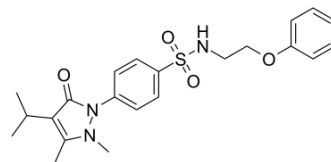


BC-LI-0186

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|---------------------------|---|
| Cat. No.: | HY-136265 |
| CAS No.: | 695207-56-8 |
| Molecular Formula: | C ₂₂ H ₂₇ N ₃ O ₄ S |
| Molecular Weight: | 429.53 |
| Target: | Aminoacyl-tRNA Synthetase |
| Pathway: | Metabolic Enzyme/Protease |
| Storage: | Please store the product under the recommended conditions in the Certificate of Analysis. |



BIOLOGICAL ACTIVITY

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|-------------------------------------|--|------------|-------------|----------------|--|------------------|---|---------|---|
| Description | BC-LI-0186 is a potent and selective inhibitor of Leucyl-tRNA synthetase (LRS; LeuRS) and Ras-related GTP-binding protein D (RagD) interaction (IC ₅₀ =46.11 nM). BC-LI-0186 competitively binds to the RagD interacting site of LRS (K _d =42.1 nM) and has on effects on LRS-Vps34, LRS-EPRS, RagB-RagD association, mTORC1 complex formation or the activities of 12 kinases. BC-LI-0186 can effectively suppress the activity of cancer-associated MTOR mutants and the growth of rapamycin-resistant cancer cells. BC-LI-0186 is a promising agent for lung cancer research ^{[1][2]} . | | | | | | | | |
| IC₅₀ & Target | IC ₅₀ : 46.11 nM (LeuRS and RagD interaction) ^[1] K _d : 42.1 nM (LeuRS and RagD interaction) ^[1] | | | | | | | | |
| In Vitro | <p>BC-LI-0186 (0-20 μM; starved for 90 min in the leucine-free medium and then in the serum-free media for 15 min) inhibits phosphorylation of S6K in a dose- and time-dependent manner, but it has no effects on hosphorylation of AKT (S473)^[1]. BC-LI-0186 (0-20 μM; 6 hours) induces cleaved poly (ADP-ribose) polymerase (PARP) and caspase-3 and an increase of p62 in A549 and H460 cells^[1].</p> <p>BC-LI-0186 exhibits cytotoxic effect at nanomolar concentration in NSCLC cells, it exhibits IC₅₀ values of 98 nM, 206 nM, 55 nM, 78 nM, 83 nM, 86 nM, 102 nM, 109 nM, 128 nM, and 206 nM in A549, H460, H2228, H1703, SNU1330, H1650, H2009, H358, H2279, H460, and H596 cells, respectively^[1].</p> <p>BC-LI-0186 overcome acquired rapamycin resistance and inhibits the mTORC1 pathway in isogenic HCT116 cell lines that harbored either M TOR WT (HCT116 MW) or S2035I mutations (HCT116 MM), it exhibits little changed efficacy between the wild-type and mutant cells (GI₅₀: 39.49 nM and 42.03 nM, EC₅₀: 105.03 nM and 100.45 nM)^[1].</p> <p>MCE has not independently confirmed the accuracy of these methods. They are for reference only.</p> <p>Cell Viability Assay^[1]</p> <table border="1"> <tr> <td>Cell Line:</td> <td>NSCLC cells</td> </tr> <tr> <td>Concentration:</td> <td>0 μM, 0.1 μM, 0.2 μM, 1 μM, 2 μM, 5 μM, 10 μM, 20 μM</td> </tr> <tr> <td>Incubation Time:</td> <td>Starved for 90 min in the leucine-free medium and then in the serum-free media for 15 min</td> </tr> <tr> <td>Result:</td> <td>Suppressed leucine-mediated mTORC1 activation in NSCLC cells.</td> </tr> </table> | Cell Line: | NSCLC cells | Concentration: | 0 μM, 0.1 μM, 0.2 μM, 1 μM, 2 μM, 5 μM, 10 μM, 20 μM | Incubation Time: | Starved for 90 min in the leucine-free medium and then in the serum-free media for 15 min | Result: | Suppressed leucine-mediated mTORC1 activation in NSCLC cells. |
| Cell Line: | NSCLC cells | | | | | | | | |
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| Incubation Time: | Starved for 90 min in the leucine-free medium and then in the serum-free media for 15 min | | | | | | | | |
| Result: | Suppressed leucine-mediated mTORC1 activation in NSCLC cells. | | | | | | | | |
| In Vivo | BC-LI-0186 (intraperitoneal injection; 50 mg/kg; alone or combines with cisplatin alone; 2 weeks; bid for 5 days per week) exhibits antitumor effects and significantly reduces tumor size compared with treatment with vehicle in an LSL K-ras G12D lung cancer animal model ^[1] . | | | | | | | | |

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

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|-----------------|---|
| Animal Model: | K-ras mouse lung cancer model and LSL K-ras G12D lung cancer animal model ^[1] |
| Dosage: | 50 mg/kg |
| Administration: | Intraperitoneal injection; 50 mg/kg; alone or combines with cisplatin alone; 2 weeks; bid for 5 days per week |
| Result: | Shown activated caspase-3-positive cells higher in the BC-LI-0186-treated group than in the vehicle or cisplatin-treated group. Reduced p-S6 and p-AKT level whereas cisplatin alone has minimal effect on both p-S6 and p-AKT expression. Shown a slight (not statistically significant) increase in body weight during the treatment period. Exhibited a specific inhibition of mTORC1 and not mTORC2. |

REFERENCES

[1]. Jong Hyun Kim, et al. Control of leucine-dependent mTORC1 pathway through chemical intervention of leucyl-tRNA synthetase and RagD interaction. Nat Commun. 2017 Sep 29;8(1):732.

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

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