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Early Steroid Withdrawal Compared With Standard Immunosuppression in Kidney Transplantation - Interim Analysis of the Amsterdam-Leiden-Groningen Randomized Controlled Trial

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BACKGROUND. The optimal immunosuppressive regimen in kidney transplant recipients, delivering maximum efficacy with minimal toxicity, is unknown. **METHODS.** The Amsterdam, LEiden, GROningen trial is a randomized, multicenter, investigator-driven, noninferiority, open-label trial in 305 kidney transplant recipients, in which 2 immunosuppression minimization strategies—one consisting of early steroid withdrawal, the other of tacrolimus minimization 6 months after transplantation—were compared with standard immunosuppression with basiliximab, corticosteroids, tacrolimus, and mycophenolic acid. The primary endpoint was kidney function. Secondary endpoints included death, primary nonfunction, graft failure, rejection, discontinuation of study medication, and a combined endpoint of treatment failure. An interim analysis was scheduled at 6 months, that is, just before tacrolimus minimization. **RESULTS.** This interim analysis revealed no significant differences in Modification of Diet in Renal Disease between the early steroid withdrawal group and the standard immunosuppression groups (43.2 mL/min per 1.73 m^2 vs 45.0 mL/min per 1.73 m^2, $P = 0.408$). There were also no significant differences in the secondary endpoints of death (1.0% vs 1.5%; $P = 0.737$), primary nonfunction (4.1% vs 1.5%, $P = 0.159$), graft failure (3.1% vs 1.5%, $P = 0.370$), rejection (18.6% vs 13.6%, $P = 0.289$), and discontinuation of study medication (19.6% vs 12.6%, $P = 0.348$). Treatment failure, defined as a composite endpoint of these individual secondary endpoints, was more common in the early steroid withdrawal group ($P = 0.027$), but this group had fewer serious adverse events and a more favorable cardiovascular risk profile. **CONCLUSIONS.** Based on these interim results, early steroid withdrawal is a safe short-term immunosuppressive strategy. Long-term outcomes, including a comparison with tacrolimus minimization after 6 months, will be reported in the final 2-year analysis.

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Immunosuppression with basiliximab, prednisolone, calcineurin inhibitors, and mycophenolic acid results in low rejection rates and excellent graft survival in kidney transplant recipients.[1-7] Despite this success, mortality and morbidity rates remain relatively high due to infectious complications, malignancies, an increased cardiovascular risk, and other long-term side effects of immunosuppression.

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The Amsterdam, LEiden, GROningen (ALLEGRO) trial was designed to compare 2 immunosuppression minimization strategies—early steroid withdrawal and tacrolimus minimization after 6 months—to standard immunosuppression with basiliximab, corticosteroids, tacrolimus, and mycophenolic acid. The aim of the study is to assess whether early steroid withdrawal or tacrolimus minimization can provide equivalent outcomes in terms of kidney function while limiting immunosuppressive toxicity. In this interim analysis, the 6-month results of early steroid withdrawal are compared to those of standard immunosuppression. The final analysis will report the 2-year outcomes and will also include the results of the tacrolimus minimization group.

MATERIALS AND METHODS

Study design

We conducted a prospective, open label, multicenter, randomized, investigator-driven trial comparing standard immunosuppression (basiliximab/corticosteroids/tacrolimus/mycophenolic acid) to early steroid withdrawal and to tacrolimus minimization after 6 months.

In this trial, kidney transplant recipients from 3 participating Dutch academic medical centers were included: the Academic Medical Center in Amsterdam, Leiden University Medical Center, and the University Medical Center Groningen. Approval from the Institutional Review Board of the participating institutions was obtained, and the trial was conducted in compliance with the principles of Good Clinical Practice, the Declaration of Helsinki, and national laws and regulations. All patients provided written informed consent and could withdraw from the study at any time.

Patients between the ages of 18 and 80 years who were scheduled to receive a first or second kidney transplant from a living donor, donation after brain death (DBD) donor, or donation after cardiac death (DCD) donor were eligible to participate in this trial. Patients receiving a kidney from an HLA-identical related donor were excluded, as were patients who had more than 75% current or historic panel reactive antibodies, patients with diabetes mellitus type I, and female patients who were unwilling to use adequate contraception during the study.

