Does ATG Induction Prevent Donor-Specific Antibodies After Heart Transplantation?

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Abstract

Purpose: Sensitized patients awaiting heart transplantation (HTx) are known to have poor outcome post-transplant but also are known to develop more donor-specific antibodies (DSA) particularly if anti-HLA antibodies were present prior to transplant. Some reports have suggested that the use of ATG induction will decrease the development of anti-HLA antibodies in the first-year after HTx. However, it is not well established whether the use of ATG for sensitized patients decreases the development of DSA.

Methods: Between 2010 and 2016, we assessed 685 heart transplant patients and isolated those patients who were sensitized prior to transplant (PRA >=10%, n=217). Patients were then divided into those that received ATG (n=162) and those that did not (n=55). Furthermore, we divided the patients who received ATG induction into those with (n=13) and without (n=149) pre-transplant DSA and analyzed outcomes. Endpoints included 1-year freedom from DSA development, 1-year survival, 1-year freedom from any-treated rejection (ATR), acute cellular rejection (ACR), and antibody mediated rejection (AMR).

Results: Sensitized patients treated with ATG appear to have greater freedom from 1-year DSA development post-transplant compared to the no ATG group (86.4% vs 74.5%, p=0.038). Between the ATG group and no ATG group, there was no difference in 1-year survival, any-treated rejection, acute cellular rejection, or antibody mediated rejection (see table). Within the ATG group, the presence of pre-transplant DSA did not alter post-transplant de novo DSA development or outcome (data not shown).

Conclusion: In sensitized patients, ATG induction appears to have benefit in reducing DSA development post- heart transplant.

Background

- Sensitized patients awaiting heart transplantation (HTx) are known to have poor outcome post-transplant but also are known to develop more donor-specific antibodies (DSA) particularly if anti-HLA antibodies were present prior to transplant.
- Some reports have suggested that the use of ATG induction will decrease the development of anti-HLA antibodies in the first-year after HTx.

Purpose

- To establish whether the use of ATG for sensitized patients decreases the development of donor-specific antibody.

Methods

- Between 2010 and 2016, we assessed 685 heart transplant patients and isolated those patients who were sensitized prior to transplant (PRA >=10%, n=217).
- Patients were then divided into those that received ATG (n=162) and those that did not (n=55).
- Furthermore, we divided the patients who received ATG induction into those with (n=13) and without (n=149) pre-transplant DSA and analyzed outcomes.
- Endpoints included:
  - 1-year freedom from DSA development
  - 1-year survival
  - 1-year freedom from any-treated rejection (ATR)
  - 1-year freedom from acute cellular rejection (ACR)
  - 1-year freedom from antibody mediated rejection (AMR)

Demographics

Demographic	ATG Induction (n=162)	No ATG Induction (n=55)	P-Value
Mean Recipient Age, Years ± SD	53.4 ± 13.6	53.6 ± 13.7	0.925
Mean Donor Age, Years ± SD	34.4 ± 12.9	32.7 ± 11.9	0.390
Body Mass Index, Mean ± SD	25.2 ± 4.9	25.3 ± 4.4	0.894
Female (%)	51.9%	38.2%	0.088
Previous Pregnancy in Females (%)	81.0%	76.2%	0.761
Ischemic Time, Mean Mins ± SD	160.4 ± 65.0	150.2 ± 49.7	0.289
Primary Reason for Transplant, Underlying Diagnosis of Coronary Artery Disease (%)	35.8%	30.9%	0.623
Status 1 at Transplant (%)	82.1%	89.1%	0.290
Cytomegalovirus Mismatch (%)	40.4%	20.0%	0.009
Diabetes Mellitus (%)	33.3%	18.2%	0.040
Treated Hypertension (%)	53.0%	54.2%	1.000
Insertion of Mechanical Circulatory Support Device (%)	30.4%	41.8%	0.013
Prior Blood Transfusion (%)	60.5%	72.5%	0.192
Pre-Transplant Creatinine, Mean ± SD	1.6 ± 1.4	1.2 ± 0.7	0.043

Outcomes

Endpoints	ATG Induction (n=162)	No ATG Induction (n=55)	P-Value
1-Year Survival	92.0%	85.5%	0.200
1-Year Freedom from de novo DSA Development	86.4%	74.5%	0.038
1-Year Freedom from Any-Treated Rejection	84.0%	78.2%	0.425
1-Year Freedom from Acute Cellular Rejection	96.3%	94.5%	0.599
1-Year Freedom from Antibody-Mediated Rejection	88.9%	92.7%	0.379

Results Summary

- Sensitized patients treated with ATG appear to have greater freedom from 1-year DSA development post-transplant compared to the no ATG group (p=0.038).
- Between the ATG group and no ATG group, there was no difference in 1-year survival, any-treated rejection, acute cellular rejection, or antibody mediated rejection (see table).
- Within the ATG group, the presence of pre-transplant DSA did not alter post-transplant de novo DSA development or outcome (data not shown).

Conclusion

- In sensitized patients, ATG induction appears to have benefit in reducing DSA development post- heart transplant.

Author Disclosures

J. Patel: G; C; Alexion, Pfizer, Alnylam. O; C; Therakos. **M. Kittleson:** None. **L. Czer:** G; C; St. Jude Medical. **D.H. Chang:** G; C; Mesoblast, Amgen. S; C; Abbott Laboratories, AbbVie, Repligen. **E. Kransdorf:** None. **S. Dimbil:** None. **R. Levine:** None. **K. Norland:** None. **A. Hage:** C; C; Bayer. G; C; United Therapeutics, Actelion, Bellerophon Therapeutics, Lung Biotechnology, Reata Pharmaceuticals. **D. Ramzy:** None. **J. Kobashigawa:** G; C; CareDx, Sanofi, CSL Behring.