More intensive chemotherapy dramatically improves recurrence, survival in younger patients with aggressive lymphoma

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Younger patients with diffuse large B-cell lymphoma given a more intensive regimen of chemotherapy combined with rituximab survive significantly longer, and are approximately twice as likely to remain in remission 3 years later, compared with patients given standard chemotherapy treatment plus rituximab, according to an article published Online First in the *Lancet*.

Over the past decade, combined treatment with the monoclonal antibody rituximab and a standard chemotherapy regimen CHOP (cyclophosphamide, doxorubicin, vincristine, and prednisone) has substantially improved outcomes in lymphoma patients younger than 60 years. But some patients still relapse after a complete response to treatment, and the optimum chemotherapy regimen to combine with rituximab has yet to be established. Recent studies suggest that intensive chemotherapy (higher doses with shortened intervals between treatments) might benefit younger patients with aggressive lymphomas.

This study, conducted by the Groupe d'Etude des Lymphomes de I'Adulte (GELA), randomly assigned 379 patients aged 18 years with early intermediate-stage diffuse large B-cell lymphoma (one of the most common and aggressive forms of non-Hodgkin's lymphoma) to receive either four cycles of dose-intensive chemotherapy (doxorubicin, cyclophosphamide, vindesine, bleomycin, and prednisone) plus rituximab (R-ACVBP)* at 2 week intervals, or eight cycles of the

standard treatment (R-CHOP) at 3 week intervals.

After 3 years, event-free survival (patients not experiencing unplanned treatment for lymphoma, disease progression or recurrence, or death) was significantly better for patients in the dose-intensive group compared with those receiving standard treatment (81% vs 67%), with the more intensive chemotherapy reducing the risk of experiencing an event by 44%.

Additionally, patients assigned to the intensified regimen had a 56% lower risk of death and were 52% less likely to experience disease progression compared with those given standard treatment.

But increasing the treatment intensity also significantly increased the likelihood of serious side effects. In particular, haematological and mucosal toxic effects were significantly more common in the dose-intense group, and a much higher proportion of patients experienced febrile neutropenia (38% vs 9%).

The authors say: "Intensified immunochemotherapy with R-ACVBP represents an alternative to R-CHOP to improve survival in patients younger than 60 years with diffuse large B-cell lymphoma of low-intermediate risk."

They conclude by calling for further research to identify subsets of patients who are more likely to benefit from this intensive regimen.

In a Comment, Julie Vose from Nebraska Medical Center, Omaha, USA, cautions: "This dose-intense regimen should only be used in patients in whom the expected relapse rate is sufficient to justify the higher toxic effects and cost profile."

More information: Paper online: www.thelancet.com/journals/lan …

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