Progression free survival (PFS) and Event Free Survival (EFS) from a Global Randomized Phase 3 study of Guadecitabine (G) VS Treatment Choice (TC) in 815 Patients with Treatment Naive (TN) AML Unift for Intensive Chemotherapy (IC): ASTRAL-1 Study

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METHODS

• Eligibility: TN AML patients ineligible for age due to 75 years, or comorbidities, or poor ECOG PS 2 or 3
• Patients randomized 1:1 to G: 60 mg/m² SC dailyx5 or preselected TC (AZA, DEC, or LDAC) using their approved dose and regimen. Cycles repeated Q 28 days. Treatment to be continued till progression or unacceptable toxicity
• Complete Response (CR) was assessed by an independent central pathologist blinded to randomization assignment
• CR and Overall Survival (OS) were co-primary endpoints. PFS was a secondary endpoint
• PFS: defined as from date of randomization to disease progression or death defined as the earliest occurrence of relapse in a responding patient; clinically significant increase in blasts % that necessitate alternative therapy; investigator determined progression, or death
• DFS: defined as from date of randomization to the earliest occurrence of treatment discontinuation, start of alternative therapy, or death. This simple definition avoids assigning a progression date, and is inclusive of patients who may continue treatment due to clinical benefit in the absence of response or overt clinical progression that necessitate alternative therapy

RESULTS

Table 1. Treatment Exposure

<table>
<thead>
<tr>
<th>Treatment Choice</th>
<th>Guadecitabine 100 mg/m²</th>
<th>Treatment Choice n=392</th>
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<tbody>
<tr>
<td>Patients with ≥ 4 cycles</td>
<td>42.4%</td>
<td>40.8%</td>
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<tr>
<td>Patients with ≥ 6 cycles</td>
<td>54.2%</td>
<td>51.8%</td>
</tr>
</tbody>
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• All patients with ≥ 4 cycles were included for OS and DFS analyses

Table 2: Table 2: OS; PFS; EFS results for ITT; and subgrouping receives at least 4 or 6 cycles

<table>
<thead>
<tr>
<th>Overall Survival (OS)</th>
<th>ITT Population n=815</th>
<th>Patients who had ≥ 4 cycles n=476</th>
<th>Patients who had ≥ 6 cycles n=375</th>
</tr>
</thead>
<tbody>
<tr>
<td>HR (95% CI, p value)</td>
<td>0.88 (0.73-1.06), 0.17</td>
<td>0.86 (0.70-1.07), 0.17</td>
<td>0.84 (0.69-1.00), 0.12</td>
</tr>
</tbody>
</table>

- Number of patients balanced in each comparison: ITT (G, 408 patients; TC 407 patients); Subgroup with ≥ 4 cycles (G, 235 patients; TC 241 patients); Subgroup with ≥ 6 cycles (G, 187 patients; TC 188 patients)
- OS: no difference between G and TC for the ITT analysis. G better than TC in the subgroups receiving ≥ 4 and ≥ 6 cycles

Figure 3. EFS in the Primary ITT Population (N=815)

Figure 4. EFS in subgroup who received at least 4 cycles (N=476)

SUMMARY/CONCLUSIONS

• ASTRAL-1 was the largest randomized study conducted in TN AML unift for IC
• Primary ITT analyses showed no significant differences between G and TC in the co-primary endpoints of CR rate or OS
• ~ 41 to 54% of patients (balanced between the 2 arms) did not receive the minimum of 4 to 6 cycles recommended to achieve maximum benefit with HMAs. G was superior to TC in OS subgroups who received at least 4 or 6 cycles
• EFS defined as from date of randomization to the earliest of treatment discontinuation, start of alternative therapy, or death. Using EFS as defined, G treatment was associated with superior OS benefit over TC in the ITT population, as well as in the subgroups of patients who received at least 4 or 6 cycles, and the subgroup of patients who responded to treatment
• The data suggest that continuation of HMA treatment with guadecitabine is associated with survival benefit

REFERENCES


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