EPSTEIN BARR VIRUS (EBV)- POST TRANSPLANT MANAGEMENT UHL RENAL TRANSPLANT GUIDELINE	University Hospitals of Leicester NHS NHS Trust C22/2022

1. Introduction and Who Guideline applies to

This guideline is written to help clinicians manage Epstein Barr seronegative patients receiving kidney transplant from Epstein Barr seropositive donors in Leicester transplant unit.

EBV transmission to naive recipients (D+/R-) increases the risk of post-transplant lymphoproliferative disorders. The risk of PTLD in renal transplant recipients is between 1 to 2 %. The risk of PTLD is more than 6 times higher for D+/R- transplants compared with D+/R+ transplants. There is no prophylactic treatment that can prevent primary EBV infection. Therefore EBV- DNA monitoring and early intervention should be considered for all D+/R- recipients. This includes reduction of immunosuppression and, in selected cases, rituximab if there is a significant rise in viral load(> 10 3 IU/ ml).

Imaging by whole-body 18-fluoro-deoxyglucose positron emission tomography (FDG-PET) is used in most European centres to rule out PTLD and complemented computer tomography is used in 50%.

Kidney Disease: Improving Global Outcomes guidelines suggest monitoring high-risk kidney transplants (defined as donor EBV seropositive and recipient EBV seronegative) for EBV by nucleic acid testing after transplantation once in the first week, monthly for the first 3 to 6 months, then every 3 months until the end of the first post transplant year, and additionally after treatment for acute rejection.

Kidney Disease: Improving Global Outcomes guidelines recommend reducing immunosuppressive medication in EBV-seronegative patients with an increasing EBV viral load (VL) and in patients with EBV disease, including PTLD.

Status	Risk of EBV infection	Prophylaxis	Monitoring	When to treat?
D-/R-	Low	None		
D-/R+ D+ /R+	Mod	None		Any PCR >10^3 copies / ml, reduce IS / Rituximab
D+/R-	High		Check EBV PCR every 2 weeks for 3 months	Any PCR >10^3 copies / ml, reduce IS / Rituximab

2. Guideline Standards and Procedures

This guideline is written to help clinicians identify high risk renal transplant recipients, to assist them in monitoring viremia and intervene in case of elevated viremia.

FREQUENCY OF PCR CHECK

- Lower risk patients (D-/R+, D+/R+):
    - Monthly EBV PCR for first 3 months post transplant.
    - Three monthly from 3 month until 1 year post transplant.

- High risk patients (D+/R-):
    - Fortnightly EBV PCR for first 3 months post transplant
    - Monthly from 3 month to 6 month post transplant
    - Three monthly from 6 month until 1 year post transplant

ACTIONS UPON RESULTS

If titres are greater than 1000 copies/ml (620 IU/ml)

- Reduce Immunosuppression (Mycophenolate/ Azathioprine/Tacrolimus/Cyclosporine).

- Discuss with Virologist about performing EBV DNA PCR on whole blood and plasma. The rational is that elevated viremia in whole blood compared to plasma would indicate that the virus is mainly intracellular, potentially less clinically significant.

- Check titres two weeks later.

