

Product Data Sheet

Product Name: Bendamustine HCl

Cat. No.: GC10744

Chemical Properties

Cas. No. 3543-75-7

Chemical Name 4-[5-[bis(2-chloroethyl)amino]-1-methylbenzimidazol-2-yl]butanoic acid;hydrochloride

SMILES CN1C2=C(C=C(C=C2)N(CCCl)CCCl)N=C1CCCC(=O)O.Cl

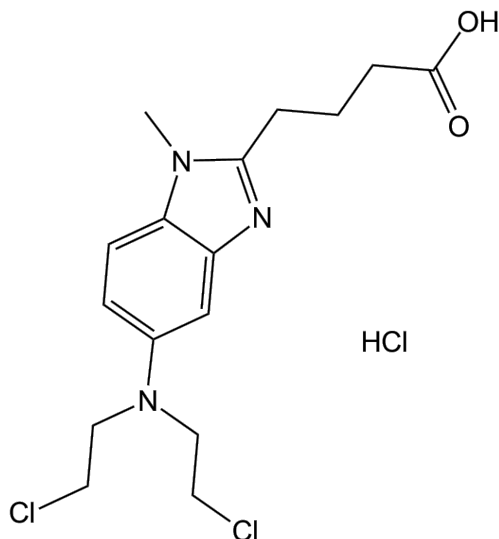
Formula $C_{16}H_{21}Cl_2N_3O_2 \cdot HCl$ M.Wt 394.72

Solubility $\geq 19.736\text{mg/mL}$ in DMSO Storage 4°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



Protocol

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

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Cell experiment: Cytotoxicity of both Bendamustine and melphalan on multiple myeloma (MM) cells is calculated as inhibition of cell viability by measuring the percentage of cell survival by MTS assay. Briefly, cells (1×10^4 /well) are seeded in 96-well plates with increasing concentrations of the drug and analyzed after 24, 48, 72 and 96 h of incubation. To this end, 1 μ g/mL of MTS solution is added to each well and, after 1 h at 37 °C, the dark blue formazan crystals are dissolved by isopropanol 1 N and HCl (24:1, vol/vol). Finally, the absorbance is measured at 490 nm in a 96-well plate reader. Cell survival is estimated as the percentage of the absorbance of untreated controls and each test is performed in triplicate. The inhibitory concentrations 50 (IC₅₀) and 25 (IC₂₅) of each drug, being the amount able to reduce cell growth to 50% and 25%, respectively, of that of untreated control cells, are calculated, and the tests are performed in parallel using equitoxic concentrations of Bendamustine and melphalan. The relative resistance index (RRI) is expressed as the ratio of the IC₅₀ of 8226-LR5 to the IC₅₀ of RPMI-8226 cells[2].

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Animal experiment: Mice[3]C.B.-17 scid mice (DoHH-2, Granta 519) or C.B.-17 scid-bg mice (SuDHL-4, RAMOS) are inoculated with 1×10^6 (DoHH-2, RAMOS), 3×10^6 (SuDHL-4) or 5×10^6 (Granta 519) cells s.c. in the right flank. For flank xenografts, inoculation volume is 0.2 mL consisting of a 50:50 mixture of cells in growth medium and Matrigel. Tumour volume is estimated by two to three weekly measurements of the length and width of the tumour by electronic calipers and applying the following equation: $V = L \times W^2 / 2$. Tumours are allowed to reach approximately 250 mm³, and mice are size-matched (day 0) into treatment and control groups. For systemic Granta 519 tumour models, 2×10^6 cells are injected via the tail vein in 0.1 mL volume of cell medium on day 0, and treatment is initiated on day 14. All animals are ear-tagged and monitored individually throughout the experiment. Navitoclax is administered by oral gavage once daily in a mixture of Phosal 50PG : PEG400 : ethanol. Bendamustine and rituximab are administered i.v. at 25 mg/kg and 10 mg/kg, respectively, on day 1. Navitoclax is administered approximately 2 h before Bendamustine and rituximab. All trials are comprised of 10 mice per group. Mice are humanely killed when tumours reach a size >2000 mm³ or when any signs of distress are monitored. Signs of distress include loss of ambulation, laboured breathing or weight loss > 20% mean body weight per cage[3].

References:

- [1]. Leoni LM, et al. Bendamustine (Treanda) displays a distinct pattern of cytotoxicity and unique mechanistic features compared with other alkylating agents. Clin Cancer Res. 2008 Jan 1;14(1):309-17.
- [2]. Minbo Zang, et al. Effects of chemotherapeutic agent bendamustine for non-hodgkin lymphoma on spermatogenesis in mice. J Biomed Res. 2017 0(0): 1-12.
- [3]. Cives M, et al. Bendamustine overcomes resistance to melphalan in myeloma cell lines by inducing cell death through mitotic catastrophe. Cell Signal. 2013 May;25(5):1108-17.
- [4]. Ackler S, et al. Navitoclax (ABT-263) and bendamustine $\pm$ rituximab induce enhanced killing of non-Hodgkin's lymphoma tumours in vivo. Br J Pharmacol. 2012 Oct;167(4):881-91.

Background

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Bendamustine HCl is an alkylating agent associated with DNA damage with IC₅₀ of 50 μ M [1].

It has been reported that bendamustine is activated under DNA damage stress and apoptosis. Bendamustine inhibits mitotic checkpoints and induces mitotic catastrophe by inhibiting several mitosis-related genes such as Polo-like kinase 1, Aurora kinase A, and Cyclin B1 [1]. In myeloma cell lines, bendamustine induced apoptosis by cleavage of caspase 3, and resulted in G2 cell cycle arrest [2]. In chronic lymphocytic and mantle cell lymphoma cell lines, bendamustine HCL has been shown to activate both the mitochondrial cell death pathway and caspase-dependent apoptosis. Some assays showed that bendamustine exhibited anti-proliferation effects on dexamethasone-sensitive (MM1.S) and -resistant (MM1.R) multiple myeloma cells in a dose-dependent manner, with IC₅₀s of 119.8 μ M (MM1.S) and 138 μ M (MM1.R), respectively. The apoptosis by activation of caspase-3 and caspase-8 was induced in both MM1.S and MM1.R cell lines [4].

References:

- [1]. Leoni LM, Bailey B, Reifert J, Bendall HH, Zeller RW, Corbeil J, Elliott G, Niemeyer CC. Bendamustine (Treanda) displays a distinct pattern of cytotoxicity and unique mechanistic features compared with other alkylating agents. Clin Cancer Res. 2008 Jan 1;14(1):309-17.
- [2]. Gaul L, Mandl-Weber S, Baumann P, Emmerich B, Schmidmaier R. Bendamustine induces G2 cell cycle arrest and apoptosis in myeloma cells: the role of ATM-Chk2-Cdc25A and ATM-p53-p21-pathways. J Cancer Res Clin Oncol. 2008 Feb;134(2):245-53.
- [3]. Roué G, López-Guerra M, Milpied P, Pérez-Galán P, Villamor N, Montserrat E, Campo E, Colomer D. Bendamustine is effective in p53-deficient B-cell neoplasms and requires oxidative stress and caspase-independent signaling. Clin Cancer Res. 2008 Nov 1;14(21):6907-15.
- [4]. Cai B, Wang S, Huang J, Lee CK, Gao C, Liu B. Cladribine and bendamustine exhibit inhibitory activity in dexamethasone-sensitive and -resistant multiple myeloma cells. Am J Transl Res. 2013;5(1):36-46.

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