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cGvHD: evidenze e nuove esperienze con la ECP

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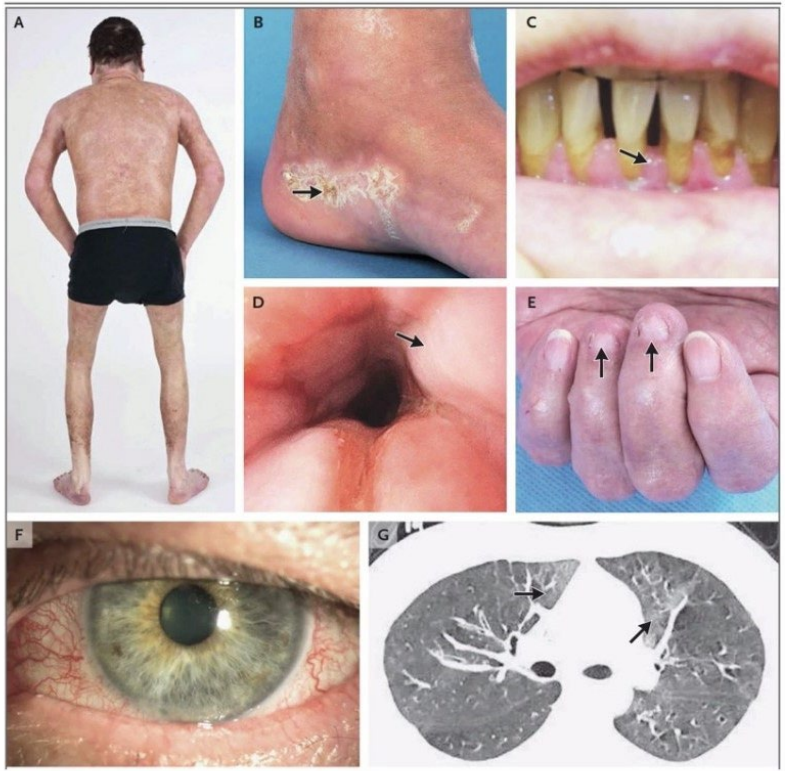
Disclosures of Patrizia Chiusolo

Company name	Research support	Employee	Consultant	Stockholder	Speakers bureau	Advisory board	Other
Sanofi	X		X				
Therakos					X		
Novartis						X	

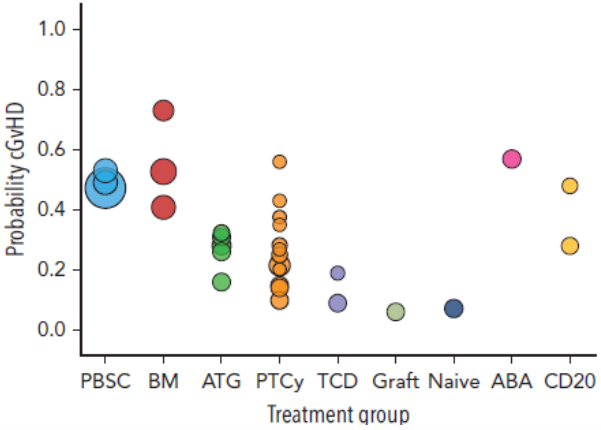
Overview cGvHD

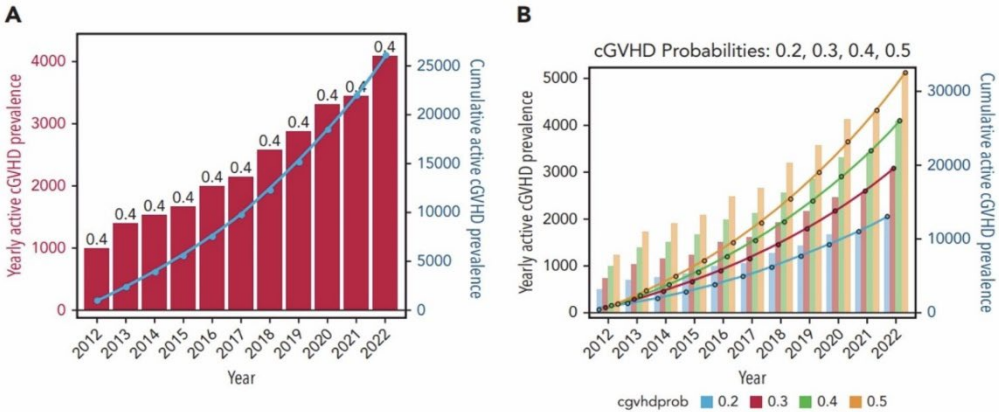
- Chronic GVHD is a multiorgan condition characterized by inflammation and fibrosis which is associated with morbidity, mortality, and impaired quality of life.
- Historically, chronic GVHD impacts 30-50% of allogeneic HCT recipients.



Zeiser R, et al. N Engl J Med. 2017

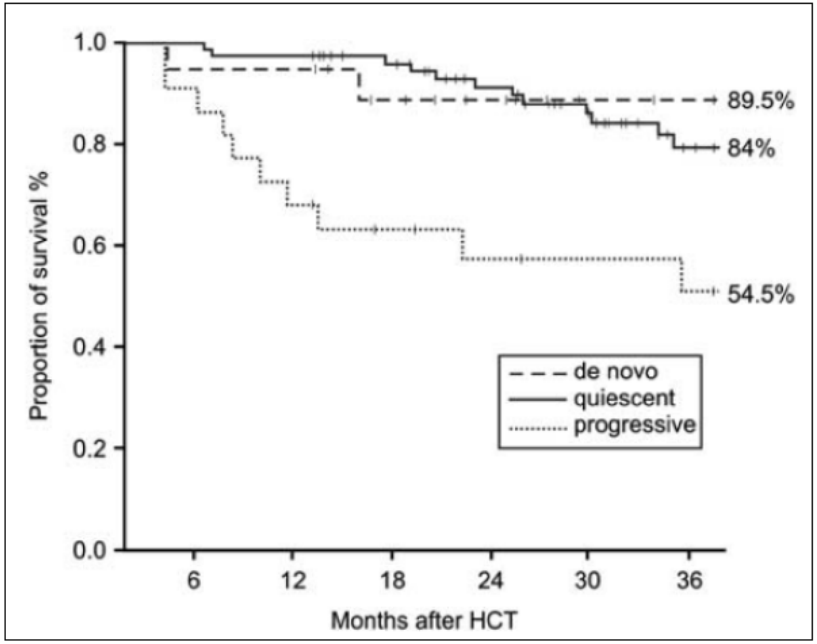
Range of cGVHD incidence following different initial GVHD prevention strategies





Estimated prevalence of active cGvHD

Pidala et al, Blood 2024



- Steroids are still standard first-line therapy of moderate/severe cGvHD.
- Improved understanding of pathophysiology of cGvHD.
- Improved staging/severity scoring and response assessment due to NIH consensus.
- Ruxolitinib, Ibrutinib, Belumosudil, Axatilimab FDA/EMA approved for refractory cGvHD.
- Dismal prognosis in high-risk cGvHD has remained.
- cGvHD is main reason for late NRM.

