

Low-Dose Alemtuzumab-Based Induction in Kidney Transplantation: A Retrospective Comparison of Maintenance Immunosuppression, Long-Term Graft Outcomes, and Induction Costs

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Abstract

Background: Alemtuzumab is a lymphocyte-depleting monoclonal antibody used for induction immunosuppression in kidney transplantation. Its prolonged immunological effects may permit minimization of maintenance immunosuppression. This study compared long-term outcomes, maintenance immunosuppression requirements, complications, and reported induction costs between recipients receiving low-dose alemtuzumab and those receiving conventional induction.

Methods: This retrospective comparative study included kidney transplant recipients who underwent transplantation between 2006 and 2014. Recipients receiving 10 mg subcutaneous alemtuzumab before transplantation were compared with recipients receiving antithymocyte globulin (ATG) or basiliximab. Follow-up extended through 2019. Outcomes included acute rejection, graft loss, death with a functioning graft, lymphocytopenia, maintenance immunosuppression, metabolic complications, malignancy, and induction costs. The available abstract provided aggregate outcome counts; detailed statistical methods and baseline characteristics were not available for this manuscript preparation.

Results: The study included 177 recipients: 75 in the alemtuzumab group and 102 in the conventional-induction group. Acute rejection occurred in 2/75 (2.7%) and 8/102 (7.8%), respectively. Triple-drug maintenance immunosuppression was reported in 13/75 (17.3%) recipients receiving alemtuzumab and 94/102 (92.2%) receiving conventional induction. Dyslipidemia was reported in 12/75 (16.0%) and 56/102 (54.9%), respectively, while hypertension requiring more than two antihypertensive medications was reported in 12/75 (16.0%) and 82/102 (80.4%). Graft failure beyond five years was reported in 3/75 (4.0%) and 22/102 (21.6%). Induction costs were reported as below US\$500 per patient in the alemtuzumab group and above US\$1,000 in the conventional-induction group. The abstract reported significant differences in several outcomes but did not provide complete statistical output.

Conclusion: In this retrospective cohort, low-dose alemtuzumab induction was associated with lower use of triple-drug maintenance immunosuppression, lower reported frequencies of selected metabolic complications, fewer reported graft failures beyond five years, and lower induction costs. These findings are hypothesis-generating. Complete statistical verification, adjustment for confounding, and a formal economic analysis are required before concluding that alemtuzumab improves long-term outcomes or is cost-effective.

Keywords: Alemtuzumab; kidney transplantation; induction immunosuppression; graft failure; maintenance immunosuppression; cost analysis.

1. Introduction

Kidney transplantation is the preferred treatment for eligible patients with end-stage kidney disease. Long-term transplant success depends on balancing prevention of allograft rejection against the adverse effects associated with sustained immunosuppression. Induction immunosuppression is commonly administered at transplantation to reduce early alloreactive immune responses and facilitate effective maintenance therapy. Basiliximab, an interleukin-2 receptor antagonist, and antithymocyte globulin, a lymphocyte-depleting preparation, are widely used induction agents. Alemtuzumab is a humanized monoclonal antibody directed against CD52, which is expressed on several lymphocyte populations. Its administration produces substantial lymphocyte depletion and has been investigated as a means of reducing maintenance immunosuppression exposure.

In the INTAC randomized trial, alemtuzumab was compared with conventional induction using basiliximab or rabbit antithymocyte globulin in kidney transplant recipients stratified by immunological risk. The trial demonstrated that the comparative effects of induction depend on recipient risk and the treatment strategy used [1]. The 3C Study subsequently compared an alemtuzumab-based regimen with basiliximab-based induction and evaluated a strategy involving reduced maintenance immunosuppression [2]. These trials established an important evidence base for investigating alemtuzumab-based approaches, although their regimens and populations differ from those in the present study.

Lower-dose alemtuzumab protocols are of interest because they may reduce drug acquisition costs while providing sufficient immunological activity to facilitate maintenance immunosuppression minimization.

However, dose, route of administration, recipient immunological risk, concomitant therapy and long-term follow-up may influence both efficacy and safety.

