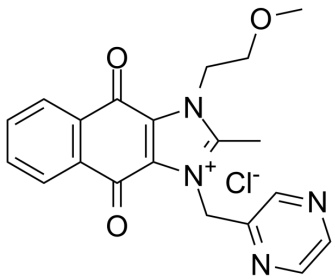
Sepantronium hydrochloride

Cat. No.:	HY-10194A
CAS No.:	355406-09-6
Molecular Formula:	$C_{20}H_{19}ClN_4O_3$
Molecular Weight:	398.84
Target:	Survivin; Autophagy
Pathway:	Apoptosis; Autophagy
Storage:	Please store the product under the recommended conditions in the Certificate of Analysis.



BIOLOGICAL ACTIVITY

Description	Sepantronium hydrochloride (YM-155 hydrochloride) is a novel survivin suppressant with an IC_{50} of 0.54 nM for the inhibition of survivin promoter activity[1].
IC_{50} & Target	IC50: 0.54 nM (survivin)
In Vitro	Sepantronium bromide (YM155; 30 μM) is not sensitive to survivn gene promoter-driven luciferase reporter activity. Sepantronium bromide shows significant supression on endogenous survivin expression in PC-3 and PPC-1 human HRPC cells with deficient p53 via transcriptional inhibition of the survivin gene promoter. Sepantronium bromide (100 nM) does not affect protein expression of c-IAP2, XIAP, Bcl-2, Bcl-xL, Bad, α-actin, and β-tubulin. Sepantronium bromide potently inhibits human cancer cell lines (mutated or truncated p53) such as PC-3, PPC-1, DU145, TSU-Pr1, 22Rv1, SK-MEL-5 and A375 with IC_{50}s ranging from 2.3 to 11 nM, respectively[1]. Sepantronium bromide (YM155) resultin in an increase in sensitivity of NSCLC cells to γ-radiation. Sepantronium bromide combined with γ-radiation increases both the number of apoptotic cells and the activity of caspase-3. In addition, Sepantronium bromide delays the repair of radiation-induced double-strand breaks in nuclear DNA[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	Sepantronium bromide (YM155; 3 and 10 mg/kg) inhibits the tumor growth in PC-3 xenografts, without obvious body weight loss and blood cell count decrease. Sepantronium bromide is highly distributed to tumor tissue in vivo. Sepantronium bromide shows 80% TGI at a dose of 5 mg/kg in PC-3 orthotopic xenografts[1]. Sepantronium bromide (YM155) in combination with γ-radiation shows potent antitumor activity against H460 or Calu6 xenografts in nude mice[2]. In this orthotopic renal and metastatic lung tumors models, Sepantronium bromide (YM-155) and IL-2 additively decreases tumor weight, lung metastasis, and luciferin-stained tumor images[3]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Cell Assay [1]	The antiproliferative activity of Sepantronium bromide is measured. After treatment with Sepantronium bromide for 48 h, the cell count is determined by sulforhodamine B assay. The GI_{50} value is calculated by logistic analysis, which is the drug concentration resulting in a 50% reduction in the net protein increase (as measured by sulforhodamine B staining) in control cells during the drug incubation. The assay is done in triplicate, and the mean GI_{50} value is obtained from the results

	of four independent assays. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Animal Administration [1]	Five-week-old male nude mice (BALB/c nu/nu) are used for the assay. PC-3 cells (2×10^6-3×10^6) are injected into the flanks of the mice and allowed to reach a tumor volume of > 100 mm^3 in tumor volume (length×$width^2$×0.5). Sepantronium bromide is s.c. administered as a 3-day continuous infusion per week for 2 weeks using an implanted micro-osmotic pump or i.v. administered five times a week for 2 weeks. The percentage of tumor growth inhibition 14 days after initial Sepantronium bromide administration is calculated for each group using the following formula: MTV=100×{1-[(MTV of the treated group on day 14)-(MTV of the treated group on day 0)]/[(MTV of the control group on day 14)-(MTV of the control group on day 0)]}, where MTV is mean tumor volume. For both the frozen tumors and plasma samples, survivin expression levels are analyzed by Western blotting and Sepantronium bromide concentration by high-performance liquid chromatography/triple quadrupole mass spectrometry (LC/MS/MS) using validated methods. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- Cancer Lett. 2018 Jul 1;425:54-64.
- Cell Death Dis. 2020 Nov 15;11(11):982.
- Cancers. 2019 Oct 14;11(10):1550.
- Cancers. 2019 Jul 5;11(7):947.
- Stem Cell Res Ther. 2020 Jun 10;11(1):229.

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REFERENCES

[1]. Nakahara T, et al. YM155, a novel small-molecule survivin suppressant, induces regression of established human hormone-refractory prostate tumor xenografts. Cancer Res. 2007 Sep 1;67(17):8014-21.

[2]. Iisa T, et al. Radiosensitizing effect of YM155, a novel small-molecule survivin suppressant, in non-small cell lung cancer cell lines. Clin Cancer Res. 2008 Oct 15;14(20):6496-504.

[3]. Guo K, et al. A combination of YM-155, a small molecule survivin inhibitor, and IL-2 potently suppresses renal cell carcinoma in murine model. Oncotarget. 2015 Aug 28;6(25):21137-47.

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