Kuzmina et al, Leukemia 2012, 26: 746-756

Prophylaxis and management of graft-versus-host disease after stem-cell transplantation for haematological malignancies: updated consensus recommendations of the European Society for Blood and Marrow Transplantation

Olaf Penack, Monia Marchetti*, Mahmoud Aljurf, Mutlu Arat, Francesca Bonifazi, Rafael F Duarte, Sebastian Giebel, Hildegard Greinix, Mette D Hazenberg, Nicolaus Kröger, Stephan Mielke, Mohamad Mohty, Arnon Nagler, Jakob Passweg, Francesca Patriarca, Tapani Ruutu, Hélène Schoemans, Carlos Solano, Radovan Vrhovac, Daniel Wolff, Robert Zeiser, Anna Sureda, Zinaida Peric*

Recommendations on cGVHD treatment published previously without need for update

- The decision to start treatment for cGVHD is made on the basis of symptom type, severity (moderate and severe according to National Institutes of Health, and dynamics of progression in the context of other relevant variables, such as disease risk, chimerism and minimal residual disease results (NCCN classification 2C)

- The first-choice corticosteroid is prednisone at a dose of 1 mg per kg orally (NCCN classification 2C)

Lancet Haematol 2024; 11: e147–59

Phase III studies combining prednisone (>1mg/kg) with other therapies for first line of cGvHD

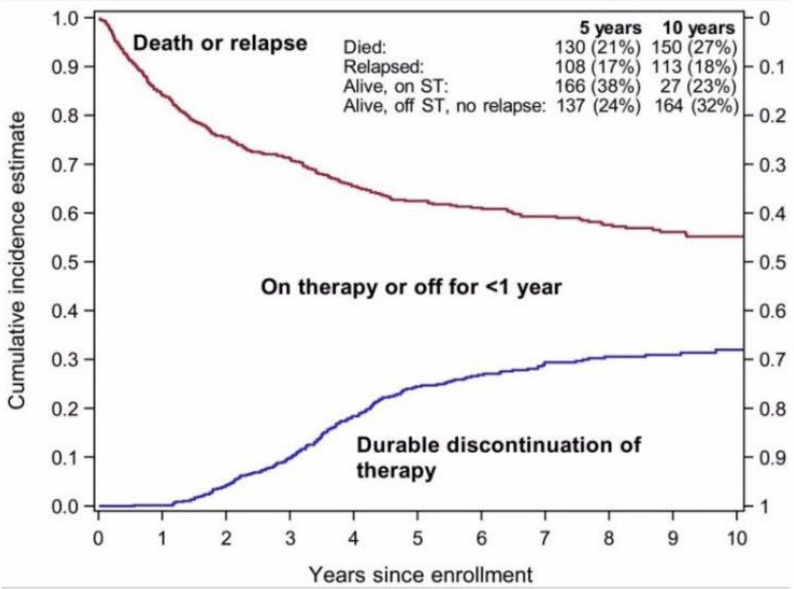
Recommended first-line treatment for cGvHD is corticosteroids

Author	Agents compared	Double-blind?	N	Results
Sullivan, *et al.*[1]	Prednisone + azathioprine	Yes	179	Decreased survival
Koc, *et al.*[2]	Prednisone + cyclosporine	No	287	Limited benefit
Arora, *et al.*[3]	CSP/prednisone + thalidomide	No	54	No benefit
Martin, *et al.*[4]	CNI/prednisone + MMF	Yes	151	No benefit
Gilman, *et al.*[5]	CNI/prednisone + hydroxychloroquine	No	54	Terminated early
Carpenter, *et al.*[6]	Sirolimus/prednisone + CNI	No	151	2 drugs less toxic than 3

cGvHD, chronic graft-versus-host disease; CNI, calcineurin inhibitor; CSP, cyclosporine; MMF, mycophenolate mofetil.

1. Sullivan KM, et al. *Blood*. 1988;72(2):546-554. **2.** Koc S, et al. *Blood*. 2002;100(1):48-51. **3.** Arora M, et al. *Biol Blood Marrow Transplant*. 2001;7(5):265-273. **4.** Martin PJ, et al. *Blood*. 2009;113(21):5074-5082. **5.** Gilman AL, et al. *Biol Blood Marrow Transplant*. 2012;18(1):84-91. **6.** Carpenter PA, et al. *Haematologica*. 2018;103(11):1915-1924.

- Few patients achieve and maintain a response (CR/PR) without requiring secondary treatments within 1 year of diagnosis.
- Most patients will require multiple lines of therapy that are administered over multiple years.

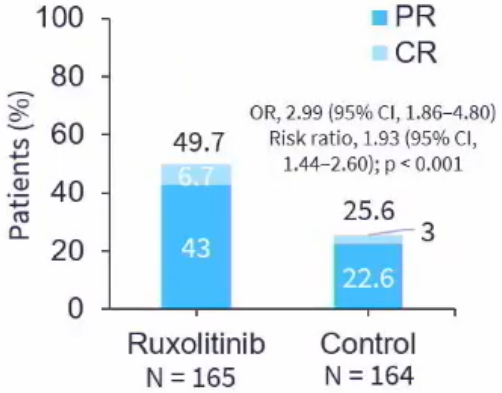


Chen GL, et al. Haematologica. 2023

SR-cGvHD-New drugs

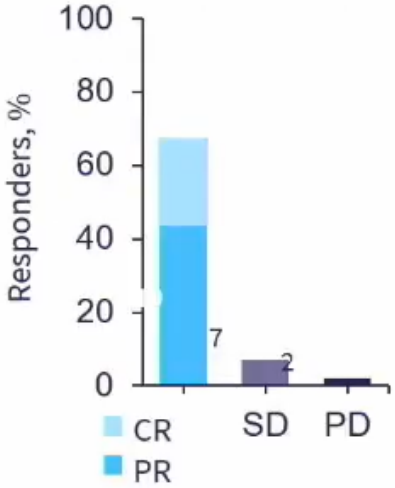
2024: Axatilimab FDA approved for cGvHD after failure of at least two prior lines of systemic therapy

- Ruxolitinib in phase III REACH3 ORR 49.7% vs 25.6% (ruxolitinib vs control)[3]



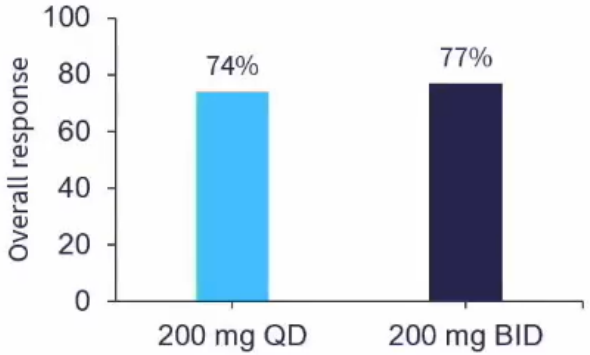
- Grade 3 infection rate similar in two groups (19.4% vs 18.4%)[3]
- 16.4 % vs **7.0% discontinued** treatment due to AEs[3]
- Approved in Sep 2021 (U.S. FDA) and May 2022 (EMA)[3]

- Until 2021 only 1 approved agent for SR-cGVHD – phase Ib/II study ibrutinib; ORR, 67%[1,2]



- Often discontinued due to adverse events[1,2]

- Belumosudil in phase II in 132 patients after 2–5 lines of previous therapy; ORR 74–77%[4,5]



- Median time to response 5 weeks, 7 patients achieved CR in all affected organs[4,5]
  12% discontinued due to SAEs[4,5]
- Most common pneumonia (7%)[4,5]
- Approved for cGvHD (U.S. FDA) after failure of at least 2 prior lines of therapy in Jul 2021[4,5]

Zeiser R et al. NEJM 2021; 385: 228, Miklos D et al Blood 2017; 130: 2243, Cutler C et al. Blood 2021; 138: 2278

Prophylaxis and management of graft-versus-host disease after stem-cell transplantation for haematological malignancies: updated consensus recommendations of the European Society for Blood and Marrow Transplantation

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New recommendations

A second-line treatment for cGvHD is recommended if corticosteroid resistance or dependence occurs.	Recommendation made from standard practice and expert opinion.
In adults with SR-cGvHD, we recommend ruxolitinib (NCCN classification 1).	Large beneficial effect on ORR and FFS in a randomised trial, a propensity-adjusted retrospective analysis and three meta-analyses. Fan S.2022;Hui L.2020;Zhang MY.2022;Zeiser R.2021;Novitzky-Baso I.2023.
In adults with SR-cGvHD, belumosudil is a potential therapeutic option (NCCN classification 2C).	Encouraging ORR in non-randomised trials showing a low drug induced toxicity profile. Cutler C.2021;Jagasia M.2021;Lee SJ.2022;DeFilipp Z.2022.
In adults with SR-cGvHD, ibrutinib is a potential therapeutic option (NCCN classification 2B).	Encouraging ORR in non-randomised trials in patients with moderate GvHD burden and an acceptable toxicity profile. Doki N.2021;Miklos D.2017;Waller EK.2019;Chin KK.2021;Kaloyannidis P.2021.

