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Overlap cGVHD: assessment in the real life

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Disclosures of Drazen Pulanic

Company name	Research support	Employee	Consultant	Stockholder	Honoraria	Advisory board	Other
Novartis					Yes		
Takeda					Yes		



Chronic *Graft-versus-Host Disease* (cGvHD)

- Multiorgan allo- and auto-immune disorder
- Increasing risk for cGvHD with new transplant procedures, older age of patients and longer long-term survival
- Chronic GvHD is today the most important risk factor for non-relapse morbidity and mortality after alloHSCT



Chronic GvHD

Dry eyes

Oral lesions

Nail dystrophy

Skin sclerosis

Deep sclerosis

BOS

Loss of biliary ducts

Fasciitis

Skin ulcers

Genitourinary
Autoantibodies
Infections
Endocrinology
Nutrition
Coagulation
Pain
Neurology
Quality of life



Chronic *Graft-versus-Host Disease* (cGvHD)

Seattle Classification of cGvHD

- **Limited**
 - Localized skin and/or hepatic dysfunction due to cGvHD
- **Extensive**
 - Generalized skin involvement
 - Localized skin involvement and/or hepatic dysfunction plus liver histology or cirrhosis or involvement of eye or minor salivary glands or oral mucosa or any other target organ

Shulman HM et al, Am J Med 1980; 69: 204-217



2005: NIH consensus development project of criteria for clinical trials in cGvHD

Co-chairs: S.Pavletic, NCI
G.Vogelsang, Johns Hopkins

1. Diagnosis and staging

Filipovich A. et al, BBMT 11:945, 2005

2. Histopathology

Shulman H. et al, BBMT 12:31, 2006

3. Biomarkers

Schultz K. et al, BBMT 12:126, 2006

4. Response criteria

Pavletic S. et al, BBMT 12: 252, 2006

5. Ancillary and supportive care

Couriel D. et al, BBMT 12: 375, 2006

6. Clinical trials design

Martin P. et al, BBMT 12: 491, 2006



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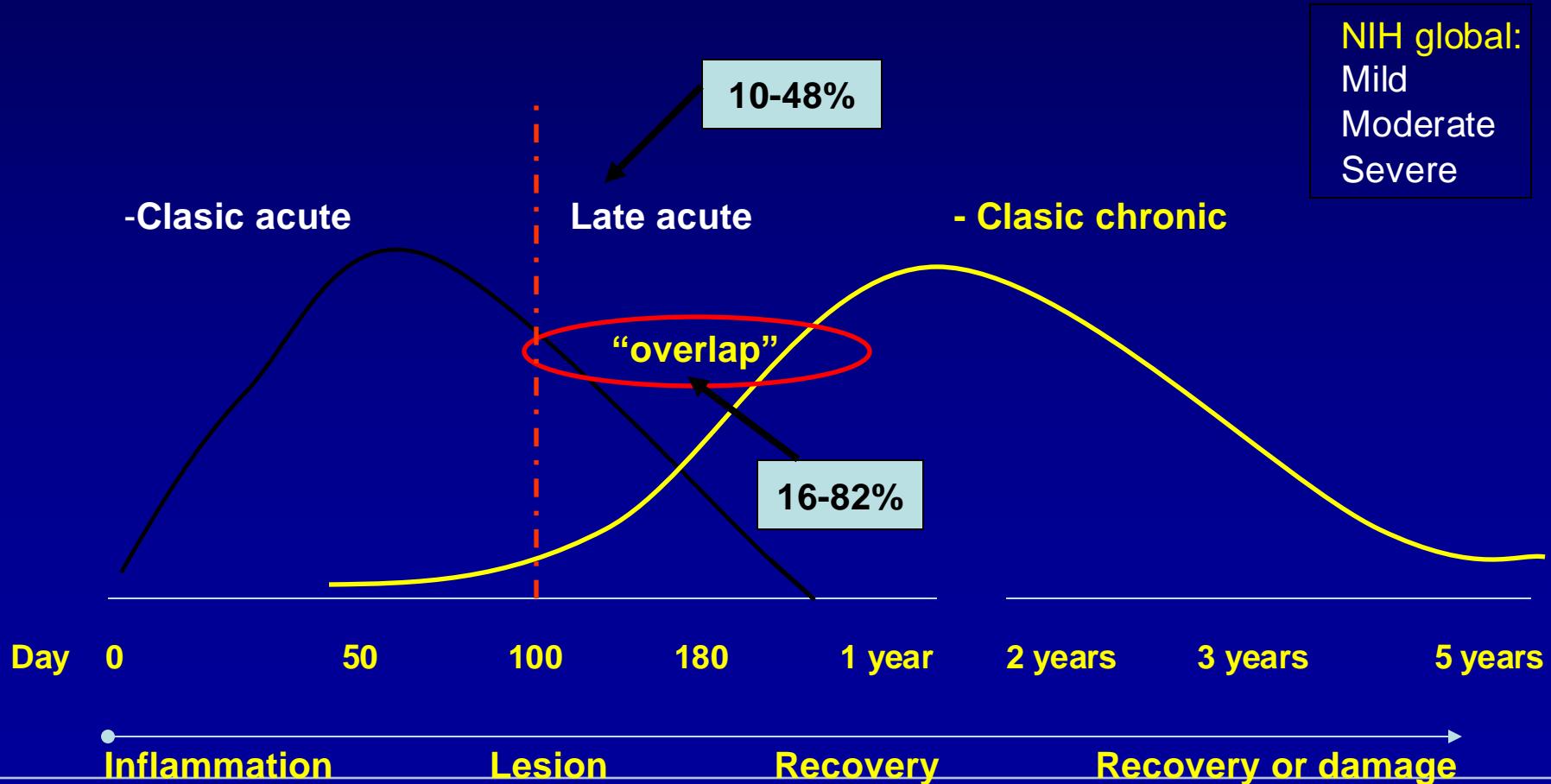


