Kidney Transplantation

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INTRODUCTION

Solid organ transplantation, adult and pediatric, is an established therapeutic option for patients with end-stage kidney, liver, heart, and lung disease.

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INTRODUCTION

Unfortunately, many more patients are in need of transplantation than there are organs available. In 2021, about 30,000 organ transplants were performed by August 2021, whereas 117,260 people were waiting for all organs

During the 1960s, azathioprine, prednisone, antilymphocyte serum, and antilymphocyte globulin made the success of kidney transplantation possible.

TRANSPLANTATION IMMUNOLOGY

Successful organ transplantation has evolved from a greater understanding and application of pharmacology, microbiology, molecular and cellular biochemistry and biology, genetics, and immunology.

Suppression of the host's immune system and prevention of rejection are vital for host acceptance of the transplanted organ.

The ultimate goal is permanent acceptance or tolerance, a situation in which the new organ is seen as "self" by the host's immune system.

In general, the currently used immunosuppressive drugs provide a nonpermanent form of tolerance and lifelong immunosuppression is required.

A basic understanding of the immune system and the mechanisms of rejection is key to the effective use of immunosuppressive drugs in organ transplantation.

Major Histocompatibility Complex and Human Leukocyte Antigen

The degree to which allogeneic grafting (eg, donor and recipient from same species) is successful depends on the genetic similarities or differences between the donor organ and the recipient's immune system.

The recipient recognizes the transplanted graft as either self or foreign.

This recognition is based on the recipient’s reaction to alloantigens or antigens (ie, substances that initiate an immune response that can lead to rejection of the transplanted organ).

These substances, also known as histocompatibility antigens, play a very important role in organ transplantation.

The ABO blood group system of red blood cells is also important, and, in most cases, the donor and recipient should be ABO compatible; otherwise, immediate graft destruction can occur because of antibodies directed against the ABO antigens.

IMMUNOSUPPRESSIVE AGENTS

Immunosuppressives, based on an improved understanding of their mechanisms of action and the mechanisms of rejection, have had the most significant impact on patient and graft survival.

The currently used immunosuppressives are shown in Table 34-1.

These agents can be categorized as induction or maintenance therapy.

Sites of action and the role of the currently used agents are discussed here.

Drug (Brand Name)	Usual Dose/Route (How Supplied)	Therapeutic Use(s)	Major Adverse Effects
Alemtuzumab (Campath-H1)	IV or SC 0.3 mg/kg or 30 mg × 1 dose (30-mg vial for injection)	Prevention and treatment of acute cellular and antibody-mediated rejection; steroid-free protocols	Lymphopenia, leukopenia, infection
Azathioprine (Imuran)[a]	IV or oral 1–3 mg/kg/day (50-mg tablet; 100-mg vial for injection)	As maintenance agent to prevent acute rejection	Leukopenia, thrombocytopenia, hepatotoxicity, nausea and vomiting, diarrhea, pancreatitis, infection
Antithymocyte globulin, equine (Atgam)	IV 10–20 mg/kg/day (250 mg/5-mL ampoule for injection)	Treat acute rejection (including severe or steroid-resistant forms); as induction agent in high-risk patient to prevent acute rejection	Anemia, leukopenia, thrombocytopenia, arthralgia, myalgias, nausea and vomiting, diarrhea, fevers, chills, hypotension, tachycardia, anaphylaxis, infection
Antithymocyte globulin, rabbit (Thymoglobulin)	IV 1.5 mg/kg/day given daily for 4–10 days (25 mg/5-mL vial for injection)	Treat acute rejection (including severe or steroid-resistant forms); as induction agent in high-risk patient to prevent acute rejection	Fever, chills, nausea and vomiting, hypotension, neutropenia, flushing, rash, itching, joint pain, myalgias, thrombocytopenia, infection
Basiliximab (Simulect)	IV 20 mg × 2 doses 10 mg; 2 doses for children if <35 kg (10- and 20-mg vial for injection)	As induction agent to prevent acute rejection	Abdominal pain, dizziness, insomnia, hypersensitivity reaction (rare)

Belatacept (Nulojix)	IV initial maintenance: 10 mg/kg on days 0, 4, 14, and 28; and weeks 8 and 12 and monthly thereafter Conversion from CNI: 5 mg/kg q 2 weeks for five doses, then q 4 weeks thereafter	As maintenance agent to prevent acute rejection; conversion agent from CNIs in patients with intolerances	Anemia, neutropenia, diarrhea, UTIs, headaches, peripheral edema, PTLD
Cyclosporine[a] (Sandimmune)	Oral 5–10 mg/kg/dose bid IV 1.5–2.5 mg/kg/dose (100 mg/mL oral solution; 25- and 100-mg capsule; 250 mg/5-mL ampoule for injection)	As maintenance agent to prevent acute rejection	Nephrotoxicity, hypertension, neurotoxicity, hair growth, gingival hyperplasia, hyperglycemia, hyperkalemia, dyslipidemia, hypomagnesemia, infection, neoplasm
Cyclosporine (Neoral, Gengraf, various others)[a]	Oral 4–8 mg/kg/day bid (100-mg solution; 25-, 50-, and 100-mg capsules)	As maintenance agent to prevent acute rejection; conversion agent from tacrolimus in patients with intolerance	Same as given earlier
Everolimus (Zortress)	Oral 0.5–1.5 mg bid (0.25-, 0.5-, 0.75-mg tablets)	As maintenance agent to prevent acute rejection; conversion agent from CNI in patients with intolerance or poor response	Dyslipidemia, thrombocytopenia, neutropenia, impaired healing, mouth ulcers, proteinuria, pneumonitis (rare)

