Efficacy of Desensitization in Lung Transplant Recipients with Preformed Donor-Specific Antibodies

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BACKGROUND

Lung transplantation remains the definitive treatment for patients with end-stage lung disease.

The presence of preformed DSA are associated with an increased risk of antibody-mediated rejection (AMR), chronic lung allograft dysfunction (CLAD), and reduced graft survival.

Consequently, sensitized candidates often experience prolonged wait times, limited donor availability, and increased waitlist mortality.

To expand transplant opportunities for these patients, desensitization strategies have been employed to reduce circulating HLA antibodies and mitigate the pathogenic effects of DSA.

Several studies have demonstrated that perioperative desensitization can facilitate successful transplantation in DSA-positive recipients, achieving short-term and long-term outcomes comparable to DSA negative recipients.

AIM

The aim of this study is to characterize the patterns of preformed DSA, response to desensitization and post-transplant outcomes.

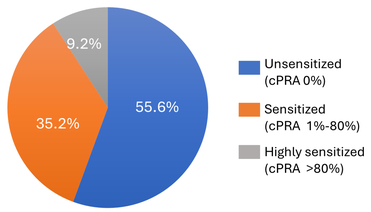
METHODS

We conducted a retrospective study of 392 lung transplant recipients at UCLA from 2021 to 2026.

We analyzed sensitization status, DSA specificity and strength were evaluated along with clinical outcomes including rejection.

RESULTS

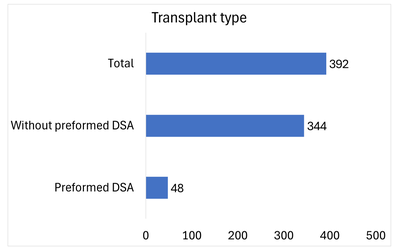
Figure 1. Sensitization status



Approximately 55.6% of patients were unsensitized, 35.2% were sensitized, and 9.2% were highly sensitized based on their degree of HLA sensitization.

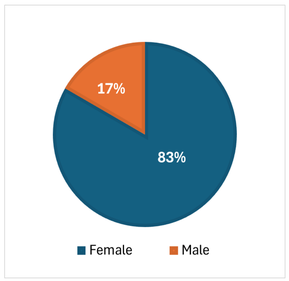
Sensitized and highly sensitized patients demonstrated varying levels of preformed alloantibodies, reflecting immunologic barriers to transplantation and a potentially higher risk of antibody-mediated rejection.

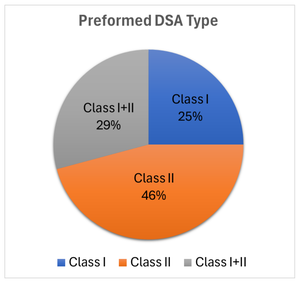
Figure 2. Transplant type and pre-formed DSA type



Among the 392 patients, 48 (12.2%) were transplanted with preformed DSA. Preformed DSA represent an important immunologic barrier to transplantation and are associated with an increased risk of antibody-mediated rejection, graft dysfunction, and reduced graft survival.

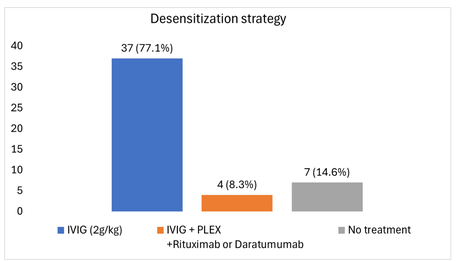
Among patients with preformed DSA, 40 (83.3%) were female and 8 (16.7%) were male.





The majority of preformed DSA were directed against HLA Class II antigens (46%), followed by combined Class I/Class II DSA (29%), with Class I DSA alone (25%) accounting for the smallest proportion. This pattern highlights the predominance of Class II sensitization in transplant recipients.

Figure 3. Desensitization strategy



Of the 48 patients transplanted with preformed DSA, 37 (77.1%) received high-dose intravenous immunoglobulin (IVIG) therapy, while 4 (8.3%) received combination desensitization therapy, including IVIG with either rituximab or daratumumab. The remaining 7 patients (14.6%) did not receive desensitization treatment prior to transplantation.

These findings indicate that the majority of patients with preformed DSA were managed with IVIG-based desensitization strategy.

RESULTS

Figure 4. Outcome by DSA type

Outcome by DSA Type				
DSA Type	Resolution	Transient	Persistent	Indeterminate
Class I	5 (41.7%)	4 (33.3%)	2 (16.6%)	1 (8.4%)
Class II	9 (42.9%)	7 (33.3%)	4 (19%)	1 (4.8%)
Both Clas I &II	5 (33.3%)	6 (40%)	3 (20%)	1 (6.7%)
Total	19	17	9	3

Persistent DSA		
Pateint ID	Class I	Class II
P-1		DQ
P-2	B	DR, DP
P-3	Cw	DQ
P-4		DQ
P-5		DQ
P-6	B	
P-7	A	DQ
P-8		DQ
P-9	B	
Persistent DSA were mainly against HLA-DQ followed by HLA-B		

Resolution (DSA no longer detected after transplant)
Persistent (DSA persistently detected)
Transient (DSA detected then resolved)
Indeterminate (no follow up DSA testing available)

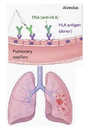
Resolution and Transient DSA were common in Class I and Class II HLA-DR, whereas persistent DSA was common against HLA-DQ.

Figure 5. Outcome by desensitization Strategy

DSA Outcome by desensitization Strategy				
DSA Type	Resolution	Transient	Persistent	Indeterminate
IVIG (2g/kg)	15 (40.6%)	12 (32.4%)	8 (21.6%)	2 (5.4%)
IVIG + PLEX + Rituximab or Daratumumab		4 (100%)		
No Treatment	3 (43%)	2 (28.5%)	1 (14.3%)	1 (14.3%)
Total	18	18	9	3

- Among IVIG-treated patients, most experienced DSA resolution or only transient DSA detection, with persistent DSA observed in 8 patients (21.6%).
- All combination treated patients had Transient DSA.
- Only one untreated patient had Persistent DSA.

Figure 6. Post transplant clinical outcome



Antibody Mediated Rejection

Occurred in 3 patients

- 1 patient with resolution DSA
- 2 patients with persistent DSA

AMR developed in 3 patients, corresponding to an incidence of approximately 6%. One patient from DSA resolution group and two from persistent DSA group.



Obliterative bronchiolitis

Occurred in 2 patients

- 1 patient with resolution DSA
- 1 patient with persistent DSA

Two patients (4%) developed obliterative bronchiolitis (OB). One patient from DSA resolution and one from DSA persistent group.

CONCLUSIONS

High dose IVIG or combined desensitization strategy enabled lung transplantation across preformed DSA, resolving HLA Class I and Class II DR DSA, though persistent HLA class II DQ DSA remained a challenge.