Product Name: Linsitinib
Cat. No.: GC15749

Chemical Properties

- **Cas No.**: 867160-71-2
- **Chemical Name**: 3-[8-amino-1-(2-phenylquinolin-7-yl)imidazo[1,5-a]pyrazin-3-yl]-1-methylcyclobutan-1-ol
- **Canonical SMILES**: CC1(CC(C1)C2=NC(=C3N2C=CN=C3N)C4=CC5=C(C=C4)C=CC(=N5)C6=CC=CC=C6)O
- **Formula**: C_{26}H_{23}N_{5}O
- **M.Wt**: 421.51
- **Solubility**: ≥ 21.1mg/mL in DMSO
- **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.

Protocol

**Cell experiment: [1]**

- **Cell lines**: HepG2, Hep3B, Huh-7, PLC/PRF/5, SNU-387 and SNU-423 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.
- **Reaction Conditions**: 3 μM, 20 hours

**Caution: Product has not been fully validated for medical applications. For research use only.**
All 6HCC cell lines showed higher IR phosphorylation than IGF-1R, suggesting the significance of IR activity in HCC. Furthermore, all 3 HCC cell lines (HepG2, Hep3B, and HuH-7) that are sensitive to OSI-906 had much higher phosphorylation levels of both IGF-1R and IR than insensitive cell lines. This suggests that sensitivity to OSI-906 associates with activation of both IGF-1R and IR in HCC cell lines.

**Animal experiment:** [2]

**Animal models**
Female athymic nude mice injected with NCI-H292 or NCI-H441 cells

**Dosage form**
Oral administration, 60 mg/kg

The NCI-H292 xenografts (sensitive to OSI-906 treatment) show a significant decrease (p<0.05) in 18FDG uptake at 2, 4 and 24 hours post dosing with OSI-906 compared to vehicle treated controls. NCI-H441 xenografts (insensitive to OSI-906 treatment) did not demonstrate a significant change in uptake of 18FDG at any time point evaluated. The decreased %ID/g in the NCI-H292 xenografts is suggestive of a rapid PD effect observed by 18FDG imaging mediated by the inhibition of IGF-1R and IR pathways by OSI-906. Conversely, for the NCI-H441 xenograft model no difference in uptake of the radiotracer was observed in the tumor samples between vehicle controls and the OSI-906 treatment group.

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.

**References:**

**Background**

Linsitinib (OSI-906) is a potent and novel small-molecule inhibitor inhibiting insulin receptor (IR) and IGF-1 receptor (IGF-1R) kinases with IC50 value of 75nM and 35nM, respectively.

Studies in 3T3/huIGF-1R(LISN) cells showed that linsitinib inhibits the ligant-dependent autophosphorylation of IGF-1R and its downstream signaling pathways including pERK1/2, pAKT, p-p70S6K. Linsitinib showed anti-proliferative effects in different cancer cell lines including colorectal cells (SW620), breast tumor cells (DY4475) and mouse fibroblast cells (3T3/huIGF-1R) with EC50 of 21nM, 86nM, and 78nM, respectively.

Linsitinib administrated orally in LISN derived xenograft model has been shown to suppress the tumor growth in a dose-dependent manner.
References: