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P592 GILTERITINIB IN COMBINATION WITH VENETOCLAX, LOW DOSE CYTARABINE AND ACTINOMYCIN D FOR FLT3 MUTATED RELAPSED OR REFRACTORY ACUTE MYELOID LEUKEMIA

Topic: 04. Acute myeloid leukemia - Clinical

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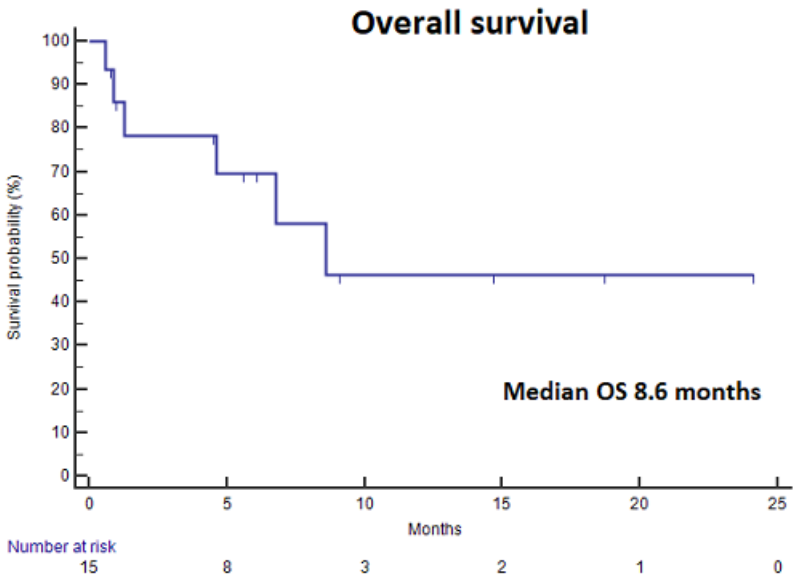
Background: A second generation *FLT3* inhibitor Gilteritinib has become a standard of care for *FLT3* mutated relapsed or refractory acute myeloid leukemia (*FLT3*m R/R AML). However, remission duration and overall survival remain unsatisfactory. Preliminary results of doublet Gilteritinib + Venetoclax and triplet Gilteritinib + Venetoclax + Hypomethylator regimens are encouraging. Herein, we report the quadruplet regimen consisting of Gilteritinib, Venetoclax, Low Dose Cytarabine and Actinomycin D (ACTIVE + G) for the treatment of *FLT3*m R/R AML in the clinical practice setting.

Aims: To evaluate the efficacy and safety of the ACTIVE + G regimen.

Methods: This was an observational, retrospective study. The patients were at least 18 years of age and had *FLT3*m R/R AML. All patients provided informed consent for treatment and data collection. The ACTIVE + G regimen consisted of Venetoclax 600mg/d p/o from day 1 up to day 28, Cytarabine 20mg/m2 s/c on days 1-10, Actinomycin D 12.5 µg/kg i/v on days 1-3 (on days 1-2 for patients ≥65 years) and Gilteritinib 120mg/d p/o starting from either day 4 or day 10 and continued up to day 28. Indications for stopping Venetoclax and Gilteritinib before day 28 were life-threatening infections or faster hematological recovery in responding patients. A second ACTIVE + G cycle was administered in non-responders without evidence of progressive disease after Cycle 1 or in responders with positive measurable residual disease (MRD). Responders after ACTIVE + G could proceed to either allogeneic stem cell transplantation (alloSCT) or maintenance therapy with Venetoclax, Low Dose Cytarabine and Gilteritinib. We evaluated baseline characteristics, composite CR (CRc = CR + CRi + CRp), overall response (ORR = CRc + MLFS), MRD negativity rates (<0.1% by multiparameter flow cytometry), overall survival (OS), relapse-free survival (RFS), grade 3-5 non-hematological toxicities and day 30 and day 60 mortality rates.

Results: Fifteen patients had been treated with ACTIVE + G, of whom 8 (53%) were female. The median age was 66 years (34-87), median ECOG was 2 (0-3). *FLT3-ITD* mutation was confirmed in 80% (12/15) of cases and 20% (3/15) had *FLT3-TKD*. The most common co-mutations were NPM1 (53%, 8/15), *DNMT3A* (27%, 4/15), *IDH1* (20%, 3/15) and *IDH2* (20%, 3/15). Three patients (20%) had adverse cytogenetics. The median number of previous treatment lines was 2 (1-5). Twelve patients (80%) had received prior intensive chemotherapy, 3 patients (20%) had prior Venetoclax exposure and 9 patients (60%) had been previously treated with *FLT3* inhibitors (Midostaurin – 7, Sorafenib – 1, Gilteritinib – 1). Three patients (20%) had relapsed after alloSCT. The majority of patients (80%, 12/15) had received 1 cycle of ACTIVE + G, 3 patients (20%) had been treated with 2 cycles. The CRc and the ORR were 67% (10/15) and 93% (14/15), respectively. MRD negativity was confirmed in 50% (5/10) of CRc cases. The median OS and RFS were 8.6 and 12.9 months, respectively. The most common non-hematological grade 3-5 adverse events were febrile neutropenia (73%, 11/15), sepsis/bacteremia (53%, 8/15), pneumonia (33%, 5/15) and secondary hemophagocytosis (13%, 2/15). Day 30 and day 60 mortality rates were 13% (2/15) and 20% (3/15), respectively.

Image:



Summary/Conclusion: A quadruplet regimen ACTIVE + G demonstrated high efficacy in this small group of R/R *FLT3*m AML patients irrespective of their prior exposure to *FLT3* inhibitors or Venetoclax. The main toxicities were infectious complications attributable to prolonged myelosuppression. Prospective clinical trials are needed to verify our results.