(PB2728) EFFICACY AND SAFETY OF GILTERITINIB-BASED COMBINATION THERAPY IN RELAPSED/REFRACTORY FLT3-MUTATED ACUTE MYELOID LEUKEMIA: A REAL-WORLD MULTICENTER STUDY

Topic: 04. Acute myeloid leukemia - Clinical

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Background

Relapsed or refractory acute myeloid leukemia with fms-like tyrosine kinase 3 mutations (R/R FLT3^{mut+}AML) remains a major clinical challenge. Although gilteritinib monotherapy resulted in improved overall survival (OS) compared to salvage chemotherapy for R/R FLT3^{mut+}AML patients, the remission rates and survival with gilteritinib monotherapy are still unsatisfactory. Gilteritinib-based combination therapy demonstrated increased response rates, but the survival did not improve because of increased toxicities. Thus, the optimal regimen for R/R FLT3 mutated AML remained unclear.

Aims

To compare the efficacy and safety of gilteritinib-based combination therapy for R/R FLT3^{mut+}AML.

Methods

Patients with R/R FLT3^{mut+}AML in six hospitals of China were screened from July 2019 to July 2025. Eligible criteria include: (1) aged ≥18 years with confirmed FLT3^{mut+}AML; (2) relapse or refractory (R/R) to first or greater lines of AML treatment (3) received gilteritinib-based therapy: gilteritinib plus venetoclax (Gil+Ven), gilteritinib plus venetoclax and "X" (gilteritinib plus venetoclax and azacitidine, gilteritinib plus venetoclax, azacitidine and homoharringtonine), or gilteritinib combined with intensive chemotherapy (Gil+Chemo). The primary endpoint was the composite complete remission (CRc) rate after 1-2 cycle of treatment. The secondary endpoints were safety, OS, event-free survival (EFS) and relapse.

Results

54 patients were enrolled with a median age of 44.8 years old. 42 patients had FLT3-ITD mutation, 11 had FLT3-TKD mutation and 1 had both mutations. 14 received Gil+Ven, 29 received Gil+Ven+X and 11 received Gil+Chemo. There were no significant differences among the three groups in baseline patient characteristics. Gil+Ven group showed a trend toward higher CRc (85.7%) compared to Gil+Ven+X (65.6%) and Gil+Chemo (63.6%) groups (p=0.341). The CR rate of Gil+Ven group was 71.4%, numerically higher than Gil+Ven+X (41.4%) and Gil+Chemo (54.5%) groups (p=0.127). The MRD-negative rate in the Gil+Ven group (50%) was comparable with the Gil+Ven+X group (56%, p=0.749) and higher than the Gil+Chemo group (28.6%, p=0.401). The proportion of bridging to allogeneic hematopoietic stem cell transplantation were comparable across the Gil+Ven, Gil+Ven+X, and Gil+Chemo groups (57.1% vs. 55.2% vs. 63.6%, respectively, p=0.894). With a median follow-up of 18 months, the median OS was longer in Gil+Ven group (not reached) than that in Gil+Ven+X (7.0 months) or Gil+Chemo (19.0 months) group (p=0.19). Gil+Ven group had a higher 2-year OS (74.48%) than Gil+Ven+X group (31.78%, p=0.009) and Gil+Chemo group (38.35%, p=0.083), respectively. The 2-years EFS were also higher in Gil+Ven group (68.18%) than Gil+Ven+X (24.52%, p=0.006) and Gil+Chemo group (34.09%, p=0.090). Furthermore, the 2-year cumulative incidence of relapse (CIR) was lower in Gil+Ven group (12.5%) than Gil+Ven+X (36.91%, p=0.147) and Gil+Chemo group (46.43%, p=0.144). Gil+Ven group was associated with fewer grades 3 or higher hematologic and non-hematologic adverse events (AEs) compared to the other two groups. In Gil+Ven group, neutropenia (p=0.023), anemia (p=0.048) and BLOOD infection (p=0.045) were significantly less frequent than the other two groups.

Summary/Conclusion

Gilteritinib plus venetoclax demonstrated a trend toward better efficacy and fewer adverse events than other gilteritinib-based combination therapy, suggesting it might be the optimal salvage strategy for R/R FLT3^{mut+}AML.