

Table 2. Characteristics of Small-Molecule Immunosuppressive Drugs Used in Organ Transplantation or in Phase 2–3 Trials.*

Drug	Description	Mechanism	Nonimmune Toxicity and Comments
Cyclosporine	11-amino-acid cyclic peptide from <i>Tolypocladium inflatum</i> ³¹	Binds to cyclophilin; complex inhibits calcineurin phosphatase and T-cell activation	Nephrotoxicity; hemolytic-uremic syndrome, hypertension, neurotoxicity; gum hyperplasia, skin changes, hirsutism, post-transplantation diabetes mellitus, hyperlipidemia; trough monitoring or checking levels two hours after administration required
Tacrolimus (FK506)	Macrolide antibiotic from <i>Streptomyces tsukubaensis</i> ^{32,33}	Binds to FKBP12; complex inhibits calcineurin phosphatase and T-cell activation	Effects similar to those of cyclosporine but with a lower incidence of hypertension, hyperlipidemia, skin changes, hirsutism, and gum hyperplasia and a higher incidence of post-transplantation diabetes mellitus and neurotoxicity; trough monitoring required
Sinolimimus (rapamycin)	Triene macrolide antibiotic from <i>S. hygroscopicus</i> from Easter Island (Rapa Nui) ³⁴	Binds to FKBP12; complex inhibits target of rapamycin and interleukin-2-driven T-cell proliferation	Hyperlipidemia, increased toxicity of calcineurin inhibitors, thrombocytopenia, delayed wound healing, delayed graft function, mouth ulcers, pneumonitis, interstitial lung disease; lipid monitoring required; recipients whose risk of rejection is low to moderate can stop cyclosporine treatment two to four months after transplantation
Everolimus	Derivative of sinolimimus		
Mycophenolate mofetil and enteric-coated mycophenolate	Mycophenolic acid from penicillium molds ³⁵⁻³⁷	Inhibits synthesis of guanosine monophosphate nucleotides; blocks purine synthesis, preventing proliferation of T and B cells	Gastrointestinal symptoms (mainly diarrhea), neutropenia, mild anemia; blood-level monitoring not required but may improve efficacy; absorption reduced by cyclosporine
FK778 and malononitrilamide	Modification of A771726 (active derivative of leflunomide)	Inhibits pyrimidine synthesis, blocking proliferation of T and B cells	Anemia; other effects not known; in phase 2 trials
Azathioprine	Prodrug that releases 6-mercaptopurine	Converts 6-mercaptopurine to tissue inhibitor of metalloproteinase, which is converted to thioguanine nucleotides that interfere with DNA synthesis; thioguanine derivatives may inhibit purine synthesis	Leukopenia, bone marrow depression, macrocytosis, liver toxicity (uncommon); blood-count monitoring required
FTY720	Sphingosine-like derivative of myriocin from ascomycete fungus ³⁸	Works as an antagonist for sphingosine-1-phosphate receptors on lymphocytes, enhancing homing to lymphoid tissues and preventing egress, causing lymphopenia	Reversible first-dose bradycardia, potentiated by general anesthetics and beta-blockers; nausea, vomiting, diarrhea, increased liver-enzyme levels
CP-690,550 ³⁹ and Tyrphostin AG 490 ⁴⁰	Synthetic molecule	Binds cytoplasmic tyrosine kinase JAK3, inhibiting cytokine-induced signaling	Anemia caused by potential effects on JAK2

* Data about drugs come from the manufacturer's inserts for health care professionals unless otherwise indicated.

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