ADVERSE EVENTS AND CLINICAL BURDEN ASSOCIATED WITH CHEMOTHERAPY IN PATIENTS WITH RELAPSED OR REFRACTORY EBV+ PTLD FOLLOWING SOT: A RETROSPECTIVE CHART REVIEW STUDY FROM GERMANY AND FRANCE

H. ZIMMERMANN[1], S. CHOQUET[2], C. HERBAUX[3], P. CHAUVET[3], J. REN[4], Y. ZHANG[4], D. THIRUMALAI[4], H. XU[4], A. BARLEV[5], J. REITAN,[6] R. TRAPPE[1]

[1]Internal Medicine II: Hematology and Oncology, DIAKO Hospital, Bremen, Germany; [2] La Pitié Salpêtrière, Sorbonne Université, Paris, France; [3]Centre Hospitalier Régional Universitaire de Lille, Lille, France;[4]Atara Biotherapeutics, Thousand Oaks, USA; [5] Atara Biotherapeutics, South San Francisco, USA; [6]RJM Group, LLC, Crown Point, USA.

INTRODUCTION

- Post-transplant lymphoproliferative disease (PTLD) is a rare complication of immunosuppression after organ transplantation[1,2]
- PTLD are a heterogeneous group of diseases, over 80% cases of PTLD after SOT are associated with Epstein-Barr virus (EBV)[3,4]
- In adult patients with CD20+ PTLD after solid organ transplantation (SOT), risk-stratified sequential treatment with rituximab induction followed by rituximab consolidation or R-CHOP chemotherapy (CT) yields favorable treatment outcomes[1,2]
- However, adverse events (AEs), mortality and overall clinical burden associated with first or subsequent lines of chemotherapy (CT) for EBV+ PTLD pts who are refractory to or relapse (R/R) after rituximab or rituximab plus CT remains unclear.

OBJECTIVE

To characterize AEs, mortality and hospitalizations associated with CT for EBV+ PTLD pts following SOT who are R/R to rituximab or rituximab plus CT in the real-world setting.

METHODS

Study design

We conducted a retrospective chart review study from 2 centers in France and the German PTLD Registry (2000-2017).

Inclusion and exclusion criteria

We included pts diagnosed with EBV+ PTLD following SOT who were R/R to rituximab or rituximab plus CT. Pts diagnosed with primary central nervous system PTLD were excluded.

Data collection and measures

Medical charts were reviewed independently by a trained reviewer and an experienced physician. Mortality and AEs related to CT were adjudicated by physicians, and hospitalizations due to CT-related AEs were adjudicated by trained personnel. AE-related hospitalization was defined as hospitalization with a primary or secondary diagnosis of CT-related AE.

Statistical analysis

Descriptive analyses were conducted in this study. Mean, standard deviation, median and range were used to report continuous variables, while frequency and percentage were used to report categorical variables.

RESULTS

Table 1. Patient characteristics at PTLD diagnosis

Characteristics	Total (n=51)	Characteristics	Total (n=51)
Age at PTLD diagnosis in years, mean(SD)	47.0 (16.1)	CD20 negative at diagnosis, n (%)	2 (3.9)
Years to PTLD onset from transplant, mean(SD)	6.5 (7.6)	Lactate Dehydrogenase Elevated*, n (%)	31 (72.1)
Female, n (%)	11 (21.6)	PTLD Stage (Ann Arbor), n (%)	
Transplant organ type, n (%)		I	12 (23.5)
Kidney	23 (45.1)	II	4 (7.8)
Liver	9 (17.6)	III	5 (9.8)
Heart	8 (15.7)	IV	30 (58.8)
Lung	5 (9.8)	PTLD involving sites#, n (%)	
Multiple organs	1 (2.0)	Lymph nodes	5 (9.8)
Intestine	5 (9.8)	Liver	3 (5.9)
PTLD histology type, n (%)		Lung	3 (5.9)
DLBCL	32 (62.7)	Bone marrow	1 (2.0)
Polymorphic	10 (19.6)	Multiple sites	33 (64.7)
Burkitt	3 (8.3)	Other	6 (11.8)
Other	6 (11.8)	Patients with extra nodal sites, n (%)	46 (90.2)

DLBCL, diffuse large B-cell lymphoma; PTLD, post-transplant lymphoproliferative disorder; SD, standard deviation
* Elevated LDH≥250 U/l measured within 60 days after PTLD diagnosis
# Mutually exclusive

