Enfermedad Injerto vs Huésped Crónica (GVHDcr)

Centro Impasa de Trasplante de Médula Osea

Dr. Hugo Isaurralde

GVHD crónica

- Incidencia : 50 % (30 – 70 %, en ↑)

- Principal causa de MRT tardía (25 %)

- Morbilidad / Principal determinante de calidad de vida post TPH

- Mortalidad : 30 – 50% en los 1ros 5 años

La Infección es la causa más frecuente

- Resultados del Trasplante : > GVL, < recaída, Sobrevida ?

GVHD, GVL y Mortalidad

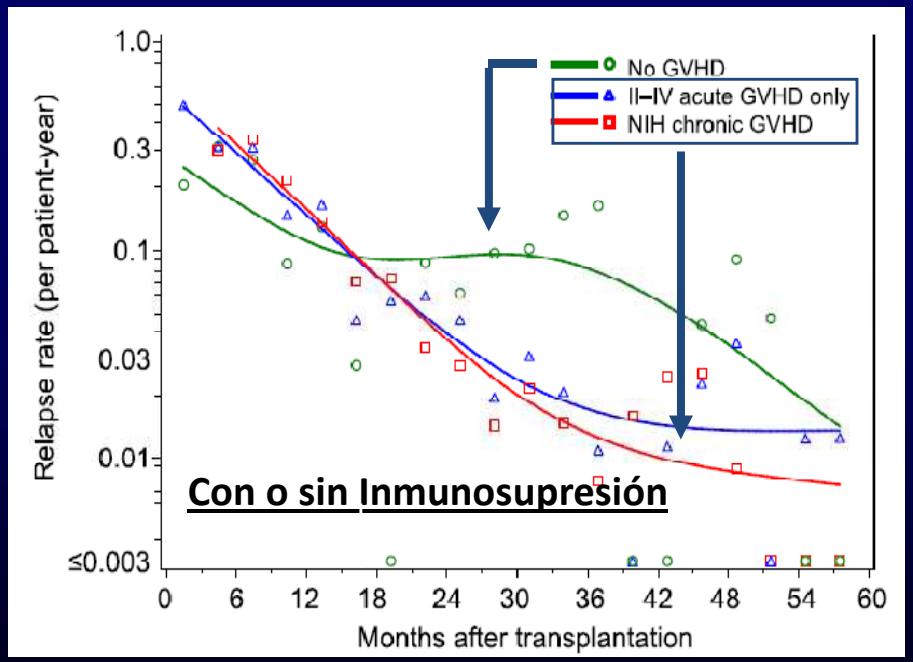
Influence of immunosuppressive treatment on risk of recurrent malignancy after allogeneic hematopoietic cell transplantation

Fred Hutchinson Cancer Research Center

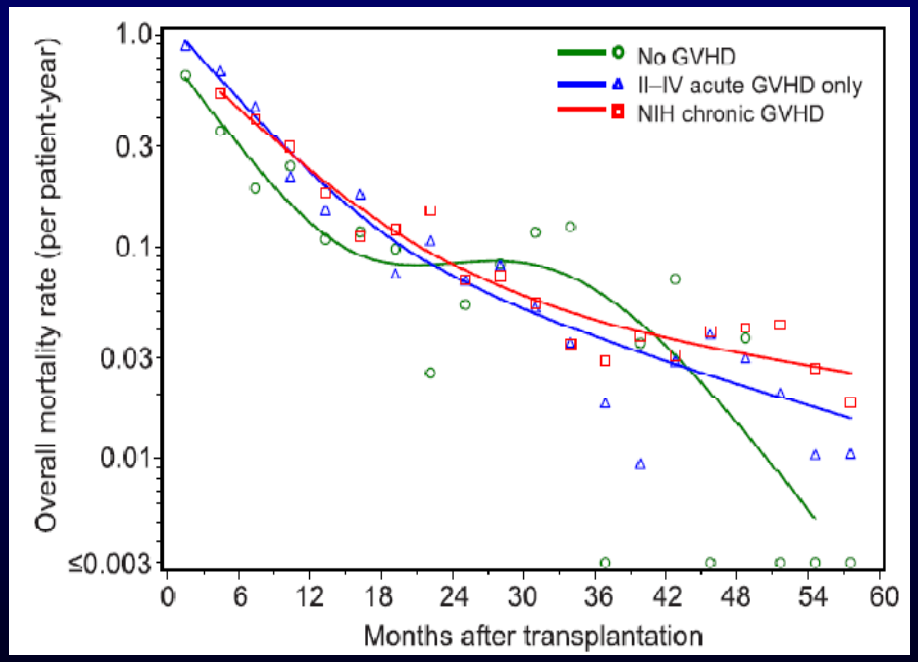
E. de cohorte retrosp. / 2656 pts / REL y NO- REL match

M. Ablativo **/ SCSP o MO / CsA + Mtx**

RECAIDA



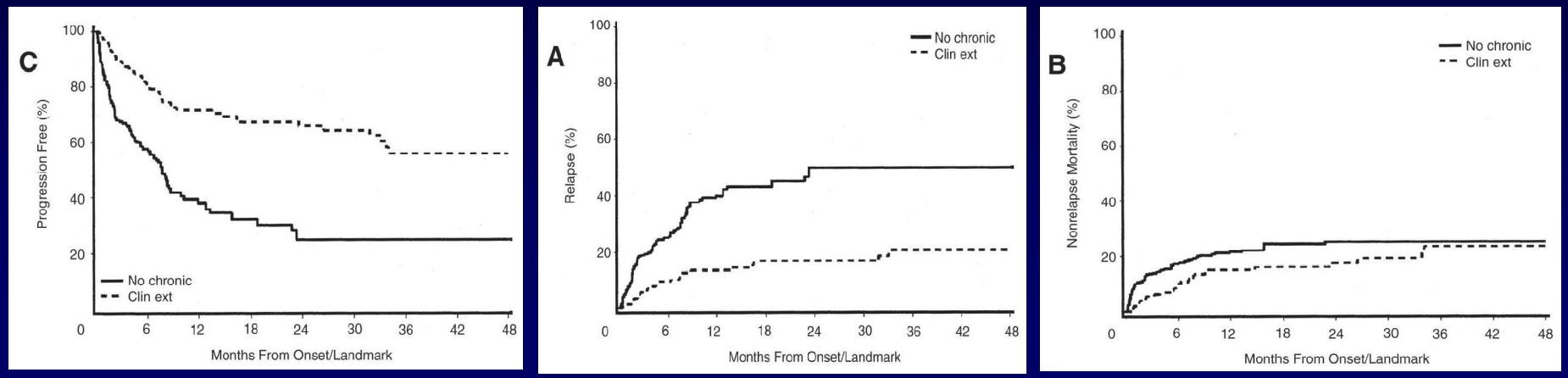
MORTALIDAD GLOBAL



Yoshihiro Inamoto et al. *Blood*. 2011;118(2): 456-463

Graft-Versus-Tumor Effects After Allogeneic Hematopoietic Cell Transplantation With Nonmyeloablative Conditioning

GVHD cr extensiva, recaída y SLP / n: 322 pts / REL y no-REL



Frédéric Baron et al, J Clin Oncol 23:1993-2003. © 2005

- La GVHD cr no significa siempre peores resultados del TPH.
- En gral. se asocia a < Recaida y > SLP (efecto GVL).
- La SG dependerá de la severidad y factores pronósticos de la GVHD y del riesgo de recaída de la enfermedad de base
- La Calidad de Vida se ve alterada

GVDH crónica

Factores de riesgo

GVHD AGUDA PREVIA ES EL MÁS IMPORTANTE

GVHD aguda

G I : 60 % GVHD cr

G II–IV : 80 % GVHD cr

Comparative analysis of risk factors for acute graft-versus-host disease and for chronic graft-versus-host disease according to National Institutes of Health consensus criteria

