Troy R. Torgerson, MD PhD

Associate Professor, Pediatric Immunology/Rheumatology
Director, Immunology Diagnostic Laboratory (IDL)
Co-Director, Non-Malignant Transplant Program
University of Washington & Seattle Children’s Hospital

Common Variable Immunodeficiency (CVID) - Some (hopefully) Practical Management Ideas

Parts you see

Troy R. Torgerson, MD PhD

Parts you don’t
Disclosures:

Shire/Baxalta – Consulting, DSMB, Grant funding
CSL Behring – Consulting, Grant funding
Grifols Bioscience – Consulting
UCB Pharmaceuticals – Consulting
Topics

1. 2 Informative Cases
2. Definitions and Prognosis
3. Diagnosis and Treatment
   A. Infections
   B. Autoimmunity
4. Hematopoietic Cell Transplant (HCT)
Patient #1 - 66 y/o Male Construction Worker

- Diagnosed with CVID almost 30 years ago – so far, just infections. Avid dirt bike rider and motocross racer.
Patient #1 - 66 y/o Male Construction Worker

- **Challenges:**
  Very active. Enjoys riding his dirt bike and going to motocross events on weekends. Lives in a rural area not near an infusion center.

- **Needs:**
  Simplicity, wants to just get infusion done and doesn’t want to think about it.

- **Solution:**
  Taught to place his own IV’s and infuse a 10% IVIG product that he infuses at home once per month.
Patient #2 - 34 y/o Female Patient Advocate

• 7 y/o watery diarrhea, no blood, diagnosed as “Crohns disease” based on biopsy. Various treatments tried.

• 11 y/o found to have low IgG and absent IgA after workup for history of recurrent sinus infections and bronchitis. Started on IVIG.

• 17 y/o worsening shortness of breath, chest CT showed ground glass opacities and multiple nodules, lung biopsy = ILD. IV steroid pulses then oral taper.

• 19 y/o developed massive ascites while doing humanitarian work in Gaza Strip. Extensive infectious w/u negative. Liver biopsies showed Nodular Regenerative Hyperplasia (NRH). Treated with TIPS.
Patient #2 - 34 y/o Female Patient Advocate

- 20 y/o profound fatigue, diagnosed with autoimmune hypothyroidism.
- 21 y/o developed psoriasis and joint pain thought to be psoriatic arthritis.
- 21 y/o Type I diabetes. Treated with insulin and diet.
- 22 y/o severe flare of interstitial lung disease, worsening bronchiectasis. Treated with pulse and oral steroids, azathioprine, Rituximab, etc. with poor response.
- 23 y/o Married
- 24 y/o MUD-BMT, non-myeloablative regimen, CVID cured but has chronic GvHD.
Patient #2 - 34 y/o Female Patient Advocate

- **Challenges:**
  Infections + severe autoimmunity with progressive organ damage that was difficult to control.

- **Needs:**
  Prevent infections + control autoimmunity. Desire to survive.

- **Solution:**
  IgG replacement + prophylactic antibiotics to prevent and control infections. Aggressive immune suppression to try to control autoimmunity. Ultimately bone marrow transplant.
Topics

1. 2 Informative Cases

2. Definitions and Prognosis

3. Diagnosis and Treatment
   A. Infections
   B. Autoimmunity

4. Hematopoietic Cell Transplant (HCT)
Common Variable Immunodeficiency (CVID)  
2014 ESID Diagnostic Criteria

At least ONE of the following:
• Increased susceptibility to infection
• Autoimmune manifestations
• Granulomatous disease
• Unexplained polyclonal lymphoproliferation
• Affected family member with antibody deficiency

AND marked decrease of IgG and marked decrease of IgA with or without low IgM levels (measured at least twice: <2 SD of the normal levels for their age.

AND at least one of the following:
• Poor antibody response to vaccines (and/or absent isohemagglutinins); i.e. absence of protective levels despite vaccination where defined.
• Low switched memory B cells (<70% of age-related normal values)

AND secondary causes of hypogammaglobulinemia have been excluded.

AND Dx is established after the 4th year of life but symptoms may be present before.

