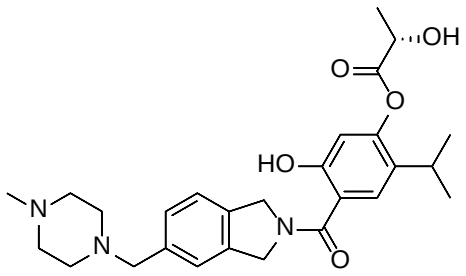
Product data sheet

MedKoo Cat#: 206740 Name: Onalespib lactate CAS: 1019889-35-0 (lactate) Chemical Formula: $C_{27}H_{37}N_3O_6$ Molecular Weight: 499.608	
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:

Onalespib lactate, also known as ATI-13387A, is a second-generation, potent and selective HSP90 Inhibitor. Onalespib Blocks mRNA Splicing of Androgen Receptor Variant 7 in Prostate Cancer Cells. Inhibition of HSP90 by AT13387 delays the emergence of resistance to BRAF inhibitors and overcomes resistance to dual BRAF and MEK inhibition in melanoma models. AT13387 induces senescence in EBV-positive nasopharyngeal carcinoma cells and suppresses tumor formation. AT13387, displays a long duration of action in vitro and in vivo in non-small cell lung cancer.

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
TBD	TBD	TBD

4. Stock solution preparation table:

Concentration / Solvent Volume / Mass	1 mg	5 mg	10 mg
1 mM	2.00 mL	10.01 mL	20.02 mL
5 mM	0.40 mL	2.00 mL	4.00 mL
10 mM	0.20 mL	1.00 mL	2.00 mL
50 mM	0.04 mL	0.20 mL	0.40 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. Lundsten S, Spiegelberg D, Stenerlöw B, Nestor M. The HSP90 inhibitor onalespib potentiates 177Lu-DOTATATE therapy in neuroendocrine tumor cells. Int J Oncol. 2019 Dec;55(6):1287-1295. doi: 10.3892/ijo.2019.4888. Epub 2019 Sep 30. PMID: 31638190; PMCID: PMC6831206.
2. Mehta RK, Pal S, Kondapi K, Sitto M, Dewar C, Devasia T, Schipper MJ, Thomas DG, Basrur V, Pai MP, Morishima Y, Osawa Y, Pratt WB, Lawrence TS, Nyati MK. Low-Dose Hsp90 Inhibitor Selectively Radiosensitizes HNSCC and Pancreatic Xenografts. Clin Cancer Res. 2020 Oct 1;26(19):5246-5257. doi: 10.1158/1078-0432.CCR-19-3102. Epub 2020 Jul 27. PMID: 32718999; PMCID: PMC7541797.

In vivo study

1. Lundsten S, Spiegelberg D, Raval NR, Nestor M. The radiosensitizer Onalespib increases complete remission in 177Lu-DOTATATE-treated mice bearing neuroendocrine tumor xenografts. Eur J Nucl Med Mol Imaging. 2020 Apr;47(4):980-990. doi: 10.1007/s00259-019-04673-1. Epub 2020 Jan 7. PMID: 31912256; PMCID: PMC7075859.
2. Mehta RK, Pal S, Kondapi K, Sitto M, Dewar C, Devasia T, Schipper MJ, Thomas DG, Basrur V, Pai MP, Morishima Y, Osawa Y, Pratt WB, Lawrence TS, Nyati MK. Low-Dose Hsp90 Inhibitor Selectively Radiosensitizes HNSCC and Pancreatic Xenografts. Clin

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Cancer Res. 2020 Oct 1;26(19):5246-5257. doi: 10.1158/1078-0432.CCR-19-3102. Epub 2020 Jul 27. PMID: 32718999; PMCID: PMC7541797.

7. Bioactivity

Biological target:

Onalespib lactate, also known as ATI-13387A, is a second-generation, potent and selective HSP90 Inhibitor.

In vitro activity

The effect of AT13387 on in vitro radio-sensitization was assessed using a clonogenic assay. The amplitude of the effects of 100 nM AT13387 on the global proteome was significantly lower than that of 3 μM AT13387. Interestingly, except for Hsp70, the abundance of any other protein did not reach beyond the 1.5-fold abundance (log scale) level. The magnitude observed on protein levels (total 2145 significantly affected protein out of 5086) suggests that the 3 μM AT13387 concentration would not be selective. Therefore, when given at a dose producing such drug levels in patients, it seems unlikely that the cumulative effect of the drug would be selective for cancer treatment. Altogether, the data suggest that a sub-toxic concentration of AT13387 can cause radio-sensitization regardless of the specific oncogenic driver(s) present in the cell lines.

Clin Cancer Res. 2020 Oct 1; 26(19): 5246–5257. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7541797/

In vivo activity

Following the determination of the pharmacokinetic profile of AT13387, it was sought to determine the duration for which AT13387 can exert its effects in vivo. To investigate these effects, a single 40 mg/kg dose of AT13387 was administered at 0 hours, and a second 40 mg/kg dose at 96 hours, to mice bearing UMSCC74B xenografts. The expression of Hsp70 was analyzed in the tumor at the various time points as previously described. Following administration, pharmacodynamics studies showed that the expression of chaperone protein Hsp70, our biomarker for Hsp90 activity, was upregulated after AT13387 treatment (Figure 5B). This result was confirmed by densitometry analysis, which showed an 8-fold upregulation of Hsp70 expression at 24 and 120 hours (Figure 5B). Nearly 2 to 5-fold increased Hsp70 expression was demonstrated using immunohistochemistry (Figure 5C). This upregulation suggests that AT13387 treatment showed the desired inhibitory effect of Hsp90 inhibition in vivo.This indicates a potential role of the immune component in radiosensitization by AT13387.

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