

**ROLE OF IMMUNOSUPPRESSANTS IN ORGAN TRANSPLANTATION**

Dr. Anjana Male<sup>1</sup>, Nandyala Bhargavi Reddy<sup>2\*</sup>, Puchakayala Krishna Swetha<sup>2</sup>, Undrakonda Ajay<sup>2</sup>,  
Palepu Priyanka<sup>2</sup>

<sup>1</sup>Professor and HOD in Department of Pharmaceutical Chemistry and Phytochemistry, Nirmala College of Pharmacy, Atmakuru, Mangalagiri, Andhra Pradesh, India.

<sup>2</sup>Pharm D, Department of Pharmacology and Pharmacy Practise, Nirmala College of Pharmacy, Atmakuru, Mangalagiri, Andhra Pradesh, India.

\*Corresponding Author: Nandyala Bhargavi Reddy

Pharm D, Department of Pharmacology and Pharmacy Practise, Nirmala College of Pharmacy, Atmakuru, Mangalagiri, Andhra Pradesh, India.

Article Received on 23/03/2018

Article Revised on 13/04/2018

Article Accepted on 03/05/2018

**ABSTRACT**

Immunosuppressants are the class of drugs that suppress the immune response through various mechanisms according to their categories. In organ transplantation immunosuppressants are used to prevent the body from either recognition or attacking the foreign organ via various immune responses. Other immunosuppressants are calcineurin inhibitors, corticosteroids, sirolimus derivatives, used to prevent rejection of a transplanted organ and to treat autoimmune diseases.

**KEYWORDS:** Immunosuppressants, organ transplantation, auto immune diseases.

**INTRODUCTION**

Any agents that can suppress or prevent the immune response are called Immunosuppressant's.

They are used to prevent rejection of a transplanted organ and to treat auto immune diseases such as psoriasis, rheumatoid arthritis and chrons disease transplantation. The process of taking an organ or living tissue and implanting it in another part of the body or in another body.<sup>[1]</sup>

**Roles of Immunosuppressants**

The class of drugs that suppress the immune response through various mechanisms in organ transplantation.

Immunosuppressant are used to prevent the body either recognition or attacking the foreign organ via various immune responses.<sup>[2,3]</sup>

**Organs Used In the Transplantations**

- Cornea
- Kidney
- Skin
- Bone marrow
- Heart and heart valves
- Intestine
- Lungs
- Liver
- Pancreas.<sup>[4]</sup>

**Types of Transplantation**

- **Auto graft:** A tissue removed from one part of the body and transplanted to another site in the same individual.  
**Ex:** skin grafting, several types of tissue can be grafted including bone, nerves, tendons, blood vessels.
- **Allograft:** An allograft uses tissue transplanted from a donor in one species to another body in the same species, as in bone from one human to another human.  
**Ex:** skin, bone, blood vessel.
- **Isograft:** An isograft is a graft tissue between two individuals who are genetically identical (i.e., monozygotic twins).  
**Ex:** kidney transplant.
- **Xenograft:** Organ of the tissue from a individual of one species transplanted into or grafted onto an organism of another species, genus, or family.  
**Ex:** pig heart valves in humans.<sup>[5]</sup>

**EXPERIMENT****List of Immunosuppressants**

The drug or drugs will be prescribed depends on whether you have an organ transplant, an autoimmune disorder or another condition. Many people who receive immunosuppressant drugs are prescribed medications from more than one of these categories. immunosuppressants are drugs or medicines that lower the body ability to reject a transplanted organ.<sup>[6,7]</sup>

There are two types of Immunosuppressant's.

**Induction drugs:** Powerful anti-rejection medicine used at the time of transplant.

**Ex:** Mycophenolatemofetil and Azathioprine along with immunosuppressant drugs such as Basiliximab, Daclizumab, Muromonab.

**Maintenance drugs:** Anti rejection medications used for the long term.

- **Calcineurin inhibitors:** Tacrolimus & cyclosporine.
- **Ant proliferative agents:** Mycophenolatem of etil, mycophenolate sodium, azathioprine.
- **MTOR inhibitors:** E.g. sirolimus, everolimus.
- **Steroids:** E.g.: prednisolone.
- **Biologics:** E.g: adalimumab, etanercept, rituximab.
- **Monoclonal antibodies:** Eg: basiliximab, daclizumab.

