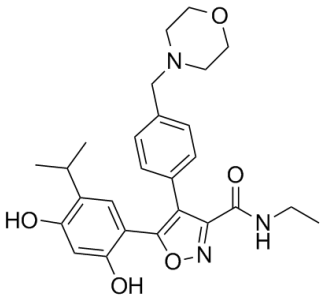
Data Sheet

Product Name:	NVP-AUY922
Cat. No.:	HY-10215
CAS No.:	747412-49-3
Molecular Formula:	$C_{26}H_{31}N_3O_5$
Molecular Weight:	465.54
Target:	Autophagy; HSP
Pathway:	Autophagy; Cell Cycle/DNA Damage; Metabolic Enzyme/Protease
Solubility:	DMSO: ≥ 62 mg/mL



BIOLOGICAL ACTIVITY:

NVP-AUY922 is a potent **HSP90** inhibitor with **IC_{50}**s of 7.8 nM/21 nM for HSP90α/β, respectively, and has weaker potency against the HSP90 family members GRP94 and TRAP-1 (**IC_{50}**, 535 nM, 85 nM, respectively).
IC50 & Target: IC50: 7.8 nM (HSP90α), 21 nM (HSP90β), 535 nM (GRP94), 85 nM (TRAP-1)[1]
In Vitro: NVP-AUY922 is a potent and selective HSP90 inhibitor, with IC_{50}s and K_is of 21 ± 16, 8.2 ± 0.7 nM against HSP90β and of 7.8 ± 1.8, 9.0 ± 5.0 nM for HSP90α. NVP-AUY922 shows weak activity against GRP94 and TRAP-1 wich IC_{50}s of 535 ± 51 nM (K_i, 108 nM) and 85 ± 8 nM (K_i, 53 nM), respectively. NVP-AUY922 exhibits inhibitory effect on proliferation of various human tumor cell lines (2.3-49.6 nM), induces cell cycle arrest and apoptosis and depletes client proteins in human cancer cells (80 nM)[1]. NVP-AUY922 (100 nM) significantly reduces CD40L fibroblast-induced changes in immunophenotype and STAT3 signaling but with no effect on the viability of chronic lymphocytic leukemia (CLL) cells. NVP-AUY922 (500 nM) in combination with fludarabine more effectively induces apoptosis in cells in co-culture than either drug alone, and overcomes fibroblast-derived resistance to Hsp90 inhibitor[2]. NVP-AUY922 shows great inhibition of pancreatic cancer cells with IC_{50} of at 10 nM. NVP-AUY922 (10 nM) reduces the expression and the epidermal growth factor (EGF)-mediated activation of EGFR and substantially disrupts EGF signaling in terms of diminishing downstream phosphorylation of $ERK^{Thr202/Tyr204}$. NVP-AUY922 (10 nM) significantly blocks pancreatic cancer cell migration and invasion both in the absence and presence of EGF[3].
In Vivo: NVP-AUY922 (50, 75 mg/kg, i.p.) significantly inhibits tumor growth rate, reducing the mean weights of tumors on day 11 in human tumor xenografts[2]. NVP-AUY922 (50 mg/kg/week, 3×25 mg/kg/week) significantly reduces tumor growth rates and lowers tumor weights in the L3.6pl pancreatic cancer cell-bearing mice model[3].

PROTOCOL (Extracted from published papers and Only for reference)

Cell Assay: [1]Cell lines are grown in DMEM/10% FCS, 2 mM glutamine, and nonessential amino acids in a humidified atmosphere of 5% CO_2 in air. All lines are free of *Mycoplasma*. Cell proliferation is determined using the SRB assay for **tumor cells and prostate epithelial cells**, the WST-1 assay for MCF10A and HB119, or an alkaline phosphatase assay for HUVEC and HDMEC. GI_{50} is the compound concentration inhibiting cell proliferation by 50% compared with vehicle controls. Active caspase-3/7 is measured using a homogenous caspase assay kit[1]. **Animal Administration:** NVP-AUY922 is dissolved in DMSO and diluted in sterile saline/Tween 20[1].[1]Mice[1]
For efficacy studies, human tumor xenografts are established s.c. in **athymic mice**. **WM266.4 cells** are also injected i.v. to generate experimental lung metastases and PC3LN3 prostate carcinoma cells are implanted into the prostates of male mice. Dosing by **i.p. with NVP-AUY922** commences when tumors are well established. Tumor growth is monitored and at study end samples are harvested for analysis[1].

References:

[1]. Eccles, Suzanne A., et al. NVP-AUY922: A Novel Heat Shock Protein 90 Inhibitor Active against Xenograft Tumor Growth, Angiogenesis, and Metastasis. Cancer Research (2008), 68(8), 2850-2860.

[2]. Best OG, et al. Heat shock protein-90 inhibitor, NVP-AUY922, is effective in combination with fludarabine against chronic lymphocytic leukemia cells cultured on CD40L-stromal layer and inhibits their activated/proliferative phenotype. Leuk Lymphoma. 2012 Jul 9.

[3]. Moser C, et al. Stoeltzing O.Targeting HSP90 by the novel inhibitor NVP-AUY922 reduces growth and angiogenesis of pancreatic cancer. Anticancer Res. 2012 Jul;32(7):2551-61.

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