Journal of Nephrology and Kidney Diseases
Volume 3 | Issue 1
ISSN: 2455-7633

Research Article Open Access

Evaluation of Infectious and Malignant Complications in Elderly Renal Transplant Recipients Receiving Alemtuzumab Compared to Basiliximab

Lang K*[1], Cunningham K[1], D'Agostino C[1], Kapugi M[1], Kane C[1], Novak A[1], Leventhal J[2] and Schulte J[1]

[1]Department of Pharmacy, Northwestern Memorial Hospital, Chicago, IL, United States
[2]Division of Transplant Surgery; Northwestern Memorial Hospital, Chicago, IL, United States

***Corresponding author:** Lang K, Department of Pharmacy, Northwestern Memorial Hospital, Chicago, IL, United States, Tel: +1-3126958900, kyle.505.lang@gmail.com

Citation: Lang K, Cunningham K, D'Agostino C, Kapugi M, Kane C, et al. (2022) Evaluation of Infectious and Malignant Complications in Elderly Renal Transplant Recipients Receiving Alemtuzumab Compared to Basiliximab. J Nephrol Kidney Dis 3(1):101. doi:10.15744/2767-9225.3.101

Abstract

Summary

The choice of induction immunosuppression can affect several outcomes after kidney transplant (KTx). We aimed to evaluate infectious and malignant complications between alemtuzumab and basiliximab in elderly KTx recipients. Patients ≥ 65 years old who received alemtuzumab or basiliximab induction for their primary KTx from 2006 – 2018 were included.

Of the 255 patients evaluated, 132 (51.8%) experienced an infectious complication within 1 year of transplant. Although the overall infection rate was similar, more patients treated with alemtuzumab developed CMV viremia (14% vs 6.1%, p=0.05), and more patients treated with basiliximab developed urinary tract (19.7% vs 31.6%, p=0.031) and *C. difficile* infections (0.6% vs 8.2%, p=0.002). Malignancy occurred more frequently in alemtuzumab treated patients (29.3% vs 16.3%, p=0.019). Biopsy proven acute rejection (BPAR) at 1 year was higher in the basiliximab group (35.7% vs.15.3%, p<0.001). There was no difference in overall mortality.

Induction with alemtuzumab may increase the risk of malignancy in elderly KTx recipients relative to basiliximab, without a significant impact on incidence of infection or mortality. Alternative induction immunosuppression in elderly KTx recipients should be considered.

Keywords: Kidney Transplantation; Immunosuppression; Induction Immunosuppression; Malignancy; Infection Risk

Abbreviations

BPAR-Biopsy proven acute rejection; CMV-Cytomegalovirus; cPRA-Calculated panel reactive antibody; HIV- Human immunodeficiency virus; HCV- Hepatitis C virus; HLA-Human leukocyte antigen; IL2-RA-Interleukin 2 receptor antagonist; KDIGO-Kidney Disease-Improving Global Outcomes; OPTN-Organ procurement and transplantation network; PRA-panel reactive antibody; PTLD-Post-transplant lymphoproliferative disorder; UNOS- United Network of Organ Sharing

Introduction

The choice of induction immunosuppression, utilized at the time of organ transplantation, can affect post-transplant outcomes such as acute rejection and infection. [1] Interleukin-2 receptor antagonists (IL2-RA) are recommended by the 2009 Kidney Disease: Improving Global Outcomes (KDIGO) clinical practice guideline for kidney transplant recipients as a first line induction therapy, while lymphocyte-depleting agents' anti-thymocyte globulin or alemtuzumab are recommended for patients at high immunologic risk. [2]

As life expectancy in the general population continues to increase, healthcare professionals are improving the management of chronic disease states known to cause chronic kidney disease and subsequently delaying the need for dialysis and kidney transplantation. The Organ Procurement Transplantation Network (OPTN) and Scientific Registry of Transplant Recipients (SRTR) 2018 Annual Data Report indicates that the proportion of patients age 65 years and older on the kidney transplant waiting list continues to increase, and now comprises nearly 25% of the national kidney waitlist.[11] Despite these demographic changes, kidney transplantation remains a treatment option for elderly patients with end stage kidney disease conferring a survival advantage compared to those who remain on long-term dialysis.[12]

A kidney transplant recipient's age may be an important factor to consider when selecting an induction agent. Older organ recipients are considered to carry a lower risk of acute rejection following transplantation compared to younger recipients, [3] likely due to changes in the immunologic function that occur with aging. In the elderly population there is a decreased capacity of antigen-recognition and T-cell differentiation resulting in the host's inability to mount a complete immune response. [4] As such, elderly renal transplant recipients may be more prone to infection and malignancy after transplantation with a lower risk of acute allograft rejection, especially in the presence of lymphocyte depleting induction immunosuppression. [5-7]