Mary E. D. Flowers, Fred Hutchinson Cancer Research Center, Seattle, WA

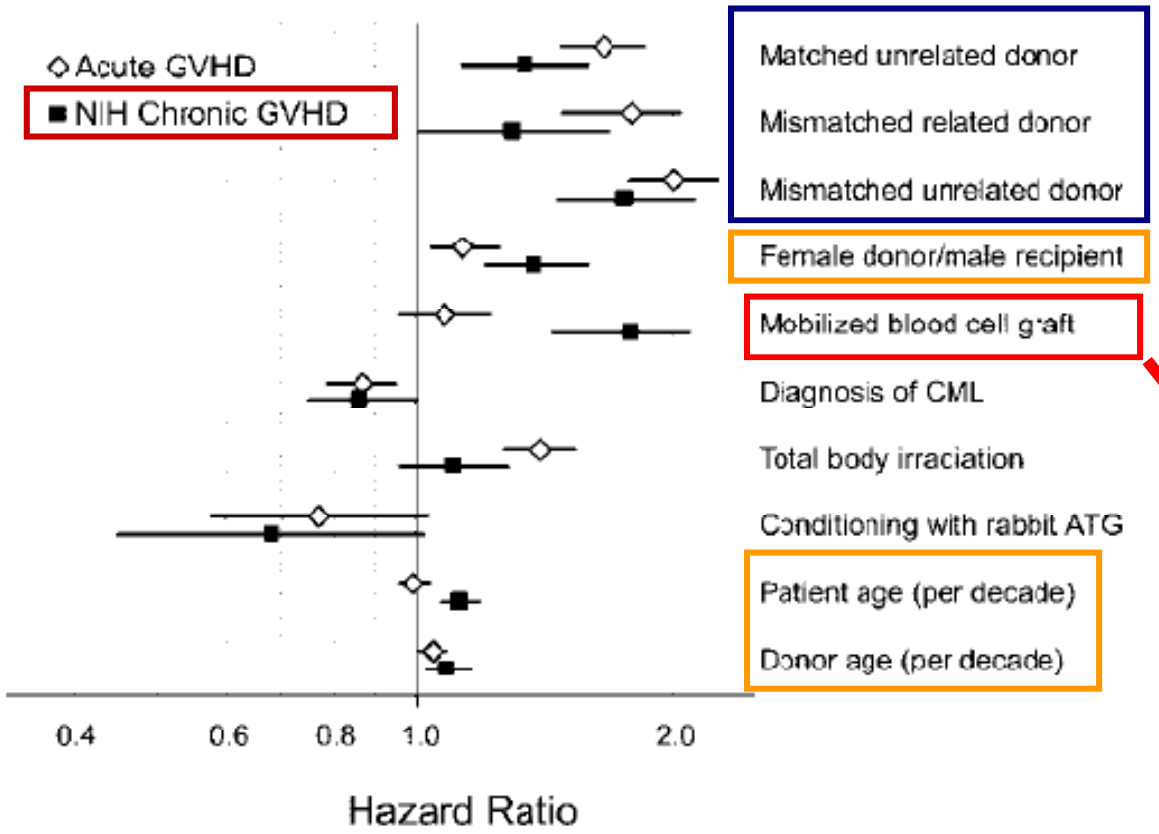
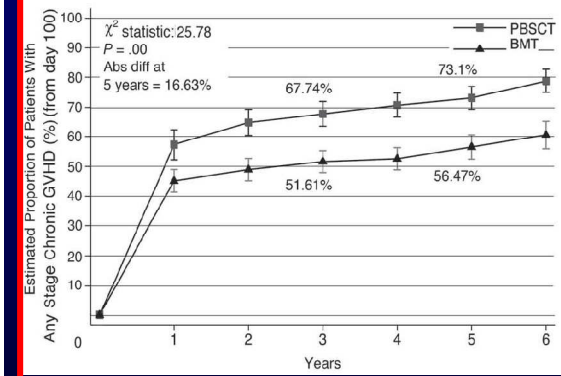


Figure 2. Multivariate risk factor profiles for grades 2-4 acute GVHD and NIH chronic GVHD. Hazard ratio and 95% CI for each risk factor are shown. The analysis included 2355 grades 2-4 acute GVHD events and 1022 NIH chronic GVHD events. Hazard ratios are relative to patients without the risk factor.

- Pts : 2941
- 1992-2005
- Reg. MA
- MO o SCSP

Allogeneic Peripheral Blood Stem-Cell Compared With Bone Marrow Transplantation in the Management of Hematologic Malignancies: An Individual Patient Data Meta-Analysis of Nine Randomized Trials

Stem Cell Trialists' Collaborative Group



< recaida / ventaja de SG en alto riesgo

(*Blood*. 2011;117(11):3214-3219)

GVDH crónica

Factores de riesgo

Intensidad del Régimen Condicionante

Chronic graft-versus-host disease in the era of reduced-intensity conditioning

DS Subramaniam[1,2], DH Fowler[1] and SZ Pavletic[1]

Chronic GVHD in non-randomized comparison trials

First author	N	Conditioning	Donor type	Stem cell source	GVHD prophylaxis	cGVHD incidence RIC vs CST (p)	Median follow-up
Comparison trials:							
Couriel DR[37]	RIC: 63 CST: 74	RIC: Flu-C-I, Flu-P-I, FluCy CST: BuCy, BuMel	MRD	RIC: 95% PB CST: 72% PB	TAC+MTX D1,3,6+11	Cumulative: 14 vs 40%[a] (NA)	20 mo
Perez-Simon JA[38]	RIC: 150 CST: 88	RIC: FluMel, FluBu CST: BuCy, CyTBI±VP16	MRD	100% PB	CSP+MTX D1,3,6±11	Cumulative: 71 vs 63% (.004) Limited: 36 vs 12% (.01) Extensive: 64 vs 88% (NS)	406 days
Mielcarek M[39]	RIC: 44 CST: 52	RIC: lowTBI±Flu CST: CyTBI, BuCy, FluBu	MRD MUD	RIC: 86% PB CST: 79% PB	RIC: CSP+MMF CST: CSP+MMF or MTX	Cumulative: 73 vs 71% (.96)	RIC: 13.9 mo CST: 11.1 mo
Kim DH[40]	RIC: 63 CST: 41	RIC: Flu-Bu or -Cy, -Mel, -Ida/AraC or BuCy or lowTBI CST: TBI-based or BuCy-based	MRD 99%	RIC: 100% PB CST: 100% PB	RIC: CSA±MTX or MMF CST: CSA+MTX	57.4 vs 71.9% (NS) Extensive: 33 vs 47% (NS)	17 mo
Aoudjhane M[42]	RIC: 315 CST: 407	RIC: FluBu, lowTBI CST: High Bu-, TBI-	MRD	RIC: 90% PB CST: 69% PB	CSP±MTX or MMF	Cumulative: 48 vs 58% (0.64)	RIC: 14 mo CST: 13 mo

Leukemia (2007) 21, 853–859

GVHD cr : RIC vs MA

- < incidencia de GVHD ag
- Igual incidencia de GVHD cr
- En gral. más leve

GVDH crónica

Factores de riesgo

Dosis de CD34

↓

Fuente de SC : MO vs SCSP

Dosis de CD34 y Resultados

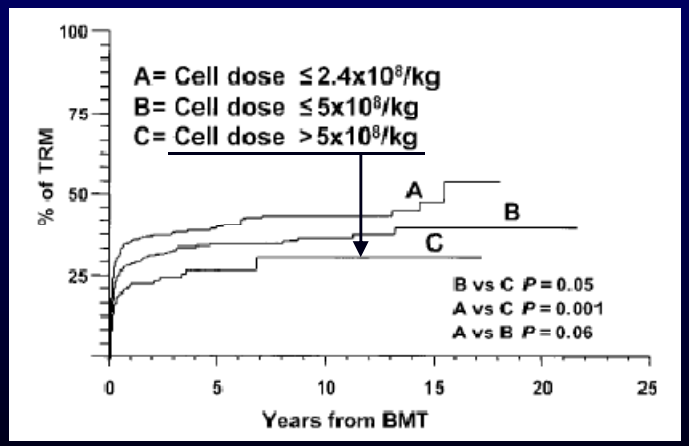
Efecto positivo en SC de MO con > dosis

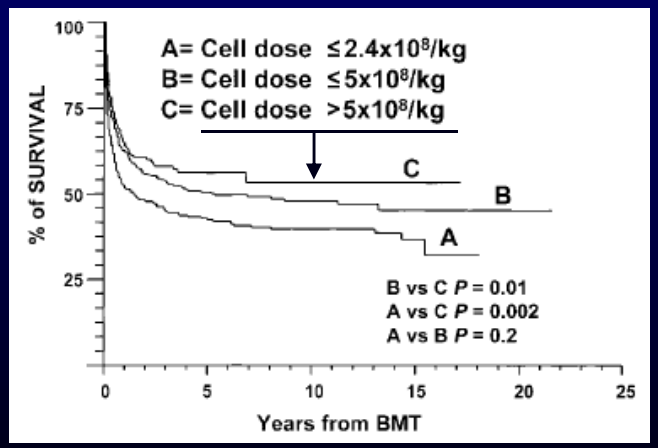
Transplant-related mortality and long-term graft function are significantly influenced by cell dose in patients undergoing allogeneic marrow transplantation

Alida Dominietto et al. Blood. 2002;100:3930-3934

Dosis > 5 x 10^8/k :

- < MRT
- < GVHD aguda III-IV / **Igual GVHD crónica**
- > Sobrevida Global
- > SLE





n : 905 pts

Retrospectivo

RC Mielo Ablativo

HLA-ID, REL y no REL

Dosis de CD34 y Resultados del TPH

Efecto en SCSP (+) con G-CSF depende de :

