LETTER TO THE EDITORS

Reply to Sabah et al.

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We appreciate the valuable comments to our report [1]. Epitope matching or total eplet mismatch could indeed be an attractive explanation for the favorable outcome of the subjects in our report, at least for those without rejection. This relatively novel view of immunological assessment could be very important although its true value remains to be determined [2].

Low recipient age at kidney transplantation was certainly an important prerequisite to achieve such favorable long-term graft survival, as comorbidities can affect graft function and survival [3]. With today's average recipient's age of 50 years at the time of transplantation in most European transplant centers, the competing endpoint to graft loss is death with functioning graft in approximately 50% [4].

We completely agree with the comments on donor age as one of the important factors for long-term graft function. In a recent analysis of kidney transplants of the past decade, we found a continuous relationship between donor age and evolution of graft function within the first transplant year in patients ($n = 315$) whose clinical course was not complicated by acute rejection (Fig. 1; I. Scheffner, B. Kettler & W. Gwinner, unpublished data). The bigger this "capital of function," the longer the organ will last in the presence of natural GFR decline, drug toxicity, hypertension, infections, and other injuries. Moreover, in the 39 long-term survivors of our current report who had no biopsies, there was an inverse correlation ($r = -0.41$; $P = 0.01$) between graft function at last follow-up and donor age (Fig. 2). Such correlation was not observed in subjects undergoing biopsy ($r = 0.06$; $P = 0.76$).

Skin cancer was prevalent in 28 subjects (39%) of our cohort. One subject had a lymphoma. Solid tumors were diagnosed in 11 subjects (15%), with four cases of breast cancer, two cases of bladder cancer, and one case each with colon and hepatocellular cancer. Of the three cases of renal cancer reported in our study, two were detected in the transplanted kidney. Occurrence of solid tumors or skin cancer was not associated with more intense maintenance immunosuppression because of rejection or with calcineurin inhibitor-containing immunosuppressive therapy. Regarding skin cancer, subjects were more likely to receive mono- or di-immunosuppressive therapy instead of triple regimens ($P = 0.046$), suggesting treatment bias. Subjects without malignancies had lower age at transplantation compared with those with skin cancer or with solid tumors (26.6 ± 11.3 vs. 33.7 ± 12.9 vs. 33.9 ± 12.5 years; $P = 0.045$), lower age at last follow-up (55.3 ± 10.7 vs. 64.4 ± 10.9 vs. 63.2 ± 12.2 years; $P = 0.004$) and a shorter duration of transplantation, with 27.9 ± 3.2 vs. 30.2 ± 3.5 vs. 28.9 ± 3.6 years; $P = 0.05$ (all P values refer to the results of one-way ANOVA; in the post-testing, only skin cancer was significantly different from the group without malignancies). This suggests that age is the most important factor and length of immunosuppressive therapy has also some importance. However, the results must be interpreted cautiously because of the small number of cases.

Only eight subjects had type 2 diabetes at last follow-up. There was no predilection of diabetes onset with calcineurin inhibitor therapy. Three of the 41 subjects with cyclosporine A developed diabetes, none of the eight subjects with tacrolimus, and 5 of 23 without calcineurin inhibitors. Also, body mass index was not explanatory, with 24.1 ± 8.2 in subjects with diabetes and 25.8 ± 4.9 without.

Until last follow-up, 12 subjects (17%) had developed coronary heart disease and five subjects (7%) had peripheral artery disease or had experienced a stroke. According to a recent survey in Germany, this rate equals individuals of the general population aged 65–69 years, and for mean ages of 55 years (like our subjects) the expected lifetime prevalence is approximately 10% [5].

doi:10.1111/tri.13522

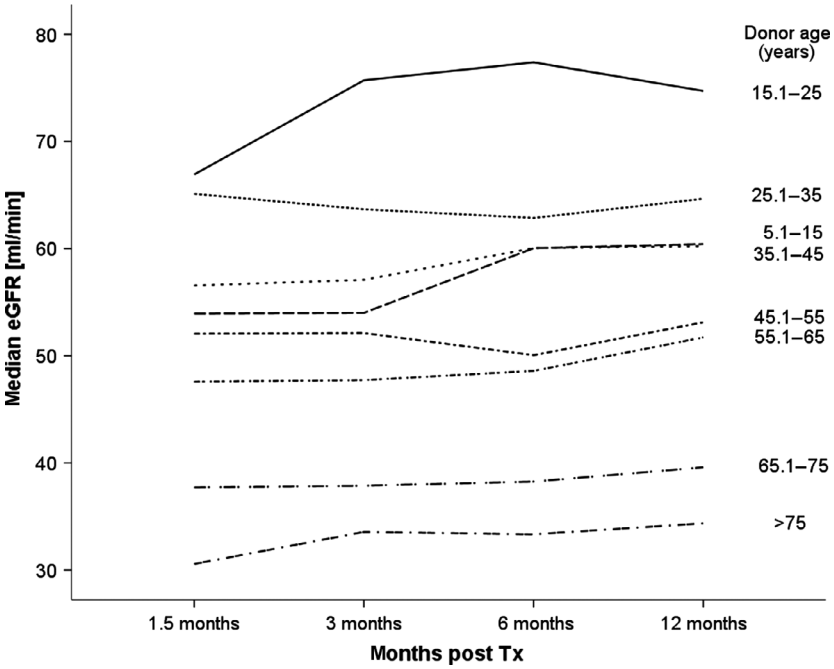

Figure 1 Evolution of median eGFR in patients transplanted between the years 2000–2007 (n = 315) who had no rejections within the first transplant year (I. Scheffner, B. Kettler & W. Gwinner, unpublished results).

Figure 2 Cystatin C-estimated glomerular filtration rate (cystatin C-eGFR) at the last follow-up in relation to the donor age in the 39 subjects with long-term graft survival who had no biopsy.

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