

## Immunomodulatory Drugs and its Applications

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**Received:** September 08, 2021; **Accepted:** September 22, 2021; **Published:** September 29, 2021

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**Citation:** Rita B (2021)  
Immunomodulatory Drugs and its  
Applications. Insights Biomed Vol.6  
No.9:43

### Commentary

Immunomodulatory Drugs (IMiDs) have been used in hematologic malignancies for the last decade. The mechanism of action of IMiDs is largely unknown. Here we provide a comprehensive overview of pivotal studies, recent advances in the application of IMiDs in cancer as well as their effects on hematopoietic stem cells including the risk of secondary malignancies. IMiDs have a well-established role as first-line therapy for patients with newly diagnosed and relapsed/refractory Multiple Myeloma (MM).

Immunomodulatory drugs are increasingly being developed for treatment of human diseases, including inflammatory disorders. Because of the similarities of nonhuman primates to humans, these can be tested in monkey models for efficacy, potential exacerbation of infections and toxicity.

Immunomodulatory drugs can be used to treat systemic or exocrine autoimmune and inflammatory manifestations. Hydroxychloroquine is often given for milder systemic manifestations of autoimmune disorders, such as fever, arthritis and rashes. It remains unclear whether hydroxychloroquine is effective for the exocrine component of the disease, although serological measures improve in SS patients on this drug. Methotrexate, azathioprine, prednisone and other immunomodulatory drugs have been used in patients with prominent systemic manifestations of SS as is done in patients with systemic lupus erythematosus.

The immunomodulatory drug thalidomide inhibits angiogenesis and induces apoptosis of established neovasculature in experimental models. Thalidomide is an oral cancer drug which has been used to treat some Non-Hodgkin's Lymphoma (nhl) and multiple myeloma. The known toxicities of thalidomide include peripheral neuropathy, sedation, constipation and fatigue.

Leflunomide an immunomodulatory drug inhibits pyrimidine synthesis in activated lymphocytes which is used in treatment of autoimmune disorders and rheumatoid arthritis which has been associated rarely with significant lung injury.

Certain immunomodulatory drugs affect thyroid function by inducing thyroid autoimmunity. Interferon alfa (IFN $\alpha$ )31 has been implicated in a destructive thyroiditis-like syndrome. It may

be more apt to lead to thyroid dysfunction when used in the treatment of hepatitis C.

Lenalidomide is an immunomodulatory drug and an analogue of thalidomide, a known teratogen. Thalidomide and lenalidomide are immunomodulatory Drugs (IMiDs) are used in the treatment of multiple myeloma. Lenalidomide is also being studied for treatment of relapsed lymphomas. They have direct cytotoxic effects and induce apoptosis or growth arrest of myeloma cells. They also have anti-inflammatory effects and potent antiangiogenic that appear to inhibit cell growth.

FTY720 is a novel immunomodulatory drug with a unique mechanism of action. It is a synthetic structural analogue of myriocin, a metabolite of an ascomycete. FTY720 shares structural and functional homology with Sphingosine-1-phosphate (S1P), a natural ligand to several G-protein-coupled receptors. FTY720 shows a novel mechanism of action characterized by sequestration of lymphocytes into secondary lymphoid organs without affecting their function.

Immunomodulatory drugs helps to modify the response of the immune system as immunostimulators or immunosuppressives of the production of serum antibodies. Immunostimulators are prescribed to enhance the immune response against infectious diseases, primary or secondary immunodeficiency, tumours, and alterations in antibody transfer, among others. Immunosuppressive drugs are used to decrease the immune response against transplanted organs and to treat autoimmune diseases such as pemphigus, allergies or lupus.