

Drugs	Prednisone	Azathioprine	Mycophenolate	Cyclophosphamide
<b>Dosing Protocol</b>	A. 0.5 mg/kg/day x 1 mth, 0.4 mg/kg/day x 1 mth, 0.3 mg/kg/d x 1mth, then decrease over the next 3 months to 10 mg daily, continue 10 mg daily for 6 months B. 1 mg/kg/d x 1 mth, then down 10 mg/d q2wks, until reach 10 mg daily, then down 2.5 mg q2wks (if wt >100 kg, down 20 mg q2wk until reach 10 mg, then down 2.5 mg q2wk until off	<u>Starting dose:</u> 50 mg qd x 1 wk, then increase by 50 mg q wk until goal. <u>Goal therapeutic dose:</u> 2 mg/kg/d (using actual NOT ideal body weight)	Starting dose: 1 gm po bid Max: 3 gm daily (250 mg or 500 mg tablets)	IV PO: Dosing of CYC will be initiated at 1.5 mg/kg once daily, to the nearest 25 mg dose, and will increase monthly by 25 mg until a maximum dose of 2 mg/kg once daily is reached as the daily treatment dose. (25 mg tablets) <u>Use cytoxan dosing from recent article looking at response of nonrenal manifestation or from Japanese cyc in ild article.</u>
<b>Other Medications</b>	Calcium (1500 mg/d) Vitamin D (1200 IU/d), Alendronate (35 qwk if nl bmd or 75 mg qwk if abnormal Bactrim (or alternate) if taking a 2nd immunosuppressant			
<b>Contraindications</b>		WBC < 4000 Tbili, alt, ast, alk phos > 1.5x ULN	WBC < 4000, plt < 150,000 Tbili, alt, ast, alk phos > 1.5x ULN Creatinine >2.0	WBC < 4000, plt < 150,000
<b>Lab Monitoring (2 weeks after starting or increasing dose, then qmonth)</b>	CBC w diff, chem7	CBC w diff, LFTs, chem7	CBC w diff, chem7, LFTs,	CBC w diff, chem.7, LFTs, urinalysis
<b>Other Monitoring</b>	DEXA (baseline, q12 mths), eye exam (q12mths),	Eye exam (q12 mths)		
<b>Common Side Effects</b>	Short term: Irritability, poor sleep, weight gain, hyperglycemia Long term: accelerated bone density loss, cataract	Hepatitis, leukopenia, anemia	Nausea (may need to switch Myfortic®), Diarrhea (may need to reduce dose if >3-4 bm's/day)	Fill
<b>Adjustments in Dosing</b>			Decrease dose by 1/3 if wbc < 4000, plt < 150,000, or tbil/alt/ast/or alk phos >1.5x ULN (If no improvement in 2 weeks, continue to decrease dose. Check weekly labs. If continues to get worse. hold medicine)	
<b>Additional Counseling</b>		No ETOH	Contraception No ETOH	Contraception No ETOH Contraception May interfere w future pregnancy

Disease-specific therapy IPF: Prednisone (A) + Azathioprine + NAC 600 mg PO tid Idiopathic NSIP: Prednisone (B) +/- Azathioprine or MMF or CYC RBILD: smoking cessation DIP: smoking cessation + prednisone (B) +/- ? COP: prednisone (B) +/- azathioprine or CYC or MMF CTD-ILD: prednisone (B) +/- azathioprine or MMF or CYC Scleroderma-ILD: NO prednisone. MMF or CYC Special Considerations for Celcept and Cytoxan (this section is being revised Bone Marrow Suppression: For leukopenia (WBC < 2500 and/or ANC < 1000), thrombocytopenia (< 100,000), or anemia (Hgb < 10 gm/dl) the study drug will be managed as follows: • Hold study drug until there is resolution of the hematologic abnormality above threshold levels (WBC > 3500, platelets > 100,000, Hgb >12 gm/dl). • Once

threshold values are exceeded, the study drugs (MMF or CYC/Placebo) will be reintroduced at 2 capsules twice daily for 2 weeks followed by 3 capsules twice daily for 2 weeks and then 4 capsules twice daily for 2 weeks as tolerated. • Follow-up should be every 1-2 weeks, as clinically indicated, until the investigator is satisfied that it is safe to return to the protocol-defined dosing schedule. • In the event of repeat toxicity, the same cycle should be repeated except with the intention of achieving a maintenance dose equal to 2 capsules per dosing less than the original target dose. For surgery or infections requiring antibiotics or hospitalization: The study drug should be discontinued until the infection is cleared and the subject is off antibiotics or two weeks after surgery. Other severe or dangerous adverse events: For adverse events that are considered clinically serious by the investigator, the study drug will be managed as follows: • Hold study drug until there is resolution of the adverse event. • Once stable, restart the study drugs (MMF or CYC) at 2 capsules twice daily for 2 weeks followed by 3 capsules twice daily for 2 weeks and then 4 capsules twice daily for 2 weeks as tolerated. • Follow-up should be every 1-2 weeks, as clinically indicated, until the investigator is satisfied that it is safe to return to the protocol-defined dosing schedule. • In the event of repeat toxicity, the same cycle should be repeated except with the intention of achieving a maintenance dose equal to 2 capsules per dosing less than the original target dose. For less severe or dangerous adverse events (e.g., dyspepsia) not responding to concomitant medications: the study drugs are to be discontinued until the adverse event disappears. At that point they can be restarted at one-half of the original dose. The subject can return to the full dose of medications or one capsule less than the full dose, as clinically indicated, after 2 weeks at the half dose of medications.