- Intensidad del RC (MA / RIC)
- Profilaxis de GVHD (Depleción Cel T / No)
- Riesgo de Recaída

CD34 cell dose in granulocyte colony-stimulating factor–mobilized peripheral blood mononuclear cell grafts affects engraftment kinetics and development of extensive chronic graft-versus-host disease after human leukocyte antigen–identical sibling transplantation

- Retrospectivo / n : 181 pts
- Fuente : SCSP / Mieloablativo

•*Dosis > de 8 x 10^6/k*: Más rápido engrafment

> incidencia de GVHD cr extensiva

HR 5 2.3; 95% CI, 1.4-3.7; *P* = .001

Más severa y dificil de tratar

No relación : aGVHD, SG ni recaída

J. Maciej Zaucha, et al. Blood. 2001;98:3221-3227

Dosis de CD34 : RIC

1. High doses of transplanted CD34$^+$ cells are associated with rapid T-cell engraftment and lessened risk of graft rejection, but not more graft-versus-host disease after nonmyeloablative conditioning and unrelated hematopoietic cell transplantation

116 pts / No REL

F Baron et al. Leukemia (2005) 19, 822–828

2. Allogeneic peripheral blood stem cell graft composition affects early T-cell chimaerism and later clinical outcomes after non-myeloablative conditioning

125 pts / REL

J. P. Panse et al. BJ of H, 128, 659–667

3. Results of Genoidentical Hemopoietic Stem Cell Transplantation With Reduced Intensity Conditioning for Acute Myelocytic Leukemia: Higher Doses of Stem Cells Infused Benefit Patients Receiving Transplants in Second Remission or Beyond—The Acute Leukemia Working Party of the European Cooperative Group for Blood and Marrow Transplantation

253 pts / REL

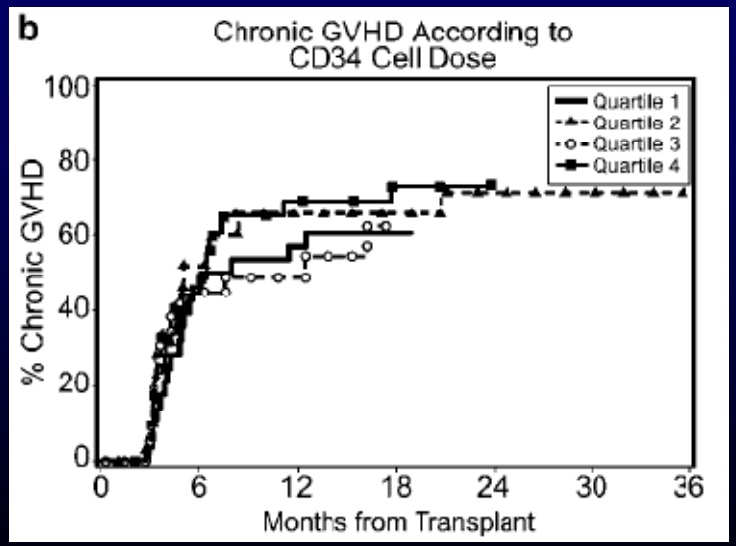
J Clin Oncol 24:3959-3966

RC : TBI 2Gy c/s Flu

Profilaxis : CsA + MMF

Media CD34 : 5.83 – 6.8 – 9.2 / 10^6/k

No correlación entre dosis de CD34 con GVHDcr ni otros resultados del TPH



Dosis de CD34

4. Impact of CD34$^+$ cell dose on the outcome of patients undergoing reduced-intensity-conditioning allogeneic peripheral blood stem cell transplantation

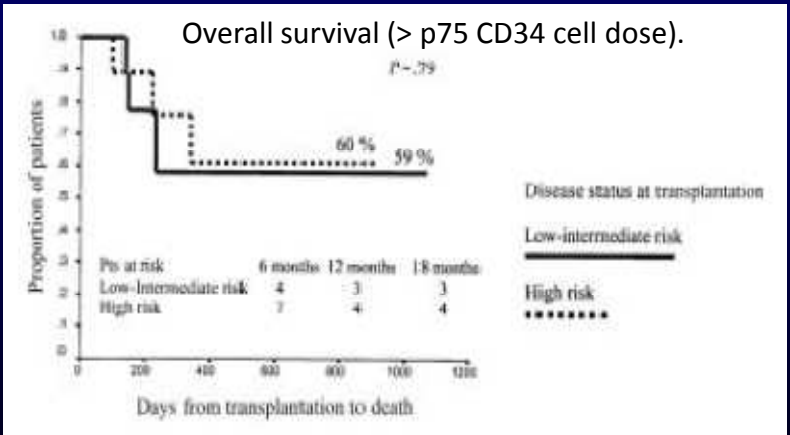
Flu / Bu o Mel. 86 pts. CsA + Mtx x 3 / REL /

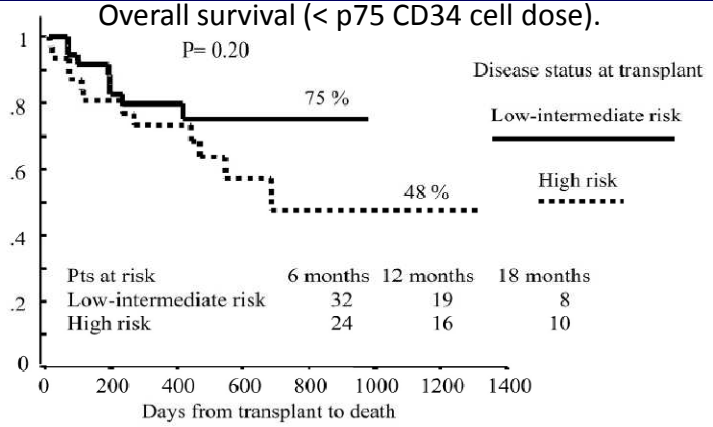
m CD34 : 5.68 x 10^6/ K (2.58-15.6)

Dosis > del percentil 75 : > GVHD cr extensiva : 74 vs 47 %

Enf. de Alto Riesgo :

< Recaída : 9% (p > 75) vs 36 % (p < 75)



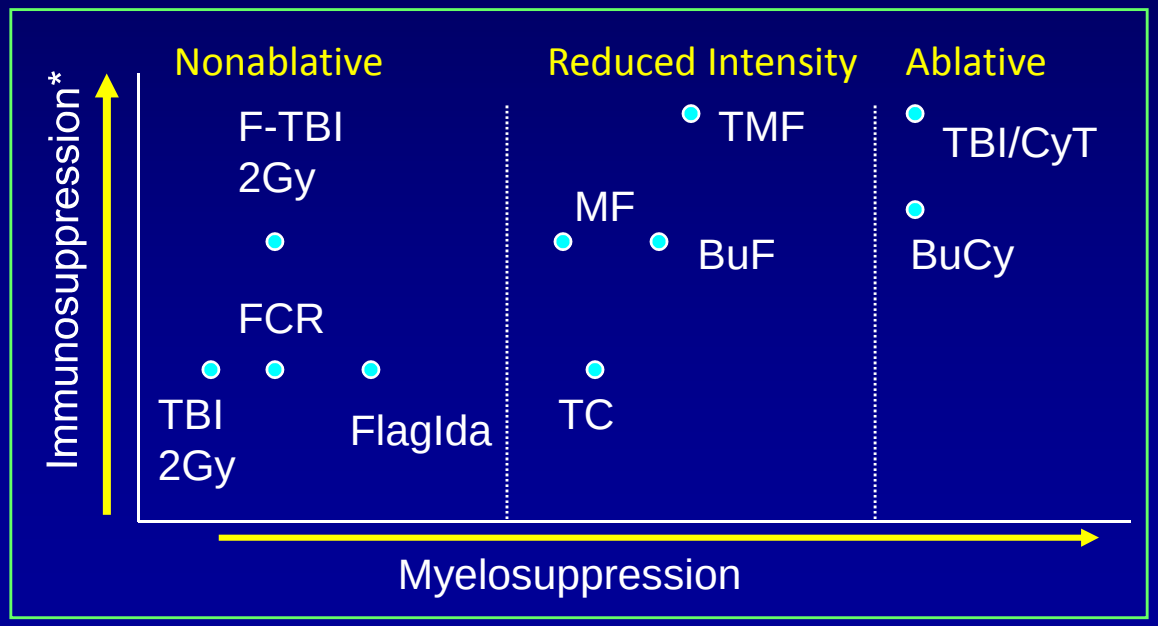


José A. Pérez-Simón, María Díez-Campelo (Blood. 2003;102:1108-1113)

