Incidence, Characteristics and Outcomes in Relapsed and Refractory CD20+ PTLD: An Institutional Retrospective Cohort Study

Zain El-amir, [1] Michael McLane, [1] Mark Kaminski, [1] Tycel Philips, [2] Ryan Wilcox, [1] Dahlia Sano, [1] Yasmin H. Karimi[1] and Shannon A. Carty[1]

[1]Michigan Medicine, Ann Arbor MI; [2]City of Hope, Duarte CA



Introduction

- Post-transplant lymphoproliferative disorder (PTLD) has significant morbidity and mortality after solid organ transplant (SOT).
- Frontline treatment of CD20+ PTLD is well established; however, there is a lack of data on the treatment of relapsed/refractory (R/R) PTLD, especially in the era of novel therapies approved since 2017 for diffuse large B-cell lymphoma.[1,2]

Objective

- To understand the treatments and respective response rates for R/R PTLD.

Design

- Using data from a tertiary academic medical center, this retrospective study reviewed SOT patients with CD20+ PTLD who were diagnosed from 01/01/2012 to 12/31/2022.
- Inclusion criteria were age ≥18 and use of an adult regimen including rituximab for frontline therapy.

Results

- 71 cases of CD20+ PTLD were included. Median overall survival (OS) was 62 months.
- 21 (29.6%) patients relapsed (N=13) or were refractory (N=8) to frontline treatment. Median time to relapse was 12.0 months. In the R/R setting: 3 patients transitioned to comfort care; 8 had reductions in immunosuppression (RIS).
- Second-line treatments included: R-CHOP, R-mini-CHOP, RICE, R-gemcitabine and oxaliplatin (R-GemOx), lenalidomide/tafasitamab (len/tafa), R-ibrutinib.
- Overall response rate (ORR) for second-line treatment was 72.2%. 50% required dose reductions. Median OS was 17 months and progression-free survival (PFS) was 4.5 months in the second-line setting.
- 6 patients received a third line of therapy. Regimens included polatuzumab-BR, CAR-T cell therapy, R-GemOx, len/tafa, and loncastuximab with ORR 83%. 50% had RIS. 33% required dose reductions.
- At data cutoff, 2 patients who were on third-line therapy had stable disease. Causes of death in the third-line setting included: perforation (N=1), COVID (N=1), fungemia (N=1), cardiac arrest likely unrelated to PTLD (N=1). 3 patients had active PTLD at time of death.
- ORR for novel agents in second- and third-line treatment (N=8) was 88% compared to 63% for traditional cytotoxic therapy (CTx) (N=16).
- 25% of patients who received novel therapy in the second- and third-line settings required dose reductions compared to 50% who received CTx. No patients had graft rejection in the second- or third-line settings.

Characteristic	N = 71 (%)
Sex	
Male	51 (72)
Female	20 (28)
COO subtype	
GCB	14 (29)
Non-GBC	27 (38)
Transplant type	
Kidney	33 (47)
Liver	15 (21)
Lung	12 (17)
Heart	10 (14)
Pancreas	1 (1)

Table 1. Baseline characteristics of the PTLD cohort.

Treatment	Rituximab	R-CHOP	R-ICE	R-ICE to autoSCT	R-GemOx
N = 21	3	4	2	1	2
ORR (CR)	67% (67%)	75% (50%)	50% (0%)	100% (100%)	50% (0%)
Toxicities	Hypogamma-globulinemia, C. difficile infection, AKI	Bowel perforation -> septic shock (fatal), neutropenia, mucositis, AKI	Fungemia -> septic shock (fatal), neurotoxicity/confusion, GI bleed, diarrhea, AKI	Panic attack, neutropenic fever, thrombocytopenia, GI bleed, nausea	Septic shock (fatal), volume overload, A-fib, infectious diarrhea, nausea, mucositis, neuropathy

Treatment	R-ibruitinib	Tafasitamab/ Lenalidomide	Loncastuximab	BR-Polatuzumab	CAR-T	Tabelecleucel
N = 21	1	2	1	2	1	1
ORR (CR)	0% (0%)	100% (0%)	100%	50%	100% (0%)	100% (0%)
Toxicities	Intracranial bleed, diarrhea, AKI	Nausea	COVID-19, bacterial pneumonia, DVT, weakness	Fungemia, septic shock, HTN, tachycardia, thrombocytopenia, GI bleed, nausea	CRS (G2), ICANS (G3), prolonged pancytopenia, A-fib, bilateral pleural effusions	Hypogammaglobulinemia, Rhinoenterovirus infection, bacterial pneumonia

Table 2. Treatment regimens, overall response rates (ORR), and toxicities in the R/R setting.

Conclusion

- R/R CD20+ PTLD after SOT remains a therapeutic challenge.
- Novel therapies have been used in R/R setting, and larger studies could further evaluate efficacy and toxicities of these therapies in this unique population.

References

1. Trappe R, Oertel S, Leblond V, et al. Sequential treatment with rituximab followed by CHOP chemotherapy in adult B-cell post-transplant lymphoproliferative disorder (PTLD): the prospective international mutlicentre phase 2 PTLD-1 trial. *Lancet Oncol*, 2012; 13:196-206.
2. Zimmermann H, Koenecke C, Dreyling M, et al. Modified risk-stratified sequential treatment (subcutaneous rituximab with or without chemotherapy) in B-cell post-transplant lymphoproliferative disorder (PTLD) after solid organ transplantation (SOT): the prospective multicentre phase II PTLD-2 trial. *Leukemia*, 2022 Oct; 36(10):2468-2478.