# Optimizing Outcome of Transplantation in Highly Sensitized Recipients

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**Canada**

# Outline

- Why special consideration for this group?
- Assessment of Sensitization
- Definition of Highly Sensitized
- Approaches to Transplantation of the Highly Sensitized
- Conclusions

# Sensitization

- Development of anti-HLA antibodies as a consequence of prior exposure
  - Pregnancy
  - Prior transplant
  - Transfusion

# Why Concern re Highly Sensitized?

- Transplantation improves survival
- Increased waiting time associated with worse outcomes
- High degrees of sensitization reduce the likelihood of finding a compatible kidney and increase waiting time
- Successful transplantation of this group requires a unique approach

# Detecting and Interpreting HLA Antibodies

**PRA: Panel reactive antibody**

- **Cell based assays: ESTIMATE percent of donors from "a population" to whom a recipient has cytotoxic antibodies**
  - **15% FP and FN**
  - **Cannot tell you WHICH antibodies in detail**
  - **Exquisitely dependent on cells chosen for the panel**

- **Solid phase assays**
  - **Improved specificity**
  - **Up to 30% more sensitive**
  - **Single Antigen Beads – give a list of antibodies or "unacceptable" antigens**

# List of Antibodies→ cPRA

- cPRA: Calculated PRA
- Estimates the number of donors in a population to whom a recipient has at least one HLA antibody (or unacceptable antigen)

- Depends on when you look
  - Frequent testing to capture full spectrum of immunity
  - Current versus historical antibodies
- Depends on the population
- Depends on the loci included – what do you want to avoid?

# Impact of Antibody Quantity

Higher Titer Antibody

| Test | How much antibody? | Consequence |
|---|---|---|
| Cytotoxic crossmatch | LOTS,<br>Binds C’ | Hyperacute, accelerated AMR<br>(Terasaki et al NEJM 1969) |
| Flow cytometry crossmatch | Some,<br>may or may not bind C’ | Early AMR, late AMR, higher graft loss |
| DSA only | Low,<br>may or may not bind C’ | Later AMR (less), CABMR<br>More immunosuppression needed |

Longer time to outcome

# Impact on Access

- cPRA 95% → 1:20 donors
- cPRA 99% → 1:100 donors
- cPRA 99.6% → 1:250 donors
- cPRA 99.9% → 1:1000 donors

- In a region with 100 donors a year…. Up to 10 years?
- If access to 1000 donors .... Maybe only a year or two?

**THE BEST TREATMENT (IF AVAILABLE) FOR A HIGHLY SENSITIZED PATIENT IS ACCESS TO MORE DONORS TO FIND ONE THAT IS DSA NEGATIVE**

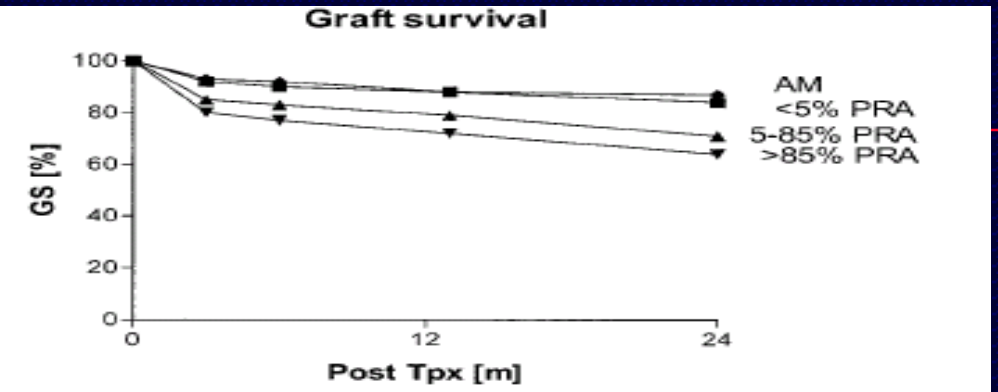
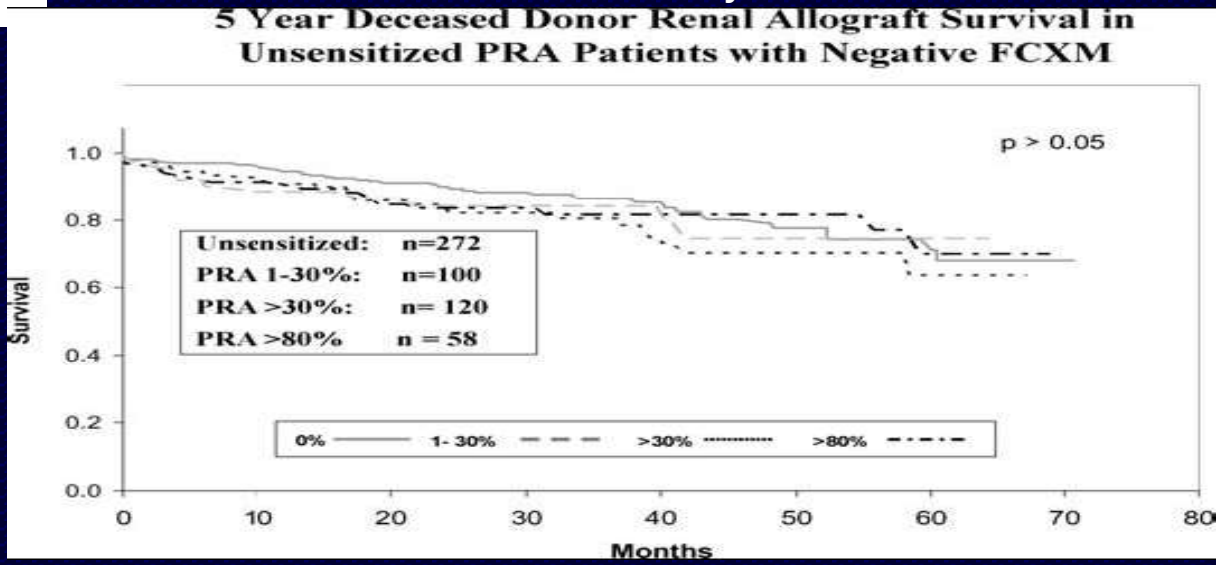



**FIGURE 2.** Comparison of graft survival between acceptably mismatched patients (n=112) and nonsensitized (≤5% panel reactive antibody [PRA]), sensitized (6%–84% PRA), and HS (≥85% PRA) recipients whose transplants were arranged through the ET-KAS (14.328). GS, graft survival.

Claas et al. Transplantation, 2004

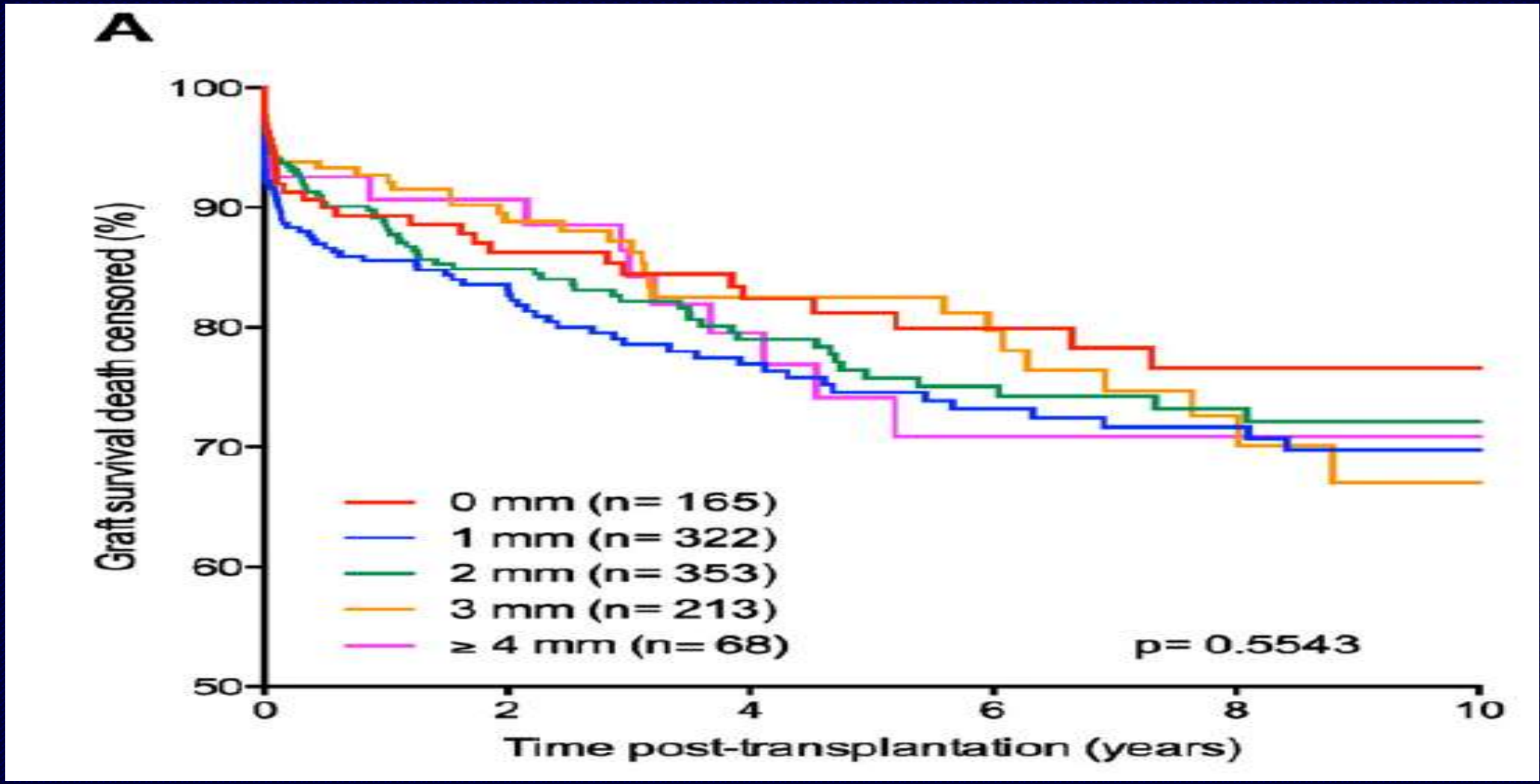
# PRA does *not* drive risk in isolation
# DSA drives risk

Bray et al. AJT Oct 2006



# No Effect of HLA Mismatch in Acceptable Mismatch Programme

**Heidt et al Transplant Immunology, 2015**



THE BEST RESULT WITH LEAST IMMUNOSUPPRESSION AND RISK OF ASSOCIATED MORBIDITY/MORTALITY IS FROM TRANSPLANTATION OF A DSA NEGATIVE KIDNEY

# Optimal Transplantation of the Highly Sensitized Requires Collaboration!!

## With the HLA Lab

## Across/Between Countries

# Approaches to Transplanting Highly Sensitized Patients

- Sensitized with Incompatible Living Donor
  - -Kidney Paired Donation
  - -Desensitization
  - -Combined approach
- Highly Sensitized Without Living Donor
  - -Large Registries/focused allocation strategies to prioritize DSA negative deceased donor kidneys for highly sensitized patients

# Paired Exchange

## Registered Pair A

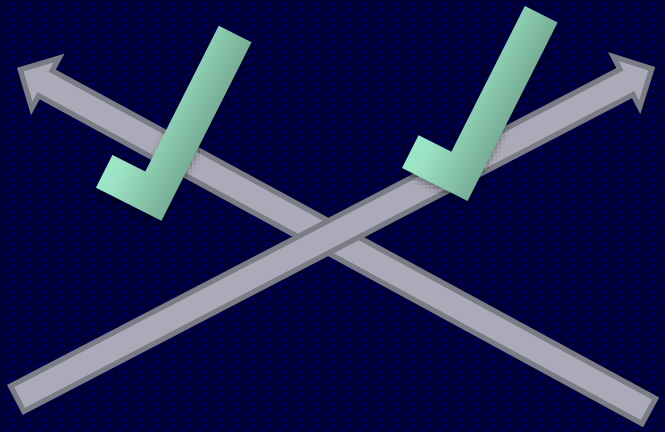
Candidate : Andree

Donor: John

## Registered Pair B

Candidate: Suzanne

Donor: Todd



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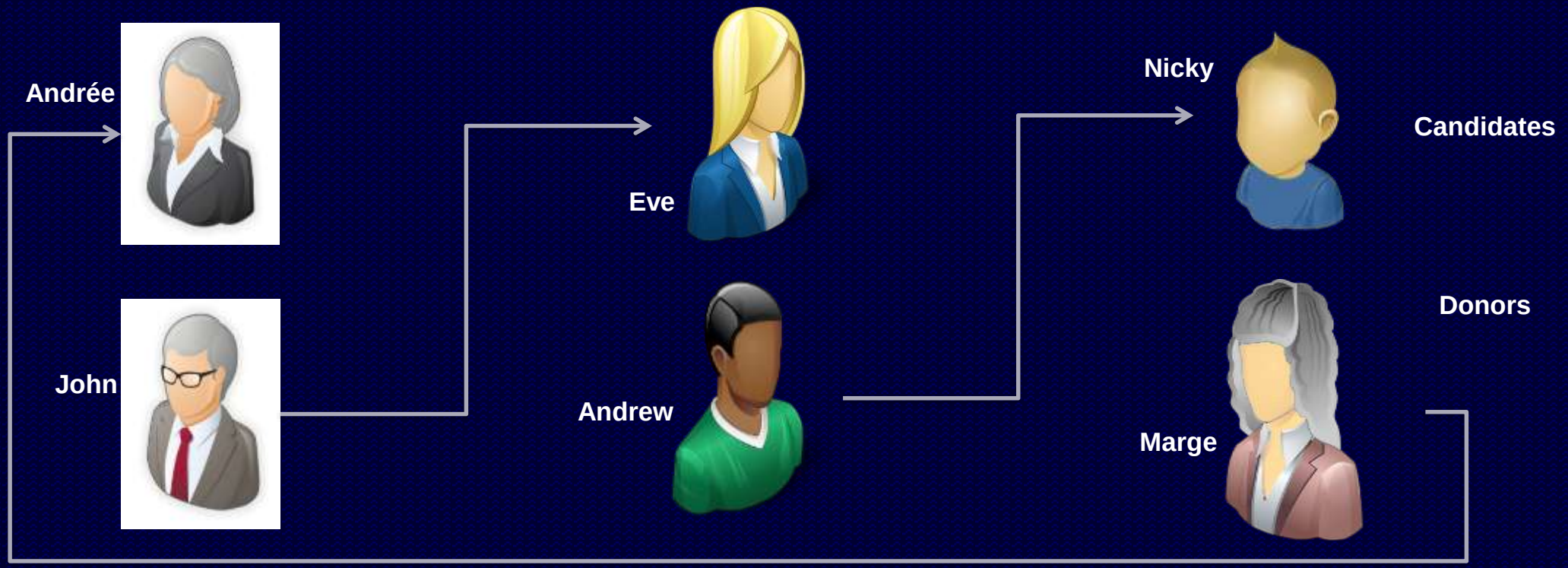
# N-Way (Closed) Chain

Registered Pair A

Registered Pair B

Registered Pair C

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# Domino Chain

Registered Pair A

Registered Pair B

Registered Pair C

Faith

Non-directed Donor

Nicky

Marge

Andrée

John

Tracy

Tony

Eve

Person on Transplant Waitlist

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# Kidney Paired Donation Program

Advisory Committee

Published Match Run

Proposed Matches

Matching Algorithm

Patient Records

Canadian Transplant Registry

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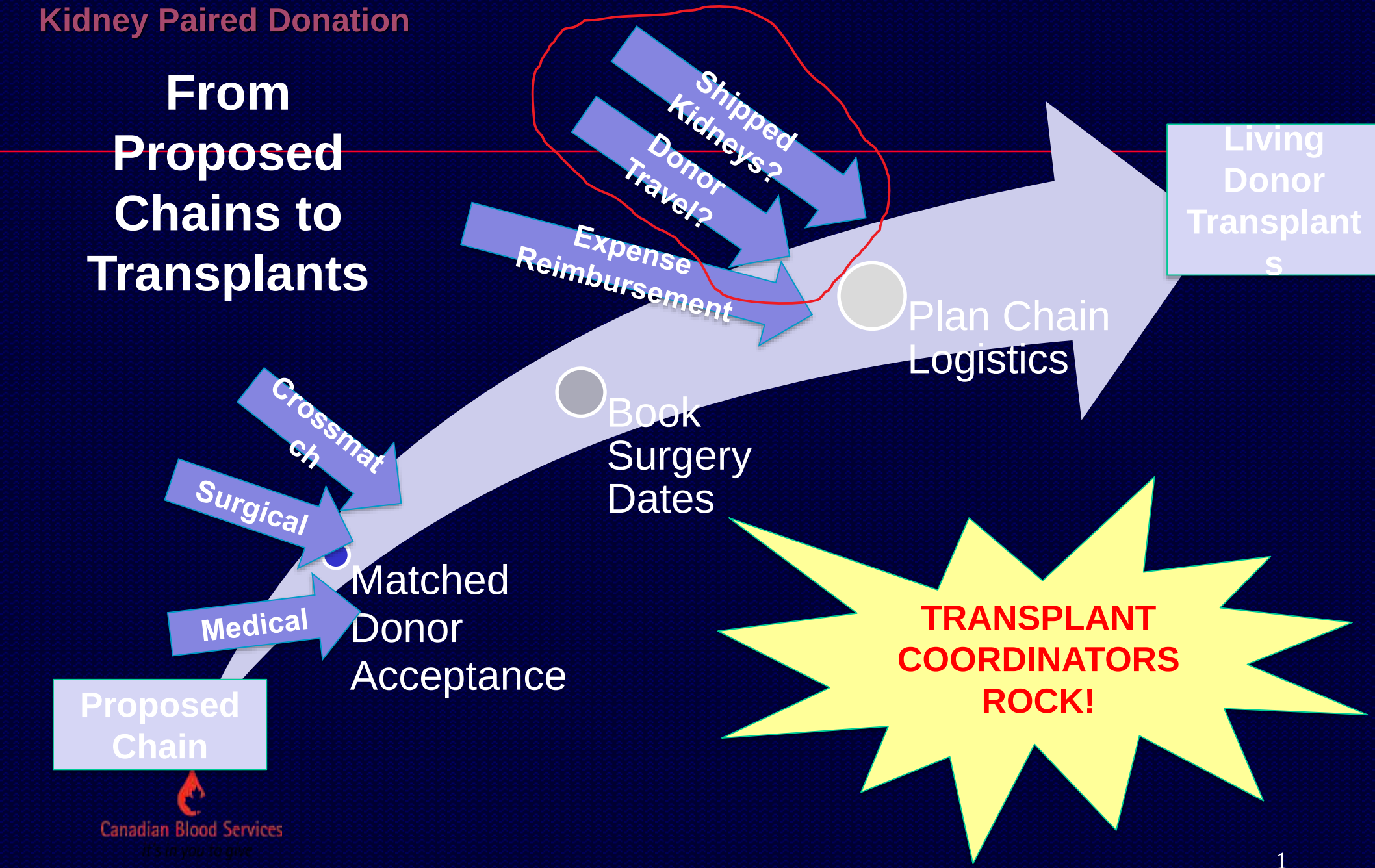
# From Proposed Chains to Transplants