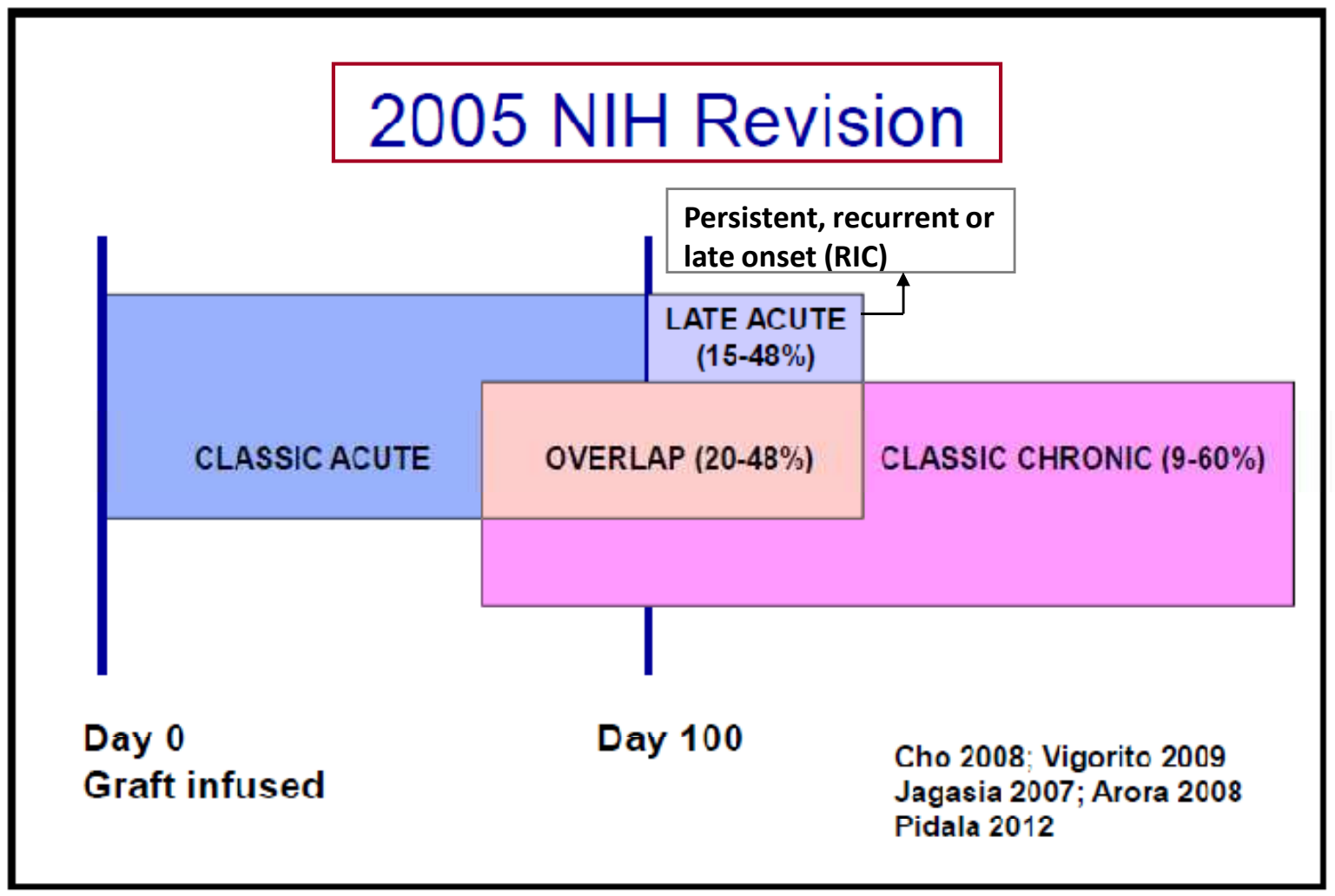
GVHD crónica y dosis de CD34

- En SCSP

En RIC : Efecto dependiente del RC



GVHD - Clasificación



Intensity

Se
Mo
Mi

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

- Signos Diagnósticos
- Signos Distintivos
- Signos Inespecíficos
- Signos Comunes con GVHD ag

GVHD crónica : 1 Signo Diagnóstico o

1 Signo Distintivo + Confirmación : HISTOLOGICA

LABORATORIO

IMAGEN

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

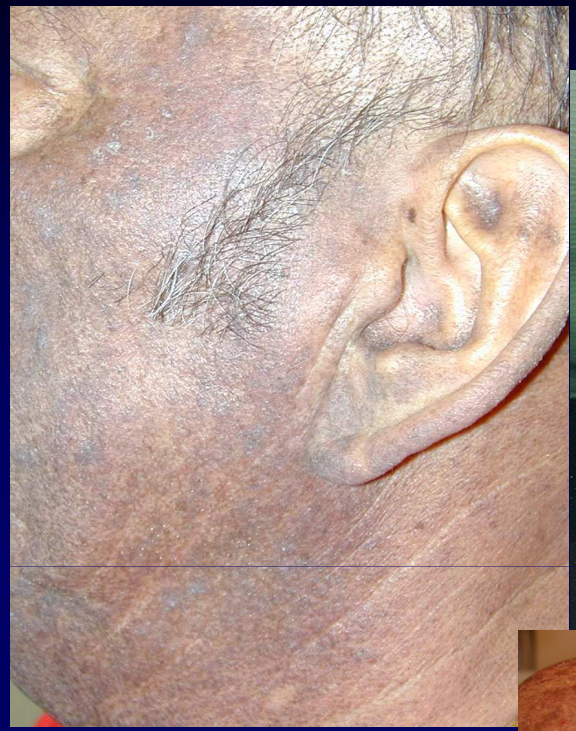
Signos Diagnósticos

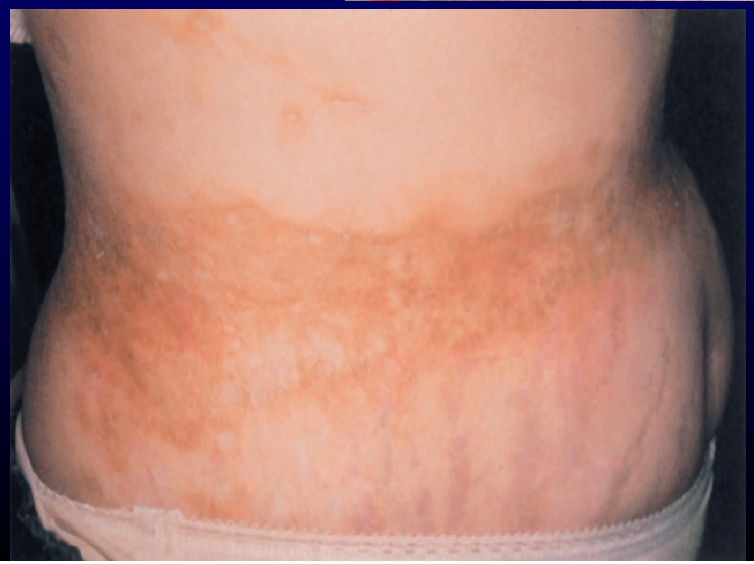
- Piel
- Cavidad oral
- Ap. Genital Femenino
- Esófago
- Ap. Respiratorio
- Tejido Conectivo

Signos Diagnósticos

PIEL

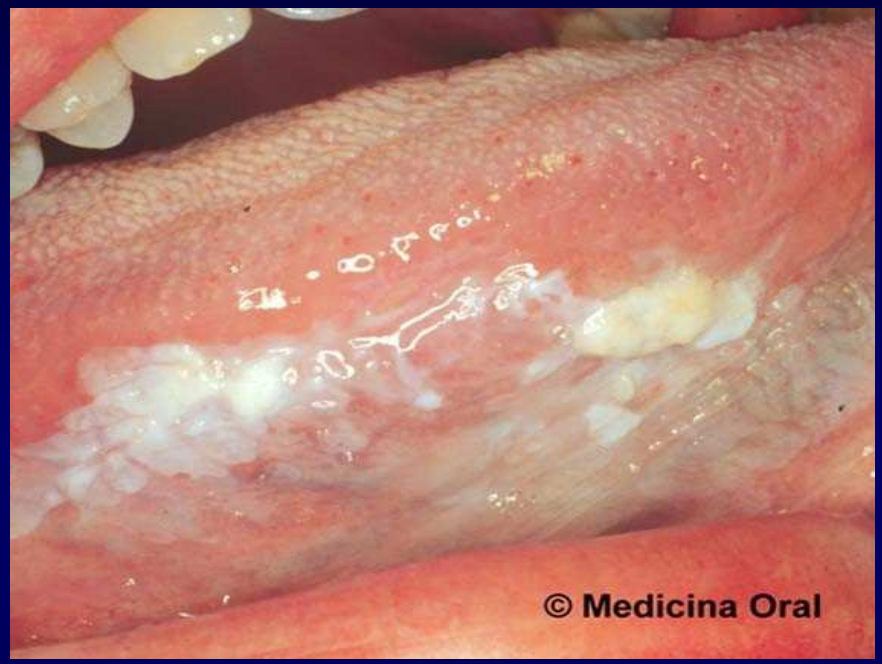
- Liquen plano
- Liquen escleroso
- Morfea
- Esclerosis
- Poiquiloderma

