

Product Data Sheet

Product Name: diABZI STING agonist-1

Cat. No.: GC35853

Chemical Properties

Cas. No. 2138299-33-7

SMILES O=C(N)C1=CC(N=C(NC(C2=CC(C)=NN2CC)=O)N3C/C=C/CN4C(NC(C5=CC(C)=NN5CC)=O)=NC6=C4C(OCCCN7CCOCC7)=CC(C(N)=O)=C6)=C3C(OC)=C1

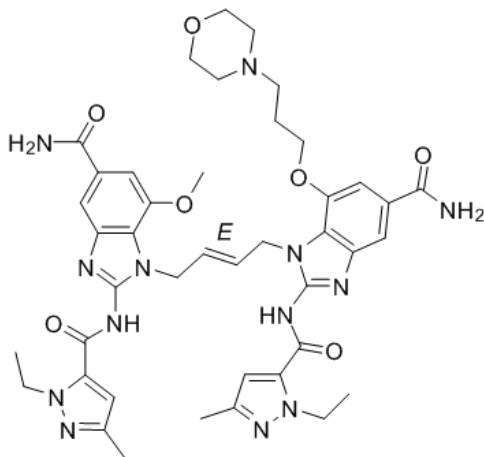
Formula $C_{42}H_{51}N_{13}O_7$ M.Wt 849.94

Solubility DMSO : 100 mg/mL (117.66 mM; Need ultrasonic) Storage Store at -20°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

Cell experiment [1]:

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Cell lines	Human NSCLC cell lines (H460 and A549)
Preparation Method	Human NSCLC cell lines (H460 and A549) were cultured in RPMI 1640 (Gibco) and Ham's F-12 K (Procell), respectively. Irradiation (IR) was carried out with a ¹³⁷Cs-irradiator (Gammacell-40, Atomic Energy of Canadian Inc.) at a dose rate of 0.9Gy/min. Cells were irradiated with 0, 2 and 4Gy γ-ray after pretreatment with diABZI STING agonist-1 trihydrochloride or DMSO for 2h. In this study, diABZI STING agonist-1 was used at a 20nM concentration according to previous studies. Briefly, cells (3×10^3 cells/well) were plated in 96-well plates and when they had grown to 70%–80% confluence, were treated with 20nM diABZI STING agonist-1 or DMSO. After 24, 48 and 72h treatment, respectively, cell counting kit-8 (CCK-8) (Biosharp) was added to each well. After incubation for 3h, absorbance at 450nm for each well was measured using a microplate reader (Infinite M200).
Reaction Conditions	20nM; 24、48 and 72h
Applications	Compared to the control cells, the proliferation of both H460 and A549 cells was obviously inhibited by diABZI STING agonist-1. The inhibitory effect of diABZI STING agonist-1 combined with a low dose of IR (2Gy) on the proliferation of NSCLC cells was closer to that of a higher dose of IR.
Animal experiment [2]:	
Animal models	BALB/cJ mice

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Mice were injected on day 1 with a diABZI STING agonist-1 trihydrochloride (GLPBIO, Montclair, CA, USA) in 40% PEG300 (MilliporeSigma, St. Louis, MO, USA) (2.5mg/kg, 0.05mL/mouse, subcutaneous (sc) route) on a shaved back. One day before the diABZI STING agonist-1 injection, on day 0, some mice were pre-treated with poly (I:C) (HMW, InvivoGen Corp, San Diego, CA, USA) in Preparation Method saline (2mg/kg body weight, 0.2ml/mouse, intraperitoneal (ip) route). Mice injected with saline (ip) followed by 40% PEG300 (sc) or poly (I:C) (ip) followed by 40% PEG300 (sc) served as control groups. Tail bleeds were collected from all mice four hours after each injection on days 0 and 1. Sera were stored at -80 °C for cytokine analysis. The skin on the back of the mice was monitored daily for inflammatory changes.