AND no evidence of profound T cell deficiency defined as two of the following:
• CD4 number/µL: 2-6 y/o <300, 6-12 y/o <250, >12 y/o <200
• % Naïve CD4: 2-6 y/o <25%, 6-16 y/o <20%, >16 y/o <10%
• T cell proliferation to mitogens absent

Reference: European Society for Immunodeficiency – Diagnostic Criteria for PID
http://www.esid.org/clinical-diagnostic-criteria-for-pid-73-0#Q3
CVID – Other Features

• Autoimmunity (25-30%):
  – Heme (AIHA/ITP)
  – Lung (ILD/LIP/GLILD)
  – GI (lymphocytic colitis)
  – Endocrine (thyroiditis/diabetes)
  – Skin (Psoriasis/Eczema)
  – Joints (RA/PsA)
  – Other

• Granulomatous disease (10-22%): multi-system, non-caseating Sarcoid-like, frequently associated with autoimmunity.

• Neoplasia: Non-Hodgkins lymphoma most common but solid organ tumors (gastric Ca, etc.) also occur.
Long-term Outcomes in CVID


Figure 2. Kaplan-Meier curve for patients with and without noninfectious complications. Patients with noninfectious complications were significantly more likely to die than those with infections only (P < .0001).
Topics

1. 2 Informative Cases
2. Definitions and Prognosis
3. Diagnosis and Treatment
   A. Infections
   B. Autoimmunity
4. Hematopoietic Cell Transplant (HCT)
# Summary of Factors that affect choice of IgG replacement: IVIG vs. SCIG

<table>
<thead>
<tr>
<th></th>
<th>IVIG</th>
<th>SCIG</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Pharmacokinetics</strong></td>
<td>Wide range of serum IgG levels (peak / trough)</td>
<td>Consistent serum IgG levels</td>
</tr>
<tr>
<td><strong>Systemic Side Effects</strong></td>
<td>Common</td>
<td>Infrequent</td>
</tr>
<tr>
<td><strong>Infusion Site Reactions</strong></td>
<td>Infrequent</td>
<td>Common</td>
</tr>
<tr>
<td><strong>Location of Infusions</strong></td>
<td>Infusion center or home</td>
<td>Anywhere</td>
</tr>
<tr>
<td><strong>Patient Satisfaction</strong></td>
<td>Often better for needle-phobic patients</td>
<td>Very flexible - minimizes impact on quality of life</td>
</tr>
<tr>
<td></td>
<td>Preferable in patients who have compliance issues</td>
<td></td>
</tr>
</tbody>
</table>

**Facilitated SCIG**
Prophylactic Antibiotics

- Good data for efficacy in few PIDD (CGD, etc.)
- Little definitive data in hypogammaglobulinemia/CVID
- There is however data from the chronic lung disease literature including COPD, Bronchiectasis, and the lung transplant literature that may be informative.
- Recent set of Cochrane Reviews published in 2018 on this topic.
Use of Prophylactic Antibiotics in COPD

• Seven RCTs published between 2001 and 2011.
• 3170 patients
• Five studies were of continuous antibiotics and two studies were of intermittent antibiotic prophylaxis (termed ‘pulsed’).
• Antibiotics investigated were azithromycin, erythromycin, clarithromycin and moxifloxacin.
• The study durations varied from 3 to 36 months and all used intention-to-treat analysis.
• primary outcomes of review: number of exacerbations and QoL
Use of Prophylactic Antibiotics in COPD

Continuous prophylactic antibiotics:
• Number of patients experiencing an exacerbation was reduced (odds ratio (OR) 0.55; 95% confidence interval (CI) 0.39 to 0.77, 3 studies, 1262 participants, high quality). This represented a reduction from 69% of participants in the control group compared to 54% in the treatment group (95% CI 46% to 63%) and the number needed to treat to prevent one exacerbation (NNTb) was therefore 8 (95% CI 5 to 18).
• Frequency of exacerbations was also reduced.

