(S1560) IVOSIDENIB (AG-120) IN MUTANT IDH1 RELAPSED/REFRACTORY ACUTE MYELOID LEUKEMIA: RESULTS OF A PHASE 1 STUDY

Daniel A. Pollyea, et al.

Abstract: S1560

Type: Oral Presentation

Presentation during EHA23: On Sunday, June 17, 2018 from 08:00 - 08:15

Location: Victoria Hall

Background

Ivosidenib (IVO; AG-120) is an oral, targeted inhibitor of mutant isocitrate dehydrogenase 1 (mIDH1) that is being evaluated in a phase 1 dose escalation and expansion study of mIDH1 advanced hematologic malignancies (NCT02074839).

Aims

To report updated efficacy and safety data from all patients with relapsed/refractory acute myeloid leukemia (R/R AML) receiving IVO 500 mg once daily (QD).

Methods

All patients provided written informed consent. The primary efficacy endpoint was the CR+CRh rate (complete remission [CR] according to modified IWG 2003 criteria plus CR with partial hematologic recovery [CRh]). CRh was defined as absolute neutrophil count >0.5 × 10^9/L *and* platelet count >50 × 10^9/L. The overall response rate (ORR) comprised CR, CR with incomplete hematologic or platelet recovery, partial response, and morphologic leukemia-free state. The data cutoff date for this analysis was Nov 10, 2017.

Results

A total of 258 patients were treated with IVO. Among 179 R/R AML patients who received IVO 500 mg QD, 17 (9.5%) remained on treatment at data cutoff. In R/R AML patients, the CR+CRh rate was 31.8% (95% CI: 25.1%, 39.2%), including CR in 24.0% (95% CI: 18.0%, 31.0%). Median duration of CR+CRh was 8.2 months (95% CI: 5.6, 12.0), and median duration of CR was 10.1 months (95% CI: 6.5, 22.2). The ORR was 41.9% (95% CI: 34.6%, 49.5%). Treatment was well tolerated; the most common adverse events (AEs) of any grade, irrespective of causality and occurring in ≥25% of 179 R/R AML patients were diarrhea (33.5%), leukocytosis (31.3%), nausea (31.3%), febrile neutropenia (29.1%), fatigue (28.5%), and electrocardiogram QT prolonged (25.7%). The majority of these AEs were grade 1–2 and unrelated to treatment. IDH differentiation syndrome (IDH-DS) was reported in 19 of 179 (10.6%) patients, including grade ≥3 IDH-DS in 9 (5.0%); study drug was held owing to IDH-DS in 6 patients (3.4%), and no instances of IDH-DS led to dose reduction, permanent treatment discontinuation, or death. Updated mutation clearance results will be provided.

Conclusion

In a high-risk, molecularly defined R/R AML patient population, IVO induced durable remissions and was well tolerated. Studies in previously untreated AML populations are ongoing.

Session topic: 4. Acute myeloid leukemia - Clinical

Keyword(s): Acute Myeloid Leukemia, AG-120, Clinical Trial, Relapsed acute myeloid leukemia