Clinical Outcomes of EBV+ PTLD Patients Following HCT Who Fail Rituximab: A Retrospective Chart Review Study from France

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INTRODUCTION

- Post-transplant lymphoproliferative disease (PTLD) occurs as a consequence of immunosuppression following allogeneic hematopoietic stem cell transplantation (Post-HCT)
- In most cases, PTLD is associated with Epstein-Barr Virus (EBV) infection of B cells, either due to reactivation of the virus after transplantation, or from primary EBV infection[1,2,3]
- Clinical practice treatment guidelines recommend rituximab as preemptive therapy for EBV reactivation (based on EBV virus load) and for EBV+ PTLD following HCT
- Treatment options for EBV+ PTLD patients (pts) who fail rituximab are not clearly defined and outcome is usually very poor

METHODS

- It is a retrospective chart review study of pts diagnosed with EBV+ PTLD following HCT who received rituximab or rituximab plus chemotherapy (CT) between 2000-2017 at 4 centers across France and who were refractory (failed to achieve complete [CR] or partial response [PR]) to rituximab or rituximab plus CT, or relapsed at any point after such therapy
- Primary CNS-PTLD excluded
- Medical charts were reviewed independently by a trained reviewer and an experienced physician
- Kaplan-Meier (KM) method was used to estimate the distribution of overall survival (OS) for pts who failed rituximab or rituximab plus CT post-HCT
- Index date for rituximab failure: The earliest date when pts became refractory to or relapsed after first line rituximab or rituximab plus CT

RESULTS

Table 1. Patient Characteristics at Transplant (n=18)

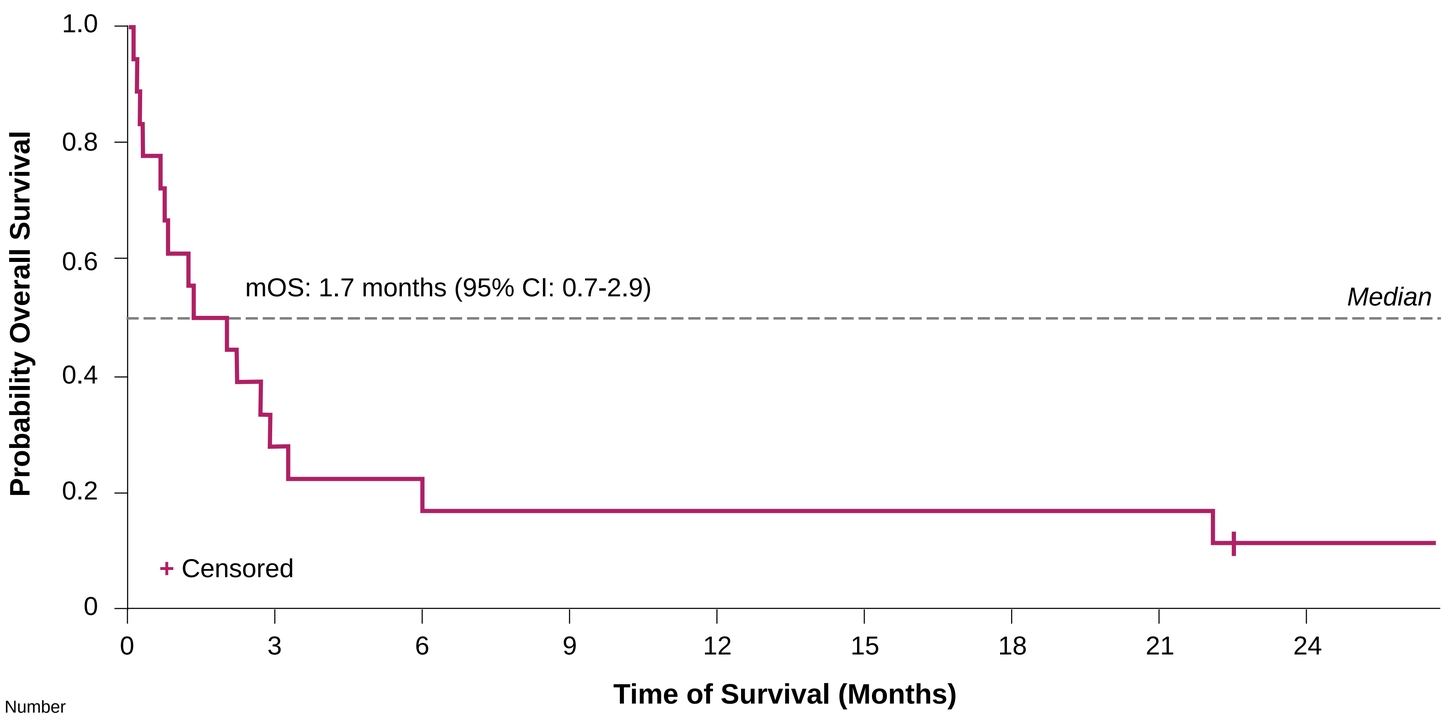
Median age at transplant, years (range)	54.8 (18-75)
	n (%)
Female	9 (50)
Initial diagnosis leading to HCT	
AML	6 (33.3)
ALL	2 (11.1)
MDS	2 (11.1)
CLL	1 (5.6)
NHL	1 (5.6)
Aplastic anemia	3 (16.7)
Multiple myeloma with light chains	1 (5.6)
Myelofibrosis	1 (5.6)
Severe medullary aphasia	1 (5.6)
Primary disease status leading to HCT	
In remission	12 (66.7)
Not in remission	6 (33.3)
Allograft donor type	
Matched unrelated donor	10 (55.6)
Matched related donor	4 (22.2)
Haploidentical	3 (16.7)
Mismatched unrelated donor	1 (5.6)
Stem cell source	
PBMC	13 (72.2)
Bone marrow	5 (27.8)
Conditioning regimen	
Reduced intensity conditioning	10 (55.6)
Myeloablative conditioning	8 (44.4)

