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Blood 142 (2023) 5892–5893

The 65th ASH Annual Meeting Abstracts

ONLINE PUBLICATION ONLY

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

The Efficacy and Safety of the Third Generation TKI Olverembatinib in Adult Ph+ Acute Lymphoblastic Leukemia with Relapsed Disease or Persistent MRD Bridging to Allo-HSCT: A Case Series from a Single Center

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Background
The value of achieving hematology remission and MRD negativity before HSCT is substantial for ph+ALL patients. Olverembatinib, a novel third-generation TKI developed in China, has been approved in CML with T315I mutation since 2021. In this study, we report a retrospective analysis of the efficacy and safety of the Olverembatinib-involved regimen in adult Ph/BCR-ABL1+ ALL with relapsed disease or persistent MRD prior to allo-HSCT. Herein, we report our preliminary results.
Method
In this retrospective analysis, all enrolled ph+ALL patients with relapsed disease or persistent MRD were treated with Olverembatinib involving regimen, before bridging to HSCT. The Olverembatinib involving regimen included: Olverembatinib and Venetoclax in combination with VP based low intensive chemotherapy (Vindesine /Prednisone), Olverembatinib+Blinatumomab, Olverembatinib + INO. Efficacy was assessed by complete remission (CR) rate, MRDneg (<0.01%) rate by flow cytometry, and CMR (BCR-ABL1 transcript<10-4) rate by real-time quantitative polymerase chain reaction (RT-qPCR). Safety events were also monitored.
Result
From April 2022 to February 2023, 13 Ph+ ALL pts were treated with Olverembatinib involving therapy due to disease recurrence (n=2) and persistently molecular positive (n=11). The median age was 40 years (range, 23-56), and 9/13 were males. BCR::ABL1 p190 and p210 fusion were found in 7 and 6 patients, respectively. Three patients had T315I mutations, and one had G250E mutation. Three patients had IKZF mutations. Four patients had received 2 types of TKIs previously. One patient relapsed with both BM and CNS involved. The median time from diagnosis of Relapse or molecular positive to the administration of Olverembatinib was 181 (range, 51-1284) days.
Totally, ten patients achieved CMR, and the overall CMR by PCR rate was 76.92%, while the MRDneg rate by flow cytometry was 100%. All patients with T315I mutations achieved CMR. Among patients with hematology relapse, the hematology remission rate and CMR rate reached both 100% after only one cycle of Olverembatinib involved regimen, including Olverembatinib + Blinatumomab, Olverembatinib + INO, respectively. For patients with persistent molecular diseases, eight patients achieved CMR. With respect to the different olverembatinib involving regimen, the CMR in olverembatinib+Venetoclax+ VP, olverembatinib+Blinatumomab, olverembatinib + INO, were 71.43%. 75% and 100%, respectively. The median regimen cycle times were 2 (range 1-3). All patients succeeded to bridge to allo-HSCT. With a median follow-up of 249(60-376)days post-HSCT, the estimated one-year overall survival (OS), and relapse-free survival (RFS) were 92.3±7.39% and 92.3±7.39%, respectively. One patient died of severe infection and CNS complications. Meanwhile, the Olverembatinib-based therapy was well tolerated. Only one patient reported gastrointestinal symptoms, such as nausea and vomiting. One patient complained about dizziness due to hypertension. No drug-related death or permanent discontinuation was reported due to toxicity.
Conclusion

This work suggests that Olverembatinib showed a profound response rate and was well tolerated in MRD clearance prior to allo-HSCT in Ph+ALL with disease recurrence and persistently MRD positive. Larger prospective studies are needed.

Disclosures No relevant conflicts of interest to declare.

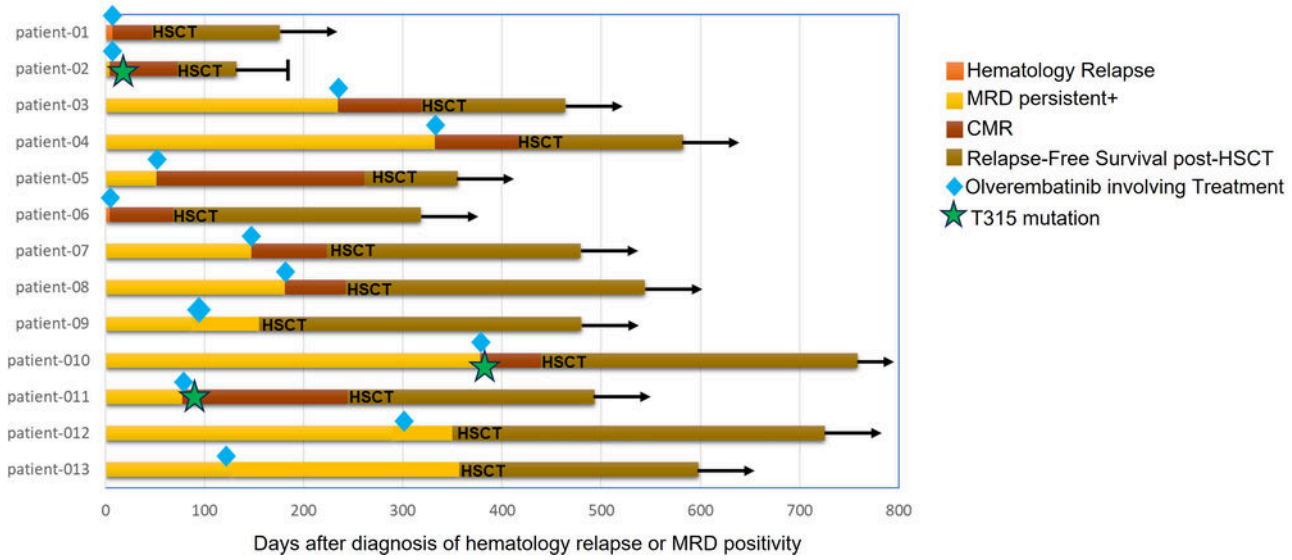

Figure 1

https://doi.org/10.1182/blood-2023-184400