Clinical and Treatment-Related Features Determining the Risk of Late Relapse in Patients with Diffuse Large B-cell Lymphoma

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BACKGROUND:

In diffuse large B-cell lymphoma (DLBCL), 35-40% of patients achieving complete remission (CR) will experience a relapse. Most will relapse within the first 2yrs and 10-20% will achieve a 2nd CR upon salvage treatment. Of all patients who relapse, a subset will do so late, i.e. several years after CR achievement. Little is known about the frequency of late relapses (LR) and about their predisposing factors. There is no consensus on the definition of LR with proposed cut-offs ranging from 24mo to 5yrs after achievement of CR. Despite earlier attempts to clarify this issue, it is still unclear whether there are clinically exploitable differences in the biology and behaviour of early relapse (ER) vs. LR.

AIM:

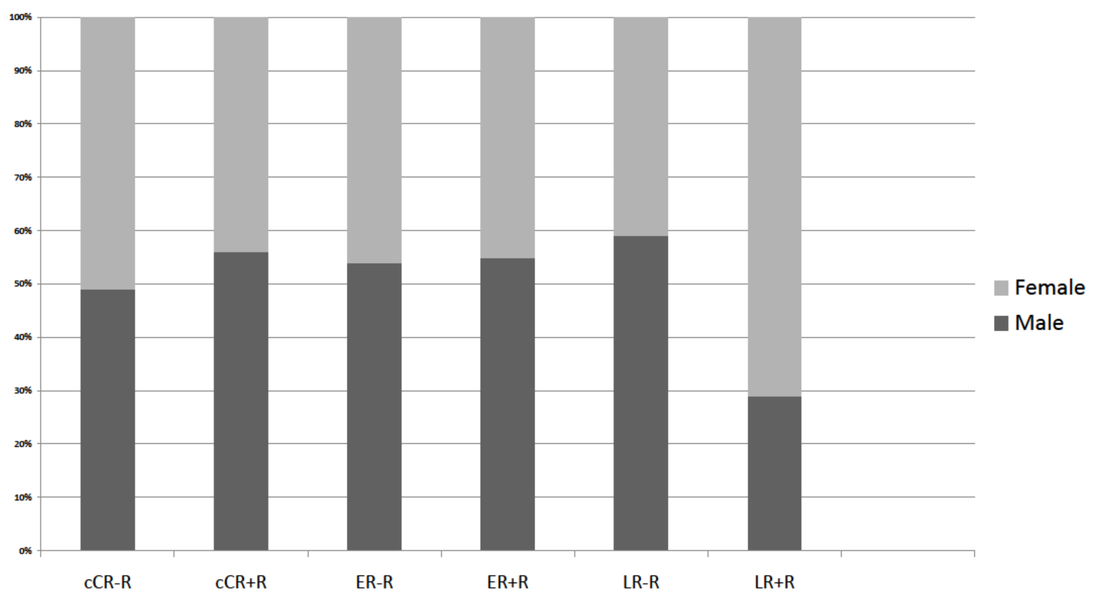
The aim of the present study was to analyse a large population-based DLBCL-cohort in order to identify :

1. The frequency of LR
2. Parameters influencing the risk of LR
3. The impact of Rituximab on the occurrence of LR

STUDY POPULATION:

The data sets of 7,247 DLBCL patients diagnosed within the period of 1983-2014 were obtained from the population-based Danish Lymphoma Registry. ER was defined as biopsy-proven reoccurrence of disease maximum 2 years after achievement of 1st CR. Likewise, the disease-free interval required in order to fulfil the definition of LR was 5 years or more after 1st CR. 4,097 patients (57%) achieved a CR upon 1st line treatment. Of these, 3,279 (80%) remained in continuous CR (cCR), whereas 818 (20%) had a registered relapse. 556 (68% of all relapses) had an ER, while 78 (10% of all relapses) relapsed more than 5 years after CR. Patients with relapse occurring between 2 and 5 yrs were excluded in order to better discriminate between truly early vs. late event features. In all cases of relapse, the diagnosis was histologically verified.

Fig. 1: Association between gender and Rituximab (R) treatment in relapse-groups



RESULTS:

Patients with LR presented with a more favourable IPI (p=0.019) and better performance score (p=0.004) than ER patients. LDH elevation was found more frequently in relapse patients (ER and LR alike) compared to patients in cCR (p<0.0001). The use of radiotherapy was associated with a lower rate of ER (p<0.0001), while it did not affect the rate of LR or cCR. The use of Rituximab lowered the occurrence of both ER and LR (p<0.0001). An intriguing finding was a significant female overrepresentation among LR patients that had received a Rituximab-containing 1st line treatment (p=0.031) (Fig. 1). With regard to outcome, we found that DLBCL patients with LR had a better 5-year overall survival (OS) compared to patients with ER (Fig. 2). The difference in outcome was no longer present for those patients who had received Rituximab upfront (Fig. 3).

