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| **PROTOCOL TITLE:** Kidney and Pancreas Post Transplant: BK Polyoma Management |
| **APPLICABLE FACILITIES:**[ ] EHC [ ] EDH [ ] EHH [ ] EHI [ ] EHN [ ] EJCH [ ] ELTAC [ ] ESJH[x] EUH [ ] EUHM [ ] EUHS [ ] EUOSH [ ] EWWH [ ] RJV-ERH [ ] RJV-ESOP [ ] TEC/ESA |
| **EFFECTIVE DATE:**  | **ORIGINATION DATE:** 03/07/2013 |

**CATEGORY:** Diagnostic/Therapeutic/Preventive

**LEVEL:** Independent

**PURPOSE:** The Emory Kidney Transplant Program is committed to caring for patients and 20% of renal transplant patients will develop BK viremia post-transplantation. Uncontrolled BK viremia can lead to nephropathy and loss of transplanted organ. Prior to institution of prospective screening at EUH for BK polyoma, 50% of patients with BK nephropathy would lose their transplanted organ within 6 months of diagnosis.1 Reduction of immunosuppression is the only currently effective means of prolonging allograft survival.2

**GUIDELINES:**

1. **BK Polyoma PCR monitoring protocol**

All patients undergoing kidney and multi organ transplantation will have a BK polyoma PCR performed at post-transplant visits, monthly in the first year. BK monitoring will be discontinued after the first annual visit on all patients who have not developed evidence of infection. Routine monitoring beyond **1 year** post-transplant is not generally recommended and should be performed only if clinically indicated.

1. For those who have developed significant BK viremia and/or disease, in addition to the prescribed frequencies below, BK polyoma PCR monitoring will occur at months 15, 18, 21, and 24. More frequent monitoring may be performed if clinically indicated
2. For those who received thymoglobulin or high dose steroids/Acthar/PLEX/Rituxan/IVIg/PLEX, BK polyoma PCR will be checked every month for the first 6 months
3. BK polyoma PCR will be obtained at the time of any renal transplant biopsy for cause (allograft dysfunction, BK viremia).

**2.** **Treatment protocols**

A. **Tacrolimus/Cyclosporine-based maintenance**

**Initial Diagnosis**:

Upon detection of BK PCR in blood, if BK PCR value is:

* + Below 4.0 log10 copies/ml
		- the BK PCR blood test should be repeated within 2 weeks and in 1 month
		- If still positive and still below 4.0 log10, BK PCR should then be monitored every 4 weeks until a stable low-level viremia is documented. (Probably asymptomatic viremia).
		- If still positive and still below 4.0 log10 on stable immunosuppression for 2 years consider monitoring at yearly visits.
	+ Between 4.0 log10 and 5.0 log10 copies/ml
		- Reduce anti-metabolite dose (MMF/Myfortic/AZA) dose by 50%
		- BK PCR should then be monitored every 2 weeks until a stable low level (<4.0 log10) viremia is documented. (Probably asymptomatic viremia).
	+ Greater than 5.0 log10
		- A kidney biopsy is indicated if there is evidence of renal dysfunction
		- Reduce anti-metabolite dose (MMF/Myfortic/AZA) dose by 50%
		- BK PCR should then be monitored at least every 2 weeks until a stable low level (<4.0 log10) viremia is documented.
	+ If biopsy proven BK nephropathy
		- In addition to reduction in MMF, reduce calcineurin inhibitor to next lower target range.
		- If patient’s biopsy shows significant inflammation, then initiate an oral steroid pulse (100mg of prednisone daily for 5 days), then go back to 5mg prednisone.

**Follow-up therapy**:

* + Within the first 4 weeks after immunosuppression reduction, if the PCR level is trending downward, no further reduction of immunosuppression is needed.
	+ At 4 weeks after immunosuppression reduction, if BK PCR has reduced by < 1.0 log10 , continue to monitor every 2 weeks until PCR 4.0 < log10 copies.
	+ At 2-4 weeks after immunosuppression reduction, if BK PCR has increased by > 1.0 log10, then consider further reduction in the calcineurin inhibitor dose, consider reduction of the anti-proliferative agent or discontinuation, or consider increasing prednisone to 10mg. Repeat BK PCR in 2 weeks and repeat cycle until BK PCR < log10 4.0 copies.