### Drug Treatment

Transplant rejection involves the body producing T&B cell and immune responses that recognize markers on foreign tissue called antigens. Treatment regimens used to prevent rejection employ drugs from different classes taking advantage of their complementary actions & minimizing toxicity.<sup>[8,9]</sup>

**Double Drug Treatment:** Usually a calcineurin inhibitor such as tacrolimus or cyclosporine with azathioprine or mycophenolate.<sup>[10,11]</sup>

**Triple Drug Treatment:** Usually a calcineurin inhibitors such as tacrolimus or cyclosporine, a corticosteroid & either azathioprine or mycophenolate.<sup>[12,13]</sup>

**Quadruple Drug Treatment:** Triple drug treatment + immunosuppressant antibody  
Immunosuppression for organ transplants usually involves triple or quadruple drug treatment.<sup>[14]</sup>

### Immunosuppressants Uses

- Preventing organ rejection & reverse acute rejection in organ transplantation
- Prevent & treat graft - versus - host disease
- Minimize destruction of affected tissues in autoimmune & inflammatory diseases.<sup>[15,16]</sup>

### RESULTS

All immunosuppressant drugs carry the serious risk of infection. When an immunosuppressant drug weakens immune system, so body becomes less resistant to infection.<sup>[17,18,19]</sup>

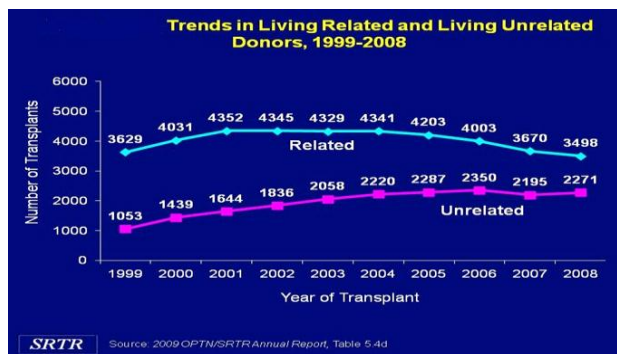
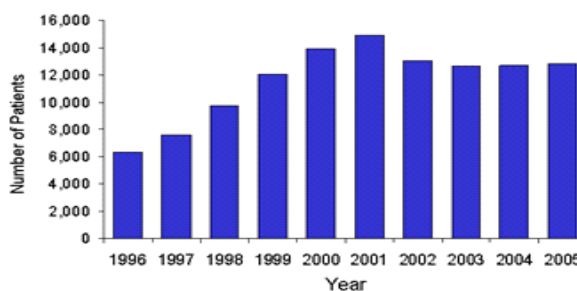
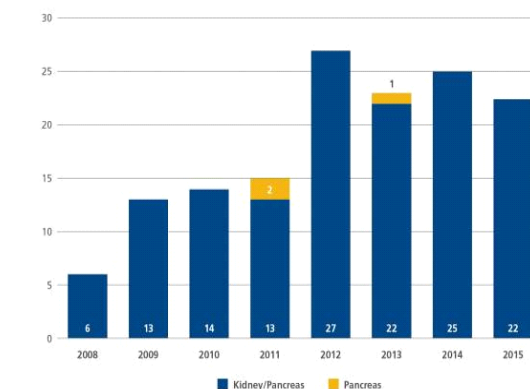


Figure V-1. Number of Patients on the Liver Waiting List, Active at Year-End, 1996-2005



COMBINED KIDNEY/PANCREAS & PANCREAS TRANSPLANTS 2008-2015  
OCHSNER MEDICAL CENTER



### Side Effects

Fever or chills, Alopecia, Pain in the side of lower back, frequent urination & pain while urinating, unusual tiredness or weakness, increased appetite, dyspepsia.

### Rare Serious Side Effects

- Muscle weakness, Amenorrhoea, Psychosis, Euphoria, Depression, Hirsutism, Gingival hyperplasia.

### CONCLUSION

More than 50,000 people waiting for compatible donor.

- Xenogeneic transplantation may be major issue of research xenograft technology including genetically modified animal may become a new source of organ supply.
- Immunosuppressants are used to prevent rejection of a transplanted organ and to treat autoimmune diseases.<sup>[20]</sup>

