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ORIGINAL ARTICLE

Scandiatransplant acceptable mismatch program—10 years with an effective strategy for transplanting highly sensitized patients

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In March 2009, the Scandiatransplant acceptable mismatch program (STAMP) was introduced as a strategy toward improving kidney allocation to highly sensitized patients. Patients with a transplantability score ≤ 2% are potential candidates for the program. Samples are analyzed and acceptable antigens (HLA-A, B, C, DRB1, DRB3/4/5, DQB1, DQA1, DPB1, DPA1) are defined by the local tissue typing laboratory and finally evaluated by a steering committee. In the matching algorithm, patients have the highest priority when the donor's antigens are all among the recipient's own or acceptable HLA antigens. In the period from 2009 to 2020, we have transplanted 278 highly sensitized kidney patients through the program. The graft survival of the STAMP patients was compared with 9002 deceased donor kidney-transplanted patients, transplanted in the same time period. The 10-year graft survival was 73.4% (95% CI: 60.3–90.0) for STAMP and 82.9% (95% CI: 81.6–84.3) for the reference group. ($p = .2$). In conclusion, the 10-year allograft survival demonstrates that the STAMP allocation algorithm is

Abbreviations: AM, acceptable mismatch; anti-HLA, antibodies against human leukocyte antigen; BMI, body mass index; CDC, complement-dependent cytotoxicity; CI, confidence interval; cPRA, calculated combined panel reactive antibodies; HLA, human leukocyte antigen; MFI, mean fluorescence intensity; PRA, panel reactive antibodies; QC, quality control; STAMP, Scandiatransplant acceptable mismatch program; TS, transplantability score.

immunological safe. The program is continuously monitored and evaluated, and the introduction of matching for all HLA loci is a huge improvement to the program and demonstrate technical adaptability as well as clinical flexibility in a de-centralized organization.

KEYWORDS
alloantibody, clinical research/practice, graft survival, health services and outcomes research, histocompatibility, kidney (allograft) function/dysfunction, kidney transplantation/nephrology, organ allocation, organ procurement and allocation, panel reactive antibody (PRA)

1 | INTRODUCTION

Scandiatransplant is the Nordic organ allocation organization including Denmark, Estonia, Finland, Iceland, Norway, and Sweden covering a population of 28.9 million inhabitants. 554 used deceased donors were realized in 2020, which resulted in 972 deceased donor kidney transplantations performed in the 11 kidney transplant centers. Within the participating transplant centers in Scandiatransplant common agreed obligations for kidney exchange between centers are incorporated in daily practise (Table 1). In total, 19% of the transplanted kidneys were exchanged between centers as a result of the pre-defined kidney exchange obligation criteria, including mandatory payback.

Broadly anti-HLA-sensitized patients on the waiting list have a lower chance of getting an organ offer. As of July 2021, 1580 patients were active on the kidney waiting list in Scandiatransplant. Of these patients, 12% had calculated combined Panel Reactive Antibodies (cPRA) in the latest serum sample above 80% and a median waiting time of 736 days, whereas non-sensitized patients on the waiting list (74%) had a median waiting time of 369 days.

In March 2009, Scandiatransplant acceptable mismatch program (STAMP) was introduced in Scandiatransplant as a dedicated strategy toward improving kidney allocation to highly sensitized patients. Under this initiative, kidneys are allocated on the basis of antigen-level match and acceptable HLA antigen-mismatch with the patient. Acceptable HLA antigens are defined by the local tissue typing laboratory and finally evaluated for eligibility to the program by the STAMP steering committee. After entry to the program, the patients are given the highest priority in the matching algorithm (Priority 1 in Table 1). Technical and clinical developments since 2009 have permitted a number of adjustments and improvements to the program. This progress has been necessary to ensure that only patients with a low transplantability are included and that the majority of these are successfully transplanted through the program. The development in the STAMP since 2009 is shown as a timeline in the bottom of Figure 1. The changes made to the program in 2009–2015 have been published earlier.[1] In our previous paper, we retrospectively examined if a calculated transplantability score (TS) could be an improvement to the program, as it is based on both ABO and HLA frequency in a common donor pool. These speculations contributed to the implementation of TS as acceptance criteria by September 2017 with the intention that only patients with the lowest a priori chance of getting a transplant were included in the program.

In this highly selected group of patients, we changed allocation from ABO identical to ABO compatible by December 2018, thereby increasing the chance of finding a compatible kidney allograft for blood groups A, B, and AB patients.

TABLE 1 Rules for exchange of kidneys from deceased donor within the Scandiatransplant cooperation

1.	Patient with STAMP-status that are ABO compatible with donor and where all donor HLA-A, -B, -C -DRB1, -DRB3/4/5, -DQA1, -DQB1, -DPA1, -DPB1 antigens are either shared with the recipient or are among those defined as acceptable.
2.	Highly immunized (PRA ≥ 80%) patients who are HLA-A, HLA-B, HLA-DRB1 compatible with donor.
3.	Immunized patients (PRA ≥ 10% but below 80%) who are HLA-A, -B, -DRB1 compatible with donor.
4.	If organ donor is <50 years of age, at least one kidney is offered to recipient <16 years of age (counted from time of registration), if there is HLA-DRB1 compatibility and in addition not more than two HLA-A, B mismatches.
5.	Patients who are HLA-A, HLA-B, HLA-DRB1 compatible with donor unless the proposed recipient is >30 years older than the donor.

