RENAL TRANSPLANT: IMMEDIATE MANAGEMENT - SCH

PRACTICE GUIDELINE ©

DOCUMENT SUMMARY/KEY POINTS

- The purpose of this protocol is to provide guidance for the admission and medical management of children who are undergoing kidney transplantation for medical and nursing staff.
- Variations from this guideline may be required for individual patients but this should only occur under consultant supervision.

CHANGE SUMMARY

- N/A – New document

READ ACKNOWLEDGEMENT

This practice guideline is relevant to the following staff:

- Medical and surgical junior staff involved in the care of kidney transplant recipients
- Medical and surgical senior staff involved in the care of kidney transplant recipients
- Nursing staff in C1S and CICU involved in the care of kidney transplant recipients

Approved by:	SCHN Policy, Procedure and Guideline Committee	
Date Effective:	1st April 2018	**Review Period:** 3 years
Team Leader:	Staff Specialist	**Area/Dept**: Renal

Date of Publishing: 6 April 2018 2:54 PM Date of Printing: 6 April 2018

TABLE OF CONTENTS

Background

Kidney transplantation is the preferred mode of renal replacement therapy in children, providing both improved quality of life and survival for children with end stage kidney disease (ESKD). [1]

The two major programs for kidney transplantation are the living related/unrelated kidney donation and deceased donor program. Living related/unelated kidney donation can be done pre-emptively, however children can only be wait listed for deceased donor kidney transplant whilst on dialysis. Living related/unrelated kidney transplantation is scheduled electively.

The purpose of this protocol is to provide guidance for the admission and medical management of children who are undergoing kidney transplantation for medical and nursing staff.

Pre-Operative Admission & Workup

Business Hours: Direct ward admission C1S

After Hours: through emergency department or direct to ward if bed available
After hours registrar/SOS will be responsible for admission

Checklist of investigations and orders

Table 1 summarises the investigations and orders required on admission

The consultant nephrologist will contact the transplant surgical consultant directly

The following people are also to be notified by the admitting medical officer regarding the kidney transplant:

- Anaesthetic Registrar on call through switch
- The transplant surgeon will notify the renal transplant fellow at Prince of Wales through switchboard. Surgical team is responsible for consent and notification of theatres.
- Request postoperative CICU bed by contacting CICU Team leader and CICU fellow.

The medical officer clerking admission will liaise with the nephrologist on call to determine:

- Whether dialysis is required preoperatively
- If the patient is medically well for kidney transplantation
- Which of the patients regular medications will be required preoperatively
- The rate and type of IV fluids to be administered whilst fasting

The dose and timing of the initial pre-operative immunosuppression and medications. Many medications will require ordering from pharmacy in advance.

Whether the child requires isolation bed due to known previous multi-resistant organism isolation.

Table 1: Pre-operative investigations to be performed on admission to SCH

Investigations		*Comments*
Bloods + IVC	***FBE***	***Send bloods urgently***
	UEC/CMP/LFTs/BSL	
	Coagulation	
	Group and hold	
	X- match two units	
	Hepatitis B/C/HIV serology	
	EBV/CMV/Herpes/Varicella IgG	
ECG		
CXR		
Microbiology	***MRSA screen swabs***	***Also swab any open wounds***
	Gastrostomy site swab	
	CVL exit site swab	
	PD catheter exit site swab	
	PD fluid culture	***Drain and cap PD catheter. Send fluid for MCS***
	MSU	
	Viral throat swab or NPA	
Weight & height		***Dry weight if on dialysis***

Initial perioperative medications

All decisions regarding transplant immunosuppression are to be discussed with the nephrologist on call.

Table 2 denotes the medications which are required to be charted and administered prior and during the transplant operation.

