Darolutamide

Cat. No.: HY-16985

CAS No.: 1297538-32-9

Molecular Formula: $C_{19}H_{19}ClN_6O_2$

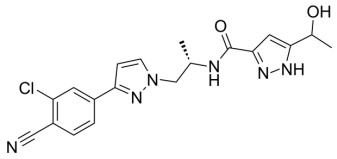
Molecular Weight: 398.85

Target: Androgen Receptor

Pathway: Vitamin D Related/Nuclear Receptor

Storage:

Powder	-20°C	3 years
	4°C	2 years
In solvent	-80°C	1 year
	-20°C	6 months



SOLVENT & SOLUBILITY

In Vitro

DMSO : 100 mg/mL (250.72 mM; Need ultrasonic)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	2.5072 mL	12.5360 mL	25.0721 mL
	5 mM	0.5014 mL	2.5072 mL	5.0144 mL
	10 mM	0.2507 mL	1.2536 mL	2.5072 mL

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

In Vivo

1. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: ≥ 2.08 mg/mL (5.21 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.08 mg/mL (5.21 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.08 mg/mL (5.21 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

Darolutamide (ODM-201;BAY-1841788) is a potent androgen receptor (AR) antagonist with an IC_{50} of 26 nM in in vitro assay.

IC_{50} & Target

IC50: 26 nM (AR-HEK293 cells, AR)[1]

In Vitro

In competitive AR binding assays, the inhibition constant (Ki) values of Darolutamide (ODM-201) are 11 nM. ODM-201and ORM-15341 suppresse androgen-induced cell proliferation more efficaciously than ARN-509, IC50 values being 230 and 170 nM for Darolutamide and ORM-15341 vs. 420 nM for ARN-509. Darolutamide has no effect on the viability of AR-negative cell

	lines tested, DU-145 prostate cancer cells and H1581 lung cancer cells confirming that the antiproliferative properties of Darolutamide and ORM-15341 are specific to AR-dependent PC cells[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	Darolutamide (ODM-201) showes a significant antitumor activity with both doses, 50 mg/kg twice daily being more efficacious compared to castrated, untreated mice ($p<0.001$), which also showes inhibition of tumor growth ($p<0.05$) vs. castrated, untreated mice. Further, there is no sign of treatment-related toxicities; the body weights of mice treated with Darolutamide twice daily do not decrease significantly during the treatment[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Cell Assay [1]	To study the antiproliferative properties of Darolutamide and ORM-15341, the VCaP cell line originally derived from a bone metastasis of a CRPC patient is used. The VCaP cell line is characterized with endogenous AR gene amplification and AR overexpression30, typical for CRPC. VCaP cells are cultured in RPMI-1640 medium and supplemented with 10% fetal bovine serum (FBS), 100 UI/mL penicillin, 100 μ g/mL streptomycin, and 4 mM VCaP[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Animal Administration [1]	To elucidate the in vivo efficacy of Darolutamide in a CRPC mouse model, castrated male nude mice with subcutaneously injected VCaP cells are treated orally with ODM-201 (50 mg/kg) once (qd) or twice daily (bid), or with enzalutamide (20 mg/kg, qd) for 37 days. The dose for enzalutamide is selected based on previously published studies9 and our pharmacokinetic (PK) analyses which reveales that in mice the systemic exposure (AUC0–24) for this dose of enzalutamide is 2.5 times higher than that for Darolutamide (50 mg/kg, bid). Moreover, enzalutamide exhibited a long plasma half-life (18.3 hours) while the half-life of Darolutamide in mice is not optimal (1.6 hours) supporting once daily dosing for enzalutamide and higher dose and more frequent dosing for ODM-201[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- Br J Cancer. 2022 May 26.
- J Dermatol Sci. 2023 Aug 29.
- Sci Rep. 2019 Sep 24;9(1):13786.

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REFERENCES

[1]. Moilanen AM, et al. Discovery of ODM-201, a new-generation androgen receptor inhibitor targeting resistance mechanisms toandrogen signaling-directed prostate cancer therapies. Sci Rep. 2015 Jul 3;5:12007. doi: 10.1038/srep12007.

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