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Treatment of refractory Hodgkin's lymphoma: a puzzle to merge

Introduction

About 80% of patients with Hodgkin's lymphoma are like to be cured by first line chemotherapy. However some patients fail to reach remission or relapse early (within 3 months) after first-line therapy. These non-responders generally have a much worse prognosis and need to be identified as early as possible to lower their risk of treatment failure, avoid unnecessary toxicity and increase the chance of long term survival.

High dose chemotherapy with autologous transplantation (HDCT) is considered the gold standard, while 40-50% of patients will have a recurrence.

Several clinical variables present at the time of disease relapse or immediately prior to HDCT have been evaluated with regard to their influence on risk of recurrence following autologous transplant such as clinical stage, number of involved regions, B symptoms, extranodal disease, bulky disease, relapse in prior radiation field, duration of first remission less than 12 months and higher risk score as described by Hasenclever and Diehl at relapse.

In "the functional imaging with positron emission tomography *era*" PET positive response at the end of induction therapy is the worst predictor of outcome.

Being in complete remission (CR) after induction therapy plays the major role for a good outcome, however the best way to achieve it a has not been established. IGEV scheme can reach 47% of CR, while other regimens obtain almost 30%.

So how can we get through this puzzle? Intensification of induction therapy before HDCT is one of the strategies to obtain normalization of FDG-PET. Also combinations of new molecules (such as bortezomib and rituximab) with chemotherapy show encouraging results even if they were tested in small cohorts of patients.

Interim PET during induction therapy is a merging tool for patients stratification and introduction of risk adapted strategies.

Add a second transplant (auto or allo transplant), in a setting of a tandem procedure, may result in durable remission for poor risk categories. Relapsed patients who previously underwent HDCT remain a clinical challenge with limited effective treatments. In this setting experimental therapies such us non mieloablative allogeneic transplant from any source (sibling, MUD, Aplo, CB) or new drugs as i-DAC are probably the keys to merge this puzzle.

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