Table 2: Perioperative medications for kidney transplantation

Drug	Dose and Route	Timing	Comments
Mycophenolate mofetil*	400mg/m^2 PO Max dose 1000mg	Given prior to theatre	Continued Q12H
Tacrolimus*	0.15mg/kg PO Max dose 5mg	Given prior to theatre	May be withheld with deceased donor
Corticosteroids	Prednisone 2mg/kg (max 120mg) PO	Given prior to theatre	Continued daily
	Methylprednisolone 10mg/kg IV Max dose 500mg	Given intra-operatively immediately prior to release of aortic clamp	
Basiliximab**	< 35kg 10mg IV >35 kg 20mg IV (adult dose)	Given intra-operatively	Infusion 50ml 5% glucose or 0.9% sodium chloride over 30 mins
Antibiotics	Piperacillin-tazobactam (Tazocin®) 100mg/kg(of piperacillin component)	Given-intraoperatively	Stat dose for surgical prophylaxis

*See appendix regarding tablet strength: round to appropriate dose
**Thymoglobulin, a T cell depleting anti body, is an alternative induction agent which is used in selected patients. If required, dosing and administration is provided in Appendix A

Anaesthetic Guidelines

All children will require a multi-lumen central venous line inserted for CVP monitoring and fluids

- An arterial line is typically inserted to monitor SBP and MAP
- A high intravascular volume and an adult blood pressure should be targeted intra-operatively due to the complication of thrombosis in paediatric transplant recipients. Assessment of intravascular volume can be achieve through direct visualisation of the IVC and also inferred from the CVP.
- Aggressive fluid replacement is generally required to achieve the high intravascular volume (generally CVP of 15mmgHg in infants and CVP of 12 mmHg in older children) at the time of vascular anastomosis and re-perfusion.

ml:ml replacement of urine output should commence intra-operatively and continue through recovery as the risk of thrombosis is greatest immediately post transplant.

Immediate post-operative CICU management

Day of transplant is referred to as Day 0

Handover of patient at the bedside from anaesthetics/surgeons should occur with CICU medical nursing staff and nephrology team present.

Post operatively renal transplant patients are managed in CICU jointly with the Nephrology team.
Patients should be nursed in a single room with barrier precautions.

The risk of graft thrombosis is greatest immediately post-operatively. Aggressive fluid replacement is required for the first 24 - 48 hours The Nephrology team in collaboration with the CICU team will set BP, CVP and UO targets at handover in CICU and at least daily on ward round. Notify Nephrologist immediately if there is sudden fall in urine output below target

Fluid Management

Note urine output target includes native urine output

Fluid replacement consists of two IV lines of the following:

IV line 1: Insensible losses : 400ml/m2 /day of 0.45% sodium chloride + 5% glucose **IV line 2: Urine replacement:** ml:ml replacement of previous hour urine output. **Fluid options:** 0.9% sodium chloride, 0.45% sodium chloride and Plasmalyte

Glucose free solutions are typically required for urine replacement due to high BSLs.
0.45% sodium chloride will need to be ordered in advance

Additional fluid bolus are commonly required to meet BP, CVP and UO targets. Patients may require inotropic support for blood pressure if fluids required is excessive.

This fluid regime is generally continued for the first 48 hours and then a constant IV fluid rate can be used.

Investigations and Observations

- FBE/UEC/CMP/glucose/VBG should be sent on arrival in CICU and every 6 hours thereafter.
- Tacrolimus trough levels should be measured each morning. The morning dose should be administered after blood has been collected. Levels are used to guide subsequent dosing as they are not available until late afternoon.
- Urinalysis should be performed daily
- Strict fluid balance
- Renal transplant USS should be arranged within the first 24 hours of arrival in CICU. If the child arrives back to CICU within working hours this will be performed on the same day, otherwise the next morning. If there are clinical concerns about graft function at which time the SCH Radiology should be contacted urgently through switchboard.

