Product Data Sheet

Chemical Properties

Product Name: ARRY-380
Cas No.: 937265-83-3
M.Wt: 569.63
Formula: C29H27N7O4S
Synonyms: ARRY380; ARRY 380
Chemical Name: 6-[[2-methylsulfonylethylamino)methyl]furan-2-yl]-N-[3-methyl-4-[(1,2,4]triazolo[1,5-a]pyridin-7-yl]oxy)phenyl]quinazolin-4-amine
Canonical SMILES: CC1=C(C=C(CC(C=C1)NC2=NC=C2C=C(C=C3)C4=CC=C(O4)CNCCS(=O)(=O)C)OC5=CC6=NC=NN6C=C5
Solubility: ≥28.5mg/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: JAK/STAT Signaling
Pathways: EGFR
Description:
IC50: 8 nM (HER2)
HER2 is a member of the human epidermal growth factor receptor (HER/EGFR/ERBB) family. Amplification or overexpression of this oncogene has been shown to play an important role in the development and progression of certain aggressive types of breast cancer. ARRY-380 is an orally bioavailable inhibitor of the human epidermal growth factor receptor tyrosine kinase ErbB-2 (also
called HER2) with potential antineoplastic activity.

In vitro: ARRY-380 is reported to be a reversible, ATP-competitive inhibitor with nanomolar activity against HER2 enzyme. In cell-based assays, ARRY-380 is ~500-fold selective for HER2 vs. EGFR and is equipotent against truncated p95-HER2 [1].

In vivo: ARRY-380 treatment significantly enhances survival in two ErbB2 driven intracranial tumor xenograft models, with superior activity compared to other ErbB2 agents in these studies. Additionally, ARRY-380 has demonstrated durable clinical activity in heavily pre-treated patients with ErbB2+ MBC. These preclinical and clinical data suggest that ARRY-380 may provide benefit to patients with ErbB2+ MBC with brain metastases. These preclinical and clinical data suggest that ARRY-380 may provide benefit to patients with ErbB2+ MBC with brain metastases and warrants further study [2].

Clinical trial: In a phase 1 clinical trial, 15 patients have been treated in 5 dosing cohorts at doses of 25 to 300 mg BID. No DLTs have been observed and drug-related adverse events have included Grade 1 nausea, rash and fatigue and Grade 2 fatigue in 2 patients at the 200 mg BID dose level. Preliminary PK analyses indicate a trend for increasing Cmax and AUC with increasing dose, a median Tmax of 2 hours and a mean t1/2 of 4.6 hours across all cohorts. Two patients with HER2+ breast cancer have had stable disease for ≥ 4 months with no significant toxicity. One of these two patients had a notable reduction in liver metastases (28%) after 2 cycles of ARRY-380 and is currently on study. These findings indicate ARRY-380 has demonstrated an acceptable safety and PK profile and preliminary signs of clinical benefit. Dose escalation continues to determine the MTD [3].

Reference:

Protocol

Cell experiment:

Cell lines BT474 cells, NIH-3T3 cells

Preparation method Soluble in DMSO >28.5mg/mL. 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

Applications ARRY-380 is an orally active, selective, small molecule inhibitor of...
ErbB2 (human epidermal growth factor receptor-2). Its activity (IC50) against ErbB2 enzyme is 14 nM and it inhibits the phosphorylation of ErbB2 in BT474 cells in culture with an IC 50 of 21 nM. ARRY-380 also potently inhibits phosphorylation of AKT (protein kinase B), induces apoptosis and inhibits growth of BT474 cells in vitro. Marked tumor growth inhibition has been demonstrated in NIH-3T3 cells stably transfected with constitutively active ErbB2 kinase (3T3-rErbB2).

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. Short-term 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.