The best Venetoclax dosing schedule in high-risk Myelodysplastic Syndrome (MDS)

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INTRODUCTION

MDS is a heterogenous disease from a morphologic and genetic perspective. It is considered a background for development of Acute Myelogenous Leukemia (AML) especially in patients with high-risk groups. A minority of patients are eligible for allogeneic bone marrow transplants. In this high-risk group, patients are treated the same way AML is treated especially with the emergence of new drugs such as anti-BCL-2 drugs in combination with hypomethylating agents (HMA)

AIM

Is to evaluate the efficacy and safety of 3 Venetoclax doses schedule in combination with Azacitidine in newly diagnosed high-risk patients with MDS.

METHOD

Patients are given azacitidine 75mg/m² for 7 days in 28 days schedule in all the 30 recruited patients. Regarding Venetoclax, 10 patients received 400mg per day in parallel with Azacitidine (Arm 1), 10 patients received 200mg per day for 21 days (Arm 2) and the rest of 10 patients received 100mg per day in continuous (Arm 3). Bone marrow aspiration performed after each cycle with morphologic and flowcytometric studies. Toxicity profile was registered in each patient including adherence to treatment. Azole antifungal prophylaxis was not given to our patients.

CONCLUSIONS

In high-risk MDS, treatment with Venetoclax and HMA demonstrates good response and survival irrespective of the dose of Venetoclax. However: low doses of Venetoclax confer good adherence and consequently good response. Bigger trials are warranted to reach the preferred dose of Venetoclax in high-risk MDS.

RESULTS

We have included 30 newly diagnosed patients with high-risk AML with ages ranging between 48 and 77 years (63 years in median). A male to female ratio 2:1. Complete response was documented in 4 patients in arm 1 (40%), 5 patients in arm 2 (50%) and 4 patients in arm 3 (40%). Adherence to treatment was 90% in arm 1, 80% in arm 2 and 70% in arm 3. Neutropenia was documented in 100% of patients in arm 1, 80% in patients of arm 2 and 30% in patients with arm 3. In general, after the second cycle, all 30 patients could not adhere to the treatment plan as scheduled before. We have lost one patient in arm 1, two patients in arm 2 and one patient in arm 3 after the end of the first induction. The overall survival rate after 12 months of follow-up was 70% in arm 1, 80% in arm 2 and 80% in arm 3. Toxicity profile was worse in arm 1 compared with the other 2 arms. Tolerance and good adherence to treatment was correlated with better response in general irrespective of the studied arm and the dose taken p value 0.05.

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