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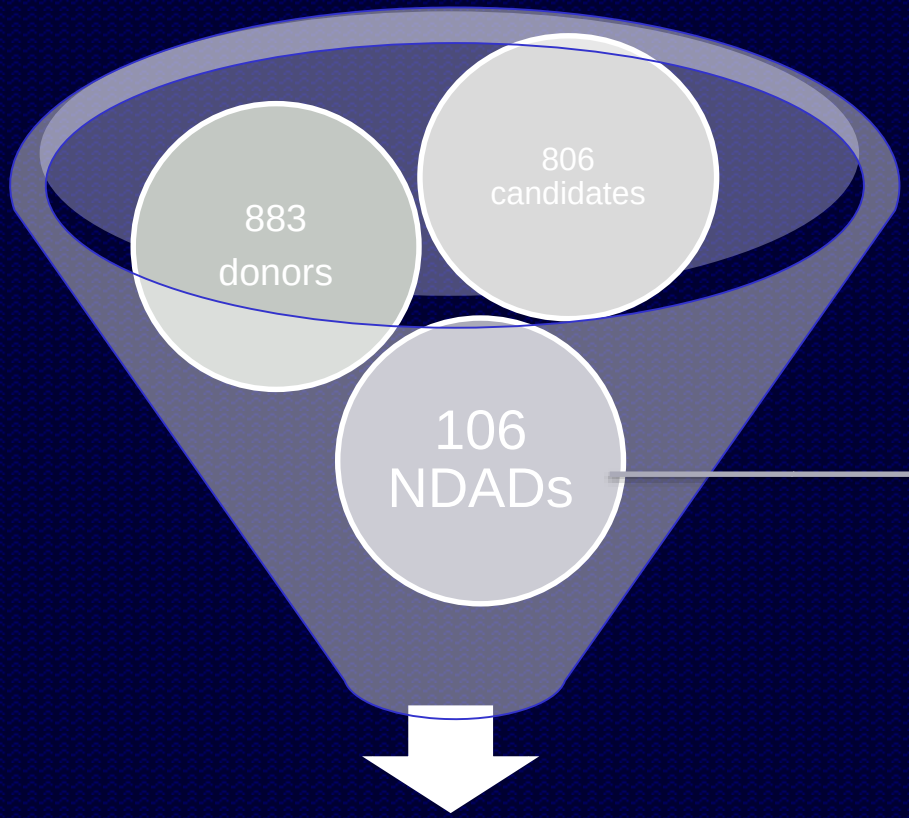
# KPD…as of October 18, 2016




**46** from Paired Exchanges

23 chains

**120** from N-Way (Closed) Chains

31 chains

**294** from Domino Chains

88 chains

**460 Transplants**

375 Registered Candidates

85 Waitlist Recipients

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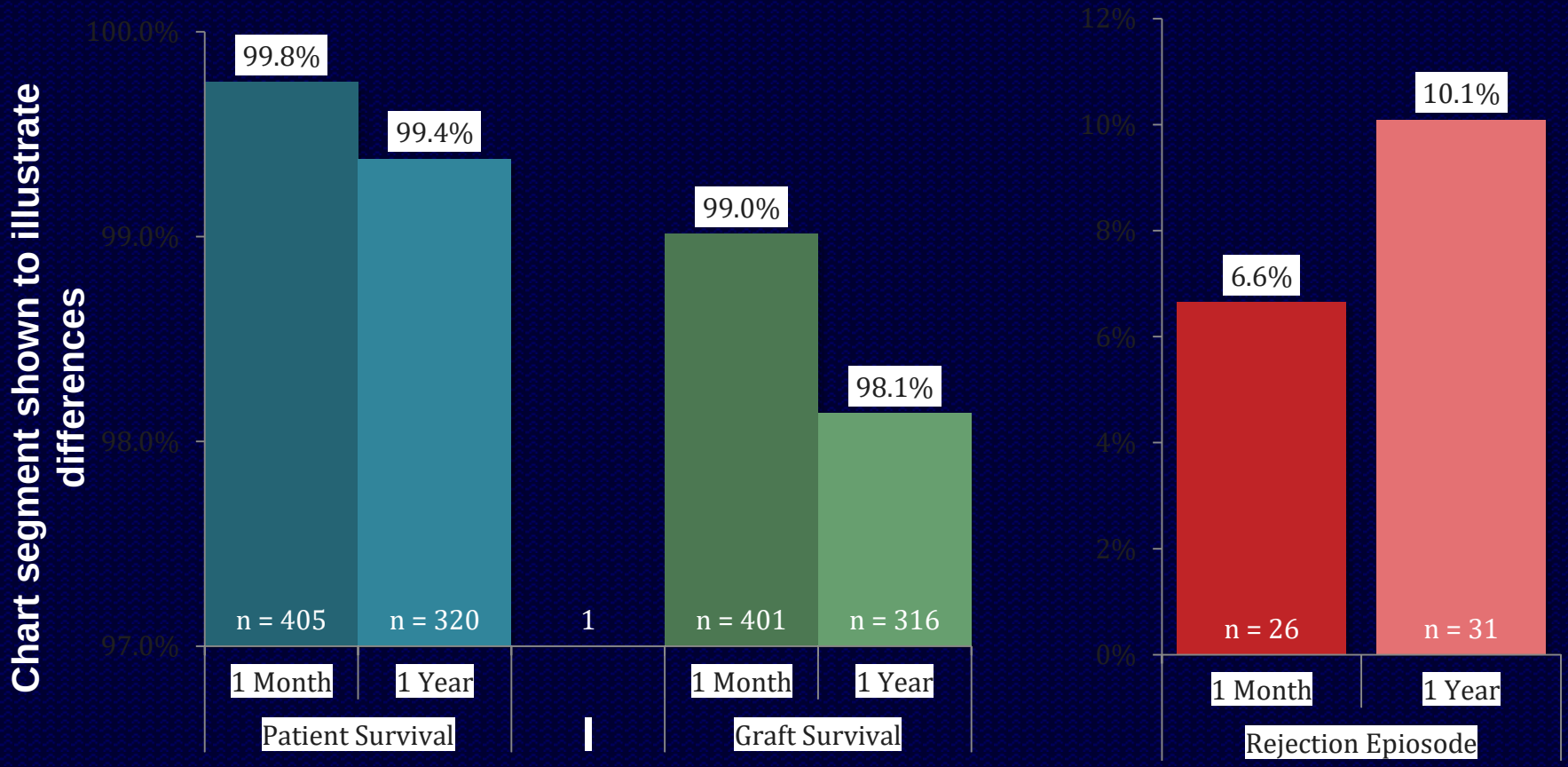
# Outcomes of Patients Reaching One Year Post-Transplant

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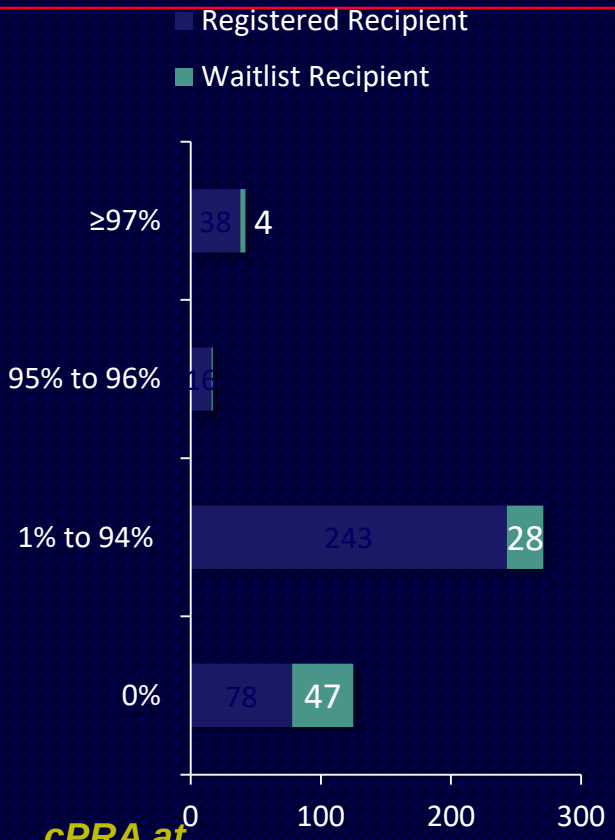
# cPRA for Candidates and Recipients




*cPRA at time of transplant*

| | 0% | 1% - 94% | 95% - 96% | ≥97% |
|---|---|---|---|---|
| *Transplants to Registered Recipients (N=375)* | 76 (20%) | 240 (64%) | 17 (5%) | 42 (11%) |
| *cPRA Distribution in Candidate Pool* | 152 (19%) | 389 (48%) | 28 (3%) | 237 (29%) |
| *% of cPRA Group Transplanted* | 50% | 62% | 61% | 18% |
| *Transplants to Wait List Recipients (N=85)* | 47 (59%) | 28 (35%) | 1 (1%) | 4 (5%) |

***cPRA is based on rating as currently calculated for all candidates registered to date. cPRA values for five (5) waitlist recipients are not available.***

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# Assessment of KPD Advantages

- Uses available living donor kidneys preserving deceased donor kidneys for those without living donors
- Living donor still facilitates transplantation for intended recipient
- Low immune risk transplant is performed (depending on acceptability criteria)
- Chain includes kidney to deceased donor list

# Assessment of KPD Disadvantages

- Donor does not give to intended recipient
- Travel or shipping needed
- May require new care team for donor or recipient. Donor and recipient surgical teams need to trust each other
- Some difficult to match pt may take a long time to find matches
- Donors putting life on hold for this
- Potential risk of donor backing out after his/her recipient already transplanted

# Domino Chain

Registered Pair A

Registered Pair B

Registered Pair C

Faith

Non-directed Donor

Nicky

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John

Tracy

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Person on Transplant Waitlist

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# THE CANADIAN HIGHLY SENSITIZED DECEASED DONOR REGISTRY

# Registry Design

- Define cutoff for inclusion
- We chose cPRA >/=95%
- All OPOs have details of unacceptable antigens for all Canadian HS recipients
- Virtual cross match neg HS recipients are assessed for all deceased donors
- 1 kidney always stays locally. Other to HS recipient if accepted by recipient centre
- Thresholds for each centre to ensure no centre winners/losers

# Highly Sensitized Registries
# Pros and Cons

- No living donor needed
- Substantial increase in donor pool/potential for transplant
- Much less administrative burden than KPD
- Compatible kidney transplanted (rules determined by Registry members)

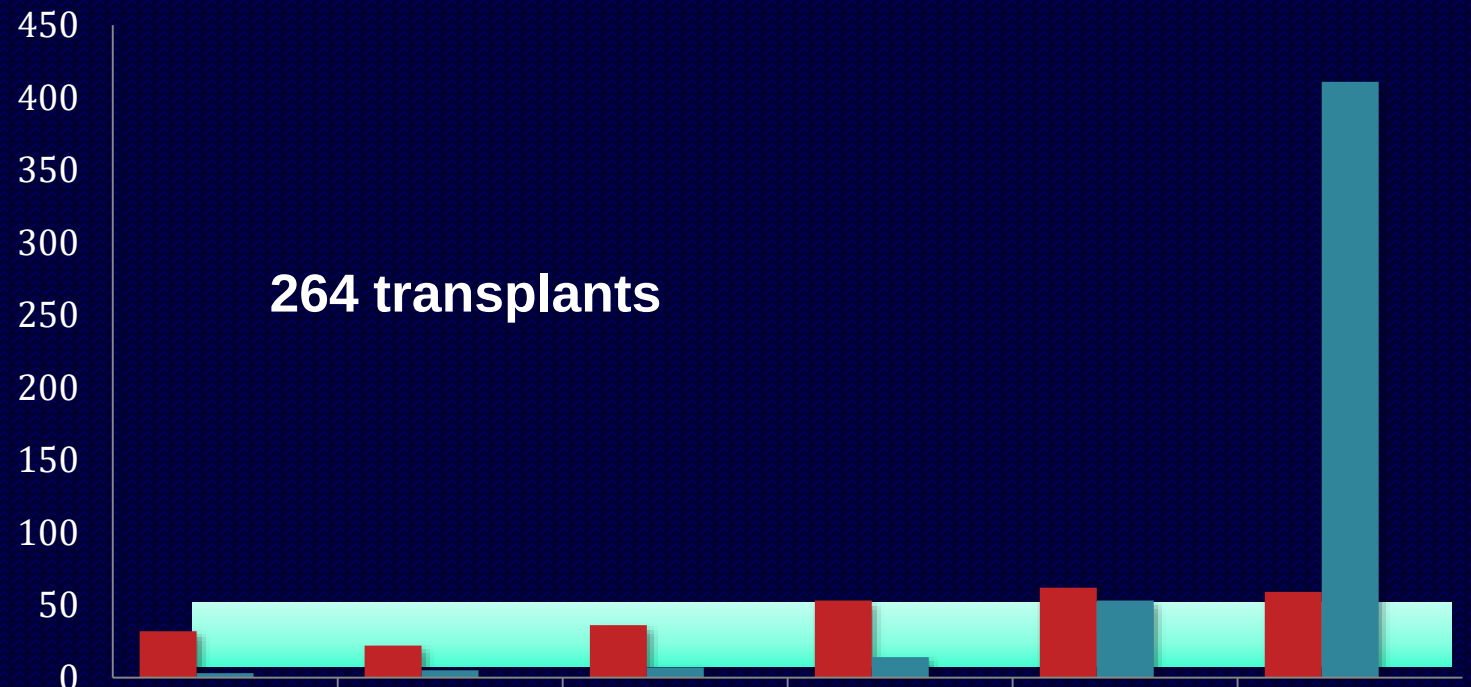
- Deceased donor kidney of variable quality
- Potential risk of higher donor regions sending net kidneys to regions with poor donor rates
- ? Payback/thresholds
- Requires shipping
- To function effectively requires HLA Lab standardization

# Problems With Determination of Highly Sensitized

- Each recipient needs to have extensive HLA Ab testing
- Significant cost
- For success, virtual crossmatch needs to be highly predictive of actual cross match
- Methodology for antibody determination and sensitivity varies by lab even within each country.
- In Canada our labs have collaborated to standardize.
- Otherwise, high likelihood that same samples get different readouts from different labs. Thus kidney that is shipped may not be used for intended recipient

- Success will also depend on deceased donor supply. Large network best
- Some groups have used PRA cutoff of >/= 80 %
- In our Canadian KPD data and that of some other areas, the likelihood of DSA neg really drops at PRA >/= 97
- Thus far our national highly sensitized Registry used 95% as cutoff but we are considering increasing that

# HSP Candidate Participation by cPRA




| cPRA | 95% | 96% | 97% | 98% | 99% | 100% |
|---|---|---|---|---|---|---|
| HSP Transplanted | 32 | 22 | 36 | 53 | 62 | 59 |
| HSP Candidates Waiting (Active) | 3 | 5 | 7 | 14 | 53 | 411 |
| % Transplanted* | 48% | 42% | 45% | 43% | 31% | 8% |

***Proportion based on all candidates who were ever active as HSP program candidates***

**Results as of October 6, 2016**

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# Allocating DD Kidneys to High PRA Recipients
# Gebel et al Clin JASN, 2016

- Simulation study of effect of algorithm change in US
- Found virtual X Match negative donors for 20% of those with PRA 100
- However about 25% unlikely to receive a single offer

# Conclusions

- Sensitization limits access to transplantation
- Efforts should be made to improve standardization of methods for defining DSA and antibody titre and strength
- Optimal long term outcomes and freedom from morbidity/mortality are achieved with DSA negative transplants
- Where feasible and if living donor available KPD Registries offer the best long term outcomes for those with living donors
- Registries prioritizing highly sensitized on the deceased donor list improve access

# Conclusions 2

- In very highly sensitized with poor prospect of finding compatible donor, survival is limited
- Therefore, if a living donor available, desensitization, with or without KPD, needs to be considered

# DESENSITIZATION

# Desensitization

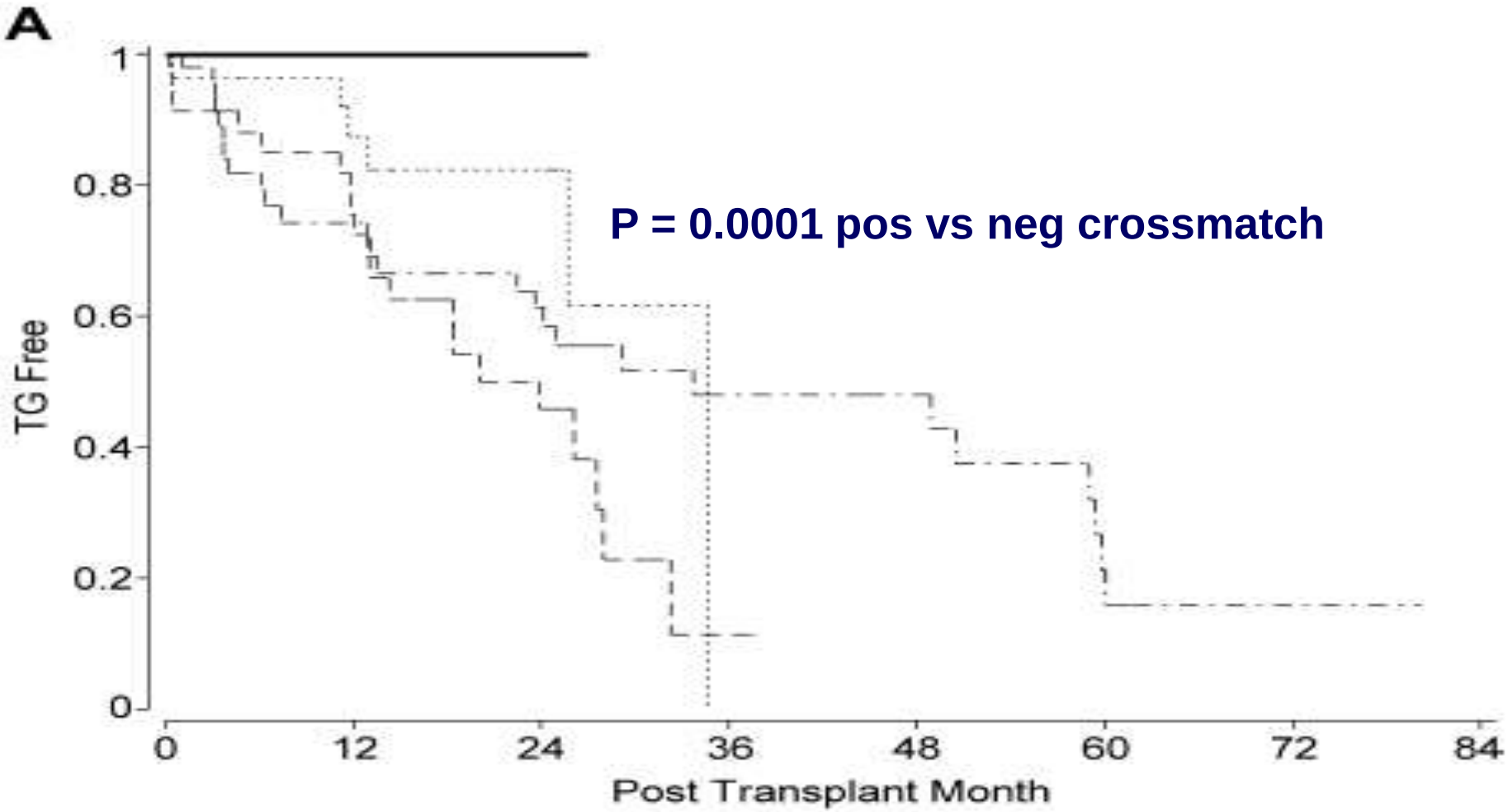
- The strategy of using various agents to reduce PRA pre transplant so that fewer/lower titre DSA, ideally with negative flow cross match
- Optimal agents not clear but include IVIg, plasma exchange, ATG, rituximab, bortezumib, eculizumab
- May be used together with kidney paired donation for very highly sensitized