Table 2. PTLD Characteristics (n=18)

Median age at PTLD diagnosis, years (range)	55 (18-75)
Median time to PTLD onset from HCT, months (range)	2 (1-4)
Median follow-up time from PTLD diagnosis, months (range)	2.6 (0.7-58.3)
	n (%)
PTLD histology type	
DLBCL	14 (77.8)
Polymorphic	3 (16.7)
Burkitt	1 (5.6)
PTLD stage (Ann Arbor)	
Stage I	1 (5.6)
Stage III	5 (27.8)
Stage IV	8 (44.4)
Unknown	4 (22.2)
PTLD involved sites*	
Lymph nodes	15 (83.3)
Liver	3 (16.7)
Lung	3 (16.7)
Gastrointestinal	3 (16.7)
Spleen	2 (11.1)
Tonsil	1 (5.6)
Kidney	1 (5.6)
Bone	1 (5.6)
Mediastinum	1 (5.6)
Extra nodal sites of PTLD	10 (55.6)
CD 20 status at diagnosis	
Positive	11 (61.1)
Negative	4 (22.2)
Unknown	3 (16.7)

*Non mutually exclusive categories

Figure 1. KM Plot for Overall Survival for EBV+ PTLD Pts Post-HCT Who Fail Rituximab (n=18)

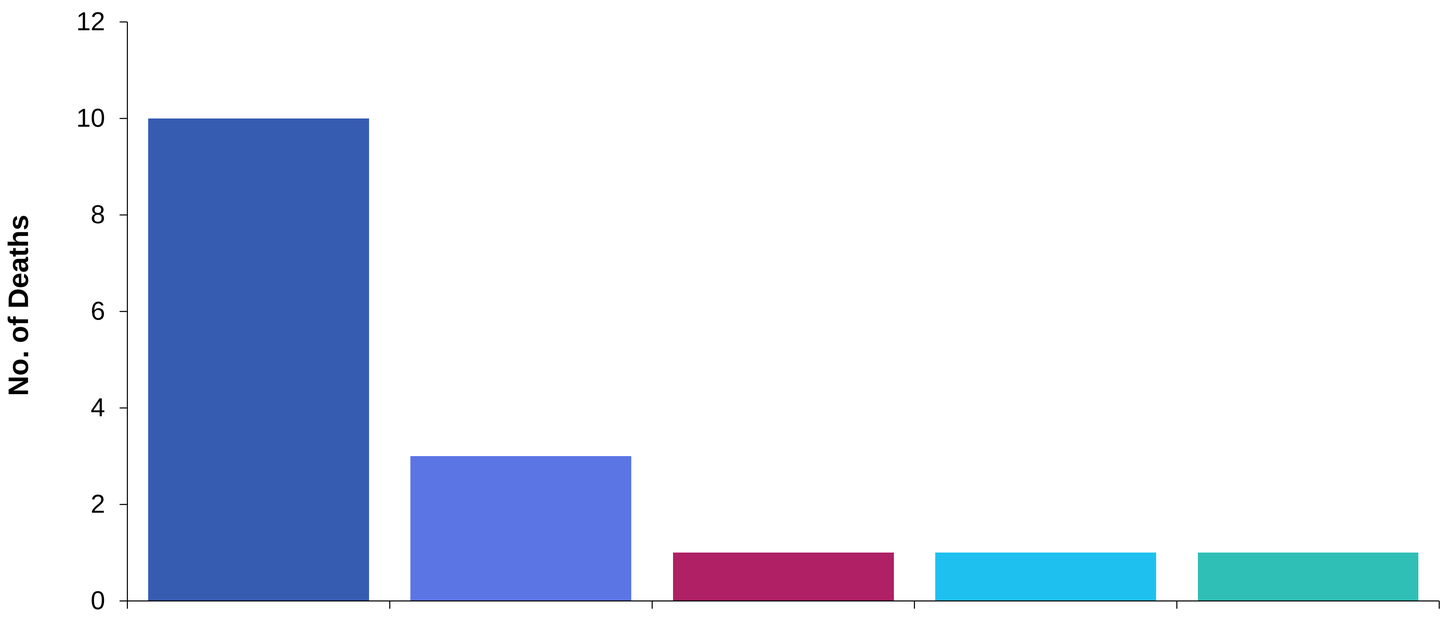


Number at risk									
(Cumulative Event)	18 (0)	5 (13)	3 (15)	3 (15)	3 (15)	3 (15)	3 (15)	3 (15)	1 (16)
OS Rate, % (95% CI)		27.8 (10.1, 48.9)	16.7 (4.1, 36.5)	16.7 (4.1, 36.5)	16.7 (4.1, 36.5)	16.7 (4.1, 36.5)	16.7 (4.1, 36.5)	16.7 (4.1, 36.5)	11.1 (1.9, 29.8)

Index date: Earliest date when pts became refractory or relapsed to rituximab.

- Median OS from PTLD diagnosis was 2.5 months (95% CI: 1.5-4.6).

Figure 2. Causes of Death (n=16)



CONCLUSIONS

- **Patients who developed EBV+ PTLD following allogenic HCT and failed rituximab had a mOS of <2 months**
- **89% of the pts died; of all deaths, 63% were related to PTLD and therapy**
- **There remains a significant unmet need for EBV+ PTLD POST-HCT pts who fail rituximab**

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