

# Incidence, Risk Factors, and Outcomes of Post-Transplant Lymphoproliferative Disorders among Epstein-Barr Virus Donor Positive, Recipient Negative Adult Solid Organ Transplant Recipients

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## Background

Epstein-Barr virus (EBV) donor positive, recipient negative (D+R-) serostatus is an important relative risk factor for post-transplant lymphoproliferative disorders (PTLD) in adult solid organ transplant recipients (SOTR)<sup>1</sup>. However:

- The absolute incidence, risk factors, and outcomes of PTLD among adult EBV D+R- SOTR remain incompletely characterized.
- Defining specific subset(s) of adult EBV D+R- SOTR with a high absolute incidence of PTLD is a necessary initial step to identify a target population for future interventional trials of preventive and therapeutic strategies.

## Objectives

- Determine the incidence and risk factors for PTLD in adult EBV D+R- SOTR
- Identify specific subgroup(s) among EBV D+R- SOT recipients in whom the incidence is high enough to feasibly target for future preventive and/or interventional strategies

## Methods

Figure 1: Experimental methods

Retrospective identification of adult SOTR who underwent first transplant between January 1, 2000 and April 30, 2018 at a single center. All patients had ≥ 2 years of follow-up.

Pre-transplant EBV serologies used to determine recipient serostatus<sup>a</sup>

Donor serologies for all R- determined; D+R- cohort identified<sup>b</sup>

Biopsy-proven PTLD cases occurring in SOTR identified using a pathological database and LEAF, an open-source, data-driven web application for cohort discovery.<sup>2</sup>

- PTLD WHO classification, timing, and vital status extracted from electronic medical record
- Mann-Whitney,  $\chi^2$ , Fisher's exact test, and Kaplan-Meier curves were used to compare PTLD features among different organ and serostatus groups

<sup>a</sup> EBNA-1 IgG and VCA IgG were measured using FDA-cleared ELISA assays

<sup>b</sup> Donors with unknown serologies were presumed to be seropositive based on >93% seropositivity in the pooled donor population.

## Results

Figure 2: SOTR study population and PTLD incidence

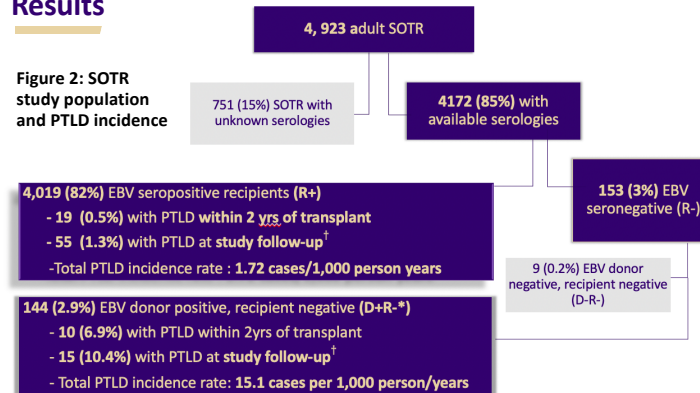


Figure 3: Cumulative Incidence of PTLD in D+R- SOTR\*

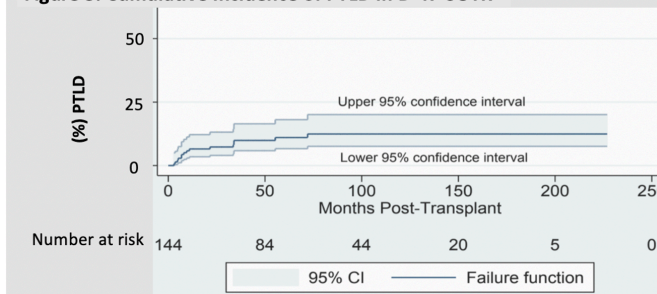
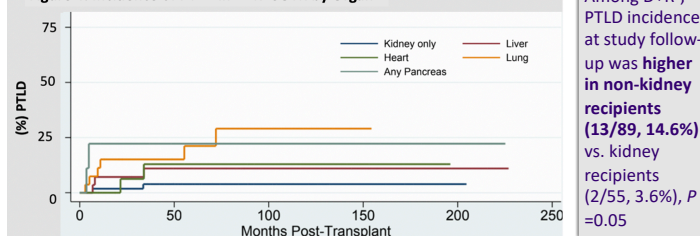


Figure 4: Incidence of PTLD in D+R- SOTR by Organ\*



\* Donor serologies were unknown for 53/153 (35%) of R- recipients and presumed to be positive. The presumed D+R- group (n=144), may include few D-R-; thus incidence of PTLD in D+R- may be underestimated

<sup>†</sup> Patients were followed until PTLD diagnosis, death, or April 30, 2020, whichever came first

Table 2: EBV D+R- Cohort Characteristics\*

PTLD characteristics	No PTLD (n=129)	PTLD (n=15)	P-value
Mean age at first transplant, years (SD)	45 (15.7)	38.3 (17.1)	0.1
Male (%)	90 (69.8)	11 (73.3)	0.88
Receipt of anti-thymoglobulin for rejection prevention or treatment	33 (25.6)	3 (20.0)	0.637
Median time from transplant to PTLD diagnosis, months (IQR)		9.6 (6.1-34.2)	
<b>PTLD histopathology</b>			
Monomorphic		9 (60.0)	
Polymorphic		3 (20.0)	
Hodgkin's lymphoma		0 (0.0)	
Other/Unknown		3 (20.0)	
<b>Tumor EBV status</b>			
Positive		12 (80.0)	
Negative		0 (0.0)	
Indeterminate/Unknown		3 (20.0)	
<b>Outcomes</b>			
Graft failure after PTLD diagnosis		2 (13.3)	
Graft failure with re-transplant after PTLD diagnosis		3 (20.0)	
Mortality within 6 months of PTLD diagnosis		3 (20.0)	

\* Because unknown donor serologies were presumed positive, may include few D-R-

## Conclusions

- EBV D+R- group comprises a small (~3%) proportion of adult SOTR, but have a ~10-fold higher incidence of PTLD compared to R+ patients
- Among EBV D+R- SOTR, the absolute incidence of PTLD is significantly higher in non-kidney vs kidney recipients
- Trials of new preventive and/or therapeutic strategies should be most feasible in this group

## References

- 1) Caillard S, Lamy FX, Quelen C, et al. *Am J Transplant.* Mar 2012;12(3):682-93.
- 2) Dobbins NJ, Spital CH, Black RA, et al. Leaf: an open-source, model-agnostic, data-driven web application for cohort discovery and translational biomedical research. *J Am Med Inform Assoc.* Jan 2020;27(1):109-118

The authors have no relevant interests to disclose