Elderly kidney transplant recipients who receive induction immunosuppression with lymphocyte-depleting agents may be at a greater risk of developing systemic infections and malignancy after transplantation. In a UNOS-OPTN database study from 2003, the risk of post-transplant lymphoproliferative disorder (PTLD) was significantly increased in renal transplant recipients who received lymphocyte depleting induction immunosuppression compared to non-lymphocyte depleting agents. [8] Similarly, there is an increased risk of infectious complications and death in elderly renal transplant recipients. [6] Therefore, IL2-RAs may be a more optimal choice for induction immunosuppression in this population. Given these considerations, there remains a lack of guideline consensus on the induction agent of choice for patients 65 years of age and older. Due to the paucity of data in this population, there is a need for further clinical studies to determine the safety and efficacy of induction immunosuppression agents in the elderly renal transplant population. The purpose of this study was to compare the safety and efficacy of alemtuzumab to basiliximab induction in elderly kidney transplant recipients.

Materials and Methods

This retrospective analysis evaluated all elderly kidney transplant recipients (age ≥ 65 years) who received a primary living or deceased donor kidney transplant at Northwestern Memorial Hospital from December 2006 to August 2018. Patients were included in the analysis if they received alemtuzumab or basiliximab induction. Exclusion criteria included: history of previous transplant, receipt of multi-organ transplant, administration of rabbit anti-thymocyte globulin or methylprednisolone alone for induction immunosuppression, history of human immunodeficiency virus (HIV), or untreated hepatitis C virus (HCV).

The primary endpoint was a composite of infection or malignancy developed within 1 year after transplant. Secondary endpoints included: malignancy developed at any time after transplant (identified via electronic medical record review), biopsy proven acute rejection (BPAR) within 1 year following transplant according to the Banff Classification of Renal Allograft Pathology [9, 10], number of infection-related hospitalizations after transplant, and patient survival after transplant. Renal transplant biopsies were obtained per protocol at three- and twelve- months post-transplant. Infectious definitions are included in **Appendix A**.

The study protocol was approved by the Northwestern University Institutional Review Board.

Immunosuppression and Opportunistic Infection Prophylaxis

Prior to 2014, all kidney transplant recipients at our center received lymphocyte depleting induction with alemtuzumab at the time of transplantation. Since the publication of Cherikh et. al [8] indicating a significantly higher risk of malignancy following alemtuzumab induction in elderly kidney transplant recipients and the increased risk of allograft loss and patient death identified by Hurst et al., [18] our center modified the approach to induction immunosuppression to stratify patients based on age to receive lymphocyte-depleting vs lymphocyte-non-depleting induction at the time of transplant. From 2014 to 2018 patients aged 65 years and older received basiliximab. Maintenance immunosuppression consisted of tacrolimus, mycophenolate mofetil, and rapid corticosteroid withdrawal by POD10. Tacrolimus was initiated on POD1 and titrated to a goal trough of 8-10 ng/mL for months 0-3, then 5-7 ng/mL thereafter. Mycophenolate mofetil was initiated at the time of transplant, with dosing dependent on body weight ranging from 1000 mg to 1250 mg twice daily. All patients received lifelong prophylaxis against *Pneumocystis jirovecii*. Cytomegalovirus (CMV) and herpes simplex virus (HSV) prophylaxis was continued for 6 months post-transplant utilizing valganciclovir 450mg daily (or equivalent renally dosed frequency) or valacyclovir 500mg daily depending on donor and recipient CMV serology. The study protocol was approved by the Northwestern University institutional review board.

Statistical Analysis

Patient demographic and clinical outcome data were compared using Student t-test for continuous variables and chi-square or Fisher's exact tests for categorical variables. Kaplan-Meier curves were constructed to illustrate patient survival and event rates with respect to the incidence of BPAR and malignancy. A P value of less than 0.05 was considered to indicate statistical significance.

Results

Demographics

A total of 255 patients were included in the analysis. Of this cohort, 157 patients (61.6%) received alemtuzumab induction while 98 (38.4%) received basiliximab induction. Baseline demographics are summarized in Table 1. Both groups were well balanced with respect to patient characteristics with a median follow up of 6.7 years (IQR 3.8-8.5 years). The majority of recipients were male who received deceased donor grafts with a mean age at transplant of 69 years. More patients who received basiliximab had a history of malignancy prior to transplant compared to the alemtuzumab group [(35.7%) vs (16.6%), p<0.01]. Additionally, there was a higher proportion of sensitized patients (calculated panel reactive antibody [cPRA] > 20%) in the alemtuzumab cohort [(28%) vs (16.3%), p=0.03].

