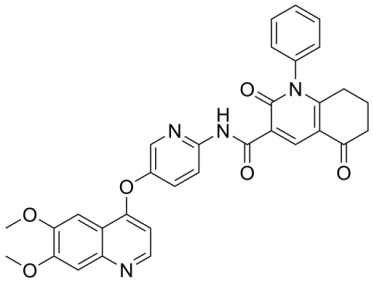
Data Sheet

Product Name:	Tamnorzatinib
Cat. No.:	CS-0083699
CAS No.:	1646839-59-9
Molecular Formula:	$C_{32}H_{26}N_4O_6$
Molecular Weight:	562.57
Target:	TAM Receptor; Trk Receptor
Pathway:	Neuronal Signaling; Protein Tyrosine Kinase/RTK
Solubility:	DMSO : 250 mg/mL (444.39 mM; Need ultrasonic)



BIOLOGICAL ACTIVITY:

ONO-7475 is a potent, selective, and orally active **Axl/Mer** inhibitor with **IC_{50}** values of 0.7 nM and 1.0 nM, respectively. ONO-7475 sensitizes AXL-overexpressing EGFR-mutant NSCLC cells to the EGFR-TKIs, suppresses the emergence and maintenance of tolerant cells. ONO-7475 combines with Osimertinib (HY-15772) provides a bright promise for the study of EGFR-mutated non-small cell lung cancer (NSCLC)[1]. IC50 & Target:IC50: 0.7 nM (AXL)[1]
IC50: 1.0 nM (MER tyrosine kinase)[2] **In Vitro:** ONO-7475 is against recombinant human AXL with **IC_{50}** values of 0.414 nM and 0.7 nM in off-chip MSA and ACD cell-based tyrosine kinase assay, respectively. It is against AXL, MER, TYRO3, TRKB, PDGFR alpha, TRKA, and FLT3 activities with IC_{50} values of 0.7 nM, 1.0 nM, 8.7 nM, 15.8 nM, 28.9 nM, 35.7 nM and 147 nM, respectively in a Cell-based Tyrosine Kinase assay[2].
ONO-7475 (0.0001 μM-1 μM; 72 hours) increases the sensitivity to Osimertinib and Dacomitinib and reduces the viability of high AXL-expressing PC-9 and HCC4011 cells, but not of low-AXL-expressing HCC827 cells. Besides, ONO-7475 enhances Osimertinib efficacy on the viability of cell lines PC-9, PC-9KGR, and HCC4011, and H1975, all of which express high levels of AXL. But it has a marginal effect on the viability of cell lines HCC827, HCC4006, and H3255 with low levels of AXL[1].
ONO-7475 (1 μM; 4 or 48 hours) combines with Osimertinib markedly inhibits the phosphorylation of AXL, AKT, and p70S6K compared with the treatment of the high-AXL-expressing cell lines treated with Osimertinib alone at 4 hours. It combines with osimertinib increases cleaved PARP in PC-9 and HCC4011 cells compared with the treatment with Osimertinib alone[1].
In Vivo: ONO-7475 (oral gavage; 10 mg/kg or combines with 5 mg/kg Osimertinib; 29 days) treatment alone has little effect on the tumor growth. Besides, Osimertinib alone causes tumor regression within one week, but the tumors reappear within three weeks. The combined initial treatment causes tumor regression and the size of tumors is maintained for 4 weeks. No apparent adverse events, including weight loss are observed during these treatments[1].

References:

[1]. Okura N, et al. ONO-7475, a Novel AXL Inhibitor, Suppresses the Adaptive Resistance to Initial EGFR-TKI Treatment in EGFR-Mutated Non-Small Lung Cancer.Clin Cancer Res. 2020 Jan 17.

[2]. Ruvolo PP, et al. Anexelekto/MER tyrosine kinase inhibitor ONO-7475 arrests growth and kills FMS-like tyrosine kinase 3-internal tandem duplication mutant acute myeloid leukemia cells by diverse mechanisms.Haematologica. 2017 Dec;102(12):2048-2057.

CAIndexNames:

3-Quinolinecarboxamide, N-[5-[(6,7-dimethoxy-4-quinolinyl)oxy]-2-pyridinyl]-1,2,5,6,7,8-hexahydro-2,5-dioxo-1-phenyl-

SMILES:

O=C(C1=CC2=C(N(C3=CC=CC=C3)C1=O)CCCC2=O)NC4=NC=C(OC5=CC=NC6=CC(OC)=C(OC)C=C56)C=C4

Caution: Product has not been fully validated for medical applications. For research use only.

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