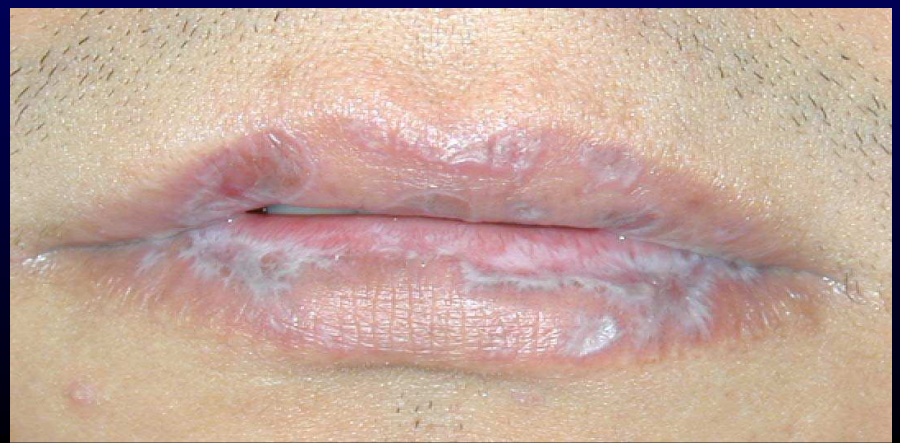




Signos diagnósticos Cavidad Oral

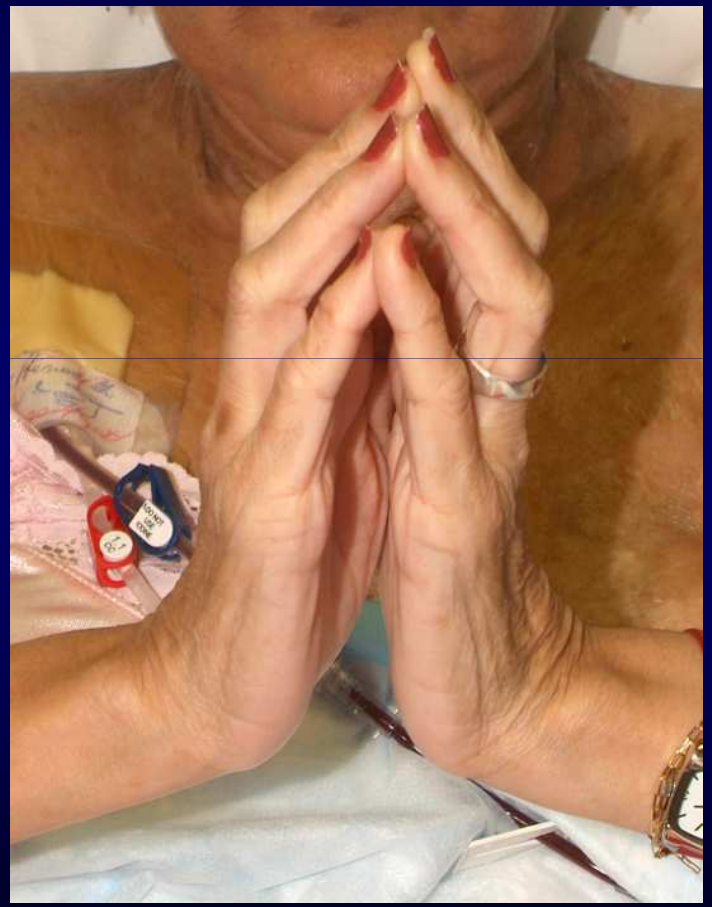
- Liquen
- Leucoplaquia
- Limitación a la apertura por Esclerosis

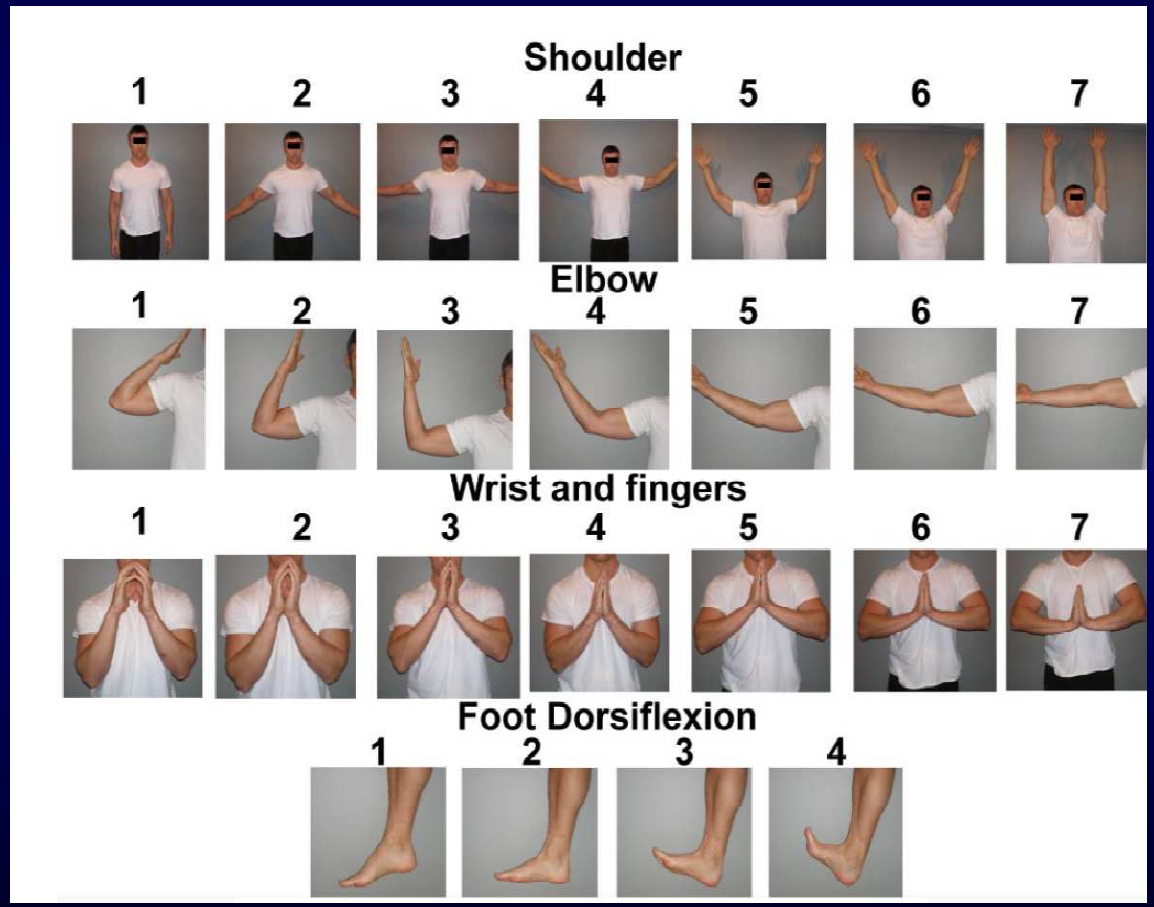




Signos Diagnósticos
Tejido Conectivo

- Fascitis : Edema (piel de naranja)/Dolor/Esclerosis





- Rigidez articular por esclerosis

Signos Diagnósticos

- Esófago : Anillos / Fibrosis / Estenosis

  Endoscopía / Radiología

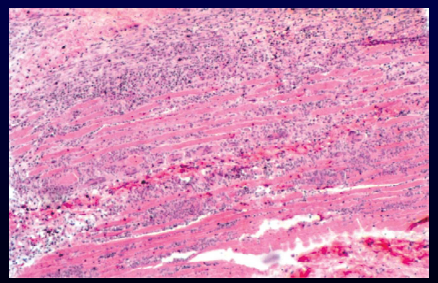
- Ap. Genital Fem. : Liquen / esclerosis / estenosis

- Pulmón : Bronquiolitis Obliterante

  - Funcional Respiratorio ($FEV_1 < 75\%$)
  - TAC de AR (atrap.aire, pared bronq.engrosada, bronquiectasias…)
  - Histología :(bronq. constrictiva)
  - Descartar Infección : (cultivos …,)

Signos Distintivos de GVHD cr

- Piel y Faneras : (Alopecia, Depigmentación,…)
- Mucosa Oral : (Xerostomía, mucoceles, úlceras,…)
- Ojos : (Queratoconjuntivitis sicca, …)
  - T. Schirmer
  - Lámpara de Hendidura
- NeuroMuscular : (PNP, Miositis, Miastenia…)



Enzimas,
Electromiograma, Biopsia

Signos comunes a GVHD aguda y crónica

- Hígado : Colestasis (BD, TGO, TGP, F.Alc….)
  No diferencias Histológicas
- Tubo Digestivo : (Anorexia, Vómitos, Diarrea,…)
- Piel : (eritema, rush, prurito…)
- Mucosa Oral : (mucositis, eritema,…)
- Pulmón : BOOP

GVHD cr
Diagnóstico

- En cada ÓRGANO O TEJIDO afectado siempre plantear : *D.DIFERENCIAL*

- INFECCION (COEXISTENCIA)
- TOXICIDAD POR DROGAS
- NEOPLASIA
- TRASTORNOS FUNCIONALES
- OTRAS

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

Severidad de sitio afectado

- Según extensión y limitación funcional
- Score de 0 – 3 (clínico, salvo Hígado)
- Sitios : (Piel, Mucosas, Ojos, Pulmón, Hígado, Articul., Fascia, T. Digestivo, Ap.Gen Fem.)