Infection and Malignancy

In regards to the primary endpoint, there was no difference in the composite incidence of infection or malignancy developed within one year after transplant (47.8% vs 59.2%, p=0.08). There was no difference in the overall incidence of infection developed within one year after transplant (47.8% vs 58.2%, p=0.11). The most frequently observed infection was urinary tract infection, which affected 19.7% of patients in the basiliximab cohort and 31.6% in the alemtuzumab cohort, p=0.03. There was a significantly higher incidence of CMV viremia in alemtuzumab treated patients (14% vs 6.1%, p=0.05). Conversely, there was an increased incidence of *Clostridium difficile* (*C. difficile)* infection in the basiliximab group (0.6% vs 8.2%, p<0.01). Basiliximab treated patients also experienced a higher incidence of infection-related hospitalizations within one year after transplant (22.9% vs 34.7%, p=0.04) (Table 2) .

There was no difference in the incidence of malignancy within one year after transplant (1.9% vs 3.1%, p=0.16). Freedom from malignancy within five years was not significantly different (log-rank = 0.443) (Figure 1). At any time after transplant, patients treated with alemtuzumab had a higher rate of malignancy compared to those who were treated with basiliximab (29.3% vs 16.3%, p=0.02) A subgroup analysis evaluated the development of malignancy in patients without a history of malignancy prior to transplant. Similar

Characteristic	Alemtuzumab (n= 157)	Basiliximab (n=98)	p-value
Age – yr, median (IQR)	69±5	69±4	0.582
Male – n (%)	85 (54.1)	64 (65.3)	0.078
Race or ethnic group – n (%)			0.831
Caucasian	79 (50.3)	53 (54.1)	
African American	30 (19.1)	18 (18.4)	
Other	48 (30.6)	27 (27.5)	
Transplant type – n (%)			
Living related	47 (30)	34 (34.7)	0.489
Living unrelated	46 (29.2)	19 (19.4)	0.104
Deceased donation	64 (40.8)	45 (45.9)	0.418
Indication for transplant – n (%)			0.571
HTN	63 (40.1)	34 (34.7)	
DM	53 (33.8)	33 (33.7)	
Other	41 (26.1)	31 (31.6)	
Time to loss to follow up – yr, median (IQR)	7.7±1.3	2.9±1.4	<0.001
History of malignancy – n (%)	26 (16.6)	35 (35.7)	<0.001
cPRA >20% – n (%)	44 (28.0)	16 (16.3)	0.032
CMV Serology – n (%)			0.060
D-/R-	9 (5.7)	17 (17.3)	
D-/R+	39 (24.8)	25 (25.5)	
D+/R+	61 (38.9)	36 (36.7)	
D+/R-	24 (15.3)	14 (14.3)	
Missing data	24 (15.3)	6 (6.2)	
EBV Serology – n (%)			0.705
D-/R-	0 (0)	0 (0)	
D-/R+	7 (4.5)	3 (3.8)	
D+/R+	122 (77.7)	90 (91.8)	
D+/R-	2 (1.3)	1 (1.0)	
Missing data	26 (16.6)	4 (4.1)	

Table 1: Patient Characteristics

to the entire study population, there was no difference in the composite incidence of infection or malignancy developed within one year after transplant (50.4% vs 50.7%, p=0.38). However, a greater percentage of patients in the basiliximab group experienced malignancy by year 3 (2.4% vs 16%, p=0.01) (Table 3).

