Introduction to Chronic GVHD

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All therapeutics are off-label
Chronic GVHD

- Most common late complication caused by transfer of stem cells from one person to another
  - Affects up to half of people
  - Average time to onset 4-6 months
  - Major cause of poor quality of life
  - Higher risk for medical complications and death if chronic GVHD is severe
What is chronic GVHD?

• Can affect almost any part of the body
• Due to “rejection” of the patient by the donor cells
  – Does not happen if a patient given their own cells back or cells from an identical twin
• Similar to autoimmune diseases - lupus, scleroderma, Sjogren’s, primary biliary cirrhosis
What does chronic GVHD look like?

- Most people with chronic GVHD have 3 or more affected body parts
- Most common:
  - Skin, mouth, eye, liver
- Less common:
  - Lung, intestines, joints, genital tract
- Rare:
  - Kidneys, heart, brain and nervous system, pancreas
How can chronic GVHD affect people?

- Worse quality of life
- Inability to work
- Financial challenges
- Changed family and societal roles
- Need for frequent clinic visits
- Need to take medications
- Increased risk of infections
- Increased risk of death
Health status

Fraser et al. Blood 2006;108:2867-2873
Is chronic GVHD ever a good thing?

• Yes, chronic GVHD is associated with less cancer relapse
  – In many studies, people who have a little chronic GVHD survive longer than those with none

• If transplant physicians could control the amount of GVHD a person has, we would want just a little for people transplanted for cancer, none for those transplanted for non-malignant diseases
Who is at greater risk for chronic GVHD?

- Older people
- Mismatched or unrelated donor vs. matched
- Female donor and male patient
- Higher numbers of T cells
  - Peripheral blood vs. bone marrow
  - Certain types of transplants are associated with a much lower risk of chronic GVHD:
    - Umbilical cord grafts, T cell depletion, Anti-thymocyte globulin (ATG)
What causes chronic GVHD?

• Not really known
• Immune cells from the donor
  – Inappropriately attack the patient
• Inflammation and scarring occur
• Severity varies
  – Some only need topical, nonabsorbed therapies
  – Others need several powerful immunosuppressive medications
How common is chronic GVHD?

- 10%-50% of people get chronic GVHD

- When chronic GVHD develops, usually happens in the first year
  - Only a 4% risk after the first year
  - Can happen very late if a person’s immunity is stimulated
How long does chronic GVHD last?

• Average length of treatment is 2-3 years
• Chronic GVHD usually eventually “burns itself out,” and people are able to stop medications
  – When chronic GVHD goes away, symptoms usually resolve
  – Some organ damage is permanent
• 15% of people are still being treated after 7 years
How do you treat chronic GVHD?

• Prednisone daily or every other day
  – additional immunosuppressive medications if needed
• Use topical or ancillary therapy whenever possible
• Treat until symptoms controlled and ongoing organ damage halted
• Taper to lowest level of medication needed
First line therapy

• Steroids at 1 mg/kg/day (90 mg for 200 lb)
  – Studies do not support the need for a calcineurin inhibitor (Koc Blood 2002; 100:49)
  – About 30% of people respond and never need additional treatment (Flowers Blood 2002; 100: 415)
  – No evidence that initial therapy should be modified based on risk of cancer relapse
  – Mycophenolate mofetil (Myfortic) should not be started as part of first line therapy (Martin Blood 2009; 113: 5074)
Second Line Therapy

• Needed if
  – New organ involvement
  – Poor or inadequate response to first line treatment
  – Intolerance of first line treatment
  – Inability to taper prednisone – “steroid-sparing”

• Broad range of options
  – Choice depends on organ involvement, anticipated toxicities, clinician experience, logistics, patient preference, insurance coverage
  – Try and see
Current Secondary Therapy

- Acitretin/etretinate
- Alefacept
- Alemtuzumab
- ATG
- Azathioprine
- Bortezomib
- Clofazimine
- Daclizumab
- Extracorporeal photopheresis (ECP)
- Etanercept
- Halofuginone
- Imatinib, nilotinib, dasatinib
- Infliximab
- IL-2
- Lidocaine
- Mesenchymal stem cells (MSC)
- Methotrexate
- Montelukast
- Mycophenolate mofetil
- Pentostatin
- Pravastatin
- Psoralen/UVA
- Rituximab
- Sirolimus
- Steroids (pulse)
- Thoraco-abdominal radiation
- T reg infusions
- Thalidomide
- Tocilizumab
- UVB

N=33 (3 not approved for any uses)
Response rate: 20-82%
Chronic GVHD Consortium

Clinical sites:
Fred Hutchinson
Stanford University
University of Minnesota
Dana-Farber Cancer Institute
Vanderbilt University
Medical College of Wisconsin
H. Lee Moffitt Cancer Center
Washington University
National Cancer Institute
Memorial Sloan Kettering
University of North Carolina
Weill Cornell Medical College
Mayo Clinics
Roswell Park Cancer Institute
Cleveland Clinic
Ohio State University

CA118953, CA163438
Long term complications of chronic GVHD

• Increased risk of infections
  – Powerful immunosuppressive medications
  – Poor nutrition
  – Mouth and skin ulcers
  – Chronic GVHD causes weakened immunity

• Increased risk of second cancers
  – Mouth, skin, thyroid

• Organ failure
  – Lung
Potential new treatments

• New medications
  – More targeted approaches

• Greater interest in preventing chronic GVHD
  – Choosing bone marrow as a stem cell source
  – Altering acute GVHD prophylactic medications
Precautions you can take

• Take prophylactic medications as directed
  – Antibiotics, antiviral, antifungal
• Use sun protection
• Maintain bone health
  – Calcium, vitamin D, weight-bearing exercise
• Routine medical follow up
  – Cancer screening
• Promptly notify your physician of changes
  – May be due to chronic GVHD or other complications
Summary

• Chronic GVHD affects up to half of people after transplantation of stem cells from another person.

• Can affect almost any organ, but skin, mouth, eye and liver are most common.

• Treatment is with powerful immunosuppressive medications and topical/local therapies.

• People with chronic GVHD need to work closely with their physicians to maintain their health.
Recommended post-transplant care
http://marrow.org/Physicians/
Post-Transplant_Care/
Post-Transplant_Care.aspx

Measuring therapeutic response in chronic GVHD Trials:
An instructional manual
http://www.asbmt.org/GVHDForms.htm