Outcomes of Primary Simultaneous Pancreas-kidney Transplants by Induction Agent in the United States

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Background. Long-term outcome data by induction type in simultaneous pancreas-kidney (SPK) transplantation is limited. Methods. Utilizing the Scientific Registry of Transplant Recipients, we examined all primary SPK transplants between 2000 and 2020, excluding crossmatch-positive recipients. We grouped recipients according to induction regimen into 3 groups: rabbit antithymocyte globulin (r-ATG) (n = 5678), alemtuzumab (n = 1199), and interleukin-2 receptor antagonist (IL-2RA; n = 1593). We analyzed the 10-y recipient and composite (kidney and pancreas) graft survival using the Kaplan-Meier survival function. Cox-proportion hazard models were generated to examine the association between induction type, the 10-y recipient, and graft survival. Models were adjusted for recipient age, sex, ethnicity, HLA-mismatch, diabetes type, dialysis dependency, cold-ischemia time, local versus imported organs, panel reactive antibody, steroid maintenance, and Pancreas Donor Risk Index. Results. r-ATG was associated with the lowest 1-y kidney and pancreas rejection rates compared with other agents (P < 0.001). In the univariable analysis, induction type was not associated with recipient (log-rank P = 0.11) or graft survival (log-rank P = 0.36). In the multivariable model for the composite graft survival, alemtuzumab use was associated with 22% increased kidney or pancreas graft loss compared with r-ATG (adjusted hazard ratio, 1.22; 95% confidence interval, 1.05–1.42), whereas IL-2RA use was not a predictor of graft survival. Induction type did not influence recipient survival in the adjusted model. Conclusions. r-ATG use was associated with the lowest SPK rejection rates. Compared with r-ATG, alemtuzumab but not IL-2RA was associated with worse long-term death-censored SPK graft outcome. Our analysis supports the common use of r-ATG for induction in US primary SPK recipients.

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Simultaneous pancreas-kidney (SPK) transplantation proved to be a durable treatment for patients with type 1 diabetes and end-stage renal disease for >3 decades. Indications for SPK transplantation continue to expand with an increasing percentage of SPK patients with uremia secondary to type 2 diabetes.1 Although the number of pancreas transplants performed per year has decreased over time, outcomes for graft and patient survival continued to improve.2,3 The improvement in short- and long-term outcomes for SPK transplants has largely been attributed to a...
variety of donor- and candidate-related aspects as well as advancements in the diagnosis and management of rejection with evolving immunosuppressive therapies.

The current immunosuppression strategy after SPK transplantation is divided into induction therapy and maintenance or lifelong immunosuppression. There are 3 forms of induction treatments in the United States. Nondepletional interleukin-2 receptor antagonists (IL-2RA), daclizumab or basiliximab, are monoclonal antibodies directed against the IL-2 receptor on T cells preventing IL-2–dependent T-cell activation and proliferation in response to immunologic stimuli. Rabbit anti-thymocyte globulin (r-ATG) consists of cytotoxic antibodies directed against antigens on human T lymphocytes, ultimately leading to lymphodepletion. Finally, alemtuzumab is a humanized monoclonal antibody against CD52, leading to profound T lymphocyte depletion. According to the most recent registry data, >90% of patients undergoing SPK transplantation receive T-cell depletion induction therapy.

Although the field agrees on the need for induction therapy in SPK transplant patients, there remains a dispute as to which induction therapy provides the most benefit concerning short- and long-term recipient and graft outcomes. Evidence from multicenter and single-center randomized controlled trials is mostly equivocal between compared groups, with the majority of the benefit derived from acute incidence of early rejection and corresponding decreases in hospital admissions without long-term follow-up data. More recent nonrandomized comparisons have suggested that alemtuzumab and thymoglobulin are associated with a lower acute rejection rate but carry a higher rate of viremia-related complications, particularly from cytomegalovirus.

Given the lack of consensus regarding induction therapy and conflicting reports from small, single-center data sets, we performed a retrospective analysis of the Scientific Registry of Transplant Recipients (SRTR) database to evaluate whether the choice of induction agent is associated with recipient and graft outcomes in SPK transplants. As the field of immune senescence continues to evolve, induction use has been linked to long-term posttransplant outcomes. Accordingly, we focused on long-term outcomes by induction type in SPK recipients.