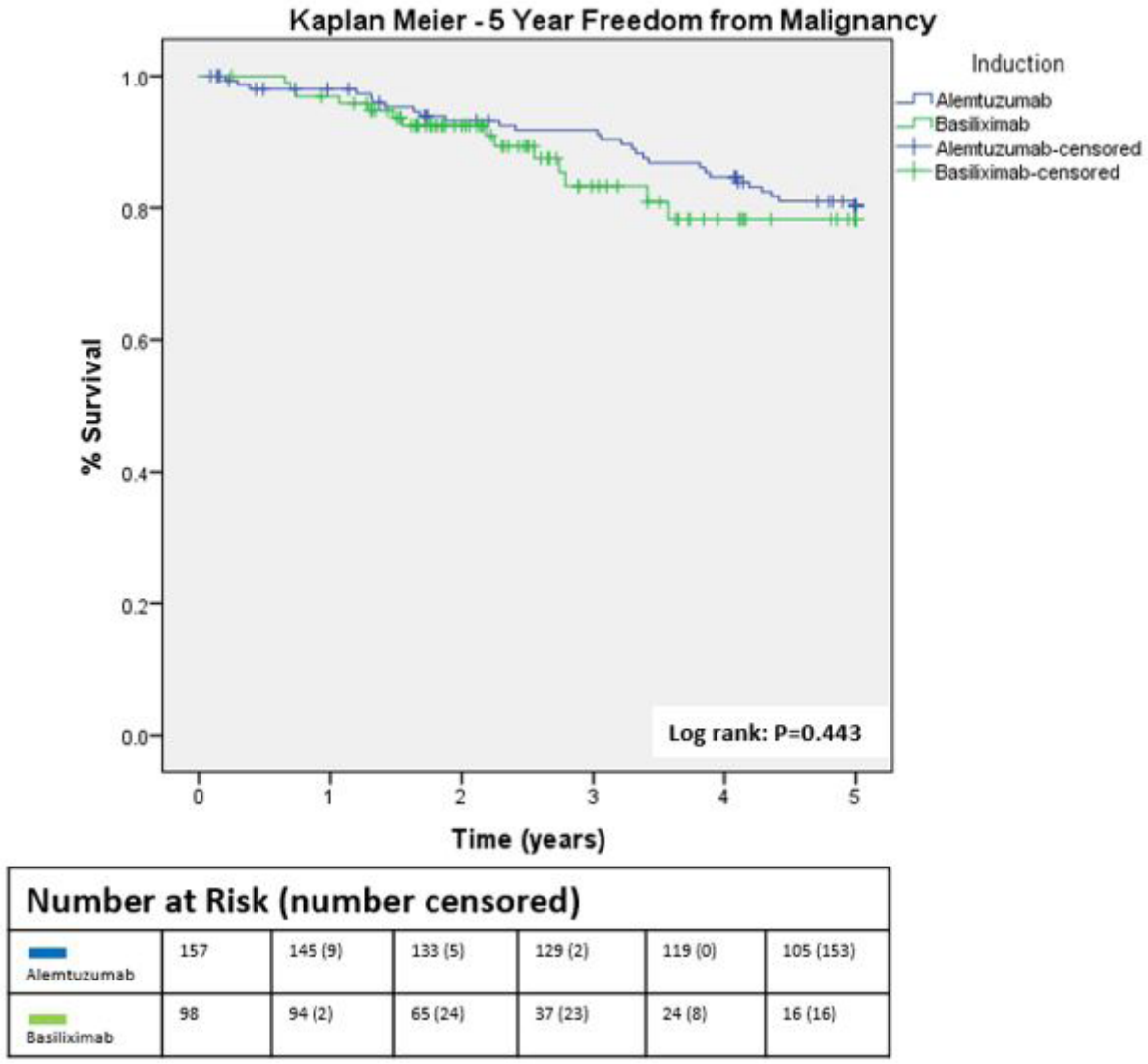

Figure 1: 5 year freedom from malignancy

End Point	Alemtuzumab (n=157)	Basiliximab (n=98)	p-value
Composite – infection or malignancy within 1 year after transplant – n (%)	75 (47.8)	58 (59.2)	0.08
Infection within 1 year after transplant– n (%)	75 (47.8)	57 (58.2)	0.11
BK viremia	13 (8.3)	15 (15.3)	0.08
BK nephropathy	8 (5.1)	5 (5.1)	1.00
CMV viremia	22 (14)	6 (6.1)	0.05
Viral infection other than CMV	6 (3.8)	0 (0)	0.09
Bacteremia	6 (3.8)	6 (6.1)	0.55
C. difficile infection	1 (0.6)	8 (8.2)	<0.01
Bacterial pneumonia	9 (5.7)	8 (8.2)	0.45
Fungal infection	2 (1.2)	2 (2)	0.64
Urinary tract infection	31 (19.7)	31 (31.6)	0.03
Skin and soft tissue infection	13 (8.3)	6 (6.1)	0.52
Intra-abdominal infection	4 (2.5)	3 (3.1)	1.00
Other infection[∞]	2 (1.3)	5 (5.1)	0.11
Malignancy within 1 year – n (%)	3 (1.9)	3 (3.1)	0.16

Hospitalized within 1 year for infection – n (%)	36 (22.9)	34 (34.7)	0.04
Malignancy at any time – n (%)	46 (29.3)	16 (16.3)	0.02
Squamous cell carcinoma	23 (14.6)	10 (10.2)	0.30
Basal cell carcinoma	6 (3.8)	3 (3.1)	1.00
Melanoma	5 (3.2)	1 (1.0)	0.41
Lung cancer	3 (1.9)	0 (0)	0.29
Breast cancer	2 (1.3)	0 (0)	0.53
Gastrointestinal cancer	4 (2.5)	0 (0)	0.30
Genitourinary cancer	2 (1.3)	1 (1.0)	1.00
Renal cell carcinoma	5 (3.2)	1 (1.0)	0.41
Other malignancies[Δ]	3 (1.9)	2 (2)	1.00
Lymphoma	5 (3.2)	0 (0)	0.16
Diffuse large B-cell lymphoma	3 (1.9)	0 (0)	0.29
Polymorphic lymphoma	1 (0.6)	0 (0)	1.00
Other lymphoma	1 (0.6)	0 (0)	1.00
Malignancy within 1 year – n (%)	3/157 (1.9)	3/98 (3.1)	0.16
Malignancy within 3 years – n (%)	13/141 (9.2)	7/43 (16)	0.26
BPAR within 1 year after transplant – n (%)	24 (15.3)	35 (35.7)	<0.01
Borderline*	11 (7)	26 (26.5)	<0.01
IA	5 (3.2)	4 (4.1)	0.74
IB	1 (0.6)	3 (3.1)	0.16
IIA	4 (2.5)	1 (1.0)	0.65
IIB	3 (1.9)	1 (1.0)	1.00
III	0 (0)	0 (0.0)	1.00
Graft failure within 1 year – n (%)	6 (3.8)	4 (4.1)	0.15
1 year all-cause mortality – n (%)	9 (5.7)	2 (2)	0.21
Treatment of rejection – n (%)			
Increase in maintenance immunosuppression	7/24 (29.2)	14/35 (40)	0.42
Glucocorticoid therapy	12/24 (50)	19/35 (54.3)	0.80
Anti-thymocyte globulin	5/24 (20.1)	0/35 (0)	<0.01