Note: The five kidney exchange obligation rules that are currently operational within Scandiatransplant in order of priority (rules effective from November 2020). Recipients with STAMP status have the highest priority.

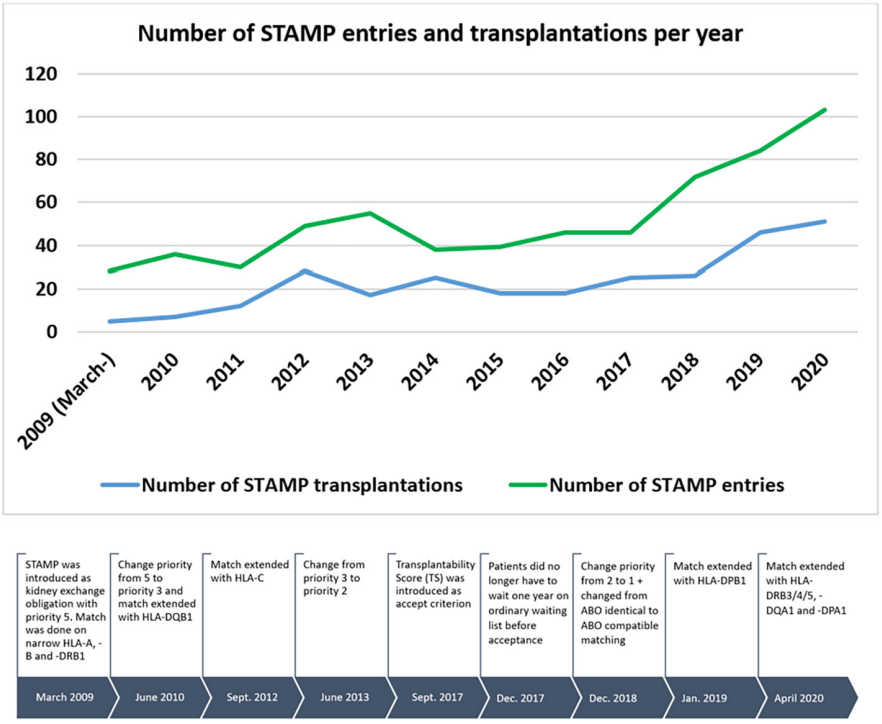

FIGURE 1 Number of STAMP entries and transplantations per year. At the top a graphical illustration of the development in numbers of entries and transplanted recipients through the STAMP in the years 2009 to 2020. The timeline at the bottom presents all the changes and developments one by one in the STAMP since the introduction in 2009.

Despite these changes, we still identified a group of broadly sensitized patients non-eligible to STAMP because of antibodies toward HLA-DPB1, -DQA1, -DPA1, and -DRB3/4/5. A main obstacle in matching on more alleles were to secure that all 10 HLA laboratories performed on-call deceased donor HLA typings for all loci, and this was accomplished by the end of 2018.The most recent changes in the program were initiated in January 2019 when matching for HLA-DPB1 was made possible. Since April 2020 STAMP patients are compared with all deceased donors in Scandiatransplant for all classical HLA loci, providing the optimal possibility to get a transplant for these immunologically challenged patients.

Other organ sharing organizations have functioning programs for transplanting highly sensitized patients. In 2014, UNOS introduced a new kidney allocation system[2] in which highly sensitized patients are prioritized through a complex point system. Waiting time, recipient age, HLA-A, -B, -DR mismatches, cPRA, and proximity to donor hospital are all included in the final score. In 2020, Jackson et al. published the 3-year posttransplant outcome for patients with cPRA-100% and showed an improved outcome after the introduction of their new allocation system, with a 3-year death censored graft failure of 6.3%.[3]

The acceptable mismatch (AM) program in Eurotransplant was initiated more than 30 years ago and more than 1700 highly sensitized patients have been transplanted. Patients eligible to the AM program must have been on dialysis for at least 2 years, PRA ≥ 85% and HLA antibodies detected in solid-phase assays only must be explained by previous immunization. Potential recipients will be selected on the basis of their own HLA-A, HLA-B, and HLA-DR antigens in combination with the HLA-A, HLA-B, and HLA-DR acceptable antigens. HLA-C and -DQ antibody specificities reported as unacceptable antigens are taken into consideration by the immunologist at the centralized laboratory.[4,5] In their most recent publication, they report death censored 15-year allograft survival of approximately 60%, which is similar to the allograft survival of non-sensitized patients transplanted through regular allocation. This was significantly better than that of highly sensitized patients transplanted outside the AM program.

In this paper, we discuss our experience with introducing TS as the single acceptance criterion for the AM program. Furthermore that Scandiatransplant, to our best knowledge, is the first organ exchange organization to implement allocation based on matching for all HLA loci in an AM program.

2 | MATERIALS AND METHODS

In Scandiatransplant, all information regarding donors, recipients, and transplantations are registered in the Scandiatransplant web application. Data entry is done locally at each of the 10 tissue typing laboratories and 11 transplant centers, which are all members of the Scandiatransplant association. The quality of the selected data entered is checked by both the local departments and the Scandiatransplant office.

