

Product Data Sheet

Product Name: DT2216
Cat. No.: GC39708

Chemical Properties

Cas. No. 2365172-42-3

SMILES CC1(C)CCC(C2=CC=C(Cl)C=C2)=C(C1)CN3CCN(C4=CC=C(C(NS(=O)(C5=CC(S(C(F)(F)F)=O)=O)=C(N[C@@H](CSC6=CC=CC=C6)CCN7CCN(C(CCCCCC(N[C@@H](C(C)(C)C)C(N8[C@@H](C[C@@H](O)C8)C(N[C@H](C9=CC=C(C%10=C(N=CS%10)C)C=C9)C)=O)=O)=O)=O)CC7)C=C5)=O)=O)C=C4)CC3

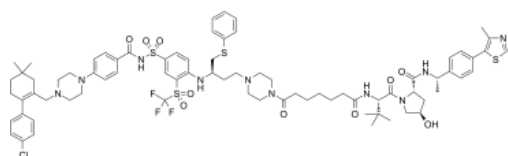
Formula $C_{77}H_{96}ClF_3N_{10}O_{10}S_4$ M.Wt 1542.36

Solubility DMSO: 25 mg/mL (16.21 mM) Storage Store at -20°C, stored under nitrogen

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



Protocol

Caution: Product has not been fully validated for medical applications. For research use only.

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Cell experiment [1]:

Cell lines MyLa cells

Preparation Method MyLa cells were pretreated with or without QVD for 4 h, and then treated with DT2216 for different duration.

Reaction
Conditions 0, 0.01, 0.03, 0.1, 0.3 μ M for 16h

Applications DT2216 dose- and time-dependently decreased the expression of Bcl-xL but had no effect on the expression of BCL2L1 (the gene that encodes Bcl-xL) mRNA in MyLa cells

Animal experiment [2]:

Animal models Pancreatic cancer PDX models were established by NSG mice

Preparation Method Animals were treated with vehicle, gemcitabine [20 mg/kg, once a week (every 7 days), i.p.], DT2216 [15 mg/kg, every 4 days, i.p.] and a combination of gemcitabine and DT2216. DT2216 was formulated in 50% phosal 50 PG, 45% miglyol 810N and 5% polysorbate 80.

Dosage form Intraperitoneal injection, 15 mg/kg, every 4 days

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Applications DT2216 inhibited tumor growth and increasing the survival of the tumor-bearing mice, whereas the combination treatment was more effective than either agent alone without any significant decrease in body weight.

References:

- [1]: He Y, Koch R, Budamagunta V, et al. DT2216—a Bcl-xL-specific degrader is highly active against Bcl-xL-dependent T cell lymphomas[J]. Journal of hematology & oncology, 2020, 13(1): 1-13.
- [2]: Thummuri D, Khan S, Underwood P W, et al. Overcoming Gemcitabine Resistance in Pancreatic Cancer Using the BCL-XL-Specific Degradar DT2216[J]. Molecular cancer therapeutics, 2022, 21(1): 184-192.

Background

DT2216 is a proteolysis targeting chimera (PROTAC), and targets Bcl-xL for degradation in T-cell lymphomas that depend on the overexpressed proteins of the Bcl-2 family, such as Bcl-2, Bcl-xL, and Mcl-1^[1,2].

DT2216 inhibited G-68 cells with IC50 value of 4.02 μ M (72hours). Combination of 0.1 μ M DT2216 and 0.1 μ M gemcitabine treatment synergistically kills pancreatic cancer cells in vitro^[3].

DT2216 showed remarkable effects in xenograft mouse model of human T-cell lymphoma (MyLa, MJ, MAC2A, and L82 cell lines) and T-cell prolymphocytic leukemia (T-PLL), with reduced platelet toxicity compared with ABT263^[1]. DT2216 effect was also present in a patient-derived xenograft tumor model of resistant T-cell ALL, when DT2216 was combined with vincristine, dexamethasone, and L-asparaginase. The median overall survival of mice reached 72 days with combination treatment versus 55 days with DT2216 monotherapy, and 47 days with chemotherapy alone^[4].

References:

- [1]. He Y, Koch R, Budamagunta V, et al. DT2216—a Bcl-xL-specific degrader is highly active against Bcl-xL-dependent T cell lymphomas[J]. Journal of hematology & oncology, 2020, 13(1): 1-13.
- [2]. Khan, S.; Zhang, X.; Lv, D.; Zhang, Q.; He, Y.; Zhang, P.; Liu, X.; Thummuri, D.; Yuan, Y.;

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Wiegand, J.S.; et al. A selective BCL-XL PROTAC degrader achieves safe and potent antitumor activity. Nat Med. 2019, 25, 1938-1947.

[3]. Thummuri D, Khan S, Underwood P W, et al. Overcoming Gemcitabine Resistance in Pancreatic Cancer Using the BCL-XL-Specific Degradation DT2216[J]. Molecular cancer therapeutics, 2022, 21(1): 184-192.

[4]. Wolska-Washer A, Smolewski P. Targeting protein degradation pathways in tumors: Focusing on their role in hematological malignancies[J]. Cancers, 2022, 14(15): 3778.

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