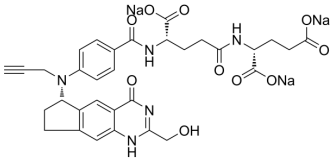
ONX 0801 trisodium

Cat. No.:	HY-10822A
CAS No.:	1097638-00-0
Molecular Formula:	$C_{32}H_{30}N_5Na_3O_{10}$
Molecular Weight:	713.58
Target:	Thymidylate Synthase
Pathway:	Apoptosis
Storage:	Please store the product under the recommended conditions in the Certificate of Analysis.



BIOLOGICAL ACTIVITY

Description

ONX 0801 (BGC 945) trisodium is a thymidylate synthase (TS) inhibitor, targeted to α-folate receptor–overexpressing tumors [1][2].

In Vitro

ONX 0801 (BGC 945) is designed to further reduce toxicity by more effectively targeting cancer cells that overexpress the α-FR[1].

ONX 0801 (BGC 945) exhibits IC_{50} values of of 6.6 μM, 1.1 nM, 3.3 nM, 90 nM and 0.32 μM in A431, A431-FBP, KB, IGROV-1 and JEG-3 cells[2].

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

In Vivo

BGC 945 (100 mg/kg, ip/iv injection) in the tumor had a longer half-life (28 hours) compared with other tissues[2].

BGC 945 (100 mg/kg daily for 16 days) does not lead to body weight loss, macroscopic signs of toxicity to the major organs, or a change in renal function[2].

BGC 945 at 100mg/kg induces a 5-20-fold increase in tumor dUrd at 4-72h without increases in the plasma, consistent with tumor targeting[2].

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Animal Model:	Mice (on the folate-free diet for 5 days were transplanted with tumor and the implants)[2].
Dosage:	100 mg/kg (Pharmacokinetic Analysis).
Administration:	Single i.p. or iv injection.
Result:	After i.p. injection, the compound was well absorbed from the peritoneal cavity. The plasma AUC was 50% higher for i.p. compared with i.v. administration and was also higher in spleen, kidney, and liver by this route. Tumor AUC was similar via either route.

REFERENCES

[1]. Anna Tochowicz, et al. Development and binding mode assessment of N-[4-[2-propyn-1-yl[(6S)-4,6,7,8-tetrahydro-2-(hydroxymethyl)-4-oxo-3H-cyclopenta[g]quinazolin-6-yl]amino]benzoyl]-l-γ-glutamyl-D-glutamic acid (BGC 945), a novel thymidylate synthase inhibitor that targets tumor cells. J Med Chem. 2013 Jul 11;56(13):5446-55.

[2]. David D Gibbs, et al. BGC 945, a novel tumor-selective thymidylate synthase inhibitor targeted to alpha-folate receptor-overexpressing tumors. Cancer Res. 2005 Dec 15;65(24):11721-8.

[3]. Chau Ng, et al. Efficacy and tolerability of the thymidylate synthase (TS) inhibitor, BGC 945 is mediated through its selective uptake via the α-folate receptor (α-FR) in IGROV-1 human tumor xenografts. AACR Annual Meeting-- Apr 12-16, 2008; San Diego, CA.

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