Figure 1. Treatment pattern

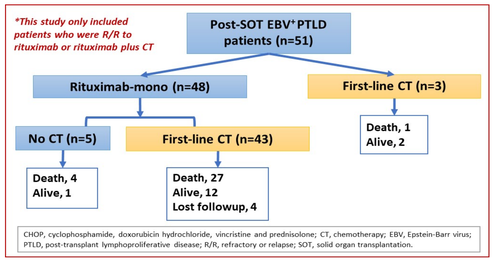


Figure 2. AEs during first-line CT

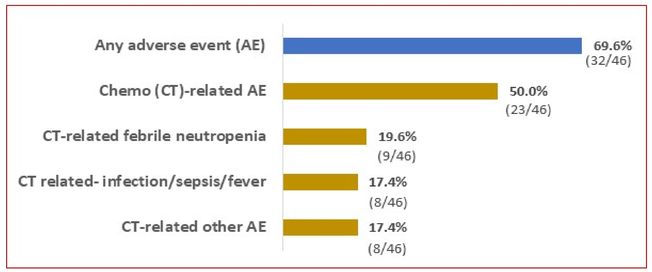


Figure 3: AE-specific deaths during the follow-up time (median 20 months) after first-line CT

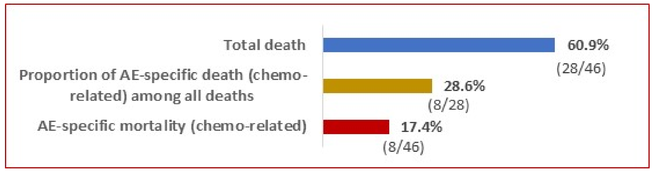


Figure 4: AE-related hospitalizations and ICU admissions among patients with first-line CT (one patient had missing data)

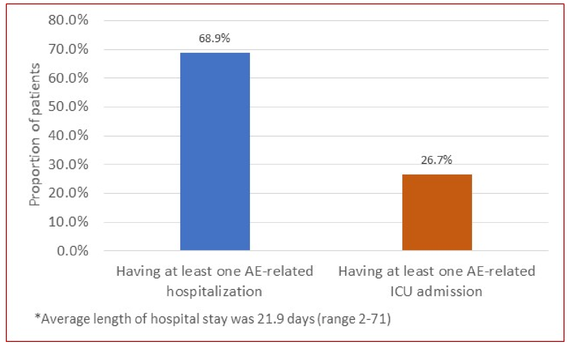
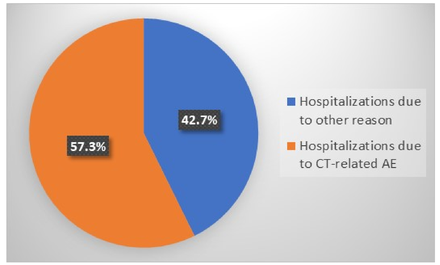


Figure 5: Proportion of hospitalizations due to CT-related AE among patients having at least one AE-related hospitalization



RESULTS (CONTINUED)

- Fifty-one patients (36 from Germany and 15 from France) with EBV+ PTLD were R/R to rituximab or rituximab plus chemo ***(Table 1).*** Of them, 45 patients were R/R to first rituximab.
- Forty-six patients received CT with a dominant regimen of CHOP/R-CHOP for first-line CT ***(Fig. 1)***, with 32.6% of patients receiving less than 4 cycles.
- During first-line CT, 69.6% reported AEs, and 50.0% reported CT-related AEs ***(Fig. 2).***
- CT-related AE led to dose reduction in 17.4% of pts and early discontinuation of CT in 10.9% of pts. Similar AE profile was observed during the second line CT with slightly higher rates.
- After first-line CT, 60.9% of patients died during the follow up time, and 28.6% of deaths were caused by CT-related AEs ***(Fig. 3).***
- 68.9% and 26.7% patients had at least one AE-related hospitalization and ICU admission, respectively ***(Fig. 4).***
- For those with at least one AE-related hospitalization, 57.3% of hospitalizations were due to CT related AEs ***(Fig. 5).***

CONCLUSIONS

- Half of patients with EBV+ PTLD following SOT who were R/R to rituximab or rituximab plus chemotherapy (CT) experienced CT-related AEs.
- Over a quarter of all deaths were due to CT-related AEs.
- These CT-related AEs pose significant clinical burden highlighting a need for effective and more tolerable therapies.

REFERENCES

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