

Product Data Sheet

Product Name: AZD4635

Cat. No.: GC19049

Chemical Properties

Cas. No. 1321514-06-0

SMILES NC1=NC(C2=CC=C(F)C=C2)=C(C3=CC(Cl)=NC(C)=C3)N=N1

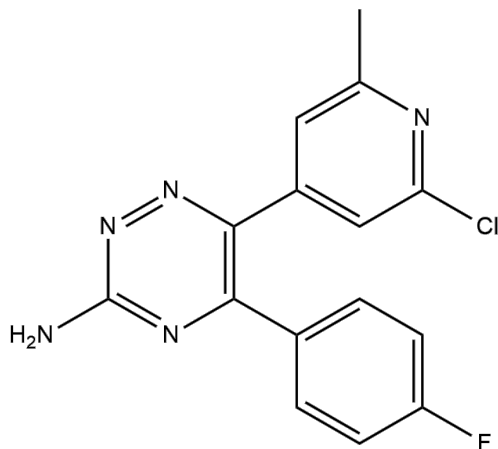
Formula $C_{15}H_{11}ClFN_5$ M.Wt 315.73

Solubility DMSO : ≥ 83.3 mg/mL (263.83 mM); Water : < 0.1 mg/mL (insoluble) Storage Store at -20°C

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]:

Cell lines Mouse bone marrow-derived progenitor cells

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

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Preparation Method Mouse bone marrow-derived precursor cells were cultured for 16 days in complete T cell medium supplemented with 200ng/ml rmFLT3L and 5ng/ml rmGM-CSF. After initial incubation with growth cytokines for 10 days, 3μM AZD4635 or DMSO (as a control) was added, and after 30 minutes of incubation, 5μM NECA was added. After that, the culture with growth cytokines was continued for 6 days before the cells were harvested for analysis.

Reaction Conditions 3μM; 30min

Applications AZD4635 treatment rescued the immunosuppressive effects of mouse bone marrow-derived progenitor cells and promoted the generation of bone marrow-derived precursors into CD103⁺ dendritic cell.

Animal experiment [2]:

Animal models C57BL/KalwRij mice

Preparation Method C57BL/KalwRij mice were raised in a standard sterile environment and injected intravenously with 2×10^5 5T33 multiple myeloma (MM) cells on day 0 and intraperitoneally with 10mg/kg monoclonal anti-CD73 antibody on days 2, 4, 8, 11, and 15. AZD4635 (25mg/kg) was administered by gavage once a day from day 0, and mice were sacrificed on day 15, and spleen tissues were collected for analysis.

Dosage form 25mg/kg/day for 15 days; p.o.

Applications AZD4635 treatment resulted in a significant decrease in the number of CD138 MM cells in the spleen of mice, an increase in the number of monocytes, and enhanced T cell activation.

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References:

- [1] Borodovsky A, Barbon C M, Wang Y, et al. Small molecule AZD4635 inhibitor of A2AR signaling rescues immune cell function including CD103+ dendritic cells enhancing anti-tumor immunity[J]. Journal for Immunotherapy of Cancer, 2020, 8(2): e000417.
- [2] Yang R, Elsaadi S, Misund K, et al. Conversion of ATP to adenosine by CD39 and CD73 in multiple myeloma can be successfully targeted together with adenosine receptor A2A blockade[J]. Journal for immunotherapy of cancer, 2020, 8(1): e000610.

Background

AZD4635 is a potent, selective, and oral adenosine 2A receptor (A2AR) inhibitor, with a K_i value of 1.7nM [1]. AZD4635 can increase the expression of CD25 (IL2Ra), an activation marker on CD8 T cells, and increase the expression of granzyme B on CD4 and CD8 T cells to improve immune activation[2]. AZD4635 has been widely used in different animal models to reduce tumor burden and enhance antitumor immunity [3].

In vitro, AZD4635 treatment at 3 μ M for 30min significantly reversed the immunosuppressive effect of 5 μ M 5'-(N-ethylcarboxamide) adenosine (NECA) on dendritic cells, and increased the expression of ovalbumin (OVA)[4]. After stimulation with anti-CD3 and anti-28 monoclonal antibodies, combined treatment with anti-PD-L1 antibody (10 μ g/ml) and AZD4635 (0.2 μ M) for 6 hours enhanced CD8⁺ T cell function and increased IL-2 and IFN- γ secretion[5].

In vivo, AZD4635 (25mg/kg) administered by gavage once daily for 15 days in combination with sodium polyoxotungstate (POM-1) and anti-CD73 antibody treatment resulted in enhanced T cell activation in the spleen and increased IFN- γ and monocyte levels in the spleen and bone marrow in a mouse model of myeloma[6].

References:

- [1] Borodovsky A, Wang Y, Ye M, et al. Preclinical pharmacodynamics and antitumor activity of AZD4635, a novel adenosine 2A receptor inhibitor that reverses adenosine mediated T cell suppression[J]. Cancer Research, 2017, 77(13_Supplement): 5580-5580.
- [2] Budhu S, Mane M, Bah M A, et al. Optimizing breast cancer therapy by inhibiting the adenosine

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- receptor and oxygen consumption[J]. Cancer Research, 2023, 83(7_Supplement): 2517-2517.
- [3] Borodovsky A, Wang Y, Ye M, et al. Inhibition of A2AR by AZD4635 induces anti-tumor immunity alone and in combination with anti-PD-L1 in preclinical models[J]. Cancer Research, 2018, 78(13_Supplement): 3751-3751.
- [4] Borodovsky A, Barbon C M, Wang Y, et al. Small molecule AZD4635 inhibitor of A2AR signaling rescues immune cell function including CD103+ dendritic cells enhancing anti-tumor immunity[J]. Journal for Immunotherapy of Cancer, 2020, 8(2): e000417.
- [5] Li J, Huang H H, Tu B, et al. Reversal of the CD8+ T-Cell exhaustion induced by chronic HIV-1 infection through combined blockade of the adenosine and PD-1 pathways[J]. Frontiers in Immunology, 2021, 12: 687296.
- [6] Yang R, Elsaadi S, Misund K, et al. Conversion of ATP to adenosine by CD39 and CD73 in multiple myeloma can be successfully targeted together with adenosine receptor A2A blockade[J]. Journal for immunotherapy of cancer, 2020, 8(1): e000610.

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