Acute myeloid leukemia (AML) has a poor prognosis, and is associated with higher disease burden and lower survival rates compared to other hematopoietic malignancies. IDH1 and IDH2 mutations in AML result in the production of 2-HG, which can accumulate in cancer cells. This accumulation leads to metabolic dysregulation and blockage of cellular differentiation, contributing to oncogenesis.

As of February 19, 2019, 10 patients (43.5%) remained on study treatment.

Azacitidine treatment has been found to prolong overall survival in patients with newly diagnosed AML. The treatment was associated with favorable outcomes, including a 28-day overall survival rate of 12/16 (75%) and 1/2 (50%) for patients with newly diagnosed and relapsed or refractory AML, respectively. The median duration of response was 1.8 (0.7–3.8) months, with a median treatment duration of 25 (4–78) days.

An independent data monitoring committee will monitor the data throughout the study. To evaluate the efficacy and safety of the AGILE study, an amendment to revise the primary endpoint to event-free survival is in progress. The study is ongoing (NCT02677922).

**Objective:**

To evaluate the efficacy and safety of ivosidenib plus azacitidine in adults with previously untreated AML who do not meet candidate criteria for intensive treatment.

**Primary Outcomes:**

- Time to event (progression-free survival, overall survival, and event-free survival) for the combination of ivosidenib and azacitidine
- Response rates
- Rates of infection and hospitalization
- Transfusion requirements
- Rates of infection and hospitalization
- Quality of life

**Secondary Outcomes:**

- Rates of infection and hospitalization
- Quality of life
- Safety
- Translation requirements
- Rates of infection and hospitalization
- Quality of life

**Statistical Analysis:**

The study has 80% power to detect a hazard ratio of 0.71 for overall survival (ivosidenib + azacitidine vs placebo + azacitidine), with a one-sided alpha of 0.05.