Lancet Haematol 2024; 11: e147–59

GITMO

GRUPPO ITALIANO PER IL TRAPIANTO DI MIDOLLO OSSEO, CELLULE STAMINALI EMOPOIETICHE E TERAPIA CELLULARE

LINEE GUIDA

PROFILASSI E TRATTAMENTO DELLA GRAFT VERSUS HOST DISEASE ACUTA E CRONICA

Versione 1.2024

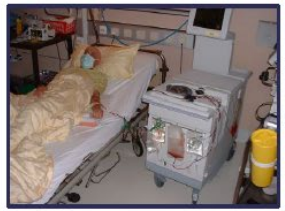
SR-cGvHD: real life practice

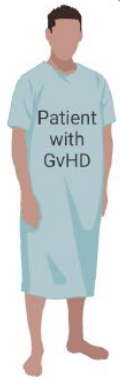
- Transplant Complications Working Party of the EBMT survey in 2021
- 145 centers in 33 countries
- 56% clinical trials, 65% centers have SOP, 35% have a multidisciplinary team
- Very heterogeneous practice with most centers reporting on the use of more than two agents (range, 3–13)

Most used agents are:
Ruxolitinib and ECP in 68%
CNI in 40%
MMF in 37%
Rituximab in 29%
Imatinib in 25%
mTOR inhibitors in 23%,
Ibrutinib and MTX in 19%
Pulse of CS in 17%
MSC in 12%
PUVA therapy in 10% of centers

EBMT-TCWP survey 2021

What is extracorporeal photopheresis?





4. The photoactivated white blood cells are returned to the patient

UVA light

+ methoxsalen

3. White blood cells are treated with methoxsalen and exposed to UVA light for photoactivation

Leukapheresis

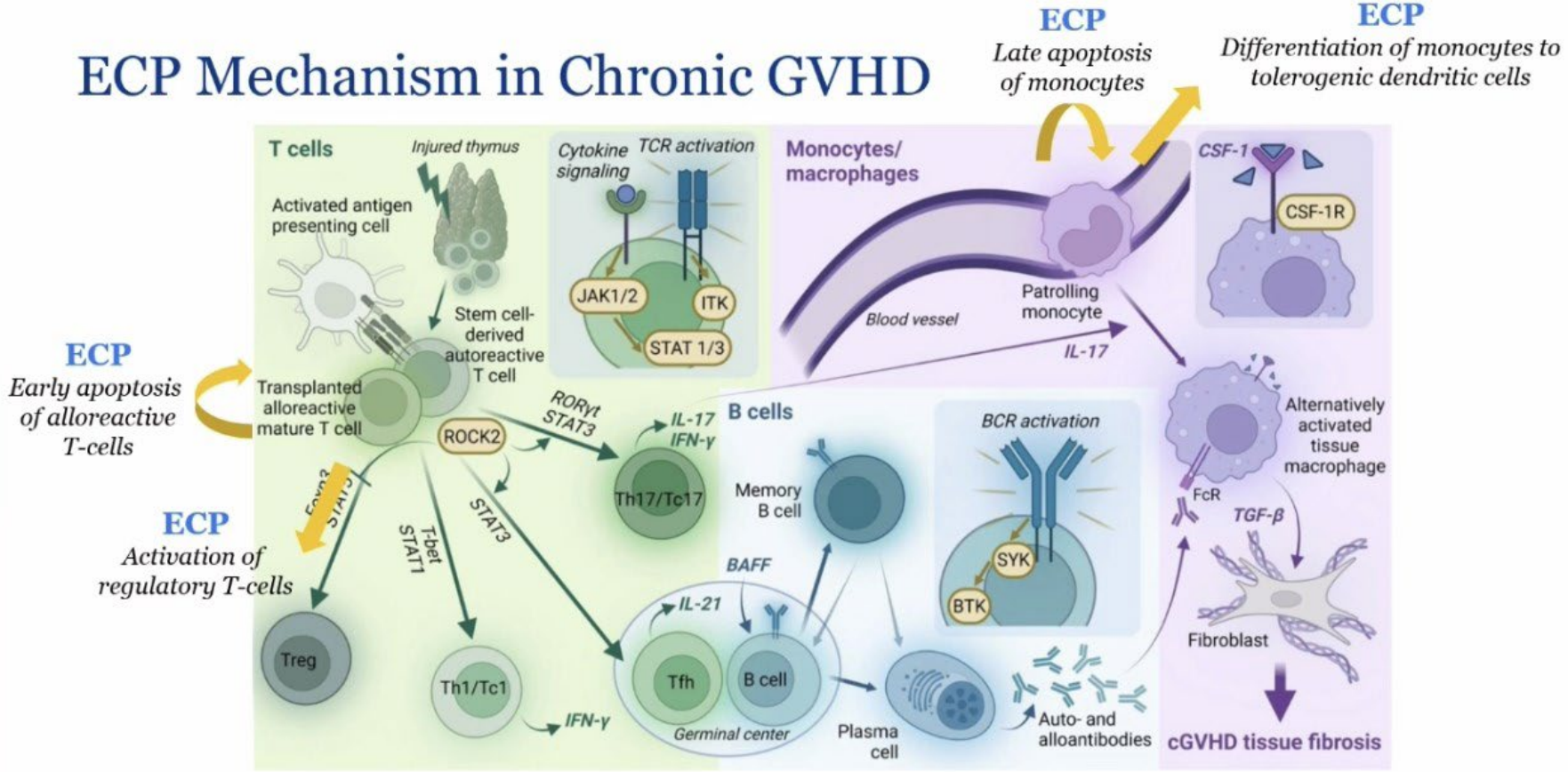
2. Blood is separated by centrifugation and red blood cells are returned

1. The ECP device draws blood from the patient

Each cycle = ~2 hours

Adapted from Knobler R, et al. *J Am Acad Dermatol*. 2009;61(4):652-65.
Created with BioRender.com.

ECP Mechanism in Chronic GVHD

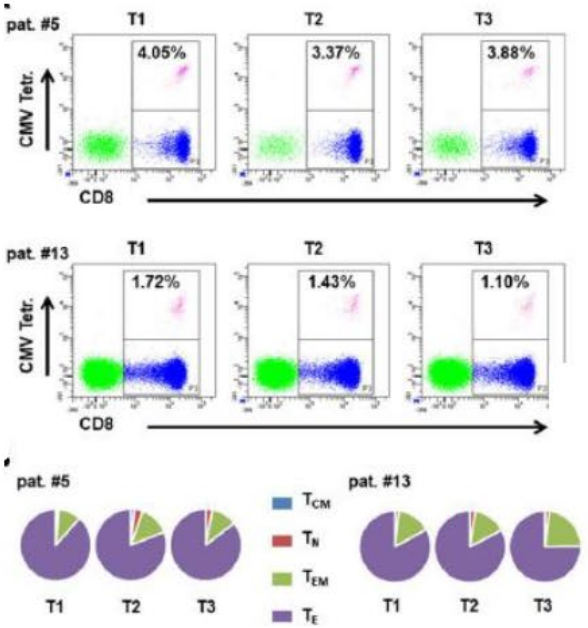


Asensi Cantó P, et al. Transplant Cell Ther. 2023; Boiko JL, et al. Transplantation. 2024; Berhan A, et al. Immunotargets Ther. 2024;