# Benefits of Desensitization

- Allows earlier transplantation with good short term success
- Permits living donor to give directly to their intended recipient
- Avoids costs/waits/complexities of KPD and Registries

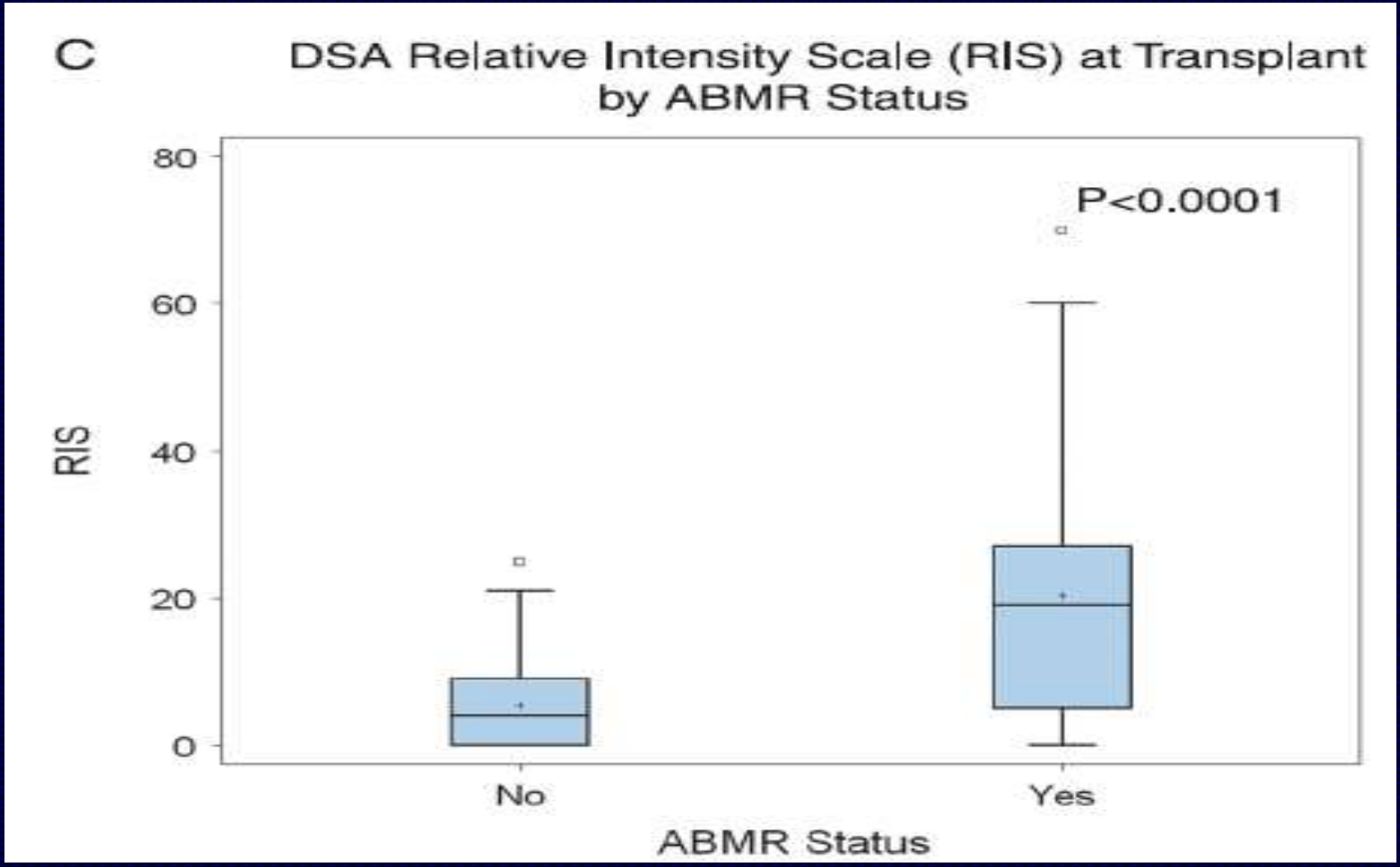
# Incidence of Transplant Glomerulopathy Pos vs Neg Cross Match

**Gloor et al AJT, 2010**



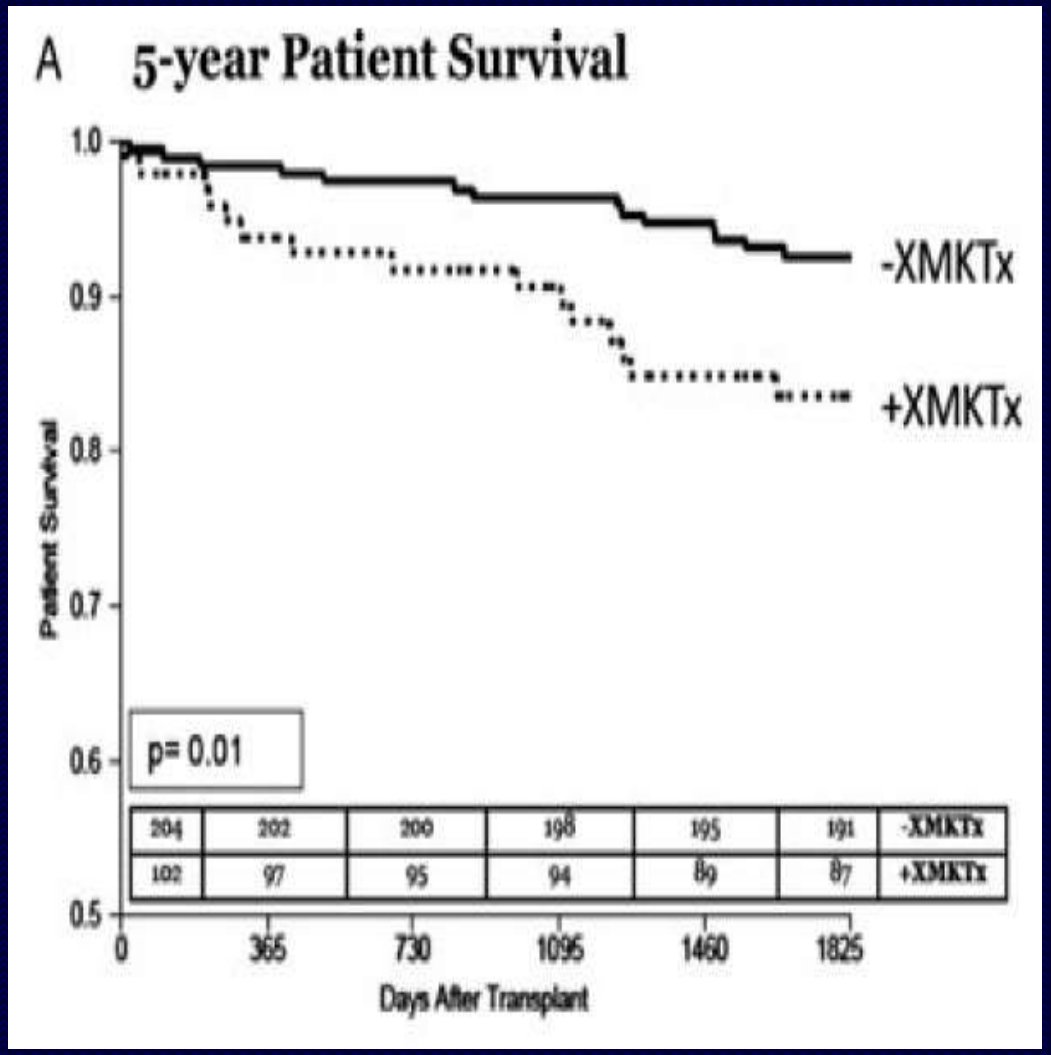
# Factors Predicting Graft Loss in Desensitized Patients

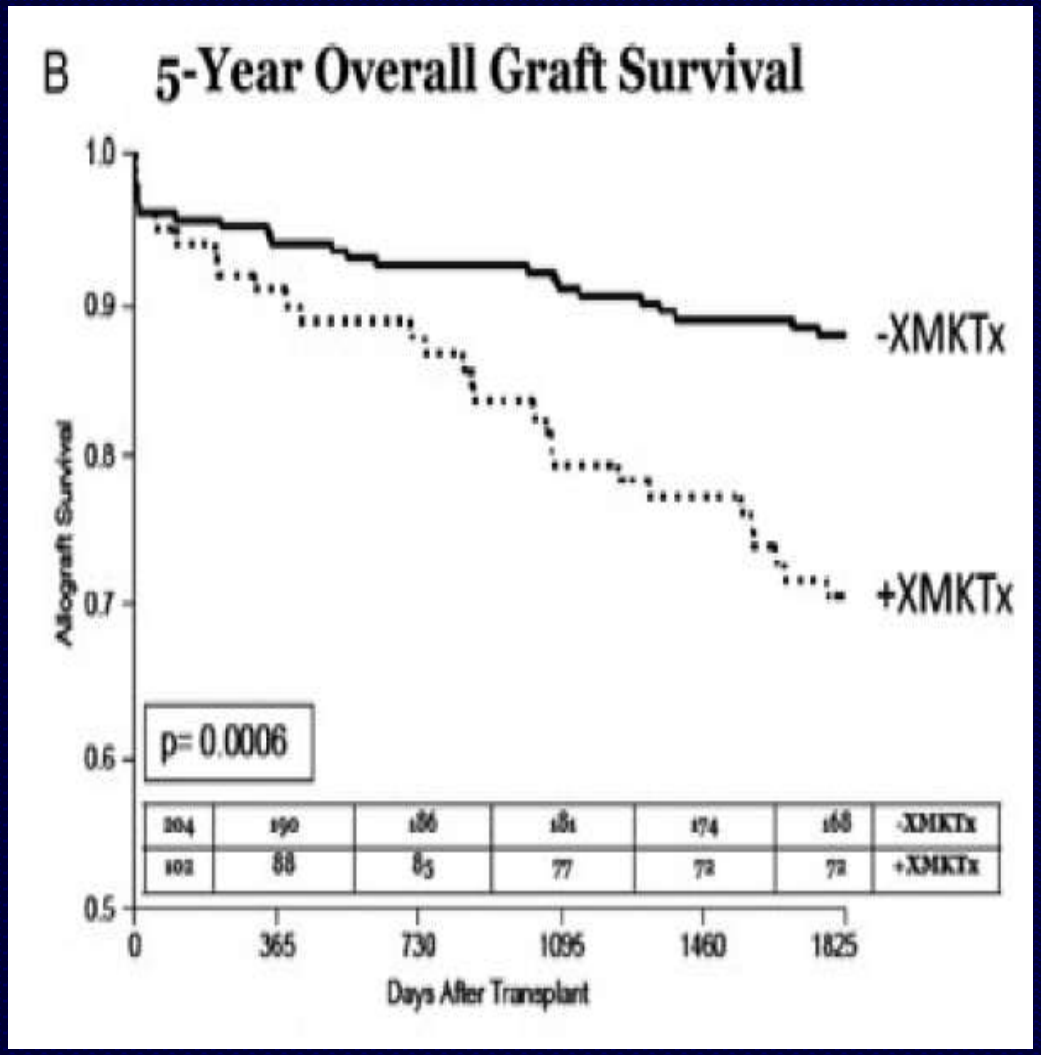
## Vo et al Transplantation, 2015



# Outcomes in DSA Positive Renal Transplantation

## Bentall et al AJT, 2013



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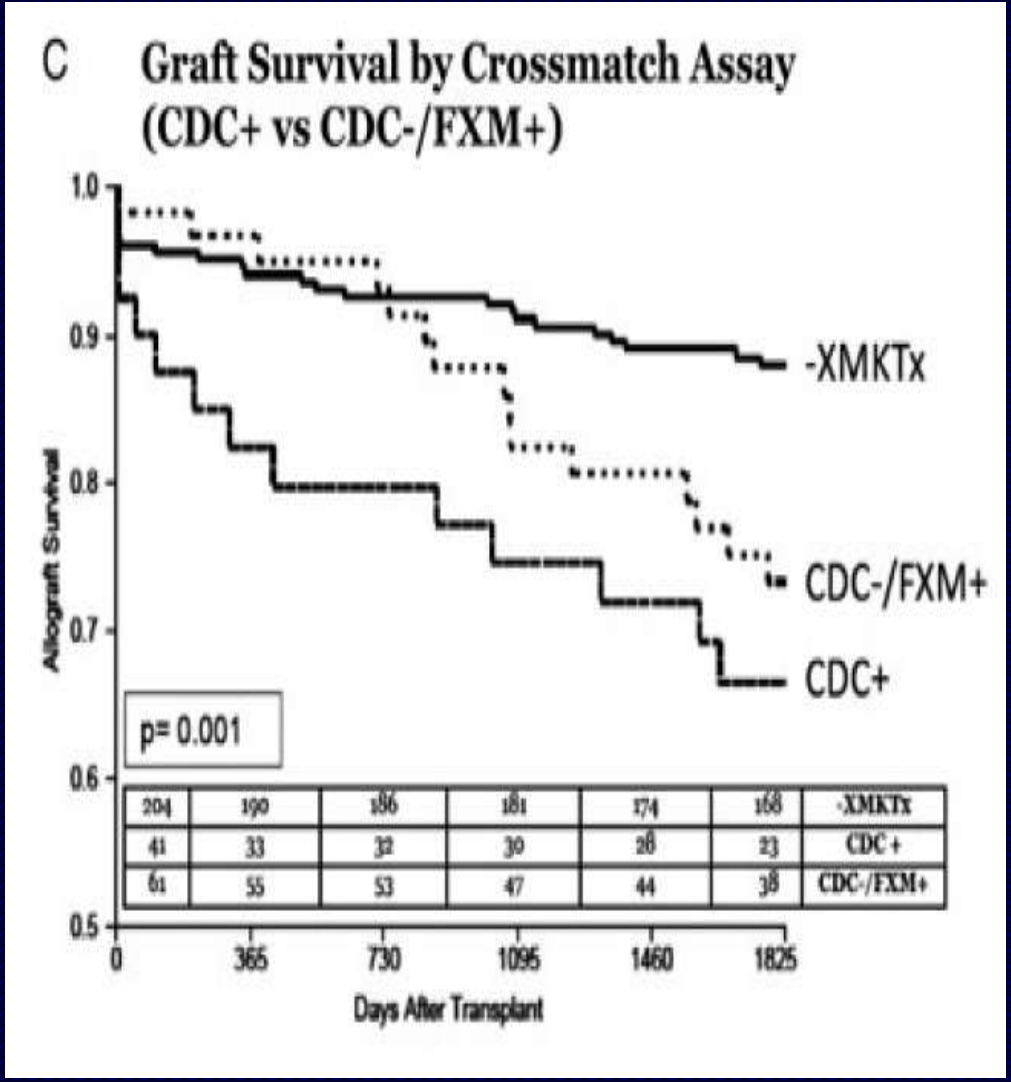
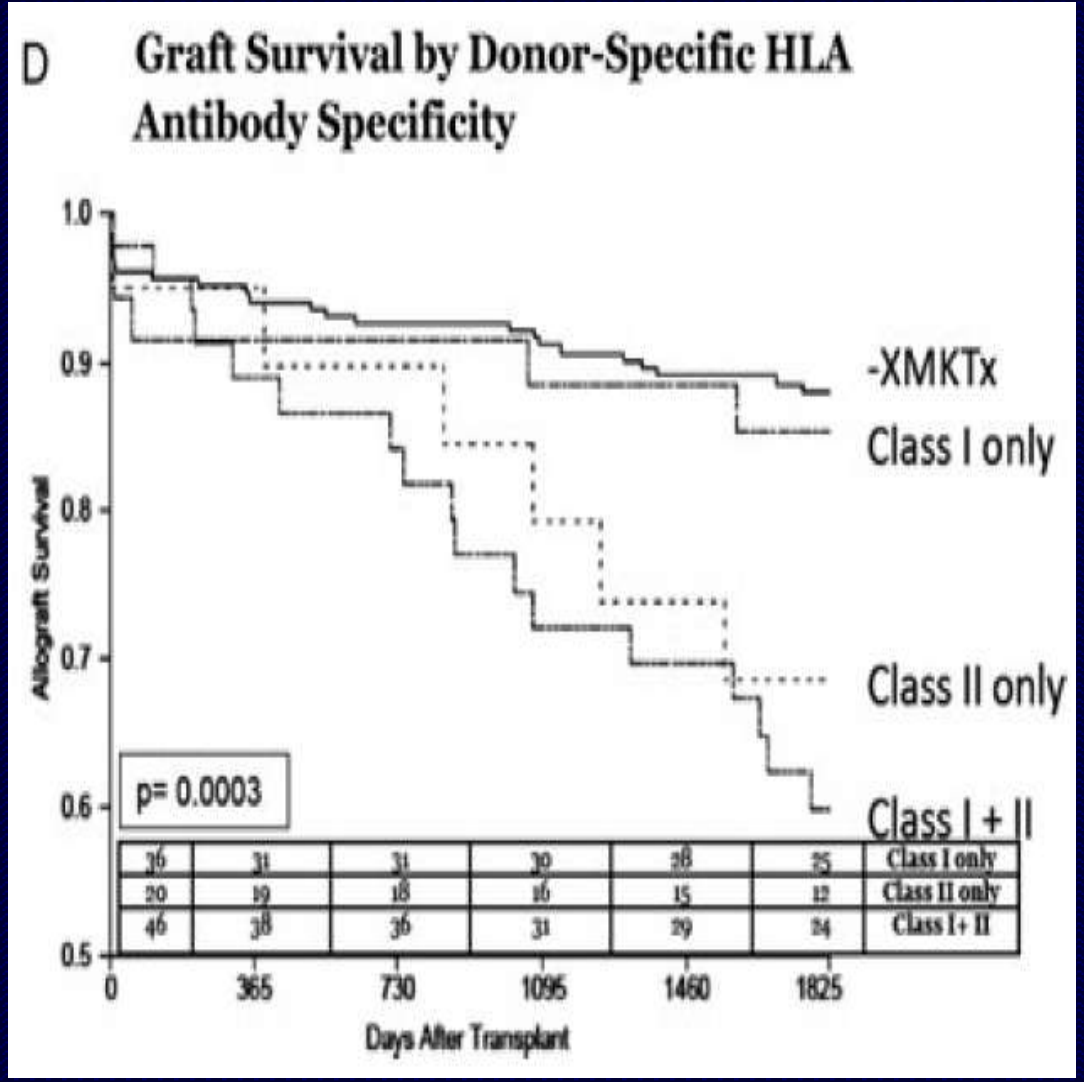


