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Answering reviewers

We would like to thank both the reviewers for their very kind and helpful comments.

Reviewer's code:02885171

Specific comments

a) Major

a-1: At the Renal Transplantation Unit of "Laiko" General hospital which is a tertiary hospital, more than 40% of the country's kidney transplantations are performed. (about 70/year). The control group was comprising of recipients with similar baseline characteristics (gender, donor/recipient age, PRAs), transplanted during the same period from ABO compatible living kidney donors.

a-2: It is well known that the cost of an ABOi transplantation is higher compared to an ABO compatible transplantation. However, we have to compare the cost of the ABOi transplantation to that of maintenance dialysis. If we also take into account the health related quality of life benefits of a successful transplant, it is clearly cost effective.

a-3: The preconditioning regimen used for ABOi kidney transplantation in our center was based on the Swedish protocol. Indeed, the optimum dosage of rituximab is still an issue that needs investigation. Lower doses have been proven efficacious in Asians; hoewever it is difficult to extrapolate the results for Caucasians. We used the dosages generally applied in Europe which have proven efficacy in depleting B-cells according to our measures of CD20 pre- and post administration.

a-4: The choice of everolimus initially was based on the consideration that the combination of an mTORi with a CNI could prove to be more potent in preventing acute rejection episodes compared to CNI plus MPA. Thus for the first trimester, we used the combination of low-dose mTOR with low CNI. This combination of two potent immunosuppressants but at low doses to avoid toxicity, was our first choice as induction therapy for this high immunological risk patient group, despite the fact that there are no studies in ABOi transplantation comparing the efficacy of CNI plus mTOR with CNI plus MPA. After three months, we switched to the immunosuppresive regimen which is the standard of care in most centers including ours, namely CNI + MPA in order to avoid nephrotoxicity long term. We considered our strategy to be safe as it is already well known that after the period of accommodation, ABOi recipients have not significantly higher immunologic risk than their ABOc counterparts.

a-5: In our center we do not perform protocol biopsies. However we perform biopsies at a minimum level of clinical indication. More than 50% of our patients underwent indication biopsy. Indeed, we could possible missed some subclinical, "silent" rejections episodes, though the impact of those episodes on long term graft function still remains controversial. Moreover, we –like many other centers- compared BPAR according to clinical indication between the two groups and we did not find a significant difference.

b) Minor

b-1 Preoperative crossmatch was made using CDC (compement dependent cytotoxicity) and flow cytometry crossmatch. See section results on patient characteristics.

A. *Reviewer's code: 03290767*

1. We have measured IgG and IgM antibodies. Changes in the IgG and IgM antibodies showed the same pattern.
   The pathogenetic role of IgM abs in ABOi transplantation is still a matter of debate. Also, IgG titers were also higher than IgM in all the patients, so when we reached the target IgG titer, IgM was already equal or lower. Additionally,

in the vast majority of published studies therapeutic guidance of apheresis sessions is the IgG and not the IgM ab titer.

2. We didn't tested donor status for A1 and A2, and we also didn't measured antibodies to A1 and A2.