

Comments for the MEDCAC On the Impact of ESA Use in Renal Transplantation

The American Society for
Histocompatibility and Immunogenetics
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Background and Issues to be Addressed

- ASHI – professional society comprised of scientists, transplant physicians and surgeons, technologists
- Expertise – histocompatibility and transplant immunology
 - Sensitization to HLA antigens
- Issues to be addressed:
 - Definition of sensitization
 - Impact of sensitization
 - Relationship of transfusion to sensitization

Definition of Sensitization: PRA and CPRA

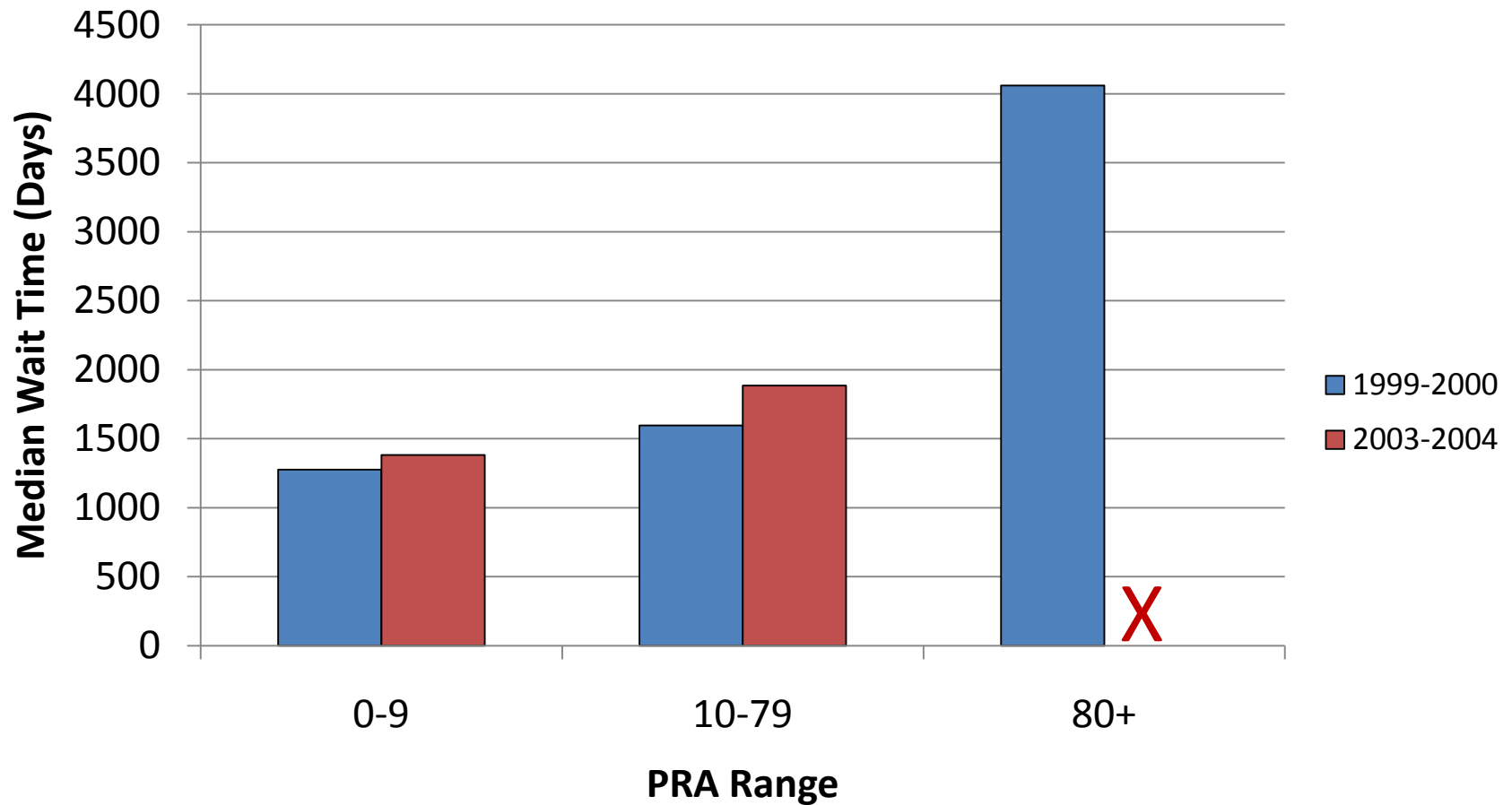
- Panel reactive antibody (PRA)
 - PRA varies with different panels and with assay method – Cells vs. solubilized HLA antigens
 - PRA is determined for either HLA class I or class II antigens, but not both
 - Inconsistency from center to center
- Calculated PRA (CPRA)
 - Represents frequency of incompatible donors to any given patient
 - Based on actual HLA frequencies in national donor pool
 - More accurate measure of sensitization because it includes both HLA class I and II specific antibodies
 - Implemented for organ allocation by OPTN on 10/01/2009.
- Identification of donor HLA specific antibodies
 - Best predictor of sensitization impact for a specific donor

