Darolutamide

Cat. No.: HY-16985
CAS No.: 1297538-32-9
Molecular Formula: C₁₉H₁₉ClN₆O₂
Molecular Weight: 398.85
Target: Androgen Receptor
Pathway: Others
Storage: Powder -20°C 3 years
         4°C 2 years
         In solvent -80°C 6 months
         -20°C 1 month

Solvent & Solubility

In Vitro DMSO : ≥ 44 mg/mL (110.32 mM)
* "≥" means soluble, but saturation unknown.

<table>
<thead>
<tr>
<th>Preparing Stock Solutions</th>
<th>Concentration</th>
<th>1 mg</th>
<th>5 mg</th>
<th>10 mg</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>1 mM</td>
<td>2.5072 mL</td>
<td>12.5360 mL</td>
<td>25.0721 mL</td>
</tr>
<tr>
<td></td>
<td>5 mM</td>
<td>0.5014 mL</td>
<td>2.5072 mL</td>
<td>5.0144 mL</td>
</tr>
<tr>
<td></td>
<td>10 mM</td>
<td>0.2507 mL</td>
<td>1.2536 mL</td>
<td>2.5072 mL</td>
</tr>
</tbody>
</table>

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

BIOLOGICAL ACTIVITY

Description
Darolutamide (ODM-201; BAY-1841788) is a potent androgen receptor (AR) antagonist with an IC₅₀ of 26 nM in vitro assay.

IC₅₀ & 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-201 and ORM-15341 suppress androgen-induced cell proliferation more efficaciously than enzalutamide or ARN-509, IC₅₀ values being 230 and 170 nM for Darolutamide and ORM-15341 vs. 410 and 420 nM for enzalutamide and 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\(^1\).

In Vivo
Darolutamide (ODM-201) shows a significant antitumor activity with both doses, 50 mg/kg twice daily being more...
efficacious compared to castrated, untreated mice (p<0.001) or Enzalutamide (p=0.0245), which also shows 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].

### 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 overexpression, typical for CRPC. VCaP cells are cultured in RPMI-1640 medium and supplemented with 10% fetal bovine serum (FBS), 100 UI/mL penicillin, 100 μg/mL streptomycin, and 4 mM VCaP.

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 studies and our pharmacokinetic (PK) analyses which reveals 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.

### REFERENCES