Product Data Sheet

Product Name: MEDI3726
Cat. No.: GC78788

Chemical Properties

Cas. No.			
Formula		M.Wt	
Solubility		Storage	Store at -80°C, protect from light
General tips	For obtaining a higher solubility , please warm the tube at 37 °C and shake it in the ultrasonic bath for a while.Stock solution can be stored below -20°C 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			

Background

MEDI3726 (ADCT-401) is a prostate-specific membrane antigen (PSMA)-targeting antibody-drug conjugate (ADC), composed of LP Tesirine and antibody J591. MEDI3726 binds PSMA 's extracellular domain, triggers endocytosis, undergoes lysosomal degradation to release a pyrrolobenzodiazepine warhead. MEDI3726 induces DNA crosslinking, DNA damage, cell death, cytotoxicity, and inhibits tumor growth in mouse xenograft models. MEDI3726 undergoes in vivo catabolism primarily via heavy-light chain dissociation, with minimal warhead deconjugation. MEDI3726 can be used for the research of metastatic castration-resistant prostate cancer and prostate cancers [1] [2] [3] [4].

Caution: Product has not been fully validated for medical applications. For research use only.
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In Vivo, MEDI3726 (0.11-1 mg/kg; i.v.; single dose) exhibits dose-dependent antitumor activity and improved survival in mouse LNCaP prostate cancer xenografts[4]. MEDI3726 (0.33-1 mg/kg; i.v.; single dose) displays dose-dependent antitumor activity in mouseCWR22Rv1 castration-resistant prostate cancer xenografts[4]. MEDI3726 (0.33-1 mg/kg; i.v.; single dose) exhibits only limited antitumor activity in mouse PSMA-negative PC-3 prostate cancer xenografts at the 1 mg/kg single dose[4]. MEDI3726 (0.1-0.9 mg/kg; i.v.; once every 3 weeks; 3 doses) demonstrates dose-dependent, statistically significant antitumor activity in highly PSMA-positive LuCaP prostate cancer mosue PDX models[4].

In Vitro, MEDI3726 (ADCT-401) exhibits potent, specific cytotoxicity in PSMA-expressing prostate cancer cell lines, with greatly reduced activity in PSMA-negative prostate cancer cell lines[3]. MEDI3726 (0.2 μg/mL; 1 h) cross-reacts with human and cynomolgus monkey soluble PSMA with similar potency, but does not cross-react with rat soluble PSMA[4]. MEDI3726 (up to 7 days) remains stable and active at 37°C in PBS, human plasma, or cynomolgus monkey plasma[4]. MEDI3726 (5-7 days) potently and specifically kills PSMA-positive human prostate cancer cell lines LNCaP (IC_{50} = 0.02 nM), LNCaP C4-2 (IC_{50} = 0.06 nM), MDA PCa 2b (IC_{50} = 0.002 nM), and CWR22Rv1 (IC_{50} = 0.29 nM), but shows no targeted cytotoxicity in PSMA-negative PC-3 (IC_{50} = 29.3 nM) and DU145 cell lines (IC_{50} = 44.9 nM)[4]. MEDI3726 (24 h) is specifically internalized and trafficked to lysosomes in PSMA-positive LNCaP cells, but not in PSMA-negative PC-3 cells[4]. MEDI3726 (6 nM; 2 h treatment) induces persistent DNA interstrand crosslinks in PSMA-positive LNCaP cells, but does not induce significant DNA crosslinking in PSMA-negative PC-3 cells[4].

References:
[1]. de Bono JS, et al. Phase I Study of MEDI3726: A Prostate-Specific Membrane Antigen-Targeted Antibody-Drug Conjugate, in Patients with mCRPC after Failure of Abiraterone or Enzalutamide. Clin Cancer Res. 2021;27(13):3602-3609.
[2]. Huang Y, et al. Multifaceted Bioanalytical Methods for the Comprehensive Pharmacokinetic and Catabolic Assessment of MEDI3726, an Anti-Prostate-Specific Membrane Antigen Pyrrolobenzodiazepine Antibody-Drug Conjugate. Anal Chem. 2020;92(16):11135-11144.
[3]. Francesca Zammarchi, et al. ADCT-401/MEDI3726, a novel pyrrolobenzodiazepine (PBD)-based

antibody-drug conjugate (ADC) targeting PSMA-expressing prostate cancers. Cancer Res 2017;77(13 Suppl):Abstract nr 3111A.
[4]. Cho S, et al. Antitumor Activity of MEDI3726 (ADCT-401), a Pyrrolobenzodiazepine Antibody-Drug Conjugate Targeting PSMA, in Preclinical Models of Prostate Cancer. Mol Cancer Ther. 2018;17(10):2176-2186.