Hospices Civils de Lyon

Photophorèse extracorporelle et maladie du greffon contre l'hôte chronique

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Congrès Société Française d'Hémaphérèse 2026

Conflits d’intérêts

Aucun

GVH chronique

- Complication fréquente : 30 à 50% des patients allogreffés
  - Essentiellement dans la 1ère année post-greffe (début médian: 6-7 mois)
  - 5 à 10 % des cas après la 1ère année post-greffe

- En augmentation sur ces 20 dernières années

- Facteurs de risque:
  - Age du patient +/- du donneur
  - CSP > MO
  - Donneur non apparenté, disparité HLA
  - GVH aigue (1/3 de GVHc de novo)
  - Greffe non T déplétée
  - Sex mismatch F-> H

GVH chronique

- Mortalité proche de 50 % pour les formes sévères :
  - Thrombopénie,
  - Evolution d'une GVH aigue
  - Atteintes pulmonaire, hépatique et digestive
- Morbidité importante induite par la GVH et les IS :
  - Dysfonction d'organe
  - Immunosuppression

GVH chronique

- Impact sur la qualité de vie
- Risque de cancers secondaires (notamment ORL et cutané)
- Durée de traitement > 2 ans (CSP > MO)
- 50-60% des patients nécessitent une seconde ligne de traitement (cortico-résistance, -dépendance)

REGULAR ARTICLE

blood advances

Nonrelapse mortality among patients diagnosed with chronic GVHD: an updated analysis from the Chronic GVHD Consortium

Zachariah DeFilipp,[1] Amin M. Alousi,[2] Joseph A. Pidala,[3] Paul A. Carpenter,[4] Lynn E. Onstad,[4] Sally Arai,[5] Mukta Arora,[6] Corey S. Cutler,[7] Mary E. D. Flowers,[4] Carrie L. Kitko,[8] George L. Chen,[9] Stephanie J. Lee,[4] and Betty K. Hamilton[10]

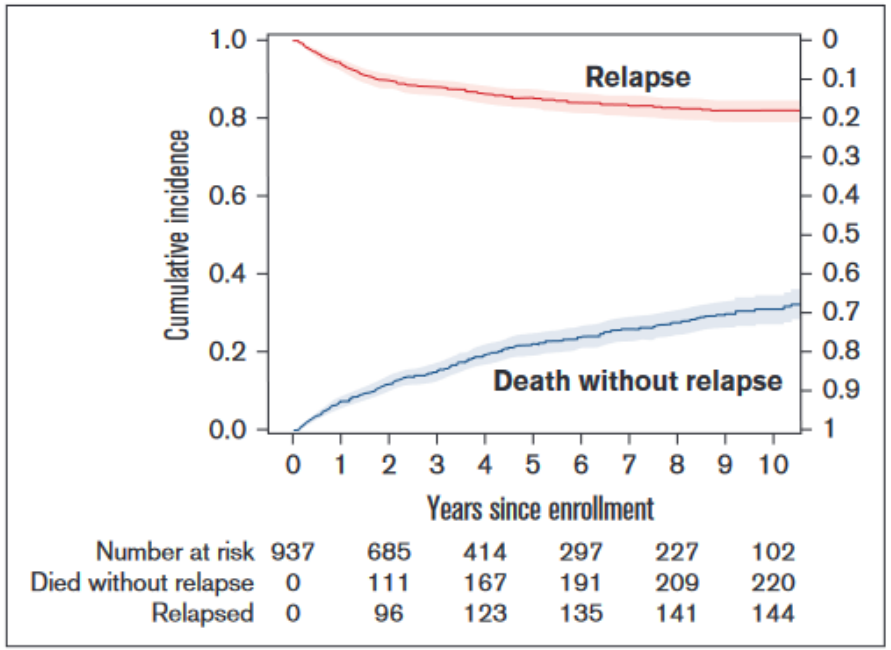


Figure 1. The cumulative incidence of NRM among patients diagnosed with cGVHD. Relapse shown as a competing risk.

Table 3. Multivariable analysis of variables associated with increased risk for NRM

Parameter	HR	95% CI	*P*	Global *P*
Conditioning regimen				
Myeloablative	1.0			
RIC/NMA	1.5	1.1-2.1	.024	
Bilirubin at enrollment, mg/dL				
≤2	1.0			
>2	2.24	1.16-4.34	.017	
Skin score at enrollment				
Not involved	1.0			.004
Mild	1.21	0.72-2.05	.47	
Moderate or severe	1.89	1.27-2.82	.002	
Lung score at enrollment				
Not involved	1.0			.002
Mild	1.68	1.14-2.49	.009	
Moderate or severe	2.25	1.35-3.75	.002	
Walk test (per 10 feet)	0.97	0.96-0.99	.001	
Modified HAP-adjusted activity score (per 10 points)	0.80	0.70-1.0	.012	

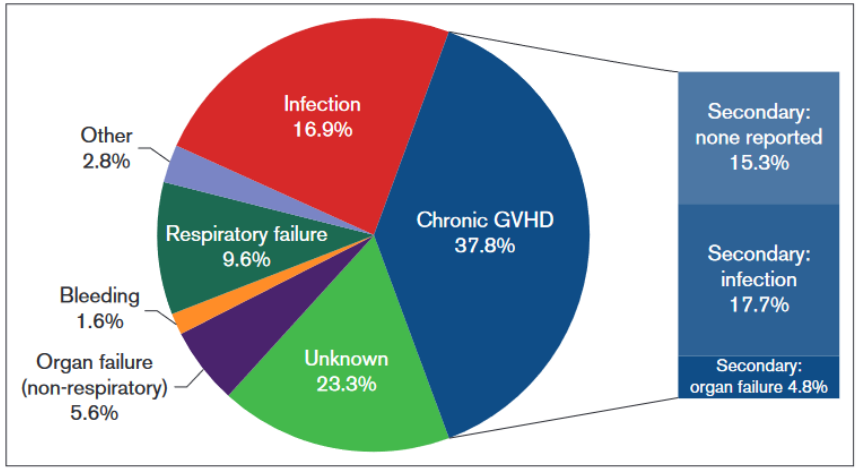


Figure 2. Reported primary causes of death for cases of NRM.

