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Title

Refractory diffuse large B-cell Lymphoma

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Introduction

Up to 20 % of patients with diffuse large B-cell lymphoma won't respond to first-line therapy. These patients require alternative therapies such as second-line chemoimmunotherapy followed by consolidative autologous hematopoietic stem cell transplantation. In this study, we aim to evaluate the factors associated with these refractory cases and describe their outcome.

Methodolgy

This is a retrospective, descriptive, and analytical study of newly diagnosed DLBCL patients followed up in an internal medicine and onco-hematology department between January 2018 and December 2021. Data were collected using a computerized system (HOSIX). Refractory DLBCL was defined as progressive disease or stable disease as the best response at any point during chemotherapy (>4 cycles of first-line or 2 cycles of later-line therapy). Statistical analysis was performed with IBM SPSS Statistics. Survival analyses with corresponding P-values were calculated using the Kaplan-Meier method.

Results

We analyzed 160 DLBCL patients treated in our hospital between 2018 and 2021. Among them, 19 patients (11.8%) were declared refractory. The median age at diagnosis of our refractory cases is 52.57 years old [16-72] and the F/M sex ratio is 1.37. The average diagnostic delay was 8.4 months. Of our refractory patients, 57.89% had B-signs at diagnosis, and 84.21% presented with clinically evident tumor syndrome. The performans status (PS) ≤1 in 14 patients. On the CT scan, 68.42% of our refractory cases had a bulky mass, and 14 patients (73.68%) had an III-IV stage disease according to the ANN-ARBOR staging system. Eleven patients had a high IPI (≥3).

Eighteen patients are refractory to R-CHOP regimen as first-line treatment, while 1 patient with a mediastinal bulky, who received DA-R-EPOCH protocol, was deemed refractory as well. After the first line, 15 patients were put on the RDHAOX regimen, 2 patients on RGEMOX, and one patient received the R-COPADEM protocol. Six of these patients passed away, seven were lost to follow-up, three achieved complete remission and three were put on a third-line treatment.

Refractory DLBCL was associated with the presence of a bulky mass (p=0.002), adrenal involvement (p=0.006), pulmonary involvement (p=0.043), lymphopenia (p=0.018), BCL2 positivity (p=0.05), BCL6 positivity (p=0.049), and CD5 positivity (p=0.048).

The 4-year survival of refractory patients was 59.4% versus 77.7% of nonrefractory cases (p=0.19).

Conclusion

Refractory cases require more aggressive therapy. Current data suggest that patients can be consolidated after second-line with hematopoietic stem cell transplantation. Chimeric antigen receptor (CAR) T-cell therapy has dramatically changed the treatment of refractory and relapsed DLBCL, and it is indicated for patients ineligible for transplantation. Tafasitamab (an anti-CD19 engineered monoclonal antibody), in addition to lenalidomide, antibody-drug conjugates, and bispecific antibodies are the new weapons in this therapeutic strategy. But, unfortunately, are still associated with significant barriers to access.