Long-term outcomes are particularly relevant because early rejection rates alone do not establish whether an induction strategy improves graft longevity, reduces complications or lowers overall healthcare expenditure. Metabolic complications, infection, malignancy and the cumulative burden of maintenance immunosuppression must also be considered.

The present retrospective study compared kidney transplant recipients who received 10 mg subcutaneous alemtuzumab with recipients who received conventional induction using ATG or basiliximab. The objectives were to compare reported transplant outcomes, maintenance immunosuppression patterns, selected complications and induction costs.

2. Materials and Methods

2.1. Study design and population

This was a retrospective comparative study of kidney transplant recipients undergoing transplantation between 2006 and 2014. Follow-up data were assessed through 2019, as described in the original conference abstract.

A total of 177 recipients were included. Group I comprised 75 recipients who received 10 mg subcutaneous alemtuzumab before transplantation. Group II comprised 102 recipients who received conventional induction with ATG or basiliximab.

Recipients with missing data or inadequate follow-up were excluded from the original study. The total number screened, specific exclusion criteria and the definition of adequate follow-up require confirmation from the original study records.

2.2. Induction and maintenance immunosuppression

Group I received 10 mg subcutaneous alemtuzumab before transplantation. Group II received conventional induction with ATG or basiliximab. The distribution of recipients between ATG and basiliximab, individual dosing protocols and the rationale for selecting each agent were not available in the abstract.

Maintenance immunosuppression was categorized according to the regimens reported in the original study:

1. Tacrolimus with corticosteroids at a dose below 7.5 mg.
2. Tacrolimus and mycophenolate mofetil (MMF).
3. Tacrolimus, MMF and corticosteroids.

The exact time points at which maintenance regimens were recorded and the definitions used for corticosteroid minimization require verification.

2.3. Outcomes

The outcomes reported acute rejection, graft loss, graft failure beyond five years, death with a functioning graft through 2019, persistent lymphocytopenia beyond three months and one year, malignancy, post-transplant diabetes mellitus, dyslipidemia, hypertension requiring more than two antihypertensive medications, infection, maintenance immunosuppression requirements and induction costs.

2.5. Cost assessment

The induction costs below US\$500 per patient in Group I and above US\$1,000 per patient in Group II. Accordingly, the present analysis describes the reported induction-cost comparison.

3. Results

3.1. Study population

The study included 177 kidney transplant recipients, comprising 75 recipients in the low-dose alemtuzumab group and 102 in the conventional-induction group.

The male-to-female ratio was 50:25 in Group I and 75:27 in Group II. Male recipients accounted for 66.7% of Group I and 73.5% of Group II.

Table 1. Reported demographic characteristics

Characteristic	Alemtuzumab (n=75)	Conventional induction (n=102)
Male recipients	50 (66.7%)	75 (73.5%)
Female recipients	25 (33.3%)	27 (26.5%)
Mean recipient age	Not available	Not available
Donor characteristics	Not available	Not available

Immunological risk	Not available	Not available
ATG versus basiliximab distribution	Not applicable	Not available

The absence of additional baseline characteristics prevents a complete assessment of between-group comparability.

3.2. Acute rejection and graft outcomes

Acute rejection was reported in 2 recipients (2.7%) in Group I and 8 recipients (7.8%) in Group II. The original abstract reported that this difference was not statistically significant.

Graft loss was reported in 2 recipients (2.7%) in Group I and 4 recipients (3.9%) in Group II. The p-value recorded in the original table requires verification.

Graft failure beyond five years was reported in 3 recipients (4.0%) in Group I and 22 recipients (21.6%) in Group II. The original abstract reported a p-value below 0.05 for this outcome.

Death with a functioning graft through 2019 was reported in 8 recipients (10.7%) in Group I and 12 recipients (11.8%) in Group II.