NIH Skin Score

	0	1	2	3
Clinical features ☐ Maculopapular rash ☐ Lichen planus-like ☐ Papulosquamous ☐ Ichthyosis ☐ Hyperpigmentation ☐ Hypopigmentation ☐ Keratosis pilaris ☐ Erythema ☐ Erythroderma ☐ Poikiloderma ☐ Sclerotic features ☐ Pruritus ☐ Hair involvement ☐ Nail involvement **% BSA involved____**	☐ No Symptoms	☐ ≤18% BSA with disease signs but **NO** sclerotic features	☐19-50% BSA **OR** involvement with superficial sclerotic features "not hidebound" (able to pinch)	☐ >50% BSA **OR** deep sclerotic features "hidebound" (unable to pinch) **OR** impaired mobility, ulceration or severe pruritus

♦ % BSA and degree of sclerosis

NIH Lung Score

0	1	2	3
☐ No Symptoms	☐ Mild symptoms (shortness of breath after climbing one flight of steps)	☐ Moderate symptoms (shortness of breath after walking on flat ground)	☐ Severe symptoms (shortness of breath at rest; requiring O_2)
☐ FEV1 ≥ 80% OR LFS=2	☐ FEV1 60-79% OR LFS 3-5	☐ FEV1 40-59% OR LFS 6-9	☐ FEV1 ≤39% OR LFS 10-12

LFS = FEV1 score + DLCO score

≥ 80%	= 1
70-79%	= 2
60-69%	= 3
50-59%	= 4
40-49%	= 5
≤ 40%	= 6

♦ Symptoms and PFTs

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

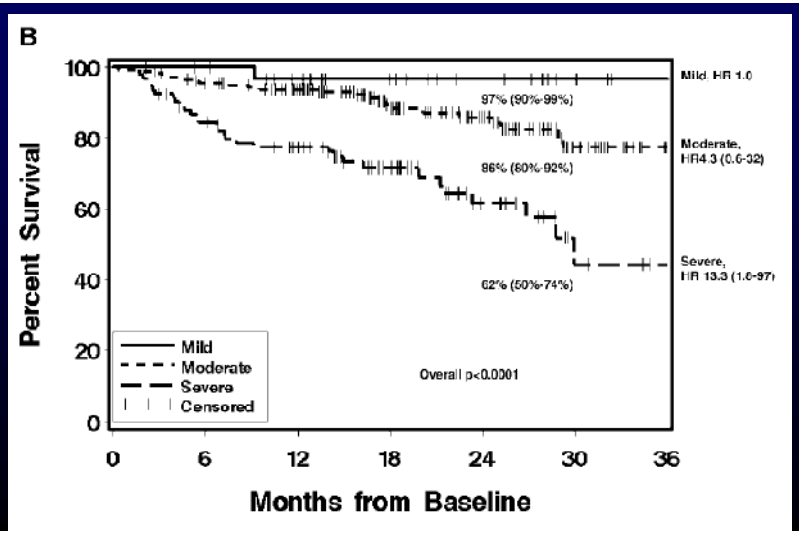
Severidad Global (Al D(+) y Evolución)

- Mínima
- Moderada
- Severa

Table 1: Global scoring of cGvHD

Number of Organs	Mild cGvHD	Moderate cGvHD	Severe cGvHD
1	Score 1	Score 2	Score 3
2	Score 1	Score 2	Score 3
3		Score 1	Score 3
Lung involvement		Score 1	Score 2

Global and organ-specific chronic graft-versus-host disease severity according to the 2005 NIH Consensus Criteria



Prospectivo

N : 298 pts

5 Centros / segu. : 18.5 m

Arai S et al. Blood 2011;118:4242-4249

GVHDcr - PRONOSTICO

Trombocitopenia < 100.000

Inicio de GVHD ag previa (superposición)

Overlap subtype of chronic graft-*versus*-host disease is associated with an adverse prognosis, functional impairment, and inferior patient-reported outcomes: a Chronic Graft-*versus*-Host Disease Consortium study

Joseph Pidala,[1] Georgia Vogelsang,[2] Paul Martin,[3] Xiaoyu Chai,[3] Barry Storer,[3] Steven Pavletic,[4] Daniel J. Weisdorf,[5] Madan Jagasia,[6] Corey Cutler,[7] Jeanne Palmer,[8] David Jacobsohn,[9] Sally Arai,[10] and Stephanie J. Lee[3]

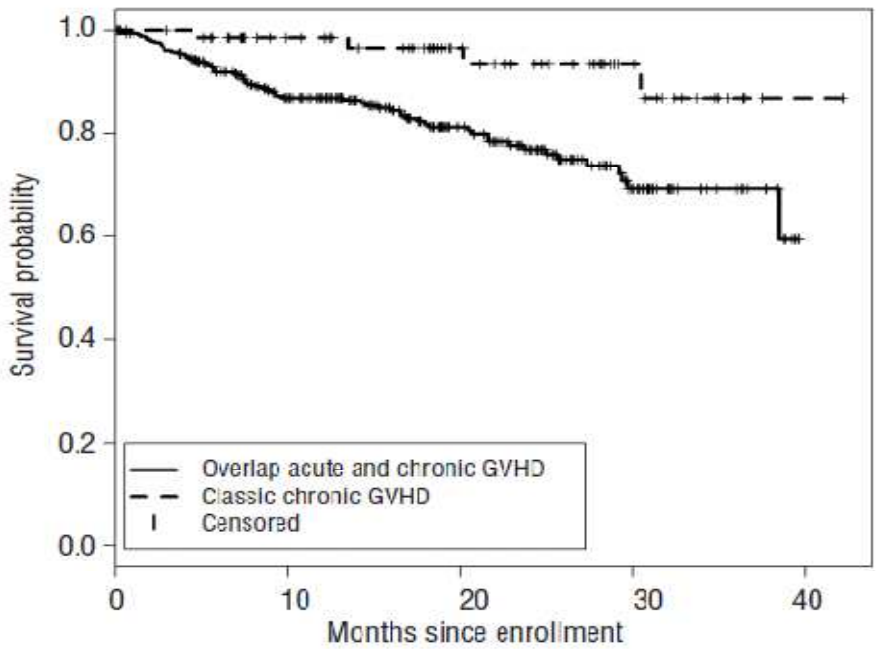


Figure 1. Overall survival according to overlap *versus* classic chronic GVHD.