# Antibody Mediated Rejection Within 1 Year Post Transplant and Outcome

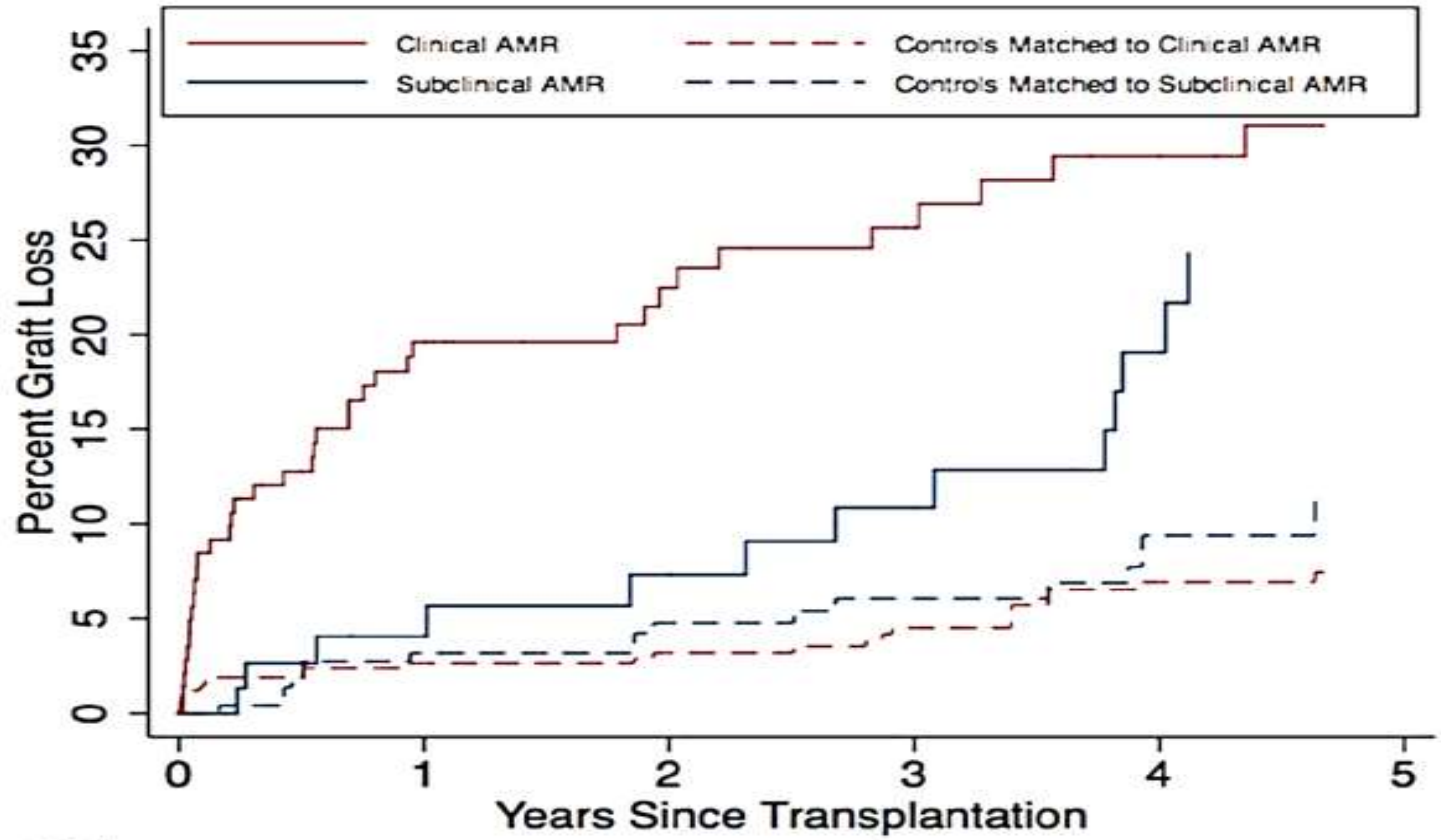
## Orandi et al AJT, 2015

**Table 2A:** Antibody-mediated rejection incidence and presentation[1] by transplant type

| Transplant type | Incidence of AMR | | |
|---|---|---|---|
| | Overall (n = 219) | Subclinical presentation[2] (n = 77) | Clin presentation (n = 142) |
| Deceased donor: compatible | 1.7% | 0.1% | 1.6% |
| Deceased donor: HLA-incompatible | 44.7% | 16.5% | 28.2% |
| Live donor: compatible | 0.7% | 0.5% | 0.2% |
| Live donor: ABO-incompatible[3] | 13.6% | 2.5% | 11.1% |
| Live donor: HLA-incompatible | 47.4% | 18.1% | 29.3% |
| Overall | 9.5% | 3.3% | 6.1% |

# Antibody Mediated Rejection Within 1 Year Post Transplant and Outcome

## Orandi et al AJT, 2015




Number at risk

| | | | | | | |
|---|---|---|---|---|---|---|
| Clinical AMR | 142 | 104 | 82 | 68 | 55 | 42 |
| Controls Matched to Clinical AMR | 426 | 396 | 337 | 289 | 229 | 184 |
| Subclinical AMR | 77 | 66 | 57 | 50 | 39 | 29 |
| Controls Matched to Subclinical AMR | 231 | 209 | 181 | 143 | 108 | 80 |

# Desensitization Outcomes- All Cause Graft Loss By Antibody Strength

**Orandi et al AJT, 2014**

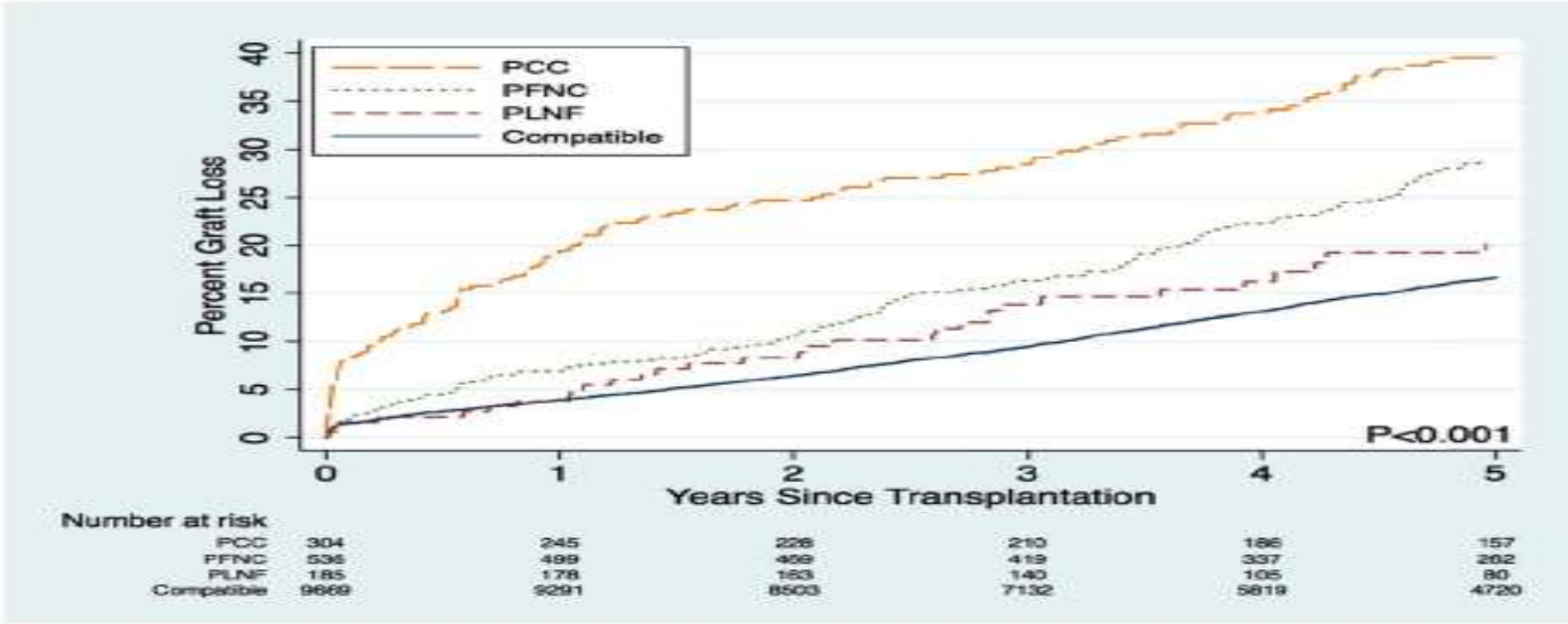



**Figure 1: All-cause graft loss, by antibody strength.** PCC, positive cytotoxic crossmatch; PFNC, positive flow, negative cytotoxic crossmatch; PLNF, positive Luminex, negative flow crossmatch.

# Desensitization Outcomes- Mortality vs Antibody Strength

## Orandi et al AJT, 2014

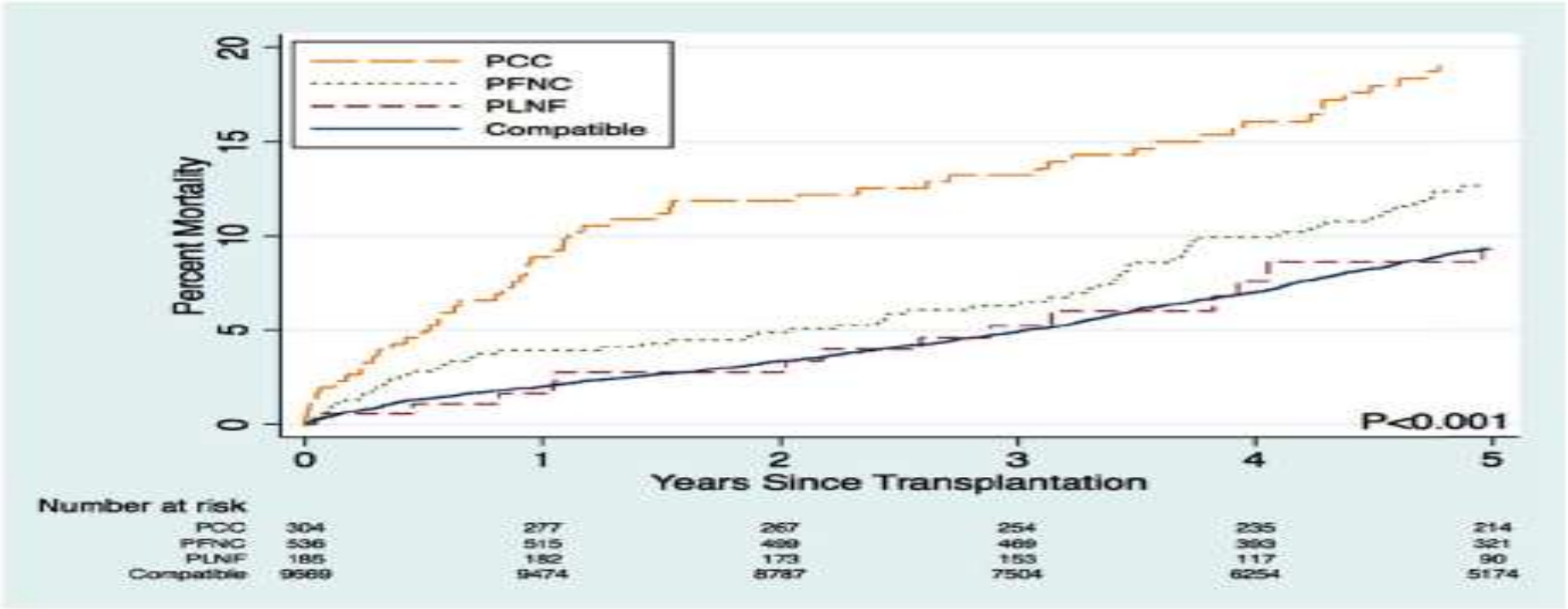


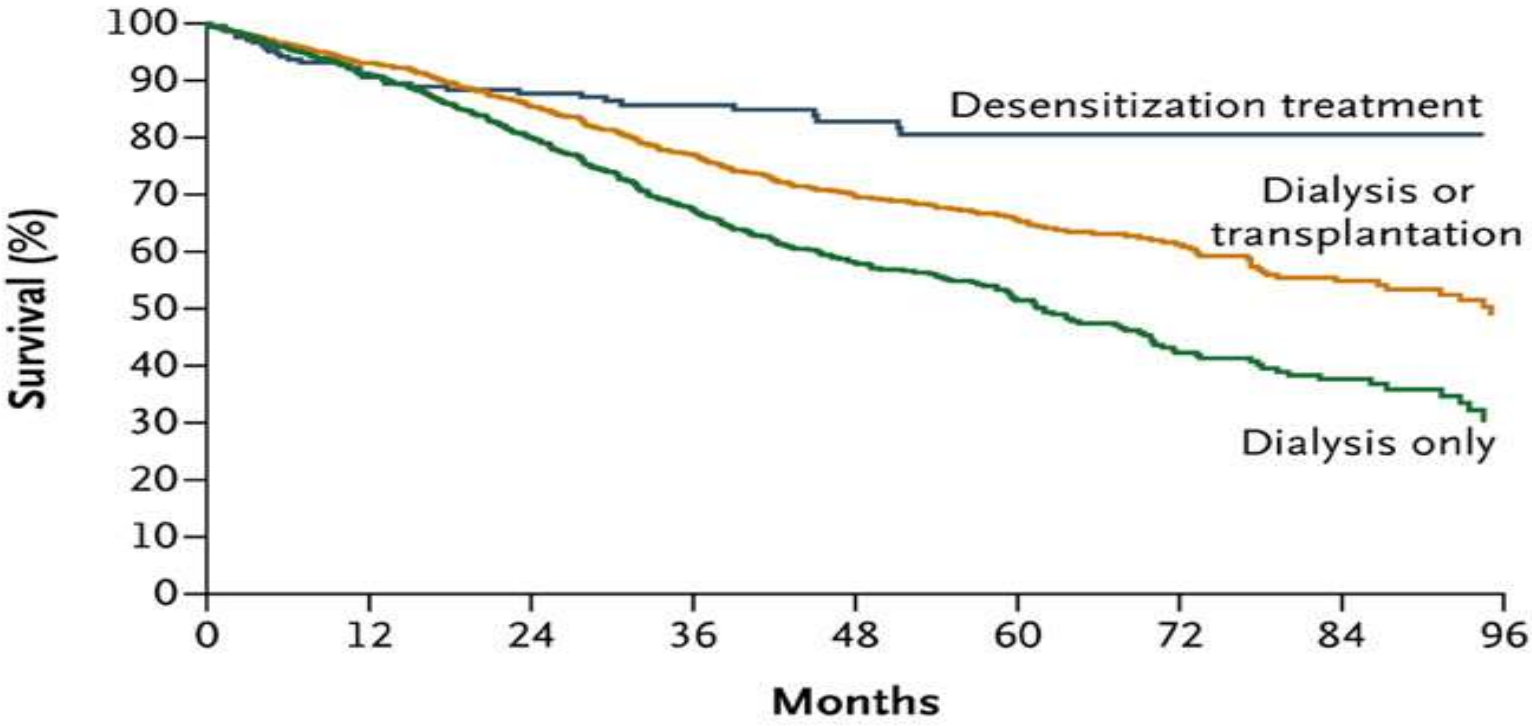

**Figure 2: Posttransplant mortality, by antibody strength.** PCC, positive cytotoxic crossmatch; PFNC, positive flow, negative cytotoxic crossmatch; PLNF, positive Luminex, negative flow crossmatch.