Before undergoing kidney transplantation, patients were randomly assigned in a 1:1:1 ratio to 3 treatment groups (groups 1, 2a, and 2b) by means of a centralized, interactive voice-response system. Randomization did not take into account any specific patient or donor organ characteristic, such as organ type. All groups received induction therapy with basiliximab and methylprednisolone. Group 1, the early steroid withdrawal group, received no prednisolone maintenance immunosuppression. Groups 2a and group 2b both received standard prednisolone, tacrolimus, and mycophenolic acid for the first 6 months. After 6 months, group 2b was switched to a low-dose tacrolimus regimen for the remainder of the study. The total study duration was set at 2 years, with a prespecified interim analysis scheduled 6 months after the last patient had been included. Figure 1 provides a schematic overview of the study.

Detailed Study Medication

All groups received induction treatment with basiliximab (Simulect, 20 mg intravenously on day 0 and day 4) and methylprednisolone (500 mg, 250 mg, 125 mg intravenously on days 0, 1, and 2). Mycophenolic acid (MyFortic) was prescribed at 720 mg twice daily for the first 2 weeks and then tapered to 540 mg twice daily for the remainder of the study. Group 1 received no maintenance prednisolone, whereas prednisolone in groups 2a and 2b was dosed at 10 mg once daily for the first 6 weeks and then lowered to 7.5 mg once daily for the remainder of the study.

All subjects were given extended-release tacrolimus (Advagraf), with a trough level target of 8 to 12 ng/mL for the first 6 weeks, which was then lowered to 6 to 10 ng/mL. For group 1 and 2a, this target trough level was continued for the remainder of the study, whereas in group 2b (the tacrolimus minimization group), target trough levels were lowered to 3 to 5 ng/mL after 6 months.

Patients with evidence of either donor or recipient cytomegalovirus seropositivity received 6 months of valgancyclovir (Valcyte) prophylaxis. In addition, all patients were prescribed 6 months of *Pneumocystis jirovecii* prophylaxis (trimethoprim/sulfamethoxazole or Cotrimoxazole).

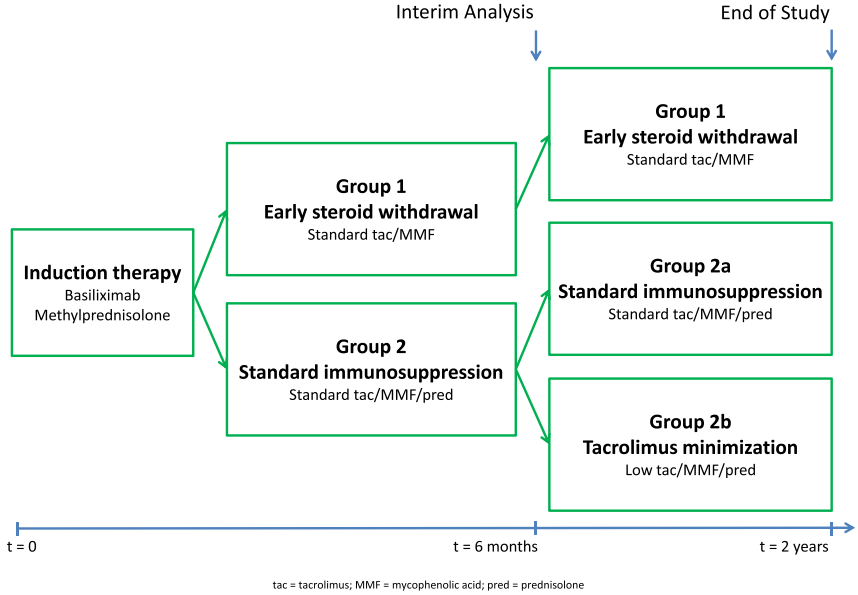

FIGURE 1. Schematic overview of the study.

Safety

All adverse events were monitored and recorded. A data safety monitoring board was formed, which met after 75 and 150 patients had been included to judge the rate of rejections and serious adverse events (SAEs). The data safety monitoring board had the right to terminate the study if the rejection rate was higher than 30%.