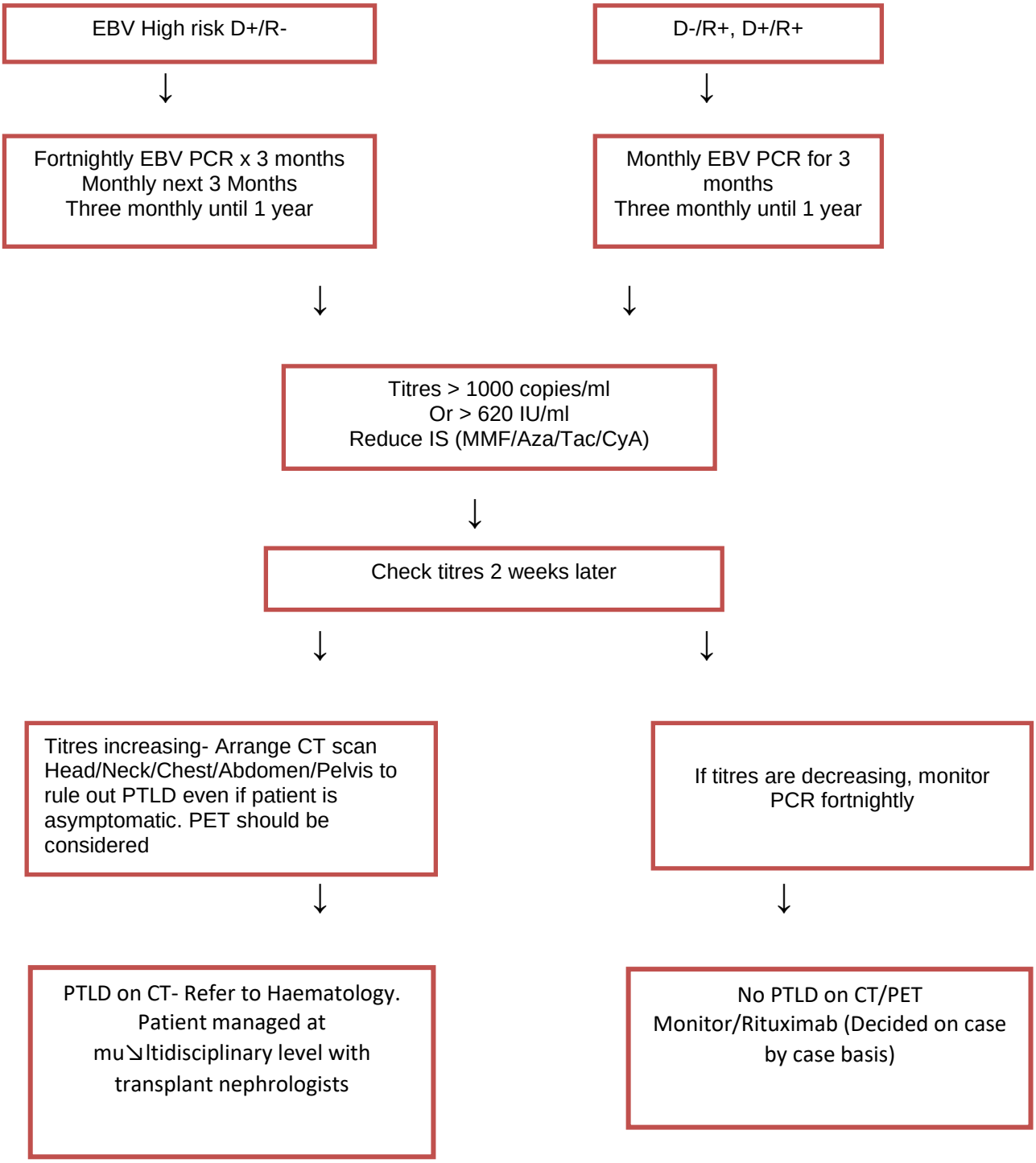
    - If titres are decreasing monitor with PCR every two weeks till negative

    - If titres are raising and even if the patient is asymptomatic, proceed to further immunosuppression reduction and arrange a Head, Neck, Chest, Abdomen and Pelvis CT scan to rule out PTLD. PET scan should also be considered.

PTLD MANAGEMENT

- If PTLD is found on CT/PET scan, then refer to Haematologist for treatment. Patient is managed at a multidisciplinary level together with transplant nephrologists.

- If no PTLD detected on CT/PET, Rituximab treatment can be considered. Treatment will be decided on case by case basis.


EBV High risk D+/R-
D-/R+, D+/R+
Fortnightly EBV PCR x 3 months
Monthly next 3 Months
Three monthly until 1 year
Monthly EBV PCR for 3 months
Three monthly until 1 year
Titres > 1000 copies/ml
Or > 620 IU/ml
Reduce IS (MMF/Aza/Tac/CyA)
Check titres 2 weeks later
Titres increasing- Arrange CT scan Head/Neck/Chest/Abdomen/Pelvis to rule out PTLD even if patient is asymptomatic. PET should be considered
If titres are decreasing, monitor PCR fortnightly
PTLD on CT- Refer to Haematology. Patient managed at mu↘ltidisciplinary level with transplant nephrologists
No PTLD on CT/PET
Monitor/Rituximab (Decided on case by case basis)

3. Education and Training

All doctors managing renal transplant recipients should read this guideline.

4. Monitoring Compliance

What will be measured to monitor compliance	How will compliance be monitored	Monitoring Lead	Frequency	Reporting arrangements
EBV PCR from seronegative recipents	Proton and iLab data		Annual	

5. Supporting References (maximum of 3)

Sampaio MS, Cho YW, Shah T, et al. Impact of Epstein-Barr virus donor and recipient serostatus on the incidence of post-transplant lymphoproliferative disorder in kidney transplant recipients. Nephrol Dial Transplant. 2012;27:2971–2979. [PubMed] [Google Scholar]

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European Directorate for the Quality of Medicines & Health Care: Guide to the quality and safety of organs for transplantation. 6th ed Strasbourg: 2016. [Google Scholar]

6. Key Words

Renal, Transplant, EBV, PTLD.

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Details of Changes made during review:	