Impact of ECP on antiviral immune response

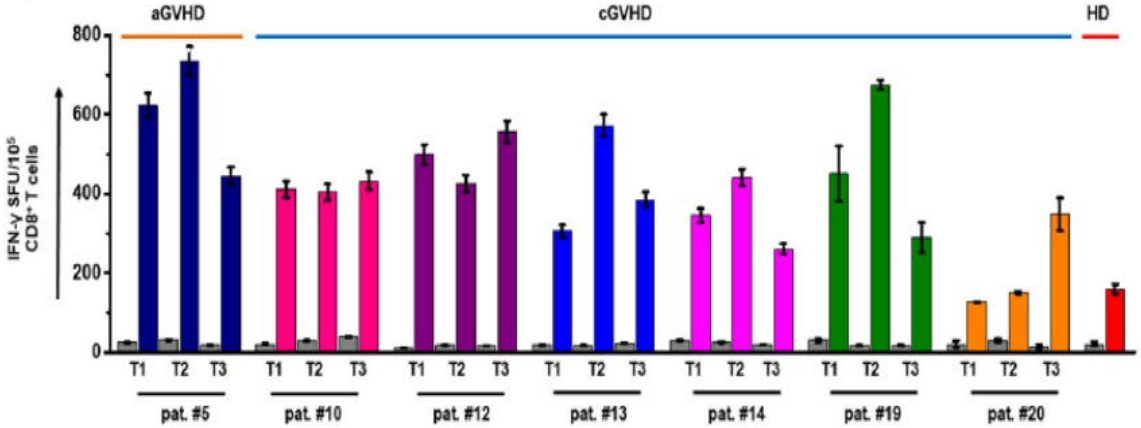
CMV-specific CD8⁺ T cells before and after ECP in acute and chronic GvHD are not different

Cell function measured by IFN-γ release remains stable



Wang L, et al. *Front Immunol.* 2018;9:2207.

ECP does not cause generalized immunosuppression



Wang L, et al. *Front Immunol.* 2018;9:2207.

ECP in SR-cGvHD: retrospective data

- ECP is the most commonly evaluated among different treatments for SR cGvHD
- Mainly small, uncontrolled studies with different endpoints and treatment regimens
- Improvements in all organs, cutaneous > gastrointestinal > hepatic > ocular/oral mucosa > pulmonary involvement

Excellent safety profile

Number of patients	>6–102
ORR, %	31–100
Steroid-sparing	Most studies
Start of treatment	Median from cGvHD 2–24 months
Schedule	Weekly>every 2 weeks>monthly
Duration	Median 6–20 months and longer
First effect	Slow

Nygaard M et al, Eur J Haematol 2020; 104: 361-365

ECP in SR-cGvHD: prospective data

- Several single-arm prospective studies and 1 randomized controlled trial
- Most studies evaluate cycles of ECP (two sequences)
- No firm evidence of superior effect using twice weekly instead once weekly sequences or initial weekly instead every 2 weeks
- **ECP should be continued for 6 months especially in cutaneous GvHD**

Authors	N	CR/PR skin, %	CR/PR liver, %	CR/PR oral, %	CR/PR lung, %	CR/PR ocular, %	CR/PR GI, %	ORR, %	Steroid sparing	OS, %
Seaton, *et al.*[1]	28	48	32	21	—	—	—	36	No	24/28 (86%)
Foss, *et al.*[2]	25	64	0	46	—	—	—	64	Yes	med 51 mo
Flowers, *et al.*[3]	**48**	**40**	**29**	**53**	**—**	**30**	**—**	**—**	**Yes**	**98**
Greinix, *et al.*[4]	29	31	50	70	57	—	—	31	Yes	100
Dignan, et al.[5]	38	65	—	29	50	55	100	50	Yes	94
Okamoto, *et al.*[6]	15	36	43	46	0	31	33	67	Yes	—

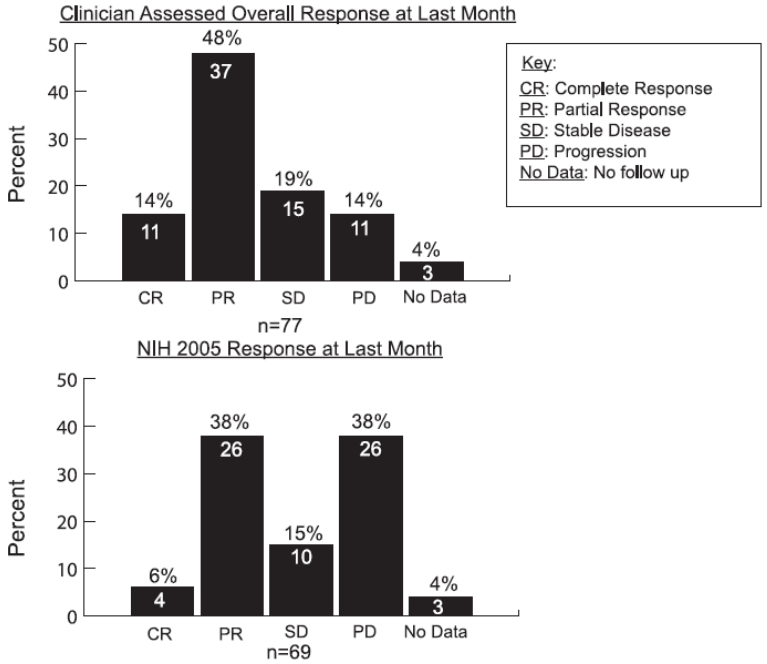
Seaton ED et al, Blood 2003; Foss FM et al BMT 2005; Flowers M et al Blood 2008; Greinix H et al BBMT 2011; Dignal FL et al BMT 2014; Okamoto S et al Int J Hematol 2018

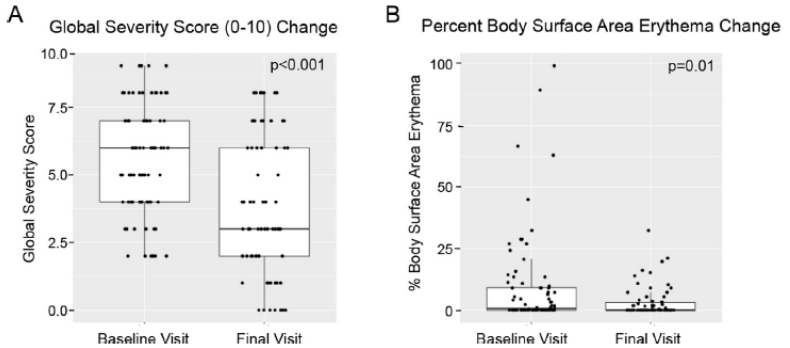
ECP in cGvHD: steroid-sparing effects

Study	Steroid-sparing effects
Greinix HT, *et al.* 1998[1]	Steroid therapy could be discontinued after a median of 80 days
Apisarnthanarax N, *et al.* 2003[2]	64% of patients achieved a steroid-sparing response while on ECP
Foss FM, *et al.* 2005[3]	52% discontinued corticosteroids; 44% had discontinuation of ≥1 immunosuppressive medication
Couriel DR, *et al.* 2006[4]	22% discontinuation of steroids at one year; 10% discontinuation of all immunosuppressive therapy at one year
Greinix HT, *et al.* 2006[5]	Accelerated tapering of steroids, which had a favourable impact on survival
Flowers MED, *et al.* 2008[6]	20.8% and 35.4% of patients had ≥50% reduction in steroid dose and final steroid dose <10 mg/day after 12 and 24 weeks of ECP, respectively
Jagasia MH, *et al.* 2009[7]	ECP led to significant decrease in steroid dose in cGvHD patients (P = 0.009)
Greinix HT, *et al.* 2011[8]	17% and 25% of patients had ≥ 50% reduction in steroid dose and final steroid dose <10 mg / day after 12 and 24 weeks of ECP, respectively
Dignan F, *et al.* 2014[9]	20 out of the 25 (80%) patients that completed six months of ECP had reduction in immunosuppression and 17 of 19 (89%) of evaluable patients had a reduction of steroids during ECP treatment