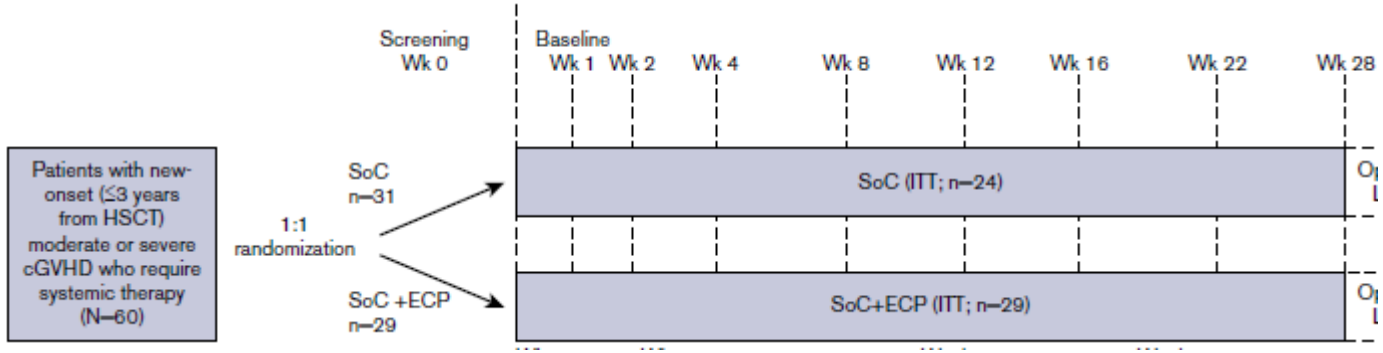
Traitement de 1ère ligne

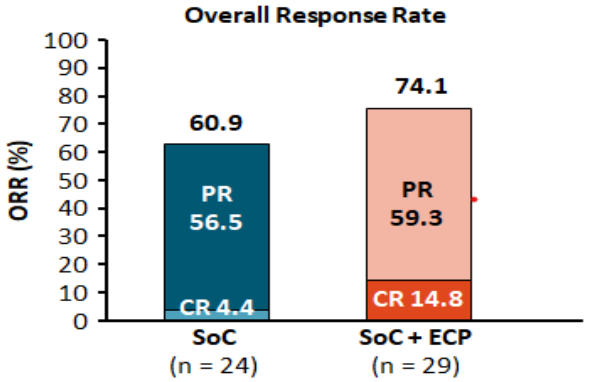
	Percentage approval (%)	Evidence and consensus category	Comments
The decision to start treatment for chronic GVHD is made basedon symptom type, severity (moderate or severe according to NIH classifications) and dynamics of progression in the context of other relevant variables, such as disease risk, chimerism, and minimal residual disease results	100	2C	This recommendation is based on standard practice and expert opinion
The first-line treatment of newly diagnosed chronic GVHD is steroids	100	2A	Randomised trials evaluated the addition of other agents (azathioprine, thalidomide, mycophenolate mofetil, hydroxychloroquine, and ciclosporin) to prednisone regimen, but a clinically meaningful benefit for patients with standard risk (according to NIH classification) chronic GVHD was reported[40–42]
In severe chronic GVHD the primary addition of another immunosuppressant to reduce steroid use is a valuable option	95	2C	This recommendation is based on expert opinion
The first-choice corticosteroid is prednisone taken orally at a dose of 1 mg/kg	100	2C	This recommendation is based on standard practice and expert opinion

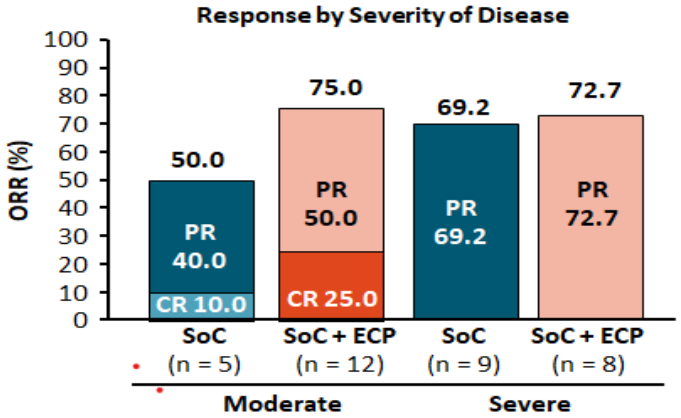
Négativité des études randomisées (azathioprine, ciclosporine, thalidomide, mycophenolate mofetil, hydroxychloroquine, ibrutinib…

Penack O. et al. Lancet Hematol. 2020

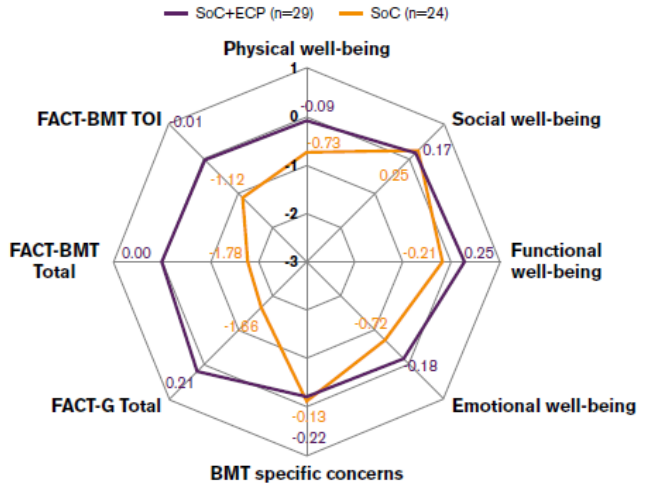
Randomized controlled study of ECP with methoxsalen as first-line treatment of patients with moderate to severe cGVHD







- Blind assessments
- No difference in mean steroid doses through Wk 28
- Slightly longer FFS in ECP arm (12.5 vs 7.8 mos)



- Déclin de la Qualité de Vie chez les patients traités avec SoC
- Maintien de la qualité de vie chez les autres in SoC+ECP

Jagasia M et al., Blood Advances 2019

Traitement de 2nde ligne

	Recommendation	NCCN classification
Prophylaxis of GvHD for patients undergoing allogeneic HSCT	For recipients of allogeneic HSCT from a matched related donor, PTCy should not be generally preferred to rATG for preventing GvHD	2A
	For recipients of allogenic HSCT from a MUD, GVHD prophylaxis including rATG or PTCy should be preferred to prophylaxis with neither rATG nor PTCy	1
	For recipients of allogenic HSCT from MMUD, GVHD prophylaxis including rATG or PTCy should be preferred to prophylaxis with neither rATG nor PTCy	2A
Recommendation on aGvHD treatment	In adults with SR-aGVHD we recommend ruxolitinib	1
Recommendations on cGvHD treatment	In adults with SR-cGVHD, we recommend ruxolitinib	1
	In adults with SR-cGVHD, belumosudil is a potential therapeutic option	2C
	In adults with SR-cGVHD, ibrutinib is a potential therapeutic option	2B