# Caveats

- No standardization of assays for antibody determination or cross match
- Different protocols for desensitization
- Different protocols for treatment of AMR
- Small number of patients at risk at 5 years especially for Flow X match negative group

# Outcomes in Highly Sensitized Pt

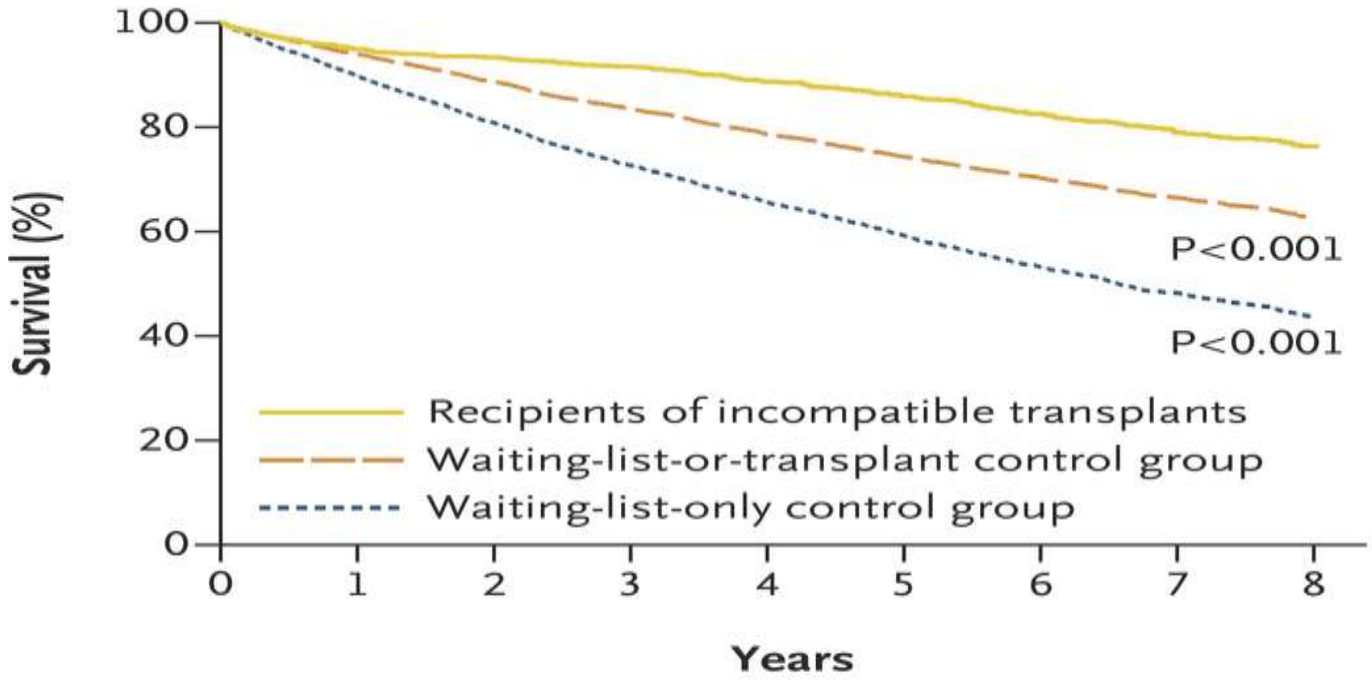
## Segev et al NEJM, 2011




| No. at Risk | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| Desensitization treatment | 210 | 170 | 143 | 110 | 75 | 58 | 42 | 28 | 14 |
| Dual therapy | 1027 | 854 | 688 | 497 | 321 | 230 | 157 | 96 | 41 |
| Dialysis only | 1012 | 822 | 626 | 419 | 250 | 159 | 93 | 54 | 17 |

# Survival in Incompatible Transplantation vs Remaining on the List

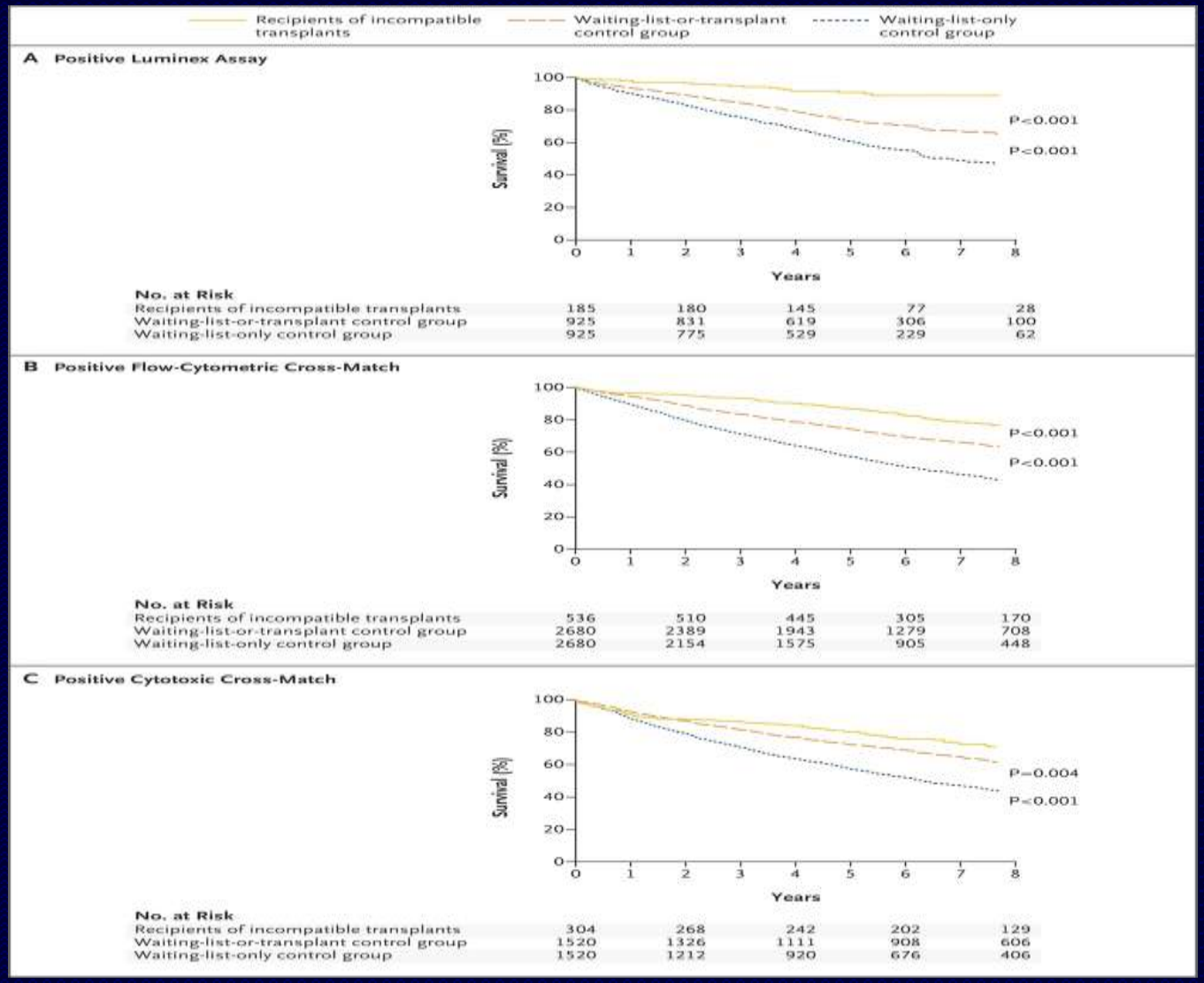
## Segev et al NEJM, 2016




| No. at Risk | | | | | |
|---|---|---|---|---|---|
| Recipients of incompatible transplants | 1025 | 958 | 832 | 584 | 327 |
| Waiting-list-or-transplant control group | 5125 | 4546 | 3673 | 2493 | 1414 |
| Waiting-list-only control group | 5125 | 4141 | 3024 | 1810 | 916 |

# Survival vs Crossmatch Type

## Segev et al NEJM, 2016



# IVIg Alone Vs IVIg plus PP/Anti CD20Ab

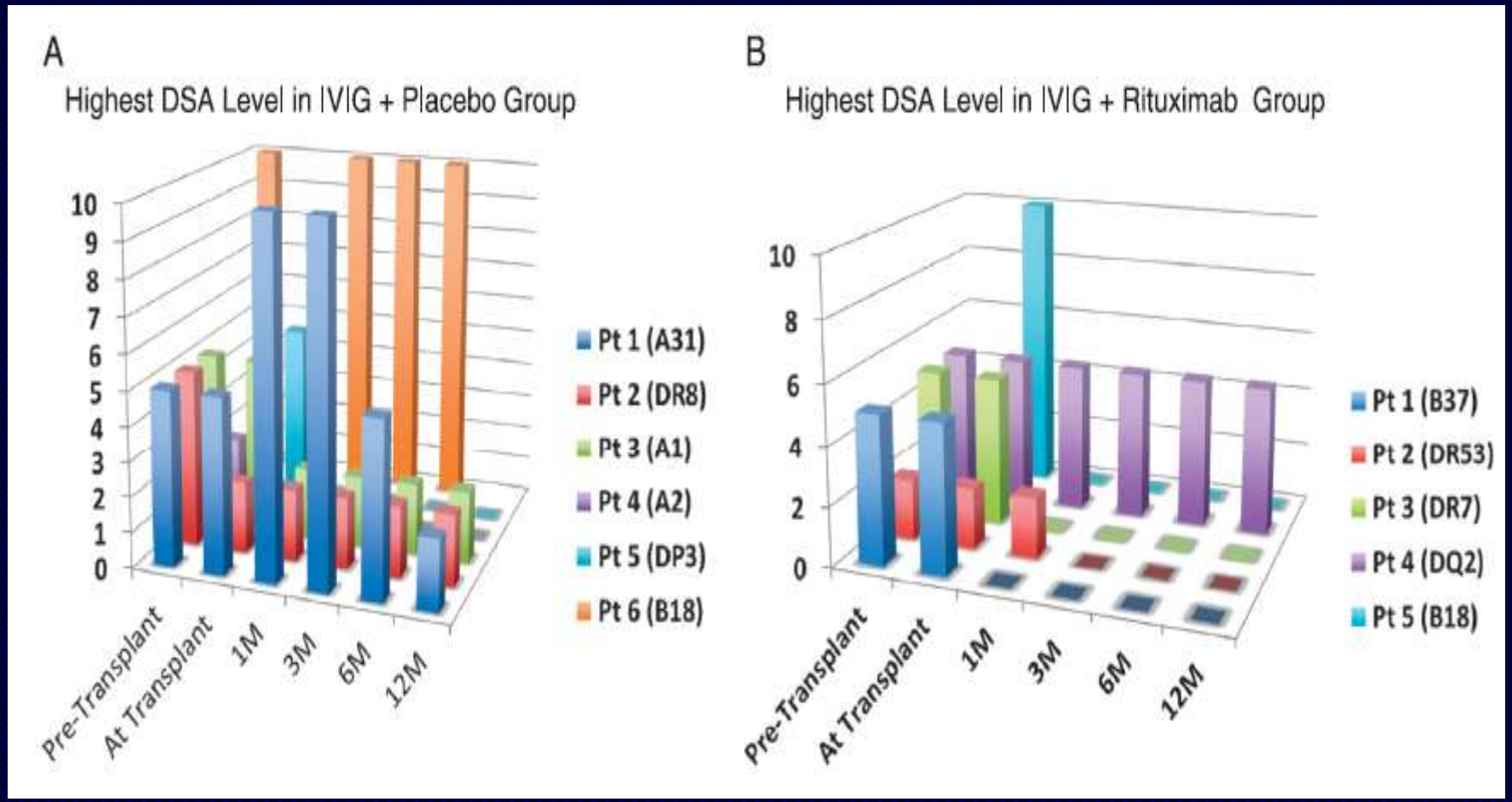
## Stegall et al AJT, 2006

**Table 4:** Humoral rejection rates

| Negative crossmatch at transplant | | N | Humoral rejection |
|---|---|---|---|
| | High-dose IVIG responders | 5 | 4/5 (80%) |
| | PP/IVIG/anti-CD20 (includes 3 IVIG nonresponders) | 30 | 11/30 (37%) |
| | PP/IVIG/monitoring | 14 | 4/14 (29%) |
| Positive crossmatch at transplant | High-dose IVIG, PP/IVIG/anti-CD20 nonresponders | 10 | 7/10 (70%) 5/10 allograft loss (50%) |

# IVIg +/- Rituximab for Desensitization

## Vo et al, Transplantation, 2014



# Systematic Review of Rituxumab in Desensitization

## Macklin et al Transplantation, 2014

**TABLE 3.** Outcomes of studies of rituximab for desensitization in recipients with positive DSA

| Study (yr) country | Inclusion criteria | No. of patients (RTX/non-RTX) | Study period, mo | Treatment regimen (RTX/non-RTX) | Baseline IS | T-cell induction therapy |
|---|---|---|---|---|---|---|
| *Retrospective cohort studies* | | | | | | |
| Hirai (2012) Japan (*27, 28, 46–50*) | DSA MFI >800 | 113 (74/39) | 60 | RTX+PP/±PP | TAC, MMF+CS | BXM |
| Loupy (2010) France (*29, 51, 52*) | DSA MFI >1000 | 96 (43/53) | 12 | RTX, IVIg +PP/IVIg | CNI, MMF+CS | ATG |

| Patient survival | Graft survival | Incidence of rejection | Graft function | Negative CDC-XM | Adverse effects | Downs and Black Score |
|---|---|---|---|---|---|---|
| Not reported | Not reported | Favors RTX | No difference | Favors RTX | Not reported | 19/32 |
| Not reported | Not reported | Favors RTX | No difference | No difference [c] | Not reported | Not applicable |

# Eculizumab vs Retrospective Control as Prophylaxis in Flow Cross Match Pos Transplants

## Stegall et al AJT, 2011

**Table 2:** Posttransplant outcomes in the eculizumab-treated and control groups

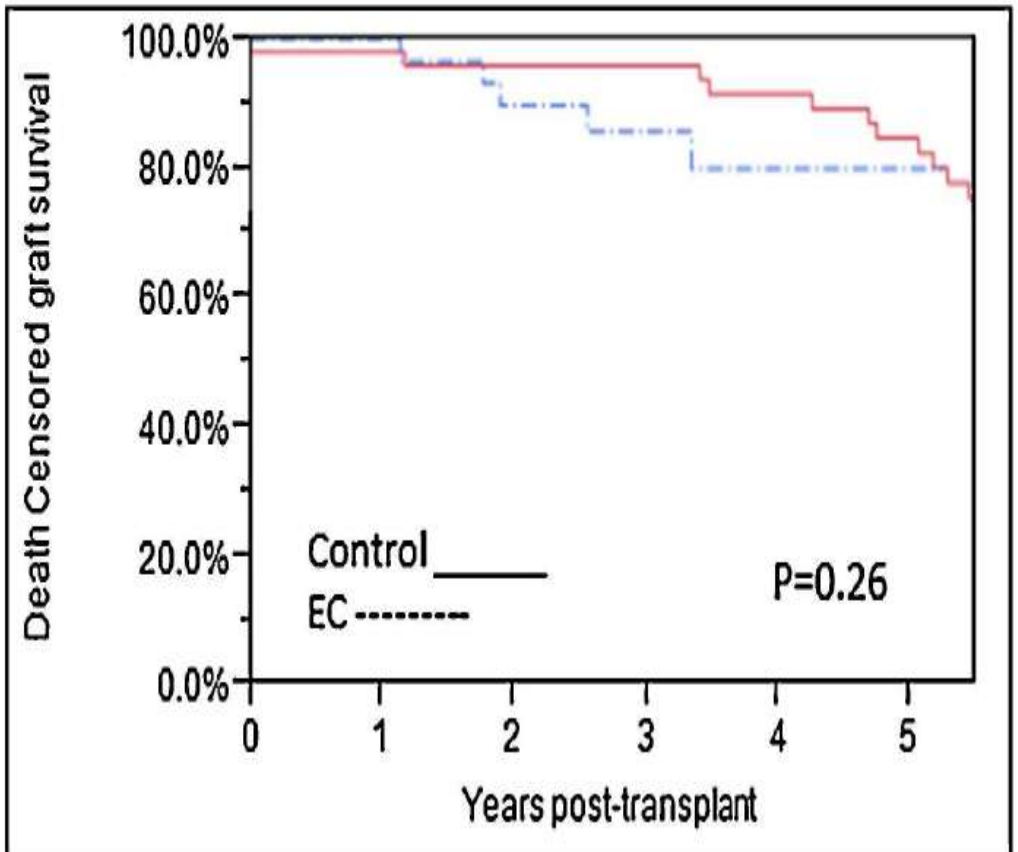
| Category | Eculizumab group (n = 26) | Control group (n = 51) | p-Value |
|---|---|---|---|
| Follow-up (mean months ± SD, range) | 11.8 ± 6.3 (3.0–27.5) | 48.8 ± 14.1 (7.8–69.8) | |
| Graft survival at 1 year (n, %) | 16/16 (100%) | 49/51 (96%) | 1.00 |
| Antibody-mediated rejection ≤ 3months (n, %) | 2 (7.7%) | 21 (41%) | 0.0031 |
| Patients developing high DSA levels ≤ 3 months[1] | 13 (50%) | 22 (43%) | 0.63 |
| High DSA biopsies C4d+ (n, %) | 13 (100%) | 20 (91%) | 0.52 |
| High DSA and C4d+ biopsies showing AMR (n, %) | 2 (15%) | 20 (100%) | <0.0001 |
| Cellular rejection ≤3 months (n, %) | 1 (6.2%) | 1 (2%) | 0.42 |
| Plasma exchange posttransplant | | | |
| Patients receiving PE (n, %) | 3 (12%) | 39 (76%) | <0.0001 |
| Number of PE treatments (mean ± SD) | 0.35 ± 1.1 | 7.9 ± 7.5 | <0.0001 |
| Splenectomy (n, %) | 0 (0%) | 9 (18%) | 0.025 |
| Graft dysfunction in first month (mg/dL) (maximum serum creatinine – nadir serum creatinine) | 0.45 ± 0.37 | 0.93 ± 1.15 | 0.05 |
| Histology at 1 year | | | |
| Transplant glomerulopathy incidence (n, %) | 1/15 (6.7%) | 15/42 (36%) | 0.044 |

# Death Censored Graft Survival and Causes of Graft Loss

## Cornell et al AJT, 2015

Cornell et al

A.