1. Greinix HT, *et al. Blood* 1998;92:3098–3104; 2. Apisarnthanarax N, *et al. Bone Marrow Transplant.* 2003;31:459–465; 3. Foss FM, *et al. Bone Marrow Transplant*. 2005;35:1187–1193; 4. Couriel DR, *et al. Blood* 2006;107:3074–3080; 5. Greinix HT, *et al. Haematologica*. 2006;91:405–408; 6. Flowers MED, *et al. Blood.* 2008;112:2667–2674; 7. Jagasia MH, *et al. Biol Blood Marrow Transplant.* 2009;15:1288–1295; 8. Greinix HT, *et al. Biol Blood Marrow Transplant*. 2011;17:1775–1782; 9. Dignan F, *et al. Bone Marrow Transplant.* 2014;49:704–708

A Prospective Trial of Extracorporeal Photopheresis for Chronic Graft-versus-Host Disease Reveals Significant Disease Response and No Association with Frequency of Regulatory T Cells





Highlights

- In a highly pretreated cohort, 62% of patients responded to this treatment.
- Treatment was associated with a meaningful decrease in prednisone dose.
- Overall, global severity and body surface area redness decreased with treatment.
- **Response was not associated with frequency of regulatory T cells**

Gandelman JS et al BBMT 2018; 24: 2373-2380

ECP for SR cGvHD

Transplantation and Cellular Therapy

Review

Systematic Review and Meta-Analysis of Extracorporeal Photopheresis for the Treatment of Steroid-Refractory Chronic Graft-Versus-Host Disease

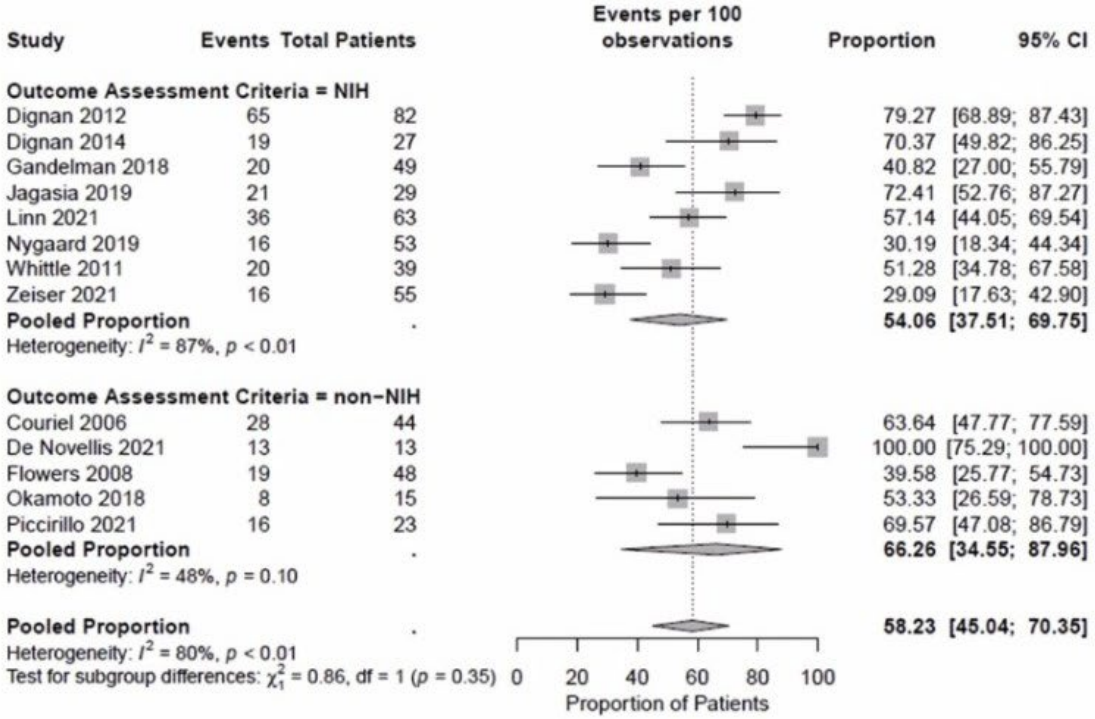
- Key efficacy outcomes were ORR, OS, and PFS
- 45 studies included

DeFilipp Z et al, TCT 2025

Response Rates

NIH Response
8 studies
397 patients
ORR 54%

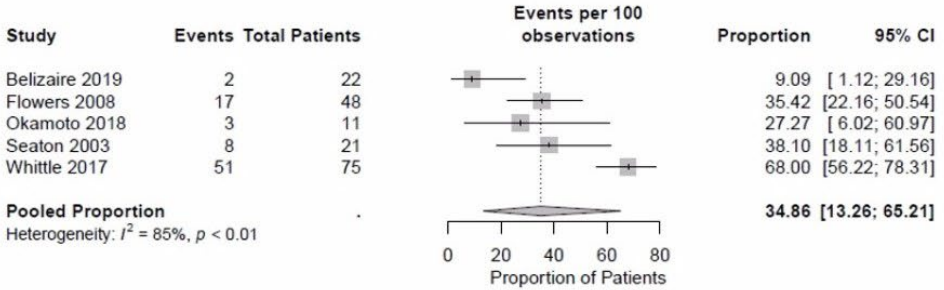
Non-NIH Response
5 studies
143 patients
ORR 66%

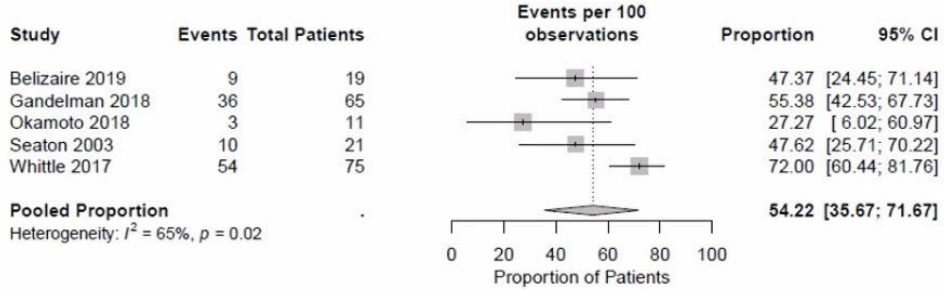


Overall response rates assessed **6-8 months** from initiation of ECP

DeFilipp Z et al, TCT 2025

Skin-specific responses





Months 2-3
5 studies
177 patients
Response rate 35%

Months 4-6
5 studies
191 patients
Response rate 54%

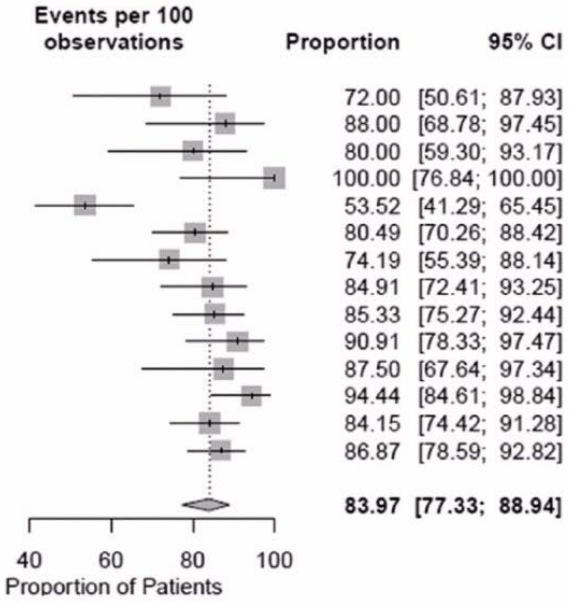
DeFilipp Z et al, TCT 2025

Overall Survival

12 months
14 studies
704 patients
OS 84%

Study	Events	Total Patients
Akhtari 2010	18	25
Amat 2021	22	25
Belizaire 2019	20	25
Bisaccia 2006	14	14
Couriel 2006	38	71
Dignan 2012	66	82
Jagasia 2009	23	31
Kansu 2022	45	53
Linn 2021	64	75
Messina 2003	40	44
Motolese 2007	21	24
Nygaard 2019	51	54
Sakellari 2018	69	82
Whittle 2017	86	99
Pooled Proportion		.