Post-operative Immunosuppression & Medications[2]

Table 3: Postoperative immunosuppression and medications

Drug	Medication	Dosing	Comments
Corticosteroids	Methylprednisolone	2mg/kg IV daily	Day 1 & Day 2 Day 4 prednisolone dose given as IV methylprednisolone as premedication for basiliximab along with promethazine
	Prednisolone PO	Wt < 20 kg: 2 mg/kg daily Wt > 20kg 1.5mg/kg daily	From Day 3: Weaning regimen see Page 13
Induction agent	**Basiliximab***	< 35kg: 10mg/m2 >35kg 20mg	Second dose Day 4 Infusion 50ml 5% glucose or 0.9% sodium chloride over 30 mins
Anti-proliferatives	Mycophenolate mofetil IV or PO	400mg/m^2 PO BD Trough levels on Day 7 and 14. To be collected and dose given immediately post Trough target > 1.4 mg/L	Commence Day 0 Give at 0800 & 2000 Switch to oral when tolerating fluids
Calcineurin inhibitors	Tacrolimus PO	0.15mg/kg PO BD Titrate to daily trough levels see Page 14 – give dose immediately post level	Commence Day 0 unless delayed graft function. Give at 0800 & 2000
Anti-infectives	Ganciclovir IV	Initial dose assume CrCl 10-25ml/min/1.73m^2 0.625 mg/kg/day	Commence Day 0 then switched to PO valganciclovir when tolerating fluids

			Not given if donor and recipient CMV negative Dose to be recalculated and sterile pharmacy to be informed by 1000 next am
	Trimethoprim-sulfamethoxazole PO	≥50kg 160mg (trimethoprim component) tablet Mon/Wed/Fri < 50 mg 5mg/kg (trimethoprim component) Mon/Wed/Fri	
	Nystatin PO	1 ml QID	Fungal prophylaxis
Other medications	Ranitidine IV	1 mg /kg BD	Modify to GFR
	Heparin		As determined by the transplant surgeon and consultant nephrologist

General postoperative ward care

Observations and monitoring fluid status

- Patient should be weighed daily prior to breakfast
- Fluid regimen and target daily fluid balance will be determined daily by nephrology team
- Strict fluid balance should be kept and calculated as per medical team orders
- On return to the ward, patients fluid balance is be assessed by evening and overnight medical cover for the first 48 hours

Medications and investigations

- Daily bloods are performed for the first month post transplant
- Tacrolimus is given immediately post blood tests: levels are used to guide subsequent dosing as they are not available until late afternoon
- Daily urinalysis to be attended

Wound and Drain Care

- Wound care to be attended as directed by transplant surgical team

- Removal of drain to be determined by the transplant surgical team

Indwelling catheter

- IDC is to remain in situ as per transplant surgical team (typically 5-7days) and is not to be removed without discussion with the transplant surgical team.
- If the IDC becomes blocked or is accidently removed, following discussion with transplant surgical team it is to be replaced immediately by nursing staff.
- Oxybutynin may be used to relieve bladder pain and spasms induce by IDC or polyuria

Ureteric Stents

- Double J stent routinely inserted at time of transplant and removed 4 weeks post transplant. Liaise with Urology team to arrange date during inpatient admission.
- If recurrent UTI or macroscopic haematuria, can be removed earlier on consultation with Urology and transplant surgical team.

Dialysis and vascular access

- Non-tunnelled CVLs should receive standard care as per CVAD guideline: these are removed as soon as possible, typically post Day 4 basiliximab. They can be used for blood sampling.
- Non-tunnelled and tunned haemodialysis lines are sometimes required for plasmapharesis – these are NOT to be used for blood sampling unless directed by the Nephrology team.

Mobilisation

- Referral to physiotherapy should be considered on return to the ward for chest physiotherapy.
- The patient should be encouraged to sit in a chair out of bed on day 2 and early ambulation should be encouraged.

Feeds and Diet

- Transplant surgical team will determine upgrade in oral intake.
- Children who have previously required supplemental feeds pre transplant will often require feeds in the immediate post transplant period. Often these can be transitioned to standard infant and paediatric formula.
- Early review by dietician is essential to encourage healthy habits and minimise post transplant weight gain.