Penack O et al, Lancet Hematol. 2024

Guidelines on the Use of Therapeutic Apheresis in Clinical Practice – Evidence-Based Approach from the Writing Committee of the American Society for Apheresis: The Ninth Special Issue

GRAFT-VERSUS-HOST DISEASE

Incidence: after allogeneic HSCT, grade II to IV aGVHD in up to 60%; cGVHD in up to 70%

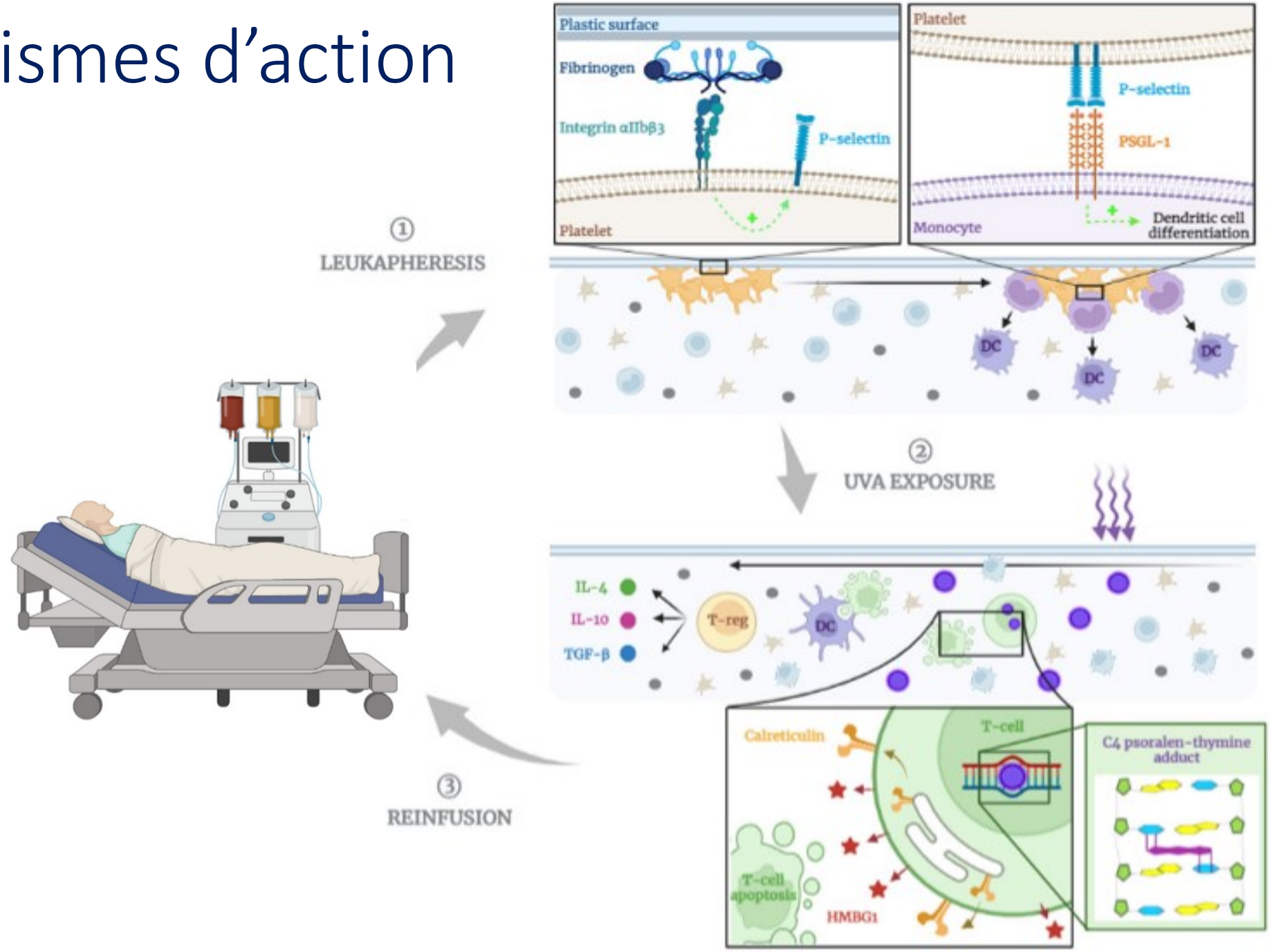
Indication	**Procedure**		**Category**	**Grade**
Acute/Chronic	ECP		II	1B
# reported patients: >300	**RCT**	**CT**	**CS**	**CR**
Acute	1 (81)	6 (296)	NA	NA
Chronic	2 (148)	8 (228)	NA	NA

- ORR = 65%
- Avantage en termes de survie globale chez les patients répondeurs
- Une introduction précoce semble améliorer la réponse

- Réponse maximale : au moins 6 mois de traitement pour la GVHc
- Epargne cortisonique/ baisse des IS
- Pas d'effet immunosuppresseur : pas d'augmentation du risque d'infections ou de rechute

Connelly-Smith L et al, J Clin Apher 2023

Mécanismes d’action



The role of extracorporeal photopheresis in the management of cutaneous T-cell lymphoma, graft-versus-host disease and organ transplant rejection: a consensus statement update from the UK Photopheresis Society

- 27 études rétrospectives et prospectives

- 725 patients adultes avec une GVH chronique cortico-dépendante ou réfractaire

- ORR : 68% (14 études)

- ORR par organe:
  - Peau: 74% (23 études)
  - Foie: 62% (15 études)
  - Muqueuse buccale: 62% (12 études)
  - Yeux: 60% (4 études)
  - Digestive : 46% (5 études)
  - Poumon: 16% (9 études)

Alfred et al., BJH, 2017

A multicenter prospective phase 2 randomized study of extracorporeal photopheresis for treatment of chronic graft-versus-host disease

*Mary E. D. Flowers,[1] Jane F. Apperley,[2] Koen van Besien,[3] Ahmet Elmaagacli,[4] Andrew Grigg,[5] Vijay Reddy,[6] Andrea Bacigalupo,[7] Hans-Jochem Kolb,[8] Luis Bouzas,[9] Mauricette Michallet,[10] H. Miles Prince,[11] Robert Knobler,[12] Dennis Parenti,[13] Jose Gallo,[13] and *Hildegard T. Greinix[14]

Table 3. Total Skin Score (TSS) and corticosteroid response to ECP treatment

	Week 12			Week 24	
Parameter	**ECP, n = 48**	**Control, n = 47**	***P***	**ECP, n = 48**	**Control, n = 47***
Median percent change from baseline in TSS	−14.5	−8.5	.48	−31.4	N/A
> 50% reduction in corticosteroid dose, n (%)†	12 (25)	6 (12.8)	.13	19 (39.6)	N/A
> 50% reduction in corticosteroid dose and > 25% improvement in TSS, n (%)	4 (8.3)	0 (0.0)	.04	11 (22.9)	N/A
> 50% reduction in corticosteroid dose and final corticosteroid dose of < 10 mg/day, n (%)†	10 (20.8)	3 (6.4)	.04	17 (35.4)	N/A