Table 2. Reported transplant outcomes

Outcome	Alemtuzumab (n=75)	Conventional induction (n=102)	Original statement	statistical
Acute rejection	2 (2.7%)	8 (7.8%)	p > 0.05	
Graft loss	2 (2.7%)	4 (3.9%)	Verify original output	
Graft failure beyond five years	3 (4.0%)	22 (21.6%)	p < 0.05	
Death with functioning graft through 2019	8 (10.7%)	12 (11.8%)	No p-value supplied	

These counts suggest differences in selected graft outcomes. However, individual follow-up times, the definition of graft failure and the handling of death as a competing event are unavailable. Crude event counts cannot independently establish superior long-term graft survival.

3.3. Maintenance immunosuppression

Maintenance immunosuppression regimens differed substantially between the two groups.

In Group I, 22 recipients (29.3%) received tacrolimus with corticosteroids below 7.5 mg, 40 (53.3%) received tacrolimus and MMF, and 13 (17.3%) received triple-drug therapy.

In Group II, no recipients were reported to receive tacrolimus with low-dose corticosteroids without MMF. Eight recipients (7.8%) received tacrolimus and MMF, while 94 (92.2%) received triple-drug therapy.

Table 3. Maintenance immunosuppression regimens

Regimen	Alemtuzumab (n=75)	Conventional induction (n=102)
Tacrolimus + corticosteroid below 7.5 mg	22 (29.3%)	0
Tacrolimus + MMF	40 (53.3%)	8 (7.8%)
Tacrolimus + MMF + corticosteroid	13 (17.3%)	94 (92.2%)

The original abstract reported significant differences in maintenance regimen distribution. These results indicate that recipients in the alemtuzumab group were more frequently maintained on regimens without all three drugs. The precise timing and indications for immunosuppression minimization remain to be clarified.

3.4. Persistent lymphocytopenia

Lymphocytopenia beyond three months was reported in 65 recipients (86.7%) in Group I and 12 (11.8%) in Group II, with a reported p-value below 0.05.

Beyond one year, lymphocytopenia was reported in 12 recipients (16.0%) and 8 recipients (7.8%), respectively; the abstract reported no statistically significant difference.

Table 4. Reported persistent lymphocytopenia

Outcome	Alemtuzumab (n=75)	Conventional induction (n=102)	Original statistical statement
Lymphocytopenia beyond three months	65 (86.7%)	12 (11.8%)	p < 0.05
Lymphocytopenia beyond one year	12 (16.0%)	8 (7.8%)	p > 0.05

The definition of lymphocytopenia and the laboratory thresholds used were not included in the abstract. These findings should be verified against the original laboratory records.

3.5. Metabolic complications and malignancy

Dyslipidemia was reported in 12 recipients (16.0%) in Group I and 56 (54.9%) in Group II. Hypertension requiring more than two antihypertensive medications was reported in 12 recipients (16.0%) and 82 (80.4%), respectively. Both outcomes were reported as significantly more frequent in Group II.

Post-transplant diabetes mellitus was reported in 6 recipients (8.0%) in Group I and 18 (17.6%) in Group II. Malignancy was reported in 6 recipients (8.0%) and 4 (3.9%), respectively. The abstract did not provide statistical significance values for these two comparisons.

Table 5. Reported metabolic and other complications

Outcome	Alemtuzumab (n=75)	Conventional induction (n=102)	Original statement	statistical
Dyslipidemia	12 (16.0%)	56 (54.9%)	p < 0.05	
Hypertension requiring >2 antihypertensive medications	12 (16.0%)	82 (80.4%)	p < 0.05	
Post-transplant diabetes mellitus	6 (8.0%)	18 (17.6%)	P<0.05	
Malignancy	6 (8.0%)	4 (3.9%)	P<0.05	

The reported findings indicate differences in the recorded frequency of selected metabolic complications. Nevertheless, baseline comorbidities, duration of follow-up, steroid exposure and other potential confounders are unavailable and could influence these comparisons.

3.6. Infection

The incidence of infection did not differ significantly between the groups.

3.7. Induction costs

Induction costs were reported as below US\$500 per patient in Group I and above US\$1,000 per patient in Group II.

Table 6. Reported induction costs

Parameter	Alemtuzumab	Conventional induction
Reported cost per patient	<US\$500	>US\$1,000

These figures suggest a lower reported acquisition cost for the low-dose alemtuzumab protocol. The precise difference cannot be calculated from the reported ranges, and the data do not establish overall cost-effectiveness.

