

Product Data Sheet

Product Name: Birinapant (TL32711)

Cat. No.: GC12426

Chemical Properties

Cas. No. 1260251-31-7

Chemical Name (2S,2'S)-N,N'-((2S,2'S)-((3S,3'S,5R,5'R)-5,5'-((6,6'-difluoro-1H,1'H-[2,2'-biindole]-3,3'-diyl)bis(methylene))bis(3-hydroxypyrrolidine-5,1-diyl))bis(1-oxobutane-2,1-diyl))bis(2-(methylanino)propanamide)

SMILES CCC(C(=O)N1CC(CC1CC2=C(NC3=C2C=CC(=C3)F)C4=C(C5=C(N4)C=C(C=C5)F)CC6CC(CN6C(=O)C(CC)NC(=O)C(C)NC(O)O)NC(=O)C(C)NC

Formula C₄₂H₅₆F₂N₈O₆

M.Wt 806.94

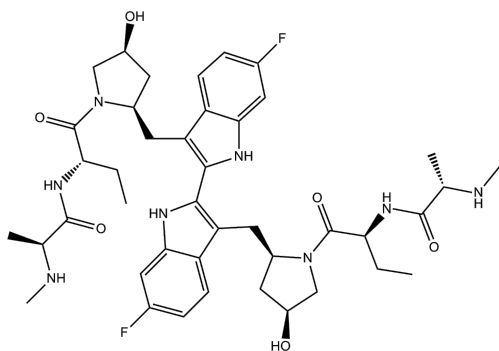
Solubility ≥ 40.35 mg/mL in DMSO, ≥ 46.9 mg/mL in EtOH

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



Protocol

IAP binding affinity of Birinapant (TL32711)[1]:

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

Tel: (909) 407-4943 Fax: (626) 353-8530 E-mail: tech@glpbio.com

Address: 10292 Central Ave. #205, Montclair, CA, USA

Product Data Sheet

Preparation Method A fluorescence polarization assay was used to determine the dissociation constants (K_d) of Smac mimetics Birinapant (TL32711) and GT13402 for XIAP and cIAP1 by monitoring the decrease in fluorescence polarization signal due to competitive displacement of an FP peptide from the BIR3/FP peptide binary complex.

Applications The binding constants (K_d) of Birinapant (TL32711) for XIAP and cIAP1 were determined to be 45 and

Cell experiment [2]:

Cell lines 451Lu and WM1366 melanoma cells

Preparation Method Cells were treated with Birinapant (TL32711) 1 $\mu\text{mol/L}$ in combination with TNF- α 1 ng/mL. Cells were then incubated for 72 hours in the presence or absence of Necrostatin-1 a RIP1 kinase inhibitor. Proliferation was assessed using the MTS assay.

Reaction Conditions 1 $\mu\text{mol/L}$ Birinapant (TL32711) for 72 hours

Applications The majority of cell lines exhibited strong combination activity of Birinapant (TL32711) and TNF- α .

Animal experiment [3]:

Animal models Male C57BL/6J mice aged 8 week old, weighing $21 \pm 1.3\text{g}$

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

Tel: (909) 407-4943 Fax: (626) 353-8530 E-mail: tech@glpbio.com

Address: 10292 Central Ave. #205, Montclair, CA, USA

Product Data Sheet

Preparation Method Before the LPS administration, mice were injected intraperitoneally with Birinapant (TL32711) (30 mg/kg body weight, Birinapant (TL32711) group) either vehicle control (vehicle group) for 24 h. Birinapant (TL32711) was dissolved in 12.5% Captisol in distilled water. Twenty-four mice in each group were euthanized and the samples of the liver and blood were harvested at 0, 6, 12 and 24 h after LPS challenge.

Dosage form 30 mg/kg Birinapant (TL32711) ip. for 24 h.

Applications Birinapant (TL32711) pretreatment significantly improved mice survival.

References:

[1]. Allensworth JL, Sauer SJ, et.al. Smac mimetic Birinapant induces apoptosis and enhances TRAIL potency in inflammatory breast cancer cells in an IAP-dependent and TNF- α -independent mechanism. Breast Cancer Res Treat. 2013 Jan;137(2):359-71. doi: 10.1007/s10549-012-2352-6. Epub 2012 Dec 7. PMID: 23225169.

[2]. Krepler C, Chunduru SK, et.al. The novel SMAC mimetic birinapant exhibits potent activity against human melanoma cells. Clin Cancer Res. 2013 Apr 1;19(7):1784-94. doi: 10.1158/1078-0432.CCR-12-2518. Epub 2013 Feb 12. PMID: 23403634; PMCID: PMC3618495.