Methylprednisolone[a] sodium succinate (Solu-Medrol, various others)	10–1000 mg/dose (40-, 125-, 250-, 500-, 1000-, and 2000-mg vial for injection)	As induction and maintenance agent to prevent acute rejection; to treat acute rejection	Hyperglycemia, psychosis, euphoria, impaired wound healing, osteoporosis, acne, peptic ulcers, gastritis, fluid, electrolyte disturbances, hypertension, dyslipidemia, leukocytosis, cataracts, cushingoid state, infection, insomnia, irritability

Mycophenolate[a] mofetil (CellCept)	1.5–3.0 g/day bid IV/PO (250-mg capsule; 500-mg tablet; 200 mg/mL oral suspension; 500-mg vial for injection)	As maintenance agent to prevent acute rejection; conversion agent from azathioprine and sirolimus in patients with intolerance or poor response	Diarrhea, nausea and vomiting, neutropenia, dyspepsia, ulcers, infection, thrombocytopenia, anemia
Mycophenolate[a] sodium (Myfortic)	360–720 mg PO bid (180- and 360-mg tablets)	As maintenance agent to prevent acute rejection. Alternative to MMF	Similar side effect profile as MMF
Prednisone[a] (Deltasone)	Oral 5–20 mg/day (1-, 2.5-, 5-, 10-, 20-, 50-, and 100-mg tablet)	As maintenance agent to prevent acute rejection	See methylprednisolone
Sirolimus[a] (Rapamune)	Oral 2–10 mg/day (0.5-, 1-, and 2-mg tablet; 1 mg/mL oral solution)	As maintenance agent to prevent acute rejection; conversion agent from CNI or mycophenolate or azathioprine in patients with intolerance or poor response	Dyslipidemia, thrombocytopenia, neutropenia, anemia, diarrhea, impaired healing, mouth ulcers, proteinuria, pneumonitis (rare)
Tacrolimus (Prograf, Astagraf XL, Envarsus XR)[a]	Oral 0.15–0.3 mg/kg/day bid IV 0.025–0.05 mg/kg/day as continuous infusion (0.5-, 1-, and 5-mg capsule; 5 mg/mL ampoule for injection) Astagraf XL: oral 0.1–0.2 mg/kg/day once daily (0.5-, 1-, and 5-mg capsules)	As maintenance agent to prevent acute rejection; conversion agent from cyclosporine in patients with intolerance or poor response	Nephrotoxicity, hypertension, neurotoxicity, alopecia, hyperglycemia, hyperkalemia, dyslipidemia, hypomagnesemia, infection, neoplasm

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Bortezomib (Velcade)	1.3 mg/m^2 on days 1, 4, 8, and 11 IV bolus or SC (3.5-mg single-use vial)	Inhibits plasma cells	Bone marrow suppression, thrombocytopenia, neuropathy, hypotension, gastrointestinal
Eculizumab (Soliris)	600- to 1200-mg IV infusion (300-mg single-use vial [30 mL of 10 mg/mL solution])	Inhibits complement	Infusion reaction, headache, hypertension, leukopenia, infections
Rituximab (Rituxan)	375 mg/m^2 × 1–5 doses or 500 mg/m^2	Inhibits B-cell production	Infusion reactions (fever, chills, rigors); pain at infusion site, infections

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Intravenous Immunoglobulin (Carimune NF, Flebogamma, Gammagard S/D, Gamunex, Iveegam EN, Octagam, Polygam)	100 mg/kg to 2-g/kg IV infusion (vial size varies based on manufacturer, ranging from 1, 2.5, 5, 6, 10, 12, 20, 30, and 40 g; usually concentrations are 5% and 10%)	Immunomodulation of T and B cells and/or immunoglobulin replacement	Infusion reactions (fever, chills, rigors); pain at infusion site, thrombosis, hemolytic anemia, acute renal failure, septic meningitis

Induction

POLYCLONAL ANTIBODIES: Antithymocyte globulins

MONOCLONAL ANTIBODIES: Basiliximab

Alemtuzumab

OTHER AGENTS

Maintenance

AZATHIOPRINE

MYCOPHENOLIC ACID DERIVATIVES (MYCOPHENOLATE MOFETIL AND MYCOPHENOLATE SODIUM)

CORTICOSTEROIDS

CALCINEURIN INHIBITORS

KIDNEY TRANSPLANTATION

Donor And Recipient Matching

ANTITHYMOCYTE GLOBULINS

Postoperative Course and Delayed Graft Function

Rejection

HYPERACUTE REJECTION

ACCELERATED REJECTION

ACUTE REJECTION

ANTIBODY-MEDIATED REJECTION

CHRONIC REJECTION

Acute Rejection Treatment