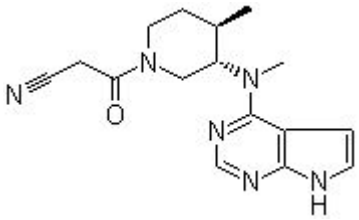
Product Introduction

Tofacitinib (CP-690550,Tasocitinib)

Tofacitinib 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):	312.37	
Formula:	$C_{16}H_{20}N_6O$	
Solubility (25°C) * <1 mg/ml means slightly soluble or insoluble:	DMSO 62 mg/mL	
	Water <1 mg/mL	
	Ethanol <1 mg/mL	
Purity:	>98%	
Storage:	3 years -20℃Powder	
	6 months-80℃in DMSO	
CAS No.:	477600-75-2	

Biological Activity

CP-690550 is a specific, orally inhibitor of JAK3, it is 20- to 100-fold less potent for JAK2 and JAK1 with IC50 of 20 nM and 112 nM, respectively. CP-690550 doesn't have potent activity against 30 other kinases (all median IC50 > 3000 nM). CP-690,550 inhibits IL-2–induced proliferation with 30-fold greater potency than its effects on GM-CSF–induced proliferation. [1] CP-690550 effectively inhibits a murine mixed lymphocyte reaction (MLR) (IC50 = 91 nM). [2] CP-690550 potently inhibits IL-4 induced upregulation of

CD23 (IC50=57 nM) and class II major histocompatibility complex (MHCII) expression (IC50=71 nM) on murine B cells. [3] A recent research indicates low dose of CP-690550 accelerates the onset of experimental autoimmune encephalomyelitis by potentiating Th17 differentiation. [4]

In a murine model of heterotopic heart transplantation (DBA2 donor heart into C57/BL6 host), CP-690550 results in a dose-dependent increase in survival of transplanted hearts.The EC50 (drug concentration in blood at which 50% of mice will maintain their graft for >28 days) to be ~60 ng/mL.CP-690550 prevents rejection of allogeneic kidneys in nonhuman primate (NHPs, macaca fascicularis) (MST of 62 and 83 days for the 50 to 100 ng/ml groups and 200 to 400 ng/ml groups, respectively). [1] Mice chronically dosed with CP-690550 (1.5-15 mg/kg/day) demonstrates dose and time-dependent alterations in lymphocyte subsets when examined by flow cytometry. The most dramatic change observed is a 96% reduction in splenic NK1.1+TCRb-cell numbers following 21 days of treatment. Delayed-type hypersensitivity (DTH) responses in sensitized mice are reduced in a dose-dependent manner following treatment with CP-690550 (1.87–30 mg/kg, s.c.). Extended survival of neonatal Balb/c hearts implanted into the ear pinna of MHC mismatched C3H/HEN mice is observed with CP-690550 monotherapy (10–30 mg/kg/day), but improved upon combination with cyclosporin (10 mg/kg/day). [2]

References

[1] Changelian PS, et al, Science, 2003, 302(5646), 875-878.

[2] Kdlacz E, et al, Am J Transplant, 2004, 4(1), 51-57.

[3] Kudlacz E, et al, Eur J harmacol, 2008, 582(1-2), 154-161.

[4] Yoshida H, et al, Biochem Biophys Res Commun, 2012, 418(2), 234-240.

[5] Borie DC, et al, Transplantation, 2005, 80(12), 1756-1764.

[6] Kudlacz E, et al. Am J Transplant, 2004, 4(1), 51-57.

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