GITMO Symposium
HOT TOPICS IN CHRONIC GVHD

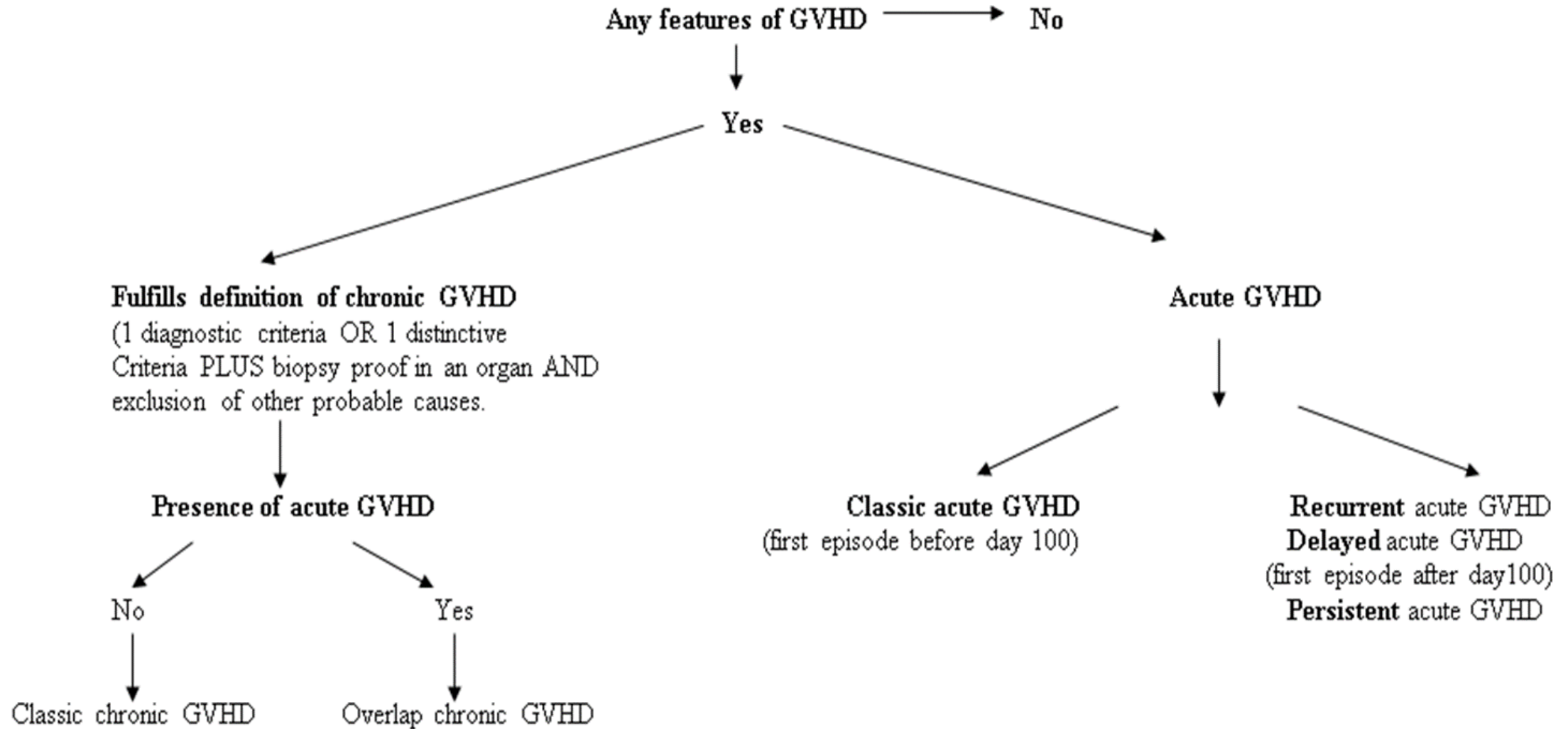
GvHD after NIH consensus conference 2005