Heterogeneity: $I^2 = 72\%$, $p < 0.01$



DeFilipp Z et al, TCT 2025

Meta-analysis: strengths and limitations

Strenghts

- Summarize efficacy outcomes which support the established role of ECP in SR-cGvHD

Limitations

- Heterogeneity of cGvHD characteristics and lines of therapy
- Heterogeneity in reported outcomes (varying length of follow-up, lack of uniform applications of NIH response criteria, sparse reporting of failure-free survival)
- Conducted before current era with new approved cGVHD drugs

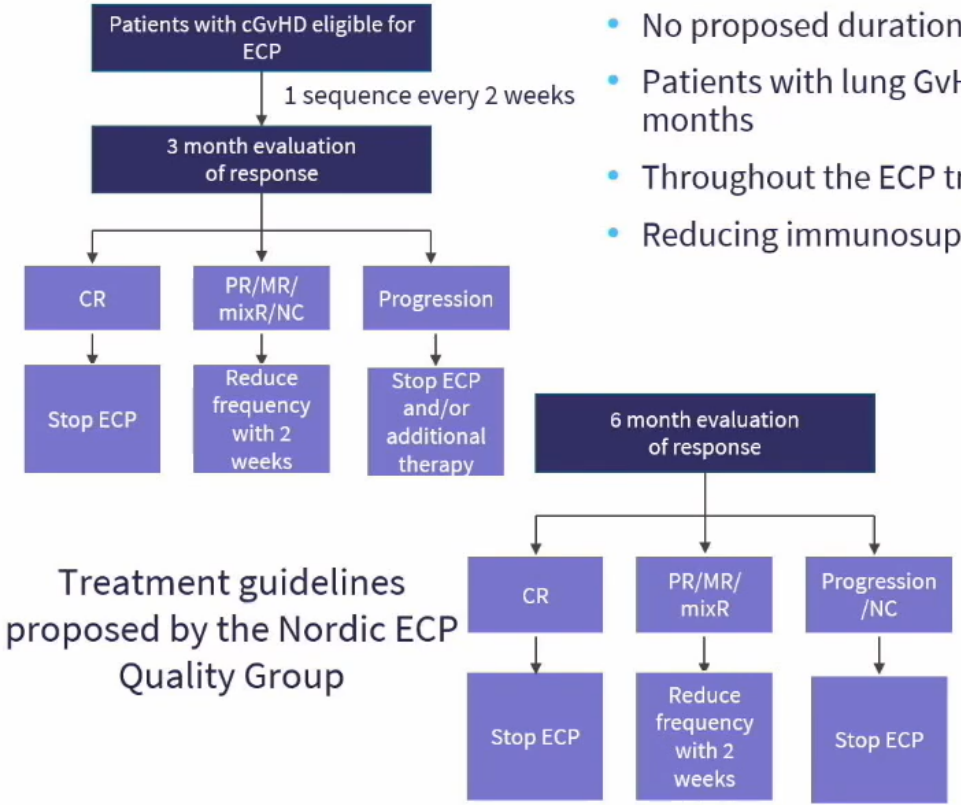
ECP in SR-cGvHD: Lack of Schedule Guidelines

Author	Schedule	Assessment
Scarisbrick, et al.[1]	Two consecutive procedures every 2 weeks; evaluation after 3 months if PR reduction to every 4 weeks. If no response, stop ECP. If some improvement, ECP every 2 weeks until PR.	Every 3 months
Pierelli, *et al.*[2]	Two procedures weekly until maximum response and then taper.	Every 8–12 weeks
Knobler, *et al.*[3]	Two procedure every 1–2 weeks for 3 months; then taper for 1 week every 3 months	By NIH criteria
Howell, *et al.*[4]	Two consecutive treatments for at least 3 months	No recommendations
Schwartz, *et al.*[5]	Two consecutive treatments weekly until response or for 8–12 weeks and then taper to every 2–4 weeks until maximal response	No recommendations
Alfred, *et al.*[6]	Two consecutive treatments every 2 weeks for 3 months; if CR or PR continue every 4 weeks until maximal response; if minimal response, continue 1 cycle every 2 wk after 6 months; if CR, taper/stop ECP; If PR, continue every 4 weeks until maximal response; if minimal response, continue every 4 weeks for 3 months, and if no further response or PD, taper/stop ECP	NIH consensus criteria every 3 months
Knobler, *et al.*[7]	Two consecutive treatments weekly for 3 months then two treatments every 2 weeks	NIH consensus criteria

CR, complete response; ECP, extracorporeal photopheresis; NIH, National Institute of Health; PR, partial response.

1. Scarisbrick JJ, et al. *Br J Dermatol*. 2008;158(4):659-678. **2.** Pierelli L, et al. *Transfusion*. 2013;53(10):2340-2352. **3.** Knobler R, et al. *J Eur Acad Dermatol Venereol*. 2014;28(1):1-37. **4.** Howell C, et al. *Transfus Med*. 2015;25(2):57-78. **5.** Schwartz J, et al. *J Clin Apher*. 2016;31(3):149-162. **6.** Alfred A, et al. *Br J Haematol*. 2017;177(2):287-310. **7.** Knobler R, et al. *J Eur Acad Dermatol Venereol*. 2020;34(12):2693-2716.

ECP in SR-cGvHD: Guidelines



Treatment guidelines proposed by the Nordic ECP Quality Group

- No proposed duration, evaluation should be done every 3 months
- Patients with lung GvHD/scleroderma should continue ECP for at least 6 months
- Throughout the ECP treatment steroid tapering should be done
- Reducing immunosuppression shouldn't be done with reducing ECP

Contraindications:

- Unstable circulatory or respiratory condition
- Known sensitivity to psoralen compounds
- Known photosensitivity
- Aphakia (absence of lens in the eye)
- Pregnancy
- Low white blood cell count (<1 × 109/L)

Precautions:

- Low haematocrit
- Low platelet count
- Active bleeding or risk of bleeding
- Active infection
- Low body weight

cGvHD, chronic graft-versus-host disease; CR, complete response; ECP, extracorporeal photopheresis; MR, minimal response; mixR, mixed response; NC, no change; PR, partial response; SR, steroid-refractory.

1. Lee S, et al. *Biol Blood Marrow Transplant*. 2015;21(6):984-999. **2.** Nygaard M, et al. *Eur J Hematol*. 2020;104:361–375.

Il trattamento della graft-versus-host disease (GvHD) con terapie extracorporee non farmacologiche: aggiornamento 2022 delle raccomandazioni della Società Italiana di Emaferesi e Manipolazione Cellulare (SIdEM) e del Gruppo Italiano per il Trapianto di Midollo Osseo, cellule staminali emopoietiche e terapia cellulare (GITMO).
Versione 2.2 del 30 gennaio 2024

Raccomandazione:
Nei pazienti con GvHD cronica refrattaria alla prima linea di trattamento si suggerisce di eseguire l'ECP **in seconda linea e successive** (raccomandazione positiva condizionata, qualità delle prove bassa).

