First Results of a 10-Day Regimen of SGI-110 (Guadecitabine), a Second Generation Hypomethylating Agent (HMA) in Previously Untreated Elderly AML Who are Not Candidates for Intensive Chemotherapy

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Background

• Elderly and unfit individuals with AML are often ineligible to receive intensive chemotherapy
• Hypomethylating agents (HMA) such as decitabine and azacitidine have shown efficacy and acceptable safety in these patients
• SGI-110 (guadecitabine) is a next generation HMA given as a small volume subcutaneous (SC) administration

We previously presented Phase 2 data of SGI-110 using the standard 5-day regimen which showed good clinical activity in these patients1. We present preliminary results for the 10-day regimen (SGI). We present results for the 10-day regimen (SGI), which showed good clinical activity and more cycling leukemic cells as a result of the exposure time (Figure 1). This allows decitabine incorporation into DNA of more cycling leukemic cells as a result of the longer exposure time

ogy 1 (SC) administered which showed good clinical activity

Figure 1: Guadecitabine SC Results in Prolonged Exposure Window to Active Metabolite Decitabine

Open-label single arm phase 2 study of guadecitabine given as a 10-day regimen q 28 days for up to 4 cycles followed by 5-day regimen in previously untreated elderly AML patients who are not candidates for intensive chemotherapy (TN IC-Ineligible AML).

Overall Study Goals

• Primary: Evaluate the activity of SC guadecitabine given as a 10-day regimen in TN IC-ineligible AML as measured by the Overall Composite Complete Remission (CRc) rate (CR+CPR+CRi). Secondary: Duration of response, overall survival (OS), and safety

Major Eligibility Criteria

• Adults > age 65 with treatment naive AML ineligible for IC
• ECOG Performance Status 0-2
• No symptomatic CNS involvement
• No limits on WBC or blasts
• Adequate hepatorenal function
• Informed consent

Table 2: Clinical Responses in Treatment Naive TN IC-Ineligible AML

Table 4: All-Cause Early Mortality

Table 3: Most Commonly Reported Grade > 3 AEs Regardless of Relationship (>10%)

References

1. Nye K et al. (2016). European Hematology Association, abstr 5467

Figure 4: Cycle 1 LINE-1 Demethylation 5-Day vs 10-Day Regimen

In treatment naive AML patients, the 10-day schedule shows a longer duration of LINE-1 demethylation compared to the 5-day regimen

Figure 2: Guadecitabine 10-Day regimen for AML

Guadecitabine was given as 60 mg/m²/d SC days 1-5 and 8-12 Q28 days for up to 4 cycles based upon tolerance followed by treatment on days 1-5 Q28 days for a total of at least 6 cycles

Table 1: Treatment Naive IC-Ineligible AML Patient Characteristics

RESULTS

73% of patients (38/52) received 2 cycles of guadecitabine 10-day regimen 48% of patients (25/52) continue on treatment with 5-day regimen