Pulsed prophylactic antibiotics:
• Non-significant reduction in the number of people with exacerbations, (moderate quality) and significantly different from the effect on exacerbations with continuous abx.
• Statistically significant improvement in quality of life with both continuous and pulsed.
• Neither pulsed nor continuous antibiotics showed a significant effect on secondary outcomes of frequency of hospital admissions, change in lung function, serious adverse events or all-cause mortality (moderate quality evidence).
Use of Prophylactic Macrolides in Bronchiectasis

- 14 parallel-group RCTs and one cross-over RCT with interventions lasting from 8 weeks to 24 months.
- 11 adult studies with 690 participants, six used azithromycin, four roxithromycin, and one erythromycin.
- Four studies with 190 children used either azithromycin, clarithromycin, erythromycin, or roxithromycin.
- 9 adult studies included in comparison between macrolides and placebo and two in comparison with no intervention.
- 1 study included with children in comparison between macrolides and placebo and 1 in comparison with no intervention.
Use of Prophylactic Macrolides in Bronchiectasis

Adults:
• Macrolides reduced exacerbation frequency to a greater extent than placebo (OR 0.34, 95% confidence interval; moderate-quality evidence). Number needed to treat for an additional beneficial outcome of 4 (95% CI 3 to 8).
• Macrolides were also associated with a significantly better quality of life compared with placebo.
• No evidence of a reduction in hospitalizations (low-quality evidence), in the number of participants with serious adverse events, including pneumonia, respiratory and non-respiratory infections, hemoptysis, and gastroenteritis (low-quality evidence), or in the number experiencing adverse events with macrolides compared with placebo.

Children:
• No significant reduction exacerbation frequency compared to placebo, (1 study, low-quality evidence).
• Increase in macrolide-resistant Streptococcus pneumoniae (OR 13.20, 95% CI 1.61 to 108.19; 89 children; one study), and Staphylococcus aureus (OR 4.16, 95% CI 1.06 to 16.32; 89 children; one study) with macrolides compared with placebo.
Topics

1. 2 Informative Cases
2. Definitions and Prognosis
3. Diagnosis and Treatment
   A. Infections
   B. Autoimmunity
4. Hematopoietic Cell Transplant (HCT)
Primary Immune Deficiency Disorders
- Infections Dominant
- May have autoimmunity/autoinflammation
  - CVID – Bowel, Lungs, Liver, Skin, etc.
  - CGD – Bowel, etc.
  - WAS – Vasculitis, etc.
Primary Immune Deficiency Disorders
- Infections Dominant
- May have autoimmunity/autoinflammation
  - CVID – Bowel, Lungs, Liver, Skin, etc.
  - CGD – Bowel, etc.
  - WAS – Vasculitis, etc.

Primary Immune Regulatory Disorders
- Immune Pathology Dominant (Autoimmune, Autoinflammatory, etc.)
- May have infections
  - STAT1-GOF – CMC, Mycobacteria
  - PIK3CD – EBV, etc.

IUIS Immune Deficiencies (2017)

344 Total

Infections
PIDD

Immune Dysregulation
PIRD

229
115
Genetics of CVID

Genetic defects can now be identified in approximately 1/3 of patients with the complicated form of CVID:

- PIK3CD
- PIK3R1
- hCTLA4
- STAT1-GOF
- STAT3-GOF
- IZKF1
- BTK
- RAG1/2
- CECR1 (ADA2)
**LRBA binds the cytoplasmic Tail of LRBA and plays a role in recycling to cell surface**
STAT1-GOF Disease – Targeted Therapy

Treatment:

Jakafi (Ruxolitinib – JAK 1/2 inhibitor) highly effective in anecdotal cases. Not much pediatric dosing guidance. Usual adult dose is 20 mg po BID. Thrombocytopenia most common side effect. Risk for Herpes viral infections.
Activated PI3 Kinase Targeted Therapy

Effective Targeted Therapy for APDS

GOF mutations

PI3Kδ

Leniolisib

INCREASED
pAKT
Lymphoproliferation
T cell senescence
Transitional B cells
IgM, IFNγ, CXCL13
Cytopenias
Fatigue

DECREASED
pAKT
Lymphoproliferation
T cell senescence
Transitional B cells
IgM, IFNγ, CXCL13
Cytopenias
Fatigue

10 mg bid

Leniolisib

12 weeks

70 mg bid

30 mg bid

V. Koneti Rao et al. Blood 2017;130:2307-2316
Organ Involvement & Management

- **Heme** – AIHA, ITP, Autoimmune Neutropenia.
- **GI** – Enteropathy, Liver
- **Lungs** – LIP, Follicular bronchiolitis, Granulomas
- **Skin** – Eczema, Psoriasis, Pemphigus nodularis
- **Endocrine** – Thyroiditis, Type I DM, Other
Diagnosis

Autoimmune Hemolytic Anemia:
- CBC with differential
- Direct Coombs – may be positive if on IgG supplementation