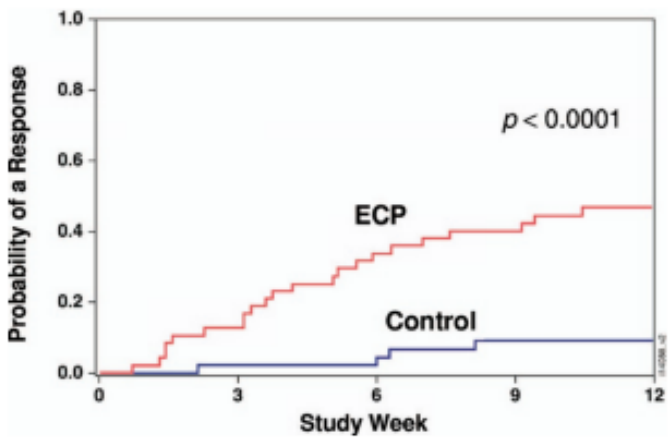


Figure 4. Cumulative incidence of complete or partial skin response.

- Epargne cortisonique de la PCE
- Meilleure réponse
- Evaluation de la réponse trop tôt

Flowers et al, Blood, 2008

Progressive Improvement in Cutaneous and Extracutaneous Chronic Graft-versus-Host Disease after a 24-Week Course of Extracorporeal Photopheresis—Results of a Crossover Randomized Study

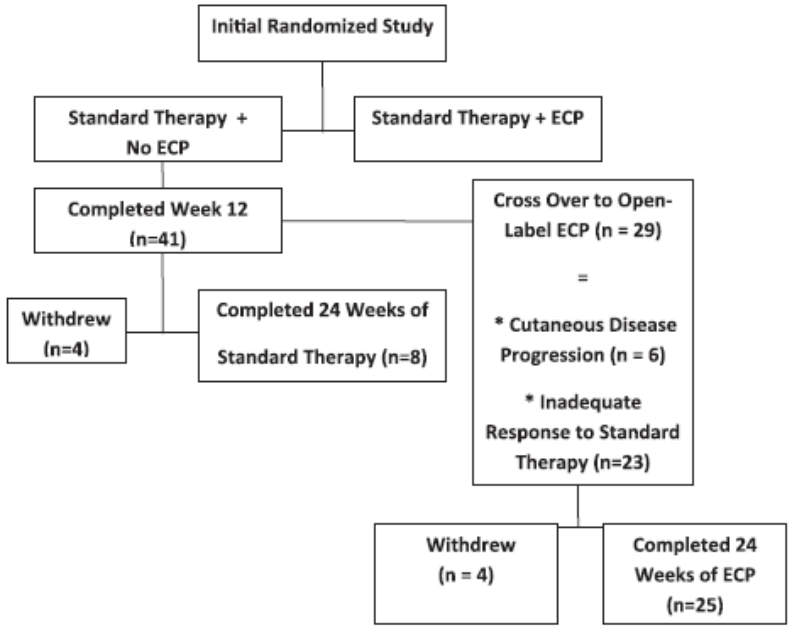
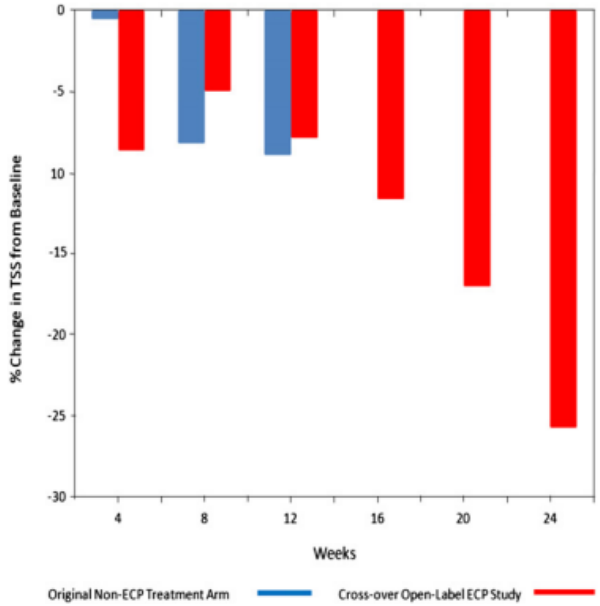


Table 2. Cutaneous Response to Crossover ECP and Steroid-Sparing

	Weeks after Start of ECP	
	12	24
Number of patients	24*	24*
Cutaneous response		
- Complete and partial response (nonblind clinical investigator assessment), n (%)	7/27† (26)	9/29‡ (31)
- Median percent change in TSS from baseline (blind observer)	−7.9	−25.8
Corticosteroid-sparing effect		
≥50% Reduction in corticosteroid dose, n (%)	4/24 (17)	8/24 (33)
≥50% Reduction in corticosteroid dose and corticosteroid dose < 10 mg/day.	4/24 (17)	6/24 (25)