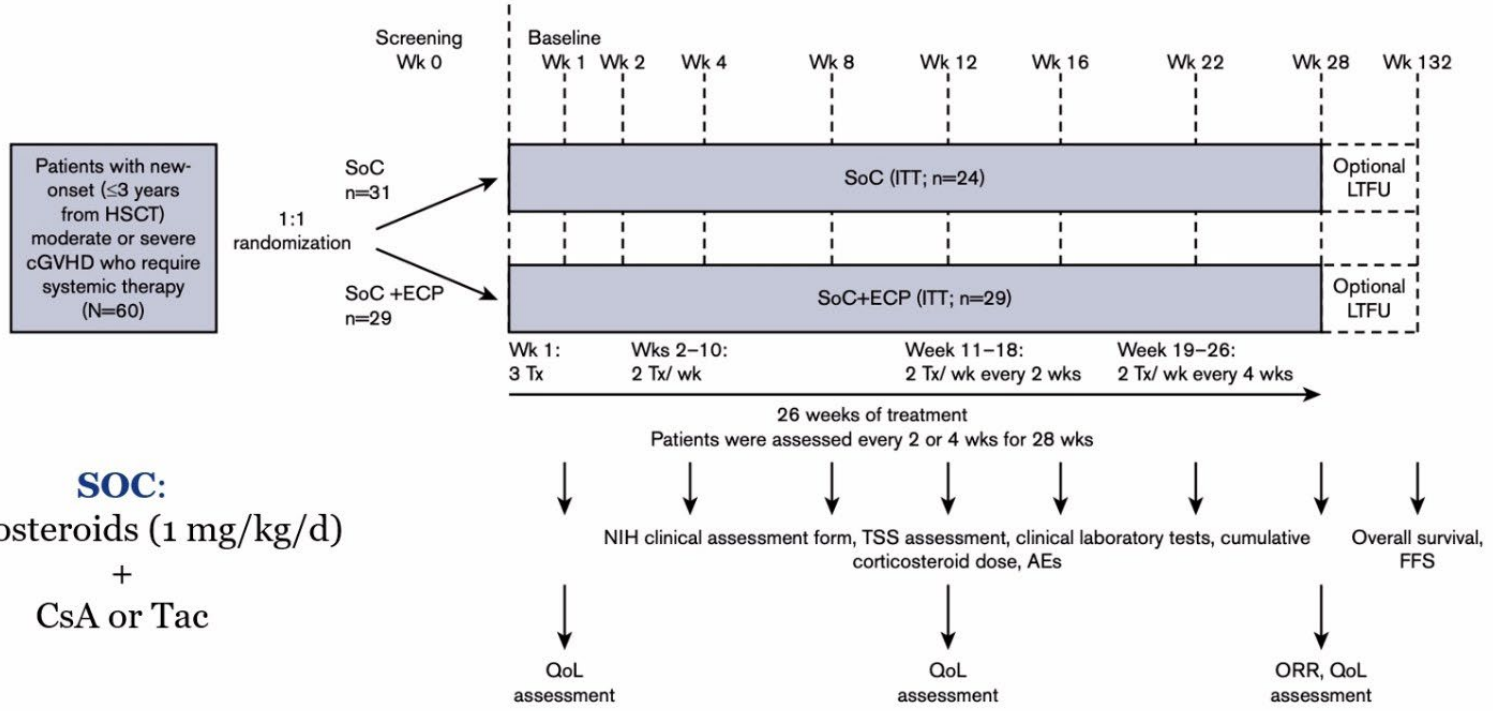
Raccomandazione:
Nei pazienti con GvHD cronica candidati a ECP si suggerisce **un ciclo ECP (due sedute) a settimane alterne per le prime 12 settimane** per il trattamento iniziale (raccomandazione positiva condizionata, qualità delle prove bassa).

Implementation, tools and tips:
Si raccomanda di **correggere l'anemia e la piastrinopenia** prima di eseguire una seduta di ECP. Al momento attuale **non ci sono evidenze a supporto della definizione di un valore soglia dei leucociti** al di sotto del quale sia controindicata l'esecuzione dell'ECP.

Si raccomanda di non eseguire l'ECP in pazienti con **instabilità cardiocircolatoria e respiratoria o infezione severa in atto**.

Si raccomanda inoltre di non eseguire l'ECP in presenza di **afachia, gravidanza in atto, ipersensibilità nota ai composti psoralenici** (come 8-MOP) o all'anticoagulante utilizzato (se non può essere utilizzato un anticoagulante alternativo), fotosensibilità nota all'8-MOP e ai raggi UV-A.

ECP for First-Line Chronic GVHD

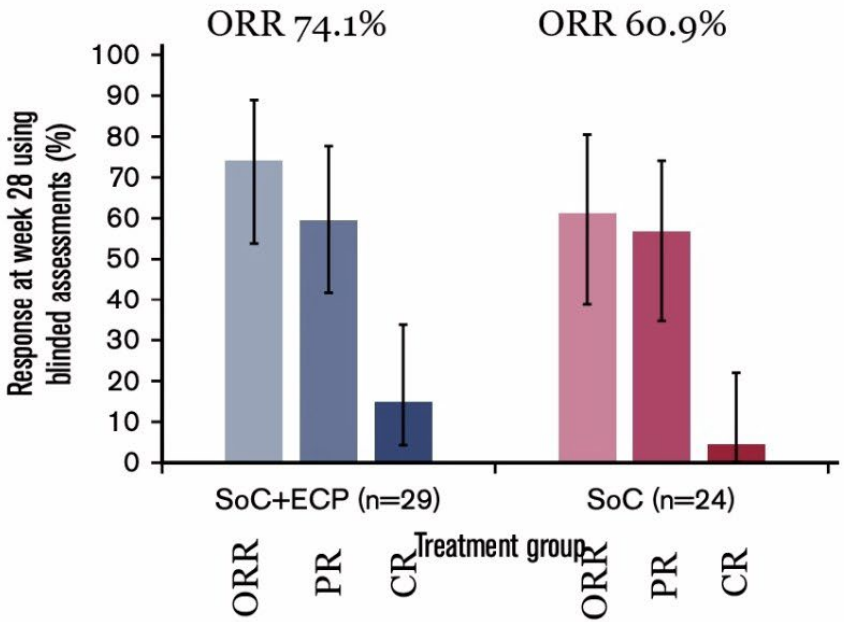


SOC:
corticosteroids (1 mg/kg/d)
+
CsA or Tac

Jagasia M, et al. Blood Adv. 2019

ECP for First-Line Chronic GVHD

	SOC + ECP (n=29)	SOC (n=24)
Chronic GVHD severity		
Moderate	17 (59%)	11 (46%)
Severe	12 (41%)	13 (54%)
Chronic GVHD onset		
De novo	14 (48%)	14 (58%)
Progressive	6 (21%)	1 (4%)
Quiescent	9 (31%)	9 (38%)
Organs involved with chronic GVHD		
Skin	15 (52%)	12 (50%)
Liver	4 (14%)	1 (4%)
GI tract	7 (24%)	3 (13%)



