

EICRc: más allá de hematología. Necesidad de equipos multidisciplinares para un control óptimo

Mesa GETH 2023

EICRc 360º: abordaje integral para optimizar el control y la Calidad de Vida del
paciente con EICR crónica

Málaga, 15 de marzo de 2024

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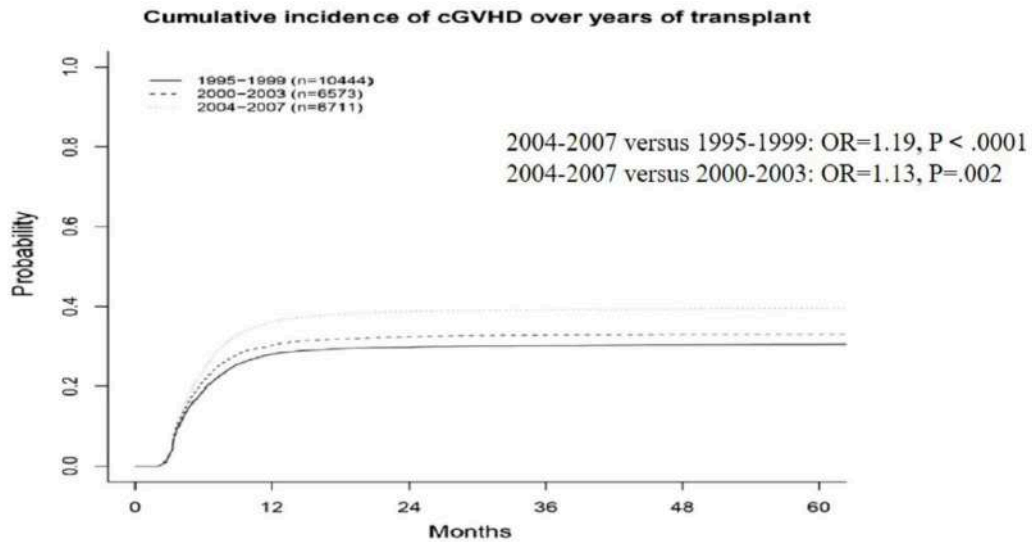
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- 2. Afectación Orgánica en EICRc**
- 3. Manejo EICRc**
- 4. Consulta multidisciplinaria**
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1. Introducción