MATERIALS AND METHODS

Data Source
This study used data from the SRTR. The SRTR data system includes data on all donors, wait-listed candidates, and transplant recipients in the United States, submitted by the members of the Organ Procurement and Transplantation Network. The Health Resources and Services Administration. US Department of Health and Human Services provides oversight to the activities of the Organ Procurement and Transplantation Network and SRTR contractors. The study complied with the SRTR data use agreement and was approved by the University of Minnesota Institutional Review Board.

Study Population
We analyzed the SRTR standard analysis files for all adult primary SPK transplant recipients between January 1, 2000, and January 12, 2020 (N = 15 854). We focused our analysis on those who received one of the three most common forms of induction: alemtuzumab, IL-2RA, or r-ATG. Additionally, all subjects included in the study had a negative crossmatch and were discharged on tacrolimus and mycophenolate with or without steroid avoidance. Because SPK transplants are utilized frequently in type 2 uremic diabetics, we only included recipients with clearly documented diabetes type. Finally, we included those who survived their initial transplant hospitalization without technical graft failures or losses caused by surgical complications.

We excluded: (1) 2903 recipients who were not discharged on tacrolimus and mycophenolate; (2) 3575 recipients with unknown, missing, or other than specified induction types and positive or missing crossmatch; (3) 383 recipients with missing or discordant diabetes type data; and (4) 523 recipients who had technical grafts loss or did not survive the initial transplant hospitalization.

The remaining 8470 recipients were grouped according to induction agent into 3 groups: alemtuzumab group (n = 1199), IL-2RA (n = 1593), and r-ATG (n = 5678) (Figure 1).

Outcomes of Interest
The primary outcomes were recipient and a composite outcome of the death-censored pancreas and kidney graft survival. Secondary outcomes included rates of delayed graft function (defined as needing dialysis in the within the first week of transplant), and 6-mo and 1-y acute rejection rates. Also, we reported the rates of 1-y posttransplant lymphophoric disorder (PTLD) by induction received. For the binary outcomes of acute rejection and PTLD, we utilized the 6-mo and 1-y transplant recipient follow-up worksheets. We considered patients to have the event if either form listed “yes” to the related question. Patients were considered not to have the event if both forms listed “no.” If both forms had a missing value or one missing value and one no value, the outcome was set to missing.

Statistical Analyses
Recipient and donor pretransplant variables and posttransplant outcomes not subject to censoring were compared between the 2 groups using chi-square or Wilcoxon tests. Kaplan-Meier curves were generated to show time to death and composite pancreas and kidney graft loss. Follow-up was censored at 10 y from transplantation. Missing data were not imputed.

Multivariable mixed effect Cox-proportional hazard regression was used to evaluate the association between induction type and the primary outcomes of interest. We considered the transplant center a random effect to account for center-specific effects as patient characteristics and outcomes within a center are potentially more comparable than those across different centers. The models were adjusted for recipient age, sex, ethnicity, HLA-mismatches, Pancreas Donor Risk Index (PDRI), panel reactive antibody (PRA), pretransplant dialysis, diabetes type, local versus imported organs, cold-ischemia time transplant year, and steroid maintenance.

RESULTS

Baseline Characteristics
Recipient and organ characteristics by induction type are detailed in Table 1; r-ATG was used in over two-thirds of the study population. The IL-2RA group accounted for 18.8% of
Alemtuzumab debuted in the SPK arena as early as 2003, and it slowly gained popularity and quickly leveled off (Figure 2). Since the early 2000s r-ATG appeared to be the mainstay of induction in SPK transplants. Recipients in the alemtuzumab group were slightly older and had a higher body mass index. Proportions of Black recipients varied between groups, with the IL-2RA group having the lowest proportion of Black recipients, 12.4%, compared with the r-ATG group, 20.6%, and the alemtuzumab group, 19.2% (P < 0.001).

The proportion of the least sensitized recipients (PRA < 20) was the highest in the IL-2RA group, whereas more sensitized (PRA > 20) recipients were observed more frequently in the r-ATG group. PDRI varied between groups, and IL-2RA recipients had the highest PDRI compared with the other groups. The highest proportion of recipients discharged without steroid maintenance was in the alemtuzumab group.

Short-term Outcomes

Delayed kidney graft function was observed at a similar frequency across the study cohort without a significant difference by induction type. Although the 6-mo kidney allograft rejection was not statistically different, the 12-mo kidney rejection was significantly higher in the alemtuzumab group (13%) compared with 9.5% in the IL-2RA and 8.9% in the r-ATG group.