Concerning allograft survival, patients transplanted through STAMP in the time period 2009–2020 are compared with all other deceased donor kidney transplantations performed within Scandiatransplant in the same time period.

All other comparisons are done between groups of patients transplanted through STAMP in different time periods.

2.1 | HLA typing

For patients to be eligible to STAMP, HLA genotyping is recommended on the following loci: HLA-A, HLA-B, HLA-C, HLA-DRB1, HLA-DRB3/4/5, HLA-DQB1, HLA-DQA1, HLA-DPA1, HLA-DPB1. Genomic HLA typing is performed at all the local tissue typing laboratories.

One laboratory does not routinely perform 11 loci HLA typing on the patients in STAMP but comply with the STAMP guidelines by defining acceptable antigens on all 11 loci.

2.2 | HLA antibody identification

In all laboratories in Scandiatransplant, the identification of anti-HLA specificities is primarily assessed by analyzing sera with Labscreen® Single Antigen (One Lambda, Inc.). The test is performed according to the manufacturer's instruction. The STAMP guidelines recommend the inclusion of HLA antibody specificities with reactivity above 1000 MFI as unacceptable. The majority of the laboratories are using the possibility of automatic transferral of HLA antibody specificities and MFI values from the analysis software program to the Scandiatransplant web application, reducing registration errors and most importantly in context of the STAMP increasing the transparency and objectivity.

2.3 | Recipient acceptable HLA-antigens

Acceptable HLA-mismatches are defined by the tissue typing laboratory at the recipient center and may be on HLA-A, HLA-B, HLA-C, HLA-DRB1, HLA-DRB3/4/5, HLA-DQA1, HLA-DQB1, HLA-DPA1, and HLA-DPB1 loci. AMs for all loci except HLA-DPB1 are on antigen split level. For HLA-DPB1 AMs are defined on second field resolution and only among those represented on the solid-phase assay beads. Acceptable antigens are defined by the lack of antibody reactivity. It is possible to define repeated mismatches as acceptable antigens. Whether repeated mismatches are accepted relies on each transplant center.

In the data entry process, the Scandiatransplant web application can automatically provide suggestions for AMs. Furthermore, the program has several quality control functionalities, which help the users in the registration and evaluation process.

2.4 | Current acceptance criteria to STAMP

Current acceptance criteria to STAMP were the following: (i) TS ≤ 2% (ABO identical) and (ii) the last serum sample drawn and analyzed for HLA antibodies less than 3 months before acceptance.

2.5 | Transplantability score

A donor pool based on 2000 most recently antigen-level HLA typed (HLA-A, HLA-B, HLA-C, HLA-DRB1, HLA-DRB3/4/5, HLA-DQA1, HLA-DQB1, HLA-DPA1, HLA-DPB1) deceased donors registered in the Scandiatransplant web application forms the basis of the calculation of the TS.

TS is based on the percentage of donors that are ABO identical or compatible and have HLA antigens on split level that are a match to the recipient.

2.6 | Allocation on STAMP

Recipients own HLA antigens and the defined AMs are given equal priority in the matching algorithm. Recipients in the program must be screened for HLA antibodies at least every 3 months, and HLA antibody specificities must be re-evaluated at least once a year. Once accepted on STAMP, patients will stay included even if the level of HLA sensitization decreases. For each donor search with the matching algorithm, a specific search among STAMP recipients is performed. Exchange obligation to a STAMP patient is marked as priority 1 when the donor's HLA-A, HLA-B, HLA-C, HLA-DRB1, HLA-DRB3/4/5, HLA-DQA1, HLA-DQB1, HLA-DPA1, and HLA-DPB1 antigens are all among the recipient's own or acceptable HLA antigens. If an exchange obligation is identified, the kidney is offered to the recipient center and, if accepted, transported together with donor blood samples. Prospective crossmatch is mandatory to perform at the recipient transplant center. In Scandiatransplant, there is a mandatory payback requirement with the first available, comparable kidney.

No HLAi transplantations were performed in STAMP and, therefore, no HLAi transplantations are included in this data set.

2.7 | Statistics

Kaplan–Meier graft survival analysis (censored for death) was done by using the statistical tool R version 1.4.

The data on waiting time according to ABO blood group were not normally distributed according to Shapiro–Wilk and F-tests, so Mann–Whitney U-test was conducted to compare means of two independent samples, also in R version 1.4. Data entry in the Scandiatransplant database is dynamic, so data are subject to changes based on prospective data submissions and/or corrections.

Once a year, patient and graft survival data from all national kidney registries are imported into the Scandiatransplant database.

Data on rejection events have been collected manually by each transplant center, as it is not part of the common Scandiatransplant registry. This is also the reason why rejection data have not been obtained on the large control group and comparison of rejection frequency between the two groups is not possible. All other data used

in this paper have been extracted from the Scandiatransplant web application.

2.8 | IRB statement

According to the Consolidation Act on Research Ethics Review of Health Research Projects, Consolidation Act number 1338 of 1 September 2020 section 14 only health research studies has to be notified to the Committees. The Committees (The Central Denmark Region Committees on Health Research Etics) do not consider this study to be a health research study (Section 2).

3 | RESULTS

A total of 278 patients were transplanted through the STAMP in the period from March 9, 2009 to December 31, 2020.

