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2020 NIH Chronic GvHD Consensus Project on Criteria for Clinical Trials

November 18–20, 2020

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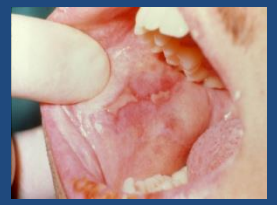
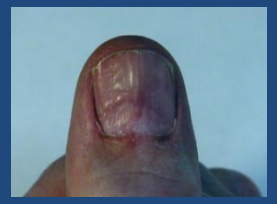
Financial Disclosure

NONE

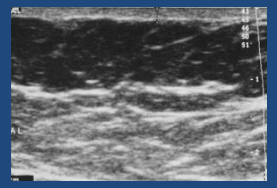
Dry eyes



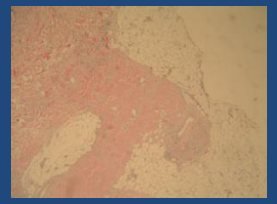
Oral lesions



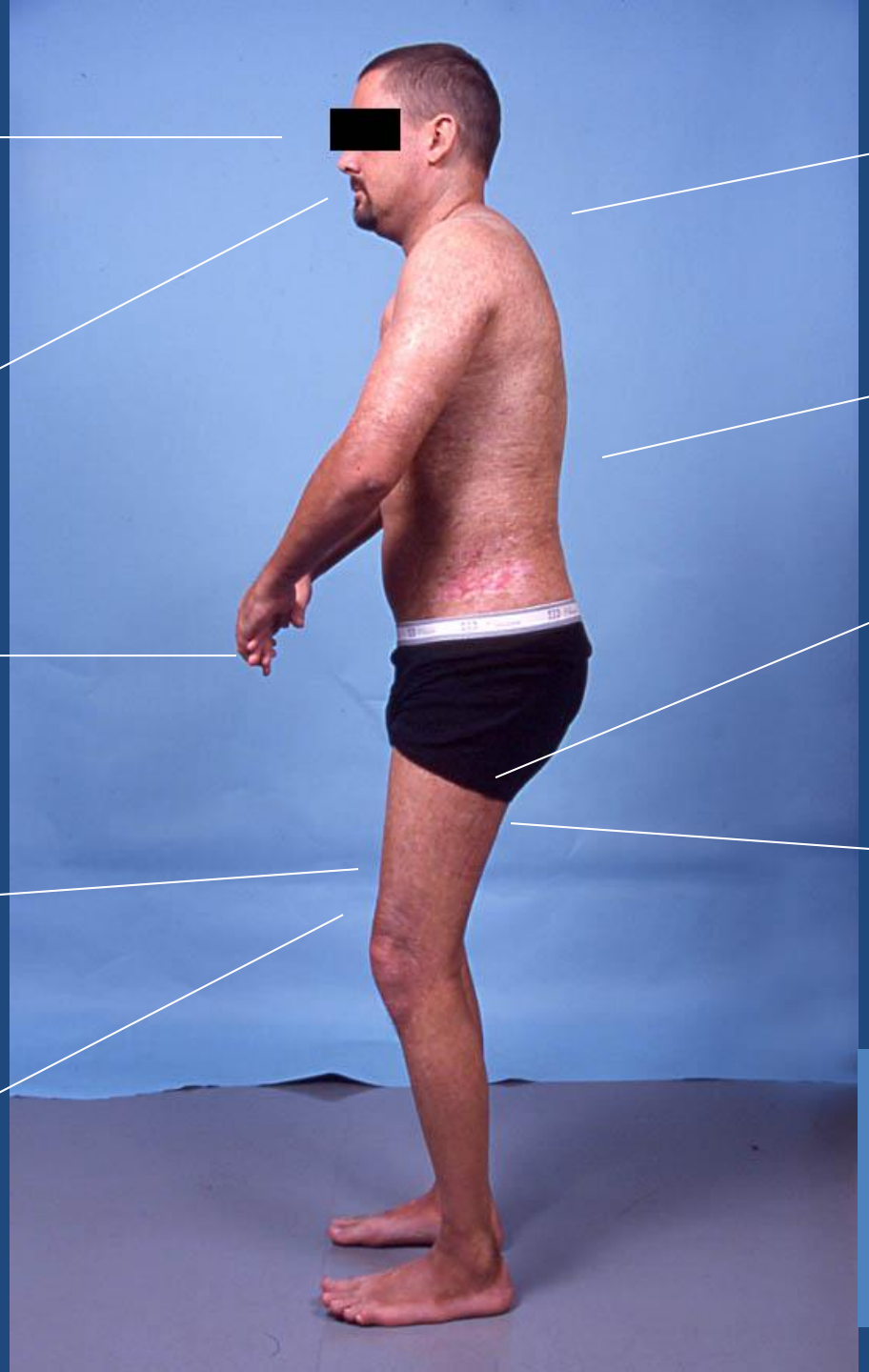
Nail dystrophy

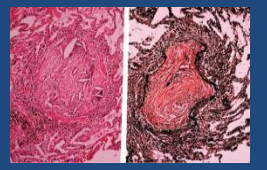


Skin sclerosis

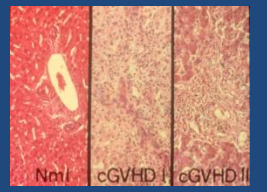


Deep sclerosis

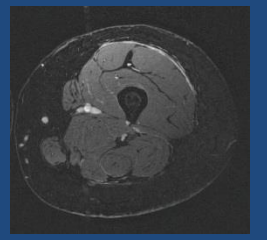




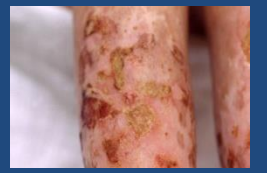
Bronchiolitis obliterans



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

Outcome	MAC-BM N=79	MAC-PB N=183	RIC-BM N=192	RIC-PB N=192	p-value
Chronic GVHD 2-years	27%	44%	25%	35%	<0.001
Overall Survival 2-years	53%	55%	58%	43%	0.07

Im et al, Biol Blood Marrow Transplant 2020; 26:1459

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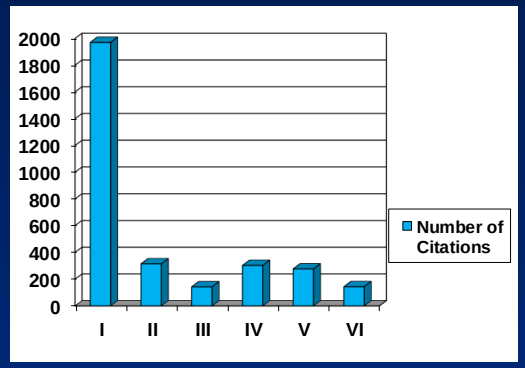
HYPOTHESIS:

Better characterization of chronic GVHD and standardization of research tools will lead to better research and ultimately improve clinical outcomes

NIH CGVHD Consensus Conferences 2005 - 2014
Moving from Expert Opinion to Evidence-Based Standards: 13 higly reference publications in BBMT

2005 Consensus Conference



Total Scopus citations: 3358 by 1/2020

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: 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

PubMed, accessed 11/1/2020

Georgia Vogelsang

Dr. Alexandra (Lisa) Hult Filipovich, MD
January 16, 1951 - May 18, 2020

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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.

Biology of Blood and Marrow Transplantation 11:945-955 (2005)

1083-8791/05/1112-0002$30.00/0
doi:10.1016/j.bbmt.2005.09.004

ASBMT American Society for Blood and Marrow Transplantation

National Institutes of Health Consensus Development Project on Criteria for Clinical Trials in Chronic Graft-versus-Host Disease: I. Diagnosis and Staging Working Group Report

Alexandra H. Filipovich,[1] Daniel Weisdorf,[2] Steven Pavletic,[3] Gerard Socie,[4] John R. Wingard,[5] Stephanie J. Lee,[6] Paul Martin,[7] Jason Chien,[7] Donna Przepiorka,[8] Daniel Couriel,[9] Edward W. Cowen,[3] Patricia Dinndorf,[10] Ann Farrell,[10] Robert Hartzman,[11] Jean Henslee-Downey,[12] David Jacobsohn,[13] George McDonald,[7] Barbara Mittleman,[14] J. Douglas Rizzo,[15] Michael Robinson,[16] Mark Schubert,[7] Kirk Schultz,[17] Howard Shulman,[7] Maria Turner,[3] Georgia Vogelsang,[18] Mary E.D. Flowers[7]