The 6-mo pancreas rejection rate was the highest in the alemtuzumab group compared with the other groups. By 12 mo, pancreas rejection was observed in 14.1% in the alemtuzumab group, 12.4% in the IL-2RA group, and 9.5% in the r-ATG group (P < 0.001). The 1-y PTLD rate did not differ statistically between groups (Table 2).

Recipient Survival Outcome

In the Kaplan-Meier analysis, recipient survival did not differ by the type of induction used (log-rank P = 0.11) (Figure 3). The 1-, 5-, and 10-y recipient survival was 97.6%, 90%, and 71% in the alemtuzumab group. In the IL-2RA group, recipient survival was 97.1%, 89.8%, and 74.4% at 1, 5, and 10 y, respectively. The recipient survival in the r-ATG group was 97.4%, 91%, and 76.2% at 1, 5, and 10 y. In the Cox-proportional multivariable model (Table 3), compared with r-ATG, neither IL-2RA nor alemtuzumab was associated with different recipient survival. Recipient older age, higher PDRI, dialysis requirement before transplant and PRA > 80...
were poor predictors of survival. Compared with imported organs, local organs were associated with 24.9% improved survival (hazard ratio, 0.751; 95% confidence interval, 0.631-0.893; \(P = 0.001\)).

### TABLE 1.
Baseline characteristics of recipient and SPK allografts by induction type

| Variable            | Alemtuzumab, \(N = 1199\) | IL-2RA, \(N = 1593\) | r-ATG, \(N = 5678\) | \(P\)   |
|---------------------|-----------------------------|-----------------------|---------------------|--------|
| Recipient age       | 42.72 (9.34)                | 41.57 (8.40)          | 42.03 (8.66)        | 0.003  |
| Recipient sex (male)| 767 (64.0)                  | 986 (61.9)            | 3535 (62.3)         | 0.478  |
| Recipient BMI (kg/m\(^2\)) | 25.28 (3.67)     | 24.89 (4.02)          | 25.21 (4.04)        | 0.012  |
| Recipient ethnicity |                             |                       |                     | <0.001 |
| Black               | 230 (19.2)                  | 197 (12.4)            | 1169 (20.6)         |        |
| Other               | 52 (4.3)                    | 28 (1.8)              | 169 (3.3)           |        |
| White               | 917 (76.5)                  | 1368 (85.9)           | 4320 (76.1)         |        |
| Diabetes type II    | 165 (13.8)                  | 57 (3.6)              | 515 (9.1)           | <0.001 |
| HLA-mismatch        | 4.54 (1.15)                 | 4.42 (1.26)           | 4.53 (1.14)         | 0.004  |
| Peak PRA            |                             |                       |                     | <0.001 |
| 0–20                | 1047 (87.3)                 | 1537 (96.5)           | 4851 (85.4)         |        |
| >20–80              | 132 (11.0)                  | 46 (2.9)              | 659 (11.6)          |        |
| >80                 | 20 (1.7)                    | 10 (0.6)              | 168 (3.0)           |        |
| Cold ischemia time (h) | 10.59 (4.55)              | 12.75 (5.64)          | 10.79 (4.62)        | <0.001 |
| Donor age (y)       | 25.73 (9.44)                | 26.23 (10.49)         | 25.06 (8.82)        | <0.001 |
| Donor sex (male)    | 809 (67.5)                  | 1088 (86.3)           | 3976 (70.0)         | 0.133  |
| Donor ethnicity     |                             |                       |                     | <0.001 |
| Black               | 203 (16.9)                  | 226 (14.2)            | 1052 (18.5)         |        |
| Other               | 42 (3.5)                    | 32 (2.0)              | 184 (3.2)           |        |
| White               | 954 (79.6)                  | 1335 (83.8)           | 4442 (78.2)         |        |
| Donor BMI (kg/m\(^2\)) | 23.84 (3.86)              | 23.97 (4.22)          | 23.99 (3.90)        | 0.484  |
| PDRI                | 1.10 (0.36)                 | 1.15 (0.44)           | 1.07 (0.33)         | <0.001 |
| Local organs        | 984 (82.1)                  | 1445 (90.7)           | 4719 (83.1)         | <0.001 |
| Pretransplant dialysis | 941 (78.5)               | 1263 (79.6)           | 4599 (81.3)         | 0.052  |
| Dialysis vintage (y) \(^a\) | 2.07 (1.77)            | 1.98 (1.87)           | 2.18 (1.78)         | 0.001  |
| Steroid maintenance | 617 (51.5)                  | 1532 (96.2)           | 4189 (73.8)         | <0.001 |

\(^a\) Only for those on dialysis pretransplant. Values are presented as mean (SD) or N (%).