The graft survival of the 278 patients transplanted through STAMP was compared with 9002 deceased donor kidney-transplanted patients (reference group), transplanted in the same time period. (Figure 2). The 10-year allograft survival was 73.4% (95% CI: 60.3–90.0) for STAMP and 82.9% (95% CI: 81.6–84.3) for the reference group ($p = .2$).

Focusing on 5-year allograft survival, thus increasing the number of patients in the analysis, also no significant difference in allograft survival was found between the STAMP group 91.5% (95% CI: 87.8–95.4) and the reference group 91.4% (95% CI: 90.7–92.1).

Demographics of the two groups (Table 2) illustrates that 62% of the STAMP patients were kidney re-transplantations, compared with 14% in the reference group. The data also disclose that the transplanted STAMP recipients are more HLA sensitized and have a longer waiting time. Table 2 shows the HLA mismatch for HLA-A, B, DRB1 for both STAMP patients and the reference patients, and it is obvious that the patients transplanted in STAMP are not allocated to minimize HLA mismatch, but instead allocated on pre-defined acceptable antigens.

Five-year allograft survival relative to the degree of HLA match is shown in Figure 5. No impact of HLA match was found in the STAMP group.

In Table 3, we have documented all cases of acute rejections according to the consensus rules of the international Banff classification criteria.[6] The overall rejection rate the first year posttransplant among the STAMP patients were found to be 13.5% (Table 3). The majority of the patients experienced no rejection the first year (86%), and among the remaining patients, 11% had one rejection, 1.9% had two rejections and only one patient experienced three rejection episodes the first year. Humoral rejections were detected in 6/42 rejection episodes.

The top of Figure 1 illustrates graphically the total number per year of patients entering the STAMP waiting list and the realized transplantations through the program. In general, there is a tendency toward an increased activity in the program over the years. It is worth noticing the significant increase in the number of new entries to the program between 2017 and 2018 when the acceptance criterium was changed from PRA to TS. Along with this the requirement of 1 year on the waiting list before acceptance was abolished. The mean number of entries in the period from 2009 to 2017 were 40.8 per year, and in the year following the change to TS, 72 patients were accepted on the program. As expected, the increased number of difficult-to-transplant patients did not initially lead to more transplantations in the program. As the program has evolved through a number of adjustments, especially in the first years, we have investigated the dynamics on the waiting list and

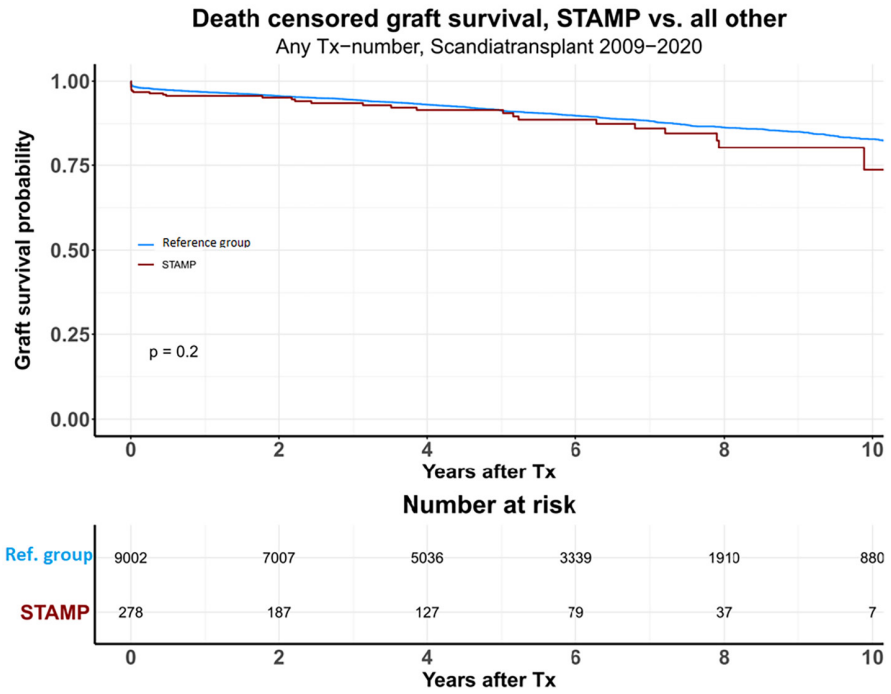

FIGURE 2 Death censored graft survival. Graft survival of the 278 patients transplanted through STAMP compared with 9002 deceased donor kidney-transplanted patients, transplanted on the general waiting list. The 10-year allograft survival is 73.4% (95% CI: 60.3–90.0) for STAMP and 82.9% (95% CI: 81.6–84.3) for the other kidney transplanted patients.

