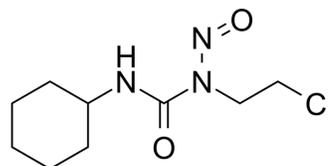


Lomustine

Cat. No.:	HY-13669		
CAS No.:	13010-47-4		
Molecular Formula:	C ₉ H ₁₆ ClN ₃ O ₂		
Molecular Weight:	233.7		
Target:	DNA Alkylator/Crosslinker; Autophagy; Apoptosis		
Pathway:	Cell Cycle/DNA Damage; Autophagy; Apoptosis		
Storage:	Powder	-20°C	3 years
		4°C	2 years
	In solvent	-80°C	2 years
		-20°C	1 year



SOLVENT & SOLUBILITY

In Vitro

DMSO : ≥ 100 mg/mL (427.90 mM)
 H₂O : < 0.1 mg/mL (ultrasonic;warming;heat to 60°C) (insoluble)
 * "≥" means soluble, but saturation unknown.

Preparing Stock Solutions	Solvent Concentration	Mass		
		1 mg	5 mg	10 mg
	1 mM	4.2790 mL	21.3950 mL	42.7899 mL
	5 mM	0.8558 mL	4.2790 mL	8.5580 mL
	10 mM	0.4279 mL	2.1395 mL	4.2790 mL

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

In Vivo

- Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
Solubility: ≥ 2.5 mg/mL (10.70 mM); Clear solution
- Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
Solubility: ≥ 2.5 mg/mL (10.70 mM); Clear solution
- Add each solvent one by one: 10% DMSO >> 90% corn oil
Solubility: ≥ 2.5 mg/mL (10.70 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

Lomustine (CCNU; NSC 79037) is a DNA alkylating agent, with antitumor activity.

IC₅₀ & Target

DNA Alkylator^[1]

In Vitro

Lomustine (CCNU; NSC 79037) is a DNA alkylating agent. Lomustine (CCNU, 0-250 μM) is cytotoxic to the U87-MG cells

expressing tumor-derived mutant IDH1, and has little effect on the expression of wild-type IDH1. The combination of Lomustine and procarbazine or vincristine has no additive effect on the killing of cells expressing mutant or wild-type IDH1. Moreover, overexpression of either ALKBH2 or ALKBH3 partially reduces the death HT1080 cells exposed to Lomustine^[1]. Lomustine (CCNU) suppresses U87-MG growth with an ED50 of 68.1 μM . Lomustine (CCNU) (30, 40 μM) in combination with docosahexaenoic acid (DHA) dramatically inhibits 2 additional human-derived glioblastoma cell lines, and induces U87-MG apoptosis and necrosis. Lomustine (30 μM) causes G2/M arrest^[2]. Lomustine (CCNU) reduces the viability of F98 rat orthotopic glioma cells and Tu-2449 mouse glioma cell line, with IC₅₀s of 20.8 μM and 18.6 μM , respectively^[3]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

In Vivo

Lomustine (CCNU; NSC 79037) (30 mg/kg) in combination with Toca 511 + 5-FC prolongs survival in rats bearing F98 tumor cells. Lomustine (CCNU) (30 mg/kg) combined with Toca-511 + 5-FC also exhibits antitumor activity in the B6C3F1 mice bearing Tu-2449 glioma cells^[3]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Cell Assay ^[2]

Initially, cells (5000 cells/well) are cultured in 96-well flat-bottom plates overnight in complete medium to establish a linear growth rate. Spent medium is replaced with new medium supplemented with 2% FBS and varying treatments (100 μL total volume/well). Ethanol-supplemented cells (< 0.5%) serve as the vehicle control. Cells are maintained at 37°C in 5% CO₂ in a humidified atmosphere for 24 hours prior to assessment of cell growth with the WST-1 assay reagent. Medium alone combined with the WST-1 assay reagent establishes nonspecific values that are subtracted from the experimental optical density (OD) readings (OD at 450 nm). Vehicle control OD readings serve as standard proliferative potential normalized to 100%. The proliferation index is calculated by dividing the average OD treatment reading by the average OD vehicle reading and multiplying by 100^[2].

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Animal Administration ^[3]

Mice^[3]

Groups of B6C3F1 mice receive PBS or 5-FC only as a control during the study (n = 8 per group). One group of mice (Lomustine Day 1 + PBS) receive one dose of Lomustine (30 mg/kg) on day 1 and a total of six cycles of PBS (800 $\mu\text{L}/\text{day}$, BID for 4 consecutive days every 10 days). The rest of the mice receive 5-FC (500 mg/kg/dose, IP, BID) for 4 consecutive days, plus Lomustine at day 1 (Lomustine (CCNU) Day 1 + 5-FC) or day 43 (Lomustine (CCNU) Day 43 + 5-FC). Cycles of 4-days on, 10-days off 5-FC or PBS are repeated a total of 6 times. Each experiment is terminated at the end of the last 5-FC treatment. All tissues are collected and saved for histopathology. Toxicity in groups receiving Lomustine is compared to the groups receiving PBS or 5-FC alone or in combination with 5-FC at designated time points^[3].

Rats^[3]

Groups of rats receive PBS or 5-FC only as controls during the study (n = 8 per group). One group of rats (Lomustine (CCNU) Day 1 + PBS) receive one dose of Lomustine (30 mg/kg) at day 1 and a total of six cycles of PBS (8 mL/day, BID). The rest of the rats receive 5-FC (500 mg/kg/dose, IP, BID) for 5 consecutive days, followed by 2 days off drug, plus Lomustine on day 1 (Lomustine (CCNU) Day 1 + 5-FC) or day 22 (Lomustine (CCNU) Day 22 + 5-FC). Cycles of 5-days on, 2-days off 5-FC or PBS are repeated a total of 6 times^[3].

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- Acta Pharmacol Sin. 2021 Jan;42(1):108-114.
- Int J Oncol. 2022 Nov;61(5):139.
- J Mol Med (Berl). 2019 Aug;97(8):1183-1193.
- Mol Imaging Biol. 2020 Feb;22(1):124-133.

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- bioRxiv. 2023 Jul 17.

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REFERENCES

- [1]. Wang P, et al. Oncometabolite D-2-Hydroxyglutarate Inhibits ALKBH DNA Repair Enzymes and Sensitizes IDH Mutant Cells to Alkylating Agents. Cell Rep. 2015 Dec 22;13(11):2353-2361.
- [2]. Harvey KA, et al. Enhanced anticancer properties of lomustine in conjunction with docosahexaenoic acid in glioblastoma cell lines. J Neurosurg. 2015 Mar;122(3):547-56.
- [3]. Yagiz K, et al. Toca 511 plus 5-fluorocytosine in combination with lomustine shows chemotoxic and immunotherapeutic activity with no additive toxicity in rodent glioblastoma models. Neuro Oncol. 2016 Oct;18(10):1390-401.
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Caution: Product has not been fully validated for medical applications. For research use only.

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