Product data sheet

MedKoo

MedKoo Cat#: 205746 Name: Taselisib (GDC0032) CAS#: 1282512-48-4 Chemical Formula: $C_{24}H_{28}N_8O_2$ Exact Mass: 460.23352 Molecular Weight: 460.53	
Product supplied as:	Powder
Purity (by HPLC):	$\geq 98\%$
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:

Taselisib, also known as GDC0032 or RG7606, is a selective, potent, orally bioavailable inhibitor of PI3Ka with a Ki = 0.2nM, and with reduced inhibitory activity against PI3Kβ. This selectivity profile, and excellent pharmacokinetic and pharmaceutical properties, allowed for greater efficacy in vivo at the maximum tolerated dose relative to a pan Class I PI3K inhibitor in PIK3CA mutant xenografts. Notably, GDC-0032 preferentially inhibited PIK3CA mutant cells relative to cells with wild-type PI3K. GDC-0032 potently inhibits signal transduction downstream of PI3K and induces apoptosis at low concentrations in breast cancer cell lines and xenograft models that harbor PIK3CA mutations.

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	63.33	137.52
Ethanol	7.0	15.20

4. Stock solution preparation table:

Concentration / Solvent Volume / Mass	1 mg	5 mg	10 mg
1 mM	2.17 mL	10.86 mL	21.71 mL
5 mM	0.43 mL	2.17 mL	4.34 mL
10 mM	0.22 mL	1.09 mL	2.17 mL
50 mM	0.04 mL	0.22 mL	0.43 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. Moore HM, Savage HM, O'Brien C, Zhou W, Sokol ES, Goldberg ME, Metcalfe C, Friedman LS, Lackner MR, Wilson TR. Predictive and Pharmacodynamic Biomarkers of Response to the Phosphatidylinositol 3-Kinase Inhibitor Taselisib in Breast Cancer Preclinical Models. Mol Cancer Ther. 2020 Jan;19(1):292-303. doi: 10.1158/1535-7163.MCT-19-0284. Epub 2019 Sep 18. PMID: 31534012.

2. Lopez S, Schwab CL, Cocco E, Bellone S, Bonazzoli E, English DP, Schwartz PE, Rutherford T, Angioli R, Santin AD. Taselisib, a selective inhibitor of PIK3CA, is highly effective on PIK3CA-mutated and HER2/neu amplified uterine serous carcinoma in vitro and in vivo. Gynecol Oncol. 2014 Nov;135(2):312-7. doi: 10.1016/j.ygyno.2014.08.024. Epub 2014 Aug 27. PMID: 25172762; PMCID: PMC4270135.

In vivo study

1. Lopez S, Schwab CL, Cocco E, Bellone S, Bonazzoli E, English DP, Schwartz PE, Rutherford T, Angioli R, Santin AD. Taselisib, a selective inhibitor of PIK3CA, is highly effective on PIK3CA-mutated and HER2/neu amplified uterine serous carcinoma in vitro and

in vivo. Gynecol Oncol. 2014 Nov;135(2):312-7. doi: 10.1016/j.ygyno.2014.08.024. Epub 2014 Aug 27. PMID: 25172762; PMCID: PMC4270135.

2. Ndubaku CO, Heffron TP, Staben ST, Baumgardner M, Blaquiere N, Bradley E, Bull R, Do S, Dotson J, Dudley D, Edgar KA, Friedman LS, Goldsmith R, Heald RA, Kolesnikov A, Lee L, Lewis C, Nannini M, Nonomiya J, Pang J, Price S, Prior WW, Salphati L, Sideris S, Wallin JJ, Wang L, Wei B, Sampath D, Olivero AG. Discovery of 2-{3-[2-(1-isopropyl-3-methyl-1H-1,2-4-triazol-5-yl)-5,6-dihydrobenzo[f]imidazo[1,2-d][1,4]oxazepin-9-yl]-1H-pyrazol-1-yl}-2-methylpropanamide (GDC-0032): a β-sparing phosphoinositide 3-kinase inhibitor with high unbound exposure and robust in vivo antitumor activity. J Med Chem. 2013 Jun 13;56(11):4597-610. doi: 10.1021/jm4003632. Epub 2013 Jun 3. PMID: 23662903.

7. Bioactivity

Biological target:

Taselisib (GDC-0032) is a potent PI3K inhibitor targets PIK3CA mutations, with Kis of 0.12 nM, 0.29 nM, 0.97 nM, and 9.1 nM for PI3Kδ, PI3Kα, PI3Kγ and PI3Kβ, respectively.

In vitro activity

Phosphorylated HER2 (pHER2), along with phosphorylated HER3 and phosphorylated EGFR, were induced following taselisib treatment in both the HER2^{+}/*PIK3CA*[WT] AU565 and the HER2^{+}/*PIK3CA*[mut] KPL-4 cells (Fig. 2C). Immunoblot analysis of a larger subset of HER2^{+} cell lines confirmed a consistent pattern of pHER2 upregulation following taselisib treatment in HER2^{+}/*PIK3CA*[mut] cells, but this was not seen in HER2^{+}/*PIK3CA*[WT] cells (Fig. 2D). PI3K pathway suppression and induction of apoptosis, as assessed by cleaved PARP and cleaved caspase 3, was induced by inhibition with the dual EGFR and HER2 inhibitor lapatinib in the HER2^{+}/*PIK3CA*[WT] cell lines, whereas these effects were primarily induced by PI3K inhibition in the HER2^{+}/*PIK3CA*[mut] cell lines (Fig. 2D; Supplementary Fig. S2B).

Reference: Mol Cancer Ther. 2020 Jan;19(1):292-303. https://mct.aacrjournals.org/content/19/1/292.long

In vivo activity

Ten mice were randomized in two groups, control and taselisib. No signs of general toxicity were seen in any of the 2 treatment groups harboring the USC-xenograft and no animal died during the experiments or had to be prematurely sacrificed due to signs of systemic drug toxicity. One mouse in the control group had to be sacrificed after 7 days because it reached 1 cm^3 in tumor volume while the remaining control animals had to be sacrificed within 2 weeks secondary to their tumor volume. Taselisib group showed a significant tumor growth inhibition after 14 days of treatment (P=0.007; Figure 5 panel A) and significantly improved OS when compared to the control group (P<0.0001; Figure 5 panel B). The mean survival of the taselisib-treated mice was 45 days.

Reference: Gynecol Oncol. 2014 Nov; 135(2): 312–317. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4270135/

Note: The information listed here was extracted from literature. MedKoo has not independently retested and confirmed the accuracy of these methods. Customer should use it just for a reference only.