TABLE 2 Demographics

Demographics	STAMP	Reference group
Recipient	*N* = 278	*N* = 9002
Median age at transplantation (years)	50	56
ABO blood group (%)		
A	39	45
B	20	13
AB	4	7
O	36	35
Transplant number (%)		
1	38	86
2	45	12
3	12	2
4	5	<1
5	<1	<1
Combined cPRA (%)*		
80–100	98	10
60–79	2	5
40–59	0	5
20–39	0	6
0–19	0	73
Gender (%)		
Female	60	35
Male	40	65
Median age at donation (years)	56	57
Donor		
Median age at donation (years)	56	57
ABO blood group (%)		
A	34	46
B	13	12
AB	<1	5
O	51	37
Median BMI	26	25
Median latest creatinine (μmol/L)	66	67
Gender (%)		
Female	41	45
Male	59	55
HLA mismatches (%)		
0 HLA-A mismatches	36	23
1–2 HLA-A mismatches	64	77
0 HLA-B mismatches	23	12
1–2 HLA-B mismatches	77	88
0 HLA-DRB1 mismatches	29	25
1–2 HLA-DRB1 mismatches	71	75

Note: Demographics on the 278 patients transplanted through STAMP and the reference group of 9002 deceased donor kidney-transplanted patients transplanted in the same time period from 2009 to 2020.

[a]Information for cPRA is missing on many of the recipients in the reference group; estimate is done based on latest PRA entry before transplantation.

TABLE 3 Rejections in the STAMP group and reference group

Rejection events within year 1 after transplantation	STAMP *N* = 259[a]
Rejection event(s) (%)	
Yes	13.9%
No	86.1%
Median rejection days after transplantation	14
Number of rejections	
0	224
1	29
2	5
3	1
Type of rejection, all rejections within year 1 (number)	42
Humoral	6
Cellular	32
Both	4
Banff grade, all rejections within year 1 (number)	
Antibody-mediated rejection	7
Borderline	12
T cell–mediated	20
Unknown	3

Note: All recorded cases of acute rejections according to the consensus rules of the international Banff classification criteria.[6] The overall rejection rate the first year posttransplant among the STAMP patients were found to be 13.5%.

[a]On 19 recipients, rejection data were not available.

transplantations in a 3-year period before and after the change as illustrated in Figure 3. This confirms the significant increase in numbers of entries and transplantations. In the same time period, we did not see an increase in the number of entries to the general kidney waiting list (data not shown). Additionally, examining a 3-year period after the change, we find that the increased activity in the program appears to be persistent.

Following the change in allocation regarding the blood groups in 2018, where ABO identity was exchanged for ABO compatibility, a steep increase in the number of realized transplantations were seen (Figure 1). In the period of 2009–2018, the average number of STAMP transplantations per year was 18. In 2019, 46 patients were transplanted through STAMP.

Table 4A shows the allocation of the blood group identical deceased donor kidneys, which was standard procedure from March 2009 to December 2018. In total, 175 kidneys were allocated for ABO identical recipients in the program. The only exception to ABO identity was the allocation of five blood group A kidneys to AB group recipients.

One of the main concerns when allowing also ABO-compatible transplants is the risk of favoring the non-O blood groups, which could potentially affect the waiting time for blood group O patients both on STAMP and the ordinary waiting list.

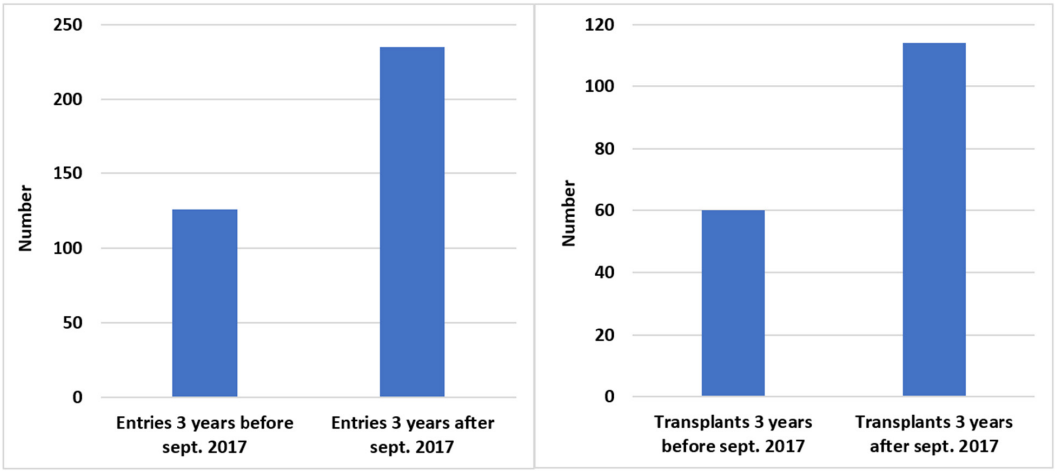

FIGURE 3 Entries and transplantations in STAMP before and after introduction of transplantability score. Number of recipients entering and transplanted through STAMP in a 3-year period before and after introducing the transplantability score as accept criteria.

TABLE 4 Allocation of kidneys before and after introduction of ABO compatibility

(A) Before introducing ABO compatibility matching in STAMP 175 recipients were transplanted with an ABO identical kidney				
Recipient→				
↓Donor	**0**	**A**	**AB**	**B**
0	75			
A		75	5	
AB			2	
B				23
(B) After introducing ABO compatibility matching, 98 recipients were transplanted and 42% of these were transplanted with an ABO-compatible kidney				
Recipient→				
↓Donor	**0**	**A**	**AB**	**B**
0	26	16	2	22
A		18	2	
AB			0	
B			1	11

Therefore, a retrospective simulation was conducted for 180 blood group O deceased donors in the Scandiatransplant database prior to implementation of the ABO change. The simulation resulted in an expected rate of allocation to recipients of other blood groups to be less than 8% (data not shown).