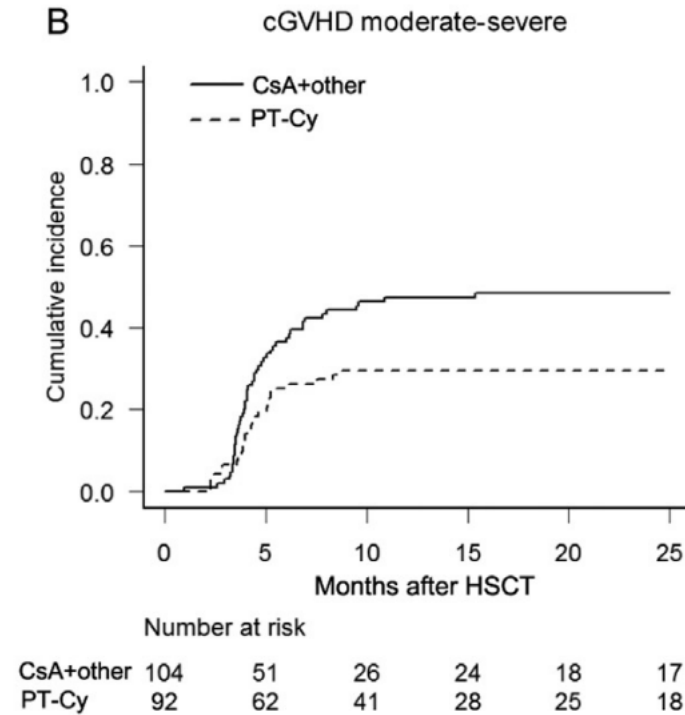
Menor incidencia de EICRc

EICRc según los años



Arai S et al. Biol Blood Marrow Transplant 2015;21:266-274

PTCY vs CsA en TPH HLAid

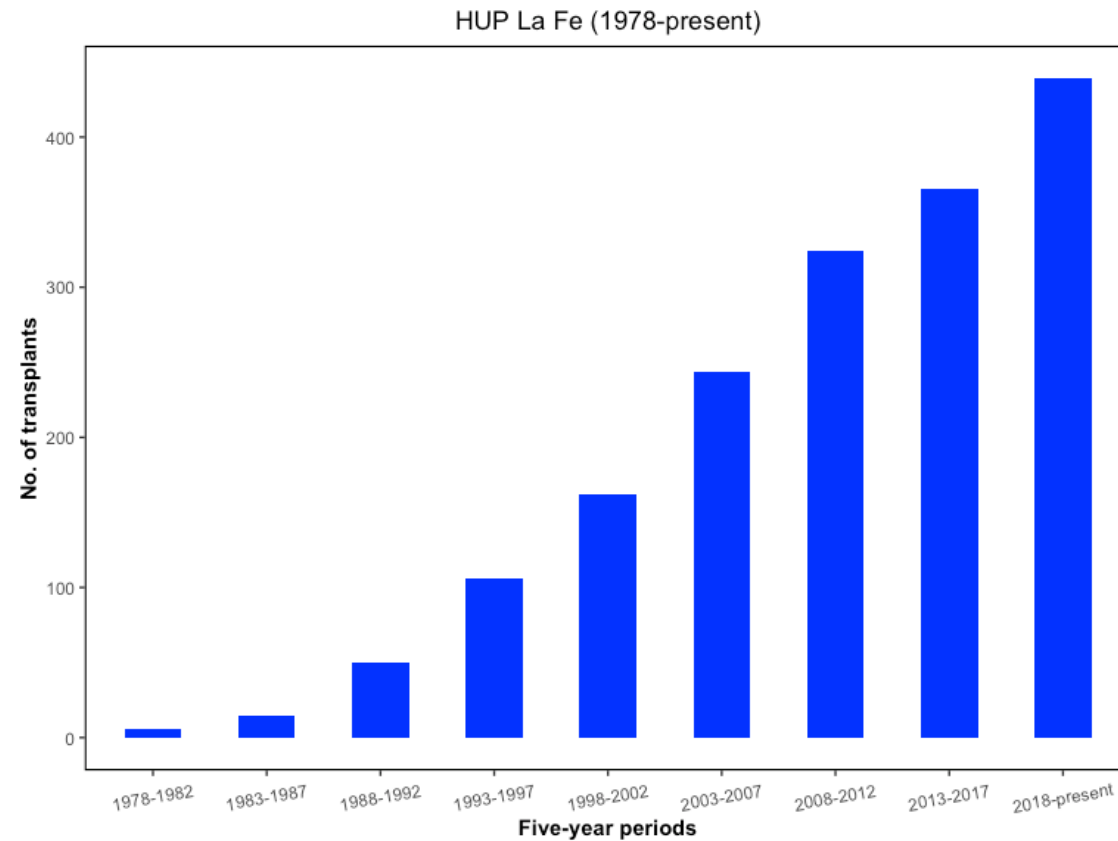


Marco-Ayala J. *Transplant. Cell. Ther.* 2023

1. Introducción

Mayor actividad TPH

Actividad de TPH por periodos





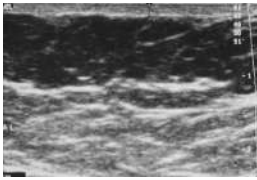
Ocular sicca



Oral ulcers



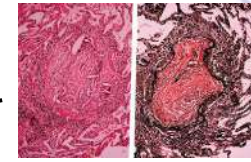
Nail dystrophy



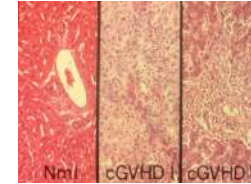
Skin sclerosis



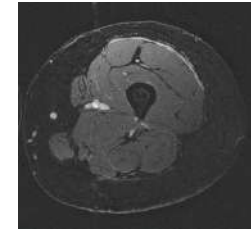
Deep sclerosis



Bronchiolitis obliterans



Loss of bile ducts



Fasciitis



Skin ulcers

Infections
Disability
Quality of life
Endocrine
Metabolism
Nutrition
Pain

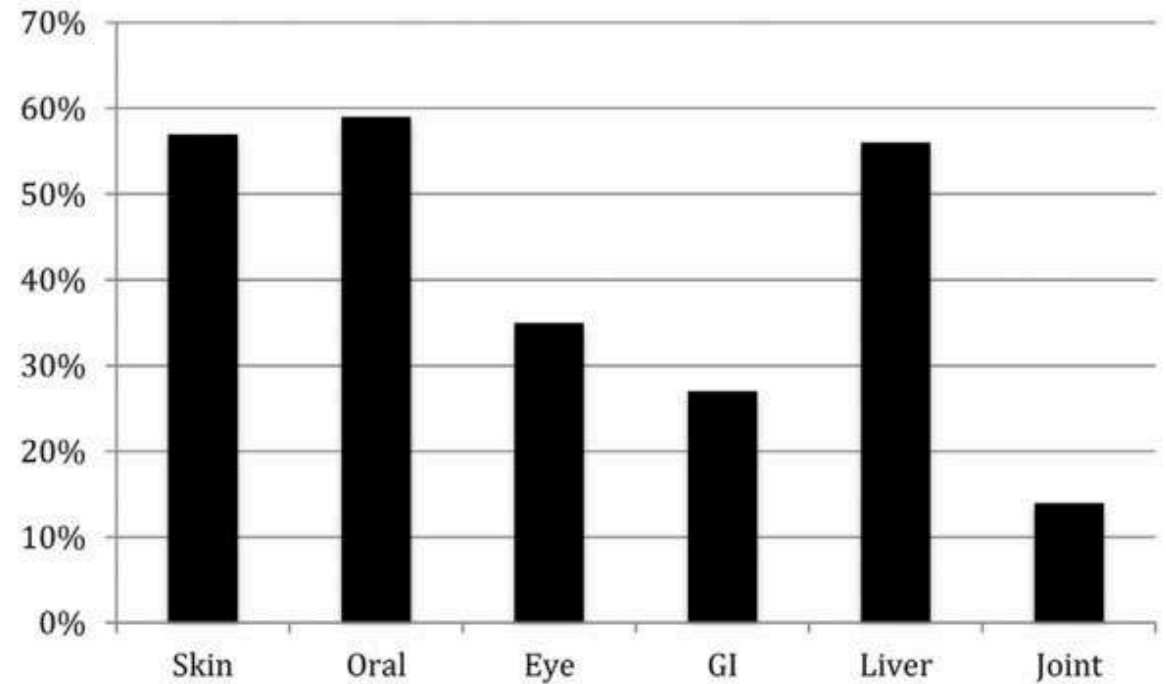
Spectrum of
manifestations
in chronic GVHD

