An Analysis of Patients Treated with Weekly Salvage Chemotherapy Regimens for High Grade Lymphoma

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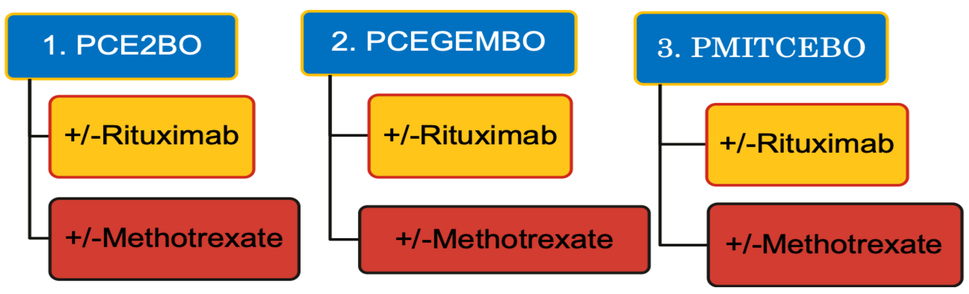
Introduction

Diffuse Large B-cell Lymphoma (DLBCL) is potentially curable, however 13% have refractory disease[2] and a further 30-40% relapse after front line therapy. Outcomes are poor among these patients, with response rates of approximately 50% in the second line setting.

In the transplant eligible patients the aim of salvage chemotherapy is to reduce disease sufficiently to proceed to stem cell autologous transplant (ASCT). There is no clear evidence that one salvage regimen is more efficacious than another, often R-GDP or R-GemP is preferred due to it being an outpatient regimen, associated with decreased toxicity and equivalent efficacy to other salvage regimens.

Prior to CAR-T being available in the UK, or in patients unsuitable for CAR T, in our centre, weekly salvage chemotherapy (WSC) were considered for patients with R/R DLBCL, who have failed ≥1 salvage regimens. The aim of the chemotherapy regimen is to allow patients to proceed to ASCT in those achieving a sufficient response; as holding or bridging treatment prior to CAR T or to prolong survival in those who are unsuitable for consolidation or CAR-T therapy.

Specific WSC regimens were based on frailty, co-morbidities and prior therapy history and consisted of :



Abbreviation (dose): P: Prednisolone; E: Etoposide (300mg/m²); C: Cyclophosphamide (300mg/m²); B: Bleomycin (10 000IU/m²); O: Vincristine (1.4mg/m²); Mit: Mitoxantrone (7mg/m²); Methotrexate (100mg/m²); Rituximab (275mg/m²).

Method and Measures

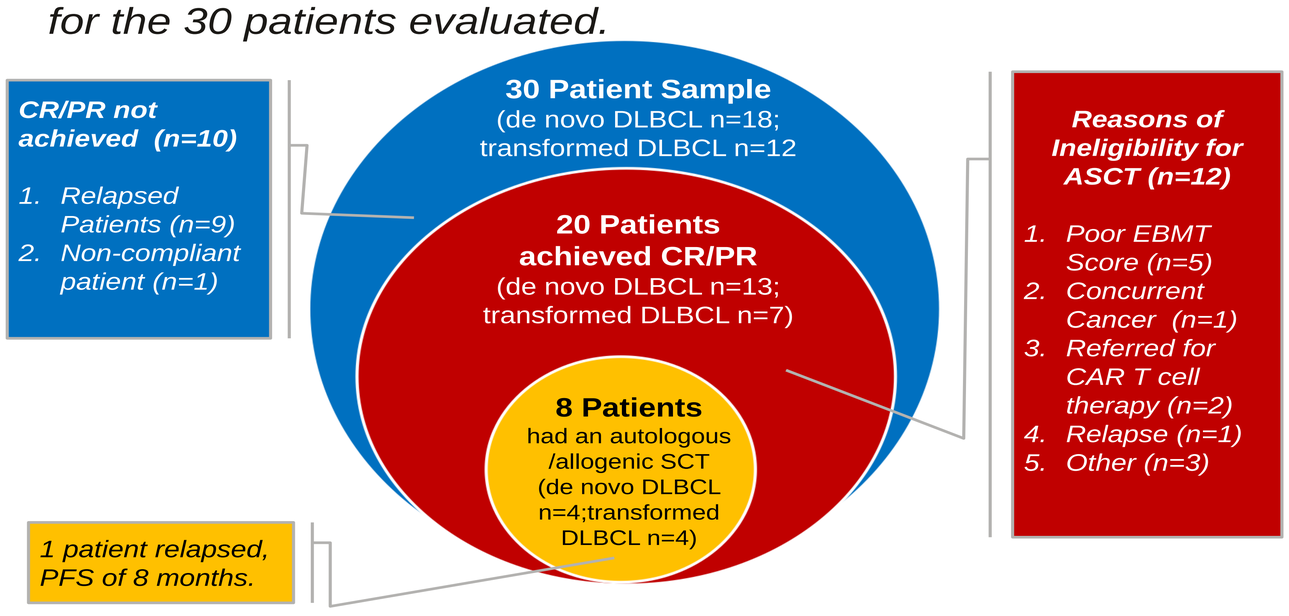
A retrospective electronic patient record (EPR) search:
Inclusion criteria:

