Product Data Sheet

Chemical Properties

Product Name: GDC-0941 dimethanesulfonate

Cas No.: 957054-33-0

M.Wt: 705.85

Formula: C25H35N7O9S4

Synonyms: GDC-0941 (2 MeSO3H salt); GDC0941 dimethanesulfonate; GDC-0941; GDC0941; GDC 0941

Chemical Name: 4-[2-(1H-indazol-4-yl)-6-[(4-methylsulfonylpiperazin-1-yl)methyl]thieno[3,2-d]pyrimidin-4-yl]morpholine; methanesulfonic acid

Canonical SMILES: CS(=O)(=O)N1CCN(CC1)CC2=CC3=C(S2)C(=NC(N3)=C=C5C=NCC5=C=C4)N6CCOC6.CS(=O)(=O).CS(=O)(=O)

Solubility: $\geq 207.6$ mg/mL in DMSO

Storage: Store at -20°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.

Shopping Condition: Evaluation sample solution: ship with blue ice
All other available size: ship with RT, or blue ice upon request

Biological Activity

Targets: PI3K/Akt/mTOR Signaling

Pathways: PI3K

Description:

GDC-0941 is a novel selective class I phosphatidylinositol-3-kinase (PI3K) inhibitor. Activation of PI3K/Akt signaling pathway is frequently associated with tumorigenesis. Deregulation of this
pathway occurs frequently with a variety of cancers and may contribute to the resistance to many anticancer agents. [1] Developing novel small molecules that specifically block the PI3K/Akt pathway may inhibit tumor growth. GDC-0941 is designed to bind the ATP-binding pocket of PI3K and to prevent formation of phosphatidylinositol-3, 4, 5-triphosphate (PIP3), a second messenger that transmits PI3K downstream signals. [2, 3] It binds to PI3K in an ATP-competitive manner. GDC-0941 is a potent small-molecule thieno[3,2-d]pyrimidine inhibitor of the class I PI3K. It is highly selective against isoforms p110α and p110β with IC50 of 3 nM, and moderately selective against isoforms p110δ and p110γ with IC50s of 33 nM and 75 nM, respectively. GDC-0941 inhibits cell proliferation in vitro and in vivo. It causes growth inhibition in a variety of cancer cell lines, including A2780, MDA-MB-361, PC3, and U87MG. [2] It also inhibits the growth of trastuzumab-sensitive and –resistant HER2-amplified cancer cells which harbor p110α mutations or PTEN loss. [4] GDC-0941 also reduces tumor volume in different xenograft models. [4] GDC-0941 can be taken orally.

Reference:

Protocol

Cell experiment:

Cell lines MDA-MB-231 and SKBR3 cells
Preparation method The solubility of this compound in DMSO is >10 mM. General tips for obtaining a higher concentration: Please warm the tube at 37 °C for 10 minutes and/or shake it in the ultrasonic bath for a while. Stock solution can be stored below -20°C for several months.
Reacting conditions 10 μM for MDA-MB-231 cells 1.25 μM for SKBR3 cells 72 hours
Applications The cytotoxicity was determined using MTT assay, after 72 h exposure to GDC-0941, ABT-737 and the combination. 10-times greater concentration of ABT-737 as a single agent resulted in a less than 50% increase in cytotoxicity. Regardless of the sensitivity to single agents, the combination of GDC-0941 and ABT-737 induced a more significant reduction of viable cells, indicating potent
synergistic effect of GDC-0941 and ABT-737.

**Animal experiment [3]:**

<table>
<thead>
<tr>
<th>Animal models</th>
<th>Female severe combined immunodeficient mice injected with breast cancer cells</th>
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<tbody>
<tr>
<td>Dosage form</td>
<td>Oral administration, 100 or 150 mg/kg</td>
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<tr>
<td>Applications</td>
<td>GDC-0941 showed excellent antitumor activity in xenograft models with HER2 amplification, PIK3CA mutations, or concomitant alterations in two pathway components (e.g., PTEN loss and PIK3CA mutation), but little or no effect in xenografts of basal-like KRAS mutant MDA-MB-231 cells. Treatment with GDC-0941 at a dose of 100 mg/kg substantially down-regulated levels of pAKT(S473) in xenograft tumors of both sensitive KPL-4 cells and resistant MDA-MB-231 cells after 1 hour, suggesting effective pharmacodynamic inhibition of PI3K signaling at this dose in both models.</td>
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<td>Other notes</td>
<td>Please test the solubility of all compounds indoor, and the actual solubility may slightly differ with the theoretical value. This is caused by an experimental system error and it is normal.</td>
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**Reference:**


**Caution**

**FOR RESEARCH PURPOSES ONLY.**

**NOT FOR HUMAN, VETERINARY DIAGNOSTIC OR THERAPEUTIC USE.**

Specific storage and handling information for each product is indicated on the product datasheet. Most ApexBio products are stable under the recommended conditions. Products are sometimes shipped at a temperature that differs from the recommended storage temperature. Shortterm storage of many products are stable in the short-term at temperatures that differ from that
required for long-term storage. We ensure that the product is shipped under conditions that will maintain the quality of the reagents. Upon receipt of the product, follow the storage recommendations on the product data sheet.