Immune Thrombocytopenic Purpura:
- CBC with differential
- Platelet autoantibodies – problems with specificity
Autoimmune neutropenia:

- CBC with differential
- Neutrophil autoantibodies
Comparison - B Cell Directed Therapy

Old Standby’s:
• Steroids
• Cyclophosphamide
• High-dose IVIG

- Anti-CD20
- Bortezomib
- Ecalizumab
- Plasmapheresis

Blys/BAFF

*Steroids (Old) + Rituxan (New)
# Time to Response – Rituximab

## Systematic Review: Efficacy and Safety of Rituximab for Adults with Idiopathic Thrombocytopenic Purpura

Donald M. Arnold, MD, MSc; Francesco Dentali, MD; Mark A. Crowther, MD, MSc; Ralph M. Meyer, MD; Richard J. Cook, PhD; Christopher Sigouin, MSc; Graeme A. Fraser, MD; Wendy Lim, MD, MSc; and John G. Kelton, MD

<table>
<thead>
<tr>
<th>Variable</th>
<th>Median</th>
<th>Interquartile Range</th>
<th>Range</th>
<th>Contributing Reports (Patients), n (n)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Time to response, wk</td>
<td>5.5</td>
<td>3.0–6.6</td>
<td>2.0–18.0</td>
<td>6 (123)</td>
</tr>
<tr>
<td>Response duration, mo</td>
<td>10.5</td>
<td>6.3–17.8</td>
<td>3.0–20.0</td>
<td>16 (252)</td>
</tr>
<tr>
<td>Follow-up, mo</td>
<td>9.5</td>
<td>6.0–21.3</td>
<td>2.0–25.0</td>
<td>10 (187)</td>
</tr>
</tbody>
</table>
**Time to Response – Rituximab**

Acta Derm Venereol 2015; 95: 928–932

**SPECIAL REPORT**

**Efficacy of Rituximab for Pemphigus: A Systematic Review and Meta-analysis of Different Regimens**

Hsiao-Han WANG¹, Che-Wei LIU², Yu-Chuan LI¹ and Yu-Chen HUANG¹

¹Department of Dermatology, Wan Fang Hospital, Taipei Medical University, and ²Department of Surgery, Cathay General Hospital, Taipei, Taiwan

Table 1. Key issues

1. Rituximab is efficacious and well-tolerated in patients with pemphigus.
2. Complete remission rate after 1 cycle of Rituximab was 76%. Mean time to complete remission was 5.8 months, complete remission duration 14.5 months and overall relapse rate 40%. Eighteen patients (3.3%) developed major adverse effects.
3. High-dose (≥2,000 mg) Rituximab was associated with longer complete remission compared with low-dose Rituximab (<1,500 mg).
4. No significant difference in time to complete remission, complete remission or relapse rates between the high-dose and low-dose Rituximab. No superiority of lymphoma protocol over rheumatoid arthritis in all outcomes.
5. Immunoabsorption-combined regimens resulted in the fastest control of disease before completion of Rituximab therapy.
6. Choice of optimal regimen may depend on the overall condition of the individual patient.
Bortezomib

- An N-protected di-peptide with a boronic acid instead of carboxylic acid at C-term
- Given IV on days 1, 4, 8, and 11 of a 21 day cycle – 8 cycles for MM
- May not need to give full course for cytopenias in PIDD patients
- Short half-life: 9-15 hours
- Side effects: Peripheral neuropathy in 30%, myelosuppression (neutropenia, thrombocytopenia), Shingles.
Treatment – MAC Inhibitors

Classical Pathway (Immune Complexes)
- C1q
- C1r
- C1s
- C2
- C4

Lectin Pathway (Pathogen Oligosaccharides)
- MBL
- MASP
- C2
- C4

Alternative Pathway (Pathogen Surfaces)
- C3b
- Factor B
- Factor D

Membrane Attack Complex (MAC)
- C5
- C6
- C7
- C8
- C9

Complement Proteins (MAC)

Eculizumab
Lineage-Specific Growth Factors

- Eltrombopag - Platelets
- Romiplostim – Platelets
- G-CSF – Neutrophils
- Epo - RBC
Organ Involvement & Management