Figure 3B displays the 98 kidneys allocated to STAMP recipients after December 2018 to December 2020. During this 2-year period, 66 blood group O kidneys were allocated, of which 26 (39%) were transplanted to blood group O recipients and the remaining 40 kidneys (61%) were transplanted to recipients with other blood groups (16 to blood group A, 2 to blood group AB, 22 to blood group B). In the same 2-year period, 436 blood group O donors were realized, and in agreement with the retrospective simulation, 40 kidneys were transplanted to ABO-compatible recipients (40/436 = 9%).

We found that in 6 of the 40 cases (15%) when a blood group O kidney was transplanted to a blood group compatible STAMP patient, a blood group identical STAMP candidate was also eligible.

Figure 4 displays the overall median waiting time on the ordinary waiting list until transplantation before and after the change of ABO identical to compatible allocation in STAMP. It illustrates an increase in the waiting time for patients of all blood groups, while statistically insignificant for A ($p = .38$), AB ($p = .25$), longer and still insignificant for blood group B ($p = .09$). We find a significant increase ($p < .01$) in waiting time for blood group O recipients.

ABO-compatible allocation of kidneys on the ordinary waiting list has not increased after the introduction of ABO-compatible allocation in the STAMP program. This is illustrated in Table 5. The current STAMP inclusion criteria includes TS calculated as ABO identical, reflecting the chance of getting transplanted on the general waiting list. For blood groups AB, B, and A, the ABO identical TS is an underestimation of their transplantability in the ABO compatible STAMP. This is illustrated in Figure 6, in which we see a significant difference between TS ABO-compatible and TS ABO identical scores for a group of patients.

4 | DISCUSSION

Transplanting the broadly sensitized kidney patients on the waiting list is the principal purpose of STAMP. In this paper, we have shown that over the years the number of transplantations in this immunologically challenging group of patients has increased. Another main purpose of STAMP is to ensure that the allograft survival is comparable with that in non-sensitized patients. In an earlier publication,[1] we found that the 5-year graft survival in STAMP recipients was comparable with a group of sensitized patients transplanted with a

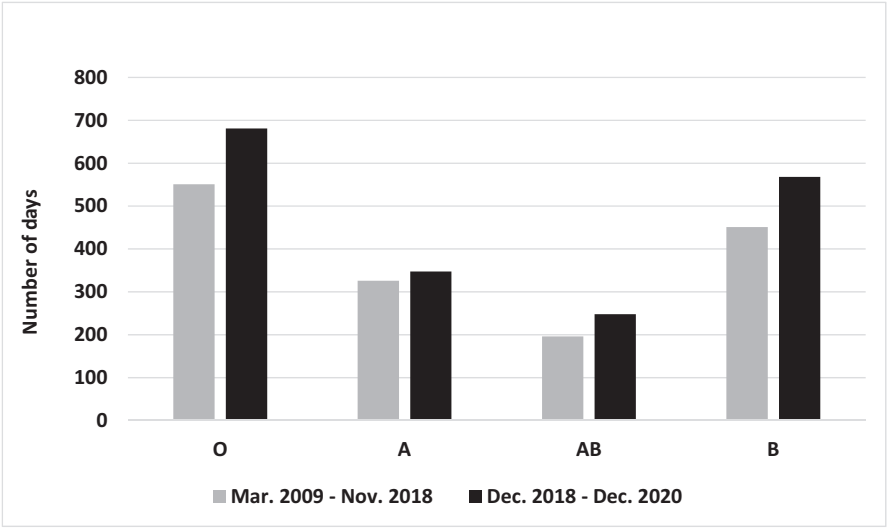

FIGURE 4 Waiting time on the general waiting list. Median waiting time in days on the general kidney waiting list before and after introducing ABO compatibility matching in the STAMP.

