Chronic GVHD

• If you are on the call, you or someone else you love is likely experiencing chronic GVHD

• Please check these out:

Mary Flowers  Annie Im

Outline

• Our goal as providers and researchers in this field is to educate

• We want to improve your lives by providing care AND to let you know more about chronic GHVD and what we’re trying to do behind the scenes about it.

  ✓ Immune effects of donor (allogeneic) stem cell transplant
  ✓ Immune toxicity (graft versus host disease)
  ✓ Individual/”personalized” treatments
  ✓ It’s an exciting hopeful time!!

I have a clinical trial with an inhibitor and that is a conflict of interest. Nothing I’m about to say is meant to guide treatment or persuade you to do anything. Go to your provider for advice!
Allogeneic Stem Cell Transplantation (HCT)

Day 0

Month Post-

GVHD

Graft versus Host (GVHD)

Stem Cells Infused

Graft/donor

Host/patient

GVL

Acute GVHD

Chronic GVHD

Allo→Autoimmunity

Insidious onset

SIRS

Month Post-HSCT
Infections
Disability
Quality of life
Endocrine
Metabolism
Nutrition
Pain

Ocular sicca
Oral ulcers
Nail dystrophy
Skin sclerosis
Deep sclerosis
Bronchiolitis obliterans
Loss of bile ducts
Fasciitis
Skin ulcers

Spectrum of manifestations in chronic GVHD

Courtesy of Steve Pavletic MD, NCI
Report

National Institutes of Health Consensus Development Project on Criteria for Clinical Trials in Chronic Graft-versus-Host Disease: V. The 2014 Ancillary Therapy and Supportive Care Working Group Report

Consensus Groups & Consortia

• NIH Consensus Criteria, 2005, 2015

• NIH Consensus on Immune Deficiency after HCT, 2016

• Chronic GVHD consortium member

• Chronic GVHD natural history study at NCI, collaborate w/ Steve Pavletic
cGVHD Team at Duke!

Rambi Cardones, MD

Barbara Alexander, MD Jen (Horan) Saullo

Diana Cardona, MD

Keith Sullivan, MD

Rambi Cardones, MD

Ankoor Shah, MD

Victor Perez, MD

Scott Palmer MD

Jamie Todd MD

Barbara Alexander, MD
Studies Using Patient Samples have advance our Understanding of cGVHD
Schematic overview of the cellular and molecular mediators, known and implicated, contributing to the continuum of aGVHD and cGVHD pathology.

Targeted Treatment is Being Developed in Hopes of Preventing both cGVHD and Cancer Development

Commentary by Daniel H. Fowler, and Steven Z. Pavletic

Blood 2015;125:3974-3975
©2015 by American Society of Hematology
Mechanistic interventions for the prevention or treatment of chronic GVHD.

Corey S. Cutler et al. Blood 2017;129:22-29
What are we thinking when we see you in our clinic? Ruling out the worst case.

Assessment of worsening cGVHD reflective of cGVHD pathophysiology that requires urgent attention.

<table>
<thead>
<tr>
<th>‘Red Flag’ Poor Prognostic Marker</th>
<th>Ongoing cGVHD Pathophysiology (histochemical patient/basic science data)</th>
<th>Additional Urgent Work-up</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>A</strong></td>
<td>Airway blockage and/or constriction</td>
<td>High resolution expiratory chest CT Scan</td>
</tr>
<tr>
<td>↓ Forced expiratory volume (FEV1) if FEV1/FVC &lt;0.7</td>
<td>ECM</td>
<td>Diagnostic Bronchoscopy (rule out infection)</td>
</tr>
<tr>
<td>Hypoxia after 2 min. ambulation</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dry cough, abnormal lung exam</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>B</strong></td>
<td>Biliary Duct ‘withering and drop-out’</td>
<td>Serum PCR tests for viruses (CMV, HSV, adeno, EBV, Hepatitis virus if indicated)</td>
</tr>
<tr>
<td>↑3x normal Total Bilirubin (T. bili)</td>
<td></td>
<td>Consider liver biopsy to rule out drug toxicity or infection</td>
</tr>
<tr>
<td>↑3x normal Alkaline phosphatase (Alk Phos, AP)</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>C</strong></td>
<td>Mouth ulcerations → precludes eating</td>
<td>PCR of feces for enteroviruses</td>
</tr>
<tr>
<td>&gt;10% weight loss</td>
<td>Esophageal strictures</td>
<td>Endoscopy</td>
</tr>
<tr>
<td>Acute diarrhea</td>
<td>Lower gut GVHD</td>
<td></td>
</tr>
<tr>
<td><strong>D</strong></td>
<td>Immune attack</td>
<td>Plasma virus</td>
</tr>
<tr>
<td>↓ Platelets</td>
<td>Bone marrow Thymus Secondary lymph organs</td>
<td>Blood culture Bone marrow biopsy</td>
</tr>
</tbody>
</table>

Stefanie Sarantopoulos et al. Blood 2019;133:1191-1200
How to we decide if you’re responding to treatment and what to do next?

Refractory cGVHD

NIH moderate-severe cGVHD, worsening*

or

'Steroid-refractory disease'

Potential Next Steps:

Add and Perhaps Modify IST
--consider slow steroid wean
--consider weaning of other ineffective IST

Unresponsive cGVHD

Not worse clinically and no worsening of PFT or LFT (so-called ‘Steroid-dependent disease’)†

or

Fixed or irreversibly damaged organ(s)†

or

'Steroid-intolerant disease'‡

Potential Next Steps:

Wean steroids
Continue other IST

NIH global severity assessments to determine need for intervention in patients with ongoing cGVHD.

Our approach to patients seen in our multidisciplinary clinic for ongoing refractory cGVHD entails assessment of global severity score

Stefanie Sarantopoulos et al. Blood 2019;133:1191-1200

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Chronic Graft-versus-Host Disease: A Long Road Ahead

Sarah Anand 1, Stefanie Sarantopoulos 2,*

1 Adult Blood and Marrow Transplantation, Division of Hematology and Oncology, Department of Medicine, University of Michigan, Ann Arbor, Michigan
2 Duke Cancer Institute, Division of Hematological Malignancies and Cellular Therapy, Department of Medicine, Duke University, Durham, North Carolina

National Cancer Institute Consensus Project
Steve Pavletic

https://www.asbmt.org/practice-resources/nih-chronic-gvhd-consensus-project

Stephanie Lee
U of Wash, Fred Hutch

Meredith A. Cowden Foundation