**Supplementary Material**

**Supplementary Methods**

***Study medication***

Kidney transplant recipients were assigned according to a 1:1:1 central randomization procedure. They received either standard immunosuppression comprising basiliximab (Simulect®, Novartis, 20 mg intravenously on day zero before allograft reperfusion and day four), prolonged release tacrolimus administered once daily (Advagraf®, Astellas Pharma GmbH), mycophenolate mofetil (MMF) (CellCept®, Roche Pharma AG,), and prednisolone (group A) or RSWD within the first week after transplantation with identical immunosuppressive medication as in the standard group (group B). In the RSWD group C, basiliximab induction was replaced by rabbit ATG (Thymoglobulin®, Sanofi).

***Inclusion and exclusion criteria***

In the original Harmony trial, adult kidney transplant recipients (18 to 75 years) with low immunological risk were scheduled to receive a single-organ renal transplant from either a living donor or a deceased donor. In the follow-up trial, all patients alive after Harmony trial and recruited by centers participating in the follow-up investigation were eligible. Patients receiving a second renal transplant were eligible, if the first allograft was not lost due to acute rejection within the first year after transplantation. Donor and recipient had to be AB0-compatible and the direct cross-match had to be negative (complement-dependent cytotoxicity crossmatch, CDC-test). Grafts with pre-transplant-existing donor-specific HLA antibodies were not eligible and the recipients exhibited a current PRA level ≤ 30%. Pregnant women and nursing mothers were excluded. Further exclusion criteria were receipt of a multi-organ transplantation, pediatric en-bloc kidney transplantation, HLA-identical or non-heart-beating donors, past history of cancer within the last five years except for non-melanoma skin cancer.

In the follow-up trial, all patients alive after the original Harmony trial and recruited by centers participating in the follow-up investigation were eligible.

***Study endpoints***

Most of the endpoints of the original Harmony trial were investigated at the three and five-year visits of the Harmony FU study. Hereby, investigators were asked for results of relevant parameters or *de novo* incidences of events either between the end of the core Harmony trial at one year up to the three-year visit or during the time from the three-year visit up to the five-year FU visit. Patients were followed up until death, graft loss or until year five after transplantation.

The primary endpoint of the original Harmony trial was the incidence of biopsy-proven acute rejections (BPAR) in-/excluding borderline changes within the first year after renal transplantation. During FU period, only episodes of acute rejection confirmed by biopsy, with histologic characteristics described according to the Banff criteria of 2015, were counted.8-12 Protocol biopsies were not performed during the FU period.

Secondary end points were: patient and graft survival, incidence of PTDM, bacterial and opportunistic infections including CMV (PCR > 400 copies/µl) or BKV (PCR > 8,000 copies/µl) infections, malignancies, ESA-treated anemia, cardiovascular diseases, or bone fractures; assessment of graft function with calculated GFR by the Cockcroft Gault formula9 or CKD-EPI equation10,percentage of steroid-free maintenance medication, systolic and diastolic blood pressure, lipids (HDL, LDL, triglycerides), or body weight. For incidence of PTDM (according to the ADA recommendations) during FU period, fasting glucose levels, HbA1c levels, oral glucose tolerance tests, as well as center diagnosis were considered11.

***Role of the funding source***

The FU trial was designed and run by the first and last author who received financial support from Astellas Pharma GmbH and Sanofi (Investigator-Initiated Trial: NCT 00724022, follow-up study DRKS00005786). Neither of the funders had any role in data collection, data analysis, data interpretation, or writing of the manuscript. An independent contract research organization (Coordination Center for Clinical Studies of the Technical University of Dresden, Dresden, Germany) was responsible for data collection, monitoring and statistical analyses. All authors had full access to all the data in the study and accept responsibility to submit for publication.

**Supplementary Results**

***FU-study characteristics***

Recipient gender consisted of 66% males and 34% females, mean age was 54.6 ± 11.7 years. For the Harmony follow-up population, pre-transplant panel-reactive antibody levels of 0% were detected in 88% of the transplant recipients indicating an immunologically low-risk population. Only 4 % of FU patients received their second renal transplant and mean HLA-antigen matching for A, B, DR in all study arms was one or lower. The donor pool consisted of 89% deceased donors and only 11% living donors; 41% of the donor allografts were transplanted with expanded criteria12, with a mean donor age of 53.1± 15.5 years. Diabetes mellitus as a complicating risk factor at the time of transplantation existed in 15% of original as well as FU patients. CMV high-risk serologic status was noted in 25% of the original and 26% of the FU patient set.

