NVP-TAE 226

Cat. No.: HY-13203
CAS No.: 761437-28-9
Molecular Formula: C₂₃H₂₅ClN₆O₃
Molecular Weight: 468.94
Target: FAK; Pyk2; IGF-1R; Insulin Receptor; Apoptosis
Pathway: Protein Tyrosine Kinase/RTK; Apoptosis
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: 50 mg/mL (106.62 mM; Need ultrasonic)

<table>
<thead>
<tr>
<th>Preparing Stock Solutions</th>
<th>Solvent Concentration</th>
<th>Mass</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>1 mg</td>
<td>5 mg</td>
</tr>
<tr>
<td>1 mM</td>
<td>2.1325 mL</td>
<td>10.6623 mL</td>
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<tr>
<td>5 mM</td>
<td>0.4265 mL</td>
<td>2.1325 mL</td>
</tr>
<tr>
<td>10 mM</td>
<td>0.2132 mL</td>
<td>1.0662 mL</td>
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</tbody>
</table>

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: ≥ 2.5 mg/mL (5.33 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (5.33 mM); Clear solution

BIOLOGICAL ACTIVITY

Description
NVP-TAE 226 (TAE226) is a potent and ATP-competitive dual FAK and IGF-1R inhibitor with IC₅₀ values of 5.5 nM and 140 nM, respectively. NVP-TAE 226 (TAE226) also effectively inhibits Pyk2 and insulin receptor (InsR) with IC₅₀ values of 3.5 nM and 44 nM, respectively[1][2].

IC₅₀ & Target
IC₅₀: 5.5 nM (FAK), 3.5 nM (Pyk2), 140 nM (IGF-1R), 40 nM (InsR), 0.16 μM (c-Met), 0.36 μM (KDR), 0.48 μM (Flt3)[1]

In Vitro
NVP-TAE 226 (TAE226), a potent ATP-competitive inhibitor of several tyrosine protein kinases, in particular FAK and IGF-1R kinases. In a cell-based kinase assay, FAK, IGF-1R kinase, and IR kinase are inhibited with an IC₅₀ range of 100 to 300 nM compared with the other kinases tested, which are >10-fold less sensitive. In culture, NVP-TAE 226 inhibits extracellular matrix-induced autophosphorylation of FAK (Tyr³⁹⁵). NVP-TAE 226 also inhibits IGF-I-induced phosphorylation of IGF-1R and...
activity of its downstream target genes such as MAPK and Akt. NVP-TAE 226 retards tumor cell growth as assessed by a cell viability assay and attenuates G2-M cell cycle progression associated with a decrease in cyclin B1 and phosphorylated cdc2 (Tyr15) protein expression. NVP-TAE 226 treatment inhibits tumor cell invasion by at least 50% compared with the control in an in vitro Matrigel invasion assay. Interestingly, TAE226 treatment of tumor cells containing wild-type p53 mainly exhibits G2-M arrest, whereas tumor cells bearing mutant p53 underwent apoptosis[1].

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

<table>
<thead>
<tr>
<th>In Vivo</th>
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<tr>
<td>Treatment with NVP-TAE 226 (TAE226) at 50 or 75 mg/kg extends the median survival of U87 xenograft animals by 6 and 7 days, respectively (P=0.084 and P=0.042, respectively, compared with vehicle-treated animals). However, NVP-TAE 226 treatment of LN229-engrafted animals significantly prolongs their median survival by 19 days (P&lt;0.004 for both dosages, compared with vehicle-treated animals)[1].</td>
</tr>
<tr>
<td>MCE has not independently confirmed the accuracy of these methods. They are for reference only.</td>
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</tbody>
</table>

**PROTOCOL**

**Cell Assay**[1]

Glioma cell cultures are harvested with 0.05% trypsin and seeded in triplicate at 2×10^4 in 24-well culture plates for 24 h before drug treatment. Culture medium is used for mock treatment. Cells are harvested at the indicated day after treatment, and viable cells are counted using the Vi-cell viability analyzer. The antiproliferative activity of NVP-TAE 226 (ranging from 0.25 to 1 μM) on cells growing in culture is determined using a tetrazolium-based colorimetric MTT assay[1].

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**Animal Administration**[1]

Mice[1]

Male nude mice used for this study are 6 to 8 weeks old. In DMEM/F12 serum-free media (5 μL), 5×10^5 of U87 cells and 1×10^6 of LN229 cells per mouse are implanted intracranially through a guide-screw system. Four days after injection of the tumor cells, mice are randomized into three groups for each cell line (n=6). Mice in group 1 are treated with 50 mg/kg NVP-TAE 226 in 200 μL of 0.5% methylcellulose, via an oral gavage. The mice in group 2 receive 75 mg/kg NVP-TAE 226 in 200 μL of 0.5% methylcellulose. The mice in group 3 the same vehicle used for administration of NVP-TAE 226 (control). Treatment frequency is once a day for 5 days and off for 2 days, for a duration of 4 weeks. Mice are monitored daily. Mice are euthanized when they are moribund, and the whole brain is extracted for rapid freezing in liquid nitrogen and storage at -70°C.

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**REFERENCES**