Impact of Sensitization

- 39.5 % of active candidates on waiting list for renal transplants are sensitized; 17.2% are highly sensitized with PRAs>80 (corresponding CPRA >85%).
- Reduced access to transplantation
 - Significantly longer waiting times
 - Highly sensitized patients may not have a compatible donor
- Lower graft survival
- Increased incidence of antibody mediated rejection episodes

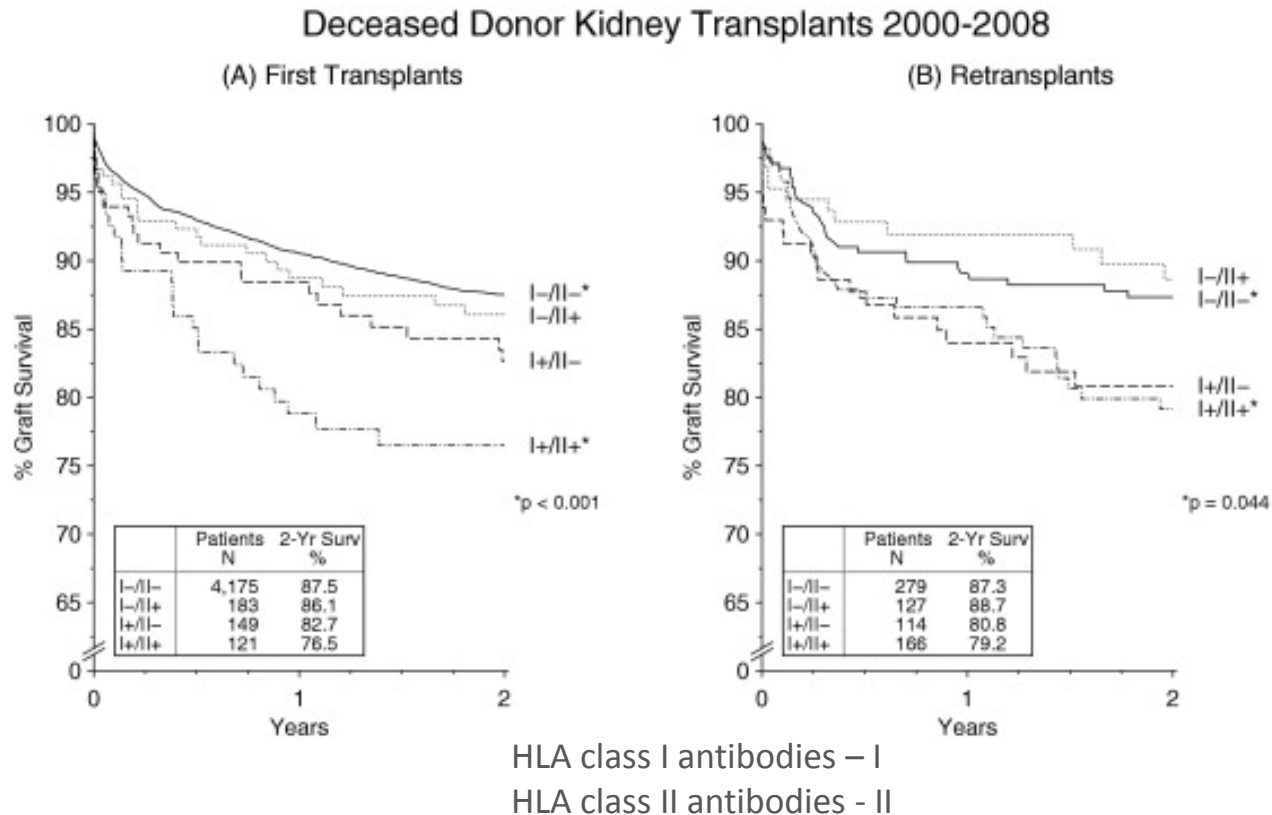
Sensitization and Median Waiting Time

OPTN Data as of 12/10/2010



Sensitization and Graft Survival

Collaborative Transplant Study

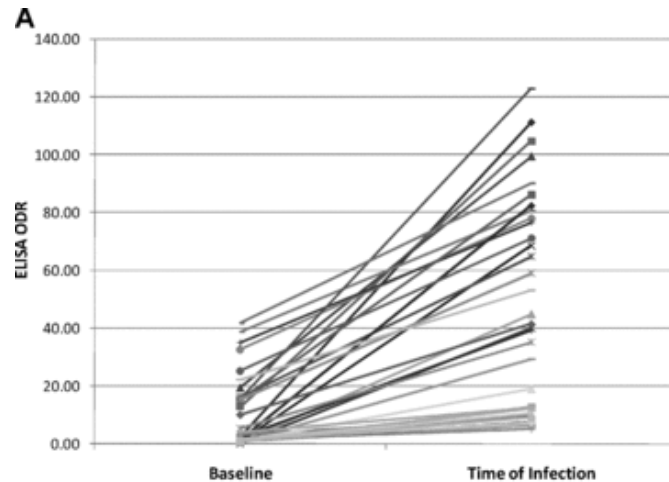


Susal C, Dohler B, Opelz G. Human Immunol.2009;70:569

Transfusion and HLA Sensitization

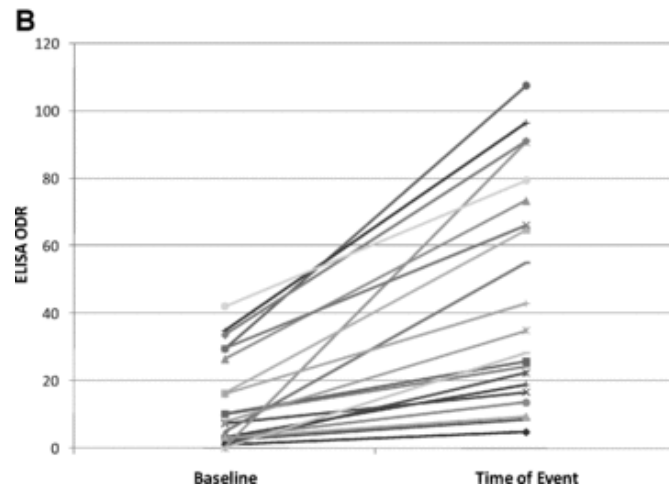
- Sensitization rates among males with no previous transplant
 - Transfusion is the most likely cause
 - 23.5% - Johns Hopkins CTC
 - 12.1% - MD Anderson Medical Center
 - Impact of leukoreduced blood transfusion among sickle cell disease patients
 - 34% overall rate of sensitization
- (McPherson ME, et al. Pediatr Blood Cancer 2010;54:552)

Increases in HLA Antibodies Induced by Infection and Inflammation



Infection or inflammatory events:

- Increase antibody titer
- Expansion of antigen specificities



Thus, even low levels of HLA antibody may become problematic.

Do ESAs Reduce Incidence of Sensitization?

- Data from earlier studies indicated that erythropoietin reduced sensitization and might improve allograft outcomes
 - # of patients sensitized by transfusion decreased from 63% pre-epo to 28% post-epo (Vella, et al. Nephrol Dial Transplant 1998;13:2027).
- Sensitization rates today cannot be compared to earlier reports
 - more sensitive methods for detection of HLA antibodies

Reasons for Continued Use of ESAs for Renal Transplant Candidates

- HLA sensitization occurs even with leukoreduced blood.
- Even low levels of HLA specific antibody adversely impact transplant candidates.
- Sensitization should be avoided in children and young adults, as these candidates will likely require a second kidney transplant.