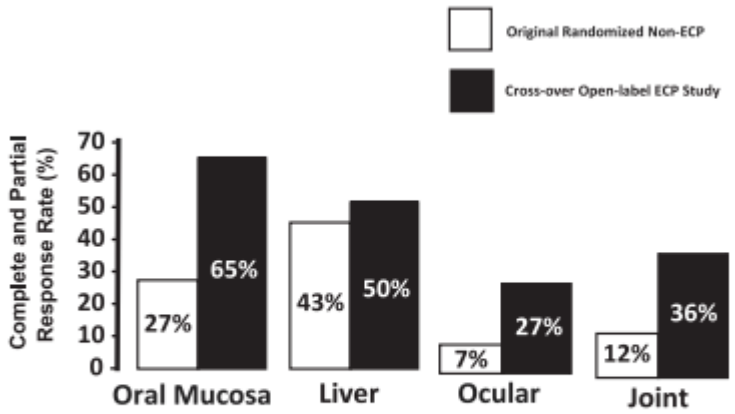
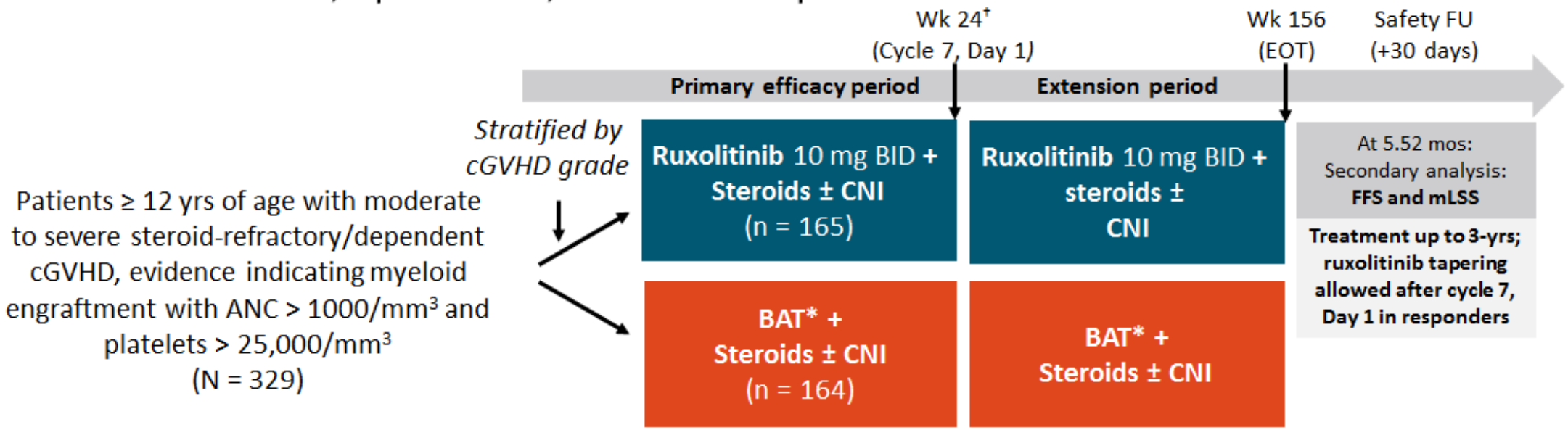


Figure 3. Complete and partial response of extracutaneous manifestations during standard non-ECP therapy and after crossover to adjunct ECP: comparison of results after 12 weeks.

Greinix et al., BBMT, 2011

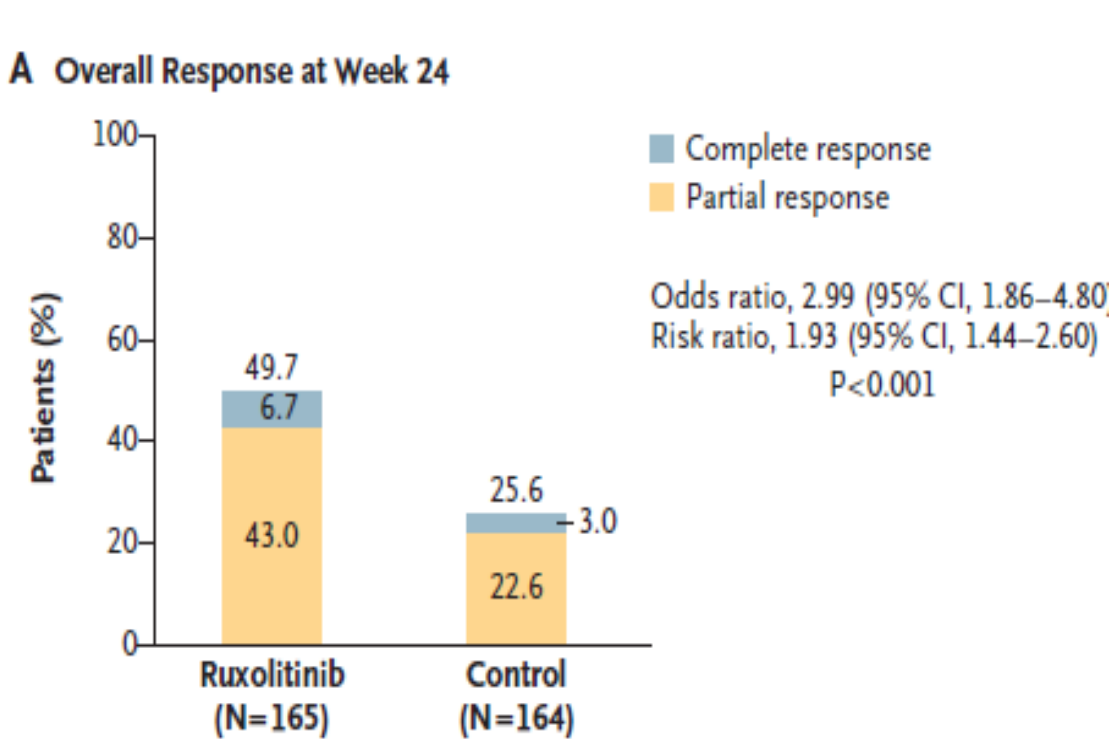
REACH3: Study Design

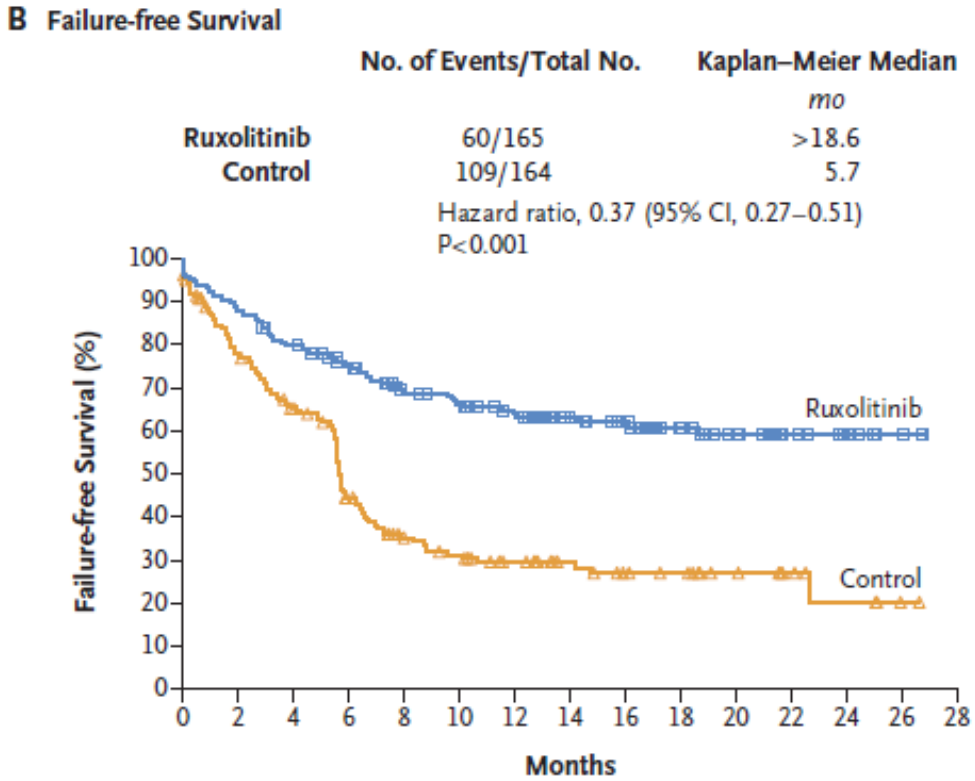
- Multicenter, open-label, randomized phase III trial[1,2]



*Investigator choice of BAT: ECP, low-dose methotrexate, mycophenolate mofetil, everolimus, sirolimus, infliximab, rituximab, pentostatin, imatinib, or ibrutinib.
†Patients receiving BAT who progressed, had mixed or unchanged response, developed toxicity to BAT, or experienced a cGVHD flare could cross over to ruxolitinib.

