MLN8237 (Alisertib) Datasheet

**Technical Data**

<table>
<thead>
<tr>
<th>Molecular Weight (MW)</th>
<th>518.92</th>
</tr>
</thead>
<tbody>
<tr>
<td>Formula</td>
<td>C27H32ClF6N4O4</td>
</tr>
<tr>
<td>CAS No.</td>
<td>102846-01-2, 1186318-95-5, 102846-06-7 (sodium salt)</td>
</tr>
<tr>
<td>Synonyms</td>
<td>N/A</td>
</tr>
<tr>
<td>Solubility (25°C)</td>
<td>DMF: 1 g/mL, water &lt; 1 mg/mL, ethanol &lt; 1 mg/mL</td>
</tr>
<tr>
<td>Storage</td>
<td>2 years at -20°C in Powder, 2 weeks at 4°C in DMSO, 6 months at -80°C in DMSO</td>
</tr>
</tbody>
</table>

**Biological Activity**

**Description**: MLN8237 (Alisertib) is a selective Aurora A inhibitor with IC50 of 1.2 nM.

**Targets**: Aurora A

**IC50**: 1.2 nM[1]

**In vitro**: MLN8237 shows >200-fold higher selectivity for Aurora A than the structurally related Aurora B with an IC50 of 396.5 nM, and does not have any significant activity against 205 other kinases.[1] MLN8237 (0.5 μM) treatment inhibits the phosphorylation of Aurora A in MM1.S and OPM1 cells, without affecting the Aurora B mediated histone H3 phosphorylation. MLN8237 significantly inhibits cell proliferation in multiple myeloma (MM) cell lines with IC50 values of 0.003-1.71 μM. MLN8237 displays more potent anti-proliferation activity against primary MM cells and MM cell lines in the presence of BM stroma cells, as well as in L-6 and IGF-1 than against MM cells alone. MLN8237 (0.5 μM) induces 2- to 6-fold increase in G2M phase in primary MM cells and cell lines, as well as significant apoptosis and senescence, involving the up-regulation of p53, p21 and p27, as well as PARP, caspase 3, and caspase 9 cleavage. In addition, MLN8237 shows strong synergistic anti-MM effect with doxetmab, as well as additive effect with doxorubicin and bortezomib.[2] MLN8237 (0.5 μM) treatment causes the induction of cell formation of FLO-1, OE19, and OE33 esophageal adenocarcinoma cell lines, and induces a significant increase in the percentage of polyploid cells, and subsequently an increase in the percentage of cells in the sub-G1 phase, which can be further enhanced in combination with cisplatin (2.5 μM), involving the higher induction of TAp73p38, PUMA, NOXA, cleaved caspase-3, and cleaved PARP as compared with a single-agent treatment.[3]

**In vivo**: MLN8237 significantly reduces the tumor burden with tumor growth inhibition (TGI) of 42% and 80% at 15 mg/kg and 30 mg/kg, respectively, and prolongs the survival of mice compared with the control.[2]

**Clinical Trials**: A Phase II study of MLN8237 for treatment of patients with ovarian, fallopian tube, or peritoneal carcinoma has been completed.

**Features**: First orally available inhibitor of Aurora A

**Protocol (Only for Reference)**

**Kinase Assay:**[1]

- **Aurora A radioactive Flashplate enzyme assay**: Aurora A radioactive Flashplate enzyme assay is conducted to determine the nature and degree of MLN8237-mediated inhibition in vitro. Recombinant Aurora A is expressed in Sf9 cells and purified with GST affinity chromatography. The peptide substrate for Aurora A is conjugated with biotin (Biotin-GLRRASLG). Aurora A kinase (5 nM) is assayed in 50 mM Hepes (pH 7.5), 10 mM MgCl₂, 5 mM DTT, 0.05% Tween 20, 2 μM peptide substrate, 3.3 μCi/mL [γ-33P]ATP at 2 μM, and increasing concentrations of MLN8237 by using Image FlashPlates.

**Cell Assay:**[2]

- **Cell Lines**: MM1.S, MM1.R, L55, RPMI 8226, DOX40, OPM1, OPM2, INA6, and U266
- **Concentrations**: Dissolved in DMSO, final concentrations ~10 μM
- **Incubation Time**: 24, 48, and 72 hours

**Methods**: Cells are exposed to various concentrations of MLN8237 for 24, 48, and 72 hours. Cells viability is measured using MTT assay, and cell proliferation is measured using [3H]-thymidine incorporation. For cell cycle analysis, cells are permeabilized by 70% ethanol at -20 °C, and incubated with 50 μl/gi, PI and 20 units/mL RNase-A. DNA content is analyzed by flow cytometry using BDFACS-Canto II and FlowJo software. For the detection of apoptosis and senescence, cells are stained with fluorescein isothiocyanate-annexin V and PI. Apoptotic cells are determined by flow cytometric analysis using BDFACS-Canto II and FlowJo software.

**Animal Study:**[2]

- **Animal Models**: Severe combined immune-deficient (SCID) mice inoculated subcutaneously with MM1.S cells
- **Formulation**: Formulated in 10% 2-hydroxypropyl-β-cyclodextrin/1% sodium bicarbonate

---

1. **Toll Free**: (877) 796-6397
2. **Fax**: +1-713-796-9816
3. **Orders**: +1-832-582-8158
4. **Tech Support**: +1-832-582-8158 Ext3
5. **Website**: www.selleckchem.com
Doses
~30 mg/kg/day
Administration
Orally

References

Customer Reviews

Inhibition of Aurora A (12.5 nM) by MLN8054 or MLN8237 was assessed in duplicate radiometric assays containing 100 μM [γ-32P] ATP and quantified by p81 phosphocellulose assay and scintillation counting. Kinase activity is reported as a percentage of control calculated from duplicate incubations containing 2.5% (v/v) DMSO. IC50 values represent the mean ±SEM calculated from two independent experiments.

The effects of T217D and T217N Aurora A mutations were directly compared to WT Aurora A-expressing cells. Each well was treated with either DMSO or 500 nM MLN8054 (E), or 30 nM MLN8237 (F) on day one of the experiment and cells were cultured for 8 days, at which point they were fixed. For all colony assays, an area encompassing >90% of the colonies per dish is shown. Similar results were seen in two independent duplicate experiments.

PLEASE KEEP THE PRODUCT UNDER -20°C FOR LONG-TERM STORAGE.

NOT FOR HUMAN, VETERINARY DIAGNOSTIC OR THERAPEUTIC USE

Specific storage and handling information for each product is indicated on the product datasheet. Most Selleck products are stable under the recommended conditions. Products are sometimes shipped at a temperature that differs from the recommended storage temperature. Many products are stable in the short-term at temperatures that differ from that required for long-term storage. We ensure that the product is shipped under conditions that will maintain the quality, but save your shipping charges by using the most economical storage conditions for an overnight shipment. Upon receipt of the product, follow the storage recommendations on the product datasheet.