Potential medical and surgical complications

Table 4: Summary medical and surgical complications immediately post kidney transplant

Graft thrombosis **EMERGENCY**	Highest risk first 48 hours post transplant Presents with sudden decrease in urine output Flush IDC to see if it blocked using sterile technique **Needs urgent return to theatre and USS to confirm diagnosis – notify nephrology and transplant surgical team IMMEDIATELY**
Sepsis **INFORM NEPHROLOGY TEAM IF T > 38.5C**	Common sources include chest infection, CVL infection and urosepsis Culture MSU, blood peripheral and CVL, PD and drains. Consider CXR. **Discuss with Nephrology and ID re antibiotics:** typically IV piperacillin/tazobactam (tazocin®) and consider antifungal cover
Rejection	Rejection is often subclinical with an elevated creatinine the primary presentation. Hyperacute rejection is uncommon today as tissue typing techniques have improved significantly. This presents with fever, tender graft and raised creatinine.
Wound infection	Ensure any organisms grown from pre-op swabs are covered
Bowel obstruction	Higher risk with intra-abdominal transplants
Lymphocoele	Often conservatively managed, sometimes requires marsupialisation
Ureteric anastomosis dehiscence	Presents with abdominal distension and urinary ascites. Check ascites fluid creatinine. Acute management is for reinsertion of IDC and likely to require surgical correction
Decrease in urine output	Flush IDC to see if it blocked Review fluid balance and discuss with Nephology Team regarding management

Common fluid and electrolyte problems encountered post operatively

- **Hyperglycaemia:** Due to the large volume of fluid replacement and use of corticosteroids at induction, transient hyperglycaemia is often seen immediately post transplant. It can be prevented by the use of glucose free fluids for urine replacement.

However, a small number do develop new onset diabetes after transplantation (NODAT).

- **Acidosis:** Quite common as there may be a significant amount of lactic acid released into the circulation with reperfusion of the lower extremity. Acidosis typically self-resolves without intervention. Persistent acidosis with bicarbonate of less than 15 can be managed by switching to Plasmalyte or Hartmanns and or addition of bicarbonate to IV fluids.

  Dosing PO: sodium bicarbonate 1mmol/kg/**dose BD**

  Dosing IV: Add sodium bicarbonate 2mmol/kg/**day** to compatible fluids.

- Phosphate: large amounts of phosphorous may be excreted by the new kidney. Oral dosing is preferred.

  Dosing PO: Starting dose 1mmol/kg/**day**

  Phosphate Sandoz® effervescent tablets contain 16mmol phosphate per tablet

  Dosing IV: sodium or potassium dihydrogen phosphate

  0.15 to 0.3mmol/kg/**dose** given over 4-6 hours

  Ideally to be given at slower rate of 0.06mmol/kg/hour

  Max rate is 0.2mmol/kg/hour with cardiac monitoring.

  Do not exceed 10mmol/hr

- Magnesium: If magnesium is less than 0.5mmol/L and IV replacement is required give magnesium sulfate. Note that hypotension is a potential complication. Ongoing oral replacement with oral magnesium may be required.

  Dosing PO: 0.1 to 0.8 mmol/kg/**dose** daily to QID

  Available as magnesium chloride solution 1mmol/ml & Magmin® (magnesium aspartate) 1.55mmol per tablet

  Dosing IV: Magnesium sulphate 0.1 to 0.2mmol/kg/**dose** over 60 mins (maximum dose 10mmol)

  Max rate is 0.5mmol/kg/hour

Immunosuppression and Medications – ongoing dosing and side effects

Information from the following section is summarised from the Australian Medicines Handbook, and supplemented from other sources as referenced. Renal dosing of anti-infectives is as per Australian Therapeutic Guidelines: antibiotic.

Corticosteroids

Prednisolone: oral liquid 5mg/ml, tablets 1mg, 5mg and 25mg
Dosing: daily at 0800

	Wt <20 kg	Wt >20 kg	Max. dose
Days 3-7	2 mg/kg	1.5 mg/kg	80 mg
Days 7-14	1.5 mg/kg	1 mg/kg	60 mg
Days 15-21	1 mg/kg	0.75 mg/kg	45 mg
Days 22-28	0.7 mg/kg	0.5 mg/kg	40 mg
Wk 5	0.6 mg/kg	0.4 mg/kg	35 mg
Wk 6	0.5 mg/kg	0.3 mg/kg	25 mg
Wk 7-8	0.4mg/kg	0.25 mg/kg	20 mg
Month 3	0.3 mg/kg	0.2 mg/kg	15 mg
Month 4	0.2 mg/kg	0.15-0.2 mg/kg	10 mg

This regimen may be personalised for higher risk recipients.

