Product Data Sheet

Product Name: Guadecitabine sodium
Cat. No.: GC36196

Chemical Properties

Cas. No.	929904-85-8		
SMILES	O=C1C2=C(N([C@H]3C[C@H](O)[C@@H](COP(O[C@@H]4[C@@H](CO)O[C@@H](N5C=NC(N)=NC5=O)C4)([O-])=O)O3)C=N2)NC(N)=N1.[Na+]		
Formula	$C_{18}H_{23}N_9NaO_{10}P$	M.Wt	579.39
Solubility	DMSO: 50 mg/mL (86.30 mM); Water	Storage	Store at -20°C
General tips	For obtaining a higher solubility , please warm the tube at 37 ℃ and shake it in the ultrasonic bath for a while.Stock solution can be stored below -20℃ 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	Guadecitabine sodium		

Protocol

Cell experiment [1]:

Cell lines	Leukemic cell lines(HL60, KG1a, U937)
Preparation Method	To evaluate the effect of Guadecitabine treatment on Cancer Testis Antigen methylation, HL60, U937, and KG1a leukemic cell lines were treated with Guadecitabine and harvested on day 5.
Reaction Conditions	Leukemic cell line were treated with Guadecitabine (0.1, 1.0 and 5μM) for 5 days.

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Applications	Guadecitabine treatment resulted in significant reductions of LINE-1 and NY-ESO-1 promoter methylation in HL60, U937 and KG1a cells, as determined by quantitative bisulfite pyrosequencing.MAGE-A3/6 was also hypomethylated following Guadecitabine treatment in all cell lines.

Animal experiment [2]:

Animal models	SCID mice
Preparation Method	OVCAR3 cells were implanted into the hindquarters of SCID mice. After 2–3 weeks, when macroscopic tumors were formed, mice were treated with Guadecitabine for 5day.
Dosage form	3 mg/kg/day, subcutaneous treatment
Applications	OVCAR3 tumors were treated with 3 mg/kg/d, 5 days Guadecitabine or vehicle control subcutaneously, 3 days later, injected with NY-ESO-1-specific CD8+ T-cells or vehicle control (PBS) intra-tumorally. The combination of Guadecitabine and NY-ESO-1 specific T-cells showed delayed tumor growth in comparison with mice treated with Guadecitabine or NY-ESO-1-specific CD8 +T-cells alone.these data suggest Guadecitabine treatment enhances NY-ESO-1-specific antitumor responses in vivo.

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References:

[1]. Srivastava P, Paluch BE,et al. Immunomodulatory action of SGI-110, a hypomethylating agent, in acute myeloid leukemia cells and xenografts. Leuk Res. 2014 Nov;38(11):1332-41.

[2]. Srivastava P, Paluch BE,et al. Immunomodulatory action of the DNA methyltransferase inhibitor SGI-110 in epithelial ovarian cancer cells and xenografts. Epigenetics. 2015;10(3):237-46.

Background

Guadecitabine is a novel hypomethylating dinucleotide of decitabine and deoxyguanosine that is resistant to degradation by cytidine deaminase. Guadecitabine Sodium is the easily dissolved form of Guadecitabine[1].

Guadecitabine (0.1, 0.3, 1, 5μM, 48h) increased sensitivity to cisplatin for both the parental and the resistant A2780 cells. Although among other ovarian cancer cell lines, the parental A2780- cisplatin resistant cells is considered to be cisplatin “sensitive”, it has a relatively high IC50 for the drug[2].

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Guadecitabine (50nM-2μM, 24h) pretreatment synergistically interacted with ASTX660 to induce cell death in five AML cell lines (MOLM-13, ML-2, MV4-11, PLB-985, KG-1) with various genetic backgrounds and representing different AML subtypes?[3].

Tumor-bearing immune-deficient mice were exposed subcutaneously to Guadecitabine at doses of 3, 6.1, or 10 mg/kg, daily for 5 days, with tumors harvested on day 7. Most mice treated on the 5 day schedule with 10mg/kg/day Guadecitabine died; all mice treated with 6.1mg/kg/day Guadecitabine developed gastrointestinal toxicity. Minimal toxicity was observed in mice treated with 3mg/kg/day. Guadecitabine treatment caused hypomethylation of?LINE-1?and?NY-ESO-1?at all doses[4].

References:
[1].Issa JJ, Roboz G, et al. Safety and tolerability of guadecitabine (SGI-110) in patients with myelodysplastic syndrome and acute myeloid leukaemia: a multicentre, randomised, dose-escalation phase 1 study. Lancet Oncol. 2015 Sep;16(9):1099-1110.
[2].Fang F, Munck J, et al. The novel, small-molecule DNA methylation inhibitor SGI-110 as an ovarian cancer chemosensitizer. Clin Cancer Res. 2014 Dec 15;20(24):6504-16.
[3].Dittmann J, Haydn T, et al. Next-generation hypomethylating agent SGI-110 primes acute myeloid leukemia cells to IAP antagonist by activating extrinsic and intrinsic apoptosis pathways. Cell Death Differ. 2020 Jun;27(6):1878-1895.
[4].rivastava P, Paluch BE, et al. Immunomodulatory action of SGI-110, a hypomethylating agent, in acute myeloid leukemia cells and xenografts. Leuk Res. 2014 Nov;38(11):1332-41.

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