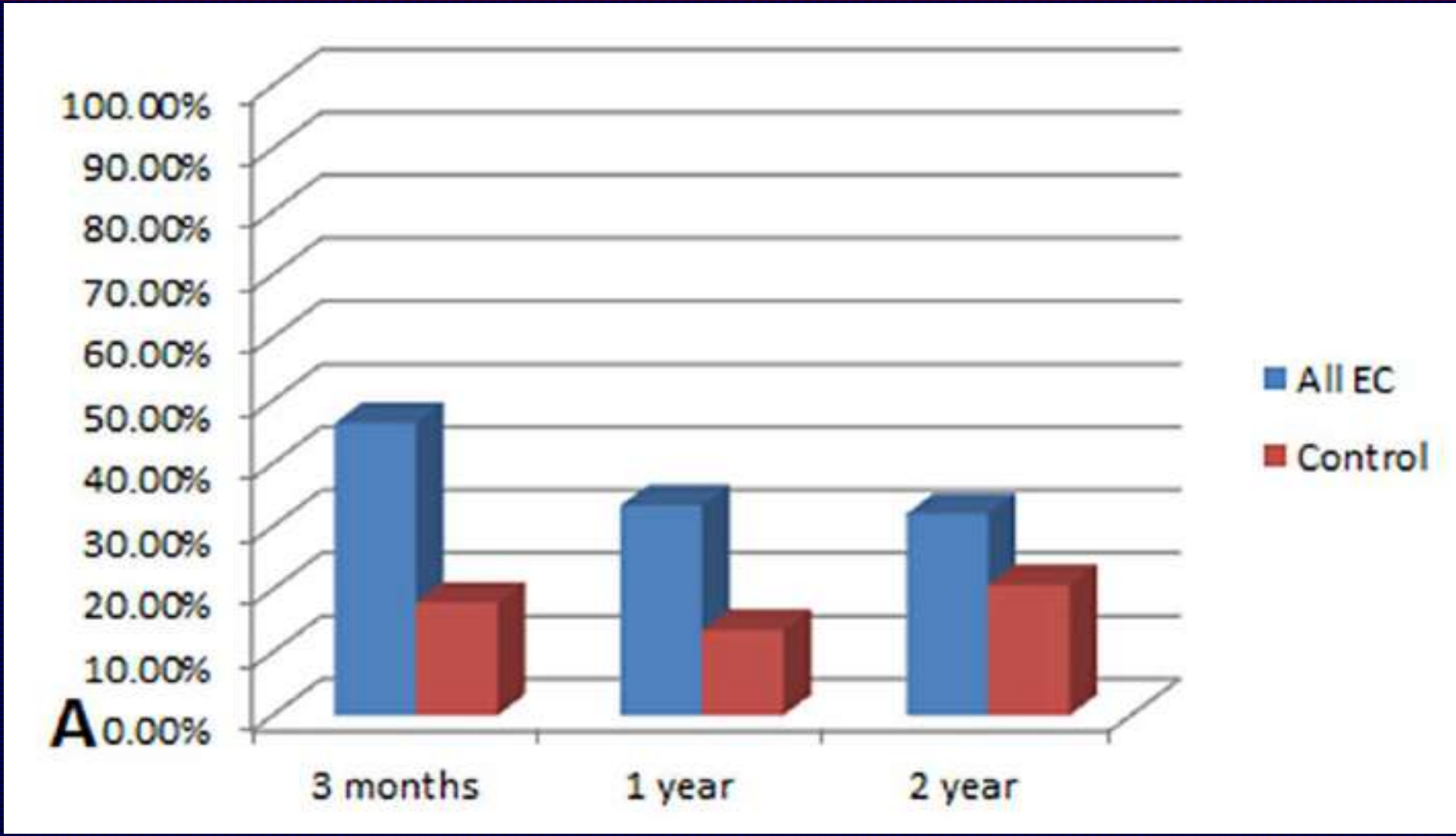



B.

| | Eculizumab n=6 | Control n=17 | p-value |
|---|---|---|---|
| Transplant glomerulopathy | 5(83.3%) | 10 (58.8%) | P=0.37 |
| Death with Function | 1 (16.7%) | 3 (17.6%) | P=1.0 |
| Recurrent Focal Segmental Glomerulosclerosis | 0 (0%) | 1 (5.9%) | P=1.0 |
| Recurrent IgA Nephropathy | 0 (0%) | 1 (5.9%) | P=1.0 |
| Late Combined Cellular & Antibody Mediated Rejection | 0 (0%) | 1 (5.9%) | P=1.0 |
| Unknown | 0 (0%) | 1 (5.9%) | P=1.0 |

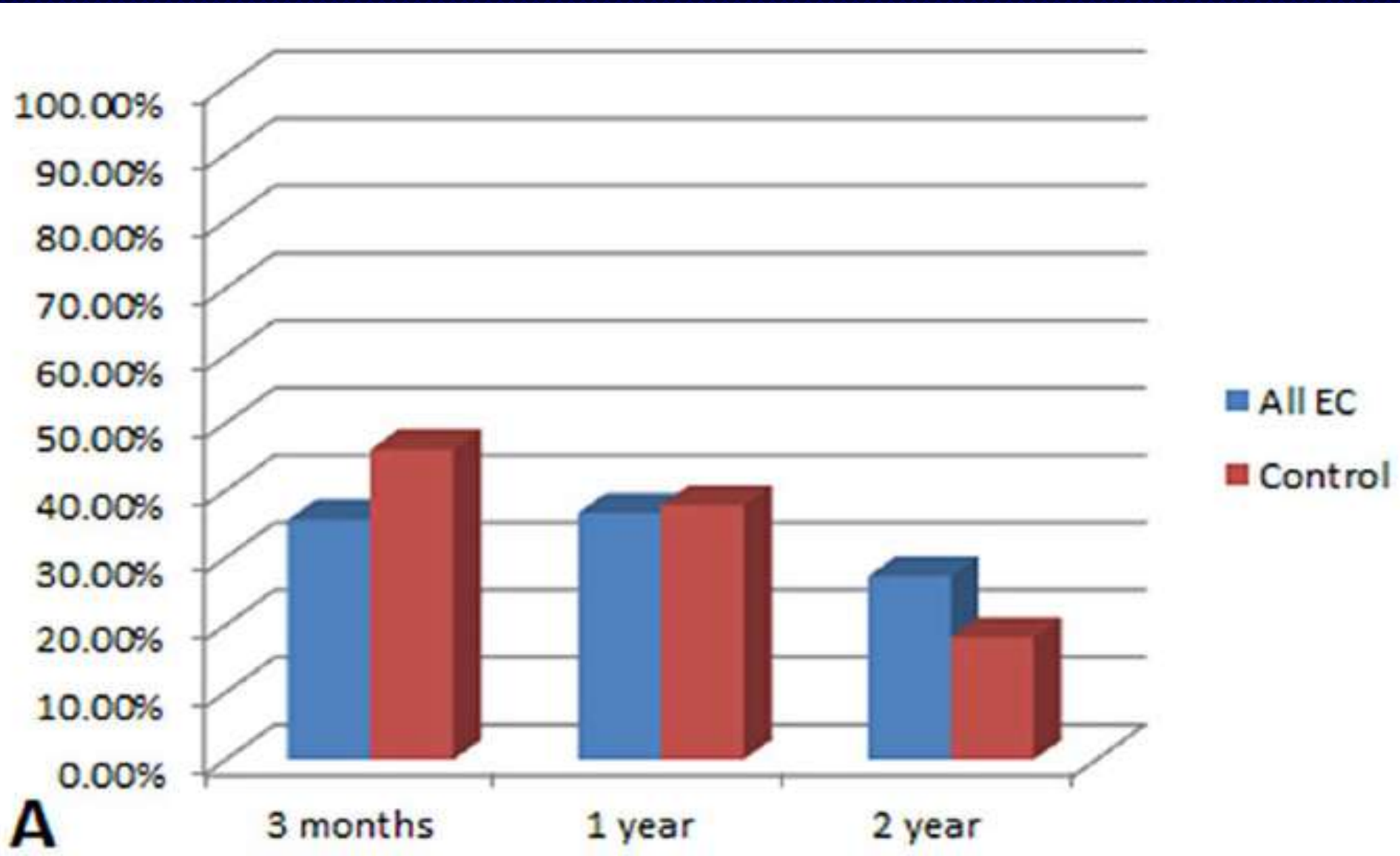
# C4d in Each Group

## Cornell et al AJT, 2015



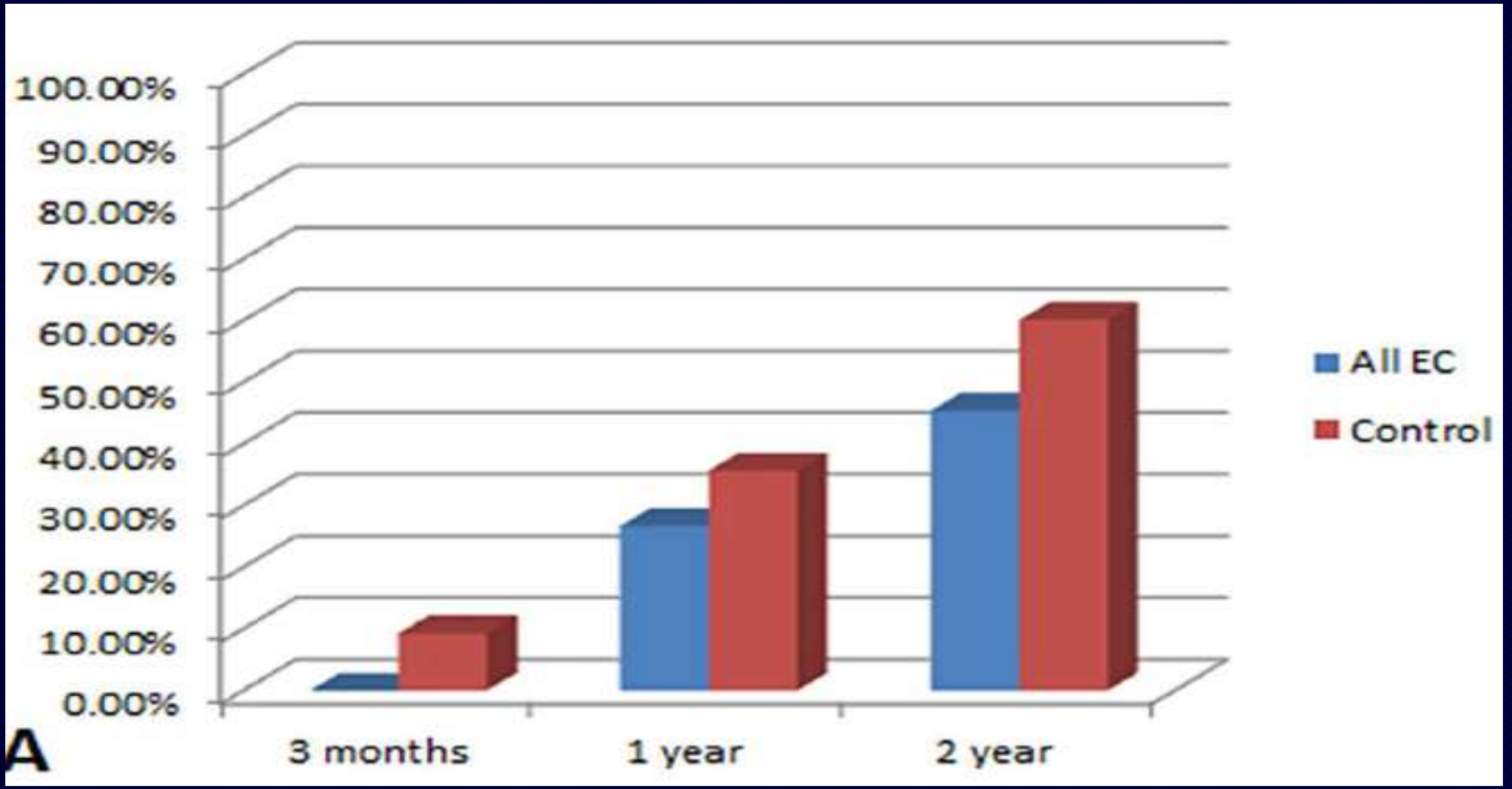
# Subclinical ABMR

## Cornell et al AJT, 2015



# Transplant Glomerulopathy

## Cornell et al AJT, 2015



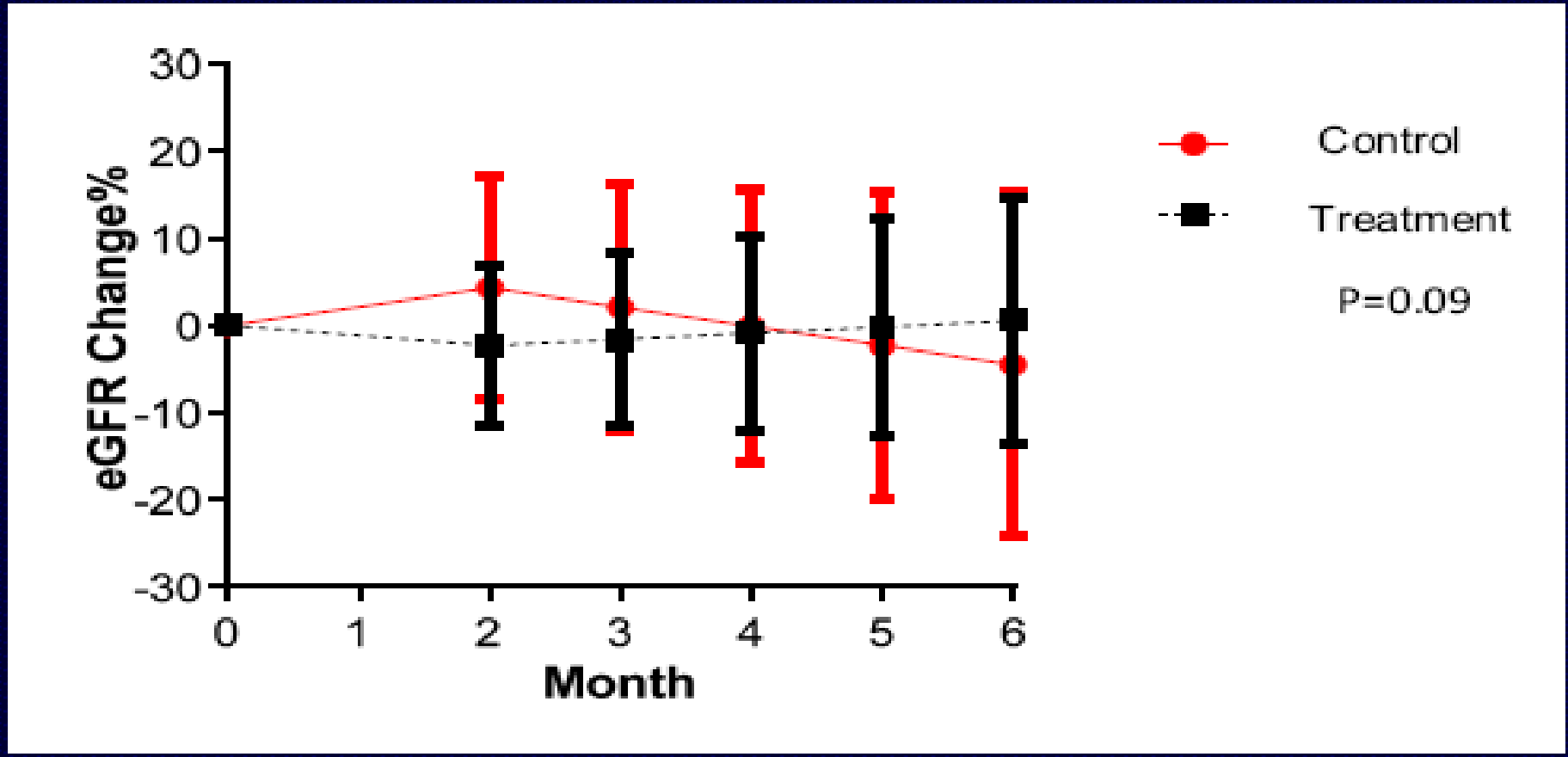
# Eculizumab in DSA pos Recipients

## Glotz et al ESOT, 2016

- 80 DSA pos recipients got Eculizumab prophylactically
- Acute ABMR at 1 year 6% vs 30% historical controls
- GS (87%) similar to DSA negative at 1 year
- Creatinine at 1 year 158uM

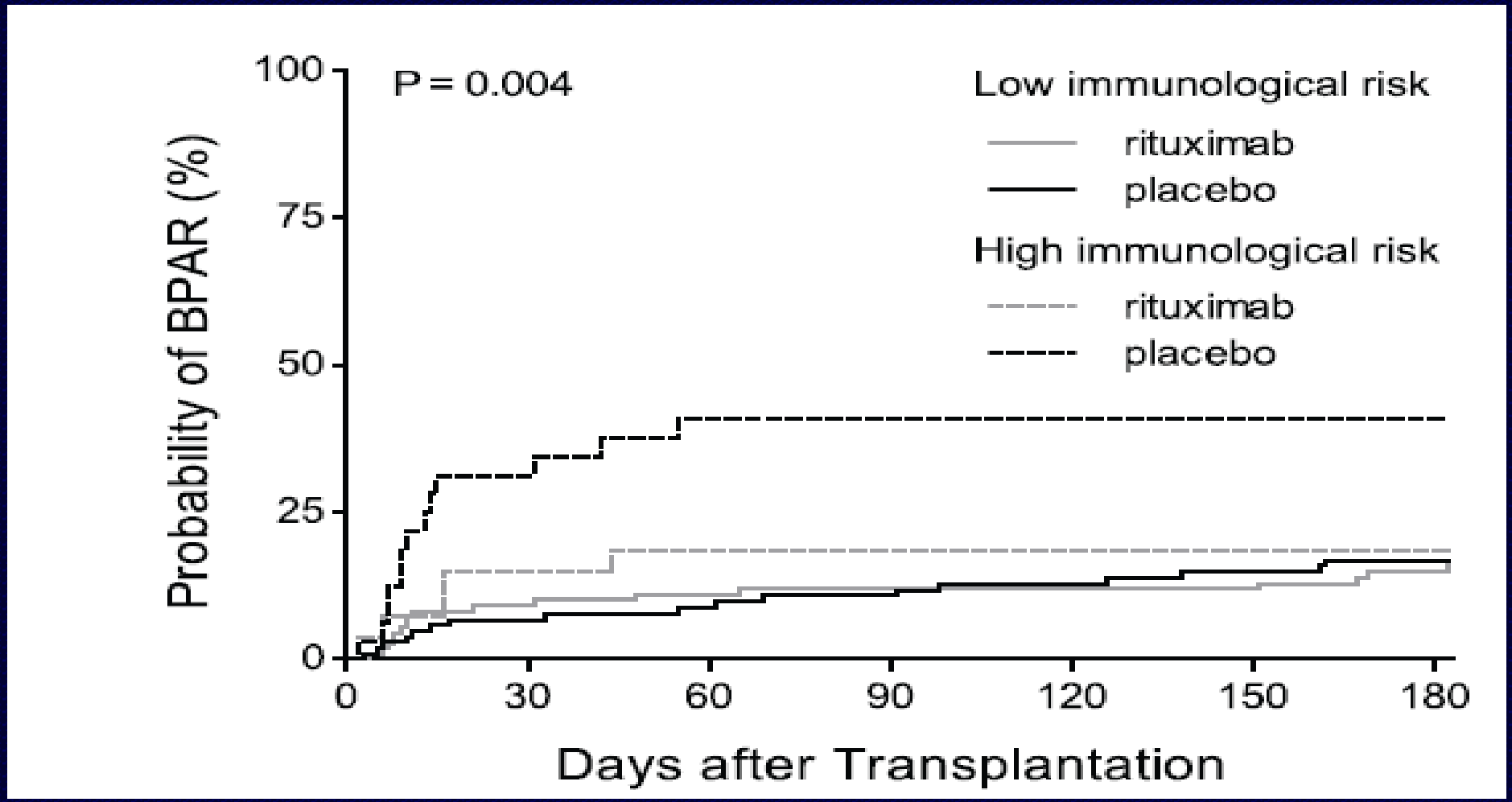
# Pilot Study to Determine Effect of Eculizumab in DSA pos and Falling GFR