BMI, body mass index; IL-2RA, interleukin-2 receptor antagonist; PDRI, Pancreas Donor Risk Index; PRA, panel reactive antibody; r-ATG, rabbit anti-thymocyte globulin; SPK, simultaneous pancreas-kidney.

Death-censored Composite SPK Graft Outcome

The composite SPK graft survival did not differ by induction type in the Kaplan-Meier analysis (log-rank 0.363) (Figure 4). The SPK 1-, 5-, and 10-y survival was 95.2%, 81.5%, and
65.2% in the alemtuzumab group. In the IL-2RA group, 94.5%, 81.8%, and 68.1% at 1, 5, and 10 y, respectively. The survival in the r-ATG group was 95.1%, 83.4%, and 68.5% at 1, 5, and 10 y posttransplant. In the multivariable Cox-proportional hazard model for the composite SPK outcome, alemtuzumab induction was associated with a 22% increased risk of kidney and pancreas graft loss compared with r-ATG (hazard ratio, 1.22; 95% confidence interval, 1.046-1.422; \( P = 0.011 \)). IL-2RA was not associated with worse graft loss. Older recipient age, recent transplant years, local organs compared with imported ones and other ethnicities compared with Black ethnicity were all associated with better graft survival. Higher PDRI, pretransplant dialysis requirement, and PRA > 80 were negative predictors of composite graft survival (Table 4).

We detailed the outcomes of each organ separately in the Supplemental Material (Figure S1, SDC, http://links.lww.com/TXD/A475; Figure S2, SDC, http://links.lww.com/TXD/A475; Table S1, SDC, http://links.lww.com/TXD/A475; and Table S2, SDC, http://links.lww.com/TXD/A475) for the pancreas and kidney, respectively.

**DISCUSSION**

Our study is the most extensive comparative report on induction therapies and outcomes of primary, crossmatch negative SPK transplant recipients discharged alive on tacrolimus and mycophenolate maintenance therapy with or without steroids. Our results can best be summarized as follows: (1) r-ATG induction was associated with the lowest kidney rejection rates at 12 mo and lowest pancreas rejection rates at both 6 and 12 mo. (2) In the multivariate analysis, compared with thymoglobulin induction, alemtuzumab was associated with a 22% increased risk of composite SPK loss by 10 y from transplant. (3) There was no patient survival difference between the 3 studied induction modalities.

Induction immunosuppression for SPK transplant has been implemented to reduce graft loss and rejection rates in transplant recipients. The basis for induction therapy choice has primarily been based on experiences from kidney transplants and revolves around r-ATG, alemtuzumab, or nondepletional IL-2RA.17-19 In 2002, Stratta et al18 compared IL-2RA induction to no antibody induction and reported a lower composite risk of acute rejection, death, and graft loss with IL-2RA induction in SPK transplant patients. Expanding on the previous findings, Kaufman et al19 conducted a multicenter, prospective, randomized, open label controlled trial comparing IL-2RA and r-ATG to no induction in SPK recipients. Reaction rates were numerically lower and less severe with antibody induction compared with no induction. Interestingly, the 1-y recipient and graft survival did not differ significantly. The same

**TABLE 2.** Short-term outcomes of SPK recipients by induction type

| Outcome | Alemtuzumab, N = 1199 | IL-2RA, N = 1593 | r-ATG, N = 5678 | \( P \) |
|---|---|---|---|---|
| Delayed graft function | 70 (5.8) | 98 (6.2) | 367 (6.5) | 0.689 |
| Kidney rejection with 6 mo | 81 (7.3) | 49 (6.6) | 274 (5.6) | 0.094 |
| Kidney rejection within 12 mo | 134 (13.0) | 68 (9.5) | 410 (8.9) | <0.001 |
| Pancreas rejection within 6 mo | 111 (10.0) | 64 (8.6) | 318 (6.6) | <0.001 |
| Pancreas rejection within 12 mo | 144 (14.1) | 98 (12.4) | 432 (9.5) | <0.001 |
| Kidney or pancreas rejection within 6 mo | 159 (14.3) | 98 (13.2) | 491 (10.2) | <0.001 |
| Kidney or pancreas rejection within 12 mo | 224 (21.9) | 130 (18.3) | 693 (15.2) | <0.001 |
| Posttransplant lymphoproliferative disorder | 3 (0.3) | 1 (0.1) | 21 (0.4) | 0.112 |

Values are presented as mean (SD) or N (%).

