VET 433A Immunosuppressive Drugs

Drug	MOA	Indication	Adverse Effects	Dosing
Glucocorticoids ***Prednisone/Prednisolone** ***Dexamethasone SP**	Inhibits phospholipase A2 and thus arachidonic acid release decreasing the production of prostaglandins and thromboxane Decreased production of leukotrienes through the lipoxygenase pathway Suppress cytokine production Decreased antibody response Reduced T-cell activation Decreased phagocytosis Decreased inflammatory cell influx Decreased Fc receptor expression by macrophages Lymphopenia, eosinophilia	First line of defense for most auto-immune diseases	PU/PD, polyphagia Panting Muscle wasting, weakness Hepatomegaly, splenomegaly Calcinosis cutis Hypercoagulability GI ulceration with anemia Alopecia, thin skin, impaired hair growth *Signs are similar to CS of Cushing's disease*	Starting dose prednisone 2 mg/kg/d Max dose of 60mg total/day Never use with NSAIDS!
Cyclosporine	Calcineurin inhibitor Interacts with cytosolic protein, cyophilin, in lymphocytes (T-lymphocytes) which blocks transcription factors for interleukin 2 leading to a down-regulation of T cell proliferation and activation	T-cell mediated auto-immune diseases Atopic dermatitis (derm) 5mg/kg q 24h until clinical improvement 1-2 months then taper to q 48h then q 72h	GI signs Gingival hyperplasia Hepatotoxicity Opportunistic infections Drug interactions P450 enzyme substrate, concentration increased by azole antifungals, macrolides, fluoroquinolones, and omeprazole May also inhibit MDR1 transporter (predispose to ivermectin toxicity)	Atopica = veterinary product 5mg/kg q 12h for immunosuppression Can start higher at 10mg/kg but will need to lower! Need to monitor clinical response, IL-2 expression, and trough concentrations

VET 433A Immunosuppressive Drugs

Azathioprine	Thiopurine competes with adenine (purine analog) leading to impaired nucleic acid synthesis. This results in faulty transcription and targets rapidly dividing cells (T and B cells) along with the intestinal epithelium.	Usually in combination with glucocorticoids as a second-line agent	Inexpensive drug but monitoring costs can add up $$$ GI upset Bone marrow suppression Hepatotoxicity Impaired hair growth Pancreatitis Profound muscle weakness and tetraparesis SEVERE adverse effects in cats (bone marrow suppression!)	Delayed onset of action 1-2 mg/kg 1 24h po for 7-14 days (loading dose) Then DECREASE to 0.5-1 mg/kg q 48h for long term use
Mycophenolate mofetil	Inhibits purine synthesis Targets rapidly dividing cells (lymphocytes)	First-line for glomerulonephritis Second-line agent for other autoimmune diseases	GI toxicity Dose-dependent diarrhea	5-10 mg/kg q 12h
Leflunomide	Inhibits pyrimidine synthesis Targets rapidly dividing cells (lymphocytes) Inhibits autoimmune T-cell proliferation and autoantibody production by B cells	IMPA Occasional utilized for other refractory disease	GI toxicity Bone marrow suppression/anemia	Dogs: 3-4 mg/kg po sid Cats: 2-3 mg/kg po sid
Chlorambucil	Alkylating agent (Leukeran)	Used most often in cats IBD vs GI lymphoma	Uncommon due to its low potency GI issues Bone marrow suppression	2mg eod to every 3rd day