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POSTER ABSTRACTS

612.ACUTE LYMPHOBLASTIC LEUKEMIAS: CLINICAL AND EPIDEMIOLOGICAL

Combination of Olverembatinib and VP Regimen As First-Line Therapy for Adult Patients with Philadelphia Chromosome-Positive Acute Lymphoblastic Leukemia

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Backgrand :
Ph+ALL is the largest genetically defined subtype in adult ALL and is considered associated with high relapse risk and inferior clinical outcomes. The combination of tyrosine kinase inhibitors (TKI) with intensive chemotherapy has achieved a major step forward in the therapy of Ph+ALL in deep response and long-term survival. The upfront use of third generation TKI ponatinib has improved the frequency of complete molecular response (CMR) and the overall survival rate to a greater extent. More interesting, the data coming from MDACC showed that combination of ponatinib in the chemotherapy in Ph+ALL maybe challenge the need for stem cell transplantation (SCT) in most patients who achieved CMR (defined BCR-ABL1 transcript < 0·01%) within 3 months after induction therapy. But the cardiovascular adverse event(AE) of ponatinib was more and severely frequently occurred in the former reports. Olverembatinib,a new third generation of TKI, which can also suppress the mutation of T315I and showed promising results in the Ph+CML. Herein we designed the clinical trial to invest the efficiency and safety of Olverembatinib combine with VP regimen (OVP) on Ph+ALL patients as the first-line therapy.
Motheds:
In this multi-centers, phase 2, single-arm trial, adult patients with previously untreated Ph+ALL were sequentially enrolled. The patients had to be aged 18 years or older, have normal cardiac function (defined by ejection fraction above 50%), and have adequate organ function (serum creatinine≦3*ULN,BUN≦3*ULN,ALT≦3*ULN,AST≦3*ULN,serum bilirubin≦3*ULN). They received three cycles of OVP regimen(for 28 days each cycle :olverembatinib 40mg qod d1-28,Vindesine 4mg d1,8,15,22,Prednisone1mg/Kg/d d1-21,0.5mg/kg/dd22-28). Twelve intrathecal injections of cytarabine alternating with methotrexate were designed as central nervous system prophylaxis in the following therapy after the diagnosis.
Findings:

32 patients were screened and 29 were eligible from June 21, 2022 until 21 July,2023. 3 Patients were withdrawn from the clinical trial(1 refused therapy after induction,1 early death due to Covid infection, 1 Protocol deviation).Among all , Male 12 and Female 17. BCR/ABL1 transcript:M-p210 (11),m-p190(18).The Median Age was 45(19-74) years old. The Median WBC was 24.8(1.06-308.00) *10E9/L. The treatment has resulted in a 100% overall response, including 96% (24/25) CR and 4% (1/25) CRp. As of data collection,23 finished 3cycles of OVP chemotherapy and 82.6% (19/23) got CMR.AS far the rest 6 patients, 1 got CMR after 1 cycle OVP,1 got CMR after 2cycles of OVP, the other 4 patients were undergoing induction therapy. The total CMR rate was 84% (21/25) at any time. The CMR rate was 36%(9/25) ,76%(19/25)and 82.6%(19/23) at 4weeks,8weeks and 12 weeks respectively. Among all the patients finished the 3 cycles, there were 4 patients not reached the CMR and all of them were M-bcr/abl-p210 protein status. The best response was MMR for 3 patients and CR for 1patient. The CMR rate was 70% (7/10) in M-bcr/abl-p210 transcript and 100% (13/13) in that of m-bcr/abl-p190. During a median follow-up of 241 days, one patient died within one month after transplantation, while all the remaining survived without relapse. During induction therapy, 4 patients had platelets consistently above normal values and 4 patients did not experience a further decrease in hemoglobin compared to baseline. The median time for the occurrence of the lowest values of platelets, hemoglobin, and neutrophils was 6th, 12th, and 11th respectively. The most common non-Hematology AE was liver function damage. AE events greater than or equal to grade 3 included 2 cases of elevated Alanine transaminase ,3 cases γ- GT elevation and 2 cases of triglyceride elevation. Other AEs were mild and less than level 3.

Discussion:

Ongoing efforts exist to optimize therapeutic options in the frontline for Ph+ALL. The future lies in using less cytotoxic and more targeted agents. The first results of our ongoing trial indicate that the OVP regimen is effective in achieving early high rate of CMR in patients with newly diagnosed Ph+ALL as first-line therapy. All these results were achieved with surprisingly few toxic effects.Until now,16 patients underwent ASCT. Will the excellent outcomes be preserved with longer? Will there be a difference in long-term outcomes between patients who underwent ASCT and those who do not?The trial is ongoing. we need more time to observe.

Disclosures No relevant conflicts of interest to declare.

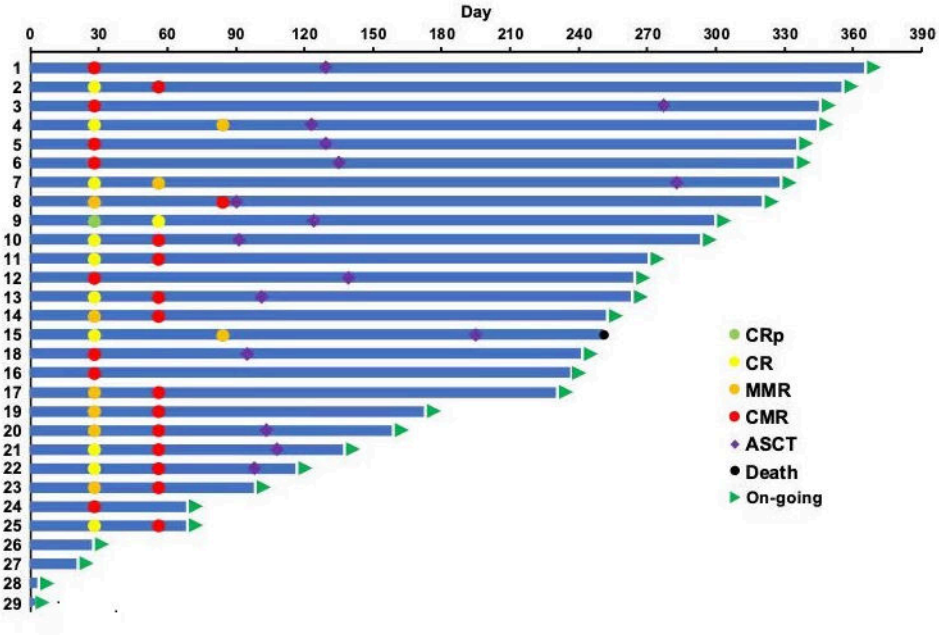

Figure:The efficacy response and survival status of these populations as of the time of data collection.

Figure 1

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