jul 12;6(8):850-5. [2]. Mace TA, et al. Single agent BMS-911543 Jak2 inhibitor has distinct inhibitory effects on STAT5 signaling in genetically engineered mice with pancreatic cancer. Oncotarget. 2015 Dec 29;6(42):44509-22.