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Lieferung & Zahlungsart

siehe unsere Liefer- und Versandbedingungen

Zuschläge

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- Trockeneiszuschlag
- Gefahrgutzuschlag
- Expressversand

SZABO-SCANDIC HandelsgmbH

Quellenstraße 110, A-1100 Wien

T. +43(0)1 489 3961-0

F. +43(0)1 489 3961-7

mail@szabo-scandic.com

www.szabo-scandic.com

linkedin.com/company/szaboscandic

Calicheamicin

Cat. No.: HY-19609

CAS No.: 108212-75-5

Molecular Formula: $C_{55}H_{74}IN_3O_{21}S_4$

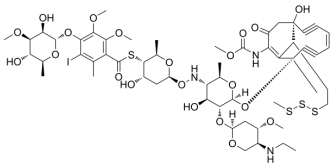
Molecular Weight: 1368.35

Target: DNA Alkylator/Crosslinker; ADC Cytotoxin; Apoptosis; Bacterial; Antibiotic

Pathway: Cell Cycle/DNA Damage; Antibody-drug Conjugate/ADC Related; Apoptosis; Anti-infection

Storage:

Powder	-20°C	3 years
	4°C	2 years
In solvent	-80°C	6 months
	-20°C	1 month



SOLVENT & SOLUBILITY

In Vitro

DMSO : 25 mg/mL (18.27 mM; Need ultrasonic)

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	0.7308 mL	3.6540 mL	7.3081 mL
5 mM	0.1462 mL	0.7308 mL	1.4616 mL
10 mM	0.0731 mL	0.3654 mL	0.7308 mL

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

In Vivo

1. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 3 mg/mL (2.19 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: ≥ 2.5 mg/mL (1.83 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: 2.5 mg/mL (1.83 mM); Suspended solution; Need ultrasonic

BIOLOGICAL ACTIVITY

Description

Calicheamicin, an antitumor antibiotic, is a cytotoxic agent that causes double-strand DNA breaks. Calicheamicin is a DNA synthesis inhibitor[1]. Calicheamicin is a click chemistry reagent, it contains an Alkyne group and can undergo copper-catalyzed azide-alkyne cycloaddition (CuAAc) with molecules containing Azide groups.

IC_{50} & Target

Calicheamicins

In Vitro	PF-06647263 (anti-EFNA4-ADC) is generated via conjugation of hE22 lysine residues to the AcButDMH-N-Ac-calicheamicin-γ1 linker-payload with an average drug-to-antibody ratio (DAR) of 4.6. PF-06647263 elicits antigen- and concentration-dependent cytotoxicity, as exposure to PF-06647263 for 96 hours results in cell death (EC_{50}= appr 1 ng/mL)[1]. CMC-544, consisting of a humanized CD22 Ab linked to calicheamicin, is effective in pediatric primary B-cell precursor acute lymphoblastic leukemia (BCP-ALL) cells in vitro. CMC-544 induces cell death in various ALL cell lines in a dose- and time-dependent way, with IC_{50} values ranging from 0.15 to 4.9 ng/mL. CMC-544 (10 ng/mL) is effective and specific in primary BCP-ALL cells[2]. In CMC-544-treated cells, the level of CD22 has decreased relative to that on G5/44-treated cells and continued to decrease[3]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	An ADC comprising a humanized anti-EFNA4 monoclonal antibody conjugated to the DNA-damaging agent calicheamicin achieves sustained tumor regressions in both TNBC and ovarian cancer PDX in vivo. PF-06647263 (0.27, 0.36 mg/kg) results in significant tumor regressions in TNBC xenografts[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Cell Assay [3]	The enhancement of the CDC effect is studied in a similar way in the presence of CMC-544 or G5/44. Specifically, after cells are incubated with or without CMC-544 (5 ng/mL calichemicin DMH) or G5/44 at 37°C for 2 h, they are washed three times to remove unbound antibodies. The viability of cells before incubation with CMC-544 is 99.8%. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Animal Administration [1]	Cohorts of tumor-bearing mice (140-180 mm^3) are randomized into study groups of 6 to 10 based on the number of available mice. The IDBS electronic notebook statistical package, Biobook, is used for automated animal randomization. Animals are dosed by intraperitoneal injection (or intravenously for 144580) twice a week for 4 cycles with ADC, or once a week for 2 cycles with 1.5 mg/kg NSC 123127 for breast PDX tumors or 5 mg/kg NSC 119875 for ovarian PDX. Study groups are followed until either individual mice or entire cohort measurements reach 1,200 mm^3, at which point sacrifice is indicated. Tumor regression is defined as a reduction in mean tumor volume after dosing. In cases where tumors regress, time to progression (TTP) is determined to be the number of days between the first dose and the time at which mean tumor volume significantly increase (regrow) after regression. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- PLoS Biol. 2020 Mar 23;18(3):e3000666.
- J Biol Chem. 2022 Jun 23;102191.
- FASEB J. 2018 Jun 6:fj201800092R.
- Research Square Preprint. 2023 Dec 4.
- bioRxiv. 2023 Aug 29.

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REFERENCES

[1]. Damelin M, et al. Anti-EFNA4 Calicheamicin Conjugates Effectively Target Triple-Negative Breast and Ovarian Tumor-Initiating Cells to Result in Sustained Tumor Regressions. Clin Cancer Res. 2015 Sep 15;21(18):4165-73

[2]. de Vries JF, et al. The novel calicheamicin-conjugated CD22 antibody inotuzumab ozogamicin (CMC-544) effectively kills primary pediatric acute lymphoblastic

leukemia cells. Leukemia. 2012 Feb;26(2):255-64

[3]. Takeshita A, et al. CMC-544 (inotuzumab ozogamicin), an anti-CD22 immuno-conjugate of calicheamicin, alters the levels of target molecules of malignant B-cells. Leukemia. 2009 Jul;23(7):1329-36.

Tel: 609-228-6898 Fax: 609-228-5909 E-mail: tech@MedChemExpress.com

Address: 1 Deer Park Dr, Suite Q, Monmouth Junction, NJ 08852, USA