[3]. Liu H, Liao R, et.al. The SMAC mimetic birinapant attenuates lipopolysaccharide-induced liver injury by inhibiting the tumor necrosis factor receptor-associated factor 3 degradation in Kupffer cells. Immunol Lett. 2017 May;185:79-83. doi: 10.1016/j.imlet.2017.02.016. Epub 2017 Mar 9. PMID: 28286228.

Background

Birinapant (TL32711) is a SMAC mimetic designed to specifically target cIAP1 and cIAP2 for degradation^[1]. Birinapant rapidly degrades cIAPs and enables cytokines (TNF α , TRAIL) to activate the extrinsic apoptosis pathway, while Birinapant rapidly turns off the canonical NF- κ B survival

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

Tel: (909) 407-4943 Fax: (626) 353-8530 E-mail: tech@glpbio.com

Address: 10292 Central Ave. #205, Montclair, CA, USA

Product Data Sheet

pathway, causing cancer cell death^[2]. Birinapant has been widely used to inhibit the growth of various cancer cells and to increase the production of TNF^[3].

In vitro, Birinapant treatment for 72 hours significantly inhibited the viability of MDA-MB-231 and A875 cells, with IC₅₀ values of 10nM and 40nM, respectively^[4]. Treatment with 1μM Birinapant for 24 hours significantly induced apoptosis in SUM190 cells, resulting in activation of caspase and NF-κB, as well as cleavage of PARP^[5].

In vivo, Birinapant treatment via intraperitoneal injection at a dose of 30mg/kg, once a week for 2 weeks, significantly promoted apoptosis and inhibited the growth of subcutaneous hepatocellular carcinoma tumors in nude mice^[6]. A single intraperitoneal injection of a 30mg/kg dose of Birinapant alleviated liver injury induced by lipopolysaccharide (LPS) in mice and increased the survival rate of mice within 72 hours^[7]. A single intravenous injection of Birinapant at 30mg/kg for 24h alleviated lung injury induced by LPS in mice and reduced the production of pro-inflammatory cytokines^[8].

References:

- [1] Condon S M, Mitsuuchi Y, Deng Y, et al. Birinapant, a smac-mimetic with improved tolerability for the treatment of solid tumors and hematological malignancies[J]. 2014.
- [2] Benetatos C A, Mitsuuchi Y, Burns J M, et al. Birinapant (TL32711), a bivalent SMAC mimetic, targets TRAF2-associated cIAPs, abrogates TNF-induced NF-κB activation, and is active in patient-derived xenograft models[J]. Molecular cancer therapeutics, 2014, 13(4): 867-879.
- [3] Chang Y C, Cheung C H A. An updated review of smac mimetics, LCL161, birinapant, and GDC-0152 in cancer treatment[J]. Applied Sciences, 2020, 11(1): 335.
- [4] Perez H L, Chaudhry C, Emanuel S L, et al. Discovery of potent heterodimeric antagonists of inhibitor of apoptosis proteins (IAPs) with sustained antitumor activity[J]. Journal of medicinal chemistry, 2015, 58(3): 1556-1562.
- [5] Allensworth J L, Sauer S J, Lysterly H K, et al. Smac mimetic Birinapant induces apoptosis and enhances TRAIL potency in inflammatory breast cancer cells in an IAP-dependent and TNF-α-independent mechanism[J]. Breast cancer research and treatment, 2013, 137(2): 359-371.
- [6] Ding J, Qin D, Zhang Y, et al. SMAC mimetic birinapant inhibits hepatocellular carcinoma growth by activating the cIAP1/TRAF3 signaling pathway[J]. Molecular medicine reports, 2020, 21(3): 1251-1257.
- [7] Liu H, Liao R, He K, et al. The smac mimetic birinapant attenuates lipopolysaccharide-induced

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

Tel: (909) 407-4943 Fax: (626) 353-8530 E-mail: tech@glpbio.com

Address: 10292 Central Ave. #205, Montclair, CA, USA

Product Data Sheet

liver injury by inhibiting the tumor necrosis factor receptor–associated factor 3 degradation in kupffer cells[J]. Immunology Letters, 2017, 185: 79-83.

[8] Hu H, Ma M, Li T, et al. The SMAC mimetic birinapant alleviates lipopolysaccharide-induced acute lung injury by inhibiting MAPK signaling[J]. Immunology Letters, 2023, 264: 31-35.

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

Tel: (909) 407-4943 Fax: (626) 353-8530 E-mail: tech@glpbio.com

Address: 10292 Central Ave. #205, Montclair, CA, USA