

## A REVIEW ON IMMUNOSUPPRESSIVE AGENTS

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### ABSTRACT

Immunosuppressive agents are commonly used in the nephrologist's practice in the treatment of autoimmune and immune-mediated diseases and transplantation, and they are investigational in the treatment of AKI and ESRD. Drug development has been rapid over the past decades as mechanisms of the immune response have been better defined both by serendipity (the discovery of agents with immunosuppressive activity that led to greater understanding of the immune response) and through mechanistic study (the study of immune deficiencies and autoimmune diseases and the critical pathways or mutations that contribute to disease).

**KEYWORDS:** Immunosuppressive, nephrologist's, AKI and ESRD.

### INTRODUCTION

Immunosuppressant drugs are a class of drugs that suppress, or reduce, the strength of the body's immune system. Some of these drugs are used to make the body less likely to reject a transplanted organ, such as a liver, heart, or kidney. These drugs are called anti-rejection drugs. Other immunosuppressant drugs are often used to treat autoimmune disorders such as lupus, psoriasis, and rheumatoid arthritis.

If your doctor has prescribed an immunosuppressant medication for you, here's what to know about what these drugs do, how they work, and how they might make you feel. The following information will tell you what to expect when taking an immunosuppressant drug and what it could do for you.

#### Autoimmune conditions

Immunosuppressant drugs are used to treat autoimmune diseases. With an autoimmune disease, the immune system attacks the body's own tissue. Because immunosuppressant drugs weaken the immune system, they suppress this reaction. This helps reduce the impact of the autoimmune disease on the body.

Autoimmune diseases treated with immunosuppressant drugs include:

- Psoriasis
- Lupus
- Rheumatoid arthritis
- Crohn's disease

- Multiple sclerosis
- Alopecia areata

#### Organ transplant

Almost everyone who receives an organ transplant must take immunosuppressant drugs. This is because your immune system sees a transplanted organ as a foreign mass. As a result, your immune system attacks the organ as it would attack any foreign cell. This can cause severe damage and lead to needing the organ removed.

Immunosuppressant drugs weaken your immune system to reduce your body's reaction to the foreign organ. The drugs allow the transplanted organ to remain healthy and free from damage.

#### Classification of ISDs<sup>[4]</sup>

The drugs commonly used to suppress the immune system are classified into several categories based on mechanism of action as shown in the table below.

Category	Types	Example
Immunophilin-binding drugs	Calcineurin inhibitors	Cyclosporine A, tacrolimus
	Non-inhibitors of calcineurin	Sirolimus
Anti-metabolites	Inhibitors of <i>denovo</i> purine synthesis	Mycophenolic acid (MPA) Mycophenolate of etil (MMF), azathioprine
	Inhibitors of <i>denovo</i> pyrimidine synthesis	Leflunomide
Biologic immunosuppression	Polyclonal antibodies	Anti-thymocyte gamma globulin thymoglobulin
	Monoclonal antibodies	Anti-CD3 monoclonal antibody (OKT3), IL-2H (humanized)

### Recent Trends in Immunosuppression

Immunosuppressive therapy has changed considerably over the past few decades with the introduction of new drugs and development of different drug regimens. The changing trends for optimizing transplantation management include:

- Multi-regimen therapies
- Calcineurin inhibitor (CNI) minimization regimens
- Calcineurin inhibitor avoidance regimens

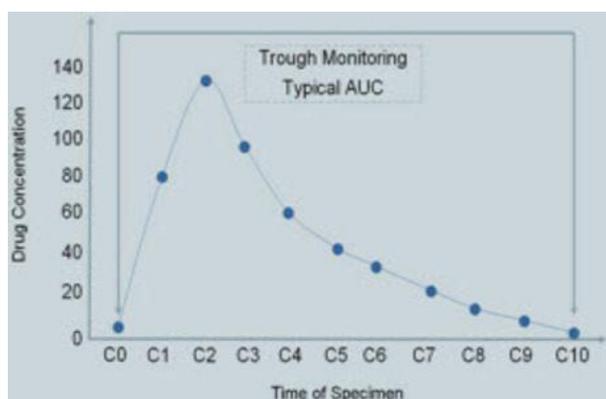
### ISD Monitoring

Rejection can occur any time post transplantation, and hence the lifelong administration of ISDs is usually required. The treatment regimen necessitates the regular monitoring and regulation of ISD doses in order to prevent probable rejection events and major adverse effects associated with supra therapeutic and sub therapeutic drug levels.