All Images Are Copyright Protected

2. Afectación Orgánica en EICRc

TARGET ORGANS

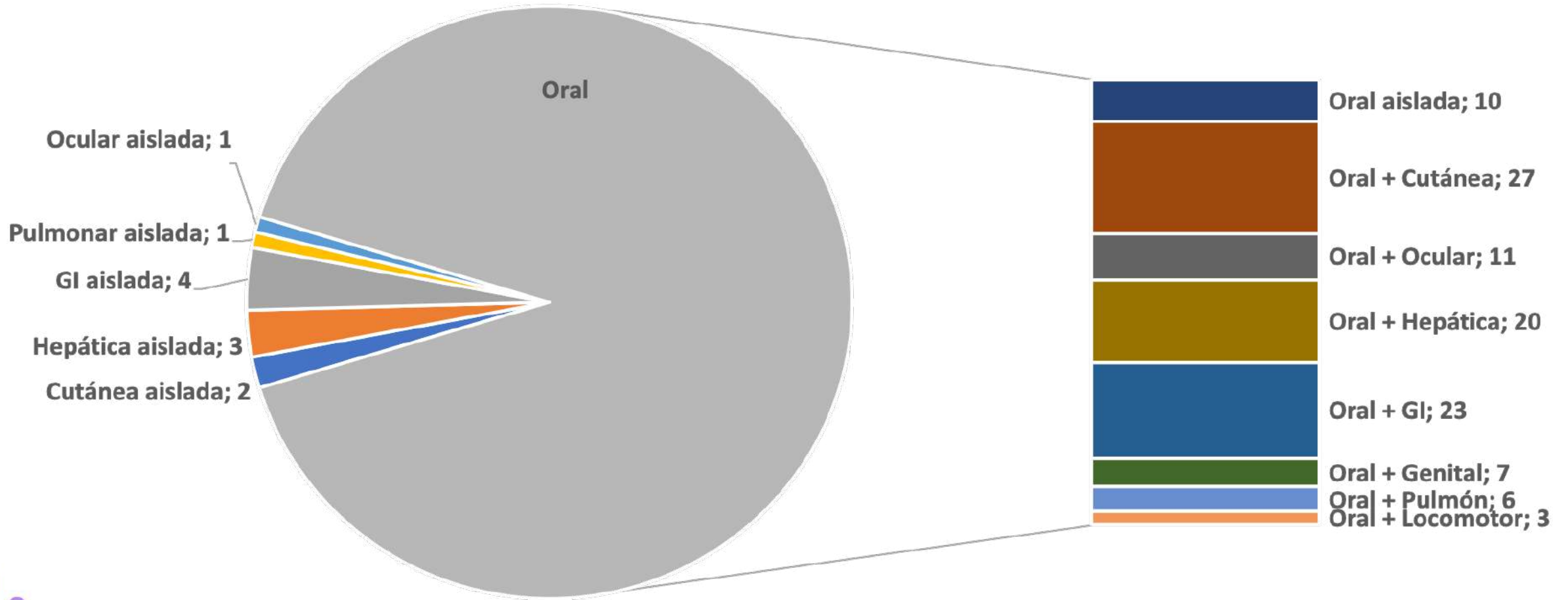
- Skin (50-55%)
- Oral mucosa (50-60%)
- Eye (30-40%)
- Liver (50%)
- Joints/fascias (40-50%)
- Gastrointestinal (20-30%)
- Lungs (10-15%)
- Genitalia (10-15%)



Abbreviations: GI: gastro-intestinal

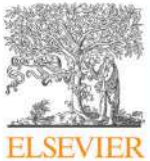
Figure 2. Organ involvement in patients with cGVHD.

2. Afectación Orgánica en EICRc



3. Manejo EICRc

Diagnóstico y Gradación



Biology of Blood and Marrow Transplantation

journal homepage: www.bbmt.org



Report

National Institutes of Health Consensus Development Project on Criteria for Clinical Trials in Chronic Graft-versus-Host Disease: I. The 2014 Diagnosis and Staging Working Group Report



Madan H. Jagasia¹, Hildegard T. Greinix², Mukta Arora³, Kirsten M. Williams^{4,5}, Daniel Wolff⁶, Edward W. Cowen⁴, Jeanne Palmer⁷, Daniel Weisdorf³, Nathaniel S. Treister⁸, Guang-Shing Cheng⁹, Holly Kerr¹⁰, Pamela Stratton¹¹, Rafael F. Duarte¹², George B. McDonald⁹, Yoshihiro Inamoto¹³, Afonso Vigorito¹⁴, Sally Arai¹⁵, Manuel B. Datile¹⁶, David Jacobsohn⁵, Theo Heller¹⁷, Carrie L. Kitko¹⁸, Sandra A. Mitchell¹⁹, Paul J. Martin⁹, Howard Shulman⁹, Roy S. Wu²⁰, Corey S. Cutler²¹, Georgia B. Vogelsang²², Stephanie J. Lee⁹, Steven Z. Pavletic⁴, Mary E.D. Flowers^{9,*}

Bone Marrow Transplantation (2018) 53:1401–1415
<https://doi.org/10.1038/s41409-018-0204-7>