Prospectivo

N : 427 pts

9 Centros

Seg. : 17- 19 m

haematologica | 2012; 97(3)

GVHDcr - Prevención

- Actuar sobre Factores de Riesgo

  Modificables

  No Modificables

- Inmunosupresión

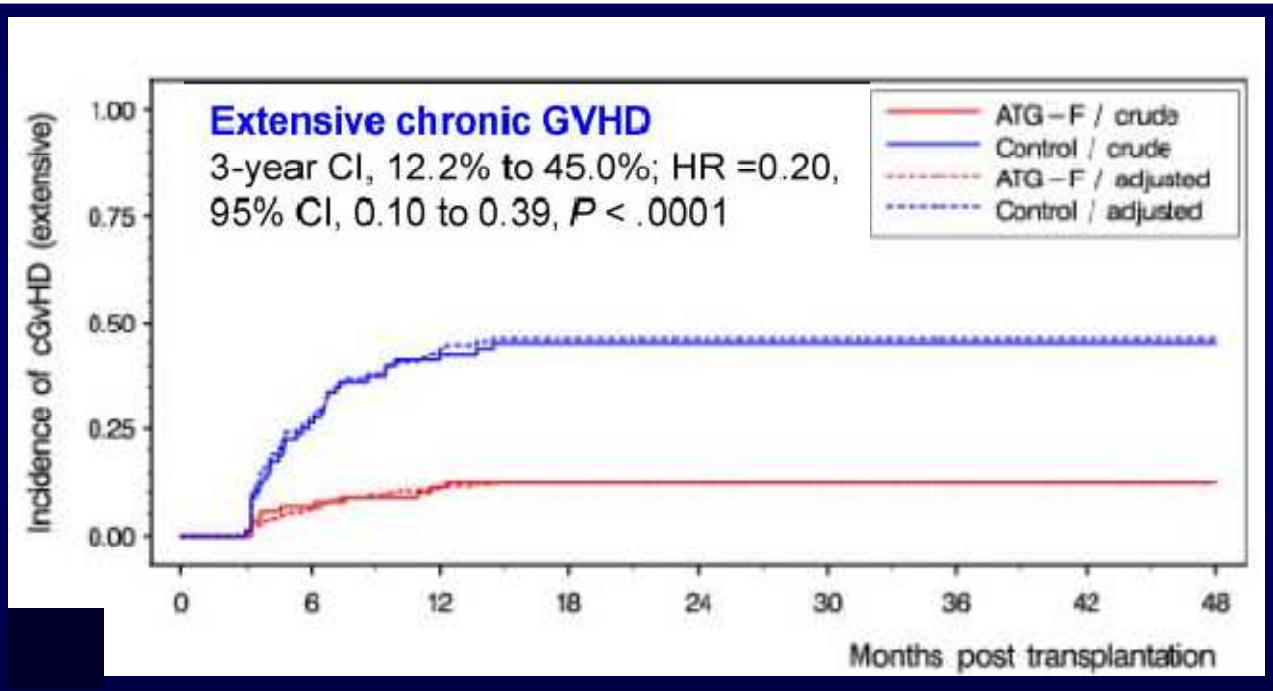
  - Actuales estrategias son de limitada eficacia
  - Prevención de GVHDag esencial pero insuficiente
  - Depleción de Cel T

Chronic graft-versus-host disease: long-term results from a randomized trial on graft-versus-host disease prophylaxis with or without anti –T-cel globulin ATG-Fresenius

ATG-Fresenius Trial Group

Randomizado / Fase III / 201 pts / SCSP o MO / No Relacionado

M. Ablativo / CsA + Mtx + ATG (20 mg/k x 3) vs No ATG



ATG : Igual Nº de Recaídas, Sobrevida Global e Infecciones

Mayor Sobrevida libre de Inmunosupresión

(*Blood*. 2011 117(23):6375-6382)

GVHD crónica
Tratamiento

- Inmunosupresión sistémica
  - 1ra Línea
  - 2da Línea y sucesivas
- Tratamiento Tópico
- Tratamiento de Soporte

GVHD crónica
Tratamiento

- Severidad (consenso NIH)
- Factores Pronósticos
- Hemopatía de Base : Riesgo de Recaída
- Toxicidad

GVHD cr
Tratamiento

- GVHDcr Mínima
  - Tópico
  - Soporte
  - Con o sin IS sistémica

F. Pronósticos

Importancia GVL

- GVHDcr Moderada - Severa
  - IS sistémica
  - Tópico / soporte

GVHD cr. Inmunosupresión Sistémica en 1ra línea

Table 2. Randomized Clinical Trials in cGVHD

Author	Arms Compared	D.Blind	Results
Sullivan (1998) **Standar risk**	PSE + placebo **(n: 63)** vs PSE + Az **(n: 63)**	Yes	Decrease Survival
Koc (2002) **Standar risk**	PSE **(n: 145)** vs PSE + CsA **(n: 142)**	No	Limited benefit
Koc (2000) **High risk**	PSE + CsA(Tacr) + plac. **(n: 26)** vs PSE + CsA (Tacr) + thal **(n: 26)**	Yes	Toxicity
Arora (2001) **Standar/High risk**	PSE + CsA **(n : 27)** vs PSE + CsA + Thal **(n : 27)**	No	No benefit
Martin (2009)	PSE ± MMF	Yes	No benefit

Biol Blood Marrow Transplant 16:S146-S151, 2010

GVHD cr : IS sistémica

Consensus Conference on Clinical Practice in Chronic Graft-versus-Host Disease (GVHD): First-Line and Topical Treatment of Chronic GVHD

Table 4. First-Line Treatment Options in cGVHD

Agent	Recommendation (citation number of references)	Evidence	Side Effects	Response rate
Steroids (1 mg/k/día)	A [16-18]	I	Osteoporosis, avascular necrosis of the bone, diabetes	~ 30 to 50% CR
CNI (Pd vs Pd + CsA : ahorro de CE)	C [16,17]	II	Renal toxicity, hypertension (<)	~ 30 to 50% CR
MMF in triple agent combinations	D [19]	II	GI complaints, infectious and relapse risk	
Azathioprine	D [18]	II	Hematologic toxicity, infectious risk	
Thalidomide	D [20,21]	II	Neurotoxicity, sedation, constipation, thrombosis	
MMF combined with steroids	C-1	III-2	GI complaints, infections	~ 30 to 50% CR

Daniel Wolff et al. *Biol Blood Marrow Transplant 16: 1611-1628 (2010)*

GVHD cr
Tratamiento con CE

- Respuestas lentas (6-8 sem., 3-6 m en esclerosis)
- Descenso lento.
- Dosis día por medio y única matinal : < efectos 2rios.
- Si :
  - Progresión durante TTO
  - Estable sin mejoría con 0.5/mg/k x 4-8 sem
  - Imposibilidad de descender dosis < 0.5 mg/k
  - Toxicidad

↓

TTO de 2da Línea (50 % pts)

GVHDcr : TTO de 2da Línea

- Recomendaciones de

  Estudios Fase II

  Análisis Retrospectivos
- "Prueba y Error"

- Corticoides
- (-) CN (CsA, Tacrolimus)
- MMF

RG : 50-70 %

RC : 10-30 %

- (-) mTOR (sirolimus, everolimus)
- Fotoféresis Extracorpórea
- Otros

GVHDcr : TTO de 2da Línea

Consensus Conference on Clinical Practice in Chronic GVHD: Second-Line Treatment of Chronic Graft-versus-Host Disease

Table 4. Second-line Treatment Options in cGVHD

Agent	Recommendation	Evidence	Side Effects
Steroids	B	III-1	osteoporosis, avascular necrosis, diabetes
Photopheresis	C-1	II	venous access required
mTOR inhibitors	C-1	III-1	TAM, hyperlipidemia, hematotoxicity
CNI	C-1	III-1	renal toxicity, hypertension
MMF	C-1	III-1	GI complaints, infectious and relapse risk

(No asociar a CNI, monitorear niveles, interacciones)

Daniel Wolff et al. *Biol Blood Marrow Transplant 17: 1-17 (2011)*

GVHDcr : TTO de 2da Línea

Consensus Conference on Clinical Practice in Chronic GVHD: Second-Line Treatment of Chronic Graft-versus-Host Disease

Falla de lo Anterior (salvo ciertas localizaciones)

MTX **Piel / Oral** **5-10 mg/m /sem**	C-2	III-1	~ 50% ~ 10 to 20% CR	Hematotoxicity **No en GVHD hepática**
High-dose steroid	C-2	III-2	50 to 75% (PR only)	Risk of infection
Thoracoabdominal radiation	C-2	III-2	~ 50% ~ 25% CR	Hematotoxicity
Hydroxychloroquine	C-2	III-2	~ 25% ~ 10% CR	GI side effects
Clofazimine	C-2	III-2	~ 50% (PR only)	GI side effects, hyperpig-mentation
Pentostatin	C-2	II	~ 50% ~ 10% CR	Hematotoxicity, risk of infection
Rituximab **Esclerosis /músculo/ autoinmune**	C-2	II	~ 50% ~ 10% CR	Risk of infection **Recurrent malignancy**
Imatinib **Esclerosis / BO**	C-2	III-1	~ 50% ~ 20% CR	Fluid retention

Daniel Wolff et al. *Biol Blood Marrow Transplant 17: 1-17 (2011)*

GVHDcr : TTO de 2da Línea

Consensus Conference on Clinical Practice in Chronic GVHD: Second-Line Treatment of Chronic Graft-versus-Host Disease

Perfil desfavorable de toxicidad. Uso en situaciones muy especiales

Thalidomide	C-3	II	~ 20 to 30% (PR only)	Neurotoxicity, drowsiness, constipation
Azathioprine	C-3	III-1	n/a	Hematotoxicity, risk of infection
Retinoids	C-3	III-2	~ 60% (PR only)	Skin toxicity, hyperlipidemia