Rejection

Indication biopsies were performed at the discretion of the treating physician. Rejections were treated identically in both groups, according to local practice. Patients in the early steroid withdrawal group with a documented rejection were switched to standard maintenance immunosuppression. Protocol biopsies in both groups were performed at 1 and 2 years after kidney transplantation and are therefore not included in this 6-month interim analysis.

Efficacy

The primary endpoint of this study was kidney function, measured as estimated glomerular filtration rate (eGFR) by means of the Modification of Diet in Renal Disease (MDRD) equation. In addition, creatinine clearance and proteinuria were obtained from 24-hour urine collections.

Secondary endpoints for the interim analysis consisted of graft and patient survival, documented rejection episodes, interruption of study medication for more than 6 weeks, SAEs and cardiovascular risk factors (blood pressure, lipid profile, and diabetes). In addition, a composite endpoint reflecting treatment failure was defined as death, primary nonfunction, graft failure (ie, death-censored graft loss), a documented rejection, or interruption of study medication for more than 6 weeks. If patients experienced multiple events, only their first event was included in the composite endpoint of treatment failure.

Statistical Methods

The sample size was calculated assuming 80% power to detect noninferiority in terms of eGFR at a significance level of 5%. Noninferiority was defined as a difference of 10 mL/min per 1.73 m^2 or less in mean eGFR. The standard deviation of eGFR was estimated at 25 mL/min per 1.73 m^2. This implies a group size of at least 75 patients for each of the 3 groups included in the final analysis. Analyses were performed both on an intention-to-treat and as-treated basis.

For the interim analysis, Student *t* tests (for MDRD and creatinine clearance) and Mann-Whitney *U* tests (for proteinuria) were used depending on the characteristics of the underlying distribution. In case of graft failure, an eGFR of 10 mL/min per 1.73 m^2 and a creatinine clearance of 10 mL/min were imputed. Sensitivity analyses were run both with and without imputations for graft failure. Secondary endpoints were compared by Kaplan-Meier analyses (for death, primary nonfunction, graft failure, rejection, interruption of study medication and the composite endpoint of treatment failure), χ^2 tests (for SAEs), and analysis of covariance analyses (for cardiovascular risk factors).

RESULTS

Patients

From June 27, 2011, to August 6, 2014, 305 patients underwent randomization (Figure 2). Eight patients had an inclusion/exclusion violation, so that 297 patients could be included in the intention-to-treat analysis. After 6 months, 53 of 98 patients had completed the assigned treatment in the early steroid withdrawal group, compared with 133 of 199 patients in the standard immunosuppression group.

The baseline characteristics of patients in the early steroid withdrawal and standard immunosuppression group are described in Table 1. It shows that both groups were well balanced in terms of demographic characteristics, underlying renal disease, previous renal replacement therapy, comorbidity, and donor and surgical characteristics.

Tacrolimus trough levels were within predefined boundaries and were identical for all groups, with the exception of week 2 trough levels, which were slightly but significantly

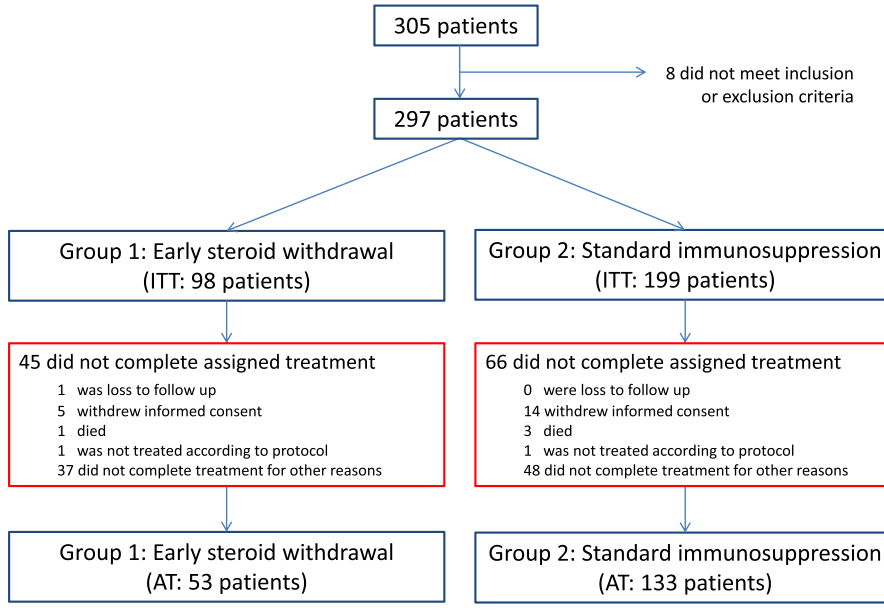

FIGURE 2. Enrollment and outcomes.

