Safety and Efficiency of ABR in Pts with TN or R/R MCL: Ph Ib Trial

Tziel Phillips, MD, Michael Wang, MD, Tezkirreki Robu, MD, PhD, David Gellerman, DO, Dan Stevenson, MD, Michael Wang, MD, PhD, Chan-Chuan Wu, PhD, PhD, Wojciech Jureczak, MD, PhD, Stephen B. Smith, MD,*

Introduction

- Acalabrutinib is an oral, Bruton’s tyrosine kinase (BTK) inhibitor that has demonstrated activity in patients with relapsed or refractory mantle cell lymphoma (MCL).
- Acalabrutinib is a novel oral medication also approved for the treatment of patients with MCL (relapsed) or stops responding to treatment (refractory). One of the treatments approved for patients with MCL included rituximab (R) followed by cyclophosphamide, doxorubicin, vincristine, and prednisone (CHOP) with rituximab maintenance.

Methods

- The current trial was a Ph Ib, single-arm, open-label, dose-escalation trial that enrolled 38 previously treated MCL patients in 2 cohorts: TN (n=18) and R/R (n=20).
- The TN cohort included patients with a time from diagnosis to treatment failure of ≤12 months, and R/R cohort included patients with relapsed or refractory MCL.
- The primary endpoint was overall response rate (ORR) and clinical benefit rate (CBR) at 12 months.
- Efficacy endpoints were assessed per Lugano criteria for non-Hodgkin lymphoma, which require PET/CT and BM biopsy confirmation of CR.

Results

- ORR: 85.0% (95% CI: 62.4, 97.1) and 74.6% (45.0, 89.8) in TN and R/R cohort, respectively.
- CBR: 80.0% (16/20 patients) in the R/R cohort and 72.7, 99.9) in the TN cohort.
- Median PFS: 15.8 months (95% CI: 15.0, 25.8) in TN cohort and 11.0 months (95% CI: 7.1, 23.8) in the R/R cohort.
- There were no cases of atrial fibrillation, ventricular arrhythmias, significant heart failure, or myocardial infarction.
- All patients had normal baseline corrected QT interval.

Data on file. All authors contributed to the study design, conduct of the study, analyses, interpretation of the data, and preparation of the manuscript.

Why was this study done?

- To evaluate the safety and efficacy of acalabrutinib in an open-label phase Ib trial for the treatment of patients with TN and R/R MCL.

What are the results?

- The trial met its primary endpoint of ORR and CBR in both TN and R/R cohorts.
- In the TN cohort, 15 of 18 patients (83.3%) achieved CR, and 3 of 18 (16.7%) achieved partial response (PR). In the R/R cohort, 15 of 20 (75.0%) achieved CR, and 5 of 20 (25.0%) achieved PR.
- The most common AEs included rash (n=8), dyspepsia (n=8), fatigue (n=7), and nausea (n=7) in both cohorts.

What are the implications for patients?

- Acalabrutinib demonstrates efficacy in both newly diagnosed and relapsed/ refractory MCL patients.
- This treatment option offers a potentially safer and more tolerable alternative to traditional chemotherapy regimens.

Key findings:

- Acalabrutinib is an orally administered BTK inhibitor with demonstrated activity in MCL.
- ORR: 85.0% (95% CI: 62.4, 97.1) and 74.6% (45.0, 89.8) in TN and R/R cohort, respectively.
- CBR: 80.0% (16/20 patients) in the R/R cohort and 72.7, 99.9) in the TN cohort.
- Median PFS: 15.8 months (95% CI: 15.0, 25.8) in TN cohort and 11.0 months (95% CI: 7.1, 23.8) in the R/R cohort.
- There were no cases of atrial fibrillation, ventricular arrhythmias, significant heart failure, or myocardial infarction.

References


Figure 3A. Maximum Change From Baseline in Simplified MIPI score. Figure 3B. Kaplan-Meier estimates for overall survival. Figure 3C. Kaplan-Meier estimates for progression-free survival. Figure 4. PFS for TN and R/R Cohorts. Figure 5. OS for TN and R/R Cohorts.
Safety and Efficacy of Acalabrutinib plus Bendamustine and Rituximab in Patients With Treatment-naive or Relapsed/Refractory Mantle Cell Lymphoma: Phase Ib Trial

Supplemental Information

### Events of Clinical Interest

#### Cardiac events
- TN cohort: 4 patients (1 with aortic valve disease [grade 2]; 1 with cardiac failure [grade 3] and tachycardia [grade 1]; 1 with tachycardia [grade 3]; and 1 with pericardial effusion [grade 3])
- R/R cohort: 4 patients (1 with tachycardia [grade 1]; 1 with unstable angina [grade 4]; 1 with angina pectoris [grade 3]; and 1 with acute coronary syndrome [grade 3])

