

Product Data Sheet

Product Name: S55746 (BLC201)

Cat. No.: GC32947

Chemical Properties

Cas. No. 1448584-12-0

SMILES O=C(C1=C2CCCCN2C(C3=C(C(N4CC5=C(C=CC=C5)C[C@H]4CN6CCOCC6)=O)C=C(OC7C7=C3)=C1)N(C8=CC=C(O)C=C8)C9=CC=CC=C9

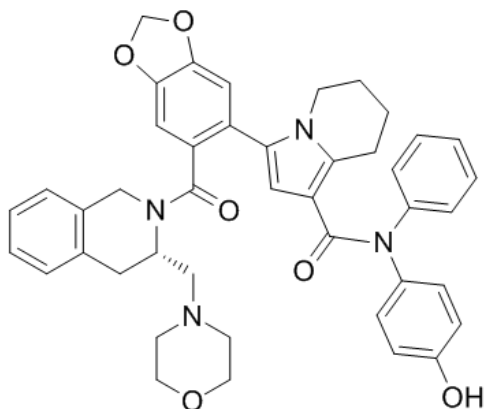
Formula $C_{43}H_{42}N_4O_6$ M.Wt 710.82

Solubility DMSO : 50 mg/mL (70.34 mM); Water : < 0.1 mg/mL (insoluble) 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.

Shipping Condition Evaluation sample solution : ship with blue ice All other available size: ship with RT, or blue ice upon request.

Structure



Background

S55746 is an orally active, selective and potent BCL-2 inhibitor, with a K_i of 1.3 nM.

S55746 is a potent inhibitor of BCL-2 ($K_i=1.3$ nM). S55746 potently induces RS4;11 cell killing after 72 h of treatment with an IC_{50} of 71.6 nM. Interestingly, S55746 exhibits a much weaker activity in

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H146 (IC₅₀=1.7 μ M), a BCL-XL-dependent cell line, which expresses a low level of BCL-2 and high level of BCL-XL whereas ABT-263, which targets BCL-2 and BCL-XL, induces equivalent cell killing in both RS4;11 and H146 (41.5 nM and 49.7 nM, respectively). S55746-induced apoptosis in RS4;11 is mediated in part by the BAX effector protein since PARP cleavage is markedly inhibited in BAX-deficient RS4;11 cells. S55746 is shown to strongly induce apoptosis in BCL-2-dependent FL5.12 cells with a minor effect in BCL-XL-dependent FL5.12 cells[1].

Caspase-3 activity after S55746 treatment at 25 and 100 mg/kg is about 11 and 28 times higher than in vehicle-treated animals, respectively. Antitumor activity of S55746 is then evaluated in RS4;11 and Toledo models, two models that display different in vitro sensitivities towards S55746 (71.6 nM in RS4;11 vs 401 nM in Toledo). In RS4;11 bearing SCID mice, daily oral gavage treatment of S55746 for 7 consecutive days induce significant anti-tumor activity compared to untreated animals. Seventeen days after beginning of treatment at 25 mg/kg, 50 mg/kg and 100 mg/kg, tumor growth inhibition is 67.1, 16.3 and -93.8 T/C respectively, with complete regression observed in all animals treated at 100 mg/kg. Efficacy of S55746 is also assessed in Toledo bearing mice. After 21 days of treatment, S55746 induces a significant tumor growth inhibition either at 200 or 300 mg/kg (13% and 2% T/C, respectively; $p < 0.05$). In this model, S55746 and ABT-199 show similar anti-tumor efficacy[1].

[1]. Casara P, et al. S55746 is a novel orally active BCL-2 selective and potent inhibitor that impairs hematological tumor growth. *Oncotarget*. 2018 Apr 13;9(28):20075-20088.

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