Acute GVHD: skin, GI, liver

Chronic GVHD: Skin, eyes, mouth, GI, liver, joints/fascia, lungs, genitourinary



Using the NIH Consensus Criteria



Assessment of Chronic GvHD

Establish diagnosis

1. Exclude acute GvHD
2. Diagnostic or distinctive signs
3. Rule out other disease

Organ score

8 organs
Based on symptoms, signs, function

Global score

Overall severity
Prognosis
Need for systemic/topical therapy



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Overlap Graft-versus-Host Disease (oGvHD)

- “Overlap syndrome” - a particular subtype of GvHD
- Characterized by a high degree of uncertainties concerning both diagnosis and treatment due to the simultaneous presence of acute and chronic GvHD features.
- Skin, liver and GI manifestations cannot be unequivocally attributable either to acute or chronic GvHD → a huge variability of the diagnosis of oGvHD, that is probably misunderstood either with late acute or early chronic GvHD.



Overlap Graft-versus-Host Disease (oGvHD)

- aGvHD together with cGvHD was associated with a worse prognosis relative to classic cGvHD: 5-year OS and GvHD specific survival (GSS) were significantly lower for oGvHD relative to classical cGvHD, 68% vs 81% ($p=0.004$) and 78% vs 94% ($p<0.001$)
- simultaneous presence of acute GvHD in a single organ (skin, liver, intestine) plus cGvHD signs was associated with reduced survival when compared with classic cGvHD
- presence of aGvHD of the lower GI or of the liver (isolated hyperbilirubinemia) in the context of cGvHD, identified a group of patients with greater risk of non-relapse mortality

Haematologica 2012;97:451-458.

Overlap Graft-versus-Host Disease (oGvHD)

- There is no consensus regarding the therapy and clinical response of overlap GvHD.
- The real world incidence of this disease is not well known.
- The real world data regarding outcome and clinical response to available treatments for oGvHD are not well known.
- Biomarkers that may help distinguishing oGvHD from other types of GvHD are needed.
- More detailed clinical and biological characterization would contribute to standardize both its diagnosis and treatment.