TABLE 1.

Baseline characteristics

	Early steroid withdrawal (98 patients)	Standard immunosuppression (199 patients)	*P*
Demographic characteristics			
Age, y	54.8 ± 14.6	57.5 ± 12.6	0.098
Sex (% male)	68.4%	67.6%	0.905
Race			0.737
White	82.7%	81.3%	
Asian	3.1%	5.1%	
Black	3.1%	4.5%	
Other	11.2%	9.1%	
Blood pressure, mm Hg	141/84	141/81	0.877/0.101
BMI	26.5	26.7	0.558
Renal disease characteristics			
Primary diagnosis			0.765
Diabetes mellitus type 2	8.2%	9.1%	
Hypertension	2.7%	22.2%	
Glomerulonephritis	8.2%	14.6%	
ADPKD	20.6%	17.7%	
FSGS	2.1%	2.5%	
Other	38.1%	33.8%	
Preemptive transplantation	27.6%	22.7%	0.389
Dialysis modality			0.784
Hemodialysis	36.7%	42.9%	
Peritoneal dialysis	20.4%	20.2%	
Both	15.3%	14.1%	
Prior renal transplantation	4.1%	5.1%	0.725
Renal risk factors			
Hypertension	82.5%	77.3%	0.303
Hypercholesterolemia	23.7%	24.2%	0.920
Diabetes	14.4%	19.7%	0.169
Smoking			0.732
None	51.0%	50.5%	
Past/current	49.0%	49.5%	
Pack-years	14 [8.2-26.9]	16.0 [7.5-36.1]	0.586
CMV status (% IgG positive)	54.1%	56.1%	0.845
EBV status (% IgG positive)	75.5%	82.3%	0.368
Donor and surgical characteristics			
Age of donor, y	54.0 ± 14.5	54.9 ± 13.3	0.585
Sex of donor (% male)	46.4%	53.5%	0.249
First or second kidney transplant (%)			0.720
First	95.9%	94.9%	
Second	4.1%	5.1%	
Postmortal donor	64.3%	55.1%	0.135
DBD	25.5%	19.4%	0.555
DCD	38.8%	35.4%	
Living donor	35.7%	44.9%	
Related	14.3%	17.2%	0.853
Unrelated	21.4%	27.8%	
Atherosclerosis (macroscopic)			0.208
None/mild	76.0%	79.0%	
Moderate	11.5%	14.1%	
Severe	12.5%	6.8%	
Cold ischemia time, h			
Postmortal donor	13.8 ± 4.7	14.5 ± 4.5	0.360
Living donor	2.6 ± 0.5	2.7 ± 0.6	0.190
Second warm ischemia time, min	37 ± 10	37 ± 12	0.267
Perioperative complications	6.1%	7.1%	0.988

All results as percentages, mean ± standard deviation or median + interquartile range.

BMI, body mass index; ADPKD, autosomal dominant polycystic kidney disease; FSGS, focal segmental glomerulosclerosis; CMV, cytomegalovirus EBV, epstein-barr virus; DBD, donation after brain death; DCD, donation after cardiac death.

