Updated Results From a Phase 2 Study of Pracinostat in Combination With Azacitidine in Elderly Patients With Acute Myeloid Leukemia

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BACKGROUND

• Elderly patients with acute myeloid leukemia (AML), deemed unsuitable for intensive therapy, have limited treatment options.
• A phase 1 study of single-agent pracinostat demonstrated clinical activity in patients with AML.
• We previously reported a high initial response rate in the first stage of this phase 2 study of pracinostat plus azacitidine in this population (ASH 2014, Abstract 894). Presented here are updated results, which include additional patients.

METHODS

Treatment Regimen
• Pracinostat 60 mg is administered orally 3 days a week (days 1, 3, and 5 of each week) for 21 days of each 28-day cycle.
• Azacitidine is administered subcutaneously or intravenously on days 1–7 of each cycle.

Eligibility Criteria

• Key inclusion criteria:
  - Age ≥65 years
  - Newly diagnosed de novo, secondary, or treatment-related AML with intermediate or unfavorable-risk cytogenetics based on the Southwest Oncology Group classifications

• Key exclusion criteria:
  - Active central nervous system disease
  - Adequate renal, cardiac, and liver function

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Eligibility Criteria: Key Exclusion

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Study Evaluations

• Primary endpoint: complete response (CR) + complete response with incomplete blood count recovery (CRi) + morphologic leukemia-free state (MLFS)
• Secondary endpoints:
  - Overall response rate (ORR)
  - Complete response rate
  - Duration of response
  - Event-free survival
  - Overall survival (OS)

RESULTS

• 50 patients have been enrolled at 15 centers.
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Table 1. Patient Disposition

<table>
<thead>
<tr>
<th>N=50</th>
<th>Number of patients evaluable (%)</th>
<th>Number of patients discontinued (%)</th>
<th>Reasons for discontinuation (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
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Table 2. Baseline Characteristics

<table>
<thead>
<tr>
<th>N=50</th>
<th>Age, years</th>
<th>Median</th>
<th>Range</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Male</td>
<td>29 (58)</td>
<td>66–84</td>
</tr>
<tr>
<td></td>
<td>Female</td>
<td>21 (42)</td>
<td>66–84</td>
</tr>
</tbody>
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Table 3. Response

<table>
<thead>
<tr>
<th>Response Assessment</th>
<th>CRi (%)</th>
<th>CR (%)</th>
<th>PR (%)</th>
<th>NR (%)</th>
<th>PD (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>CR/CRi/CRi/MLFS (primary endpoint)</td>
<td>27 (54.0)</td>
<td>17 (34.0)</td>
<td>0 (0.0)</td>
<td>6 (12)</td>
<td></td>
</tr>
</tbody>
</table>

Figure 1. Duration on Study and Best Response

Figure 2. Overall Survival (OS) by Risk Group

Table 4. Treatment-Emergent Adverse Events Leading to Drug Discontinuation (n=8)

<table>
<thead>
<tr>
<th>All Terms</th>
<th>Grades</th>
<th>Discontinuation (Cycle/Day)</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pradaxa</td>
<td>3/5</td>
<td>3/5</td>
<td>Resolved</td>
</tr>
<tr>
<td>Prolonged QTc/AF</td>
<td>3/4</td>
<td>2/4</td>
<td>Resolved</td>
</tr>
<tr>
<td>Failure to thrive</td>
<td>2/3</td>
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<td>Not recovered</td>
</tr>
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<td>Fatel</td>
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<tr>
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<td>2/2</td>
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CONCLUSIONS

• Pracinostat in combination with azacitidine demonstrates significant clinical activity in elderly patients with newly diagnosed AML.
  • To date, 27 of 50 patients (54%) achieved the primary endpoint of CR or CRi + MLFS
  • The CR rate was 32% (16/50 patients)
  • Most clinical responses occur within the first 2 cycles and continue to improve with ongoing therapy.
  • Median overall survival has not been reached in the study population.
  • The 6-month mortality rate is 12% (6/50 patients)
  • Survival of patients with intermediate-risk cytogenetic abnormalities appears greater than that for patients with high-risk cytogenetics.
  • Pracinostat in combination with azacitidine was well tolerated in this population of elderly AML patients.
  • The most common treatment-emergent AEs included febrile neutropenia, thrombocytopenia, nausea, and fatigue.
  • All results in dose reductions were uncommon and frequently related to the disease under study.

Figure 3. Baseline Characteristics

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  • The most common treatment-emergent AEs included febrile neutropenia, thrombocytopenia, nausea, and fatigue.
  • All results in dose reductions were uncommon and frequently related to the disease under study.

• Five patients to date have received the study drug beyond 1 year, reflecting long-term tolerability.

• The response rate for the combination of pracinostat plus azacitidine compares favorably with previous studies of azacitidine alone in elderly AML patients (Dombret et al. Blood. 2015).

• While overall survival is encouraging, longer follow-up is necessary to get an accurate survival estimate of the combination.

Disclosures

G. Garcia-Manero receives consultancy fees from MEI Pharma; E. Atallah reports nothing to disclose; S.K. Khaled reports nothing to disclose; M. Arellano reports nothing to disclose; M. Patnaik reports nothing to disclose; V. Esquivel is an employee of MEI Pharma; K. Wood is an employee of MEI Pharma; B. Medeiros receives research funding from MEI Pharma.