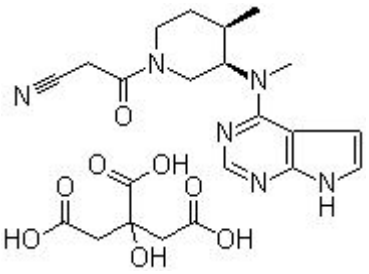
Biochempartner
瀚香生物科技

Product Introduction

Tofacitinib (CP-690550) Citrate

Tofacitinib citrate (CP-690550 citrate) is a novel inhibitor of JAK3 with IC50 of 1 nM, 20- to 100-fold less potent against JAK2 and JAK1.

Technical Data:

Molecular Weight (MW):	504.49	
Formula:	$C_{16}H_{20}N_6O.C_6H_8O_7$	
Solubility (25°C) * <1 mg/ml means slightly soluble or insoluble:	DMSO 100 mg/mL	
	Water <1 mg/mL	
	Ethanol <1 mg/mL	
Purity:	>98%	
Storage:	3 years -20℃ Powder	
	6 months-80℃ in DMSO	
CAS No.:	540737-29-9	

Biological Activity

Tofacitinib citrate inhibits IL-2-mediated human T cell blast proliferation and IL-15-induced CD69 expression with IC50 of 11 nM and 48 nM, respectively. Tofacitinib citrate prevents mixed lymphocyte reaction with IC50 of 87 nM. Tofacitinib citrate treatment of murine factor-dependent cell Patersen–erythropoietin receptor (FDCP-EpoR) cells harboring human wild-type or V617F JAK2 leads to prevention of cell proliferation with IC50 of 2.1 μM and 0.25 μM, respectively. Tofacitinib citrate inhibits

interleukin-6-induced phosphorylation of STAT1 and STAT3 with IC50 of 23 nM and 77 nM, respectively. Moreover, Tofacitinib citrate generates a significant pro-apoptotic effect on murine FDCP-EpoR cells carrying JAK2V^{V617F}, whereas a lesser effect is observed for cells carrying wild-type JAK2. This activity is coupled with the inhibition of phosphorylation of the key JAK2^{V617F}-dependent downstream signaling effectors signal transducer and activator of transcription (STAT)3, STAT5, and v-akt murine thymoma viral oncogene homolog (AKT). [2] Additionally, Tofacitinib citrate prevents IL-15-induced CD69 expression in human and cynomolgus monkey NK and CD8+ T cells in vitro. [3]

Tofacitinib citrate decrease a delayed-type hyper-sensitivity response and extended cardiac allograft survival in murine models. Furthermore, Tofacitinib citrate treatment of ex-vivo-expanded erythroid progenitors from JAK2^{V617F}-positive PV patients results in specific, antiproliferative (IC50 = 0.2 μM) and pro-apoptotic activity. In contrast, expanded progenitors from healthy controls are less sensitive to Tofacitinib citrate in proliferation (IC50 > 1.0 μM), and apoptosis assays.[2] During 2 weeks of Tofacitinib citrate dosing at 10 and 30 mg/kg/d, a significant, time-dependent decrease in NK cell numbers relative to vehicle treatment is observed. Effector memory CD8+ cell numbers in the Tofacitinib citrate-treated group are 55% less than those observed in animals treated with vehicle.[3]

References

[1] Flanagan ME, et al. J Med Chem, 2010, 53(24), 8468-8484.

[2] Manshouri T, et al. Cancer Sci, 2008, 99(6), 1265-1273.

[3] Conklyn M, et al. J Leukoc Biol, 2004, 76(6), 1248-1255.

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