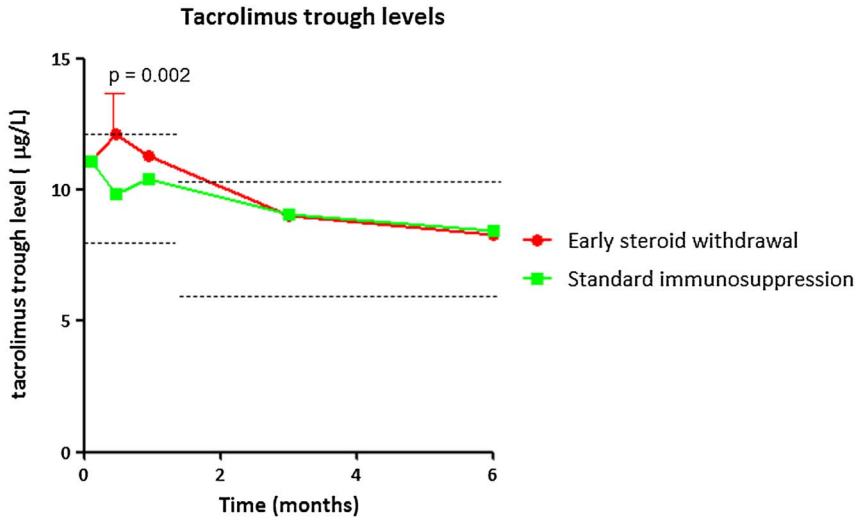

FIGURE 3. Tacrolimus trough levels.

higher in the early steroid withdrawal group (Figure 3). From the third week onward, dosages were adequately adjusted so that trough levels between the groups were indistinguishable. Average mycophenolic acid dosages were not significantly different for both groups: 930 mg daily in the early steroid withdrawal group, compared to 994 mg daily in the standard immunosuppression group ($P = 0.123$).

Primary Endpoint

There were no statistically significant differences in kidney function between the 2 groups. This was true for MDRD, creatinine clearance, and proteinuria (Table 2), both for the intention-to-treat and the as-treated analysis. Sensitivity analyses were performed with and without imputations for graft failure, without significant changes in outcome.

Secondary Endpoints

Four patients died during the first 6 months of the ALLEGRO trial, 1 (1.0%) in the early steroid withdrawal group and 3 (1.5%) patients in standard immunosuppression group. The cause of death of the patient in the early steroid withdrawal group was pneumosepsis; in the standard immunosuppression group, the causes of death were pneumosepsis and 2 cases of sudden death at home. Primary nonfunction occurred in 4.1% of patients in the early steroid withdrawal group and in 1.5% of patients in the standard immunosuppression group, whereas graft failure occurred in 3.1% and 1.5% of patients, respectively. The combined rate of death, primary nonfunction, and graft failure was not significantly different between the 2 groups ($P = 0.325$, Figure 4A). Rejection (Table 3) occurred in 18.6% of patients in the early steroid withdrawal group compared with 13.6% in the standard immunosuppression group ($P = 0.289$, Figure 4B). There was no statistically significant difference in steroid-resistant rejections ($P = 0.564$). In the early steroid withdrawal group, 19.6% of patients had to discontinue their study medication, compared with 12.6% in the standard immunosuppression group ($P = 0.164$, Figure 4C). The reasons for the discontinuation of study medication were varied (see Table 4) and included infectious complications (4.1% in both groups), mycophenolic acid toxicity (3.1% in the early steroid withdrawal group vs 1.0% in the standard immunosuppression group, $P = 0.382$), and a requirement for prednisolone for reasons other than rejection (in 4.1% of patients in the early steroid withdrawal group, eg, due to interstitial nephritis or hyponatremia). Treatment failure, defined as the composite endpoint of death, primary nonfunction, graft failure, rejection, and interruption of study medication for more than 6 weeks, occurred more frequently in the early steroid withdrawal group ($P = 0.024$, Figure 4D).

Serious adverse events were less common in the early steroid withdrawal group (44.3 vs 56.6 per 100 patients, $P = 0.048$, Table 5), which was mostly attributable to a lower rate of infections. The early steroid withdrawal group also

TABLE 2.

Primary endpoint (kidney function)

	Early steroid withdrawal	Standard immunosuppression	*P*
Intention-to-treat	98 patients	199 patients	
eGFR (MDRD, mL/min per 1.73 m^2)	43.2 ± 18.0	45.0 ± 16.1	0.408
Creatinine clearance, mL/min	58.5 ± 24.4	58.3 ± 28.6	0.949
Proteinuria, g/24 h	0.20 [0.12-0.31]	0.19 [0.11-0.30]	0.771
As-treated	53 patients	133 patients	
eGFR (MDRD, mL/min per 1.73 m^2)	50.5 ± 13.9	47.2 ± 15.4	0.175
Creatinine clearance, mL/min	67.1 ± 24.2	61.5 ± 21.7	0.137
Proteinuria, g/24 h	0.19 [0.12-0.27]	0.18 [0.11-0.30]	0.910

In case of graft failure, an eGFR of 10 mL/min per 1.73 m^2 and creatinine clearance of 10 mL/min were imputed. Sensitivity analyses were performed with and without imputation of these values and did not result in significant changes in outcome.