***Metabolic profiles***

At the year three visit, mean systolic and diastolic arterial blood pressure was 134.6 ± 16.2 and 78.3 ± 10.4 mmHg, respectively. Five years after transplantation, mean systolic and diastolic arterial blood pressure was 137.1 ± 18.8 and 80.4 ± 10.1 mmHg, respectively. 55.8% of transplant recipients had the diagnosis of arterial hypertension and almost all (> 96%) received treatment with at mean 2.7 antihypertensive agents.

At both three and five-year visits, total cholesterol levels were at mean around 5.0 mmol/l, LDL levels around 3.0 mmol/l, and triglycerides around 2.1 mmol/l. The mean weight was at baseline 78.6 ± 15.0 kg in the FU patients, at the three-year visit 80.1 ± 16.6 kg, and at the five-year visit at 81.3 ± 17.1 kg. The mean weight gain was also similar in all three groups (Table 3). The mean BMI values changed from 26.4 ± 4.5 at baseline to 26.7 ± 5.0 or 27.0 ± 5.2 at year three or five, respectively. The BMI gain during FU was not different in all groups (Table 3).

**Supplementary Figure**

***Figure S1: Flow chart***

Flow chart of the Harmony post-trial follow-up study participants.

**Supplementary Tables**

***Table S1: Causes of death in the Harmony and Harmony FU study***

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Cause of death** | **Category** | **Arm A:**  **Basiliximab/ steroids** | **Arm B:**  **Basiliximab/RSWD** | **Arm C:**  **rATG/ RSWD** | **Total-Harmony** |
| Cardiovascular | N | 6 | 2 | 3 | 11 |
| Infections | N | 2 | 0 | 3 | 5 |
| Cancer | N | 2 | 0 | 0 | 2 |
| Other | N | 15 | 11 | 8 | 34 |
| ‍ |  |  |  |  |  |
| Sum | N | 25 | 13 | 14 |  |

Table S1 depicts the causes of death of deceased patients during Harmony and Harmony FU. "Other" includes censored cases that occurred between the end of the Harmony study and the start of the Harmony Follow Up study, along with various other causes such as pulmonary embolism, bleeding, accidents and more. All deaths in the centres participating in the Harmony FU study were recorded without exception.

***Table S2: Causes of graft loss in the Harmony and Harmony FU study***

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Cause of graft loss** | **Category** | **Arm A:**  **Basiliximab/Steroids** | **Arm B:**  **Basiliximab/RSWD** | **Arm C:**  **rATG/ RSWD** | **Total-Harmony** |
| Recurrence of underlying disease | N | 2 | 1 | 2 | 5 |
| Primary non-function | N | 3 | 2 | 1 | 6 |
| Acute graft rejection | N | 0 | 2 | 2 | 4 |
| Chronic graft rejection | N | 0 | 3 | 1 | 4 |
| Other | N | 4 | 1 | 7 | 12 |
| ‍ |  |  |  |  |  |
| Sum | N | 9 | 9 | 13 |  |

Table S2 depicts the causes for graft loss during Harmony and Harmony FU. "Other" includes censored cases that occurred between the end of the Harmony study and the start of the Harmony Follow Up study, as well as various other causes such as BK virus nephropathy, graft artery thrombosis, surgical complications and more. All graft losses of the centres participating in the Harmony FU study were recorded without exception.

***Table S3: Comparison of overall survival in study arm A: Basiliximab/Steroids, Arm B: Basiliximab/RSWD and Arm C: rATG/RSWD as a function of risk factors***

**Table S3A: Comparison of overall survival in study arms A, B and C as a function of cardio- or cerebrovascular events during the Harmony FU**

