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614.ACUTE LYMPHOBLASTIC LEUKEMIAS: THERAPIES, EXCLUDING TRANSPLANTATION AND CELLULAR IMMUNOTHERAPIES

The Efficacy and Safety of Olverembatinib Combined with Monoclonal Antibodies As Salvage Therapy for RR B ALL with ABL1 Fusion Gene Positive

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Background: B cell acute Lymphoblastic Leukemia (B ALL) with ABL1 fusion gene(FG) positive(ABL1+B ALL) is classified as Ph or Ph like ALL and has a poor prognosis. With the therapy of tyrosine kinase inhibitors(TKI)CD19- or CD22-specific chimeric antigen receptor (CAR) T-cell therapy,more patients(pts)can achieve complete remission(CR) even relapsed after hematopoietic stem cell transplantation(HSCT). However, the pts relapsed/recurrence(RR)after HSCT /CART/ TKIs even ponatinib or cannot receive CART due to any reason have the worst prognosis. Recently, such pts have new hope with the wide application of a novel third-generation TKI Olverembatinib developed in China and Blinatumomab(CD19 antibody,BITE)and INOTUZUMAB OZOGAMICIN(CD22 antibody,Ino.).
Aims: Observe the efficacy and safety of Olverembatinib combined with BITE or INO. therapy in RR ABL1+B ALL pts after chemotherapy combined with TKI or CART or even after transplantation.
Methods: Four RR ABL1+B ALL pts received Olverembatinib with BITE or INO from June 2022 to July 2023. During treatment, the dose of Olverembatinib was adjusted and chemotherapy or veneclax may be given at the same time,and give appropriate treatment depending on the patient's condition.After treatment, efficacy was assessed by complete remission (CR) rate, minimal residual disease(MRD)neg (<0.01%) rate by MFC and complete molecular remission(CMR)(FG transcript<10-5) rate by real-time quantitative polymerase chain reaction (RT-qPCR).
Results: Four pts were male, the median age was 45 (range13-72) years, 3 pts were BCR-ABL1 FG positive, 1 pts was AML1-ABL1 FG positive. Before treatment,3 pts presented with 5.5%-35.5% leukemic blasts in bone marrow(BM) and only 1 pts was MRD positive by MFC.And all pts's leukemic cell showed CD19 and CD22 expression confirmed by MFC.2 pts did not undergo HSCT: both them have T315I mutation occurred during disease progression. Pts 1 was 72 years and relapsed after chemotherapy combined with TKI(include ponatinib);Pts 2 was 61 years and relapsed after chemotherapy, TKI(include ponatinib), venetoclax ,BITE and CD19-CART CD22-CART treatments. 2 pts were eventually treated with Olverembatinib combined with INO. and chemotherapy and venetoclax. The other two pts relapsed after HSCT: neither of them had T315I mutation.Pts 3 was 29 years and had recurrence after chemotherapyTKIvenetoclax HSCT and three times CART. Pts 4 was 13 years and had reccurence after chemotherapyHSCTthree times CART and TKI(include ponatinib)venetoclax DLI. 2 pts were eventually treated with Olverembatinib combined with BITE and venetoclax.All pts survived safely and achieved CR:3 pts CMR,1 pts MRDneg by MFC and BCR::ABL1:0.0023%. Pts.2 bridged HSCT;pts.3 and 4 continued oral Olverembatinib combined with venetoclax. The longest follow-up time for 3 pts was one year nearly until today. Unfortunately, pts 1 died due to a secondary fungal infection post-COVID-19 and recurrence of ALL.
Conclusions: For heavily treated RR ABL1+B ALL pts,including those after treatment with ponatinib and other TKICART and HSCT, Olverembatinib combined with monoclonal antibodies is effective and safe. In my cases, it is particularly noteworthy that one pts ,Ph like ALL with ABL1 FG, received Olverembatinib combination BITE and achieved a surprising response, so Olverembatinib may also be effective and safe for such pts. In addition, venetoclax may be used as a sensitizer for TKI or other antitumor drugs. Of course, the above needs more clinical practice to verify.

Disclosures No relevant conflicts of interest to declare.

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