- Primary endpoint: ORR at Wk 24 by NIH consensus criteria for response[3]
- Secondary endpoints: FFS, mLSS at Wk 24

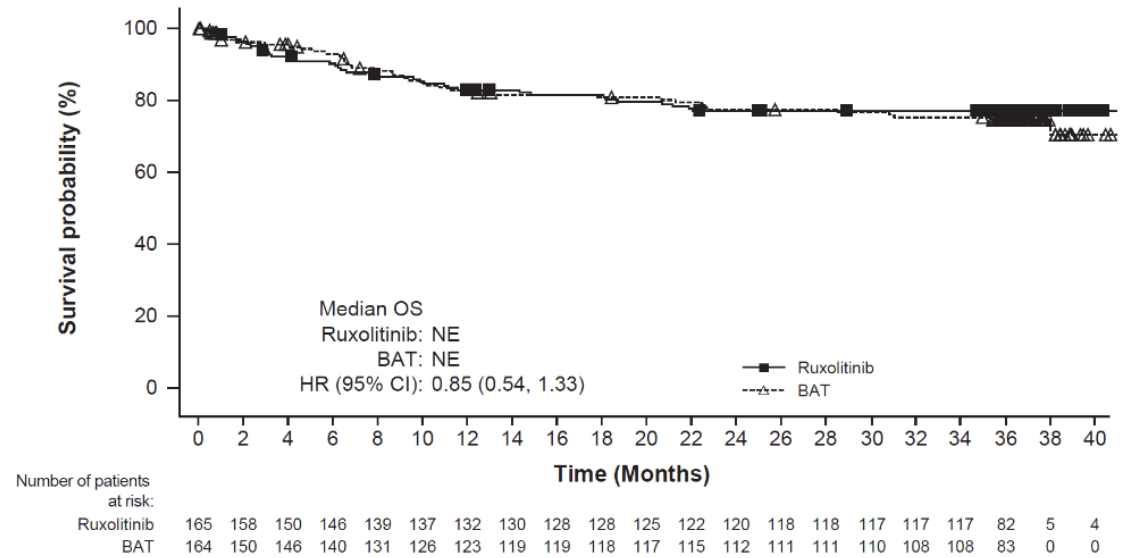




Zeiser R. et al, NEJM, 2021

	Ruxolitinib n=165		BAT n=164	
Organ	Baseline involvement[a]	Organ response[b]	Baseline involvement[a]	Organ response[b]
	n (%)	m/n (%)	n (%)	m/n (%)
Skin	119 (72.1)	49/119 (41.2)	110 (67.1)	17/110(15.5)
Eye	96 (58.2)	25/96 (26.0)	93 (56.7)	10/93 (10.8)
Mouth	96 (58.2)	48/96 (50.0)	99 (60.4)	25/99 (25.3)
Esophagus	18 (10.9)	9/18 (50.0)	17 (10.4)	5/17 (29.4)
Upper GI tract	20 (12.1)	8/20 (40.0)	21 (12.8)	8/21 (38.1)
Lower GI tract	15 (9.1)	8/15 (53.3)	10 (6.1)	3/10 (30.0)
Liver	86 (52.1)	21/86 (24.4)	83 (50.6)	18/83 (21.7)
Lung	70 (42.4)	6/70 (8.6)	49 (29.9)	3/49 (6.1)
Joints and fascia	45 (27.3)	17/45 (37.8)	44 (26.8)	7/44 (15.9)
Overall response	–	82 (49.7)	–	42 (25.6)

Kaplan-Meier plot of probability of overall survival up to 3 years (full analysis set)



ECP versus ruxolitinib in steroid-refractory chronic GVHD – a retrospective study by the EBMT transplant complications working party

