Birabresib

Cat. No.: HY-15743

CAS No.: 202590-98-5

Molecular Formula: $C_{25}H_{22}ClN_5O_2S$

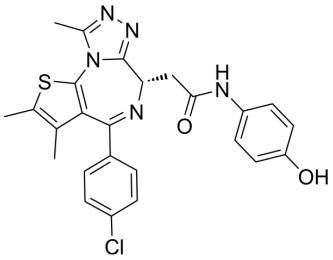
Molecular Weight: 491.99

Target: Epigenetic Reader Domain

Pathway: Epigenetics

Storage:

Powder	-20°C	3 years
	4°C	2 years
In solvent	-80°C	2 years
	-20°C	1 year



SOLVENT & SOLUBILITY

In Vitro

DMSO : ≥ 49 mg/mL (99.60 mM)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	2.0326 mL	10.1628 mL	20.3256 mL
5 mM	0.4065 mL	2.0326 mL	4.0651 mL
10 mM	0.2033 mL	1.0163 mL	2.0326 mL

Please refer to the solubility information to select the appropriate solvent.

In Vivo

1. Add each solvent one by one: 50% PEG300 >> 50% saline
   Solubility: 10 mg/mL (20.33 mM); Clear solution; Need ultrasonic and warming and heat to 60°C
2. Add each solvent one by one: 5% DMSO >> 40% PEG300 >> 5% Tween-80 >> 50% saline
   Solubility: ≥ 3 mg/mL (6.10 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: ≥ 2.5 mg/mL (5.08 mM); Clear solution
4. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: 2.5 mg/mL (5.08 mM); Suspended solution; Need ultrasonic
5. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (5.08 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

Birabresib (OTX-015) is a potent bromodomain (BRD2/3/4) inhibitor with IC_{50}s ranging from 92 to 112 nM.

IC_{50} & Target	IC50: 92-112 nM (BRD2, BRD3, BRD4)[1]
In Vitro	Birabresib (OTX-015) (500 nM) exposure induces a strong decrease of BRD2, BRD4 and c-MYC and increase of HEXIM1 proteins, while BRD3 expression is unchanged. c-MYC, BRD2, BRD3, BRD4?and?HEXIM1?mRNA levels do correlate however with viability following exposure to Birabresib (OTX-015)[2].?Birabresib (OTX-015) (0.1, 1, 5 μM) treatment induces HIV-1 full-length transcripts and viral outgrowth in resting $CD4^+$ T cells from infected individuals receiving suppressive antiretroviral therapy (ART), while exerting minimal toxicity and effects on T cell activation. Birabresib-mediated activation of HIV-1 involves an increase in CDK9 occupancy and RNAP II C-terminal domain (CTD) phosphorylation[3]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	In MDA-MB-231 murine xenografts, tumor mass is significantly (p?< 0.05) reduced by Birabresib (OTX-015) (50 mg/kg) with respect to vehicle-treated animals. Birabresib (OTX-015) in combination with 2 mg/kg RAD001 shows more effective activity than Birabresib alone[4]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Cell Assay [2]	For the MTT assay, cells are seeded in 24-well plates at 1×10^6 per well and treated with Birabresib (OTX-015) (0.01 nM-10 μM) for 72 h. Cells are transferred to 96-well plates and incubated with 0.5 mg/mL 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide (MTT) in the dark at 37°C for 4 h. Cells are then lysed with 25% sodium dodecyl sulfate (SDS) lysis buffer and absorbance is read at 570 nm using a Microplate Reader. Three independent experiments are run for each cell line and untreated cells are used as negative controls. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Animal Administration [4]	Mice are subcutaneously injected in the right flank with 10×10^6 MDA-MB-231 cells. When average tumor weight is appr 130 mg, mice are randomized (nine animals/group) to one of the following experimental groups: vehicle (for Birabresib (OTX-015), water, twice daily, oral; for RAD001 vehicle, 5% Tween-80/5% polyethylene glycol 400, thrice weekly, intraperitoneal); 50 mg/kg Birabresib (OTX-015), twice daily, oral; 2 mg/kg RAD001, thrice weekly, intraperitoneal; 50 mg/kg Birabresib (OTX-015) + 2 mg/kg RAD001, according to the single agent dosing schedules. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- Cell. 2018 Sep 20;175(1):186-199.e19.
- J Exp Med. 2021 Aug 2;218(8):e20202512.
- Hepatology. 2019 Jun;69(6):2502-2517.
- J Exp Clin Cancer Res. 2024 Mar 5;43(1):69.
- J Exp Clin Cancer Res. 2022 Nov 11;41(1):321.

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REFERENCES

[1]. J. Kay Noel, et al. Abstract C244: Development of the BET bromodomain inhibitor OTX015. Mol Cancer Ther November 2013 12; C244.

[2]. Marie-Magdelaine Coudé, et al. BET inhibitor OTX015 targets BRD2 and BRD4 and decreases c-MYC in acute leukemia cells. Oncotarget. 2015 Jul 10; 6(19): 17698–17712.

[3]. Lu P, et al. The BET inhibitor OTX015 reactivates latent HIV-1 through P-TEFb. Sci Rep. 2016 Apr 12;6:24100

[4]. Vázquez R, et al. The bromodomain inhibitor OTX015 (MK-8628) exerts anti-tumor activity in triple-negative breast cancer models as single agent and in combination with RAD001. Oncotarget. 2017 Jan 31;8(5):7598-7613.

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