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

Adapted form Paul Martin, lecture to Brazilian BMT Society

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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 form Paul Martin, lecture to Brazilian BMT Society

Towards the 3rd NIH chronic GVHD consensus conference November 18 - 20, 2020, NCI

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- 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

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Vision: To eliminate chronic GVHD as a source of patient suffering and improve outcomes after allogeneic HCT

2020 CGVHD Consensus Methods

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- 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

Chronic GVHD Research Lanes – 2020 Consensus Framework

cGVHD manifestations

Intervention based on pre-transplant characteristics	Intervention based on post-transplant information	Established chronic GVHD	Severe, advanced chronic GVHD
WG1	WG2	WG3	WG4
Etiology/Prevention	Diagnosis/Pre-emptive therapy	Systemic treatment	Highly morbid phenotypes
Understanding of biologic processes / efficacy of interventions applied based on risk factors known before transplant, regardless of when the intervention is given	Intervention determined after transplant based on a higher than previously appreciated risk of developing chronic GVHD based on secondary events, signs, symptoms or biomarkers	Systemic treatments for established chronic GVHD, including initial and subsequent therapies	Understanding of the biologic differences in highly morbid phenotypes / local and systemic interventions specifically targeting these morbid conditions

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

- **Nicolaus Kroeger**, M.D., University of Hamburg
- **Ryotaro Nakamura**, M.D., City of Hope Cancer Center
- **John DiPersio**, M.D., Washington University
- **George Chen**, M.D., University of Rochester
- **Mark Juckett**, M.D., University of Wisconsin
- **Rafael Duarte**, M.D., University Puerta de Hierro Majadahonda
- **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

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November 11, 2020

- “Miracles do not occur at random”

C.D. Bowen