FEATURE



EBMT—NIH—CIBMTR Task Force position statement on standardized terminology & guidance for graft-versus-host disease assessment

Helene M. Schoemans¹ · Stephanie J. Lee² · James L. Ferrara³ · Daniel Wolff⁴ · John E. Levine³ · Kirk R. Schultz⁵ · Bronwen E. Shaw⁶ · Mary E. Flowers² · Tapani Ruutu⁷ · Hildegard Greinix⁸ · Ernst Holler⁴ · Grzegorz Basak⁹ · Rafael F. Duarte¹⁰ · Steven Z. Pavletic¹¹ on behalf of the EBMT (European Society for Blood and Marrow Transplantation) Transplant Complications Working Party and the “EBMT—NIH (National Institutes of Health)—CIBMTR (Center for International Blood and Marrow Transplant Research) GvHD Task Force”

3. Manejo EICRc

Diagnóstico

- **DIAGNOSTIC:** sufficient for the diagnosis of cGVHD
- **DISTINCTIVE:** observed in cGVHD , but insufficient for diagnosis. Require a biopsy or other relevant test. Exclusion of other diagnoses.
- **OTHER/UNCLASSIFIED :** rare, controversial or non-specific signs. Considered part of cGVHD if the diagnosis is confirmed.
- **COMMON:** manifestations observed in aGVHD and cGVHD

3. Manejo EICRc

Diagnóstico

- **SKIN:**
 - Poikiloderma
 - Lichen planus-like features
 - Sclerotic features
 - Morphea-like features
 - Lichen sclerosus-like features
- **MOUTH:** Lichen planus-like changes
- **GENITALIA:**
 - Lichen planus-like features
 - Lichen sclerosus-like features
 - Vaginal scarring or clitoral/labial agglutination
 - Phimosis or urethral/meatus scarring or stenosis
- **GI:**
 - Esophageal web
 - Strictures or stenosis in the upper to mid third of the esophagus
- **LUNG:** BOS diagnosed with biopsy
*LFS if other distinctive feature present
- **MUSCLE/FASCIA/JOINT:**
 - Fasciitis
 - Joint stiffness or contractures secondary to fasciitis or sclerosis

3. Manejo EICRc

Gradación

	SCORE 0	SCORE 1	SCORE 2	SCORE 3
PERFORMANCE SCORE: [] KPS ECOG LPS	<input type="checkbox"/> Asymptomatic and fully active (ECOG 0; KPS or LPS 100%)	<input type="checkbox"/> Symptomatic, fully ambulatory, restricted only in physically strenuous activity (ECOG 1, KPS or LPS 80-90%)	<input type="checkbox"/> Symptomatic, ambulatory, capable of self-care, >50% of waking hours out of bed (ECOG 2, KPS or LPS 60-70%)	<input type="checkbox"/> Symptomatic, limited self-care, >50% of waking hours in bed (ECOG 3-4, KPS or LPS <60%)
SKIN† SCORE % BSA [] <i>GVHD features to be scored by BSA:</i> Check all that apply: <input type="checkbox"/> Maculopapular rash/erythema <input type="checkbox"/> Lichen planus-like features <input type="checkbox"/> Sclerotic features <input type="checkbox"/> Papulosquamous lesions or ichthyosis <input type="checkbox"/> Keratosis pilaris-like GVHD	<input type="checkbox"/> No BSA involved	<input type="checkbox"/> 1-18% BSA	<input type="checkbox"/> 19-50% BSA	<input type="checkbox"/> >50% BSA
SKIN FEATURES SCORE:	<input type="checkbox"/> No sclerotic features		<input type="checkbox"/> Superficial sclerotic features "not hidebound" (able to pinch)	Check all that apply: <input type="checkbox"/> Deep sclerotic features <input type="checkbox"/> "Hidebound" (unable to pinch) <input type="checkbox"/> Impaired mobility <input type="checkbox"/> Ulceration
<i>Other skin GVHD features (NOT scored by BSA)</i> Check all that apply: <input type="checkbox"/> Hyperpigmentation <input type="checkbox"/> Hypopigmentation <input type="checkbox"/> Poikiloderma <input type="checkbox"/> Severe or generalized pruritus <input type="checkbox"/> Hair involvement <input type="checkbox"/> Nail involvement <input type="checkbox"/> Abnormality present but explained entirely by non-GVHD documented cause (specify): _____				