Alternate day dosing is possible after 5 months.

Calcineurin Inhibitors

Inhibits calcium-calmodulin-calcineurin complex, inhibition of calcium dependent pathway of T cell activation. Tacrolimus is the preferred agent due to lower rates of acute rejection, however cyclosporine is sometimes used as an alternative. Please see Appendix A for dosing and levels of cyclosporine.

Tacrolimus (FK 506)

Tacrolimus: 1mg/ml suspension from SCH pharmacy only (compounded product)
capsules 0.5mg, 1 mg and 5 mg.
Dosing: 0.15 mg/kg BD at 0800 and 2000

Doses adjusted to maintain the following levels post transplant

An extended release (XR) form of tacrolimus is available – this is not used immediately post transplant.

Target levels (12 hour trough):

1st month 8-12 nanog/ml

2-6 months 6 -10nanog/ml

6-12 months 5-8 nanog/mL

>12 months 4-7 nanog/mL

Lower levels are to be targeted if there is delayed graft function: generally 5-8 nanog/ml until function has improved.

Tacrolimus target levels are also often personalised depending on the immunological characteristics of the transplant.

Levels are done at daily Monday-Friday and Sunday at SEALS. Levels may be performed on Saturday if negotiated with Head of Division of Medical Services and the laboratory informed.

Tacrolimus can be given as an IV infusion: starting dose is 0.03 mg/kg/day or one third of the current dose. Adjust dose to levels of 10-15 nanograms/mL as referenced POW East Coast Transplant protocol. Dose range 0.01 to 0.06mg/kg/day.

Side Effects Hypomagnasemia, hypophosphataemia, hyperkalaemia

Hypercholesterolaemia, deranged LFTs

Nephrotoxicity - acute reversible and chronic irreversible

Neurotoxicity – tremor, headaches, higher risk of PRES

New Onset Diabetes after Transplantation (NODAT)

Thrombotic microangiopathy

High levels are also seen commonly with diarrhoea

Drug interactions

Both tacrolimus and cyclosporine are substrates of CYP3A4/5 and thus there are many clinically significant drug interactions.

Drug interactions can be checked using MIMs or the drug interactions tool in Micromedex through CIAP.

Common interactions include: anticonvulsants (inducers), antifungal agents – azoles (inhibitors) and macrolide antibiotics (inhibitors).

Antiproliferatives

Most patients will start on mycophenolate mofetil as part of routine triple immunosuppression due to lower rates of acute rejection. Azathioprine is sometimes used as an alternative, particularly if there is GI intolerance. Please see Appendix A regarding dosing of azathioprine

Mycophenolate mofetil

Mycophenolate mofetil: suspension 50mg/ml & 250mg and 500mg capsules/tablets

Dosing:	with tacrolimus:	400mg/m2 (max 1000mg) BD
	With cyclosporine or sirolimus	600mg/m2 (max 1000mg) BD

There is considerable inter-individual variability in mycophenolate pharmacokinetics. There is some evidence to suggest that mycophenolate AUC > 30mg x h/L are associated with lower rates of acute rejection, which correspond to trough levels of 1.4mg/L. [3]

Side Effects: GI – diarrhoea, vomiting

Haematological - pancytopaenia

There is an alternative form of mycophenolate available: mycophenolate sodium (myfortic). Dosing is **not equivalent** with 250mg mycophenolate mofetil equivalent to 180 mg mycophenolate sodium in adults. It is enteric coated and may be of benefit if GI side effects are severe. The same therapeutic drug monitoring levels as mycophenolate mofetil apply.

