Abiraterone

Cat. No.: HY-70013

CAS No.: 154229-19-3

Molecular Formula: $C_{24}H_{31}NO$

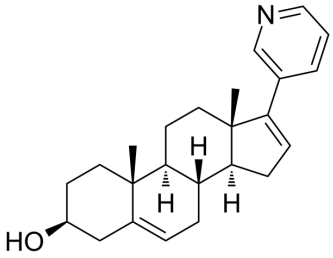
Molecular Weight: 349.51

Target: Cytochrome P450

Pathway: Metabolic Enzyme/Protease

Storage:

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



SOLVENT & SOLUBILITY

In Vitro

DMF : 8.75 mg/mL (25.04 mM; Need ultrasonic and warming)
Ethanol : 5.4 mg/mL (15.45 mM; Need ultrasonic)
DMSO : 2.5 mg/mL (7.15 mM; ultrasonic and warming and heat to 60°C)

Preparing Stock Solutions

Concentration \ Solvent \ Mass	1 mg	5 mg	10 mg
1 mM	2.8611 mL	14.3057 mL	28.6115 mL
5 mM	0.5722 mL	2.8611 mL	5.7223 mL
10 mM	0.2861 mL	1.4306 mL	2.8611 mL

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

BIOLOGICAL ACTIVITY

Description

Abiraterone is a potent and irreversible CYP17A1 inhibitor with antiandrogen activity, which inhibits both the 17α-hydroxylase and 17,20-lyase activity of the cytochrome p450 enzyme CYP17 with IC_{50}s of 2.5 nM and 15 nM, respectively.

IC_{50} & Target

IC50:17α-hydroxylase (2.5 nM), 17,20-lyase (15 nM)[6]

In Vitro

Significant inhibition of proliferation of the AR-positive prostate cancer cell lines LNCaP and VCaP with doses of Abiraterone ≥5 μM is confirmed[2]. Abiraterone shows IC_{50} values of 15 nM and 2.5 nM for the 17,20-lyase and 17α-hydroxylase (CYP17 is a bifunctional enzyme with both 17α-hydroxylase and 17,20-lyase activity). Abiraterone inhibits human 17,20-lyase and 17α-hydroxylase with IC_{50} of 27 and 30 nM respectively[3]. Abiraterone inhibits recombinant human 3βHSD1 and 3βHSD2 activity with competitive K_i values of 2.1 and 8.8 μM. 10 μM Abiraterone is sufficient to completely block synthesis of 5α-dione and DHT in both cell lines.Treatment with abi significantly inhibited CRPC progression in the robustly growing subset, effectively putting a ceiling on tumor growth over 4 weeks of treatment (P<0.00001). [^{3}H]-dehydroepiandrosterone (DHEA) depletion and Δ^4-androstenedione (AD) accumulation are inhibited by Abiraterone in LNCaP, with an IC_{50}<1 μM[4].

	MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	The 0.5 mmol/kg/d Abiraterone treatment dose is previously shown to yield serum concentrations of about 0.5 to 1 μM. Xenograft tumor growth in the control group is widely variable, with some tumors growing slowly and only a subset of tumors exhibiting robust growth[4]. Following i.v. administration (5 mg/kg) the clearance (Cl) and volume of distribution (V_d) are found to be 31.2 mL/min/kg and 1.97 L/kg, respectively. The $AUC_{0-\infty}$ (area under the plasma concentration-time curve from time zero to infinity time point) is found to be 2675 ng*h/mL. The terminal half-life ($t_{1/2}$) is 0.73 h. Because of high clearance, Abiraterone (ART) is quantifiable only until 2 h following i.v. administration[5]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Cell Assay [2]	LNCaP and VCaP cells are seeded in 96-well plates and grown in CSS-supplemented phenol red-free or FBS-supplemented media for 7 days. Cells are treated with Abiraterone (5 μM and 10 μM) at 24 and 96 hours after plating and cell viability is determined on day 7 by adding CellTiter Glo and measuring luminescence[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Animal Administration [4][5]	Mice[4] Male NOD/SCID mice 6 to 8 weeks of age are surgically orchiectomized and implanted with a 5 mg 90-day sustained release DHEA pellet to mimic CRPC with human adrenal physiology. Two days later, 7×10^6 LAPC4 cells are injected subcutaneously with Matrigel. Tumor dimensions are measured 2 to 3 times per week, and volume is calculated as length×width×height×0.52. Once tumors reach 300 mm^3, mice are randomly assigned to vehicle or Abiraterone treatment groups. Mice in the Abiraterone group are treated with 5 mL/kg intraperitoneal injections of 0.5 mmol/kg/d (0.1 mL 5% benzyl alcohol and 95% safflower oil solution) and control mice with vehicle only, once daily for 5 days per week over a duration of 4 weeks (n=8 mice per treatment). Statistical significance between Abiraterone and vehicle treatment groups is assessed by ANOVA based on a mixed-effect model. Rats[5] Male Sprague-Dawley rats (n=8, 240-260 g) are used. Blood samples (450 μL) are obtained following an i.v. 5 mg/kg dose of ART into polypropylene tubes containing Na_2-EDTA solution as an anticoagulant and at pre-dose, 0.12, 0.25, 0.5, 1, 2, 4, 6, 8 and 24 h (a sparse sampling protocol is adopted during blood collection and at each time point blood is collected from four animals). Plasma is harvested by centrifuging the blood using a Biofuge at 1760g for 5 min and stored frozen at -80±10°C until analysis. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- Nature. 2012 Jan 22;482(7383):116-9.
- Cell Res. 2020 Oct;30(10):833-853.
- Eur Urol. 2015 Aug;68(2):228-35.
- Cell Death Dis. 2022 Dec 12;13(12):1034.
- Acta Pharmacol Sin. 2021 Jan;42(1):108-114.

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REFERENCES

[1]. Attard G, et al. Phase I clinical trial of a selective inhibitor of CYP17, abiraterone acetate, confirms that castration-resistant prostate cancer commonly remains hormone

driven. J Clin Oncol. 2008 Oct 1;26(28):4563-71.

[2]. Richards J, et al. Interactions of abiraterone, eplerenone, and prednisolone with wild-type and mutant androgen receptor: a rationale for increasing abiraterone exposure or combining with MDV3100. Cancer Res. 2012 May 1;72(9):2176-82.

[3]. Stein MN, et al. Androgen synthesis inhibitors in the treatment of castration-resistant prostate cancer. Asian J Androl. 2014 May-Jun;16(3):387-400.

[4]. Li R, et al. Abiraterone inhibits 3β-hydroxysteroid dehydrogenase: a rationale for increasing drug exposure in castration-resistant prostate cancer. Clin Cancer Res. 2012 Jul 1;18(13):3571-9.

[5]. Kumar SV, et al. Validated RP-HPLC/UV method for the quantitation of abiraterone in rat plasma and its application to a pharmacokinetic study in rats. Biomed Chromatogr. 2013 Feb;27(2):203-7.

[6]. Stein MN, et al. Androgen synthesis inhibitors in the treatment of castration-resistant prostate cancer. Asian J Androl. 2014 May-Jun;16(3):387-400.

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