**Kulkarni et al AJT, 2016**



# RCT of Rituxumab vs Placebo as Induction Therapy

## Van Den Hoogen et al AJT, 2015



# Randomized Pilot of Bortezumib and Rituxumab in Sensitized Patients

## Ejaz et al AJT, 2013

**Table 4:** Rejection data for the first year following transplantation[1]

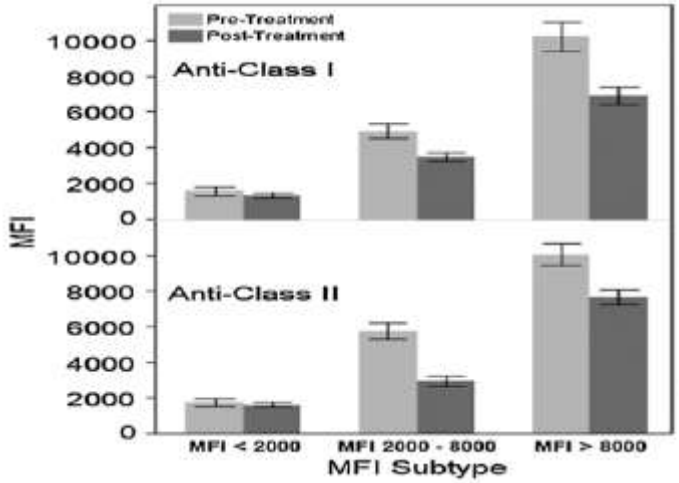
| | rATG alone (N = 10) | rATG + Ritux (N = 10) | rATG + Bortez (N = 10) | rATG + Ritux + Bortez (N = 10) | p-Value |
|---|---|---|---|---|---|
| Overall acute rejection, n (%) | 2 (20%) | 0 (0%) | 5 (50%) | 3 (30%) | 0.084 |
| Early acute rejection, n (%) | 2 (20%) | 0 (0%) | 3 (30%) | 2 (20%) | 0.46 |
| Late acute rejection, n (%) | 0 (0%) | 0 (0%) | 2 (20%) | 1 (10%) | 0.60 |
| First rejection episode, n (%) | | | | | |
| Antibody-mediated rejection | 1 (10%) | 0 (0%) | 3 (30%) | 1 (10%) | 0.36 |
| Acute cellular rejection | 1 (10%) | 0 (0%) | 1 (10%) | 0 (0%) | 1.00 |
| Mixed acute rejection | 0 (0%) | 0 (0%) | 1 (10%) | 2 (20%) | 0.60 |

**Table 5:** Patient survival, renal allograft survival and renal allograft functional outcomes for the first year after transplantation[1]

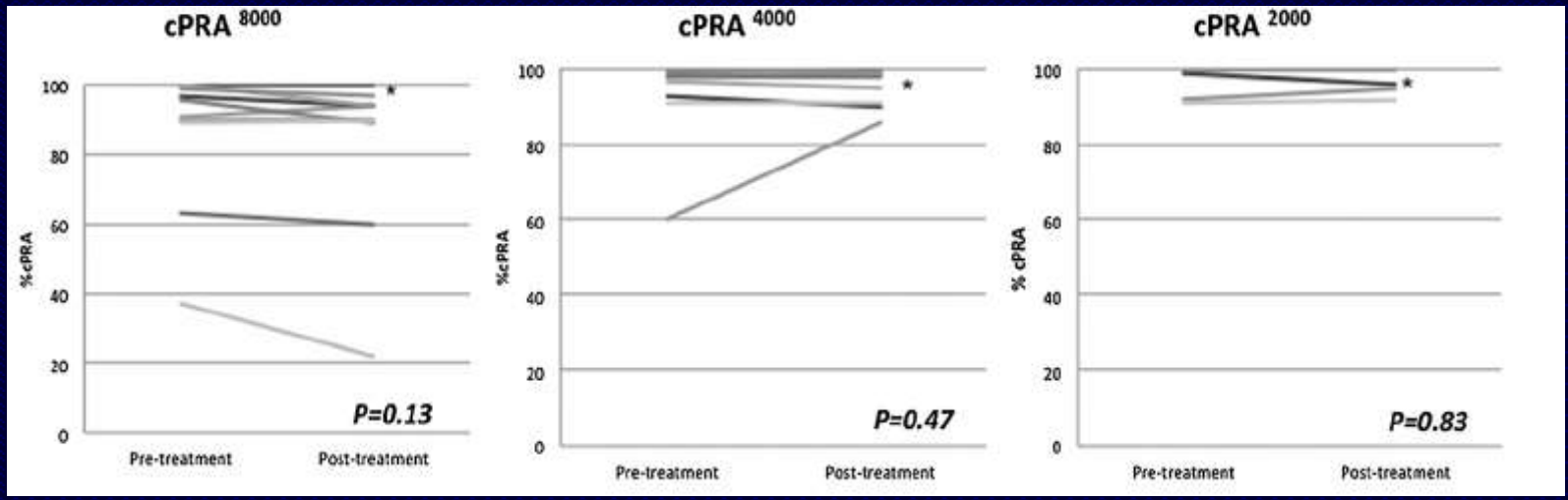
| | rATG alone (N = 10) | rATG + Ritux (N = 10) | rATG + Bortez (N = 10) | rATG + Ritux + Bortez (N = 10) | p-Value |
|---|---|---|---|---|---|
| Patient survival, n (%) | 10 (100%) | 10 (100%) | 10 (100%) | 9 (90%) | 1.00 |
| Allograft survival, n (%) | 10 (100%) | 10 (100%) | 9 (90%) | 9 (90%) | 1.00 |
| Death-censored allograft survival, n (%) | 10 (100%) | 10 (100%) | 9 (90%) | 10 (100%) | 1.00 |

# Effect of 32 Doses of Bortezumib on Sensitization in those with DSA to Living Donors

## Moreno Gonzales et al Transplantation, 2016




| MFI Subgroup | Mean Pre-BTZ | Mean Post-BTZ | Treatment Reduction | P-value |
|---|---|---|---|---|
| **Class I** | | | | |
| < 2000 | 1608 (252) | 1380 (144) | 228 (294) | 0.44 |
| 2000-8000 | 4967 (406) | 3538 (237) | 1429 (474) | <0.01 |
| >8000 | 10267 (829) | 6938 (494) | 3328 (975) | <0.01 |
| **Class II** | | | | |
| < 2000 | 1815 (221) | 1653 (138) | 162 (264) | 0.54 |
| 2000-8000 | 5809 (490) | 2984 (278) | 2824 (570) | <0.01 |
| >8000 | 10105 (617) | 7711 (425) | 2394 (757) | <0.01 |



# Phase ½ RCT of C1 Inhibitor in Flow X Match Positive Transplants

## Vo et al Transplantation, 2015

- C1INH was safe
- C1INH may reduce ischemia perfusion injury
- C1INH reduced C1q pos HLA antibodies
- Further studies needed

# C1INH in Resistant ABMR

## Lafaucheur et al ATC, 2016

- 6 pt with ABMR resistant to IVIg, PLEX, Rituximab
- Treated with C1INH for 6 months and compared to retrospective control group
- eGFR increased by 17 ml/min vs -13 ml/min in controls
- Reduced C4d on biopsy
- Reduced C1q pos DSA from 6/6 to 1/6

# Outcomes in DSA Positive Renal Transplantation

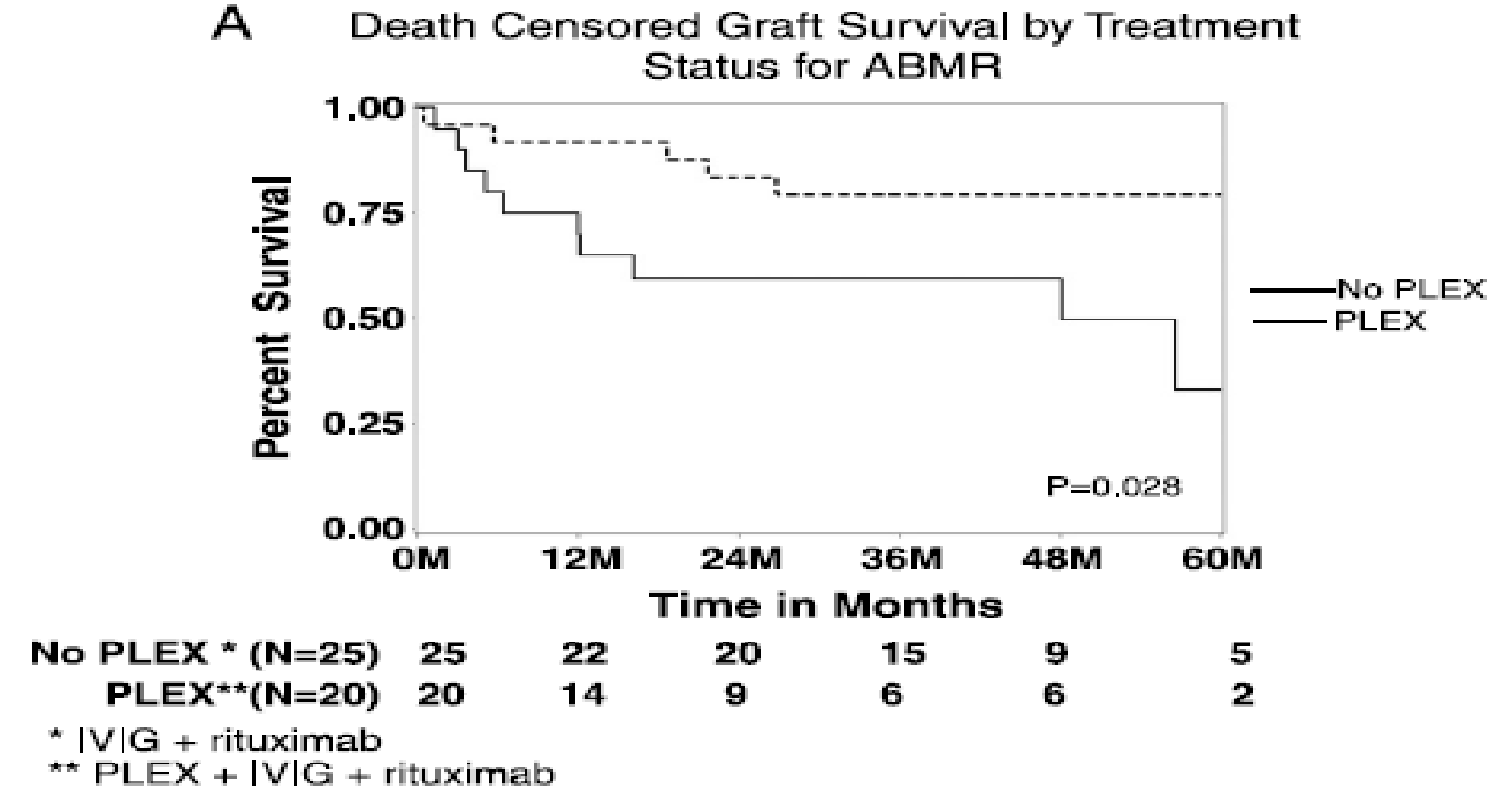
## Bentall et al AJT, 2013

**Table 2:** Summary of histologic lesions commonly associated with anti-HLA antibody. The overall incidence of histologic changes commonly associated with anti-HLA antibody found on paired surveillance biopsies obtained at 1 and 5 years after transplantation are shown

| | Chronic glomerulopathy | | Acute glomerulitis | | Peritubular capillaritis | |
|---|---|---|---|---|---|---|
| | 1 year | 5 years | 1 years | 5 years | 1 year | 5 years |
| −XMKTx | 4.2% | 7.4% | 7.4% | 6% | Not done | Not done |
| +XMKTx | 21.2% | 54.5% | 30.3% | 63.6% | 63.3% | 50% |
| Class I | 10% | 50% | 20% | 50% | 50% | 55.7% |
| Class II/I | 26.1% | 56.5% | 34.7% | 65.2% | 66.6% | 90.9% |

# Factors Predicting Graft Loss in Desensitized Patients

## Vo et al Transplantation, 2015



# Baseline DSA in Positive Crossmatch Transplantation

## Gloor et al AJT, 2010

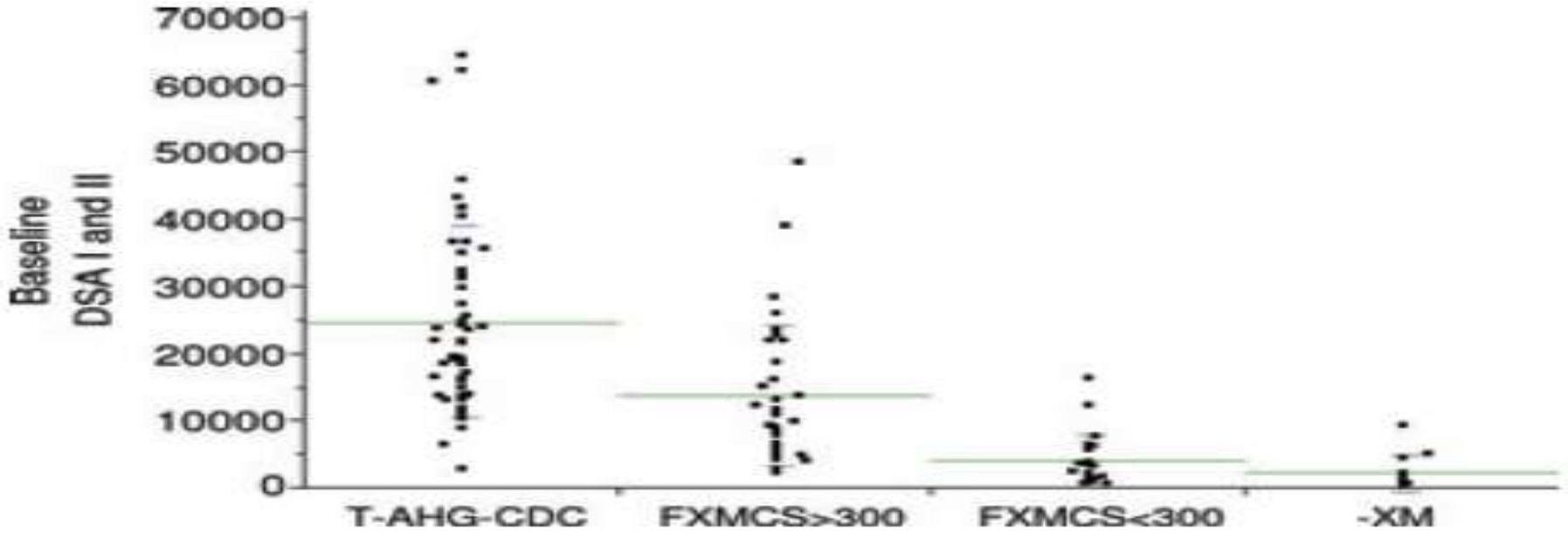
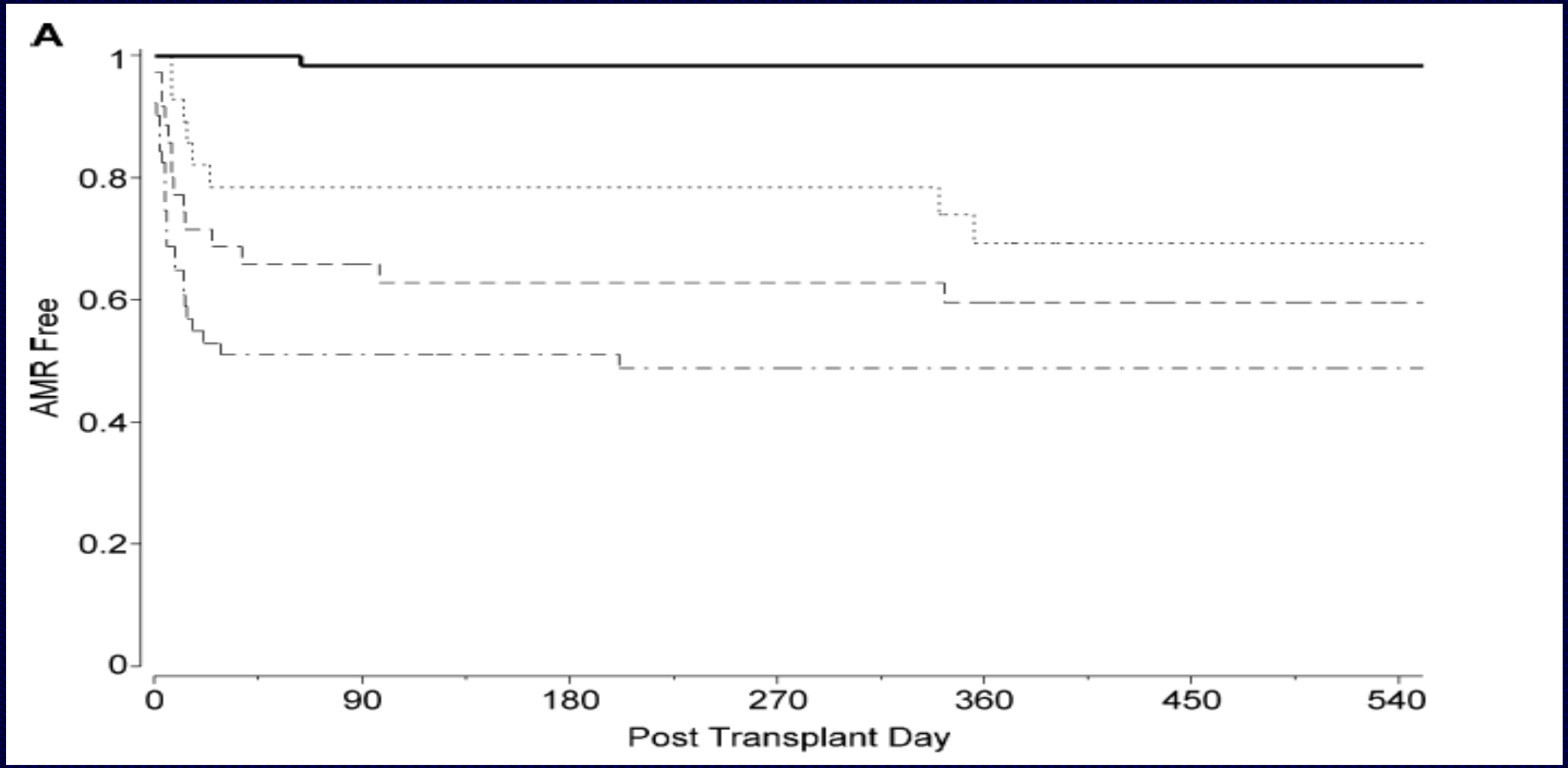



**Figure 1: Baseline DSA level analyzed using Luminex single antigen flow beads vs. cell-based crossmatch transplant group.** (A) Sum of HLA class I and II DSA combined MFI (mean ± SD): (T-AHG-CDC+: 24 649 ± 14 252; FXMCS >300: 13 722 ± 10 578; FXMCS <300: 4392 ± 4250; –XM: 2266 ± 2750). (T-AHG-CDC+ vs. FXM CS>300 vs. FXM CS <300; $p < 0.0001$).