	SCORE 0	SCORE 1	SCORE 2	SCORE 3
MOUTH <i>Lichen planus-like features present:</i> <input type="checkbox"/> Yes <input type="checkbox"/> No <input type="checkbox"/> Abnormality present but explained entirely by non-GVHD documented cause (specify): _____	<input type="checkbox"/> No symptoms	<input type="checkbox"/> Mild symptoms with disease signs but not limiting oral intake significantly	<input type="checkbox"/> Moderate symptoms with disease signs with partial limitation of oral intake	<input type="checkbox"/> Severe symptoms with disease signs on examination with major limitation of oral intake
EYES <i>Keratoconjunctivitis sicca (KCS) confirmed by ophthalmologist:</i> <input type="checkbox"/> Yes <input type="checkbox"/> No <input type="checkbox"/> Not examined <input type="checkbox"/> Abnormality present but explained entirely by non-GVHD documented cause (specify): _____	<input type="checkbox"/> No symptoms	<input type="checkbox"/> Mild dry eye symptoms not affecting ADL (requirement of lubricant eye drops ≤ 3 x per day)	<input type="checkbox"/> Moderate dry eye symptoms partially affecting ADL (requiring lubricant eye drops > 3 x per day or punctal plugs), WITHOUT new vision impairment due to KCS	<input type="checkbox"/> Severe dry eye symptoms significantly affecting ADL (special eyewear to relieve pain) OR unable to work because of ocular symptoms OR loss of vision due to KCS
GI Tract Check all that apply: <input type="checkbox"/> Esophageal web/proximal stricture or ring <input type="checkbox"/> Dysphagia <input type="checkbox"/> Anorexia <input type="checkbox"/> Nausea <input type="checkbox"/> Vomiting <input type="checkbox"/> Diarrhea <input type="checkbox"/> Weight loss ≥5%* <input type="checkbox"/> Failure to thrive <input type="checkbox"/> Abnormality present but explained entirely by non-GVHD documented cause (specify): _____	<input type="checkbox"/> No symptoms	<input type="checkbox"/> Symptoms without significant weight loss* (<5%)	<input type="checkbox"/> Symptoms associated with mild to moderate weight loss* (5-15%) OR moderate diarrhea without significant interference with daily living	<input type="checkbox"/> Symptoms associated with significant weight loss* >15%, requires nutritional supplement for most calorie needs OR esophageal dilation OR severe diarrhea with significant interference with daily living

3. Manejo EICRc

Gradación

	SCORE 0	SCORE 1	SCORE 2	SCORE 3
LIVER	<input type="checkbox"/> Normal total bilirubin and ALT or AP < 3 x ULN	<input type="checkbox"/> Normal total bilirubin with ALT ≥ 3 to 5 x ULN or AP ≥ 3 x ULN	<input type="checkbox"/> Elevated total bilirubin but ≤ 3 mg/dL or ALT > 5 ULN	<input type="checkbox"/> Elevated total bilirubin > 3 mg/dL
<input type="checkbox"/> Abnormality present but explained entirely by non-GVHD documented cause (specify):				

	SCORE 0	SCORE 1	SCORE 2	SCORE 3
LUNGS**				
Symptom score:	<input type="checkbox"/> No symptoms	<input type="checkbox"/> Mild symptoms (shortness of breath after climbing one flight of steps)	<input type="checkbox"/> Moderate symptoms (shortness of breath after walking on flat ground)	<input type="checkbox"/> Severe symptoms (shortness of breath at rest; requiring O ₂)
Lung score:	<input type="checkbox"/> FEV1 $\geq 80\%$	<input type="checkbox"/> FEV1 60-79%	<input type="checkbox"/> FEV1 40-59%	<input type="checkbox"/> FEV1 $\leq 39\%$
% FEV1	<input type="text" value=""/>			

Pulmonary function tests

- Not performed
- Abnormality present but explained entirely by non-GVHD documented cause (specify):

	SCORE 0	SCORE 1	SCORE 2	SCORE 3
JOINTS AND FASCIA	<input type="checkbox"/> No symptoms	<input type="checkbox"/> Mild tightness of arms or legs, normal or mild decreased range of motion (ROM) AND not affecting ADL	<input type="checkbox"/> Tightness of arms or legs OR joint contractures, erythema thought due to fasciitis, moderate decrease ROM AND mild to moderate limitation of ADL	<input type="checkbox"/> Contractures WITH significant decrease of ROM AND significant limitation of ADL (unable to tie shoes, button shirts, dress self etc.)
P-ROM score (see below)				
Shoulder (1-7):	___			
Elbow (1-7):	___			
Wrist/finger (1-7):	___			
Ankle (1-4):	___			
<input type="checkbox"/> Abnormality present but explained entirely by non-GVHD documented cause (specify):				

	SCORE 0	SCORE 1	SCORE 2	SCORE 3
GENITAL TRACT (See Supplemental figure ³)	<input type="checkbox"/> No signs	<input type="checkbox"/> Mild signs [†] and females with or without discomfort on exam	<input type="checkbox"/> Moderate signs [†] and may have symptoms with discomfort on exam	<input type="checkbox"/> Severe signs [†] with or without symptoms
<input type="checkbox"/> Not examined				
Currently sexually active	<input type="checkbox"/> Yes			
	<input type="checkbox"/> No			
<input type="checkbox"/> Abnormality present but explained entirely by non-GVHD documented cause (specify):				

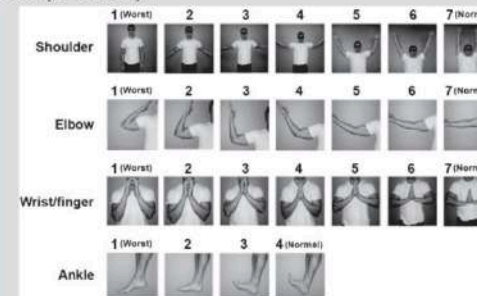
Other indicators, clinical features or complications related to chronic GVHD (check all that apply and assign a score to severity (0-3) based on functional impact where applicable none – 0, mild -1, moderate -2, severe -3)

- Ascites (serositis) ___
- Myasthenia Gravis ___
- Pericardial Effusion ___
- Peripheral Neuropathy ___
- Pleural Effusion(s) ___
- Polymyositis ___
- Nephrotic syndrome ___
- Weight loss > 5%* without GI symptoms ___
- Eosinophilia > 500/ μ l ___
- Platelets < 100,000/ μ l ___
- Others (specify):