B. **Belatacept based-maintenance treatment**

**Initial Diagnosis**:

Upon detection of BK PCR in blood if BK PCR value is:

* + Below 4.0 log10 copies/ml
		- the BK PCR blood test should be repeated within 2 weeks and in 1 month
		- If still positive and still below 4.0 log10, BK PCR should then be monitored every 4 weeks until a stable low-level viremia is documented. (Probably asymptomatic viremia).
	+ Between 4.0 log10 and 5.0 log10 copies/ml
		- < 9 months post-Transplant on bela+MMF+Tac (trough 3-5) +Pred
			* Continue bela q month
			* Reduce anti-metabolite dose (MMF/Myfortic/AZA) dose by 50%
			* Tac trough 3-5
		- > 9 months Post Transplant on bela+MMF+Tac taper+Pred
			* Continue bela q month
			* Continue anti-metabolite dose (MMF/Myfortic/AZA)
			* Start or continue taper (lowest dose of MMF while on taper 500mg bid)
		- 12-18 months Post transplant on bela+MMF+Pred
			* Continue bela q month
			* Reduce anti-metabolite dose (MMF/Myfortic/AZA) dose by 50%
				+ Lowest dose of MMF 3 months post taper 500mg bid
		- > 18 months Post transplant on bela+MMF+pred
			* Continue bela q month
			* Reduce anti-metabolite dose (MMF/Myfortic/AZA) dose by 50%
		- BK PCR should then be monitored every 2 weeks until a stable low level (<4.0 log10) viremia is documented. (Probably asymptomatic viremia).
	+ Greater than 5.0 log10
		- A kidney biopsy is indicated if there is evidence of renal dysfunction
		- Refer to plan outlined above
		- BK PCR should then be monitored at least every 2 weeks until a stable low level (<4.0 log10) viremia is documented.
	+ If biopsy proven BK nephropathy
		- If patient’s biopsy shows significant inflammation, then initiate an oral steroid pulse (100mg of prednisone daily for 5 days), then go back to 5mg prednisone.
		- Repeat BK PCR in 2weeks.

**Follow-up therapy**:

* + Within the first 4 weeks after immunosuppression reduction, if the PCR level is trending downward, no further reduction of immunosuppression is needed
	+ At 4 weeks after immunosuppression reduction, if BK PCR has reduced by less than 1.0 log10, continue to monitor every 2-4 weeks until PCR < 4.0 log10 copies.
	+ At 2-4 weeks after immunosuppression reduction, if BK PCR has increased > than 1.0 log10, in addition to above outlined pathway, consider the following interventions under the discretion of transplant nephrology and other team members:
		- Bela-consider q2 month or bela holiday
		- CNI-Selective consideration for conversion to tac
		- Reduce anti-metabolite dose (MMF/Myfortic/AZA) dose by 50%
			* If anti-metabolite is discontinued, consider increasing prednisone to 10mg
		- BK PCR should then be monitored every 2 weeks until a stable low level (<4.0 log10) viremia is documented. (Probably asymptomatic viremia).

**3. Re-address Increasing Immunosuppression**

Acute rejection can occur in 8 to 12 percent of kidney transplant recipients with BK viremia or established BK virus nephrophathy following a reduction in immunosuppression. Readdress immunosuppression once BK pcr is <4.0 log10 or if there is rapid decline in BK PCR with reduction in immunosuppression.

**4.** **Clinical Trials Patients**-Consult with study coordinator to follow any study prescribed alterations in immunosuppression.

**5.** **Policy Review:** As part of the QAPI program, policy compliance and BK viremia rates for the first twelve months post-transplant will be reviewed every six months by the transplant program’s clinical leadership and transplant infectious disease specialist.

**RELATED POLICIES / PROCEDURES:** N/A

**DEFINITIONS:** N/A

**REFERENCES AND SOURCES OF EVIDENCE:**

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**KEY WORDS:** BK virus, Polyoma BK, Kidney transplant