IL-2RA, interleukin-2 receptor antagonist; r-ATG, rabbit anti-thymocyte globulin; SPK, simultaneous pancreas-kidney.
The recipient and pancreas graft survival was similar between the groups; however, kidney survival was statistically better in the antibody induction group compared with no induction.

In 2006, Kaufman et al. retrospectively compared alemtuzumab and thymoglobulin induction in 88 SPK recipients discharged on tacrolimus/sirolimus without steroid maintenance and found no significant differences in patient or graft survival through 5 y post transplants by induction type. The rejection rates at 1 and 2 y were similar between the 2 groups.

Although patient numbers in the study were small, it established alemtuzumab as a reasonable induction choice with comparable results to r-ATG for SPK transplant patients.

Farney et al. conducted a single-center randomized trial comparing alemtuzumab and thymoglobulin induction in a mixed recipient population, including kidney, pancreas, and SPK recipients. They found higher rates of biopsy-proven acute rejection with thymoglobulin use. Contrary to Farney et al.’s findings, we detected a better rejection rate with r-ATG. We suspect the difference in results is primarily related to the

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**TABLE 3.** Multivariable Cox proportional hazard model for recipient survival

| Variable                  | Hazard ratio (95% confidence interval) | P      |
|---------------------------|---------------------------------------|--------|
| r-ATG Reference           |                                       |        |
| Alemtuzumab               | 1.154 (0.944-1.412)                   | 0.163  |
| IL-2RA                    | 1.183 (0.997-1.404)                   | 0.054  |
| Recipient age (y)         | 1.026 (1.019-1.034)                   | 0.000  |
| Recipient sex (male)      | 0.922 (0.816-1.042)                   | 0.193  |
| Recipient ethnicity       |                                       |        |
| Black                     | 0.770 (0.511-1.159)                   | 0.211  |
| White                     | 0.852 (0.725-1.001)                   | 0.051  |
| HLA-mismatch              | 1.001 (0.953-1.052)                   | 0.961  |
| Diabetes type II          | 0.954 (0.757-1.201)                   | 0.687  |
| PDRI (per 0.1 increment higher) | 1.032 (1.017-1.047) | 0.000  |
| Pretransplant dialysis (yes) | 1.591 (1.349-1.875) | 0.000  |
| Cold ischemia time (h)    | 0.994 (0.981-1.007)                   | 0.369  |
| Local organ               | 0.751 (0.631-0.893)                   | 0.001  |
| Transplant year*          | 0.998 (0.982-1.014)                   | 0.776  |
| PRA < 20                  | Reference                             |        |
| PRA > 20–80               | 1.008 (0.801-1.269)                   | 0.946  |
| PRA > 80                  | 1.621 (1.126-2.332)                   | 0.009  |
| Steroid maintenance       | 0.895 (0.76-1.054)                    | 0.185  |

*Transplant year was included as a continuous variable.

**TABLE 4.** Multivariable Cox proportional hazard model for pancreas-kidney composite graft survival

| Variable                  | Hazard ratio (95% confidence interval) | P      |
|---------------------------|---------------------------------------|--------|
| r-ATG Reference           |                                       |        |
| Alemtuzumab               | 1.220 (1.046-1.422)                   | 0.011  |
| IL-2RA                    | 0.969 (0.845-1.111)                   | 0.651  |
| Recipient age (y)         | 0.973 (0.966-0.979)                   | 0.000  |
| Recipient sex (male)      | 0.940 (0.847-1.044)                   | 0.248  |
| Recipient ethnicity       |                                       |        |
| Black                     | 0.708 (0.511-0.991)                   | 0.038  |
| White                     | 0.700 (0.618-0.794)                   | 0.000  |
| HLA-mismatch              | 1.029 (0.985-1.076)                   | 0.198  |
| Diabetes type II          | 1.178 (0.96-1.446)                    | 0.116  |
| PDRI (per 0.1 increment higher) | 1.036 (1.024-1.049) | 0.000  |
| Pretransplant dialysis (yes) | 1.308 (1.139-1.503) | 0.000  |
| Cold ischemia time (h)    | 0.989 (0.978-1)                      | 0.044  |
| Local organ               | 0.848 (0.729-0.986)                   | 0.033  |
| Transplant year*          | 0.972 (0.96-0.984)                    | 0.000  |
| PRA < 20                  | Reference                             |        |
| PRA > 20–80               | 1.131 (0.936-1.365)                   | 0.202  |
| PRA > 80                  | 1.422 (1.02-1.983)                    | 0.038  |
| Steroid maintenance       | 1.032 (0.907-1.174)                   | 0.632  |

*Transplant year was included as a continuous variable.

