The emerging role of Venetoclax in high risk newly diagnosed patients with B-cell Acute Lymphoblastic Leukemia (B-ALL)

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INTRODUCTION

Patients with high risk ALL have a relatively poor prognosis due to aggressive presentation and resistance to conventional treatment. The B-cell lymphoma 2 inhibitor venetoclax may enhance the efficacy of chemotherapy. This subgroup is treated with intensive chemotherapy such as HYPERCVAD before moving to allogeneic bone marrow transplant. Some patients are not eligible for transplants, however; they can do good with the addition of new agents to conventional chemotherapy

AIM

In our study, we are evaluating the role of Venetoclax in newly diagnosed high risk patients with ALL. Protocol is adapted according to each case including dose dense and dose intense chemotherapy with Venetoclax during the induction and consolidation phase only..

METHOD

Patients are given HYPERCVAD with the standard dose for 2 cycles as induction followed by consolidation therapy for 6 cycles including high dose Cytarabine 3grams BID for 3 days and Methotrexate 3 grams/m² on day 4. 6 mercaptopurine 100mg/m² daily in continuous. Consolidation repeated for 6 cycles every 15 days or according to the white blood count. Maintenance included Cyclophosphamide 1gram/m², vincristine 2mg, 6 mercaptopurine and oral Methotrexate 15mg every week for 2 years. Intrathecal Methotrexate every week in induction, every 2 weeks in consolidation and every 3 months in maintenance. Venetoclax was given as a single daily dose of 200 mg in continuous in both induction and consolidation setting.

CONCLUSIONS

Venetoclax shows to have a synergistic effect with chemotherapy through elimination of malignant cells expressing BCL-2. The safety profile and the tolerance make it a good partner of high dose chemotherapy in poor risk ALL patients. These findings need to be supported by comparative trials.

RESULTS

We have included 30 newly diagnosed patients with ALL with ages ranging between 18 and 55 (31 years in median). The male to female ratio was 1.5:1. The study was performed at al Bairouni university cancer center, Daffodil 88 cancer center and at the Italian hospital in Damascus, Syria. The complete response documented in 26 (86.6%) patients at the end of induction with a sensitivity of 0.0001. We have lost 1 patient in induction. 3 patients progressed in the consolidation phase. Toxicity included neutropenia in almost all patients in induction, tumor lysis syndrome in 3 patients and renal failure in 3 patients. 40% of patients could not tolerate the dose of Venetoclax and moved to intermittent dosing schedule according to their performance status. A follow-up of 36 months demonstrated an overall survival rate of 93.3% (95% CI: 87.8-95.2). change in Venetoclax schedule had no effect on response rate p value (0.04).

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