

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 mouse CWR22Rv1 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 mouse 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 (IC₅₀ = 0.02 nM), LNCaP C4-2 (IC₅₀ = 0.06 nM), MDA PCa 2b (IC₅₀ = 0.002 nM), and CWR22Rv1 (IC₅₀ = 0.29 nM), but shows no targeted cytotoxicity in PSMA-negative PC-3 (IC₅₀ = 29.3 nM) and DU145 cell lines (IC₅₀ = 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

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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.

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