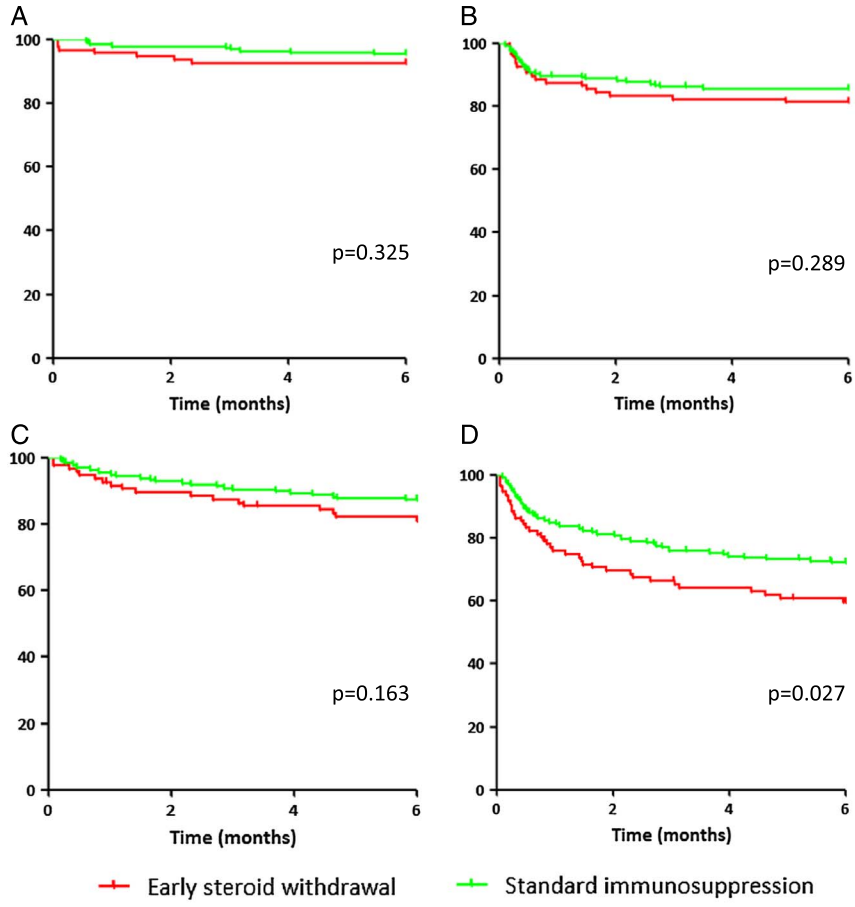

FIGURE 4. Percentage of patients free from (A) death, primary nonfunction, and graft failure, (B) rejection, (C) interruption of study medication, and (D) any type of treatment failure.

demonstrated a more favorable cardiovascular risk profile (Table 6): an improved diastolic blood pressure, and a lower total cholesterol and LDL, despite a lower percentage of patients on cholesterol lowering agents in the early steroid withdrawal group (32% vs 37.9%). The percentage of patients with new onset diabetes mellitus type II, defined as initiation of oral hypoglycemic agents or insulin for at least 30 consecutive days, was higher in the standard immunosuppression group (34.7% vs 24.3%), but due to a baseline difference in diabetes mellitus type 2 prevalence in both groups (24.2% in the standard immunosuppression group vs 14.4% in the early steroid withdrawal group), the increase was not statistically significant.

