SYNERGISTIC ACTIVITY OF EP-100 AND CHEMOTHERAPIES IN CANCER CELL LINES

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Abstract 978

Objectives

1. To determine single agent responses in vitro in multi-drug resistant cancer cell lines
2. To determine responses of cells to combination of EP-100 with standard chemotherapeutics
3. To determine responses to sequential or continuous exposure to combination of EP-100 and chemotherapeutics

Materials & Methods

Cell lines used were human sarcoma multi-drug resistant (MESA-DA5x2) and the combination with EP-100 (Graphpad Software Graphpad). In vitro efficacy studies were conducted in 96 well plate format (2,000 cells/well) with single agents (EP-100 or Paclitaxel). 5-fluorouracil, doxorubicin, vincristine, and cisplatinum (CDDP) in combination with EP-100. Inclusions were conducted for 72 h. Cell viability was determined using luminometric assays. Serial/vehicle or 0.1% Triton x100 served as controls for 100% viability and complete cell death.

Results & ctd.

<table>
<thead>
<tr>
<th>Treatment</th>
<th>MESA-DA5x2</th>
<th>MESA-DA5x2</th>
<th>Combination</th>
<th>Combination</th>
<th>Combination</th>
</tr>
</thead>
<tbody>
<tr>
<td>EP-100</td>
<td>3.04 ± 0.05</td>
<td>1.4 ± 0.3</td>
<td>0.21 ± 0.03</td>
<td>0.1 ± 0.02</td>
<td>0.01 ± 0.01</td>
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<tr>
<td>A</td>
<td>54 ± 0.6</td>
<td>19 ± 0.4</td>
<td>0.2 ± 0.01</td>
<td>0.1 ± 0.01</td>
<td>0.01 ± 0.01</td>
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<tr>
<td>C</td>
<td>25.8 ± 0.4</td>
<td>2.1 ± 0.01</td>
<td>15 ± 0.1</td>
<td>0.1 ± 0.01</td>
<td>0.01 ± 0.01</td>
</tr>
<tr>
<td>EP-100 (D)</td>
<td>23.4 ± 0.4</td>
<td>2.3 ± 0.01</td>
<td>15 ± 0.1</td>
<td>0.1 ± 0.01</td>
<td>0.01 ± 0.01</td>
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<tr>
<td>EP-100 (D)</td>
<td>8.8 ± 0.2</td>
<td>2.1 ± 0.01</td>
<td>15 ± 0.1</td>
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<td>0.01 ± 0.01</td>
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<tr>
<td>EP-100 (D)</td>
<td>66 ± 1.32</td>
<td>11 ± 0.4</td>
<td>15 ± 0.1</td>
<td>0.1 ± 0.01</td>
<td>0.01 ± 0.01</td>
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<tr>
<td>EP-100 (D)</td>
<td>66 ± 1.45</td>
<td>11 ± 0.4</td>
<td>15 ± 0.1</td>
<td>0.1 ± 0.01</td>
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Summary

EP-100 increased the potency of Paclitaxel, doxorubicin, vincristine, vinorelbine and cisplatin in drug-resistant cancer cells.

Conclusion

EP-100 sensitizes multi-drug resistant cancer cells expressing LHRH receptors to chemotherapeutics. The combination effect is highly synergistic and requires nanomolar concentrations of EP-100. These results indicate that EP-100 can be a potent anti-cancer agent when used in combination with doxorubicin, paclitaxel, vincristine, vinorelbine or cisplatin.

References


Table 1: EP-100 sensitizes multi-drug resistant cancer cell lines expressing LHRH receptors resulting in potentiation up to 7.6, and synergistic manner in combination with CDDP. The concentration is dose-dependent for IC50 but not for EP-100. Comparisons of EP-100 and CDDP were highly synergistic with CI < 1. The tested agent or cancer drugs are listed in parentheses.

Table 2: EP-100 sensitizes multi-drug resistant cancer cell lines expressing LHRH receptors resulting in potentiation up to 7.6, and synergistic manner in combination with CDDP. The concentration is dose-dependent for IC50 but not for EP-100. Comparisons of EP-100 and CDDP were highly synergistic with CI < 1. The tested agent or cancer drugs are listed in parentheses.