Anti-infectives

CMV prophylaxis

CMV is one of the most common infections seen post transplantation. Patients most at risk are CMV negative, receiving a kidney from a CMV positive donor. In addition, those patients who are CMV positive are at risk of CMV reactivation disease once immunosuppression is commenced. Prophylaxis is given for six months post transplant. Prophylaxis is also given following treatment of rejection with thymoglobulin or plasmaphoresis for five months.

Note: CrCl (ml/min/1.73m2) **= 36.5 x height (cm) /serum creatinine (micromoles/L)**

Intravenous ganciclovir prophylaxis[4]

Ganciclovir is given post-operatively on Day 0. It needs to be pre-ordered from the sterile pharmacy. For the first dose on Day 0 assume CrCl 10-25 ml/min/1.73m2.

Dosing:	CrCl > 70ml/min/1.73m2	5 mg/kg/day
	CrCl 50 – 69 ml/min/1.73m2	2.5 mg/kg/day
	CrCl 25 - 49 ml/min/1.73m2	1.25 mg/kg/day
	CrCl 10 - 25 ml/min/1.73m2	0.625mg/kg/day
	CrCl < 10 ml/min/1.73m2	0.625 mg/kg three times per week

Oral valganciclovir

Valganciclovir:Liquid 50mg/ml and 450mg tablets

Dosing: mg = 7 x BSA x CrCL (to a maximum of 150 mL/min/1.73m2) daily
maximum dose 900mg daily

Side Effects: Haematological – marrow suppression common. May need to dose reduce.

Pneumocystis

Pneumocystis can be a fatal respiratory illness in immunosuppressed patients.

Pneumocystis infection can be prevented by trimethoprim/sulfamethoxazole and is continued whilst on immunosuppression. It has been shown that a higher dose three times a week is as effective as a smaller daily dose.

Trimethoprim/Sulfamethoxazole(Bactrim®)

Note: Doses and products refer to trimethoprim component
Available as 8mg/ml trimethoprim suspension and 160mg trimethoprim tablets

Dosing: >50 kg 160 mg (of the trimethoprim component) (1 double strength tablet) Mon/Wed/Fri
<50 kg 5mg/kg (of the trimethoprim component) Mon/Wed/Fri

Side Effects: If the patient is unable to take Bactrim® because of allergy or G6PD deficiency, then intravenous pentamidine or dapsone are alternatives.

Antibiotic prophylaxis for Urinary Tract Infections
If there is a history of urinary tract infections or ureteric stent is in situ trimethoprim/sulfamethoxazole 2mg/kg can be given Tues/Thurs/Sat/Sun

Follow up post discharge

On discharge from hospital patients will be seen daily in clinic for four weeks post transplant. Summary of frequency of visits, immunosuppression dosing, viral PCR surveillance and other investigations are presented on the following page.

Investigation of graft dysfunction post-transplant

Acute rejection is most worrying cause of an acute creatinine rise post transplant. However, the following should also be considered and or excluded:

- Dehydration, especially with inter current illness
- UTI
- Obstruction
- BK nephropathy
- Recurrent disease
- Vascular insufficiency such as renal artery stenosis

School attendance

Children may attend school one month after receiving their renal transplant.

References

1. McDonald SP, Craig JC. Long-term survival of children with end-stage renal disease. *New England Journal of Medicine*. 2004;**350**:2654-62.
2. Kidney Disease Improving Global Outcomes Transplant Work Group. KDIGO clinical practice guideline for the care of kidney transplant recipients. *American Journal of Transplantation*. 2009;**9 Suppl 3**:S1-155.

3. Filler G, Alvarez-Elias AC, McIntyre C, Medeiros M. The compelling case for therapeutic drug monitoring of mycophenolate mofetil therapy. *Pediatric Nephrology*. 2017;**32**(1):21-9.
4. Kotton CN, Kumar D, Caliendo AM, Asberg A, Chou S, Danziger-Isakov L, et al. Updated international consensus guidelines on the management of cytomegalovirus in solid-organ transplantation. *Transplantation*. 2013;**96**(4):333-60.