*Borderline rejection included only if treated with enhanced immunosuppression or steroid pulse

[∞]Other infection – osteomyelitis, endocarditis, brain abscess, infectious diarrhea other than CDI, and Pseudomonas Aeruginosa otitis externa

[Δ]Other malignancies – myelodysplastic syndrome, Kaposi sarcoma, multiple myeloma, chronic lymphocytic leukemia, esophageal cancer

Table 2: Safety and Efficacy Endpoints

Acute Rejection and Patient Survival

The incidence of BPAR was 35.7% in basiliximab-treated patients, as compared with 15.3% in alemtuzumab-treated patients ($p<0.01$). The most frequently observed classification of rejection was borderline rejection (7% vs 26.5%, $p<0.01$) followed by Banff 1A rejection (3.2% vs 4.1%, $p=0.74$). In a Kaplan-Meier analysis, time to rejection was significantly longer in the alemtuzumab group, log-rank $p<0.001$ (**Figure 2**). The incidence of one-year, all-cause mortality was similar between the two groups. There was no difference in patient survival comparing alemtuzumab and basiliximab treated patients, log-rank $p=0.896$ (Figure 3).

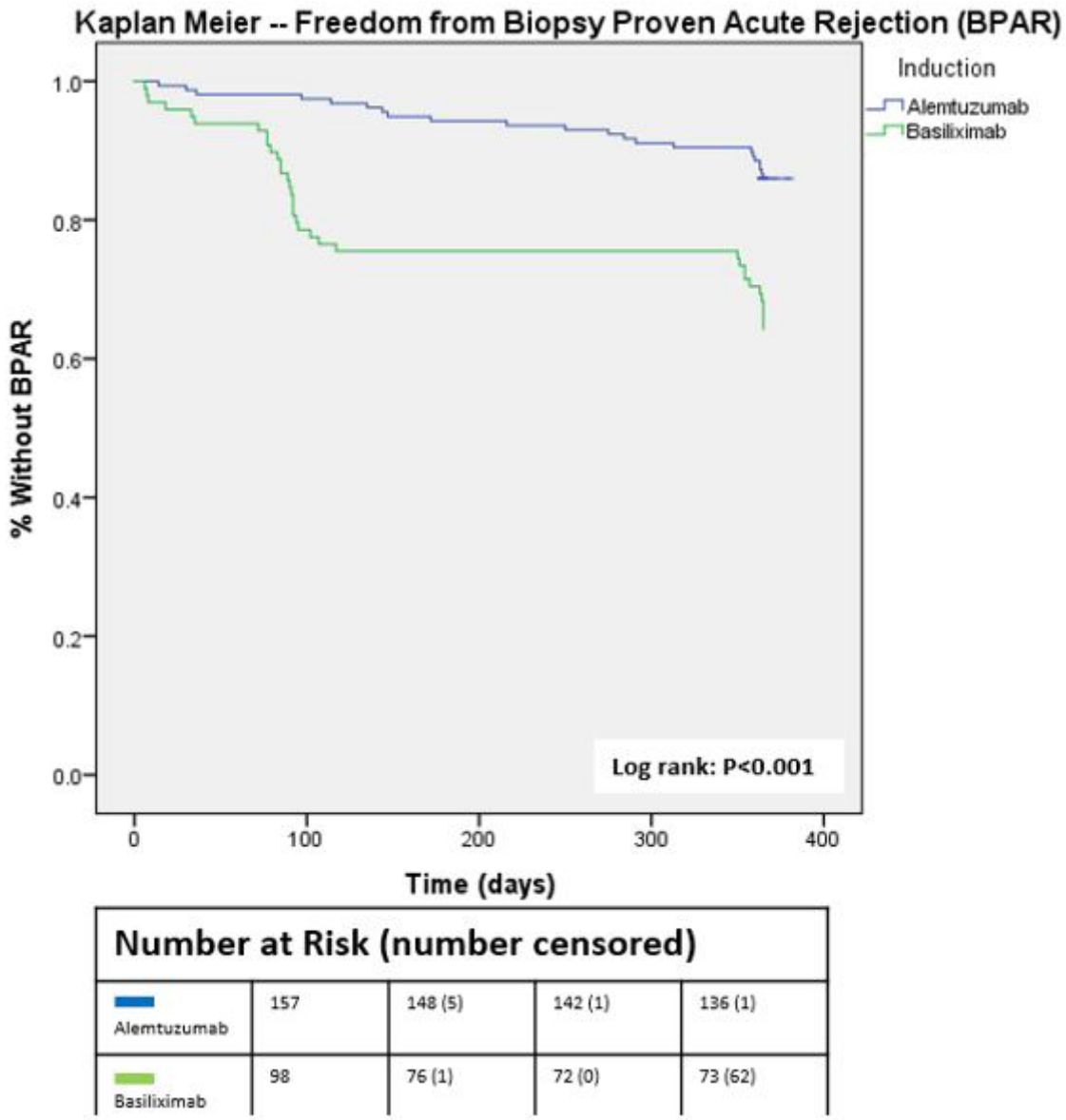

Figure 2: Freedom from BPAR

End Point	Alemtuzumab (n=131)	Basiliximab (n=63)	p-value
Composite – infection or malignancy – n (%)	66 (50.4)	36 (57.1)	0.38
Malignancy within 1 year – n (%)	3/131 (2.3)	1/63 (1.6)	0.52
Malignancy within 3 years – n (%)	3/115 (2.6)	4/25 (16)	0.01

