Tucatinib

Cat. No.: HY-16069
CAS No.: 937263-43-9
Molecular Formula: C₂₆H₂₄N₈O₂
Molecular Weight: 480.52
Target: EGFR
Pathway: JAK/STAT Signaling; Protein Tyrosine Kinase/RTK
Storage: Powder
-20°C 3 years
4°C 2 years
In solvent
-80°C 6 months
-20°C 1 month

SOLVENT & SOLUBILITY

In Vitro

<table>
<thead>
<tr>
<th>Solvent</th>
<th>Mass</th>
<th>1 mg</th>
<th>5 mg</th>
<th>10 mg</th>
</tr>
</thead>
<tbody>
<tr>
<td>Preparing Stock Solutions</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1 mM</td>
<td>2.0811 mL</td>
<td>10.4054 mL</td>
<td>20.8108 mL</td>
<td></td>
</tr>
<tr>
<td>5 mM</td>
<td>0.4162 mL</td>
<td>2.0811 mL</td>
<td>4.1622 mL</td>
<td></td>
</tr>
<tr>
<td>10 mM</td>
<td>0.2081 mL</td>
<td>1.0405 mL</td>
<td>2.0811 mL</td>
<td></td>
</tr>
</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 (5.20 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.5 mg/mL (5.20 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (5.20 mM); Clear solution

BIOLOGICAL ACTIVITY

Description
Tucatinib (Irbinitinib; ARRY-380; ONT-380) is a potent and selective HER2 inhibitor with an IC₅₀ of 8 nM.

IC₅₀ & Target
HER2

In Vitro
Tucatinib (ONT-380) is a potent, selective, ATP-competitive, orally administered small-molecule inhibitor of HER2. Tucatinib has nanomolar activity against purified HER2 enzyme and is approximately 500-fold selective for HER2.
versus EGFR in cell-based assays. Tucatinib selectively inhibits the receptor tyrosine kinase HER2 relative to EGFR. In HER2 overexpressing cell lines, Tucatinib blocks proliferation and the phosphorylation of HER2 and its downstream effector, Akt. By contrast, in the EGFR overexpressing cell lines, it weakly inhibits phosphorylation and proliferation, demonstrating that Tucatinib may have potential to block HER2 signaling without causing the toxicities of EGFR inhibition\[^{1}\].

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

### In Vivo

In preclinical studies with intracranial tumor models, treatment of mice with Tucatinib (ONT-380) compared with GW572016 or neratinib shows a survival benefit when each drug is dosed at the maximum-tolerated dose\[^{1}\]. In the Tucatinib (ARRY-380)-treated-group, 75% of the animals are alive on Day 43. Tucatinib and its active metabolite causes a significant reduction in brain pErbB2 (80%)\[^{2}\]. Tucatinib (ARRY-380) demonstrates significant dose-related tumor growth inhibition (TGI; 50% at 50 mg/kg/d and 96% at 100 mg/kg/d) with numerous partial regressions (>50% reduction from baseline size) at the higher dose level in 9/12 animals. Tucatinib (50 mg/kg/d) in combination with trastuzumab shows a 98% TGI with complete regressions in 9/12 animals and two partial regressions. At dose of 100 mg/kg/d of Tucatinib in combination with trastuzumab, there is 100% TGI and all animals have complete responses\[^{3}\].

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### PROTOCOL

**Animal Administration**\[^{3}\]

Mice: For the SKOV-3 tumor studies, female nude mice are inoculated with cells subcutaneously in the flank. Animals received: doses of Tucatinib ranging up to 200 mg/kg/d, PO; and/or Trastuzumab at 20 mg/kg, IP, Q3D or QW; and/or RP-56976 at 10 mg/kg, IV, Q3D; and/or Bevacizumab at 10 mg/kg, IP, Q4D x 3. Tumor size is measured at regular intervals and subsets of animals are monitored for up to 90 days to determine tumor-free survival\[^{3}\].

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### REFERENCES