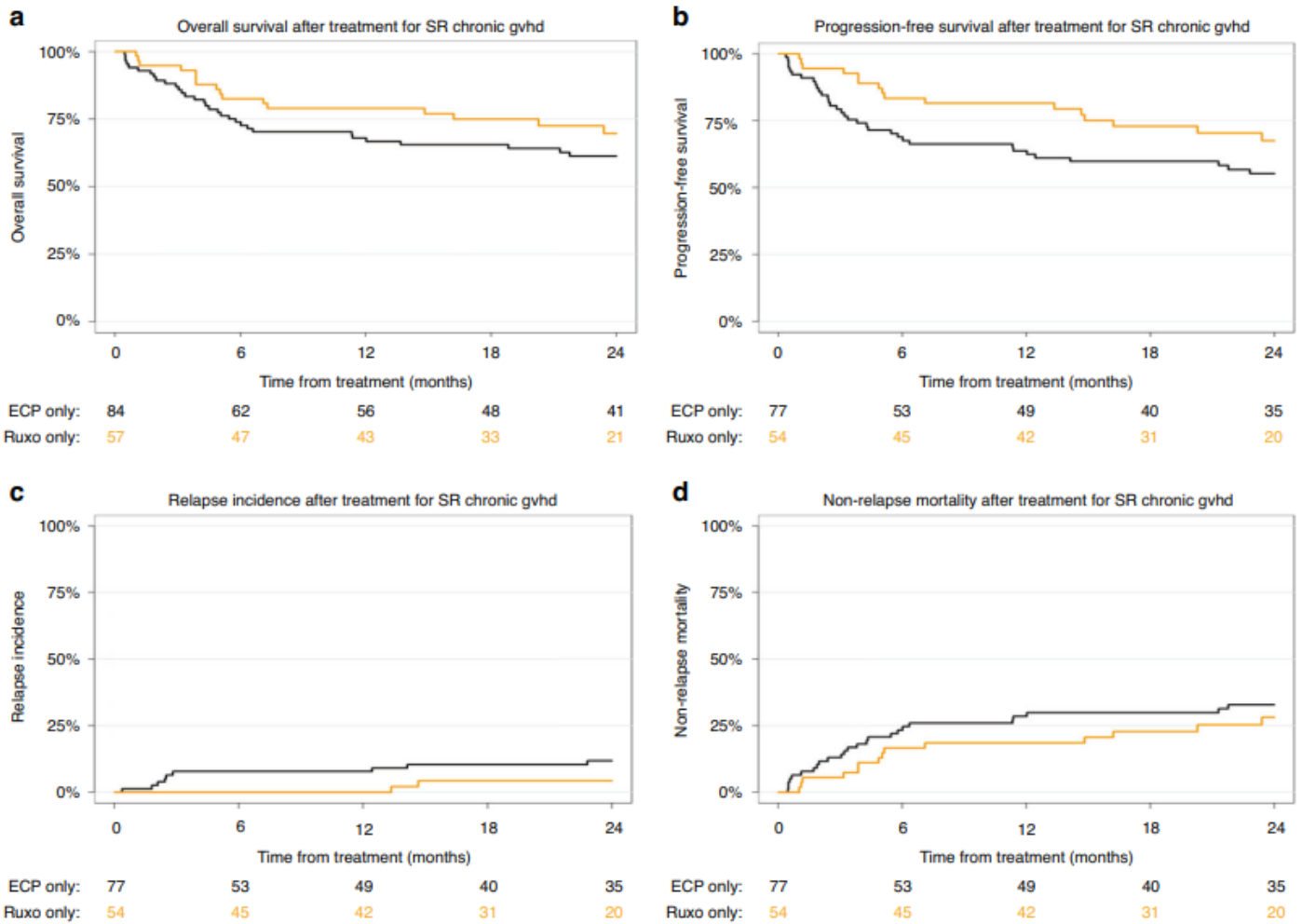


Table 3. Multivarate analyses. Results are given for the ruxolitinib group with the ECP group being the reference.

Variable	Hazard ratio/Odd ratio [95% CI]	*P*
Overall response rate at day +180	1.35 [0.64;2.91]	0.43
Overall survival	0.71 [0.32–1.6]	0.41
Progression-free survival	0.74 [0.4–1.36]	0.33
Relapse incidence	0.61 [0.17–2.15]	0.44
Non-relapse mortality	0.72 [0.32–1.63]	0.43

Pas de différence en termes d'infections bactériennes ou virales

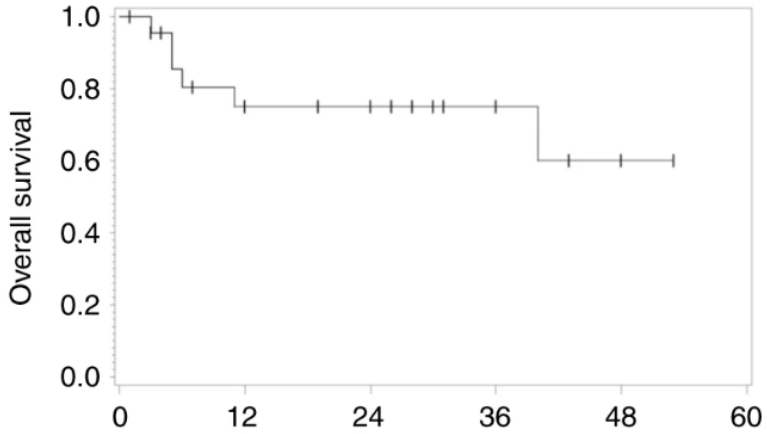
Penack O et al, BMT 2024

Ruxolitinib–ECP combination treatment for refractory severe chronic graft-versus-host disease

- 23 patients
- 60% de GVH extensive, 91% > 2 lignes, 87% > 3 organes
- 30% de patients avec PCE: 3,25 mois, RP : 3/7, NR : 4/7
- 35% de patients avec Ruxo: 15 mois, RP: 5/8, NR3/8

- ORR (PCE +Ruxo): 74% (17/23), 9% de RC, 65% de RP

75% à 24 mois



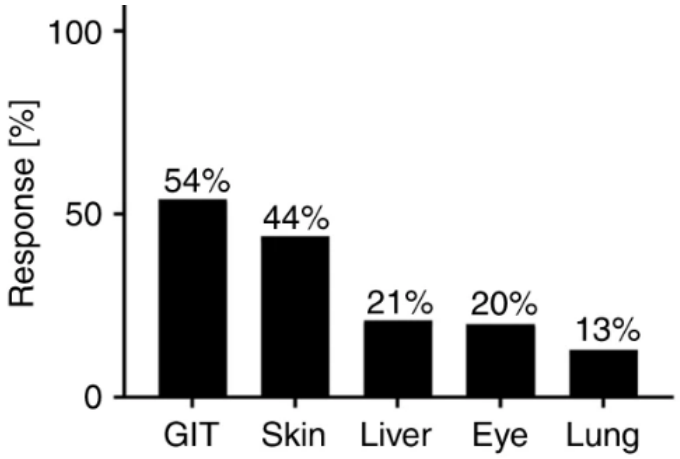


Table 2 Adverse events during treatment.

AEs	
CMV reactivation	*Absolute number (%)*
	6 (26)
Cytopenia	*Absolute number (%)*
Mild cytopenia (grade 1 and 2)	3 (13)
Severe cytopenia (grade 3 and 4)	8 (35)
Cytopenia *before* ruxolitinib	6 (26)
Relapse of Malignancy	*Absolute number (%)*
	0 (0)

Maas-Bauer et al, BMT 2021

Contre-indications

Absolues:
- Grossesse
- Infection non contrôlée
- Hypersensibilité au psoralen (8-MOP)
- Aphakie
- Photosensibilité

Relatives:
- Leucopénie (<1 × 10_9/L)
- Instabilité hémodynamique ou respiratoire

Des précautions doivent être prises chez les patients avec
- Hématocrite bas
- Thrombopénie
- Hémorragies ou risque de saignement
- Petit poids

Dunbar NM et al,. *J Clin Apher, 2017*
Colpo A et al, Transf aph Sci 2024.
Nygaard M *et al*, Eur J Hematol 2020.

