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INTRODUCTION

• Bcl-2 is an important therapeutic target that contributes to the ability of hematologic malignancies to evade apoptosis
• Upregulation of the anti-apoptotic protein Bcl-2 is a frequent event in NHL pathogenesis and contributes to chemoresistance

• ABT-199 is a selective, orally bioavailable, small molecule Bcl-2 inhibitor under investigation for the treatment of patients with NHL

• In early data, MCL is particularly responsive to ABT-199 treatment and these patients are treated with a modified dose regime to reduce the risk of TLS, similar to the treatment for chronic lymphocytic leukemia (CLL) and small lymphocytic lymphoma (SLL) patients

OBJECTIVES

• Primary
  – Assess safety
  – Determine the maximum tolerated dose (MTD) and recommended phase 2 dose (RP2D)
• Secondary
  – Pharmacokinetics (PK)
  – Efficacy

RESULTS

• As of September 30, 2013, there are 38 patients enrolled in the study and 35 are assessable

Table 1. Table of Patient Characteristics

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>MCL Subjects</th>
<th>MCL Subjects, n (%)</th>
<th>MCL Subjects, n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age years, median (range)</td>
<td>67 (25 – 80)</td>
<td>67 (25 – 80)</td>
<td>67 (25 – 80)</td>
</tr>
<tr>
<td>Gender</td>
<td>Male</td>
<td>39 (84)</td>
<td>Male</td>
</tr>
<tr>
<td>Diagnosis</td>
<td>Mantle Cell (MCL)</td>
<td>12 (26)</td>
<td>Mantle Cell (MCL)</td>
</tr>
<tr>
<td>FL</td>
<td>11 (24)</td>
<td>FL</td>
<td>11 (24)</td>
</tr>
<tr>
<td>Diffuse Large B-Cell (DLBCL)</td>
<td>9 (20)</td>
<td>Diffuse Large B-Cell (DLBCL)</td>
<td>9 (20)</td>
</tr>
<tr>
<td>High-grade T-cell lymphoma (HTLC)</td>
<td>4 (9)</td>
<td>High-grade T-cell lymphoma (HTLC)</td>
<td>4 (9)</td>
</tr>
<tr>
<td>Myeloma</td>
<td>2 (5)</td>
<td>Myeloma</td>
<td>2 (5)</td>
</tr>
<tr>
<td>Bulky nodes</td>
<td>1 (2)</td>
<td>Bulky nodes</td>
<td>1 (2)</td>
</tr>
<tr>
<td>LDH</td>
<td>30 (67)</td>
<td>LDH</td>
<td>30 (67)</td>
</tr>
<tr>
<td>Prior therapies</td>
<td>Median (range)</td>
<td>2 (1 – 6)</td>
<td>Prior therapies</td>
</tr>
<tr>
<td>Prior CHOP</td>
<td>3 (5)</td>
<td>Prior CHOP</td>
<td>3 (5)</td>
</tr>
<tr>
<td>Prior GALT</td>
<td>1 (2)</td>
<td>Prior GALT</td>
<td>1 (2)</td>
</tr>
</tbody>
</table>

Preliminary Efficacy of ABT-199

Figure 2. Current Status of Evaluable Patients

METHODS

• This is a first-in-human, phase I, open-label, dose-escalation, multicenter, international trial in patients with B- and T-cell NHL and CLL/SLL

• The data presented is an analysis of the NHL arm of the study

METHODS (CONTINUED)

• Key Patient Eligibility Criteria
  – **Histologically** confirmed NHL requiring therapy
  – Active infection
  – **14 (37)**
  – **2/3 (67)**
  – All NHL = 5.5 months (range 0.2 to 17.1)

• Initial Dose
  – 0 6 12 18 24
  – >82%

• Adequate bone marrow function: ANC ≥1,000/mL; and ECOG performance status 0 or 1

• Preliminary Efficacy
  – **8/11 (73)**
  – **1/11 (9)**
  – **1/3 (33)**
  – **10 (26)**

• Histology:
  – **2010 BEAM autograft (PR)**

• Primary endpoint: **Objective response rate**

• **3/36 (8)**

• **67 [35 – 85]**

• **2010 2 cycles RICE (PR)**

• **12 (32)**

• **11 (29)**

• **4/8 (50)**

• **Patients with post-transplant lymphoproliferative disease, DCD (or additional therapy – 1 [3])**

• **1/1 (100)**

• **5 (13)**

• **11 (29)**

• **1/8 (13)**

• **–**

CONCLUSIONS

• ABT-199 showed anti-tumor activity as monotherapy for several NHL subtypes, with an overall response rate of 31% in this R/R population

• Anti-tumor activity was seen in patients with MCL, with 82% achieving at least a PR, including 1 MCL patient achieving CR

• Across the range of ABT-199 doses, responses were observed in patients with WM, and in patients with DLBCL and FL, responses were observed at doses ≥600 mg

• Dose escalation is continuing to determine the MTD and RP2D

• Biomarker studies are also underway in various NHL subgroups to explore potential markers predictive of response

DISCLOSURES

M.S. Davids and J.M. Page have no conflicts of interest to declare.

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