• Constitutive B-cell activation via the BTK BCR has been implicated in a number of B-cell malignancies.1,2

Antibodies provided by Southern Biotech (Birmingham, AL, USA).

Table 1

<table>
<thead>
<tr>
<th>Compound</th>
<th>GI50 (μM)</th>
<th>Standardized</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ibrutinib</td>
<td>0.032</td>
<td>High</td>
</tr>
<tr>
<td>BCL-2</td>
<td>0.123</td>
<td>Medium</td>
</tr>
<tr>
<td>PI3K</td>
<td>0.245</td>
<td>Low</td>
</tr>
</tbody>
</table>

• Growth inhibition (GI) was utilized as a measure of cell viability and represented complete growth inhibition, and a GI of 200% was used to measure combination effects, which manifest as potency increase.

RESULTS

Single-Agent Dose-Response Analysis

In the absence of combination, Ibrutinib was active across all cell lines with GI50 values ranging from 0.03 to 0.24 μM (Figure 2).

Combination Activity Based on Synergy Score Analysis

• Ibrutinib combinations with BCL-2 and PI3K inhibitors were the most potent across various combinations screened.

• Strong synergy was also observed in SU-DHL-6, P3X1, and DOHH-2 cell lines.

• Dose matrices of the combination of Ibrutinib with BCL-2 and PI3K inhibitors are shown in Figure 4.

• Synergy score analysis revealed strong synergy across several histologies (DLBCL, FL, MCL, AML) with median synergy scores of 40.0 and 21.6 for the Ibrutinib/BCL-2 and Ibrutinib/PI3K combinations.

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ACKNOWLEDGMENTS

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