Appendix A

Other Immunosuppressives

Cyclosporin

Liquid 100mg/ml or capsule 10mg, 25mg, 50mg and 100mg

Dosing 14mg /kg/day in two divided doses

Target levels for 2 hour peak:

1st 4 weeks	1200-1400 microg/L
months 1-3	900-1200 microg/L
months 4-6	750-900 microg/L
months 7-12	600-750 microg/L
> 12 months	450-600 microg/L

Cyclosporin is also subject to the same drug interactions as tacrolimus

Side effects ***As per tacrolimus***

Hirstutism and gingival hyperplasia more common

Azathioprine

25mg and 50mg tablets

Also available as IV formulation

Dosing: 1-2mg/kg/day

Side Effects: Myelosuppression: check thyopurine methyltransferase (TPMT) activity. 1 in 300 will have low/non detectable TPMT activity and are risk of severe myelosuppression. Avoid or reduce dose to 10%.

GI – diarrhoea/nausea/mouth ulceration and oesophagitis, less common than with mycophenolate

Hepatitis

Hepatic sinusoidal obstruction syndrome, hypersensitivity syndrome

Precautions: allopurinol and febuxostat reduce azathioprine metabolism, increasing risk of marrow toxicity

Sirolimus

mTOR inhibitors bind to the same intracellular protein as tacrolimus but the protein drug complex blocks mTOR kinase, inhibiting cytokine induced T and B cell proliferation.

Liquid 1mg/ml or tablets 0.5mg, 1mg and 2mg

Indication: Documented evidence of toxicity on renal biopsy

Not used immediately post transplant due to increased risk of graft thrombosis, poor wound healing and increased rates of acute rejection.

Side Effects: Impaired wound healing and lymphocoele

High lipids and diabetes

Mouth ulcers, interstitial lung disease, pericardial and pleural effusion

Dosing: > 40 kg loading dose 6 mg Day 1 then maintenance 2mg daily

< 40 kg loading dose 3mg/m2 Day 1 then maintenance 1mg/m2/day

Monitoring: Without CNI < 6 months 10-14 microg/L

6-10 months 8-10 microg/L

>12 months 4-8 microg/L

Antithymocyte globulins (ATG)

Polyclonal purified horse or rabbit antibodies against human lymphocytes that deplete T lymphocytes in the circulation. They are used as an alternative to IL-2 monoclonal antibodies as induction therapy and also to treat moderate to severe rejection. The following information is from product information on MIMs.

Currently we use thymoglobulin which is rabbit derived. The horse derived thyloglobulin has different dosing.

Thymoglobulin: Rabbit polyclonal ATG

25mg vials

Dosing

Induction therapy for kidney transplantation:

1-1.5 mg/kg/day as prophylaxis for 5 - 7 days (maximum individual dose 150mg, maximum cumulative dose 13.5 mg/kg)

In obese patients dose according to ideal body weight

Some sources suggest targeting lymphocyte count 0.1 to 0.2.

Induction therapy in setting of delayed graft function (DGF) to minimise calcineurin inhibitors (CNI):

1-2mg/kg/day typically for 2-3 days.

Rejection

1.5mg/kg/day for 5-7 days (maximum individual dose 150mg, maximum cumulative dose 21mg/kg)

Dose Adjustments:

Lymphocytes < 0.05	Withhold dose
Total WCC 2.0 - 3.0	Reduce dose by 50%
Total WCC < 2.0	Withhold dose and consider discontinuation of therapy
Platelets 50 – 75:	Reduce dose by 50%

Platelets < 50 Withhold dose and consider discontinuation of therapy

Prophylactic valganciclovir, trimethoprim/sulfamethoxazole (**Bactrim®**) and nystatin should be recommenced following administration of a course of ATG for six months.

Premedications

Paracetamol 20mg/kg (maximum dose 1000mg)

Promethazine 0.5mg /kg (maximum dose 25mg)

Hydrocortisone 2mg/kg (maximum dose 100mg)

Administration

There is a high incidence of drug reactions. Reactions include both anaphylaxis and cytokine release syndrome. Resuscitation equipment should be readily available.