- **Heme** – AIHA, ITP, Autoimmune Neutropenia.
- **GI** – Enteropathy, Liver
- **Lungs** – LIP, Follicular bronchiolitis, Granulomas
- **Skin** – Eczema, Psoriasis, Pemphigus nodularis
- **Endocrine** – Thyroiditis, Type I DM, Other
• Get tissue whenever possible and ask the pathologist to do specific stains for CD4+ and CD8+ T cells and for B cells in addition to usual stains – very helpful in determining Inflammatory vs. Autoimmune.
CVID Gastrointestinal Disease

A Cross-Sectional Study of the Prevalence of Gastrointestinal Symptoms and Pathology in Patients With Common Variable Immunodeficiency

Silje F. Jørgensen, MD1,2,3, Henrik M. Reims, MD, PhD4, Didrik Frydenlund, MD, PhD4, Kristian Holm, MSc1,5, Vernund Paulsen, MD2, Annika E. Michelsen, PhD1,6, Kristin K. Jørgensen, MD, PhD1,7, Liv T. Osnes, MD, PhD8, Jorunn Brattlie, BLS1, Tor J. Eide, MD, PhD8, Christen P. Dahl, MD, PhD4, Ellen Holter, MD10, Rune R. Tronstad, MD11,12, Kurt Hanvik, MD, PhD11, Hans-Richard Brattbak, PhD11,13, Fatemeh Kaveh, PhD14, Torunn Fiskerstrand, PhD11,13, Anne-Marte B. Kran, MD, PhD12,15, Thor Ueland, PhD11,15, Tom H. Karlseth, MD, PhD11,15, Per Aukrust, MD, PhD11,15, Knut E.A. Lundin, MD, PhD11,15 and Barre Føvang, MD, PhD11,15

RESULTS:

The main findings of this study were as follows: most common GI symptoms were bloating (34%), pain (30%), and diarrhea (26%). The most frequent histopathological findings were increased intraepithelial lymphocytes in the descending part of the duodenum, i.e., “celiac-like disease” (46% of patients), decreased numbers of plasma cells in GI tract mucosa (62%), and lymphoid hyperplasia (38%), none of which were associated with GI symptoms. Reduced plasma cells in GI mucosa were associated with B-cell phenotypic characteristics of CVID, and increased serum levels of sCD14 (P=0.025), sCD25 (P=0.01), and sCD163 (P=0.04). Microarray analyses distinguished between CVID patients with “celiac-like disease” and celiac disease. Positive tests for bacterial and viral infections were scarce both in fecal samples and gut mucosal biopsies, including PCR test for norovirus in biopsy specimens (0 positive tests).

CONCLUSIONS: In conclusion, GI pathology is common in CVID, but does not necessarily cause symptoms. However, reduced plasma cells in GI mucosa were linked to systemic immune activation, “celiac-like disease” in CVID and true celiac disease appear to be different disease entities, as assessed by gene expression, and infections (including norovirus) are rarely a cause of the CVID enteropathy.
Nodular Lymphoid Hyperplasia

- Villus atrophy
- Celiac disease-like
- Loss of Goblet cells
Nodular Regenerative Hyperplasia (NRH) of the Liver

- Need liver biopsy
- AST/ALT usually elevated
GI – Diagnosis (Cont.)

• Evaluate biopsies for evidence of viral infection


• Fecal Calprotectin level


• Hepatitis Screen – AST/ALT minimum
GI - Treatment

Nutrition:

• Ask diet questions
• Enlist the help of a nutritionist
• Adjust diet – elemental formula, dietary supplementations if needed
• Bowel rest and TPN if enteropathy can’t be controlled in other ways and patient is severely malnourished.
GI - Treatment (Cont.)

• “Non-Absorbable” oral steroid (Budesonide)
• Treat based on the inflammatory infiltrate:
  • Watery diarrhea/autoimmune enteropathy – start with Rapamycin (Sirolimus), Tacrolimus, or Cyclosporin
  • Bloody diarrhea/inflammatory enteropathy – start with steroids, TNF inhibitors, etc.
• DISEASE DEPENDENT (CGD, etc.)
• If you know the gene you can use targeted therapy (CTLA4-Ig in hCTLA4, JAK inhibitors in STAT1-GOF and STAT3-GOF, etc.)
Organ Involvement & Management

- **Heme** – AIHA, ITP, Autoimmune Neutropenia.
- **GI** – Enteropathy, Liver
- **Lungs** – LIP, Follicular bronchiolitis, Granulomas
- **Skin** – Eczema, Psoriasis, Pemphigus nodularis
- **Endocrine** – Thyroiditis, Type I DM, Other
Lung – Diagnosis