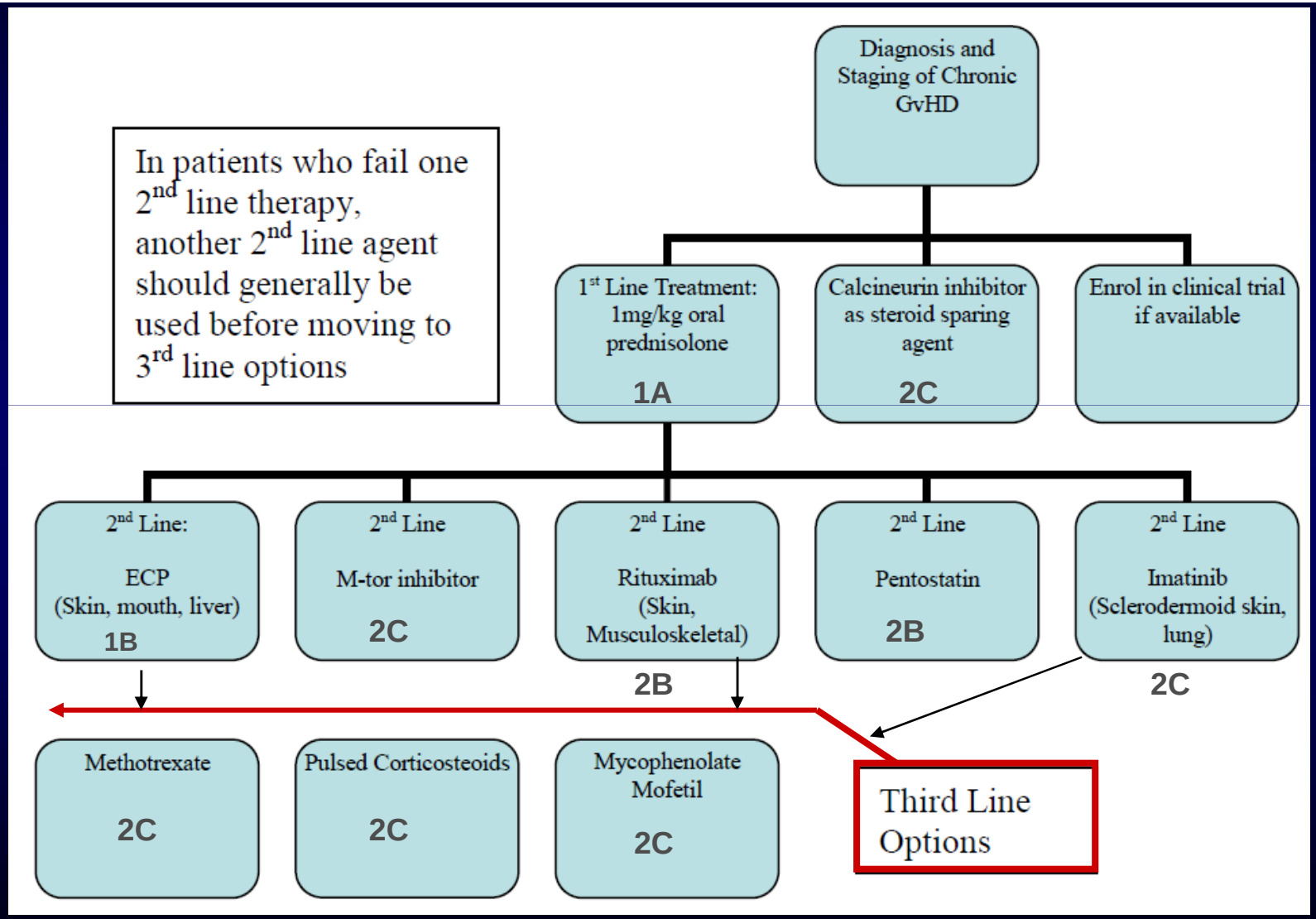
Experimental. Ensayos Clínicos

Alemtuzumab	C-4	III-3	n/a	Risk of infection
Etanercept	C-4	III-3	n/a	Risk of infection
Cyclophosphamide	C-4	III-3	n/a	Risk of infection

Stem cells Mesenquimales

Daniel Wolff et al. *Biol Blood Marrow Transplant 17: 1-17 (2011)*

BCSH/BSBMT Guideline: Diagnosis and Management of Chronic Graft- versus-Host Disease



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Tratamiento Tópico

- Importante para Mínima crGVHD
- Sin efectos sistémicos (ni beneficios)
- No compromete GVL
- IS Tópica : Corticoides, (-) calcinerina, Fototerapia

Consensus Conference on Clinical Practice in Chronic Graft-versus-Host Disease (GVHD): First-Line and Topical Treatment of Chronic GVHD

Table 5. Topical Immunosuppressive Treatment Options in cGVHD

Organ	Agent (citation number of references)	Recommendation	Evidence	Side Effects	Comments
Skin	Topical steroids [7]	C-1	III-1	Skin atrophy	Neck down: mid-strength steroids if no response upper strength steroids, face: hydrocortisone 1%
	Tacrolimus/Pimecrolimus [22-25]	C-1	III-1	Long-term risk for cutaneous malignancies	Should be given twice daily
	PUVA [26-31]	C-1	III-1	Phototoxicity, risk for cutaneous malignancies	Should not be used with phototoxic medication
	UVA [32-35]	C-1	III-1	Phototoxicity, risk for cutaneous malignancies	Requires no UV protection after treatment, should not be used with phototoxic medication
	UVB [36]	C-1	III-2	Phototoxicity, risk for cutaneous malignancies	Only effective in lichenoid cGVHD
GI	Topical steroids [37-39]	C-1	III-1		Either budesonide or beclomethasone
Lung	Topical steroids	B	III-2		May be combined with betamimetic agents
Oral	Topical steroids [40-44]	C-1	III-1-III-3	Best results with topical budesonide	Requires oral hygiene and possibly topical antifungals
	Topical tacrolimus /cyclosporine [45-51]	C-2	III-1	Burning	Potentially increases risk for oral malignancies, may be combined with topical steroids
	Topical PUVA/UVB [44,52-54]	C-2	III-1	Optional treatment option for refractory manifestations	Psoralene may be given topically or systemically
Eye	Topical steroids [55,56]	C-1	III-1	Risk for corneal thinning and infectious keratitis	Duration of exposure should be limited
	Topical cyclosporine [57-60]	C-1	III-1	Burning, stinging	Fewer long-term side effects compared to steroids, high long-term efficacy
Vaginal	Topical steroids [61-64]	B	III-3	Increased risk for infectious complications and atrophy	Topical estrogen application and antifungal prophylaxis suggested
	Topical tacrolimus/ cyclosporine/pimecrolimus [63-65]	B	III-3	Burning	Less well tolerated but better long-term efficacy

Daniel Wolff et al. *Biol Blood Marrow Transplant 16: 1611-1628 (2010)*

Tratamiento de Soporte

- Rehabilitación / Fisioterapia / Soporte Psicosocial
- Prevención de las complicaciones óseas (CE)

Osteopenia
Osteoporosis
Osteonecrosis

→

Densitometría Osea
Vit. D / Ca / Bifosfonatos / Hormonoterapia

- Reemplazo Hormonal
- <u>Prevención de Infecciones</u>

BCSH/BSBMT Guideline: Organ-Specific Management and Supportive Care in Chronic Graft-versus -Host Disease

11. Antimicrobial prophylaxis for infections in GvHD

Recommendations:

Si (+) para HVS / HZ : acyclovir

Trimet. / Sulfamet.

- Prophylaxis against viral, fungal, *Pneumocystis jiroveci* and *streptococcus pneumoniae* infection should be considered in all patients receiving immunosuppression agents for cGvHD. (1A)
- The prophylactic and/or pre-emptive strategy for prevention of CMV infection including regular monitoring of CMV PCR adopted for HSCT recipients should be continued throughout the period of acute and/or chronic GvHD. (1B)
- A mould-active azole is recommended for prophylaxis in patients undergoing treatment for GvHD. (1A); suitable agents include Posaconazole and Voriconazole (1A) or Itraconazole with regular monitoring of levels. (2B)

Pen V oral

Macrólidos

F – Quinol.

(Epstein Barr)

Rituximab

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IVIG : Niveles < de 400 IgG + Infecciones repetidas - Opcional

Alimentos, viajes, mascotas

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12. Vaccination

Recommendations:

- **Live vaccines must not be administered in patients with chronic GvHD (1A)**
- **All patients with cGvHD should receive vaccination against pneumococcus, influenza and *Haemophilus influenzae*. (1B)**

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Oportunidad : Si recibe < de 0.5 mg/k/día de Prednisona

Régimen de doble IS

Esperar si : > 0.5 mg/k/día de Pd

Régimen de IS con 3 drogas

Opción : Ac pre y post vacunación