ATG is diluted in 0.9% sodium chloride and is administered with a 0.22 micron in line filter. First dose is given over 6 hours then subsequent doses are given over 4 hours.

It is not compatible with glucose containing solutions.

Appendix B

POST TRANSPLANT FOLLOW – UP.
Site of kidney:
Donor kidney source:
Number HLA mismatches:
Pre-transplant DSA (Date):
Post-transplant DSA (Date):
Date of Transplant:
Transplant number:

JJ stent removal
Date booked:
Stent removed:

Name:
MRN:
Date of Birth:

Cause of ESRD:

Guide to Immunosuppression and Valgancyclovir doses and required levels from day of transplant.

Daily Prednisolone dose					***1 Tacrolimus Levels***	***2 Sirolimus levels LCMS – Seals****	***3 Mycophenolate doses***	***4 Duration of Valgancyclovir prophylaxis***
Day 3 to		2 mg/kg	1.5 mg/kg	80 mg	**0 - 2 months:** 8-12 nanog/mL **>2-6 months:** 6-10nanog/mL **> 6-12 months:** 5-8nanog/mL **> 12 months:** 4-7 nanog/mL	**Without CNI** **< 6 months** 10-14 microg/L**6-12 months:** 8-10 microg/L**> 12 months:** 4-8 microg/L	**1. With tacrolimus:** 400 mg/m2/dose bd to 600mg/m^2 **2. With cyclosporin or sirolimus:** 600 mg/m2/dose bd MPA trough target: 1.4 mg/L minimum	**CMV +ve to CMV -ve:** 5 months **CMV +ve/-ve to CMV +ve:** 5 mths **EBV +ve to EBV –ve:** 12 months **Dose in mg once daily = 7 x BSA x CrCL(to maximum of 150mL/min/1.73m^2)** **Cr Cl = 36.5 x ht(cm)/serum creat** **Consider further course following treatment for acute rejection.**
Day 8		1.5	1 mg/kg	60 mg				
Day 15		1 mg/kg	0.75 mg/kg	45 mg				
Day 22 to		0.7	0.5 mg/kg	40 mg				
Wk 5		0.6	0.4 mg/kg	35 mg				
Wk 6		0.5	0.3 mg/kg	25 mg				
Wk 7 & 8		0.4	0.25 mg/kg	20 mg				
Month 3		0.3	0.2 mg/kg	15 mg				
Month 4 onwards		0.2 mg/kg	0.15-0.2 mg/kg	10 mg				

The prednisolone taper will generally be slower for retransplants, transplants with a high PRA or any other high risk situation. If graft function is stable and there is still growth potential (and not multiple previous rejection episodes) then alternate day prednisone should be considered after 5 months.

Follow-up clinic visits and routine blood tests required from date of transplant – see following page for viral tests:

Week 1 to 4	Clinic daily	Daily EUC, CMP, second daily immunosuppressant drug level, twice weekly FBC, weekly LFT **EBV PCR Day 7 post transplant and MPA trough levels on Day 7 and 14**
Week 5 & 6	Clinic every 2nd day	Second daily EUC, CMP, immunosuppressant drug level, twice weekly FBC, weekly LFT
Week 7 & 8	Clinic twice a week	Twice weekly EUC, CMP, immunosuppressant drug level, weekly FBC, LFT and PTH once only
Week 9 & 10	clinic weekly	Weekly EUC, CMP immunosuppressant drug level, FBC. monthly LFT
Week 11 to 16	clinic every 2 weeks	Second weekly EUC, CMP, immunosuppressant drug level**,** FBC, monthly LFT,
4 to12 months	clinic every 4 weeks	Monthly EUC, CMP, immunosuppressant drug level, FBC, LFT.
>12 months	Clinic 4-6 weekly	Monthly EUC, CMP, immunosuppressant drug level, FBC, LFT.

1. Kotton CN, Kumar D, Caliendo AM, Asberg A, Chou S, Danziger-Isakov L, et al. Updated international consensus guidelines on the management of cytomegalovirus in solid-organ transplantation. *Transplantation*. 2013;**96**(4):333-60.