

CLINICAL GUIDELINES SUPPLEMENT

EBV Monitoring Protocol

BACKGROUND

Post-transplant lymphoproliferative disorder (PTLD) is one of the most important malignancies after solid organ transplant. The most significant risk factor for PTLD is primary EBV infection (EBV donor positive/ recipient negative) with the highest risk period occurring in the first year.

EBV DNAemia is a marker of risk but not diagnostic of PTLD. Viral load results should be interpreted along with viral load kinetics, clinical assessment, and net state of immunosuppression.

Who to monitor?

- EBV D+/R- recipients: pre-emptive monitoring during the first-year post-transplant
 - Patients who have increased immunosuppression for treatment of rejection should be considered for resumption of monitoring or increased intensity of monitoring.
- EBV R+ recipients: routine monitoring is not required

EBV Surveillance Schedule

The following schedule is suggested for EBV viral load monitoring:

- At least every 2 weeks for the first 6 months
- Monthly from months 6-12

MANAGEMENT OF EBV DNAEMIA ONCE EBV IS DETECTED

a. Adjust monitoring frequency

- Increase monitoring frequency to weekly until the viral load is falling
 - Once falling, frequency can be reduced to every 2 weeks until viral load is:
 - Negative
 - Reaches a stable, low-level set-point (e.g. similar values over multiple weeks).
 - If the value has been <1,000 IU/mL for 4 or more values, monitoring should be discontinued.

b. Clinical assessment

- Patients should be assessed for signs and symptoms of malignancy (fever, night sweats, weight loss, lymphadenopathy, unexplained GI symptoms, etc.) or graft dysfunction.

c. Imaging

- CT neck/chest/abdomen/pelvis with contrast should be done if the patient has symptoms compatible with PTLD.
- Maintain a low threshold for CT chest/abdomen/pelvis when:
 - EBV viral load is rapidly rising over time (≥ 1 log increase/10-fold increase between weekly-biweekly values) OR
 - EBV viral loads are very high when first detected ($>100,000$ IU/mL).

- Biopsy should be done if lymphadenopathy is found for histopathologic assessment. Excisional biopsy is preferred and if not feasible, core-needle biopsy is the next-best option. If infection is part of the differential diagnosis, consult transplant infectious diseases, and fresh tissue should also be sent to microbiology for bacterial, fungal and AFB cultures.

MANAGEMENT OF IMMUNOSUPPRESSION

If the patient is followed by a community transplant site, the primary transplant centre should be contacted for input with regards to immunosuppression reduction and the intensity of monitoring.

a. Consider reduction of immunosuppression

- Patients with EBV DNAemia should be assessed for reduction of immunosuppression, particularly when:
 - EBV viral load is rapidly rising over time (≥ 1 log increase/10-fold increase between weekly-biweekly values) OR
 - High level viral loads ($>10,000$ IU/mL).
 - Clinical or radiographic findings concerning for evolving PTLD

b. Continue immunosuppression with close monitoring

- Low level viral loads ($<10,000$ IU/mL) in asymptomatic patients can just be monitored without adjustment of immunosuppression

c. Re-escalation of immunosuppression

- Immunosuppression re-escalation can be reassessed based on individual patient risk when the viral load is negative or reached a stable set point (e.g. viral loads $<1,000$ IU/mL for 4 or more values)