Fig. 2: OS of ER vs. LR (without Rituximab)

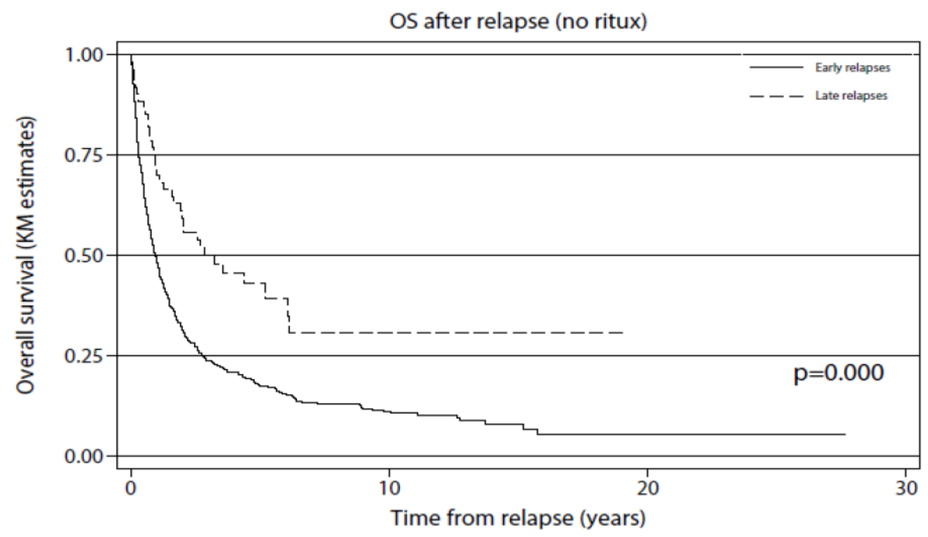
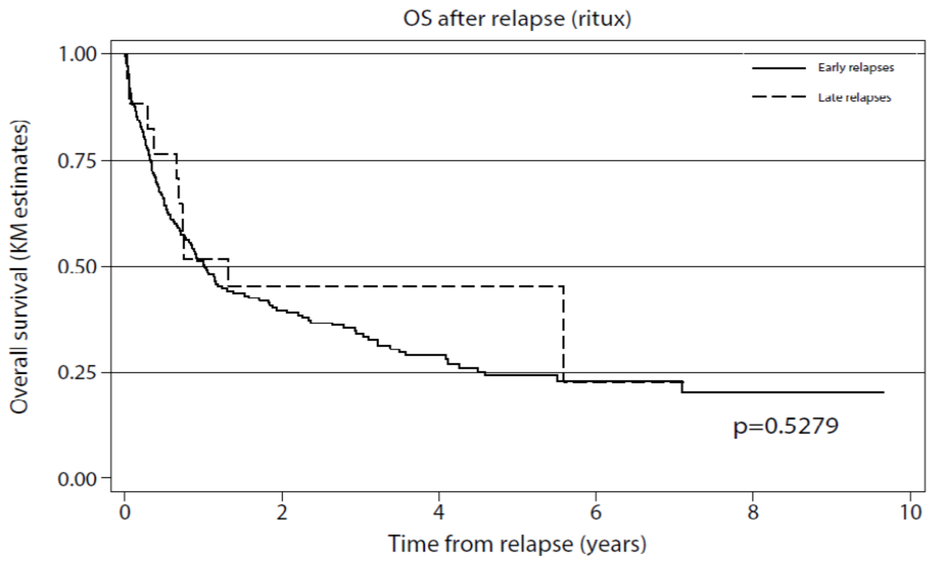


Fig. 3: OS of ER vs. LR (with Rituximab)



CONCLUSIONS

- LR was associated with low-risk features at presentation more frequently than ER [1,2]
- Radiotherapy lowered the risk of ER, but not LR
- The use of Rituximab effectively reduced the risk of both early and late events suggesting a longer-lasting biological effect
- In Rituximab-treated DLBCL, LR occurred much more frequently in women – an observation that warrants validation in other cohorts
- The use of modern immunochemotherapy regimens in DLBCL lowers the risk of both ER and LR

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Aggressive B-cell lymphoma

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