1. *Patients treated with WSC regimens between September 2002 to October 2019 for Relapsed Refractory (R/R) DLBCL.*
2. *Patients with transformed lymphoma.*
3. *Relapse refers to a disease which reappears or progresses after remission is achieved. Refractory disease describes lymphoma which is resistant to treatment following 1st, 2nd line or further lines of treatment.*

The patients were censored at last clinic.

Results

Below is a schematic diagram demonstrating the outcomes for the 30 patients evaluated.

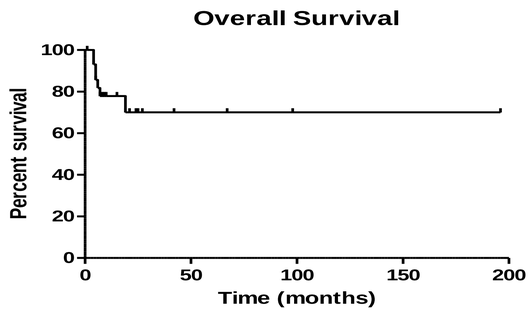


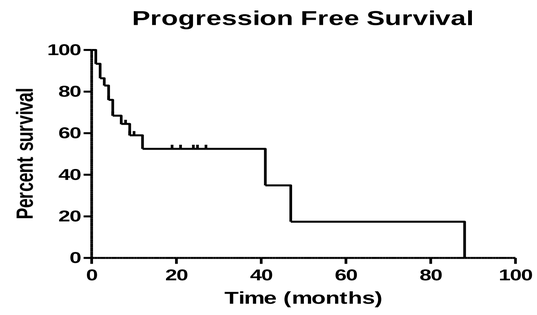
CR- Complete Remission; PR-Partial Remission; EBMT-European Society for Blood and Marrow Transplantation; CAR T- Chimeric antigen receptor; SCT- Stem cell transplant.

Thirty patient (de nova DLBCL n=18; transformed n=12) with a median age of 60 year (range 20-84) received WSC (median 4 cycles, range 2-6). Median prior lines of therapy was 3 (range 1-5).

Overall response rate was 20/30 (66%)(de nova DLBCL n=13; transformed DLBCL N=7).

Seven of the responding patients proceeded to ASCT and one to allograft. These 8 patient haD a median 6 months follow-up (range 2-16), all are still alive and only one has relapsed. Two were referred elsewhere for CAR-T therapy. Ten patient who achieved a response were unsuitable for transplant due to frailty or co-morbidities, with a median follow-up of 27 months for these patients, the median PFS for this cohort is 41 months. With a median follow-up of 15 months for the whole cohort the median PFS is 41 months (CI 95%, 6-76) and the two year OS is 77%





Conclusion

The response rates, duration of response and the number of patients able to proceed to transplant in this heavily pre-treated patient population are encouraging. We hypothesise that the reason for these results is the heavy steroid use that forms part of the regimen and the weekly "metronomic" nature of this chemotherapy that does not have prolonged breaks in the treatment between cycles. WSC was well tolerated, including in those with poor performance status and co-morbidities.

Formal studies comparing this salvage regimens to alternatives should be performed for confirmation of the results. WSC should be considered for patients with R/R DLBCL in those patients who are potential candidates for ASCT, in those patient who may need bridging for CAR-T, or in those who are in-eligible for either as it may provide responable duration of response.

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