#### Hemorrhage
- TN cohort: 8 patients (1 with hematuria [grade 2], alveolar hemorrhage [grade 4], and hematoma [grade 1]; 1 with ecchymosis [grade 1]; 1 with contusion [grade 1], hemorrhositis [grade 3], and ecchymosis [grade 1]; 1 with hemochezia, rectal hemorrhage, epistaxis, and petechiae [all grade 1]; 1 with gingival bleeding, rectal hemorrhage, contusion, and epistaxis [all grade 1]; and 1 with contusion [grade 1])
- R/R cohort: 6 patients (1 with hemoptysis [grade 1]; 1 with contusion and hemoptysis [both grade 1]; 1 with increased tendency to bruise [grade 1] and subdural hematoma [grade 3]; 1 with intestinal hemorrhage [grade 3]; 1 with gastrointestinal hemorrhage [grade 3], contusion, and petechiae [both grade 1]; and 1 with contusion [grade 1])

#### Grade ≥3 infections
- TN cohort: 5 patients (1 with appendicitis [grade 3], pneumonia [grade 3], and sepsis [grade 4]; 2 with pneumonia [each grade 3]; 1 with cellulitis and perineal cellitis [both grade 3]; and 1 with influenza and pneumonia Moraxella [both grade 3])
- R/R cohort: 6 patients (1 with infection [grade 3] and COVID-19 [grade 5]; 1 with bronchitis [grade 3]; 1 with respiratory tract infection and pneumonia [both grade 3]; 1 with appendicitis [grade 3]; 1 with pneumonia [grade 3]; and 1 with otitis [grade 3])

---

### Supplemental Table 1. ABR Discontinuation by Treatment Period – TN Cohort (n=18)

<table>
<thead>
<tr>
<th>Patients, n (%)</th>
<th>Acalabrutinib + Bendamustine + Rituximab Cycles 1–6</th>
<th>Acalabrutinib + Rituximab* Cycles 7–30</th>
<th>Acalabrutinib Monotherapy Cycles 31+</th>
<th>Entire Study Period</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>A</td>
<td>B</td>
<td>R</td>
<td>A</td>
</tr>
<tr>
<td>Ongoing treatment with drug</td>
<td>14 (77.8)</td>
<td>0</td>
<td>15 (83.3)</td>
<td>9 (50.0)</td>
</tr>
<tr>
<td>Completed treatment period</td>
<td>—</td>
<td>15 (83.3)</td>
<td>0</td>
<td>—</td>
</tr>
<tr>
<td>Discontinued treatment with drug</td>
<td>4 (22.2)</td>
<td>3 (16.7)</td>
<td>3 (16.7)</td>
<td>5 (27.8)</td>
</tr>
<tr>
<td>Clinical or objective disease progression</td>
<td>1 (5.6)</td>
<td>1 (5.6)</td>
<td>1 (5.6)</td>
<td>0</td>
</tr>
<tr>
<td>AE</td>
<td>2 (11.1)</td>
<td>2 (11.1)</td>
<td>1 (5.6)</td>
<td>4 (22.2)</td>
</tr>
<tr>
<td>Investigator’s decision</td>
<td>1 (5.6)</td>
<td>0</td>
<td>1 (5.6)</td>
<td>1 (5.6)</td>
</tr>
<tr>
<td>Other</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

*Patients with response ≥PR received rituximab maintenance every other cycle, from cycles 8–30, for 12 doses. Maintenance rituximab was available only for the TN cohort.
*aOther reasons for drug discontinuation were sponsor’s request for final database lock (n=1) and poor clinical condition (n=1).

---

### Supplemental Table 2. ABR Discontinuation by Treatment Period – R/R Cohort (n=20)

<table>
<thead>
<tr>
<th>Patients, n (%)</th>
<th>Acalabrutinib + Bendamustine + Rituximab Cycles 1–6</th>
<th>Acalabrutinib Monotherapy Cycles 7–30</th>
<th>Acalabrutinib Monotherapy Cycles 31+</th>
<th>Entire Study Period</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>A</td>
<td>B</td>
<td>R</td>
<td>A</td>
</tr>
<tr>
<td>Ongoing treatment with drug</td>
<td>18 (90.0)</td>
<td>0</td>
<td>0</td>
<td>7 (35.0)</td>
</tr>
<tr>
<td>Completed treatment period</td>
<td>—</td>
<td>14 (70.0)</td>
<td>18 (90.0)</td>
<td>—</td>
</tr>
<tr>
<td>Discontinued treatment with drug</td>
<td>2 (10.0)</td>
<td>6 (30.0)</td>
<td>2 (10.0)</td>
<td>11 (55.0)</td>
</tr>
<tr>
<td>Clinical or objective disease progression</td>
<td>1 (5.0)</td>
<td>1 (5.0)</td>
<td>1 (5.0)</td>
<td>3 (15.0)</td>
</tr>
<tr>
<td>AE</td>
<td>1 (5.0)</td>
<td>5 (25.0)</td>
<td>1 (5.0)</td>
<td>7 (35.0)</td>
</tr>
<tr>
<td>Investigator’s decision</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>1 (5.0)</td>
</tr>
<tr>
<td>Other</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

*aOne patient discontinued acalabrutinib due to withdrawal of consent.