### Need for ISD Monitoring

Some of the common techniques adopted for therapeutic drug monitoring (TDM) include the following:

**1. Trough concentration monitoring ( $C_0$ ):** In this method, the drug level that is reached prior to the administration of the subsequent dose is measured. One of the main drawbacks of this technique is that it provides just an approximate estimate of the drug levels during the dosing interval.<sup>5</sup> The advantage of  $C_0$  monitoring, however, is that it requires only one sample, eliminating the need for patients to wait in the hospital, clinic, or physician office for multiple samples to be drawn.



Blood Levels Vs Target Tissue Exposure

**2. Area under the curve (AUC) monitoring:** AUC overcame the limitations of trough monitoring and evolved as a superior technique for TDM, with benefits such as the following:

- Provides a more accurate measure of the extent to which the body is exposed to the immunosuppressive drug.
- Predicts the concentration of a drug across the entire dose interval, traditionally with serial samples (8-12) drawn over 12 hours.<sup>[5]</sup>
- Pharmacokinetic profiles such as half-life, volume of distribution, and clearance can be calculated for effectively managing the administration of the drugs.

The major drawback of AUC monitoring is that it is expensive and requires the patient to spend long hours in the hospital.

### 3. Abbreviated area under the curve monitoring:

Abbreviated AUC is a limited sampling (2-4) strategy over the dosing interval, making it more convenient and economical compared to the standard AUC monitoring.<sup>[5]</sup>

**4.  $C_2$  monitoring:** The  $C_2$  monitoring strategy further limits the number of samples to one, which is collected 2 hours following the administration of the drug. The dosing and sampling time play a vital role in accurately measuring the drug levels since it is a single sampling approach.  $C_2$  monitoring is primarily used to monitor cyclosporine A levels.

### Advantages of Effective ISD Monitoring

- Decreases incidence and severity of the rejection episodes and lowers side effects.
- Improves treatment outcome.
- Optimizes patient care and enhances quality of life.
- Reduces cost.

### Enduring Expertise for Your Immunosuppressant Drug Testing Needs

With recognized drug testing expertise, Siemens Healthcare Diagnostics offers a comprehensive and expanding menu of tests across multiple instrument solutions to meet the immunosuppressant drug (ISD) testing needs of customers in any setting.

### Treatment regimen

All immunosuppressant drugs are available only by a prescription from your doctor. Immunosuppressant drugs come as tablets, capsules, liquids, and injections. Your doctor will decide the best drug forms and treatment regimen for you. They may use a combination of drugs. The goal of immunosuppressant therapy is to find the treatment plan that will suppress your immune system while having the fewest, least harmful side effects.

If you take immunosuppressant drugs, you must take them exactly as prescribed. If you have an autoimmune disorder, a regimen change can cause a flare-up of your condition. If you're an organ recipient, even the slightest change from the medication regimen can trigger an organ rejection. No matter why you're being treated, if you miss a dose, be sure to call your doctor right away.

### Tests and dosage changes

During your treatment with immunosuppressant drugs, you'll have regular blood tests. These tests help your doctor monitor how effective the drugs are and whether dosage changes are needed. The tests will also help your doctor know whether the drugs cause side effects for you. If you have an autoimmune disease, your doctor may adjust your dosage based on how your condition responds to the medication. If you've received an organ transplant, your doctor may eventually reduce your dosage. This is because the risk of organ rejection lessens over time, so the need for these medications may decrease. However, most people who have had a transplant will need to take at least one immunosuppressant drug throughout their lifetime.

### Side effects

Side effects vary greatly for the many different immunosuppressant drugs available. To find out the side effects you may be at risk for, ask your doctor or pharmacist about the effects of your particular drug. However, all immunosuppressant drugs carry the serious risk of infection. When an immunosuppressant drug weakens your immune system, your body becomes less resistant to infection. That means they make you more likely to get infections. It also means that any infections get will be harder to treat.

If you have any of these symptoms of infection, call your doctor right away:

- Fever or chills
- Pain in the side of your lower back
- Trouble urinating
- Pain while urinating
- Frequent urination
- Unusual tiredness or weakness

### Drug interactions

Before you start taking an immunosuppressant drug, be sure to tell your doctor about all medications you take. This includes prescription and over-the-counter medications, as well as vitamins and supplements. Your

doctor can tell you about the possible drug interactions that your immunosuppressant medication might cause. Like side effects, the risk of drug interactions depends on the specific drug you take.

### Warnings

Immunosuppressant drugs can cause problems for people with certain health conditions. Tell your doctor if you have any of these conditions before you start to take immunosuppressants:

- Allergy to the specific drug
- History of shingles or chickenpox
- Kidney or liver disease.

### Pregnancy and breast-feeding

Some of these drugs can cause birth defects, while others carry milder risks during pregnancy and breast-feeding. In any case, if you're planning to become pregnant, talk to your doctor before taking an immunosuppressant drug. Your doctor can tell you about the risks of the specific drug you might be taking.

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