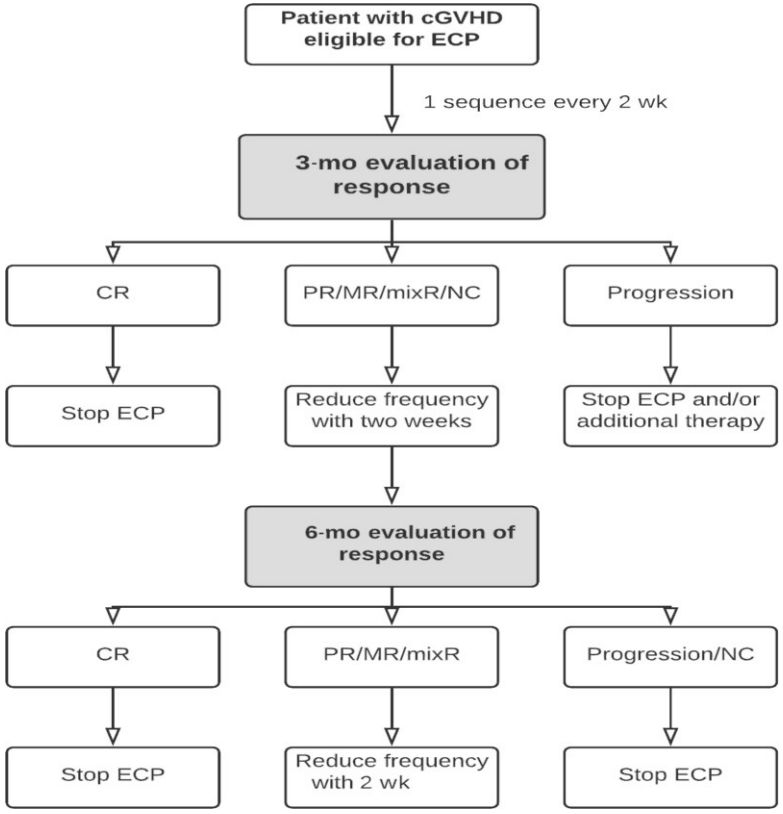
Fréquence

Volume treated: Varies.

Replacement fluid: NA

Frequency: aGVHD: 2 to 3 treatments weekly until response obtained (minimum of 8 weeks); cGVHD: one cycle weekly or every other week for up to 3 months, then, if responding, taper to one cycle per month to clinical response

Connelly-Smith L et al, J Clin Apher 2023



Nygaard M *et al*, Eur J Hematol 2020.

Recommendations: in patients with chronic GvHD who are candidates to ECP, one ECP cycle (two sessions) every other week is suggested for the first 12 weeks for initial treatment (conditional recommendation, quality of evidence low).

Colpo A et al, Transf aph Sci 2024.

Treatment patterns of extracorporeal photopheresis in steroid-refractory graft versus host disease: A delphi study

BBMT, 2025

Topic	Question to the experts	Results			
		aGvHD	Agreement %	cGvHD	Agreement %
Reasons for selecting ECP	Which factors influence you to select ECP as a treatment in SR-GvHD patients?	Rank 1: Efficacy of ECP	100	Rank 1: Efficacy of ECP	100
		Rank 2: Safety profile	100	Rank 2: Safety profile	100
		Rank 3: Steroid-sparing effect	100	Rank 3: Steroid-sparing effect	100
Combination of ECP with other GvHD therapies	What are the main reasons for choosing the combination therapy of ECP and ruxolitinib in SR-GvHD patients?	Rank 1: Severe cases	100	Rank 1: Increased efficacy	100
		Rank 2: Increased efficacy	100	Rank 2: Severe cases	100
Reducing steroid treatment	Depending on the applied treatment: What is the percentage of SR-GvHD patients where steroids could be reduced by at least 50% Do you agree on the percentages, resulting from round 1?	Proportion of patients treated with ECP: 50%	100	Proportion of patients treated with ECP: 60%	100
		Proportion of patients treated with ruxolitinib: 53%	91	Proportion of patients treated with ruxolitinib: 65%	91
		Proportion of patients treated with ECP-ruxolitinib: 50%	100	Proportion of patients treated with ECP-ruxolitinib: 50%	100
Stopping steroid treatment	Depending on the applied treatment: What is the percentage of SR-GvHD patients in your practice where steroid treatment could be stopped completely? Do you agree on these percentages, resulting from round 1?	Proportion of patients treated with ECP: 50%	100	Proportion of patients treated with ECP: 41%	100
		Proportion of patients treated with ruxolitinib: 51%	91	Proportion of patients treated with ruxolitinib: 40%	91
		Proportion of patients treated with ECP-ruxolitinib: 70%	91	Proportion of patients treated with ECP-ruxolitinib: 60%	100
ECP monotherapy	Do you agree on the selection criteria for treating SR-GvHD (both acute and chronic) patients with ECP monotherapy?	Rank 1: Low risk (e.g. skin involvement only or upper GI only)		91	
		Rank 2: Contraindication for Ruxolitinib (e.g. thrombocytopenia)		91	
Treatment duration of ECP/ruxolitinib	What is the average treatment duration of ECP/ruxolitinib in SR-GvHD in the following scenarios?	ECP: 4 to 6 months	91	ECP: 10 to 12 months	91
		Ruxolitinib: 3 to 5 months	91	Ruxolitinib: 10 to 12 months	100
		ECP in combination with ruxolitinib: 4 to 6 months	100	ECP in combination with ruxolitinib: 8 to 10 months	91
		Ruxolitinib in combination with ECP: 3 to 5 months	91	Ruxolitinib in combination with ECP: 8 to 10 months	91
Treatment schedules of ECP	When treating SR-GvHD patients with ECP alone but not with ruxolitinib - which treatment schedules do you apply?	Treatment schedule 1: 2 – 3 ECP procedures on consecutive days weekly for 4 weeks	91	Treatment schedule 1: 2 ECP procedures per week for approximately 9 weeks	55
		Treatment schedule 2: 2 ECP procedures per week at least every two weeks for approximately 8 weeks (2 months)	82	Treatment schedule 2: 2 ECP procedures per week, at least every two weeks for approximately 10 weeks	64
		Treatment schedule 3: 2 ECP procedures per week at least every month for approximately 8 weeks (2 months)	36	Treatment schedule 3: 1 – 2 ECP procedures per week at least monthly for approximately 20 weeks (5 months)	73

Conclusion

- Traitement de seconde ligne de la GVH chronique ou à visée d'épargne cortisonique
- Réponse globale entre 60 et 70%, taux de réponse plus élevée dans les atteintes cutanéo-muqueuses avec une amélioration de la survie globale chez les patients répondeurs
- Bien toléré et sans effet immunosuppresseur
- Programmation d'un cycle par semaine ou toutes les 2 semaines pendant les 3 premiers mois puis diminution de la fréquence chez les patients répondeurs
- Durée de traitement prolongée
- Les données préliminaires PCE + Ruxo sont encourageantes. Place des combinaisons avec les nouveaux traitements de la GVH à définir (Axalitimab, Belumosudil …)
- Connaissance sur les mécanismes immunitaires à approfondir pour optimiser la prise en charge des patients avec GVH chronique