## REFERENCES

1. Aull MJ, Dadhania D, Afaneh C, Leiser DB, Hartono C, Lee JB, Serur D, Del Pizzo JJ, Suthanthiran M, Kapur S. Early corticosteroid withdrawal in recipients of renal allografts: A single-center report of ethnically diverse recipients and recipients of marginal deceased-donor kidneys *Transplantation*, 2012; 94:837,844 [PubMed]
2. Batista FD, Harwood NE. The who, how and where of antigen presentation to B cells. *Nat Rev Immunol*, 2009; 9: 15–27. [PubMed]
3. Becker YT, Becker BN, Pirsch JD, Sollinger HW. Rituximab as treatment for refractory kidney transplant rejection. *Am J Transplant*, 2004; 4: 996–1001. [PubMed]
4. Beyers AD, Spruyt LL, Williams AF. Molecular associations between the T-lymphocyte antigen receptor complex and the surface antigens CD2, CD4, or CD8 and CD5. *Proc Natl Acad Sci.*, 1992; 89: 2945–2949. [PMC free article] [PubMed]
5. Busque S, Leventhal J, Brennan DC, Steinberg S, Klintmalm G, Shah T, Mulgaonkar S, Bromberg JS, Vincenti F, Hariharan S, et al. Calcineurin-inhibitor-free immunosuppression based on the JAK inhibitor CP-690,550: A pilot study in de novo kidney allograft recipients. *Am J Transplant*, 2009; 9: 1936–1945. [PubMed]
6. Brennan DC, Daller JA, Lake KD, Cibrik D, Del Castillo D, Thymoglobulin Induction Study Group. Rabbit antithymocyte globulin versus basiliximab in renal transplantation. *N Engl J Med*, 2006; 355: 1967–1977. [PubMed]
7. Bromberg J, Cibrik D, Steinberg S, West-Thielke P, Yang H, Erdman J, First R, Holman J. A phase 2 study to assess the safety and efficacy of alefacept (ALEF) in de novo kidney transplant recipients. *American Transplant Congress, Abstract*, 2011; 533.
8. Billingham RE, Brent L, Medawar PB. Actively acquired tolerance of foreign cells. *Nature*, 1953; 172: 603–606. [PubMed]
9. Brennan DC, Flavin K, Lowell JA, Howard TK, Shenoy S, Burgess S, Dolan S, Kano JM, Mahon M, Schnitzler MA, et al. A randomized, double-blinded comparison of thymoglobulin versus ATGAM for induction immunosuppressive therapy in adult renal transplant recipients. *Transplantation*, 1999; 67: 1011–1018. [PubMed]
10. Hanaway MJ, Woodle ES, Mulgaonkar S, Peddi VR, Kaufman DB, First MR, Croy R, Holman J, INTAC Study Group. Alemtuzumab induction in renal transplantation. *N Engl J Med*, 2011; 364: 1909–1919. [PubMed]
11. Hardinger KL, Wang CD, Schnitzler MA, Miller BW, Jendrisak MD, Shenoy S, Lowell JA, Brennan DC. Prospective, pilot, open-label, short-term study of conversion to leflunomide reverses chronic renal allograft dysfunction. *Am J Transplant*, 2002; 2: 867–871. [PubMed]
12. Tiede I, Fritz G, Strand S, Poppe D, Dvorsky R, Strand D, Lehr HA, Wirtz S, Becker C, Atreya R, et al. CD28-dependent Rac1 activation is the molecular target of azathioprine in primary human CD4<sup>+</sup> T lymphocytes. *J Clin Invest*, 2003; 111: 1133–1145 [PMC free article] [PubMed]
13. Tyden G, Kumlien G, Genberg H, Sandberg J, Lundgren T, Fehrman I. ABO incompatible kidney transplantations without splenectomy, using antigen-specific immunoadsorption and rituximab. *Am J Transplant*, 2005; 5: 145–148. [PubMed]
14. Everly MJ, Everly JJ, Susskind B, Brailey P, Arend LJ, Alloway RR, Roy-Chaudhury P, Govil A, Mogilishetty G, Rike AH, et al. Bortezomib provides effective therapy for antibody- and cell-mediated acute rejection. *Transplantation*, 2008; 86: 1754–1761. [PubMed]
15. Busque S, Cantarovich M, Mulgaonkar S, Gaston R, Gaber AO, Mayo PR, Ling S, Huizinga RB, Meier-Kriesche HU, PROMISE Investigators. The PROMISE study: A phase 2b multicenter study of voclosporin (ISA247) versus tacrolimus in de novo kidney transplantation. *Am J Transplant*, 2011; 11: 2675–2684. [PubMed]
16. Dello Strologo L, Guzzo I, Laurenzi C, Vivarelli M, Parodi A, Barbano G, Camilla R, Scozzola F, Amore A, Ginevri F, et al. Use of rituximab in focal glomerulosclerosis relapses after renal transplantation. *Transplantation*, 2009; 88: 417–420 [PubMed]
17. Brown MH, Cantrell DA, Brattsand G, Crumpton MJ, Gullberg M. The CD2 antigen associates with the T-cell antigen receptor CD3 antigen complex on the surface of human T lymphocytes. *Nature*, 1989; 339: 551–553. [PubMed]
18. Durrbach A, Pestana JM, Pearson T, Vincenti F, Garcia VD, Campistol J, RialMdel C, Florman S, Block A, Di Russo G, et al. A phase III study of belatacept versus cyclosporine in kidney transplants from extended criteria donors (BENEFIT-EXT study). *Am J Transplant*, 2010; 10: 547–557 [PubMed]
19. European Mycophenolate Mofetil Cooperative Study Group. Mycophenolatemofetil in renal transplantation: 3-Year results from the placebo-controlled trial. *Transplantation*, 1999; 68: 391–396 [PubMed]
20. Jordan SC, Tyan D, Stablein D, McIntosh M, Rose S, Vo A, Toyoda M, Davis C, Shapiro R, Adey D, et al. Evaluation of intravenous immunoglobulin as an agent to lower allosensitization and improve transplantation in highly sensitized adult patients with end-stage renal disease: Report of the NIH IG02 trial. *J Am Soc Nephrol*, 2004; 15: 3256–3262. [PubMed]