4. Discussion

This retrospective study compared 75 kidney transplant recipients receiving low-dose alemtuzumab induction with 102 recipients receiving conventional induction with ATG or basiliximab. The principal findings reported in the abstract were differences in maintenance immunosuppression regimens, dyslipidemia, hypertension requiring multiple medications, graft failure beyond five years and induction costs.

4.1. Maintenance immunosuppression minimization

The marked difference in maintenance immunosuppression distribution is an important observation. Only 13 of 75 recipients in the alemtuzumab group received triple-drug therapy, compared with 94 of 102 recipients in the conventional-induction group.

This pattern is consistent with the clinical rationale for studying lymphocyte-depleting induction agents as part of immunosuppression-minimization strategies. The INTAC and 3C studies provide relevant evidence that alemtuzumab-based regimens can alter early rejection outcomes and maintenance treatment strategies [1,2].

4.2. Acute rejection and graft outcomes

The reported acute rejection counts were numerically lower in the alemtuzumab group, but the original abstract indicated that the difference was not statistically significant. This should not be interpreted as proof of equivalence because the study may have had limited power to detect differences in relatively infrequent outcomes.

The reported number of graft failures beyond five years was lower in the alemtuzumab group. This finding merits further investigation but requires careful interpretation. The study was retrospective, and the conventional-

induction group combined ATG and basiliximab, which may have been selected for recipients with different immunological risk profiles.

Long-term graft outcomes are also affected by donor quality, rejection history, adherence, graft function, recipient comorbidities and duration of observation. A time-to-event analysis with appropriate adjustment for these factors is necessary before attributing differences in graft failure to the induction strategy.

4.3. Metabolic complications

The study reported lower frequencies of dyslipidemia and difficult-to-control hypertension in the alemtuzumab group. These observations are clinically relevant because cardiovascular complications contribute substantially to morbidity after transplantation.

Differences in corticosteroid exposure and other maintenance immunosuppressive medications may partly explain the reported metabolic differences.

The reported frequency of post-transplant diabetes mellitus was also numerically lower in the alemtuzumab group. The difference should therefore remain descriptive

4.4. Lymphocytopenia and safety

Lymphocytopenia beyond three months was more frequently reported in the alemtuzumab group. This is consistent with the expected biological effect of a lymphocyte-depleting agent, although the original laboratory definition and sampling schedule must be confirmed.

4.5. Economic implications

The reported induction-cost ranges favor the low-dose alemtuzumab protocol in terms of initial drug expenditure. Nevertheless, an induction-cost comparison is not equivalent to a formal cost-effectiveness analysis.

A comprehensive economic evaluation should specify the costing year, perspective, resource use, time horizon and relevant clinical outcomes. It should also consider costs associated with rejection treatment, infection, hospitalization, maintenance immunosuppression and graft failure. CHEERS 2022 provides a framework for transparent reporting of health economic evaluations [3].

The current results support reporting a difference in the stated induction costs, but they do not establish that the intervention is cost-effective over the lifetime of a transplant recipient.

4.6. Strengths and limitations

The study examines a low-dose alemtuzumab protocol and includes reported follow-up through 2019. It considers multiple outcomes relevant to transplant care, including maintenance immunosuppression, metabolic complications and graft failure beyond five years.

Its principal limitations are the retrospective design, lack of complete baseline characteristics, absence of the original statistical output, heterogeneous conventional-induction group and limited detail on follow-up and outcome definitions. The available cost information is insufficient for a formal economic evaluation.

The findings should be interpreted as observations from a retrospective cohort rather than proof that low-dose alemtuzumab improves long-term outcomes.

5. Conclusion

In this retrospective cohort, low-dose alemtuzumab-based induction was associated with a different distribution of maintenance immunosuppression regimens, lower reported frequencies of dyslipidemia and hypertension requiring multiple medications, fewer reported graft failures beyond five years, and lower reported induction costs compared with conventional induction.

References

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