EDITORIAL

Diffuse large B-cell lymphoma: R-CHOP forever?

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Diffuse large B-cell lymphoma (DLBCL) is the most frequent B-cell lymphoma, accounting for approximately 30% to 40% of all lymphoma cases.[1] The disease had been incurable until the CHOP regimen, consisting of cyclophosphamide, doxorubicin, vincristine, and prednisone, was introduced by McKelvey et al[2] in 1976. However, the success was limited, with only 20% of patients achieving 10 years of disease-free survival. Throughout subsequent years, numerous attempts had been made to improve these results, and, essentially, they all failed.[3] This was until 2002, when Coiffier et al[4] showed that the effects of CHOP could be improved in elderly patients by combining it with a newly introduced monoclonal anti-CD20 antibody, rituximab. Based on this phase III study and some phase II studies, R-CHOP became a standard initial treatment in all patients with DLBCL, with as many as almost 40% of the patients achieving 10-year disease-free survival[5] corresponding to cure. The intensification of R-CHOP by shortening the interval between cycles from 21 to 14 days was not successful.[6]

It soon became clear that DLBCL is not a homogenous disease. First, the International Prognostic Index (IPI) was introduced that categorized patients based on age, performance status, Ann Arbor stage of disease, number of extranodal lesions, and lactate dehydrogenase activity in serum.[7] Then, 3 major types of DLBCL were distinguished: primary mediastinal B-cell lymphoma, activated B-cell lymphoma, and germinal center B-cell lymphoma.[8] Finally, the so called double-hit lymphoma was identified, possessing both *MYC* and *BCL2* mutations.[9] All these findings contributed to the definition of high-risk DLBCL.

The conclusions of Coiffier et al[4] have been later extrapolated to the subpopulations of patients that were not originally included in their study. However, they have not been adequately confirmed in all these subpopulations in either prospective or retrospective analyses. Jurczak et al[10] have attempted to partially fill this gap by studying patients with high IPI values. While it is a retrospective analysis and includes only a small group of patients receiving CHOP to compare them with those receiving R-CHOP, it confirms the superiority of the latter regimen. This is in line with the results of population-based studies.[11] The question for today is how to improve the R-CHOP results? A number of reports have been published, but so far, the history repeats itself.[12,13] While for many years, there was nothing better than CHOP, a recent study on double-hit DLBCL has demonstrated that there is nothing better than R-CHOP.[13] However, new categories of compounds have become available,[14,15] such as BCL2 inhibitors, and there is hope that they will change the landscape of DLBCL treatment similarly to rituximab in the past. Promising results have been also obtained with R-CHOP by supplementing it with lenalidomide, a regimen that has become known as R2CHOP.[16]

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