Overall GVHD Severity (Opinion of the evaluator)

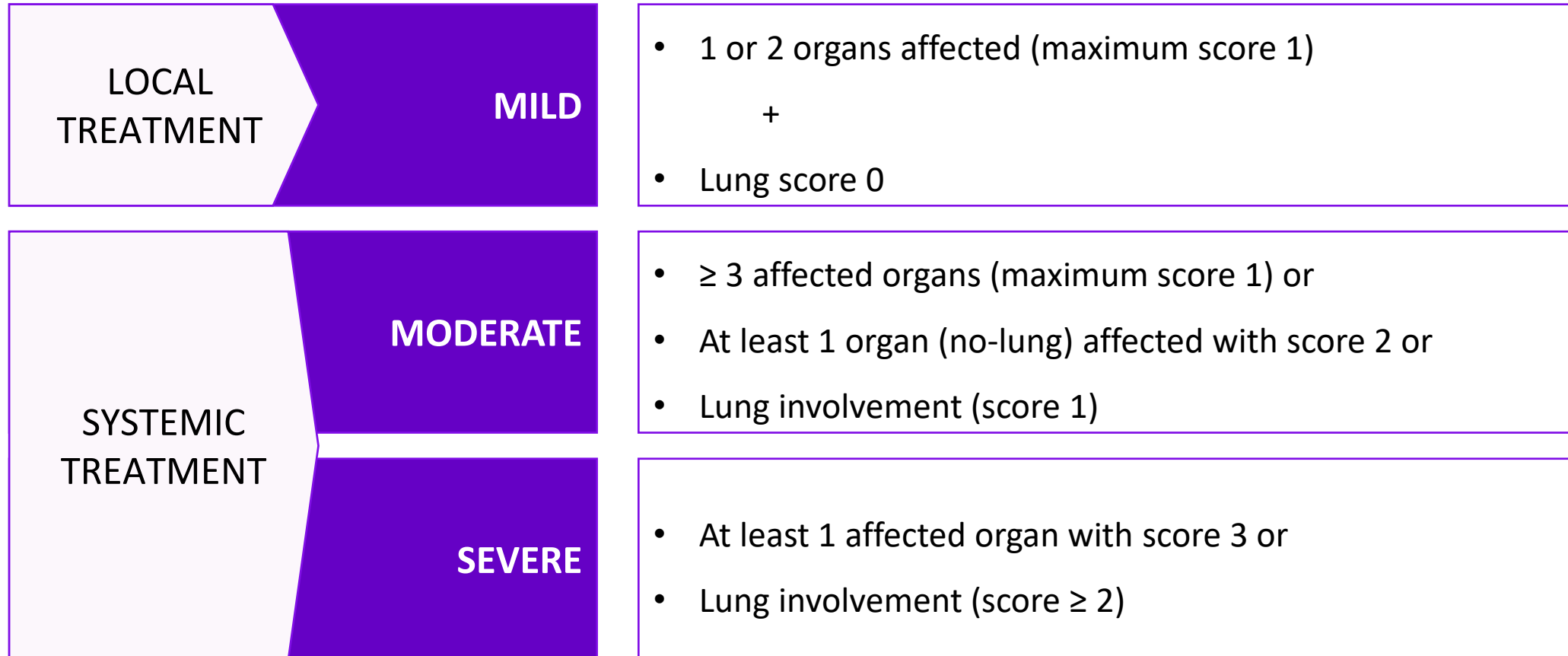
- No GVHD Mild Moderate Severe

Photographic Range of Motion (P-ROM)



3. Manejo EICRc

Gradación y tratamiento



3. Manejo EICRc

Tratamiento tópico

Biology of Blood and Marrow Transplantation 12:375-396 (2006)
© 2006 American Society for Blood and Marrow Transplantation
1083-8791/06/1204-0001\$32.00/0
doi:10.1016/j.bbmt.2006.02.003



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

Daniel Couriel,¹ Paul A. Carpenter,² Corey Cutler,³ Javier Bolaños-Meade,⁴ Nathaniel S. Treister,⁵ Juan Gea-Banacloche,⁶ Paul Shaughnessy,⁷ Sharon Hymes,¹ Stella Kim,¹ Alan S. Wayne,⁶ Jason W. Chien,² Joyce Neumann,¹ Sandra Mitchell,⁶ Karen Syrjala,² Carina K. Moravec,² Linda Abramovitz,⁸ Jerry Liebermann,⁹ Ann Berger,¹⁰ Lynn Gerber,¹⁰ Mary Schubert,² Alexandra H. Filipovich,¹¹ Daniel Weisdorf,¹² Mark M. Schubert,² Howard Shulman,² Kirk Schultz,¹³ Barbara Mittelman,¹⁴ Steven Pavletic,⁶ Georgia B. Vogelsang,⁴ Paul J. Martin,² Stephanie J. Lee,² Mary E. D. Flowers²

3. Manejo EICRc

Evaluación de respuesta



Biology of Blood and Marrow Transplantation

journal homepage: www.bbmt.org



Report

National Institutes of Health Consensus Development Project on Criteria for Clinical Trials in Chronic Graft-versus-Host Disease: I. The 2014 Diagnosis and Staging Working Group Report