**IL-2RA,** interleukin-2 receptor antagonist; PDRI, Pancreas Donor Risk Index; PRA, panel reactive antibody; r-ATG, rabbit anti-thymocyte globulin.

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**FIGURE 4.** Death-censored pancreas-kidney graft survival by induction type. IL-2RA, interleukin-2 receptor antagonist.
smaller portion of SPK recipients (N = 38), or 17% of their studied population.

In an earlier report of SPK outcomes by induction, Zachariah et al22 compared 3 antibody induction regimens, alemtuzumab, IL-2RA, and other T-cell depletional agents (all preparations), to no induction and found no differences between the 3 antibody regimens compared with no induction in terms of overall patient or graft survival.22 We identified several limitations to their analysis that we addressed in our study. The authors included all available T-cell depletional regimens other than alemtuzumab, which likely diluted the effect of r-ATG. Moreover, recipients received different maintenance regimens. We suspect these confounders did not help isolate the association between induction and outcomes of interest.

More recently, a meta-analysis of randomized clinical trials compared alemtuzumab, IL-2 antagonist daclizumab (2 doses and 5 doses), and thymoglobulin to no induction, which reported better patient and graft survival in the 2-dose daclizumab group with lowest rejection rates in the alemtuzumab group. However, this study only reported short-term outcomes and suffered from the small number of analyzed trials with small overall patient numbers in each group.23 Moreover, the meta-analysis only looked at rejection in the first 3 mo, likely contributing to lower rejection rates in the alemtuzumab group.

Todeschini et al24 illustrated that patients who receive alemtuzumab induction exhibit higher rates of de novo donor specific antibody formation and late rejection in comparison to IL-2RA and thymoglobulin groups 3 mo post transplant as they differentially populate their B-cell repertoire.

Our results explain why r-ATG use is the most popular induction modality for SPK transplantation in the United States. Our findings are validated by many earlier reports with comparable IL-2RA and thymoglobulin induction outcomes in terms of patient and graft survival. Additionally, we complement these findings with long-term data spanning 10 y from transplantation. Although alemtuzumab showed promising short-term results in single-center studies, long-term follow-up showed increased composite SPK graft loss compared with r-ATG. Taken together with the lowest rejection rate associated with r-ATG among the 3 regimens, it gives credence to r-ATG as the first choice of induction in primary SPK recipients. Nonetheless, we acknowledge that the individual center’s selection of induction and maintenance other than the popular regimen may be based on the center’s best outcomes and unique center-specific experiences, which may not be reflected in our analysis.

Strengths and Limitations

Our study offers the most comprehensive long-term SPK outcomes by induction type in the United States with the most extended follow-up. The primary outcomes of this study were patient and death-censored allograft survival, which are tightly tracked in the SRTR. Additionally, all study participants uniformly received immunosuppression maintenance with tacrolimus and mycophenolate with or without steroids. These factors, coupled with a large sample size, allowed for robust multivariable analyses isolating the association between induction regimens and the outcomes of interest. However, our study should be interpreted in the context of several limitations. As with all registry studies, variation in center reporting patterns may have led to missing or incomplete data.

Additionally, despite adjusting for the transplant year and the variabilities within and between centers, we may not have fully accounted for residual confounders such as center-specific monitoring practices, ability to biopsy the pancreas allograft or rejection treatment strategies. Additionally, although the study included those with crossmatch negative results, the crossmatch technique evolved over the study period.

In the SRTR standard analysis file, rejection episodes are reported at time intervals without specific dates, hampering our ability to perform time-to-rejection analyses. The lack of measured drug levels did not allow us to analyze or account for exposure levels of maintenance immunosuppression. Complications related to a specific induction type are not well-tracked, limiting our ability to analyze the cost implications of a particular induction type. Finally, the return to insulin data is not well tracked in the SRTR data and was not examined.

CONCLUSIONS

In primary SPK transplant recipients with negative crossmatch and on tacrolimus, mycophenolate with or without steroid maintenance, r-ATG use was associated with the lowest kidney and pancreas rejection rates. Compared with r-ATG, alemtuzumab but not IL-2RA was associated with worse long-term death-censored composite SPK graft survival. Our analysis supports the common use of r-ATG induction in US primary SPK recipients.

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