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **‍**  **‍**  **‍** | | **Planned Treatment Arm** | | | | | | | | |  | | |
| **Any cardio- or cerebrovascular disease reported during Harmony FU** | | | | | | | | | | | |
| **Arm A:**  **Basiliximab/ Steroids** | | | **Arm B:**  **Basiliximab/RSWD** | | | **Arm C:**  **rATG/ RSWD** | | | **All** | | |
| **.** | **No** | **Yes** | **.** | **No** | **Yes** | **.** | **No** | **Yes** | **.** | **No** | **Yes** |
| Overall survival |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Event | N | 22 | 1 | 2 | 13 | . | . | 13 | 1 | . | 48 | 2 | 2 |
| ColPctN | 22.68 % | 1.02 % | 18.18 % | 14.13 % | . | . | 13.54 % | 1.12 % | . | 16.84 % | 0.74 % | 6.25 % |
| Censored | N | 75 | 97 | 9 | 79 | 83 | 14 | 83 | 88 | 7 | 237 | 268 | 30 |
| ColPctN | 77.32 % | 98.98 % | 81.82 % | 85.87 % | 100.00 % | 100.00 % | 86.46 % | 98.88 % | 100.00 % | 83.16 % | 99.26 % | 93.75 % |
| All | N | 97 | 98 | 11 | 92 | 83 | 14 | 96 | 89 | 7 | 285 | 270 | 32 |
| ColPctN | 100.00 % | 100.00 % | 100.00 % | 100.00 % | 100.00 % | 100.00 % | 100.00 % | 100.00 % | 100.00 % | 100.00 % | 100.00 % | 100.00 % |

**Table S3B: Comparison of overall survival in study arms A, B and C as a function of new onset post-transplant diabetes mellitus (PTDM) in the Harmony FU cohort**

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **‍**  **‍**  **‍** | | **Planned Treatment Arm** | | | | | | | | |  | | |
| **Any diabetes criteria reported during Harmony FU** | | | | | | | | | | | |
| **Arm A:**  **Basiliximab/ Steroids** | | | **Arm B:**  **Basiliximab/RSWD** | | | **Arm C:**  **rATG/ RSWD** | | | **All** | | |
| **.** | **No** | **Yes** | **.** | **No** | **Yes** | **.** | **No** | **Yes** | **.** | **No** | **Yes** |
| Overall survival |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Event | N | . | 2 | . | . | 1 | . | . | . | . | . | 3 | . |
| ColPctN | . | 3.77 % | . | . | 1.45 % | . | . | . | . | . | 1.62 % | . |
| Censored | N | 1 | 51 | 5 | . | 68 | 7 | 1 | 63 | 4 | 2 | 182 | 16 |
| ColPctN | 100.00 % | 96.23 % | 100.00 % | . | 98.55 % | 100.00 % | 100.00 % | 100.00 % | 100.00 % | 100.00 % | 98.38 % | 100.00 % |
| All | N | 1 | 53 | 5 | . | 69 | 7 | 1 | 63 | 4 | 2 | 185 | 16 |
| ColPctN | 100.00 % | 100.00 % | 100.00 % | . | 100.00 % | 100.00 % | 100.00 % | 100.00 % | 100.00 % | 100.00 % | 100.00 % | 100.00 % |

Included in the analysis were all participants with informed consent for the Harmony FU study without evidence of Diabetes mellitus at Harmony study inclusion nor evidence of post-transplant diabetes mellitus (PTDM) during first year of the study.

**Table S3C: Comparison of overall survival in study arms A, B and C as a function of new onset post-transplant diabetes mellitus (PTDM) in the first year of the Harmony FU study**

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **‍**  **‍**  **‍** | | **Planned Treatment Arm** | | | | | | | | |  | | |
| **Post-transplant diabetes mellitus in the Harmony study during the first year**  **(ADCE or SDTM.LB)** | | | | | | | | | | | |
| **Arm A:**  **Basiliximab/ Steroids** | | | **Arm B:**  **Basiliximab/RSWD** | | | **Arm C:**  **rATG/ RSWD** | | | **All** | | |
| **.** | **No** | **Yes** | **.** | **No** | **Yes** | **.** | **No** | **Yes** | **.** | **No** | **Yes** |
| Overall survival |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Event | N |  | 11 | 6 |  | 5 | 3 |  | 5 | . |  | 21 | 9 |
| ColPctN |  | 10.58 % | 8.96 % |  | 4.03 % | 7.69 % |  | 3.97 % |  |  | 5.93 % | 6.29 % |
| Censored | N |  | 93 | 61 |  | 119 | 36 |  | 121 | 37 |  | 333 | 134 |
| ColPctN |  | 89.42 % | 91.04 % |  | 95.97 % | 92.31 % |  | 96.03 % | 100.00 % |  | 94.07 % | 93.71 % |
| All | N |  | 104 | 67 |  | 124 | 39 |  | 126 | 37 |  | 354 | 143 |
| ColPctN |  | 100.00 % | 100.00 % |  | 100.00 % | 100.00 % |  | 100.00 % | 100.00 % |  | 100.00 % | 100.00 % |

Included in the analysis were all participants without evidence of Diabetes mellitus at Harmony study inclusion