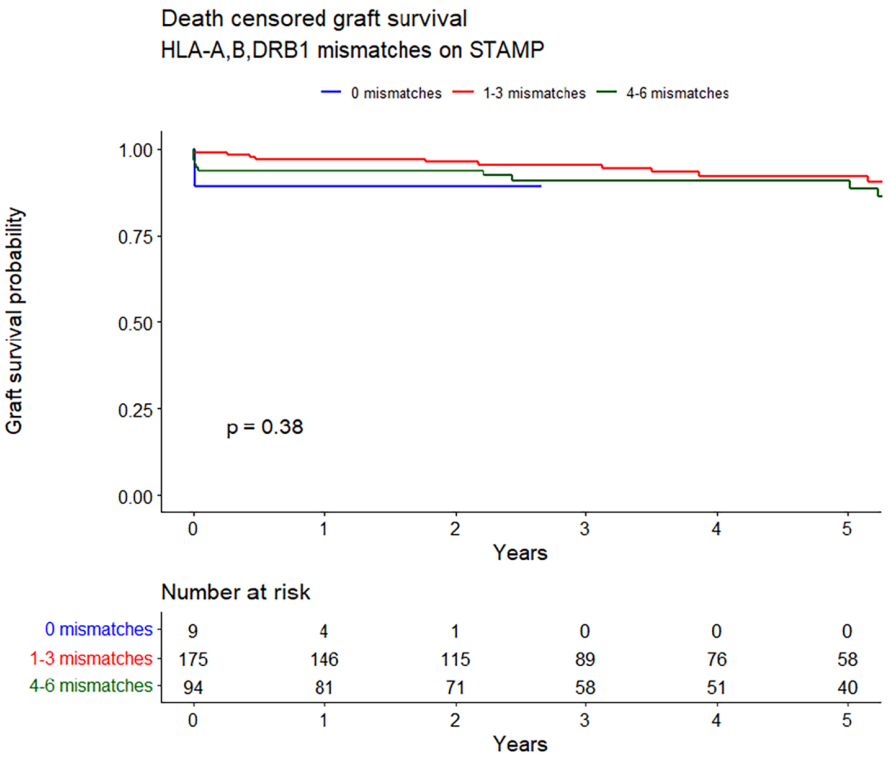

FIGURE 5 HLA mismatch and graft survival in STAMP. Five-year STAMP allograft survival relative to the degree of HLA-A, B, and DRB1 mismatches. No impact of HLA match on allograft survival was found in the STAMP group.

HLA identical allograft (HLA-A, -B, -DR identical). The rationale for choosing this group for the comparison was to obtain a high similarity in relation to HLA immunization, cold ischemia time and number of previous transplants.

In the present cohort, we decided to compare patients transplanted through STAMP with all patients transplanted within Scandiatransplant in the same time period regardless of HLA immunization and number of previous transplants. Even though we are now comparing with a group with a better expected outcome, the allograft survival among the patients transplanted though STAMP is not significantly different. The data support that the existing allocation algorithm in STAMP is a safe and efficient way to transplant this immunologically challenging patient group. It was also confirmed when comparing with the 10-year allograft survival in Eurotransplant. In their most recent publication[5] the allograft survival is approx. 68% compared with the 10-year allograft survival in STAMP of 73.4%.

Rejection rate is an important parameter in evaluating the program. The patients in our STAMP have an inherent increased immunological risk and therefore we would anticipate a higher rejection risk. If we compare our overall rejection risk to the rejection risk found in the paper by Lauronen et all,[1] they report an overall rejection risk on 15.8% in their kidney transplant population which is similar to our 13.5%. This underlines that the immunological assessment and allocation of these patients is immunological safe in the STAMP.

Comparing the rejection rate in our STAMP population to the work by Loupy et al.,[7] we also find similar overall rejections rates within the first year.

The outcome also supports that it is possible to establish and run an efficient and immunologically safe AM program with a decentralized organization.

TABLE 5 Waiting time before and after introduction of ABO compatibility

Before *N* = 7188				
Recipient→				
↓Donor	**0**	**A**	**AB**	**B**
0	2533	45	3	101
A	3	3200	89	1
AB			364	4
B			24	821
After *N* = 1814				
Recipient→				
↓Donor	**0**	**A**	**AB**	**B**
0	605	9	1	9
A		835	14	1
AB			93	1
B			9	237

Note: ABO-compatible allocation of kidneys on the ordinary kidney waiting list is stable. Before introduction of ABO-compatible allocation in the STAMP 149 of 2682 (5.6%) blood group O kidneys were transplanted ABO-compatible and after 19 of 624 (3.0%) blood group O kidneys were transplanted ABO compatible.

In the decentralized organization of Scandiatransplant, we have abstained from a common protocol for listing of patients on the waiting list. Additionally, a local assessment of patients is essential to support the need and wishes from the clinical departments. All the tissue typing laboratories have local work procedures and policies, which includes the definition of acceptable HLA antigens and own algorithms for HLA antibody detection and specification. In regard to PRA values, some laboratories conducts CDC screening analyses and generates a PRA from the panel, other laboratories use a locally HLA-typed donor pool in the Fusion software to generate a cPRA and finally others use the build-in cPRA calculation in the Scandiatransplant web application. This leads to the different foundations for estimation of PRA/cPRA in each laboratory. Using PRA/cPRA as an acceptance criterion will result in uneven access to the program depending on which method the laboratory uses for calculating the PRA. This consideration led to the introduction of TS as the sole acceptance criterium.

Following the introduction of TS as accept criterion in September 2017, we saw an increase in the number of patients accepted to STAMP. Looking at the data from each laboratory, we found that the laboratories using CDC screening-based PRA values as entry criteria had the largest increase in patients admitted to STAMP after the change (data not shown). Furthermore, as TS takes both HLA and ABO into account, we have improved the identification of patients difficult to transplant, not only due to broad HLA immunization.

