Amuvatinib (MP-470) Datasheet

**Technical Data**

<table>
<thead>
<tr>
<th>Property</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Molecular Weight</td>
<td>447.51</td>
</tr>
<tr>
<td>Formula</td>
<td>C_{23}H_{22}N_{2}O_{5}S</td>
</tr>
<tr>
<td>CAS No.</td>
<td>850879-09-3</td>
</tr>
<tr>
<td>Synonyms</td>
<td>N/A</td>
</tr>
<tr>
<td>Solubility (25°C)</td>
<td>DMF 32 mg/mL, Water &lt;1 mg/mL, Ethanol &lt;1 mg/mL</td>
</tr>
<tr>
<td>Storage</td>
<td>2 years -20°C Powder, 2 weeks 4°C in DMSO, 6 months -80°C in DMSO</td>
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</tbody>
</table>

**Biological Activity**

**Description**: MP-470 (Amuvatinib) is a potent and multi-targeted inhibitor of c-Kit, PDGFα, Flt3, with IC50 of 10 nM, 40 nM and 81 nM, respectively.

**Targets**: c-Kit\(^{D816H}\), PDGFα\(^{V561D}\), Flt3\(^{D835Y}\)

**IC50**: 10 nM 40 nM 81 nM\(^{[1]}\)

**In vitro**

The hydrochloride salt of MP-470 also inhibits several mutants of c-Kit, including c-Kit\(^{D816V}\), c-Kit\(^{D816H}\), c-Kit\(^{V650G}\), c-Kit\(^{V654A}\), as well as a Flt3 mutant (Flt3\(^{D835Y}\)) and two PDGFα mutants (PDGFα\(^{V561D}\) and PDGFα\(^{D842V}\)), with IC50 of 10 nM to 8.4 μM. MP-470 hydrochloride potently inhibits the proliferation of OVCAR-3, A549, NCI-H647, DMS-153, and DMS-114 cells, with IC50 of 0.9 μM-7.86 μM.\(^{[1]}\). MP-470 also inhibits c-Kit and PDGFα, with IC50 values of 31 μM and 27 μM, respectively. MP-470 demonstrates potent cytotoxicity against MiaPaCa-2, PANC-1, and GIST882 cells, with IC50 of 1.6 μM to 3.0 μM. MP-470 also binds to and inhibits several c-Kit mutants, including c-Kit\(^{K642E/D816V}\), c-Kit\(^{D816V}\), and c-Kit\(^{K642E/D816V}\).\(^{[2]}\) In MDA-MB-231 cells, MP-470 (1 μM) inhibits tyrosine phosphorylation of AXL.\(^{[3]}\) In LNCaP and PC-3, but not DU145 cells, MP-470 exhibits cytotoxicity with IC50 of 4 μM and 8 μM, respectively, and induces apoptosis at 10 μM. In LNCaP cells, MP-470 (10 μM) elicits G1 arrest and decreases phosphorylation of Akt and ERK1/2.\(^{[4]}\) In SF767 cells, MP-470 (10 μM) inhibits c-Abl phosphorylation and sensitizes cells to radiation. In combination with radiation, MP-470 (10 μM) inhibits glyogen synthase kinase (GSK)\(^3\beta\) activity, induces apoptosis, and disrupts the repair of dsDNA breaks probably through suppression of Rad51.\(^{[5]}\)\(^{[6]}\)

**In vivo**

In mice xenograft models of HT-29, A549, and SB-CL2 cells, MP-470 (10 mg/kg-75 mg/kg via i.p. or 50 mg/kg-200 mg/kg via p.o.) inhibits tumor growth.\(^{[4]}\) In mice bearing LNCaP xenograft, MP-470 (20 mg/kg) combined with Erlotinib significantly induces tumor growth inhibition (TGI).\(^{[4]}\)

**Clinical Trials**

MP-470 is currently under investigation in a Phase II clinical trial for small cell lung carcinoma.

**Features**

**Protocol** (Only for Reference)

**Kinase Assay**\(^{[8]}\)

**Kinase inhibition assay of c-Kit and PDGFα**: For the testing of inhibitory activity against c-Kit and PDGFα, enzymes are incubated with varying concentrations of MP-470 and radiolabeled γ\(^{32}\)P-ATP. After 30 min, the reaction mixtures are electrophoresed on an acrylamide gel and autophosphorylation, quantitated by the amount of radioactivity incorporated into the enzyme, is assayed.

**Cell Assay**:\(^{[2]}\)

**Cell Lines**: MiaPaCa-2, Panc-1, and GIST882 cells

**Concentrations**: 0–30 μM dissolved in DMSO

**Incubation Time**: 96 hours

**Methods**

Cells are plated at a density of 2 × 10\(^3\) to 1 × 10\(^4\) cells per well in 100 μL medium on day 0 in 96-well Falcon microtiter plates. On day 1, ten μL of serial dilutions of MP-470 are added to the plates in quadruplicates. After incubation for 4 days, the cells are fixed with 10% Trichloroacetic acid solution. Subsequently, they are labeled with 0.04% Sulforhodamine B (SRB) in 1% acetic acid. After multiple washes to remove the excess dye, 100 μL of 50 mM Tris solution is added to each well in order to dissolve the dye. The absorbance of each well is read on a plate reader at 570 nm. Date are expressed as the percentage of survival of control calculated from the absorbance corrected for background absorbance. The surviving percent of cells is determined by dividing the mean absorbance values of the monoclonal antibody by mean absorbance values of the control and multiplying by 100.

**Animal Study**\(^{[8]}\)

**Animal Models**: Mice (athymic nude) xenograft models of HT-29, A549, and SB-CL2 cells

**Formulation**: Dissolved in corn oil for p.o.; Dissolved in TV-10 (60% propylene glycol, 30% PEG300, 10% water, and 150 mg/mL 2-hydroxypropyl-β-cyclodextrin) or TV-10 (5% ethanol, 40% glycerol, 55% water, and 300 mg/mL cyclodextrin) for i.p.

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Toll Free: (877) 796-6397  -- USA and Canada only --
Fax: +1-713-796-9816
Orders: +1-832-582-8158
sales@selleckchem.com
Tech Support: tech@selleckchem.com
Website: www.selleckchem.com
Data independently produced by Dr. Yong-Weon Yi from Georgetown University Medical Center. MP-470 purchased from Selleck.

**Amuvatinib (MP-470) purchased from Selleck**

For MTT assays, cells (2,000 – 5,000 cells/well) were subcultured into 96-well plates according to their growth properties. Cell proliferation was assayed at 72 hr after treatment of MP-470 by adding 20 μl of 5 mg/ml 3-(4,5-Dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide (MTT) solution per 100 μl of growth medium. After incubating for 3-4 h at 37°C, the media were removed and 150 µl/well of MTT solvent (either absolute DMSO or isopropanol containing 4 mM HCl and 0.1% Nonidet-40) was added to dissolve the formazan.