**Title:** Use of Mycophenolate Mofetil in Children with Chronic, Refractory Immune Cytopenias Associated with Autoimmune Lymphoproliferative Syndrome (ALPS). V. Koneti Rao MD, Susan Price RN, Katie Perkins, CRNP, Patricia Aldridge, RN, Jean Tretler RN, Joie Davis, APRN, Kennichi Dowdell, PhD, Julie Niemela, Margaret Brown and Thomas Fleisher, MD. LCID/NIAID/NIH, Bethesda, MD, USA.

**Background:**
ALPS is a disorder of apoptosis resulting in accumulation of autoreactive lymphocytes that leads to childhood onset of marked lymhadenopathy, hepatosplenomegaly, and increased risk of lymphoma. Frequently many ALPS patients present with chronic, refractory multilineage cytopenias due to autoimmunity as well as splenic sequestration. Characteristic increases (≥1%) in circulating double negative (CD3+/CD4-/CD8- TCR alpha-beta+) T lymphocytes, and evidence of defective lymphocyte apoptosis *in vitro* establishes the diagnosis. Currently 259 individuals with ALPS, belonging to 166 families are enrolled in studies at the NIH Clinical Center and 65% of them have a heterozygous mutation in the gene Fas (ALPS Type Ia) while the remainder have either other mutations or are currently undefined in terms of a genetic defect.

**Objective:**
We have been exploring therapeutic options that might permit us to avoid splenectomy and long-term corticosteroid use in ALPS patients with chronic cytopenias. Here we report our experience using oral mycophenolate mofetil (MMF, Cellcept®) in 29 ALPS patients over the last 9 years.

**Design/Methods:**
21 boys and 8 girls, aged 6 months to 18 years (median age 8.8 years) at commencement of therapy received MMF 337-1000mg/M2/dose administered twice daily. Twenty of them had ALPS Type Ia, 2 patients had mutation is Caspase 10 gene (ALPS Type Ila), 7 of them had clinical features of ALPS with no identified genetic mutations. Concurrent multilineage cytopenias were notable; 25 patients had thrombocytopenia, 21 had anemia and 18 had neutropenia. Eleven patients had undergone splenectomy prior to starting MMF, while the remaining 18 patients had persistent splenomegaly. Four patients had failed to respond to rituximab prior to starting MMF.

**Results:**
24 patients responded over a median follow up of 49 months (range 9 months-104 months), as defined by the maintenance of an adequate hematocrit, leucocytes and platelets, with considerably reduced, often no need, for corticosteroids and avoiding splenectomy to control their autoimmunity and/or hypersplenism. None of the patients experienced any significant infections or bone marrow toxicity due to MMF. Four out of the five non-responders underwent splenectomy, while the fifth non-responding patient had a durable response to Rituximab.

**Conclusion:**
With a response rate of 82% (24/29), further accrual and long term follow up of
ALPS patients with autoimmune cytopenias are underway to study adverse effects and define an optimal dose schedule and length of therapy with MMF as a potential steroid and splenectomy sparing agent.