Product Data Sheet

Product Name: Imexon (BM 06002)
Cat. No.: GC32952

Chemical Properties

Cas. No.	59643-91-3		
SMILES	O=C1N2CC2C(N)=N1		
Formula	$C_4H_5N_3O$	M.Wt	111.1
Solubility	Soluble in DMSO	Storage	Store at -20°C
General tips	For obtaining a higher solubility , please warm the tube at 37 ℃ and shake it in the ultrasonic bath for a while.Stock solution can be stored below -20℃ for several months.		
Shipping Condition	Evaluation sample solution : ship with blue ice All other available size: ship with RT , or blue ice upon request.		
Structure	Imexon (BM 06002)		

Protocol

Cell experiment:	Cell survival for the siRNA screening experiments are calculated by the conversion of resazurin to resorufin by metabolically active cells resulting in a fluorescent product. Confirmatory growth inhibition assays with eIF2b silencing are done using the methyl-thiazolyl-diphenyl-tetrazolium bromide (MTT) assay. Cell growth inhibition data are expressed as percent survival, compared to untreated cells. The IC50 is defined as the drug concentration required to produce 50% growth inhibition.

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Animal experiment:

The effect of the combination on tumor growth in vivo is evaluated in 25-30 g male SCID mice (n=8/group). Mice receive 5×106 A375 cells subcutaneously and are pair matched on day 30, when the average tumor burden is approximately 100 mm3. Treatment begins the following day, as follows: (i) saline vehicle control; (ii) 80 mg/kg/day DTIC; (iii) 100 mg/kg/day imexon; (iv) a combination of both drugs at the same doses. Drugs are administered (i.p.) for nine consecutive days and imexon is administered 15 min before DTIC when combined. Measurement of tumor burden and body weights are made every 3-4 days. Tumor burden (mm3) is calculated as (length × width2)/2.

References:

[1]. Sheveleva EV, et al. Imexon induces an oxidative endoplasmic reticulum stress response in pancreatic cancer cells. Mol Cancer Res. 2012 Mar;10(3):392-400.
[2]. Samulitis BK, et al. Interaction of dacarbazine and imexon, in vitro and in vivo, in human A375

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melanoma cells. Anticancer Res. 2011 Sep;31(9):2781-5.
[3]. Roman NO, et al. Imexon enhances gemcitabine cytotoxicity by inhibition of ribonucleotide reductase. Cancer Chemother Pharmacol. 2011 Jan;67(1):183-92.

Background

Imexon (BM 06002) is an iminopyrrolidone aziridine with anti-cancer activity.

Imexon (BM 06002) induces oxidative stress in the ER, activates an ER stress response. Imexon (BM 06002) does not significantly alter the levels of eIF2B5, however there is a dose-dependent increase in the phosphorylation of eIF2alpha, as well as an increase in the levels of GTP exchange protein eIF2B2 in MiaPaCa-2, Panc-1, and BxPC3 cells[1]. Imexon (BM 06002) induces single-stranded breaks in the human A375 melanoma cells but only significantly at the highest concentrations for each agent compared to controls. Imexon plus DTIC cytotoxicity is additive[2]. Imexon (BM 06002) show inhibitory activities against MiaPaCa-2, Panc-1 and BxPC3, with IC50s of 275.5 ± 54.2, 147.4 ± 4.7 and 355.7 ± 114.7 μM[3].

Imexon (BM 06002) in combination with DTIC results in an increase in the peak plasma imexon level in non-tumor-bearing mice. The combination of both drugs increases

plasma imexon AUC by 22% (p=0.026). Imexon (BM 06002) (100 mg/kg/day, i.v.) treatment decreases the body weight of SCID mice bearing human A375 melanoma tumors, but there is no significant difference in tumor growth[2]. Imexon (BM 06002) (100 mg/kg) in combination with GEM shows synergistic inhibition of Panc-1 tumor growth in SCID mice.

[1]. Sheveleva EV, et al. Imexon induces an oxidative endoplasmic reticulum stress response in pancreatic cancer cells. Mol Cancer Res. 2012 Mar;10(3):392-400. [2]. Samulitis BK, et al. Interaction of dacarbazine and imexon, in vitro and in vivo, in human A375 melanoma cells. Anticancer Res. 2011 Sep;31(9):2781-5. [3]. Roman NO, et al. Imexon enhances gemcitabine cytotoxicity by inhibition of ribonucleotide reductase. Cancer Chemother Pharmacol. 2011 Jan;67(1):183-92.

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