Table 3: Malignancy developed after transplant without history of malignancy

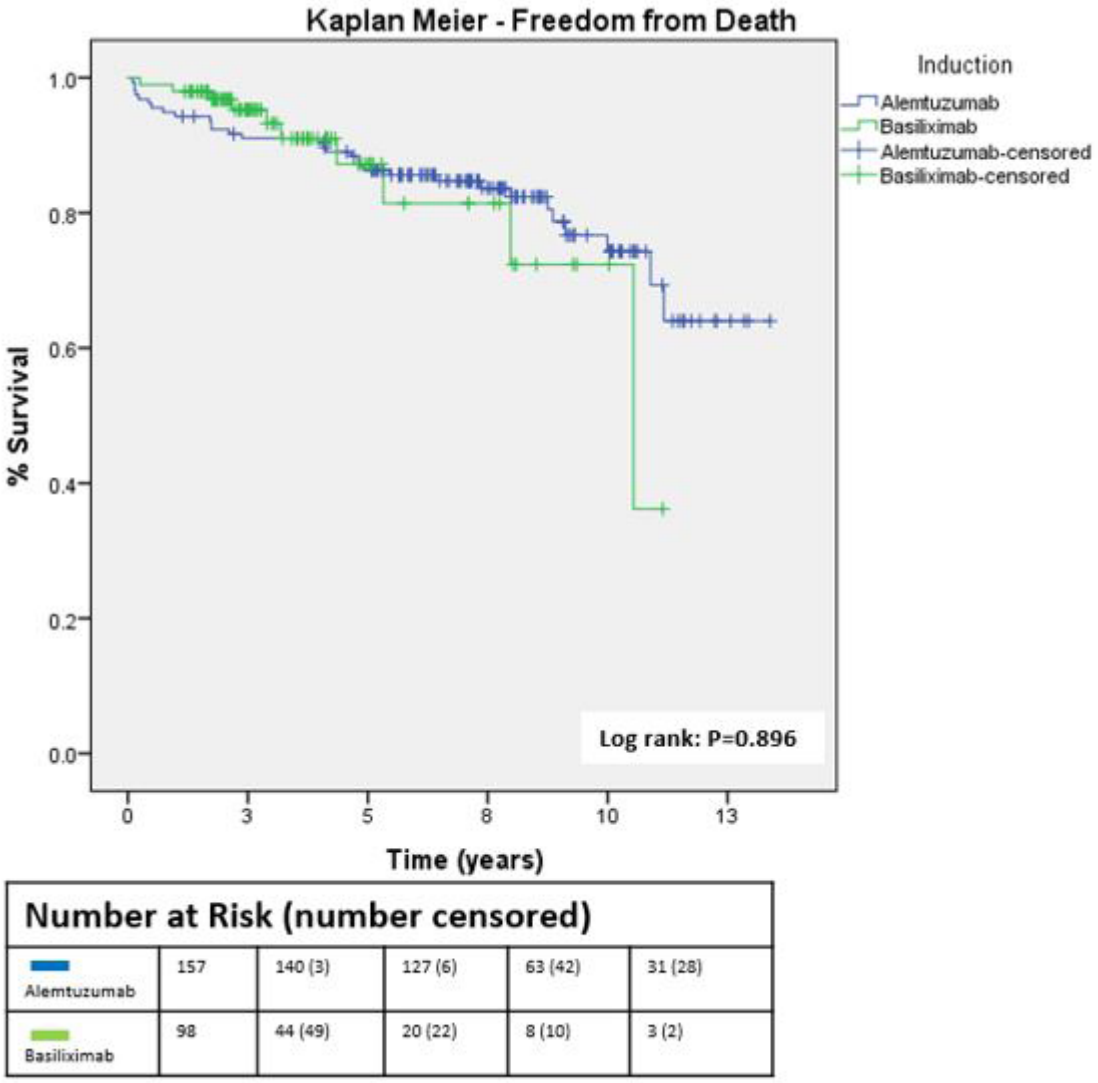

Figure 3: Patient survival

Discussion

As the proportion of elderly kidney transplant candidates continues to increase, kidney transplant centers must be diligent in selecting appropriate induction immunosuppression for this population to prevent acute allograft rejection, while also preventing serious complications. Immunosenescence is a natural process by which changes in the adaptive and innate immune system result from a dysregulation of immune cells. Thymic involution causes a decrease in naïve T cells, increased memory T cells and impaired proliferation and migration of T cells to areas of infection or inflammation. Additionally there is an effective decrease in antibody-producing B cells and a relative reduction in natural killer cells. These changes dysregulate the immune system and in the presence of immunosuppression for kidney transplantation, the patient may be at a higher risk of infectious complications and malignancy while also reducing the potential for allograft rejection.[14] Alemtuzumab causes profound lymphocyte depletion which in combination with immunosenescence can eliminate the remaining immune system reserve to combat infection and malignancy.

The primary objective of our study was to compare the infectious and malignant complications between alemtuzumab and basiliximab induction for elderly kidney transplant recipients. There was no difference in the composite primary endpoint of first incidence of infection or malignancy developed within one year after transplantation. This finding is supportive of our standard kidney transplant protocol, which risk stratifies patients who are 65 years and older to receive lymphocyte-non-depleting induction

immunosuppression. These findings further support the results of Yakubu et al., [13] which showed no significant difference in the overall incidence of infection or malignancy comparing 102 basiliximab-treated and 51 alemtuzumab-treated kidney transplant recipients age 65 years or older. In our study, which included a larger sample size, no difference in the incidence of malignancy at one and five years occurred post-transplant.. Interestingly, the subgroup analysis of malignancy outcomes among those without a prior malignancy history, did demonstrate a higher risk of malignancy at 3 years among those who received basiliximab induction. However, these data should be interpreted cautiously given the significant difference in follow up between groups, the retrospective nature of this outcome, as well as small sample size in which this was analyzed. All leading to the possibility of a false positive outcome. Nevertheless, this subgroup analysis is hypothesis generating and warrants further, larger prospective studies.

