MMAE-d_8

Cat. No.: HY-15162A

CAS No.: 2070009-72-0

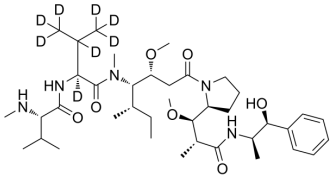
Molecular Formula: $C_{39}H_{59}D_8N_5O_7$

Molecular Weight: 726.03

Target: Microtubule/Tubulin; ADC Cytotoxin

Pathway: Cell Cycle/DNA Damage; Cytoskeleton; Antibody-drug Conjugate/ADC Related

Storage: Powder -20°C 3 years
4°C 2 years
* The compound is unstable in solutions, freshly prepared is recommended.



SOLVENT & SOLUBILITY

In Vitro

DMSO : 100 mg/mL (137.74 mM; Need ultrasonic)

Preparing Stock Solutions	Mass / Solvent / Concentration	1 mg	5 mg	10 mg
	1 mM	1.3774 mL	6.8868 mL	13.7735 mL
	5 mM	0.2755 mL	1.3774 mL	2.7547 mL
	10 mM	0.1377 mL	0.6887 mL	1.3774 mL

Please refer to the solubility information to select the appropriate solvent.

In Vivo

1. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: ≥ 2.5 mg/mL (3.44 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.5 mg/mL (3.44 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (3.44 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

MMAE-d_8 is a deuterated labeled MMAE, a potent mitotic inhibitor and a tubulin inhibitor.

IC_{50} & Target

Auristatin

In Vitro

Antibody-drug conjugates (ADC) comprise targeting antibodies armed with potent small-molecule payloads. ADCs are generated to target different receptors on the anaplastic large cell lymphoma line L-82, but delivered the same cytotoxic payload (monomethyl auristatin E, MMAE), and the intracellular concentration of released MMAE correlated with in vitro ADC-mediated cytotoxicity independent of target expression or drug:antibody ratios. LC-MS is used to measure the

	concentration of MMAE in a parallel cohort of L-82 tumors with an identical treatment regimen. Although tumor volume is not different among treatment groups 3 days after dose, the intratumoral MMAE measurement reveals two patterns. First, intratumoral MMAE concentration increases proportionally to the ADC dose, which correspondes to stronger antitumor activity. Second, the intratumoral MMAE concentration obtained from treatment with both cOKT9-vcMMAE and cAC10-vcMMAE is similar at each dose, consistent with the observation that tumor responded similarly to these two ADCs[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	Intratumoral MMAE concentrations consistently correlates with the extent of tumor growth inhibition in tumor xenograft models. IHC analysis reveals that nonbinding control-treated tumors consist of both $CD30^+$ and $CD30^-$cells, presumably because they do not kill either $CD30^+$ or $CD30^-$ Karpas 299 cells. Only $CD30^-$ cells are found in cAC10-vcMMAF-treated tumors, illustrating that cAC10-vcMMAF eliminates most $CD30^+$ cells. Interestingly, the two tumors that relapses from cAC10-vcMMAE treatment are also found to be $CD30^-$ by the end of study, indicating a small fraction of $CD30^-$ cells might have escaped from bystander killing in these two remaining tumors[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Kinase Assay [1]	Cell pellets are collected 24 hours after ADC treatment. Cell count, diameter, and circularity are determined on Vi-Cell Counter. MMAE extraction and quantification method is performed. Briefly, tumors or cell pellets are homogenized with methanol and acetonitrile containing internal standard (d^8-MMAE for MMAE detection and ^{13}C-MMAF for MMAF detection). The homogenates are centrifuged at 10,000 rpm to precipitate protein and protein-bound payloads. The supernatant is then subjected to solid phase extraction, and signals of MMAE and MMAF are detected by LC-MS[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- J Pharm Anal. 24 November 2021.
- Mol Cancer Ther. 2023 Jan 31;MCT-22-0440.
- AAPS J. 2021 Apr 15;23(3):56.
- Drug Metab Dispos. 2017 Nov;45(11):1120-1132.
- Patent. US20220356169A1.

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REFERENCES

[1]. Li F, et al. Intracellular Released Payload Influences Potency and Bystander-Killing Effects of Antibody-Drug Conjugates in Preclinical Models. Cancer Res. 2016 May 1;76(9):2710-9.

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