2020 NIH Chronic GvHD Consensus Project on Criteria for Clinical Trials

November 18–20, 2020
Financial Disclosure

NONE
Dry eyes
Oral lesions
Nail dystrophy
Skin sclerosis
Deep sclerosis
Bronchiolitis obliterans
Loss of bile ducts
Fasciitis/Myositis
Skin ulcers

Manifestations in cGVHD
- 30-60% Incidence
- 15% Life Threatening INFECTIONS
# Chronic GVHD in 2020 - leukemia patients after T-replete haploidentical HCT and PTCy (> 18 years) CIBMTR, 2013-2016

<table>
<thead>
<tr>
<th>Outcome</th>
<th>MAC-BM N=79</th>
<th>MAC-PB N=183</th>
<th>RIC-BM N=192</th>
<th>RIC-PB N=192</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chronic GVHD 2-years</td>
<td>27%</td>
<td>44%</td>
<td>25%</td>
<td>35%</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Overall Survival 2-years</td>
<td>53%</td>
<td>55%</td>
<td>58%</td>
<td>43%</td>
<td>0.07</td>
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Im et al, Biol Blood Marrow Transplant 2020; 26:1459
HYPOTHESIS: Better characterization of chronic GVHD and standardization of research tools will lead to better research and ultimately improve clinical outcomes
NIH CGVHD Consensus Conference 2005 - 2014
Moving from Expert Opinion to Evidence-Based Standards: 13 highly reference publications in BBMT

2005 Consensus Conference

2014 Consensus Conference

NIH Consensus Reports:
- Diagnosis and Staging
- Pathology
- Biomarkers
- Therapeutic Response Criteria
- Ancillary Therapy & Supportive Care
- Criteria for Clinical Trials
- Biology of CGVHD

Total Scopus citations: 3358 by 1/2020

Total Scopus citations: 969 by 1/2020

2017: FDA first drug approval for cGVHD (ibrutinib)
2018: NEJM first chronic GVHD review (Zeiser and Blazar)

Era of development of novel targeted therapies
Chronic Graft-versus-Host disease
publications/year PubMed
since 2004 1st NIH Consensus conference

First descriptions CGVHD in man

PubMed, accessed 11/1/2020
Internationally recognized leader in bone marrow transplantation and pediatric immunology. She held the Ralph J. Stolle Chair of Pediatric Immunology at Cincinnati Children’s Hospital Medical Center, served as Head of the Division of Immunology at the University of Minnesota Medical School, and was president of the Histiocyte Society. Cincinnati Children’s gained national and international prominence for the treatment of HLH.
Chronic GVHD - where are we in 2020?

- Disease and clinical course are now well characterized
- Complex pathophysiology is much better understood
- Many investigational agents are available for treatment
- Resources are available through industry collaboration
- Regulatory approval pathway has been established
- Ibrutinib has been approved for steroid-refractory disease
Chronic GVHD - where are we in 2020?

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BUT

• Initial treatment is still calcineurin inhibitor and prednisone
• Best choice of subsequent treatment is still undefined
• No standard approaches to prevention or preemption
• Highly morbid forms of chronic GVHD still exist

Adapted from Paul Martin, lecture to Brazilian BMT Society
• To implement fundamental changes in research approach to cGVHD treatment and prevention
  • Etiology and prevention
  • Diagnosis and pre-emptive treatment
  • Treatment of established chronic GVHD
  • Highly morbid forms of chronic GVHD (lungs, sclerosis)
  • Industry and advocacy summit
  • Joint ASTCT-NIH-EBMT educational committee
Towards the 3rd NIH chronic GVHD consensus conference
November 18 - 20, 2020, NCI

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Vision: To eliminate chronic GVHD as a source of patient suffering and improve outcomes after allogeneic HCT
November 2019 steering committee formed four working groups
Each working group was organized to encourage global engagement
Four groups worked individually beginning in February 2020 to review the relevant literature and prepare the initial draft of the manuscript. The Steering Committee reviewed and discussed the initial draft and offered recommendations for revisions.
Two iterative rounds of comments and revisions were collected before the November 2020 Consensus Conference.
The manuscripts are further revised for submission in early 2021 after additional suggestions from external reviewers, virtual Conference participants, and a 30-day public comment period.
2020 Chronic GVHD Consensus
Process Goals

• What has been accomplished so far
• Gaps
• What should future research address
  • In next 3 years
  • In next 5-7 years
• Four research lanes and 4 WGs
<table>
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<tr>
<th>Chronic GVHD Research Lanes – 2020 Consensus Framework</th>
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<tbody>
<tr>
<td><strong>Intervention based on pre-transplant characteristics</strong></td>
</tr>
<tr>
<td>-------------------</td>
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<tr>
<td><strong>WG1</strong></td>
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<tr>
<td>Etiology/Prevention</td>
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<tr>
<td>Understanding of biologic processes / efficacy of interventions applied based on risk factors known before transplant, regardless of when the intervention is given</td>
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<td>cGVHD manifestations</td>
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2020 CGVHD NIH Consensus Steering Committee

- Steven Pavletic, (Bethesda), co-chair
- Kirk Schultz (Vancouver), co-chair
- Daniel Wolff (Regensburg), co-chair
- Stephanie Lee (Seattle), co-chair, lead editor
- Paul Martin (Seattle), lead editor
- Hildegard Greinix (Graz)
- Sophie Paczesny (Charleston, SC)
- Bruce Blazar (Minneapolis)
- Stefanie Sarantopoulos (Durham)
- Joseph Pidala (Tampa)
- Corey Cutler (Boston)
- Gerard Socie (Paris)
- Meredith Cowden (Akron)
- Linda Griffith (Bethesda, ex officio)
2020 CGVHD NIH Consensus Reviewers

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- John DiPersio, M.D., Washington University
- George Chen, M.D., University of Rochester
- Mark Juckett, M.D., University of Wisconsin
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- Franco Locatelli, M.D., Università Sapienza, Roma
- Areej El-Jawahri, M.D., Massachusetts General Hospital
- Robert Soiffer, M.D., Dana Farber Cancer Institute
- Daniel Weisdorf, M.D., University of Minnesota
- Keith Sullivan, M.D., Duke University
- Catherine Lee, University of Utah
- Jose Antonio Perez-Simon, M.D., Instituto de Biomedicina de Sevilla
- Doris Ponce, M.D. Memorial Sloan-Kettering Cancer Center
- Andrew Harris, M.D., University of Utah
NCI Shady Grove, November 2019
3rd NIH CGVHD consensus steering committee
CGVHD Steering Committee Conference Call

November 11, 2020
• “Miracles do not occur at random”

C.D. Bowen