

Product Data Sheet

Product Name: Lenalidomide (CC-5013)

Cat. No.: GC14976

Chemical Properties

Cas. No. 191732-72-6

Chemical Name 3-(7-amino-3-oxo-1H-isoindol-2-yl)piperidine-2,6-dione

SMILES C1CC(=O)NC(=O)C1N2CC3=C(C2=O)C=CC=C3N

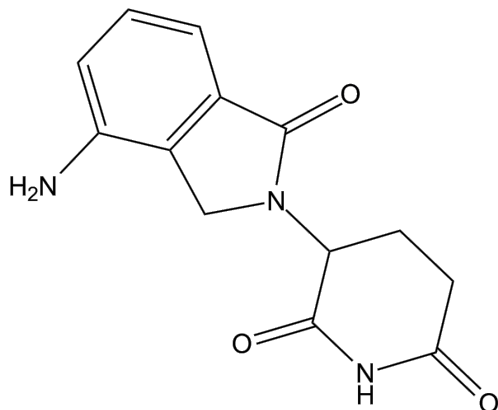
Formula $C_{13}H_{13}N_3O_3$ M.Wt 259.3

Solubility ≥ 100.8 mg/mL in DMSO Storage Store at 2-8°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]:

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Cell lines CFSE-labeled OPM1 cells and OPM1 cells co-cultured with HS-5 BMSCs

Preparation Method Lenalidomide was dissolved in DMSO.

Reaction
Conditions 0.1-10 μ M; 72h

Applications Lenalidomide significantly decreased the percentage of side population (SP) cells in a dose-dependent manner at 72 hours. Lenalidomide treatment inhibited cell proliferation of OPM1 cells either alone or with BMSCs. The percentage of CD138⁻/low⁺ population was increased after addition of Lenalidomide to OPM1 cells, alone or cocultured with BMSCs. BMSCs and lenalidomide slightly increased the proportion of CFSE⁺/7-AAD⁺ cells at 72 hours.

Animal experiment [2]:

Animal models Female NOD/SCID mice

CHLA-255-Fluc neuroblastoma cells and PBMC (0.25 $\times$ 10⁶; CD3⁺ 75.3%; CD3-CD56⁺CD16⁺ 2.7%) or NK cell depleted PBMC (PBMC-NK) (0.25 $\times$ 10⁶; CD3⁺ 82.6%; CD3-CD56⁺CD16⁺ 0.02%) were co-injected into NOD/SCID mice near Preparation Method the right and left shoulders in 25% (v/v) BD Matrigel[®] Matrix Growth Factor Reduced on day 0. Treatment began on day 1 (after imaging and randomization) with Lenalidomide alone (50mg/kg/d intraperitoneal days 1-9 and 12-16), ch14.18 alone (15 μ g/mouse intravenous days 3, 5, 8, and 12), or the combination of lenalidomide and ch14.18 using the same doses and schedules.

Dosage form 50mg/kg/d; 9+5d; i.p.

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Applications

After 14 days of treatment, Lenalidomide combined with ch14.18 most effectively suppressed tumor cell growth (AUC) compared to untreated, Lenalidomide alone, or ch14.18 alone-treated mice. Survival time was also longer for the Lenalidomide plus ch14.18-treated group than for untreated, Lenalidomide-treated or ch14.18-treated groups. When mice receiving NK-depleted PBMC were treated with Lenalidomide plus ch14.18, they had greater tumor growth and poorer survival than the PBMC group. Tumor growth was no different for these two groups treated with Lenalidomide or ch14.18 alone, and survival was no different for Lenalidomide but was marginally poorer for the NK-depleted group and ch14.18 alone-treated group. Together, these data indicate that Lenalidomide enhances survival of mice treated with ch14.18 and that this in vivo effect involves NK cells.

References:

- [1] Jakubikova J, Adamia S, Kost-Alimova M, et al. Lenalidomide targets clonogenic side population in multiple myeloma: pathophysiologic and clinical implications. *Blood*. 2011;117(17):4409-4419.
- [2] Xu Y, Sun J, Sheard MA, et al. Lenalidomide overcomes suppression of human natural killer cell anti-tumor functions by neuroblastoma microenvironment-associated IL-6 and TGFβ1. *Cancer Immunol Immunother*. 2013;62(10):1637-1648.

Background

Lenalidomide (CC-5013) is a 4-amino-glutamyl analog of thalidomide, with greater potency and without the sedative and neuropathic side effects associated with thalidomide. Lenalidomide is an immunomodulator, affecting both the cellular and humoral arms of the immune system, and has demonstrated activity in clinical trials for cancer, including anti-angiogenic, anti-proliferative, and pro-erythropoietic activities. Lenalidomide acts as a molecular glue that binds to the CRBN-CRL4 E3 ubiquitin ligase complex, promoting ubiquitination of Ikaros family zinc finger 1 (IKZF1) and IKZF3 and thereby inhibiting proliferation of multiple myeloma cells. Lenalidomide is approved in the United States for a subset of Myelodysplastic Syndromes (MDS) patients and for treatment of patients with multiple myeloma when used in combination with dexamethasone^{[1][2]}.

In vitro, Lenalidomide (0.1-10μM; 72h) dose-dependently inhibited proliferation of CFSE-labeled OPM1 cells, regardless of co-culture with HS-5 BMSCs, significantly reduced the percentage of side

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population (SP) cells, and increased the proportions of CD138⁻/low⁺ and CFSE⁺/7-AAD⁺ cells^[3]. Lenalidomide (10μM; 6h) inhibited the suppression of IL-2-induced NK cell cytotoxicity and IFN-γ secretion mediated by IL-6 and TGF-β1 in neuroblastoma/monocyte-conditioned media^[4].

In vivo, in female NOD/SCID mice injected with CHLA-255-Fluc neuroblastoma cells and PBMCs, treatment with Lenalidomide (50mg/kg/d; 9+5d; i.p.) in combination with ch14.18 improved survival^[4]. Lenalidomide (50mg/kg/d; 21d; i.p.) inhibited tumor growth and spread in xenograft mouse models of Mantle cell lymphoma (MCL)^[5].

References:

- [1] Krönke J, Hurst SN, Ebert BL. Lenalidomide induces degradation of IKZF1 and IKZF3. *Oncoimmunology*. 2014;3(7):e941742.
- [2] Kotla V, Goel S, Nischal S, et al. Mechanism of action of lenalidomide in hematological malignancies. *J Hematol Oncol*. 2009;2:36.
- [3] Jakubikova J, Adamia S, Kost-Alimova M, et al. Lenalidomide targets clonogenic side population in multiple myeloma: pathophysiologic and clinical implications. *Blood*. 2011;117(17):4409-4419.
- [4] Xu Y, Sun J, Sheard MA, et al. Lenalidomide overcomes suppression of human natural killer cell anti-tumor functions by neuroblastoma microenvironment-associated IL-6 and TGFβ1. *Cancer Immunol Immunother*. 2013;62(10):1637-1648.
- [5] Agliano, Alice et al. "Therapeutic effect of lenalidomide in a novel xenograft mouse model of human blastic NK cell lymphoma/blastic plasmacytoid dendritic cell neoplasm." *Clinical cancer research : an official journal of the American Association for Cancer Research* vol. 17,19 (2011): 6163-73.

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