Kidney transplantation, rejection prophylaxis

Adults:

→ 1.5mg/kg in 250 mLs 0.9% NaCl to run over a minimum of 6 hours for 4 days (Day 0,1,2,3) for a cumulative of 6mg/kg.
No test dose required
Day 0: First dose should be administered intra-operatively, prior to allograft reperfusion but after 500mg methyl prednisolone has been given via CVP line. **Premedication with 1g paracetamol PO and 10mg chlorpheniramine IV should also be given before thymoglobulin infusion.** Significant first dose reactions are not common and do not tend to involve hypotension or bronchospasm. If a reaction occurs intra-operatively, the infusion should be stopped, and consideration given for re-starting post-operatively.
Day 1: As for Day 0 (following second dose of 500mg methylprednisolone, with 1g paracetamol PO and 10mg chlorpheniramine IV)
Day 2,3: Premedication of Hydrocortisone 200mg IV, paracetamol 1g PO and chlorpheniramine 10mg IV before administering thymoglobulin.

Reduce the dose by half if total WCC <3 x109/l &/or Platelets <75 x109/l.

Withhold dose if total WCC < 2 x109/l or platelet count < 50 x109/l.

NB: Tacrolimus, MMF prescribed as for standard immunosuppression. Omit oral prednisolone 20mgDay 2,3,4 and start day 5. [1] [2] [3] [4]

Geriatrics:

Refer to adult dosing.

Management of SIRS:

Prophylaxis ATLG/ATG: infusion reactions can be reduced in frequency and severity by two factors: premedication and speed of infusion. Premedication is performed with steroids, antihistamine, and acetaminophen. The optimal schedule of premedication is not yet well established. Doses of prednisolone of 250 mg (higher than 1 mg/kg), given before the first infusion and followed by an additional dose in the same day, reduce the incidence of infusion reactions and cytokine release as reported. [5]

Table 26.1 Infusion of ATLG/ATG

Factors	Comments
Infusion site	– Central line is highly preferred – Risk of thrombophlebitis and drug precipitation are higher in peripheral veins
Dilution	Avoid to inject undiluted preparation; follow the manufacturer instructions for each ATLG/ATG type
Compatibility	– rATLG-Grafalon: avoid to mix concentrate solution with glucose, blood, blood derivatives, sodium heparin, and lipid-containing solutions – rATG-Thymoglobulin: avoid dilutions with other than saline and dextrose – Horse ATGAM: avoid dextrose injection or acidic solution because of precipitation or instability
Stability	Diluted solutions up to 24 h (infusion time included) stored in refrigerator
Duration of infusion	4–12 h – Slower infusion results in a lower incidence and severity of infusion reactions; therefore ≥12 h infusion is recommended Start first administration at low infusion rate (at least for the first 30–60 min)
Drug interactions	Not reported
Premedication	Mandatory; steroids, acetaminophen, antihistamines
Preinfusion test	– Not advised for rabbit sera – Recommended for ATGAM – Skin and conjunctival tests not extensively validated
Criteria for permanent discontinuation What does D/C stand for?	Anaphylaxis: severe anaphylaxis, always. De-sensitization protocols: not validated SIRS: depending on grading and clinical evaluation of pros and cons. In case of rechallenge, more stringent monitoring is required

[1]- Edren Renal Transplant Handbook. (https://edren.org/ren/handbook/transplant-handbook/immunosuppressive-drugs/atg-anti-thymocyte-globulin/)

[2] Brennan, D. C., Daller, J. A., Lake, K. D., Cibrik, D., Del Castillo, D., & Thymoglobulin Induction Study Group (2006). Rabbit antithymocyte globulin versus basiliximab in renal transplantation. The New England journal of medicine, 355(19), 1967–1977. https://doi.org/10.1056/NEJMoa060068

[3] Brennan, D. C., Flavin, K., Lowell, J. A., Howard, T. K., Shenoy, S., Burgess, S., Dolan, S., Kano, J. M., Mahon, M., Schnitzler, M. A., Woodward, R., Irish, W., & Singer, G. G. (1999). A randomized, double-blinded comparison of Thymoglobulin versus Atgam for induction immunosuppressive therapy in adult renal transplant recipients. Transplantation, 67(7), 1011–1018. https://doi.org/10.1097/00007890-199904150-00013

[4] Hardinger, K. L., Rhee, S., Buchanan, P., Koch, M., Miller, B., Enkvetchakul, D., Schuessler, R., Schnitzler, M. A., & Brennan, D. C. (2008). A prospective, randomized, double-blinded comparison of thymoglobulin versus Atgam for induction immunosuppressive therapy: 10-year results. Transplantation, 86(7), 947–952. https://doi.org/10.1097/TP.0b013e318187bc67

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[5] - Bonifazi, F. (2019). Management ATG (SIRS). In C. and M. M. and K. N. Carreras Enric and Dufour (Ed.), The EBMT Handbook: Hematopoietic Stem Cell Transplantation and Cellular Therapies (pp. 183–187). Springer International Publishing. (https://doi.org/10.1007/978-3-030-02278-5_26)

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