After introducing the TS, more patients were included in the program, which presumably would lead to more realized transplantations in this group. However, the constant development of STAMP led to a change in the matching algorithm from ABO identical to ABO-compatible allocation merely a year after introducing the TS,

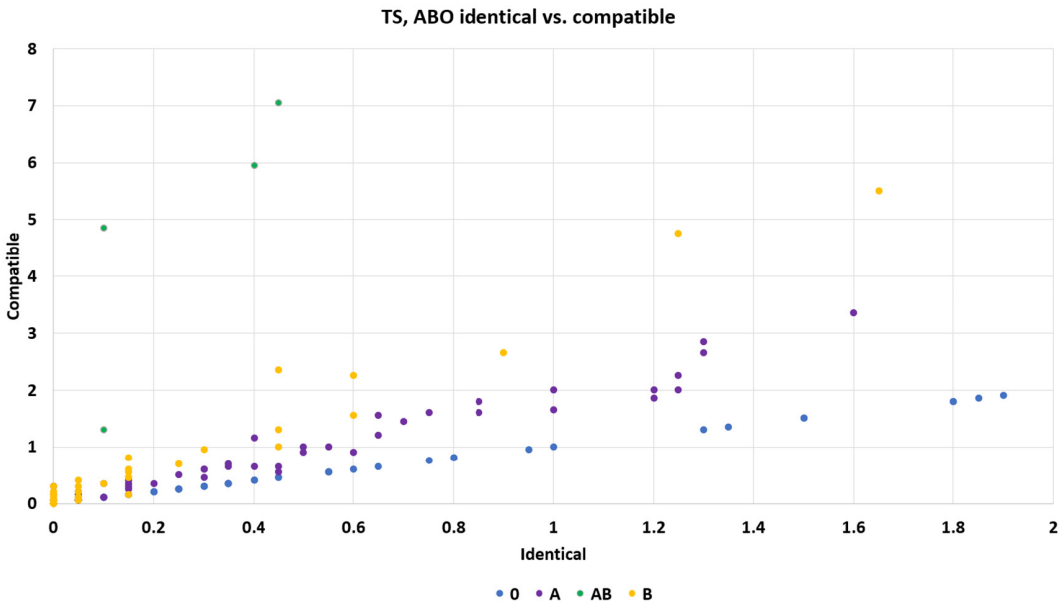

FIGURE 6 Transplantability score. On 240 HLA-typed STAMP recipients, to which acceptable mismatches have been assigned on all alleles, TS has been calculated for both ABO identical and ABO compatible. It illustrates that especially some of the blood type AB and B recipients have a very high compatible TS, which indicates that these recipient cannot be categorized as "difficult to transplant."

so the effect on realized transplantations solely by the introduction of TS is difficult to evaluate.

By far, ABO-compatible matching in STAMP has resulted in the most significant increase in the number of realized transplantations in the program. Until December 2018, almost solely ABO identical kidneys were transplanted in STAMP (Table 4A). In Table 4B, it is important to note that only 58% of the kidneys were from ABO identical donors. Theoretically, the patients with blood groups AB, B, and A would all benefit from the change in the listed order. The material from December 2018 to December 2020 (Table 4B) shows that 66% of realized transplantations among blood group B patients and 47% among blood group A patients were transplanted with a blood group O donor kidney. All blood group AB patients received kidneys with other blood groups, but it should be noted that the number of patients in this group is very small, and the blood group AB patients were previously transplanted with kidneys from blood group A donors.

Historically, there is a tradition within Scandiatransplant to transplant deceased donor kidneys for ABO identical recipients (Table 5). Therefore, introducing ABO compatibility in STAMP was considered a major change and was preceded by thorough discussions among both the Tissue Typing Group and the Nordic Kidney Group. It is a fact that blood group O patients would not benefit and could even face a prolonged waiting time.

However, the majority of the kidneys transplanted for ABO-compatible STAMP recipients would have been allocated to blood group O patients on the general waiting list.

One of the key elements in the Scandiatransplant organization is continuous monitoring of all allocation programs and adapting accordingly. With the knowledge of the O donor shortage close monitoring were done.With the current STAMP inclusion criteria where TS is calculated as ABO identical, one could argue that patients with a high TS in an ABO-compatible setting should not be eligible to STAMP. Most likely they could be transplanted with an ABO compatible kidney in their local center, while the aim of STAMP is to facilitate transplantation of the very difficult to transplant patients. This has been addressed and further changes to STAMP will be implemented in the beginning of 2022.

The newest adjustments to STAMP were introduced in January 2019 and April 2020, respectively. First matching on HLA-DPB1 allowed the centers to submit patients with HLA-DPB1 antibodies to enter STAMP instead of local AM programs.

By April 2020, STAMP includes matching for all HLA loci (HLA-A, HLA-B, HLA-C, HLA-DRB1, HLA-DRB3/4/5, HLA-DQB1, HLA-DQA1, HLA-DPB1, HLA-DPA1) allowing most broadly sensitized patients to be eligible regardless of the HLA antibody specificities. As shown in this paper, we have seen an increase in the number of patients entering STAMP, and after April 2020, 84% of the patients included in the program had antibodies toward the newly included alleles. In the following years, we will hopefully obtain data to look further into the effect of matching on all HLA loci when it comes to allograft survival.

In conclusion, the 10-year allograft survival demonstrates that the STAMP allocation algorithm is immunologically safe.

During the last 12 years, we have managed to establish, adapt and run a very efficient AM program. The program is continuously monitored and evaluated. The introduction of matching for all HLA loci is a huge improvement to the program, which demonstrates the technical adaptability as well as clinical flexibility in a decentralized organization.

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DISCLOSURE

The authors of this manuscript have no conflicts of interest to disclose as described by the *American Journal of Transplantation*. Ilkka Helanterä holds research funds from MSD and Hansa Biopharma and is receiving consultancy honoraria from Novartis, Hansa Biopharma, and Takeda. Other authors have no conflicts of interest to declare.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

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