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Title

Successful restoration of checkpoint inhibitors efficacy after allogeneic hematopoietic cell transplant for classic Hodgkin lymphoma patients

Authors

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Introduction

Classic Hodgkin's lymphoma (cHL) is a curable disease, however a minority of patients will have relapse/refractory (RR) disease and these patients are challenging to manage especially those who relapse after autologous hematopoietic cell transplant (auto-HCT). Even though a number of salvage options are available for these patients, none of them is curative except allogeneic hematopoietic cell transplant (allo-HCT) and post allo-HCT relapses remain frequent. Checkpoint inhibitors are approved for RR cHL patients and in the present practice, almost all patients will have exposure to this class of drugs before allo-HCT consideration. There are no published reports addressing the re-use of this class of drugs on patients who have been already exposed and failed. We herein report six patients who failed CPIs before allo-HCT, and were re-challenged after relapse post allo-HCT.

Methodolgy

The primary objective of this study was to evaluate the safety, efficacy and outcomes of these six patients. A retrospective chart review of these six patients was carried out after securing institutional review board (IRB) approval. All patients were started on low dose nivolumab (40 mg total dose) and monitored for GvHD. Additional doses were based on the response and the presence or absence of GvHD after each nivolumab dose. Efficacy was assessed clinically and by PET scan (positron emission tomography). Toxicities were graded according to the National Cancer Institute Common Terminology Criteria for Adverse Events (version 4.0). Acute and chronic GvHD were defined and graded according to the standard criteria. Subject's characteristics were summarized using frequencies with percentages for categorical variables and medians with interquartile range for continuous variables. Statistical analysis was carried out using IBM SPSS 24.

Results

Six cases were identified and reviewed. All patients received and failed CPIs and BV pre-allo-HCT. The median age at allo-HCT was 28.6 years (IQR 23.6-34.2), the median number of lines received prior to allo-HCT was 6.5 (range 5-9). The median duration of CPI therapy prior to allo-HCT was 8.1 months (IQR 6.7-12.9). The median time between the stop of CPI and allo-HCT was 5.78 months (IQR 3.15-15.8). The median time to progression post allo-HCT was 5.75 months (IQR 2.6-11.7). The median time between allo-HCT and the re-challenge with CPI was 7.6 months (IQR 3.2- 28.6). The median time of follow up after starting post-allo-HCT CPIs was 16 months (IQR 7.25-25.75). All patients received and failed CPIs and BV pre-allo-HCT. Table 1 is a summary of the cases and their clinical course. Figure 1: baseline and first restaging PET scans after re-challenge with nivolumab post allo-HCT.

Conclusion

The currently available strategies for cHL patients who relapse post allo-HCT are limited. Our report offers an additional option for these patients with high-unmet need. All along, this study poses many challenging questions. One thought provoking finding in our report is the fact that some patients went to CR repetitively with only one low dose of CPIs. This raises the question of whether CPIs can be used in such a fashion even before allo-HCT in patients achieving CR, where CPI holidays can be considered and then re-treatment upon progression. Another challenging issue is the immunologic correlates as well as the potency and exhaustion of T cells with response and whether DLI use can tip the balance of the immunophenotype to a favorable profile so that the patient draws the maximum benefit from this treatment strategy.