Product Data Sheet

Product Name: TAS1553
Cat. No.: GC68033

Chemical Properties

Cas. No.	2166023-31-8		
Formula	$C_{20}H_{20}ClFN_4O_5S$	M.Wt	482.91
Solubility	DMSO : 100 mg/mL (207.08 mM; Need ultrasonic)	Storage	Store at -20°C
General tips	For obtaining a higher solubility , please warm the tube at 37 ℃ and shake it in the ultrasonic bath for a while.Stock solution can be stored below -20℃ for several months.		
Shipping Condition	Evaluation sample solution : ship with blue ice All other available size: ship with RT , or blue ice upon request.		
Structure	TAS1553		

Protocol

Cell experiment [1]:

Cell lines	Human cancer cell lines (HCC38 breast cancer, MV-4-11 acute myelogenous leukemia)
Preparation Method	Cells were maintained in RPMI-1640 or DMEM supplemented with 10% fetal bovine serum (FBS) at 37°C, 5% CO_2. Cells were treated with TAS1553 at concentrations ranging from 0.228 to 10μmol/L for 30 minutes to 24 hours.
Reaction Conditions	0.228–10μmol/L; 30min–24h

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Applications	TAS1553 significantly reduced the intracellular dATP pool by disrupting the protein-protein interaction between RNR subunits R1 and R2, leading to DNA replication stress and replication fork stalling. This was accompanied by phosphorylation of Chk1 (Ser345) and RPA2 (Ser4/Ser8, Thr21) within 2 hours. TAS1553 induced apoptosis via caspase-3/7 activation and PARP cleavage, with efficacy strongly correlated with SLFN11 expression levels.

Animal experiment [1]:

Animal models	F344/NJcl-mu/rnu rats bearing MV-4-11 xenografts, BALB/cAJcl-nu/nu mice bearing HCC38 xenografts, and B6N-Tyrc-Brd/BrdCrCrl mice with systemic MLL-AF9-driven acute myelogenous leukemia (AML).
Preparation Method	Rats and mice were subcutaneously implanted with tumor cells or intravenously inoculated with AML cells. TAS1553 was administered orally once daily at doses of 50–400mg/kg for 14–21 days. For pharmacodynamic studies, tumors were collected at 1, 2, and 4 hours after a single oral dose.
Dosage form	50–400mg/kg; p.o.; Once daily for 14–21 days

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Applications	TAS1553 administration significantly suppressed tumor growth in MV-4-11 xenografts and induced complete tumor regression at 400mg/kg. TAS1553 reduced intratumoral dATP pools within 1–2 hours, triggered DNA replication stress (phospho-Chk1 elevation), and activated apoptosis (cleaved PARP and caspase-3). In the systemic AML model, TAS1553 (100mg/kg) extended median survival by 34.8%. Body weight remained stable, indicating tolerability.

References:
[1] Ueno H, Hoshino T, Yano W, et al. TAS1553, a small molecule subunit interaction inhibitor of ribonucleotide reductase, exhibits antitumor activity by causing DNA replication stress. Commun Biol. 2022 Jun 9;5(1):571.

Background

TAS1553 is a small-molecule protein-protein interaction inhibitor that effectively suppresses the activity of ribonucleotide reductase (RNR). By disrupting the DNA replication process and reducing intracellular deoxyadenosine triphosphate (dATP) levels, TAS1553 ultimately induces apoptosis[1].

In vitro, treatment of human cancer cell lines (HCC38 and MV-4-11) with TAS1553 (0.228–10μmol/L) for 30 minutes to 24 hours significantly depletes the intracellular dATP pool, induces DNA replication stress and replication fork stalling, and leads to apoptotic cell death[1].

In vivo, oral administration of TAS1553 (50–400mg/kg) once daily for 14–21 days in female NOD/SCID mice bearing MV-4-11 xenografts significantly suppresses tumor

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growth and promotes tumor regression. This is accompanied by reduced intratumoral dATP levels and activation of replication stress and apoptotic pathways [1].

References:

[1] Ueno H, Hoshino T, Yano W, et al. TAS1553, a small molecule subunit interaction inhibitor of ribonucleotide reductase, exhibits antitumor activity by causing DNA replication stress. Commun Biol. 2022 Jun 9;5(1):571.