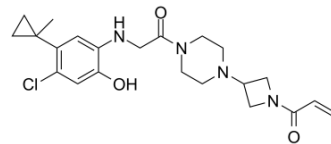


ARS-853

| | | | |
|---------------------------|---|-------|----------|
| Cat. No.: | HY-19706 | | |
| CAS No.: | 1629268-00-3 | | |
| Molecular Formula: | C ₂₂ H ₂₉ ClN ₄ O ₃ | | |
| Molecular Weight: | 432.94 | | |
| Target: | Ras; Apoptosis | | |
| Pathway: | GPCR/G Protein; Apoptosis | | |
| Storage: | Powder | -20°C | 3 years |
| | | 4°C | 2 years |
| | In solvent | -80°C | 6 months |
| | | -20°C | 1 month |



SOLVENT & SOLUBILITY

In Vitro

DMSO : 33.33 mg/mL (76.99 mM; Need ultrasonic)

| | Solvent Concentration | Mass | | |
|------------------------------|--------------------------|-----------|------------|------------|
| | | 1 mg | 5 mg | 10 mg |
| Preparing Stock Solutions | 1 mM | 2.3098 mL | 11.5489 mL | 23.0979 mL |
| | 5 mM | 0.4620 mL | 2.3098 mL | 4.6196 mL |
| | 10 mM | 0.2310 mL | 1.1549 mL | 2.3098 mL |

Please refer to the solubility information to select the appropriate solvent.

In Vivo

- Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
Solubility: ≥ 2.5 mg/mL (5.77 mM); Clear solution
- Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
Solubility: ≥ 2.5 mg/mL (5.77 mM); Clear solution
- Add each solvent one by one: 10% DMSO >> 90% corn oil
Solubility: ≥ 2.5 mg/mL (5.77 mM); Clear solution
- Add each solvent one by one: 5% DMSO >> 95% (20% SBE-β-CD in saline)
Solubility: ≥ 2 mg/mL (4.62 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

ARS-853 is a cell-active, selective, covalent KRAS G12C inhibitor with an IC₅₀ of 2.5 μM. ARS-853 inhibits mutant KRAS-driven signaling by binding to the GDP-bound oncoprotein and preventing activation^{[1][2]}.

IC₅₀ & Target

KRAS(G12C)
2.5 μM (IC₅₀)

In Vitro

ARS853 is designed to bind KRAS^{G12C} with high affinity. Treatment of KRAS^{G12C}-mutant lung cancer cells with ARS853 reduces the level of GTP-bound KRAS by more than 95% (10 μ M). ARS853 inhibits proliferation with an inhibitory concentration 50% (IC₅₀) of 2.5 μ M, which is similar to its IC₅₀ for target inhibition. ARS853 (10 μ M) inhibits effector signaling and cell proliferation to varying degrees in six KRAS^{G12C} mutant lung cancer cell lines, but not in non-KRAS^{G12C} models. Similarly, it completely suppresses the effects of exogenous KRAS^{G12C} expression on KRAS-GTP levels, KRAS-BRAF interaction, and ERK signaling. ARS-853 treatment also induces apoptosis in four KRAS^{G12C} mutant cell lines. ARS853 selectively reduces KRAS-GTP levels and RAS-effector signaling in KRAS^{G12C}-mutant cells, while inhibiting their proliferation and inducing cell death^[1]. ARS-853 inhibits mutant KRAS-driven signaling by binding to the GDP-bound oncoprotein and preventing activation^[2].

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Kinase Assay ^[1]

Purified KRAS (1 μ M) is incubated EDTA (10 mM) and GDP (1 mM) or GTPyS (1 mM) at room temperature for 1 h followed by addition of MgCl₂ (1 mM) to terminate the reaction. ARS853 (1 μ M) is then added and the mixture is incubated for another hour at room temperature. HEK293 cells expressing various KRAS mutants are treated with ARS853. Proteins are extracted using a buffer containing 9M urea, 10 mM DTT and 50 mM ammonium bicarbonate, pH 8, heated to 65°C for 15 min and alkylated using 50 mM iodoacetamide at 37°C for 30 min. The samples are desalted by gel filtration in Zeba spin desalting plates followed by addition of sequencing-grade trypsin to a concentration of 10 μ g/ml, and incubation for one hour at 37°C. Heavy isotopic standards (25 fmol) of the KRAS^{G12C} target peptide and KRAS normalization peptide are added to the samples followed by desalting in Strata-X polymeric reverse phase plates. LC-MS/MS analysis is performed in a Q Exactive quadrupole orbitrap mass spectrometer under standard condition. The amount of KRAS^{G12C} bound by the drug is determined by the ratio of the modified G12C peptide to that of the heavy isotopic standards^[1].

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- Cancer Discov. 2020 Dec;10(12):1950-1967.
- THE DEPARTMENT OF CANCER BIOLOGY.2020. 28103931.

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REFERENCES

[1]. Lito P, et al. Allele-specific inhibitors inactivate mutant KRAS G12C by a trapping mechanism. Science. 2016 Feb 5;351(6273):604-8.

[2]. Patricelli MP, et al. Selective Inhibition of Oncogenic KRAS Output with Small Molecules Targeting the Inactive State. Cancer Discov. 2016 Mar;6(3):316-29.

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

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