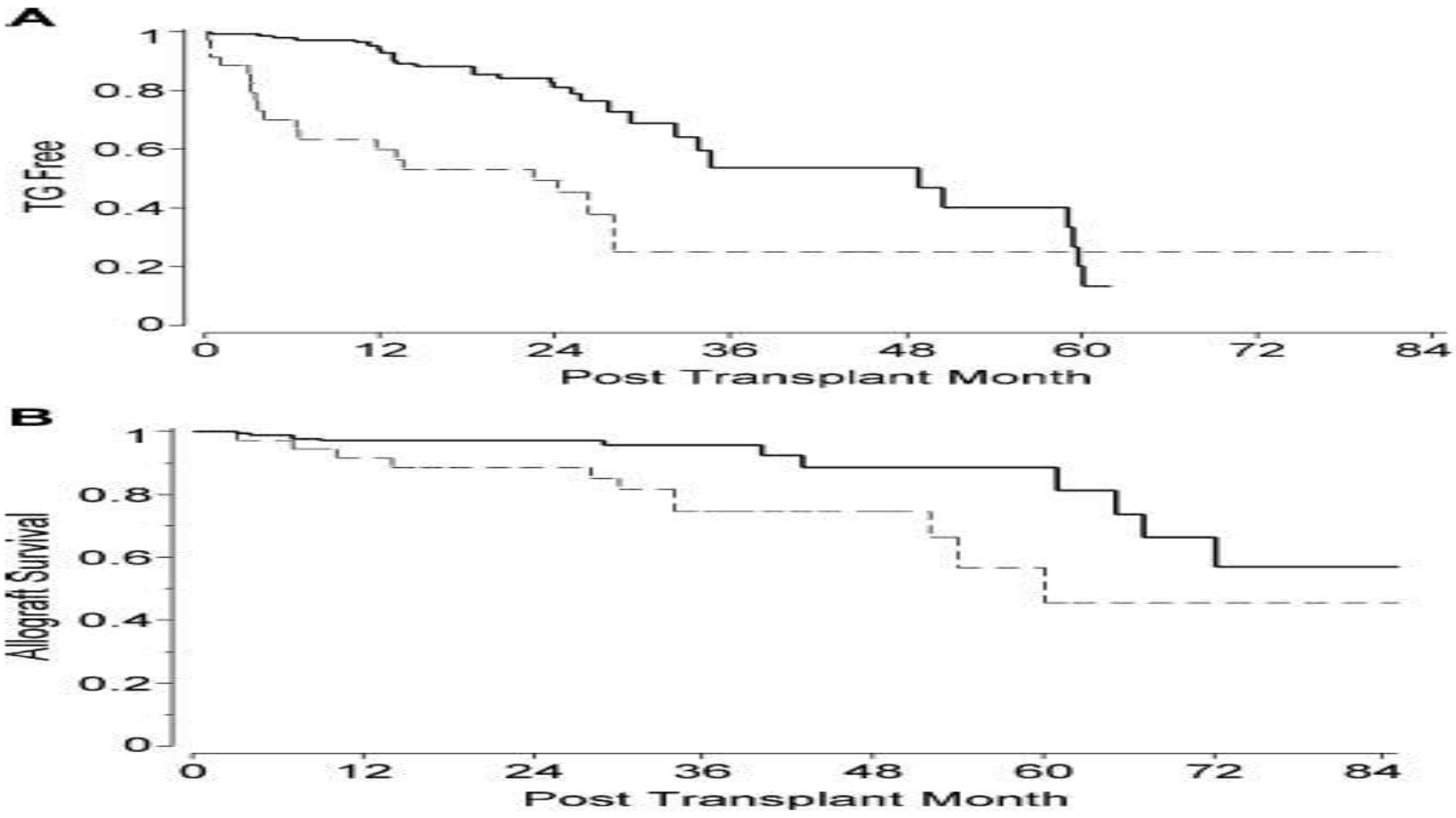
# Acute Antibody Mediated Rejection vs Crossmatch Results

**Gloor et al AJT, 2010**



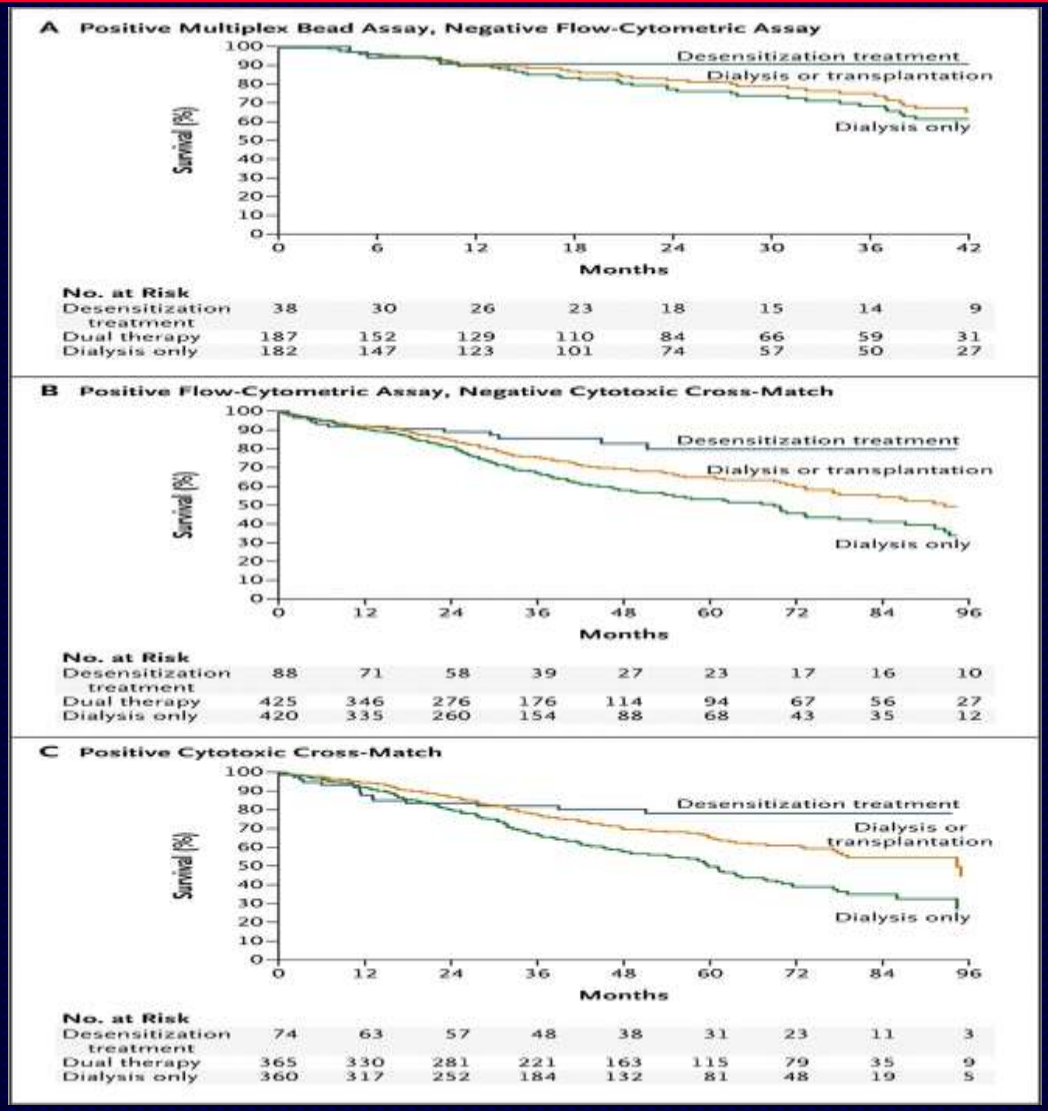
# Impact of AMR on Transplant Glomerulopathy (A) and Death Censored Graft Survival (B)

**Gloor et al AJT, 2010**



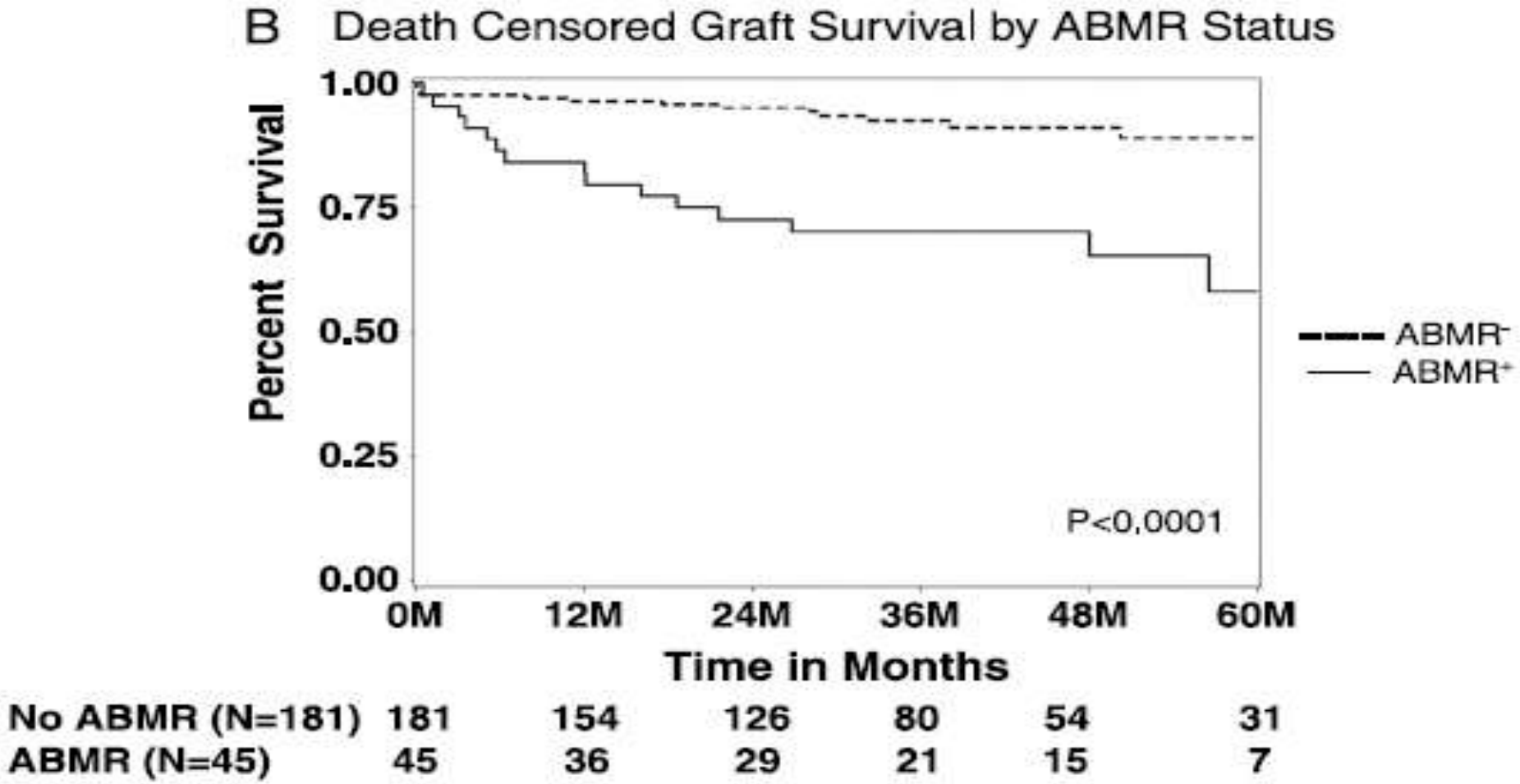
# Survival in Desensitization vs Compatible Transplantation or Dialysis

## Segev et al NEJM, 2011



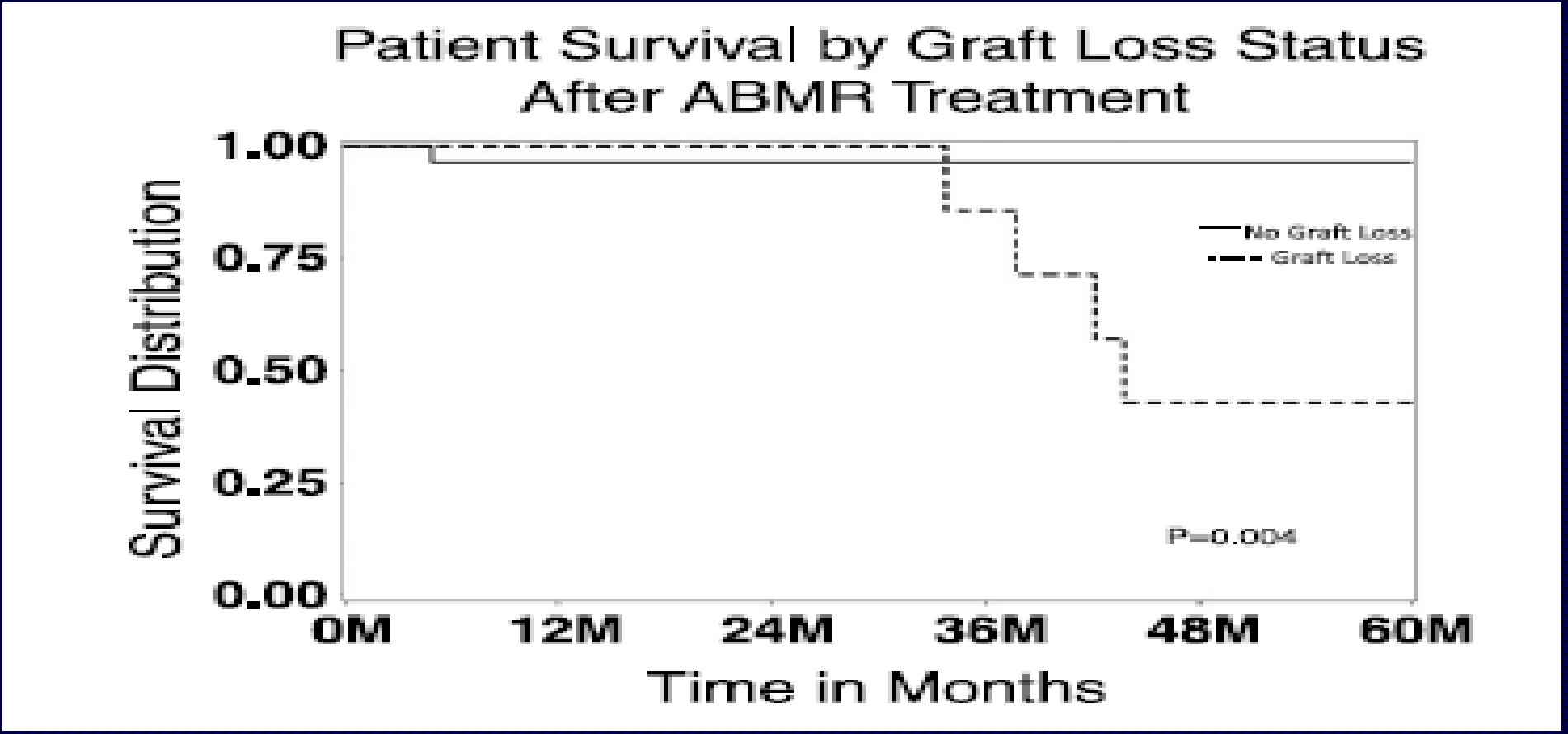
# Factors Predicting Graft Loss in Desensitized Patients

## Vo et al Transplantation, 2015



# Factors Predicting Graft Loss in Desensitized Patients

## Vo et al Transplantation, 2015



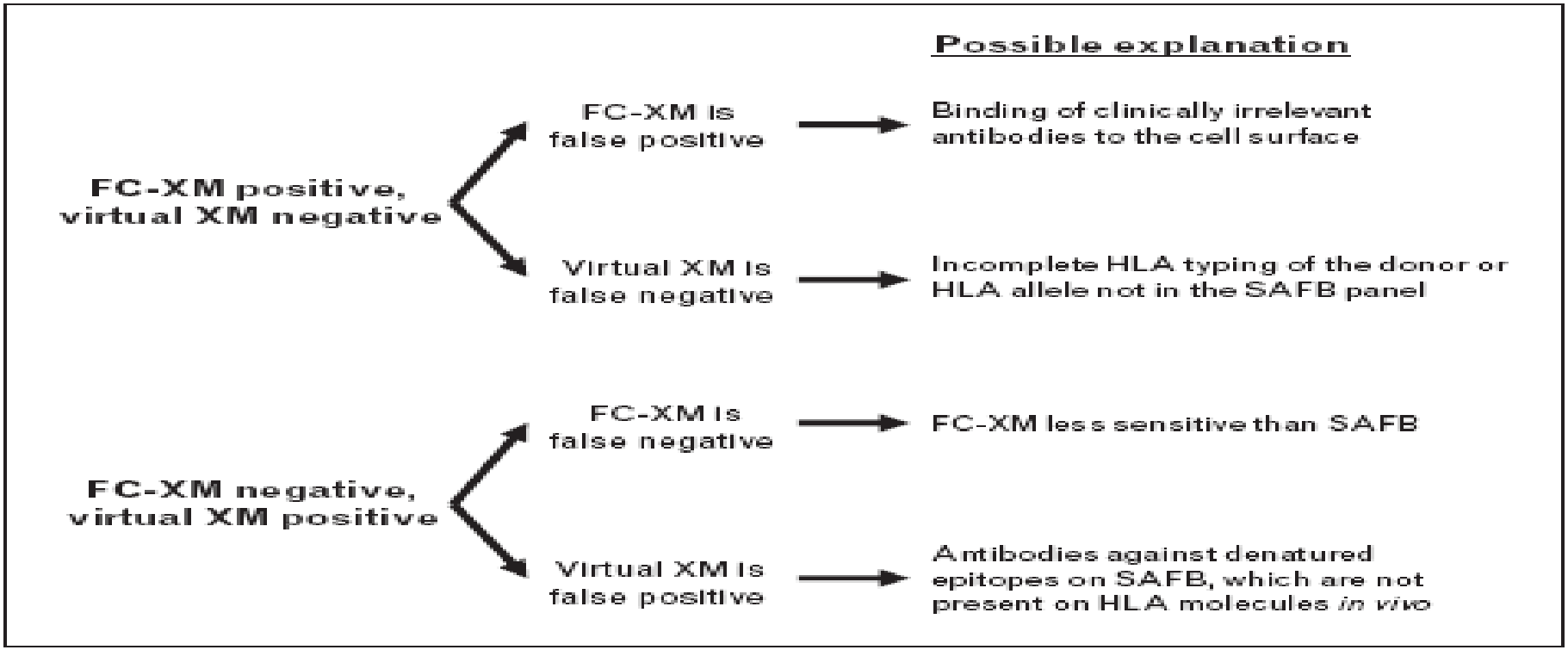
# Caveats of Desensitization

- More intense immunosuppression required
- Higher risk of acute rejection, particularly antibody mediated acute rejection
- Worse long term graft survival compared to DSA negative
- Usually only for those with living donors
- Hard to interpret data because definitions and assays vary
- Thus impossible to compare data between labs and centres

# The Virtual Cross Match

## D'Amico et al Current Opinion Organ Transpl 2009

**Figure 1 Possible explanations for divergent results of the virtual crossmatch and the flow-cytometric crossmatch**




FC-XM, flow-cytometric crossmatch; SAFB, single antigen flow-bead.