Dosage form 2.5mg/kg/d; subcutaneous injection

Applications The diABZI STING agonist-1 caused a strong local inflammatory response and skin lesions in mice, with an increase in serum IL-10 levels. Systemic pretreatment with poly(I:C) in mice led to an intensified response to diABZI STING agonist-1, higher levels of systemic cytokines, more severe skin lesions, and delayed resolution of skin inflammation.

References:

- [1] Xue A, Shang Y, Jiao P, et al. Increased activation of cGAS-STING pathway enhances radiosensitivity of non-small cell lung cancer cells[J]. Thoracic cancer, 2022, 13(9): 1361-1368.
- [2] Pyclik M, Durslewicz J, Papinska J A, et al. STING agonist-induced skin inflammation is exacerbated with prior systemic innate immune activation[J]. International Journal of Molecular Sciences, 2023, 24(4): 4128.

Background

diABZI STING agonist-1 is an agonist of the stimulator of interferon genes (STING) pathway with EC₅₀ values of 130nM in humans and 186nM in mice, respectively [1]. STING plays an important role in regulating the transcription of a large number of host defense genes (including type I IFN) and protecting cells from cancer development. diABZI STING agonist-1 demonstrated anti-tumor activity

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in mice with colon tumors [2].

In vitro, treatment of human NSCLC cell lines (H460 and A549) with diABZI STING agonist-1 (20nM) for 24, 48, and 72 hours significantly inhibited the proliferation of both cells. The inhibitory effect of diABZI STING agonist-1 combined with low-dose IR (2 Gy) on the proliferation of non-small cell lung cancer cells was closer to that of high-dose IR [2]. Treating melanoma cells with diABZI STING agonist-1 (21nM) in the culture medium for 24 hours will increase the phosphorylation levels of TBK1 and STING, and the phosphorylated STING will be located in the area near the nucleus. In addition, IRF3 was phosphorylated, indicating that the STING pathway was activated [3].

In vivo, a single subcutaneous injection of diABZI STING agonist-1 (2.5mg/kg/d) in mice caused a strong local inflammatory response and skin lesions, with elevated serum IL-10 levels. Systemic pretreatment with poly(I:C) in mice led to an exacerbated response to diABZI STING agonist-1, higher levels of systemic cytokines, more severe skin lesions, and delayed resolution of skin inflammation [4]. By treating OVX-induced osteoporosis mice with diABZI STING agonist-1 (0.5mg/kg; i.p.) for 3 times a week for 2 weeks, the concentrations of RANKL and CTX-I in serum and the RANKL/OPG ratio were significantly reduced. diABZI STING agonist-1 alleviates bone resorption induced by Ti particles and osteoporosis induced by ovarian ablation in vivo by inhibiting OC differentiation and function [5].

References:

- [1] Ramanjulu J M, Pesiridis G S, Yang J, et al. Design of amidobenzimidazole STING receptor agonists with systemic activity[J]. *Nature*, 2018, 564(7736): 439-443.
- [2] Xue A, Shang Y, Jiao P, et al. Increased activation of cGAS-STING pathway enhances radiosensitivity of non-small cell lung cancer cells[J]. *Thoracic cancer*, 2022, 13(9): 1361-1368.
- [3] Chipurupalli S, Ganesan R, Dhanabal S P, et al. Pharmacological STING activation is a potential alternative to overcome drug-resistance in melanoma[J]. *Frontiers in oncology*, 2020, 10: 758.
- [4] Pyclik M, Dursiewicz J, Papinska J A, et al. STING agonist-induced skin inflammation is exacerbated with prior systemic innate immune activation[J]. *International Journal of Molecular Sciences*, 2023, 24(4): 4128.
- [5] Huang Y, Zhang M, Zhang J, et al. diABZI and poly (I: C) inhibit osteoclastic bone resorption by inducing IRF7 and IFIT3[J]. *Journal of Bone and Mineral Research*, 2024, 39(8): 1132-1146.

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