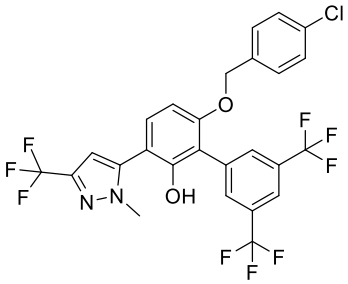
Product data sheet

MedKoo Cat#: 408062 Name: MYCi361 CAS#: 2289690-31-7 Chemical Formula: $C_{26}H_{16}ClF_9N_2O_2$ Exact Mass: 594.0757 Molecular Weight: 594.86	
Product supplied as:	Powder
Purity (by HPLC):	≥ 98%
Shipping conditions	Ambient temperature
Storage conditions:	Powder: -20°C 3 years; 4°C 2 years.
	In solvent: -80°C 3 months; -20°C 2 weeks.

1. Product description:
MYCi361, also known as NUCC-0196361, is a MYC inhibitor with the Kd of 3.2 μM for binding to MYC. MYCi361 suppresses tumor growth and enhances anti-PD1 immunotherapy.

2. CoA, QC data, SDS, and handling instruction
SDS and handling instruction, CoA with copies of QC data (NMR, HPLC and MS analytical spectra) can be downloaded from the product web page under "QC And Documents" section. Note: copies of analytical spectra may not be available if the product is being supplied by MedKoo partners. Whether the product was made by MedKoo or provided by its partners, the quality is 100% guaranteed.

3. Solubility data

Solvent	Max Conc. mg/mL	Max Conc. mM
DMSO	110	184.9

4. Stock solution preparation table:

Concentration / Solvent Volume / Mass	1 mg	5 mg	10 mg
1 mM	1.68 mL	8.41 mL	16.81 mL
5 mM	0.34 mL	1.68 mL	3.36 mL
10 mM	0.17 mL	0.84 mL	1.68 mL
50 mM	0.03 mL	0.17 mL	0.34 mL

5. Molarity Calculator, Reconstitution Calculator, Dilution Calculator
Please refer the product web page under section of "Calculator"

6. Recommended literature which reported protocols for in vitro and in vivo study
In vitro study

1. Han H, Jain AD, Truica MI, Izquierdo-Ferrer J, Anker JF, Lysy B, Sagar V, Luan Y, Chalmers ZR, Unno K, Mok H, Vatapalli R, Yoo YA, Rodriguez Y, Kandela I, Parker JB, Chakravarti D, Mishra RK, Schiltz GE, Abdulkadir SA. Small-Molecule MYC Inhibitors Suppress Tumor Growth and Enhance Immunotherapy. Cancer Cell. 2019 Nov 11;36(5):483-497.e15. doi: 10.1016/j.ccell.2019.10.001. Epub 2019 Oct 31. PMID: 31679823; PMCID: PMC6939458.

2. Ding T, Zhu Y, Jin H, Zhang P, Guo J, Zheng J. Circular RNA circ_0057558 Controls Prostate Cancer Cell Proliferation Through Regulating miR-206/USP33/c-Myc Axis. Front Cell Dev Biol. 2021 Feb 26;9:644397. doi: 10.3389/fcell.2021.644397. PMID: 33718387; PMCID: PMC7952531.

In vivo study

1. Han H, Jain AD, Truica MI, Izquierdo-Ferrer J, Anker JF, Lysy B, Sagar V, Luan Y, Chalmers ZR, Unno K, Mok H, Vatapalli R, Yoo YA, Rodriguez Y, Kandela I, Parker JB, Chakravarti D, Mishra RK, Schiltz GE, Abdulkadir SA. Small-Molecule MYC Inhibitors Suppress Tumor Growth and Enhance Immunotherapy. Cancer Cell. 2019 Nov 11;36(5):483-497.e15. doi: 10.1016/j.ccell.2019.10.001. Epub 2019 Oct 31. PMID: 31679823; PMCID: PMC6939458.

7. Bioactivity
Biological target:

Product data sheet

MYCi361 (NUCC-0196361) is a MYC inhibitor with the Kd of 3.2 μM for binding to MYC. MYCi361 (NUCC-0196361) suppresses tumor growth and enhances anti-PD1 immunotherapy.