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3. Manejo EICRc

Evaluación de respuesta

Organ	Scale	CR	PR	Progression
SKIN	NIH severity score (0-3)	0	≥ 1 point	≥ 1 point (except 0 → 1)
EYES	NIH severity score (0-3)	0	≥ 1 point	≥ 1 point (except 0 → 1)
JOINTS	NIH severity score (0-3)	0	≥ 1 point	≥ 1 point
	P-ROM (4-25)	25	≥ 1 point	≥ 1 point
MOUTH	Modified Schubert Oral Mucosa Rating Scale (4-25)	0	≥ 2 point	≥ 2 point
ESOPHAGUS	Esophagus response scales (0-3)	0	≥ 1 point	≥ 1 point (except 0 → 1)
UPPER GI	Upper-GI response scales (0-3)	0	≥ 1 point	≥ 1 point (except 0 → 1)
LOWER GI	Lower-GI response scales (0-3)	0	≥ 1 point	≥ 1 point (except 0 → 1)
LIVER	Bilirrubin / ALT	Normal	50%	2 x ULN
	Alcaline phosphatase	Normal	50%	2 x ULN

Jagasia MH, Greinix HT, Arora M, Williams KM, Wolff D, Cowen EW, Palmer J, Weisdorf D, Treister NS, Cheng GS, Kerr H, Stratton P, Duarte RF, McDonald GB, Inamoto Y, Vigorito A, Arai S, Datile MB, Jacobsohn D, Heller T, Kitko CL, Mitchell SA, Martin PJ, Shulman H, Wu RS, Cutler CS, Vogelsang GB, Lee SJ, Pavletic SZ, Flowers ME. National Institutes of Health Consensus Development Project on Criteria for Clinical Trials in Chronic Graft-versus-Host Disease: I. The 2014 Diagnosis and Staging Working Group report. Biol Blood Marrow Transplant. 2015 Mar;21(3):389-401.e1. doi: 10.1016/j.bbmt.2014.12.001. Epub 2014 Dec 18. PMID: 25529383; PMCID: PMC4329079.

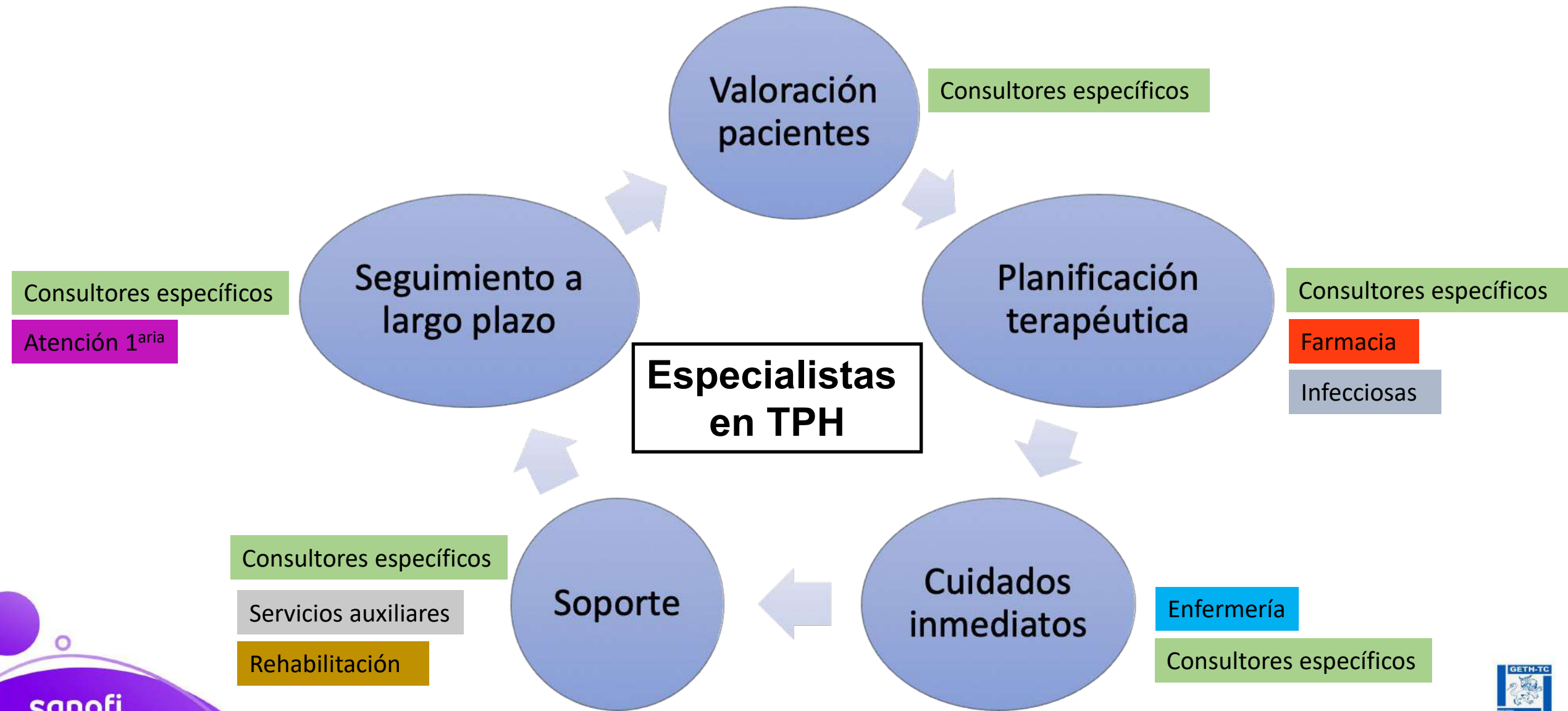
3. Manejo EICRc

Evaluación de respuesta

Organ	Scale	CR	PR	Progression
LUNG	FEV1 (L and % predicted)	Normal	≥ 10%	≥ 10%
	NIH severity score (0-3)	0	≥ 1 point	≥ 1 point
GLOBAL RATING	None-Mild-Moderate-Severe (0-3)	0	≥ 1 point	≥ 1 point
	Symptoms severity score (0-10)	0	≥ 2 point	≥ 2 point
	Change over time scale (-3-+3)	+3	≥ 2 point	≥ 2 point