We observed no statistically significant difference in the overall incidence of infection when comparing alemtuzumab with basiliximab treated patients. Interestingly there was a higher incidence of urinary tract infections and *C. difficile* infections observed in the basiliximab group. In addition there was an increased rate of hospitalizations in the basiliximab group within one year after transplant for the treatment of infection. Perhaps with the increased hospitalizations, the use of antimicrobials to treat urinary tract infections also increased which may have impacted the rate of *C. difficile* infections in the basiliximab group. There was a higher incidence of CMV viremia in the alemtuzumab group compared to basiliximab group despite observing no significant difference in the distribution of CMV donor and recipient serology between the two groups. These findings contrast the report by Korneffel et al. in which kidney transplant recipients who received alemtuzumab induction found to have a lower incidence of CMV viremia compared to a historical cohort [15], and similarly contrasts the report by Kaufman et al. in which the rate of CMV infection was no different in kidney transplant recipients who were treated with alemtuzumab compared to basiliximab regardless of age. [19]

There was a significantly higher incidence of biopsy proven acute rejection in basiliximab-treated patients. The majority of the rejection episodes were borderline changes identified on surveillance kidney biopsies that were subsequently treated with corticosteroids. Excluding borderline changes, the incidence of rejection was similar between the two groups. These results corroborate other prospective, randomized controlled trials that have demonstrated a reduction in BPAR with lymphocyte depleting induction immunosuppression [16, 17, 19]

Other retrospective studies analyzing the effects of induction immunosuppression in the elderly population have linked worse allograft outcomes with advanced age. In a United States Renal Data Base System (USRDS) study by Hurst et al.[18] alemtuzumab induction in the elderly population (age 65 years and older) was associated with an increased risk of allograft loss (HR 1.26 [95% CI 1.08 – 1.48], p=0.004) and patient death (AHR 1.31 [95% CI 1.10 – 1.56], p=0.002). Although our study did not show a difference in all-cause mortality, the conflicting results highlight the need for further investigation in this patient population.

