**Targeted Therapeutics in CLL and MCL**

**Applying Emerging BTK Inhibitor Therapy Data to Practice**

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### MoA for Approved BTK Inhibitors

<table>
<thead>
<tr>
<th>Covalent BTKi</th>
<th>Non-covalent BTKi</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ibrutinib</td>
<td>Pirtobrutinib</td>
</tr>
</tbody>
</table>

- **Ibrutinib**: a non-covalent BTKi that binds reversibly to the BTK protein in the ATP binding pocket.
- **Pirtobrutinib**: a non-covalent, reversible BTKi that binds covalently to the BTK protein in the ATP binding pocket.

### Drug Interactions

- **Avoid grapefruit juice**
- **Avoid or hold posaconazole, rifampin, rifabutin, nelfinavir**
- **Avoid or hold posaconazole, rifampin, rifabutin, nelfinavir**

### COVID-19 Considerations

- **Non-covalent, reversible BTKi**
- **Covalent BTK inhibitor**

### Dose Modifications

**Ibrutinib Dose Modifications**

- Grade 3 cardiac arrhythmias
- Grade 3 arrhythmias
- Grade 3 cardiac arrhythmias
- Grade 3 cardiac arrhythmias

**Zanubrutinib Dose Modifications**

- Grade 3 cardiac arrhythmias
- Grade 3 cardiac arrhythmias
- Grade 3 cardiac arrhythmias
- Grade 3 cardiac arrhythmias

**Pirtobrutinib Dose Modifications**

- Grade 3 cardiac arrhythmias
- Grade 3 cardiac arrhythmias
- Grade 3 cardiac arrhythmias
- Grade 3 cardiac arrhythmias

### Approximate Rates of Select AEs

<table>
<thead>
<tr>
<th>Ibrutinib</th>
<th>Acalabrutinib</th>
<th>Zanubrutinib</th>
<th>Pirtobrutinib</th>
</tr>
</thead>
<tbody>
<tr>
<td>Grade ≥3:</td>
<td>Grade ≥3:</td>
<td>Grade ≥3:</td>
<td>Grade ≥3:</td>
</tr>
<tr>
<td>Anemia:</td>
<td>Bruising or Bleeding</td>
<td>Bruising or Bleeding</td>
<td>Bruising or Bleeding</td>
</tr>
<tr>
<td>1%</td>
<td>16-23%</td>
<td>14%</td>
<td>26%</td>
</tr>
<tr>
<td>Thrombocytopenia:</td>
<td>13%</td>
<td>11%</td>
<td>13%</td>
</tr>
<tr>
<td>14%</td>
<td>13%</td>
<td>11%</td>
<td>13%</td>
</tr>
<tr>
<td>Neutropenia:</td>
<td>26%</td>
<td>23%</td>
<td>9%</td>
</tr>
<tr>
<td>41-51%</td>
<td>27%</td>
<td>9%</td>
<td>9%</td>
</tr>
<tr>
<td>Any Grade:</td>
<td>Any Grade:</td>
<td>Any Grade:</td>
<td>Any Grade:</td>
</tr>
<tr>
<td>73-81%</td>
<td>41-51%</td>
<td>9-14%</td>
<td>9-14%</td>
</tr>
</tbody>
</table>

### Dosing and Administration

- **Ibrutinib**: 56 mg twice daily
- **Acalabrutinib**: 100 mg orally twice daily or 320 mg once daily
- **Zanubrutinib**: 160 mg twice daily or 320 mg once daily
- **Pirtobrutinib**: 320 mg once daily

### Consider Switching BTKi due to AE Intolerance

<table>
<thead>
<tr>
<th>AEs</th>
<th>Ibrutinib</th>
<th>Acalabrutinib</th>
<th>Zanubrutinib</th>
<th>Pirtobrutinib</th>
</tr>
</thead>
<tbody>
<tr>
<td>33%</td>
<td>85%</td>
<td>85%</td>
<td>93%</td>
<td>86%</td>
</tr>
<tr>
<td>66%</td>
<td>85%</td>
<td>85%</td>
<td>93%</td>
<td>86%</td>
</tr>
<tr>
<td>67%</td>
<td>85%</td>
<td>85%</td>
<td>93%</td>
<td>86%</td>
</tr>
<tr>
<td>127</td>
<td>85%</td>
<td>85%</td>
<td>93%</td>
<td>86%</td>
</tr>
</tbody>
</table>

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**Abbreviations**

- AEs: adverse events
- AEG: area under the curve
- BID: twice daily
- CYP: cytochrome P450
- DDI: drug-drug interaction
- Hb: hemoglobin
- MCL: mantle cell lymphoma
- MoA: mechanism of action
- MTD: maximum tolerated dose
- NSF: nephrogenic systemic fibrosis
- PK: pharmacokinetics
- PD: pharmacodynamics
- QID: four times daily
- PPI: proton pump inhibitor
- QoL: quality of life
- SLL: small lymphocytic lymphoma
- Td: time to doubling
- TDM: therapeutic drug monitoring
- WBC: white blood cell
- W/L: wild-type/Lex

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**Source:**

- 8. Google Search: "Ibrutinib and other BTK inhibitors".
- 10. Google Search: "BTK inhibitors for chronic lymphocytic leukemia".
- 11. Google Search: "Zanubrutinib and other BTK inhibitors".
- 12. Google Search: "Pirtobrutinib and other BTK inhibitors".
- 14. Google Search: "BTK inhibitors in NHL".

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**This infographic was supported by an educational grant from Lilly.**


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