Subgroup analysis for different donor types

No differences in MDRD were found for different donor subtypes, but living donor kidney recipients had a higher creatinine clearance (64 mL/min) and a lower median proteinuria (0.16 g/d) compared to DBD (53 mL/min; 0.19 g/d;

TABLE 3.
Rejections

	Early steroid withdrawal	Standard immunosuppression	*P*
Treated rejections	18.6%	13.6%	0.289
Acute AMR	7.2%	4.0%	0.266
Acute TCMR			0.128
Grade IA	2.1%	1.0%	
Grade IB	1.0%	0%	
Grade IIA	5.2%	3.0%	
Grade IIB	3.1%	1.5%	
Grade III	0.0%	0.5%	
Borderline acute TCMR	3.1%	2.5%	0.805
Inadequate biopsy but treated as rejection[a]	0%	2.5%	0.058

Rejections graded according to Banff 2015 criteria[8].

[a] Biopsies with less than seven glomeruli.

AMR, antibody-mediated rejection; TCMR, T cell–mediated rejection.

TABLE 4.
Reasons for Discontinuation of study medication

	Early steroid withdrawal	Standard immunosuppression	*P*
Infectious complications	4.1%	4.1%	0.481
Tacrolimus toxicity	4.1%	2.5%	0.860
Inability to maintain adequate tacrolimus levels	2.1%	3.5%	0.179
MMF toxicity	3.1%	1.0%	0.382
Requirement for prednisolone for reasons other than rejection[a]	4.1%	0.0%	0.013
Other	2.1%	1.5%	0.929

[a] Initiation of prednisolone after a rejection in the early steroid withdrawal group was standard practice in the ALLEGRO trial and was therefore not included in this endpoint.

TABLE 5.

SAEs per 100 patients

	Early steroid withdrawal	Standard immunosuppression	*P*
SAEs	44.3	56.6	0.048
Urinary tract infections	11.3	12.1	
Other infections	7.2	16.2	
Cardiovascular event	3.1	2.5	
Gastrointestinal event	7.2	6.1	
Malignancy	0.0	1.5	
Urologic event	2.1	3.5	
Vascular event	0.0	2.5	
Psychiatric event	3.1	1.0	
Pulmonary event	2.1	2.0	
Other	7.2	7.1	

P = 0.012) and DCD recipients (55 mL/min; 0.20 g/d; *P* = 0.047). These trends were the same for both the early steroid withdrawal and the standard immunosuppression group. Three of 4 deaths occurred in the DCD group and 1 in a living donor kidney recipient (*P* = 0.242). No significant differences in primary nonfunction and graft failure were found for different donor types, but there was a trend of a lower rejection rate in the DBD group (8% versus 19% in living donor kidney transplant recipients and versus 16% in DCD recipients, *P* = 0.117). For all donor types, there were no significant differences in the above outcomes between the early steroid withdrawal and the standard immunosuppression group.

DISCUSSION

These interim results of the ALLEGRO trial show that early steroid withdrawal in living donor, DBD, and DCD kidney transplant recipients is noninferior compared with standard maintenance immunosuppression with basiliximab, tacrolimus, mycophenolic acid, and corticosteroids in terms of kidney function at 6 months. Early steroid withdrawal has been evaluated in 2 recent meta-analyses,[9,10] but the trials included in these meta-analyses were very heterogeneous in terms of timing of steroid withdrawal and concurrent immunosuppression. Only 4 trials are directly comparable to the ALLEGRO trial.[11-14] These trials are summarized in Table 7 and confirm the noninferiority of early steroid withdrawal in terms of kidney function. What our analysis adds to these results is that early steroid withdrawal is also noninferior in terms of proteinuria, an important predictor of graft survival.[15] We are also the first study to have included recipients of living donor, DBD, and DCD kidneys with a low to intermediate immunological risk.

In our study, early steroid withdrawal did not increase the 6-month incidence of the individual secondary endpoints of death, primary nonfunction, and graft failure. We did find a somewhat higher rate of rejection in the early steroid withdrawal group (18.6% vs 13.6%), but this difference was not statistically significant. This contrasts with the study by Woodle et al,[13] who found a significantly higher rate of biopsy-proven rejection in the steroid withdrawal group (17.8% vs 10.8%), despite using either thymoglobulin, daclizumab, or basiliximab according to local center preference, whereas we used basiliximab in all cases. However, our study could be underpowered to detect differences in the rate of rejection.