In vitro activity

To examine MYC target engagement by 361 in cells using unlabeled protein and inhibitor, the cellular thermal shift assay (CETSA) was performed. CETSA assesses drug-protein interaction in the protein's native cellular environment, based on ligand-induced changes in protein thermal stability. Treatment of PC3 cells with MYCI361 (361) (4–10 μM) or G5 (15–60 μM) for 30 min led to significant thermal destabilization of MYC protein while 360 (6 μM) had no effect (Figure 1A--1C,1C, and Figure S2A-S2E). 361 and its inactive analog 360 are regioisomers, differing only in the position of the methyl group (Figure S1J). The selectivity of 361 was assessed by using a panel of MYC-dependent and -independent cell lines. 361 inhibited the viability of MYC-dependent cancer cells including prostate cancer (MycCaP, LNCaP, PC3), leukemia (MV4–11), lymphoma (HL-60, P493–6) and neuroblastoma (SK-N-B2) with low micromolar IC50s, but had little effect on pheochromocytoma PC12 cells, which does not require MYC/MAX dimer for proliferation (Figure 3A and 3B). G5 and androgen receptor inhibitor enzalutamide were also evaluated in certain cell lines for comparison. Myc knockout Rati fibroblasts (HO15.19) were more resistant to 361 compared to wild-type Rat1 fibroblasts (TGR.1) (Figure S5A). To further examine 361 selectivity, prostate organoids were generated from MycCaP cells or their parental normal prostate epithelial cells of FVB mice. MycCaP organoids were more sensitive to 361 than the FVB mouse prostate organoids (Figure 3C). Additionally, in the P493–6 lymphoma model in which MYC protein levels could be titrated with tetracycline, sensitivity to 361 was inversely correlated with MYC levels (Figure 3D and 3E). Finally, 361 and several of its analogs were examined in the NCI60 cell line panel cell growth screen. It was found that compounds with high inhibition of MYC/MAX/DNA complex formation in EMSA showed more potent inhibition of cell growth in the NCI60 panel (Figure S5B and S5C). Activity of 361 in the NCI60 panel cells also showed a trend for inverse correlation with MYC expression levels (Figure S5D).

Reference: Cancer Cell. 2019 Nov 11;36(5):483-497.e15. https://www.ncbi.nlm.nih.gov/pmc/articles/pmid/31679823/

In vivo activity

The initial in vivo rapid screen results demonstrated that 361 inhibited MycCaP tumor growth, indicating that it has suitable pharmacokinetic properties in vivo to show efficacy. In agreement with this, pharmacokinetic analyses after intraperitoneal (i.p.) or oral (p.o.) dosing of 361 in mice indicate plasma half-lives of 44 hr and 20 hr, respectively (Figure 4A), with maximum plasma concentrations (Cmax) of 27200 ng/ml (46 μM) i.p. and 13867 ng/ml (23 μM) p.o. (Table S2). At 24 hr post-exposure, the plasma concentration was 12733 ng/ml (21 μM) for i.p. and 5283 ng/ml (9 μM) for p.o. (Table S2). 361 treatment of FVB mice bearing established MycCaP tumor allografts at 100 mg/kg/day induced tumor regression (Figure 4B). With treatment however, mice lost an average 10% of their body weight (Figure S6A). When treatment was stopped, mice regained weight. Treatment was re-started at a dose of 70 mg/kg/day after tumors had attained the original size. 361 was again effective in controlling tumor growth without additional loss in mouse body weight. Further studies confirmed 361 anti-tumor efficacy, including against a prostate PDX model with modest MYC expression as shown in the gene expression prolife (Jackson laboratory Model ID: TM00298) (Figure 4C). Ki67 proliferation marker was decreased and MYC pT58 level was increased in tumor tissues after 361 treatment (Figure 4D). Importantly, enhanced pT58 levels in tumor tissue after 361 treatment is consistent with in vitro observations, and provides pharmacodynamic evidence of 361 engaging MYC in tumor tissue. Next, 361 anti-tumor efficacy in immune-competent FVB mice was compared versus immunocompromised NSG mice. FVB and NSG mice bearing MycCaP tumor grafts were treated with 361 at 50 mg/kg/day for 4 days. 361 exhibited a stronger tumor inhibitory effect in immunocompetent FVB mice than in the immunodeficient NSG mice (Figure 4E), suggesting that full anti-tumor efficacy of 361 is dependent on an intact immune system.

Reference: Cancer Cell. 2019 Nov 11;36(5):483-497.e15. https://www.ncbi.nlm.nih.gov/pmc/articles/pmid/31679823/