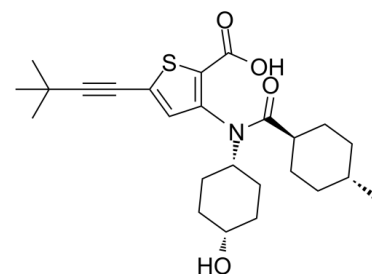


Data Sheet

Product Name:	VX-222
Cat. No.:	CS-0268
CAS No.:	1026785-59-0
Molecular Formula:	C ₂₅ H ₃₅ NO ₄ S
Molecular Weight:	445.61
Target:	HCV
Pathway:	Anti-infection
Solubility:	DMSO : ≥ 32 mg/mL (71.81 mM)



BIOLOGICAL ACTIVITY:

VX-222 (VCH-222) is a novel, potent and selective inhibitor of HCV polymerase with IC₅₀ of 0.94-1.2 μM, 15.3-fold less effective for mutant M423T, and 108-fold less effective for mutant I482L. IC₅₀ Value: 0.94 μM (HCV NS5B 1a); 1.2 μM (HCV NS5B 1b) Target: HCV
VX-222 is a small molecule non-nucleoside inhibitor of HCV NS5B polymerase that is being investigated for the treatment of hepatitis C virus infection. VX-222 exhibits non-competitive and selective inhibition in HCV NS5B of genotype 1a and 1b, with IC₅₀ of 0.94 and 1.2 μM, respectively. VX-222 selectively inhibits the replication of subgenomic HCV genotype 1a and 1b with an EC₅₀ of 22.3 and 11.2 nM, respectively. [1] Similarly, a recent study shows that VX-222 inhibits the 1b/Con1 HCV subgenomic replicon, with an EC₅₀ of 5 nM. In rats and dogs, VCH-222 displays fine pharmacokinetic profile, including low total body clearance and excellent oral bioavailability (greater than 30%) and good ADME properties. VCH-222 is biotransformed by several enzymes (CYP1A1, 2A6, 2B6, 2C8, CYP 3A4, UGT1A3) and is predicted to be actively transported in liver and excreted mainly intact in bile or as glucuronide adducts.

PROTOCOL (Extracted from published papers and Only for reference)

Cell assay [2] Huh7.5 cells harboring replicons were trypsinized and plated into 48-well plates at 40,000 cells/well. The next day the medium was changed and VX-222 was added to the cells at seven different concentrations, each pair of which differed by 3- or 10-fold dilutions in 200 μl complete medium with triplicates. After 48 h, total RNA was extracted from replicon cells using the TRIzol reagent (Invitrogen), and viral RNAs were quantified by real-time reverse transcription-PCR (RT-PCR). First-strand cDNA synthesis used 1 μg of total RNA along with Moloney murine leukemia virus (NEB) and 4 μM randomized 9-nucleotide (nt) primer mix. RT-PCR used the Bio-Rad IQ SYBR green kit (Bio-Rad), and primers were HCV 5'-UTRsense (5'-AGC CAT GGC GTT AGT ATG AGT GTC-3') and 5'-UTRanti (5'-ACA AGG CCT TTC GCG ACC CAA C-3'). Glyceraldehyde-3-phosphate dehydrogenase (GAPDH) was detected using the sense and antisense oligonucleotides 5'-GAG TCA ACG GAT TTG GTC GT-3' and 5'-TGG GAT TTC CAT TGA TGA CA-3', respectively. All reaction mixtures were heated to 95°C for 10 min, followed by 40 cycles of PCR of 15 s at 95°C, 20 s at 55°C, and 30 s at 72°C. The fold change and percent change of each group were compared to values for controls as previously described (27). The effective drug concentrations that reduced HCV RNA replicon levels by 50% (EC₅₀s) were calculated with GraphPad Prism software by nonlinear regression analysis with log curve fitting.

References:

- [1]. Yi G, Deval J, Fan B, Cai H, Soulard C, Ranjith-Kumar CT, Smith DB, Blatt L, Beigelman L, Kao CC. Biochemical study of the comparative inhibition of hepatitis C virus RNA polymerase by VX-222 and filibuvir. *Antimicrob Agents Chemother*. 2012 Feb;56(2):830-7. Epub 2011 Dec 5.
- [2]. Godzik P, Komorowski M, Cielecka-Kuszyk J, Madaliński K. [Inhibitors of hepatitis C virus--current standards and status of investigations]. *Przegl Epidemiol*.

[3]. M. Rodriguez-Torres et al. SAFETY AND ANTIVIRAL ACTIVITY OF THE HCV NON-NUCLEOSIDE POLYMERASE INHIBITOR VX-222 IN TREATMENT-NAIVE GENOTYPE 1 HCV-INFECTED PATIENTS Journal of Hepatology Volume 52, Supplement 1 , Page S14, April 2010

CAIndexNames:

2-Thiophenecarboxylic acid, 5-(3,3-dimethyl-1-butyn-1-yl)-3-[[cis-4-hydroxycyclohexyl][(trans-4-methylcyclohexyl)carbonyl]amino]-

SMILES:

O=C(C1=C(N([C@@H]2CC[C@H](O)CC2)C([C@H]3CC[C@H](C)CC3)=O)C=C(C#CC(C)(C)S1)O

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

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