Although rejection rates and patient and graft survivals were comparable in both groups, the early steroid withdrawal group was at increased risk for the composite endpoint of treatment failure. This was largely due to a higher percentage of discontinuation of study medication, for example, because of mycophenolic acid toxicity or a requirement for prednisolone for reasons other than rejection. The relatively high rate of discontinuation of study medication also explains the relatively small number of patients in our as-treated analysis, which is one of the limitations of our study. Other limitations include a relatively short follow-up duration and a heterogeneous (but real-life) study population. Lastly, the ALLEGRO study is not double-blind, but we believe that any bias would be limited, because tacrolimus levels were very comparable in both groups. The reported difference in tacrolimus levels in week 2 was most likely due to an interaction of prednisolone with tacrolimus, resulting in lower tacrolimus trough levels in the standard immunosuppression group. This phenomenon has been described previously[16] and was confirmed by an analysis of average Advagraf dosages, which were slightly higher in the standard immunosuppression group (13.5 mg vs 12.7 mg once daily) despite lower trough levels in that group.

Based on these interim results, we believe that steroid-free maintenance immunosuppression is a safe short-term strategy for living donor, DBD and DCD kidney transplant recipients with a low to intermediate immunological risk. Although associated with an increased risk of treatment failure, it does not impair kidney function at 6 months, as well as having the benefits of a decreased risk of infections and an

TABLE 6.

Cardiovascular risk factors

	Early steroid withdrawal	Standard immunosuppression	*P*
Blood pressure, mm Hg	141/84 → 138/79	141/81 → 138/80	0.303/0.030[a]
% of patients with diabetes mellitus	14.4% → 24.7%	19.7% → 34.3%	0.310
HbA1C, mmol/mol	39.4 → 42.9	39.1 → 45.1	0.811
Total cholesterol, mmol/L	4.6 → 4.8	4.5 → 5.5	0.005
HDL, mmol/L	1.3 → 1.3	1.2 → 1.5	0.010
LDL, mmol/L	2.4 → 2.7	2.3 → 3.0	0.106
Triglycerides, mmol/L	2.2 → 2.0	2.3 → 2.3	0.675
% of patients on cholesterol lowering agent	32.0%	37.9%	

[a] *P* values for systolic and diastolic blood pressure.

HDL, high-density lipoprotein; LDL, low-density lipoprotein.

TABLE 7.

Summary of studies investigating maintenance immunosuppression with tacrolimus and mycophenolic acid with or without steroids

Study	No. patients (early steroid withdrawal vs standard immune suppression)	Study duration	Immunological risk	Living/ deceased donors	Immunosuppression	Patient and graft survival	Acute rejection	Kidney function	Proteinuria	Reported composite endpoints	Other outcomes
Laftavi (2005)	28:32	1 y	PRA < 30%	80% deceased donors	ATG/Tac/MMF +/– steroids	=	=	=	N/A	N/A	Increased fibrosis in protocol biopsies in CSWD group
Rostaing (2005)	278:260	1 y	PRA < 50% or previous graft loss due to immunological reasons	living and deceased donors, % not known	Tac/MMF/steroids or Dac/Tac/MMF	=	=	=	N/A	88.8% of CSWD remained steroid-free	Less NODAT and improved lipid profile in CSWD group
Woodle (2008)	195:191	5 y	PRA < 50% or previous graft loss with PRA > 25%	44% deceased donors	ATG, Dac or Bas + Tac/MMF +/– steroids	=	More BCAR in CSWD group, no difference in steroid-resistant rejections	=	N/A	No difference in study drug discontinuation (35.1 vs 37.4%)	No difference in DMII but less insulin use, lower HbA1C and improved lipid profile in CSWD group
Kramer (2012)	139:139:143	3 y	PRA < 2%	88% deceased donors	Tac/MMF/pred, Tac/MMF or Tac/Bas	=	More BCAR in CSWD group	=	N/A	N/A	Less insulin use and improved lipid profile in CSWD group

ATG, antithymocyte globulin; Dac, daclizumab; Bas, Basiliximab; Tac, tacrolimus; MMF, mycophenolate mofetil; BCAR, biopsy-confirmed acute rejection; NODAT, new-onset diabetes after transplantation.

improved cardiovascular risk profile. Whether this will outweigh possible long-term risks, such as the possibility of increased donor-specific antibody formation or increased calcineurin inhibitor toxicity compared to the tacrolimus minimization group, will be addressed in our definitive 2-year analysis.

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