Our study comes with several limitations. First due to the retrospective nature of the analysis, we could not control for research bias. The single center study design limits external validity to other transplant centers. There was a shorter time to follow up in the basiliximab group which limits the evaluation of long term outcomes such as malignancy and patient survival. We also did not analyze the effect of maintenance immunosuppression on various outcomes such as BPAR.

In conclusion, the results from the present study indicate that compared to basiliximab induction, alemtuzumab may influence the rate of malignancy after kidney transplantation in elderly recipients without significantly influencing the rate of infection. Despite higher rates of BPAR with non-lymphocyte depleting therapy, no differences in graft or patient survival were observed. Efforts should be made to continue utilizing lymphocyte non-depleting induction strategies in the elderly renal transplant population.

References

1. Montero N, Pérez-Sáez M J, Pascual J, Abramowicz D, Budde K, et.al.,, (2016) Immunosuppression in the elderly renal allograft recipient: a systematic review. Transplantation Rev 30: 144-53.

2. KDIGO (2009) clinical practice guideline for the care of kidney transplant recipients. Am J Transplant 3: S1-155.

3. Meier-Kriesche H U, Ojo A, Hanson J, Cibrik D, Lake K, et al., (2000) Increased immunosuppressive vulnerability in elderly renal transplant recipients. Transplantation. 69:885-9.

4. McKay D, Jameson J (2012) Kidney transplantation and the ageing immune system. Nat Rev Nephrol 8:700-8.

5. Vajdic C, McDonald S P, McCredie M R E, Leeuwen M T V, Stewart J H, et.al., (2006) Cancer Incidence Before and After Kidney Transplant. JAMA. 296:2823-31.

6. Meier-Kriesche H U, Ojo A O, Hanson J A, Kaplan B (2001) Exponentially increased risk of infectious death in older renal transplant recipients. Kidney Int 59:1539-43.

7. Kasiske B L, Snyder J J, Gilbertson D T, Wang C (2004) Cancer after kidney transplantation in the United States. Am J Transplant. 4:905-13.

8. Cherikh W S, Kauffman H M, McBride M A, Maghirang J, Swinnen L J, et al., (2003) Association of the type of induction immunosuppression with posttransplant lymphoproliferative disorder, graft survival, and patient survival after primary kidney transplantation. Transplantation 76:1289-93.

9. K Solez, R B Colvin, L C Racusen, M Haas, B Sis, et al.,(2008) Banff 07 classification of renal allograft pathology: updates and future directions. Am J Transplant 8:753-60.

10. Haas M, Sis B, Racusen L C, Solez K, Glotz D, et al.,(2014) Banff 2013 meeting report: inclusion of C4d-negative antibody-mediated rejection and antibody-associated arterial lesions. Am J Transplant 14:272-83.

11. Hart A, Smith J M, Skeans M A, Gustafson S K, Wilk A R, et al., (2020) OPTN/SRTR 2018 Annual Data Report: Kidney. Am J Transplant 1:20-130.

12. Heldal K, Hartmann A, Grootendorst D C, J de Jager D, Leivestad T, et al., (2010) Benefit of kidney transplantation beyond 70 years of age. Nephrol Dial Transplant 25:1680-7.

13. Yakubu I, Ravichandran B, Sparkes T, Barth R N, Haririan A, et al., (2019) Comparison of Alemtuzumab versus basiliximab induction therapy in elderly kidney transplant recipients: a single-center experience. J Pharm Pract 34:199-206.

14. Krenzien F, ElKhal A, Quante M, Biefer H R C, Hirofumi U, et al., (2015) A Rationale for Age-Adapted Immunosuppression in Organ Transplantation. Transplantation 99:2258-68.

15. Korneffel K, Mitro G, Buschor K, Rees M, Ortiz J, (2019) Low dose valganciclovir as cytomegalovirus prophylaxis in post-renal transplant recipients induced with alemtuzumab: a single-center study. Transpl Immunol 56:101226.

16. Hanaway M J, Woodle E S, Mulgaonkar S, Peddi V R, Kaufman D B, et al. , (2011)Alemtuzumab Induction in Renal Transplantation. N Engl J Med 364:1909-19.

17. Brennan D C, Daller J A, Lake K D, Cibrik D, Castillo D D (2006) Rabbit Antithymocyte Globuoin versus Basiliximab in Renal Transplantation. N Engl J Med. 9;355:1967-77.

18. Hurst F P, Altieri M, Nee R, Agodoa L Y, Abbott K C, et al., (2011) Poor outcomes in elderly kidney transplant recipients receiving alemtuzumab induction. Am J Nephrol 34:534-41.

19. Kaufman D B, Leventhal J R, Axelrod D, Gallon L G, Parker M A, et al., (2005) Alemtuzumab induction and prednisone-free maintenance immunotherapy in kidney transplantation: comparison with basiliximab induction--long-term results. Am J Transplant. 5:2539-48.