



# Infectious Complications According to Recipient Age and Ethnicity in a Randomized Prospective Trial of Depleting Antibody Induction in Kidney and Pancreas Transplantation

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## Introduction

- Increased risk of infectious complications (ICs) after kidney (K) and pancreas (P) transplant (Tx) is a major concern, especially when using lymphocyte depleting antibody agents such as alemtuzumab (Alem) and rabbit anti-thymocyte globulin (rATG).
- These agents cause profound and durable lymphopenia that may increase the risk of infection compared to other induction agents.
- Previous studies have suggested differential risks of infection according to either recipient age or ethnicity.

## Methods

- We conducted a single center, prospective, randomized trial comparing single dose Alem (30 mg) to alternate day rATG (1.5 mg/kg) induction in adult KTx and PTx patients.
- Maintenance therapy was tacrolimus, mycophenolic acid, and risk stratification to determine early steroid elimination.
- Infection prophylaxis was given for fungal (1 month KTx; 2 month PTx), Pneumocystis (12 months minimum), and CMV (3 months; 6 months for primary CMV exposure) infection.
- Infectious complications were graded according to NIH Clinical Toxicity Criteria (CTCAE version 3.0).

## Risk Stratification

- High Risk
  - Rapid steroid taper to 5 mg daily within 2 months of transplant for:
    - PRA level >20%
    - African-American recipient (< 40 years)
    - Re-transplant
    - Delayed graft function
    - Patients already on steroids
- Low Risk
  - Total of 6 doses of steroids
    - Did not meet high risk criteria
    - Steroids stopped after POD #5

## Grading Infections: CTCAE v3.0

- Grade 1: Mild
- Grade 2: Moderate
- Grade 3: Severe
- Grade 4: Life-Threatening or Disabling
- Grade 5: Death

## Results

Outcome	Alem (n = 113)	rATG (n = 109)	P value
Patient Survival	109 (96%)	104 (95%)	NS
Kidney Graft (not ECD)	78/85 (92%)	84/95 (88%)	NS
Kidney Graft (ECD)	28/33 (85%)	22/28 (79%)	NS
Kidney Graft (SPK)	21/24 (88%)	12/14 (86%)	NS
Pancreas Graft (SPK)	21/24 (88%)	13/14 (93%)	NS
Pancreas Graft (PAK)	4/4 (100%)	N/A	-
Biopsy-proven acute rejection	16 (14%)	28 (26%)	0.02
Infections (# patients)	56 (50%)	75 (69%)	0.02

ECD – Expanded criteria donor  
SPK – Simultaneous Pancreas-Kidney  
PAK – Pancreas after kidney

## Study Groups

- Over a 2.5 year period (median follow-up 24 months), 222 patients were enrolled (113 randomized to Alem, 109 to rATG induction).
- Demographics were similar between groups.
- 52 patients (23%) were ≥60 years of age (27 received Alem induction).
- 70 (31.5%) were African-American (AA; 35 received Alem induction).
- No differences were noted in the 2 induction arms either according to recipient age (< or ≥60) or ethnicity.

## Infectious Complications by Recipient Ethnicity

Outcome	Caucasian (n = 152)	AA (n = 70)	P value
Total Infections	201 (1.3/pt)	78 (1.1/pt)	NS
# Patients with Infections	92 (60.5%)	41 (58.6%)	NS
Grade 1 Infections	1	2	NS
Grade 2 Infections	92	40	NS
Grade 3 Infections	98	34	NS
Grade 4-5 Infections	10	2	NS
Biopsy-proven acute rejection	27 (18%)	18 (26%)	NS

Infection	Caucasian (n = 152)	AA (n = 70)	P value
Bacterial	120	51	NS
Empiric	28	8	NS
Fungal	20	4	NS
Viral	33	15	NS

## Infectious Complications by Recipient Age

Outcome	Age <60 (n = 170)	Age ≥60 (n = 52)	P value
Total Infections	216 (1.3/pt)	67 (1.3/pt)	NS
# Patients with Infections	112 (66%)	29 (56%)	NS
Grade 1 Infections	4	0	NS
Grade 2 Infections	107	31	NS
Grade 3 Infections	95	35	NS
Grade 4-5 Infections	10	1	NS
Biopsy-proven acute rejection	35 (21%)	10 (19%)	NS

Infection	Age <60 (n = 170)	Age ≥60 (n = 52)	P value
Bacterial	133	42	NS
Empiric	28	8	NS
Fungal	18	5	NS
Viral	37	12	NS

- Patients ≥60 years of age did not have either more infections or less acute rejection (p=NS).
- African-American patients did not have either a higher risk of acute rejection or infection.
- Incidence of biopsy proven acute rejection (BPAR) was lower in all patient groups receiving Alem compared to rATG induction.
- The presence of BPAR increased the risk of infection from 41% to 72% (p<0.001).

## Conclusions

- Alemtuzumab is associated with a lower incidence of acute rejection and infection compared to rATG induction regardless of patient age or ethnicity.
- Older recipient age was not associated with either an increased incidence or severity of infections or less acute rejection.
- AA patients did not have either more acute rejection or a higher incidence or severity of infectious complications.
- Acute rejection was associated with more infections in each group.

## References

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