

Product Data Sheet

Product Name: PRIMA-1MET

Cat. No.: GC11247

Chemical Properties

Cas. No. 5291-32-7

Chemical Name 2-(hydroxymethyl)-2-(methoxymethyl)-1-azabicyclo[2.2.2]octan-3-one

SMILES COCC1(C(=O)C2CCN1CC2)CO

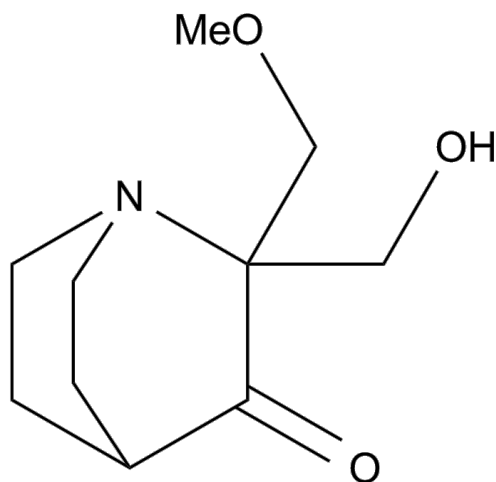
Formula $C_{10}H_{17}NO_3$ M.Wt 199.25

Solubility $\geq 19.9\text{mg/mL}$ in DMSO, $\geq 102\text{mg/mL}$ in EtOH with ultrasonic, $\geq 104.2\text{mg/mL}$ in Water
Storage Store at 4°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 KKU-100 cell

KKU-100 cells were cultured in the modified Eagle medium (DMEM) supplemented with 10% heat-inactivated fetal bovine serum (FBS), 2mg/ml sodium bicarbonate and 1% antibiotic solution. All cells were cultured in a humidified incubator at 37°C with a concentration of 5% CO₂. KKU-100 cells

Preparation Method (2×10³) suspended in 100μl of medium were inoculated into 96-well plates in triplicate. Cells were treated with PRIMA-1MET at different concentrations (0, 20, 40, 60, 80, and 100μM) for 48 hours. Cell viability was determined using sulfonylrhodamine B (SRB). The absorbance was measured at 540nm using a microplate reader.

Reaction
Conditions 0, 20, 40, 60, 80, and 100μM; 48h

Applications PRIMA-1MET significantly inhibited the viability of KKU-100 cells in a dose-dependent manner.

Animal experiment [2]:

Animal models Balb/c mice

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Five Balb/ c mice in three groups were subcutaneously inoculated with 5×10^5 MCO4 cells. On the 7th day after inoculation, PBS or PRIMA-1MET at a dose of 100mg/kg was intravenously injected into the tail vein of mice once a day for 10 consecutive days. During the observation period, body weight and tumor size were monitored starting from vaccination. The tumor was immediately fixed in 4% formaldehyde for 12 hours after resection, stored in 70% ethanol at 4°C, and then embedded in paraffin. Hematoxylin and eosin staining were carried out according to the standard protocol. According to the manufacturer's instructions, apoptotic cells were detected in situ using TUNEL.

Dosage form 100mg/kg for 10 days; i.v.

Applications PRIMA-1MET treatment significantly suppressed tumor growth, and increased the survival rate of mice without obvious toxicity.

References:

- [1] Piyawajanusorn C, Kittirat Y, Sa-Ngiamwibool P, et al. PRIMA-1MET induces cellular senescence and apoptotic cell death in cholangiocarcinoma cells[J]. Cancer Genomics & Proteomics, 2019, 16(6): 543-552.
- [2] Zache N, Lambert J M R, Wiman K G, et al. PRIMA-1MET inhibits growth of mouse tumors carrying mutant p53[J]. Analytical Cellular Pathology, 2008, 30(5): 411-418.

Background

PRIMA-1MET is a small molecule organic compound that can restore tumor suppression function, mainly targeting mutant p53 and inducing cell death in various types of cancer cells^[1]. PRIMA-1MET is hydrolyzed into the active form of methylquinine cycloketone within cells and covalently binds to the thiol group of the core domain of the mutant p53 protein, thereby causing structural changes and restoring the active conformation of p53 protein^[2]. PRIMA-1MET has been widely used in anti-cancer research^[3].

In vitro, PRIMA-1MET inhibits the cell viability of BWM-1 cells (IC₅₀ value=30μM) and MWCL-1 cells

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(IC₅₀ value= 28μM) after treatment of 48 hours^[4]. PRIMA-1MET treatment (60μM) for 24 hours significant induced autophagy and enhanced the mTOR/AMPK-ULK1-Vps34 autophagic signaling cascade in colorectal cancer (CRC) cells^[5]. PRIMA-1 MET (100μM; 72H) effectively inhibited the growth of small cell lung cancer (SCLC) cell lines expressing mutant p53 induced apoptosis, accompanied by an increase in the proportion of DNA fragmented cells, caspase-3 activation, and downregulation of Bcl-2 expression^[6].

In vivo, PRIMA-1MET treatment (100mg/kg/day; i.p.) for 15 consecutive days can inhibit the growth of multiple myeloma tumors containing mutant p53 in multiple myeloma xenograft SCID mouse models^[7]. Intraperitoneal injection of PRIMA-1MET at the dosage of 100mg/kg/day for 5 consecutive days significantly reduced the tumor size and tumor volume in the mouse model of rectal cancer xenograft tumors, decreased ERK1/2 phosphorylation, and inhibited MEK activity^[8].

References:

- [1] Perdrix, A.; Najem, A.; Saussez, S.; Awada, A.; Journe, F.; Ghanem, G.; Krayem, M. PRIMA-1 and PRIMA-1Met (APR-246): From Mutant/Wild Type p53 Reactivation to Unexpected Mechanisms Underlying Their Potent Anti-Tumor Effect in Combinatorial Therapies. *Cancers* 2017, 9, 172.
- [2] Xie X, Fan C, Luo B, et al. APR-246 enhances colorectal cancer sensitivity to radiotherapy[J]. *Molecular cancer therapeutics*, 2023, 22(8): 947-961.
- [3] Menichini P, Monti P, Speciale A, et al. Antitumor effects of PRIMA-1 and PRIMA-1Met (APR246) in hematological malignancies: still a mutant p53-dependent affair?[J]. *Cells*, 2021, 10(1): 98.
- [4] Sobhani M, Kwan K, Saha M N, et al. Small molecule PRIMA-1 met sensitizes Waldenstrom macroglobulinemia cells to apoptosis and displays synergistic cytotoxicity with bortezomib[J]. *Blood*, 2013, 122(21): 5143.
- [5] Li X L, Zhou J, Xia C J, et al. PRIMA-1met induces autophagy in colorectal cancer cells through upregulation of the mTOR/AMPK-ULK1-Vps34 signaling cascade[J]. *Oncology Reports*, 2021, 45(5): 86.
- [6] Zandi R, Selivanova G, Christensen C L, et al. PRIMA-1Met/APR-246 induces apoptosis and tumor growth delay in small cell lung cancer expressing mutant p53[J]. *Clinical Cancer Research*, 2011, 17(9): 2830-2841.
- [7] Saha M N, Jiang H, Yang Y, et al. PRIMA-1Met/APR-246 displays high antitumor activity in multiple myeloma by induction of p73 and Noxa[J]. *Molecular cancer therapeutics*, 2013, 12(11): 2331-2341.

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[8] Lu T, Zou Y, Xu G, et al. PRIMA-1Met suppresses colorectal cancer independent of p53 by targeting MEK[J]. Oncotarget, 2016, 7(50): 83017.

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