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High-dose CHOP in the rituximab era: still a place?

The combination of rituximab plus CHOP (R-CHOP) has dramatically changed the outcome of patients with diffuse large B-cell lymphoma but there are still eras where the results obtained with R-CHOP chemotherapy are not so satisfying. If R-CHOP is associated with 5-year progression-free survival (PFS) and overall survival (OS) of 70% and 80%, respectively, in patients with good risk presentation (IPI score <3), this is not the case in higher risk patients. For elderly patients, increasing the risk of chemotherapy dose is not a possibility because of the potential toxicity; however, this is the case for young patients with adverse prognosis.

The increase efficacy of ACVBP, the high-dose regimen used by the GELA since 1984 was demonstrated in a randomized study comparing it to standard CHOP (H Tilly *et al.* Blood 2003;102:4284). Because of the improvement of R-CHOP, the question of whether rituximab may replace the benefit of higher dose chemotherapy without its increased toxicity. Three studies has been realized by the GELA to respond to this important question.

In the first studies, the 3531 patients treated with ACVBP in different randomized studies were analyzed regarding the comparison with or without rituximab for OS and PFS (results not published). Results obtained with R-ACVBP were always superior to those obtained with ACVBP alone, except for patients without any adverse prognostic factor. These results were independent of the IPI score or other adverse prognostic factors.

In the second study, young patients with IPI score of 2 and 3 treated with R-ACVBP followed by intensification with autotransplant (study 03-3B) were compared with the historical cohort of identical patients treated by the same regimen without rituximab (study 98-3B) (C. Gisselbrecht ASH 2007). Patients treated with the rituximab combination had a PFS significantly longer.

The last study is a randomized study comparing R-CHOP to R-ACVBP in patients with one adverse prognostic factor (study 03-2B). This study has included 380 patients and is now closed for accrual. The first interim analysis did not show a significant difference (DSMB report) has all scheduled patients have been included. Results are not available yet.

In conclusion, R-CHOP is not sufficient for a subgroup of patients with aggressive presentation. The young ones may have better outcome with higher doses than CHOP regimen.