- High resolution Chest CT
- Pulmonary function tests with DLCO and evaluation of reversibility with bronchodilators
- Lung biopsy – VATS usually much more informative than transbrochial. Stain biopsy for CD4 and CD8 T cells and for B cells.
- BAL with lavage – fluid for stains, cultures, and PCR for viruses, etc.
- Genetic Testing
Follicular Bronchiolitis & Granulomas

Light microscopy: Expansion of alveolar septa by multifocal dense nodular and diffuse interstitial infiltrates composed of mature lymphocytes and plasma cells. Multiple lymphoid aggregates with active germinal centers also seen.
Rituximab in CVID GLILD

Use of Combination Chemotherapy for Treatment of Granulomatous and Lymphocytic Interstitial Lung Disease (GLILD) in Patients with Common Variable Immunodeficiency (CVID)

Nicole M. Chase • James W. Verbsky • Mary K. Hintermeyer • Jill K. Waukau • Aoy Tomita-Mitchell • James T. Casper • Sumit Singh • Kaushik S. Shahir • William B. Tisol • Melodee L. Nugent • R. Nagarjun Rao • A. Craig Mackinnon • Lawrence R. Goodman • Pippa M. Simpson • John M. Routes

Key Point:
• Lung biopsy is essential to make sure you know what you are dealing with
• Rituximab + Azathioprine
Organ Systems

- **Heme** – AIHA, ITP, Autoimmune Neutropenia.
- **GI** – Enteropathy, Liver
- **Lungs** – LIP, Follicular bronchiolitis, Granulomas
- **Skin** – Eczema, Psoriasis, Pemphigus nodularis
- **Endocrine** – Thyroiditis, Type I DM, Other
Topics

1. 2 Informative Cases
2. Definitions and Prognosis
3. Diagnosis and Treatment
   A. Infections
   B. Autoimmunity
4. Hematopoietic Cell Transplant (HCT)
HCT for CVID

- 25 patients (European)
- Age at transplant 8-50 years
- Mutation known in 3 patients at transplant
- RIC & MAC regimens
- Overall survival 48%, survival if transplant for lymphoma 83%.
- 13 deaths – 9 infections, 2 cGvHD, 1 VOD, 1 lymphoma recurrence.

Timing of Transplant - CGD

287 patients from 244 kindreds

Abx Antifungal +/- IFN-γ

Early BMT

Residual NADPH Oxidase and Survival in Chronic Granulomatous Disease

Douglas B. Kuhns, Ph.D., W. Gregory Alvord, Ph.D., Theo Heller, M.B., Ch.B., Jordan J. Feld, M.D., M.P.H., Kristen M. Pike, M.S., Beatriz E. Marciano, M.D., Gulbu Uzel, M.D., Suk See DeRavin, M.D., Ph.D., Debra A. Long Priel, M.S., Benjamin P. Soule, M.D., Kol A. Zarember, Ph.D., Harry L. Malech, M.D., Steven M. Holland, M.D., and John I. Gallin, M.D.

NEJM 363:2600-10 (2010)
Timing of Transplant

CGD

Early BMT

CVID

287 patients from 244 kindreds

Figure 2. Kaplan-Meier curve for patients with and without noninfectious complications. Patients with noninfectious complications were significantly more likely to die than those with infections only (P < .0001).

Morbidity and mortality in common variable immune deficiency over 4 decades

Elena S. Reznick, Erin L. Moosheer, James H. Godbold, and Charlotte Cunningham-Rundles

Immunology Institute and Departments of Medicine, Preventive Medicine, and Pediatrics, Mount Sinai School of Medicine, New York, NY

BLOOD, 16 FEBRUARY 2012 - VOLUME 119, NUMBER 7
Transplant – Burning Questions

- When do I transplant (Timing)?
- How do I transplant (Regimen)?

- Disease and complication specific
- Changes with new data & experience
- Outcomes often poor to moderate in first experience & reports
Summary

1. CVID is a spectrum of disease
2. Need to treat and prophylax for infections AND autoimmunity
3. Genetic testing can be very valuable in the CVID+autoimmunity population
4. Hematopoietic Cell Transplant (HCT) should be considered in severe cases.