Jagasia MH, Greinix HT, Arora M, Williams KM, Wolff D, Cowen EW, Palmer J, Weisdorf D, Treister NS, Cheng GS, Kerr H, Stratton P, Duarte RF, McDonald GB, Inamoto Y, Vigorito A, Arai S, Datile MB, Jacobsohn D, Heller T, Kitko CL, Mitchell SA, Martin PJ, Shulman H, Wu RS, Cutler CS, Vogelsang GB, Lee SJ, Pavletic SZ, Flowers ME. National Institutes of Health Consensus Development Project on Criteria for Clinical Trials in Chronic Graft-versus-Host Disease: I. The 2014 Diagnosis and Staging Working Group report. Biol Blood Marrow Transplant. 2015 Mar;21(3):389-401.e1. doi: 10.1016/j.bbmt.2014.12.001. Epub 2014 Dec 18. PMID: 25529383; PMCID: PMC4329079.

El manejo óptimo requiere de un equipo multidisciplinario



4. Consulta Multidisciplinar

Organización



Oftalmóloga



Dermatólogo



Reumatóloga



Hematóloga



Ginecólogo



Digestiva

Indicaciones

- Todo nuevo dx
- Candidatos a EC
- Fallos a tratamiento



- Casos difíciles
- Convocado por cualquiera de los especialistas

4. Consulta Multidisciplinar

Organización

Notas consulta multidisciplinar

Notas Médicas de Evolución CCEE

Seguimiento actual

CONSULTA EICH MULTIDISCIPLINAR
FR +

Retinitis autoinmune ya conocida con atrofia macular y retiniana

AV: CD/ PL

BMA AO catarata SCP

FO AO atrofia retiniana ya conocida, atrofia vascular, no edema de papila

Papila oblicua

DERMATOLOGÍA : solo afectación de la mucosa oral con lesiones liquenoides leves a nivel de la mucosa oral . No mucha relevancia clínica . Eich oral liquen plano like grado I .

REUMATOLOGÍA:

Refiere artralgias de ritmo inflamatorio en hombros, rodillas, muñecas de años de evolución (no mesabe especificar). Toma AINE, noltol, con mejoría escasa.

En la exploración se aprecia limitación severa a la abd, rotación interna y supraelevación de ambos brazos, tanto activa como pasiva. Se objetiva también sinovitis en ambas muñecas, con dolor a la flexo-extensión máxima.

Realizaré eco en consulta.

Notas hematología

EVOLUCIÓN ACTUAL: Hoy valorado en comité EIHC multidisciplinar.

Hematología: buenos recuentos, negativiza bcr/abl (RMM 5.0)

Neurológico: Suspendió asciminib hace unos días por nueva clínica neurológica (desorientación y dificultad al habla), resuelta tras su suspensión.

Amaurosis bilateral secundaria a retinitis autoinmune. d

Inicia EICH crónico tras ILD, actualmente sin IS.

Actualmente EICH c severo (afectación pulmonar G2 y articular G3).

GRADACIÓN DE EICH CRÓNICA POR ÓRGANOS:

- Estado general: grado 3 (afectación sobretodo por la ceguera)

- Piel: grado 0

- Boca: Liquen plano SÍ. Grado 0 (no síntomas)

- Ojos. Grado 0. Sin embargo Ceguera bilateral (completa en OD) de causa disimmune (retinitis autoinmune con atrofia macular y retiniana).

-Tracto gastrointestinal: grado 0

- Hígado: Grado 0 (función hepática normal);

- Pulmón. Grado 2 (disnea al caminar sobre llano; FEV1 40-59%); PFR 20/10/22: FEV1 57%; FVC 83%

FEV/FVC: 0.68 (patrón obstructivo). DLCO 67 % Grado 2 (disnea al caminar sobre llano; FEV1 40-59%);

- Aparato locomotor: grado 3 (rigidez, contracturas o fascitis, con significativa limitación funcional);

Puntuación P-ROM 16/25. Hombro: 4, Codo: 3, Muñeca/dedos: 7, Tobillo 2.

-Genital: Grado 0 (no síntomas);

-Otros (de 0 a 3). ceguera causa disimmune, FR positivo

5. Conclusiones

- Manejo de EICH crónico es muy complejo y se dispone de poco tiempo y recursos
- Creación de un equipo multidisciplinar y trabajo en equipo
 - Mucha satisfacción para pacientes y profesionales
 - Mejora la calidad asistencial: diagnóstico, gradación, tratamiento y respuesta
- Limitaciones / dificultades
 - Depende de iniciativa y esfuerzo individual
 - Escasos recursos para formación/investigación en especialidades consultoras



¡Gracias!