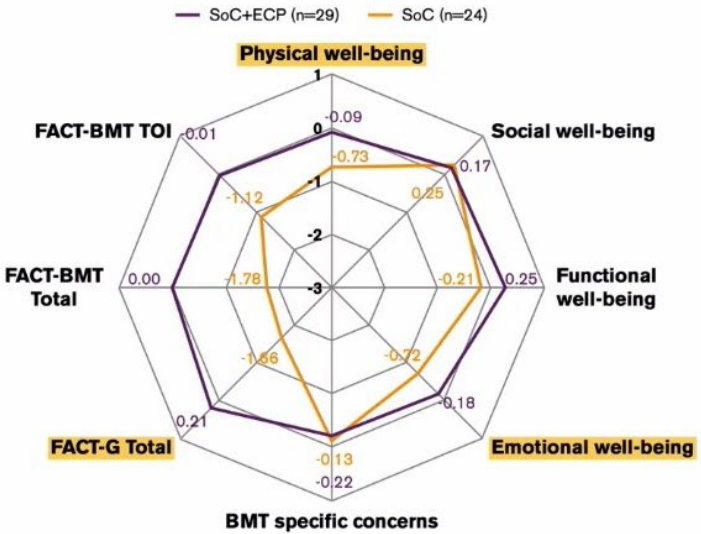
Jagasia M, et al. Blood Adv. 2019

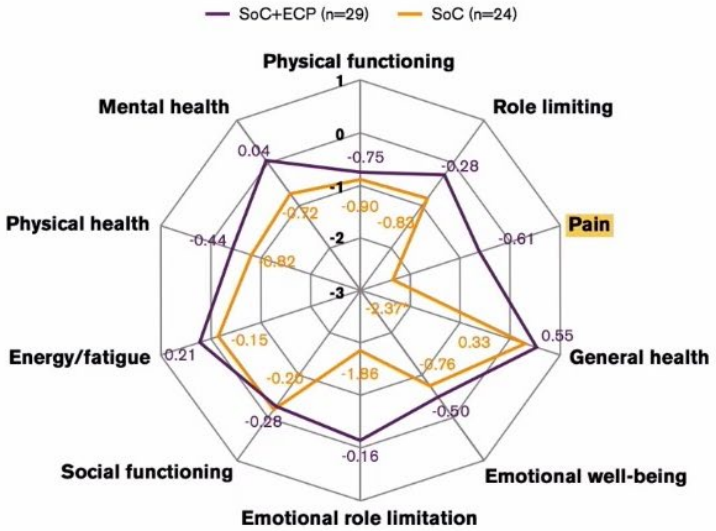
blood advances

REGULAR ARTICLE

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

Madan Jagasia,[1] Christof Scheid,[2] Gérard Socié,[3] Francis Ayuketang Ayuk,[4] Johanna Tischer,[5] Michele L. Donato,[6] Árpád Bátai,[7] Heidi Chen,[8] Sheau-Chiann Chen,[8] Thomas Chin,[9] Henri Boodée,[9] Ghaith Mitri,[9] and Hildegard T. Greinix[10]





SOC : Worsening of QoL in FACT-BMT measures

- Physical well-being (-.7326; P = .032),
- Emotional well-being (-.7151; P = .006)
- FACT-G[1] : (-1.6618; P = .018)

SoC- ECP : No changes in any QoL domains

[1]*Functional Assessment of Cancer Therapy–General*

SOC : Worsening of Pain measure (- 2,3728; P = .009),

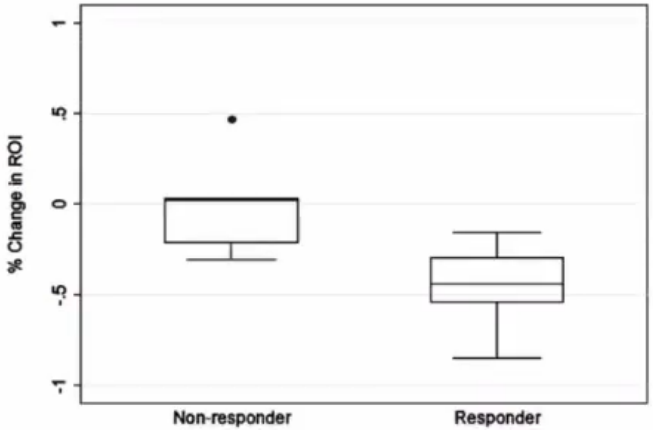
SOC- ECP : No change

What about combinations of ECP with newer targeted agents?

- ECP is almost never administered as a monotherapy, but rather in combination with historical "standard of care" chronic GVHD medications.
  - *Corticosteroids, cyclosporine, tacrolimus, MMF, sirolimus, etc.*

ECP+Imatinib for SR-cGvHD

- Imatinib inhibits TGF-β and PDGF-R pathways: both involved in fibrotic diseases, as cGvHD with fibrotic features[2] and systemic scleroderma
- Phase II imatinib study in 39 SR cGvHD patients showed 46% response in SR GvHD (PR or MR): best responses in lung, gut and skin[1]
- Significant decrease in PDGF-R stimulatory activity in 7 responders[1]
- Combination of imatinib and ECP is not evaluated
- Recent report of 7 patients receiving imatinib + ECP with sclerotic cGvHD: CR, 57%[3]
- Steroids could be discontinued in all patients at a median of 8 months



Svegliati S et al, Blood 2007; Olivieri A et al Blood 2013; Alsuliman T et al Curr Res Transl Med 2020

Complementary mechanisms of action of ECP plus ruxolitinib

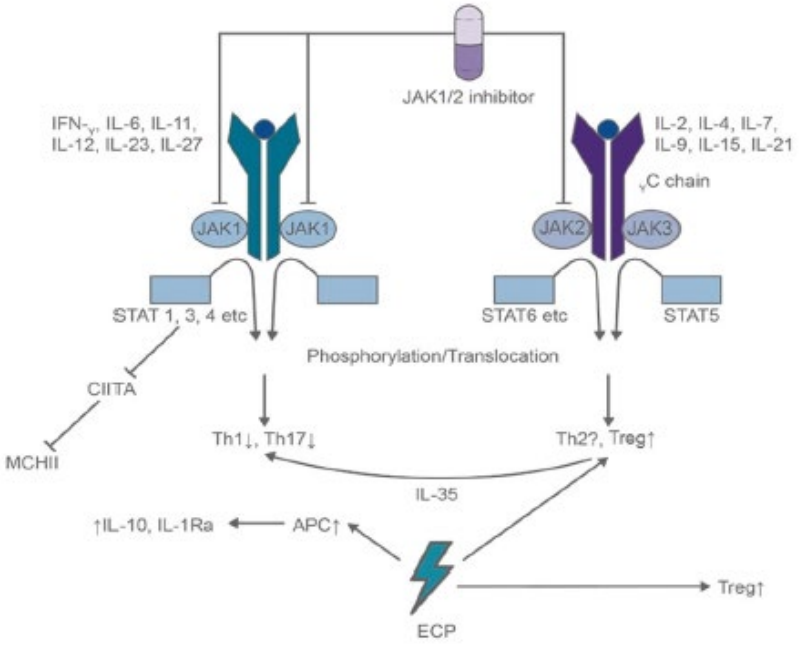
REVIEW ARTICLE OPEN

STEM CELL TRANSPLANTATION

Extracorporeal photopheresis in acute and chronic steroid-refractory graft-versus-host disease: an evolving treatment landscape

Hildegard T. Greinix[1✉], Francis Ayuk[2] and Robert Zeiser[3]

- JAK1/2 selective inhibition spared the IL-2–JAK3–STAT5 signal and therefore may spare T-regs.
- Reinfusion of ECP-treated cells leads to phagocytosis by APCs, secretion of anti-inflammatory cytokines, modulation of T Cells toward a Th2 phenotype and promotion of Treg cell generation.



Greinix et al, Leukemia 2022; 36: 2558-2566

ECP+Ruxo for SR-cGvHD

Ruxo twice daily: 5-10mg

Retrospective survey in 23 patients

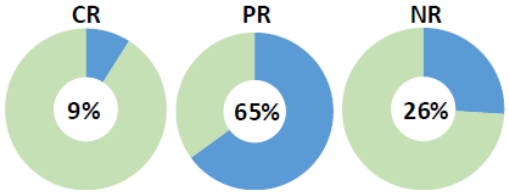
Patient characteristics	Patients, n (%)
>1 organ with GvHD features	20 (87)
Organ affection	
Skin	18 (78)
Liver	14 (61)
GI	13 (57)
Eye	10 (43)
Lung	8 (35)
cGvHD NIH Grade III	13 (57)
Beyond second-line treatment	21 (91)

Treatment

- Two treatments of ECP (on consecutive days) every 2–4 weeks
- Median time of RUX-ECP was 6 months (1–27 month)
- 35% (8/23) started ruxolitinib first, median 15 months (range, 1–29 months) of ruxolitinib prior to combination therapy

Results

Response rate after >1 week of combined therapy



- Best response (CR or PR) at any time point, 74% (17/23)
- 2-year OS, 75% (CI, 56.0–94.1)

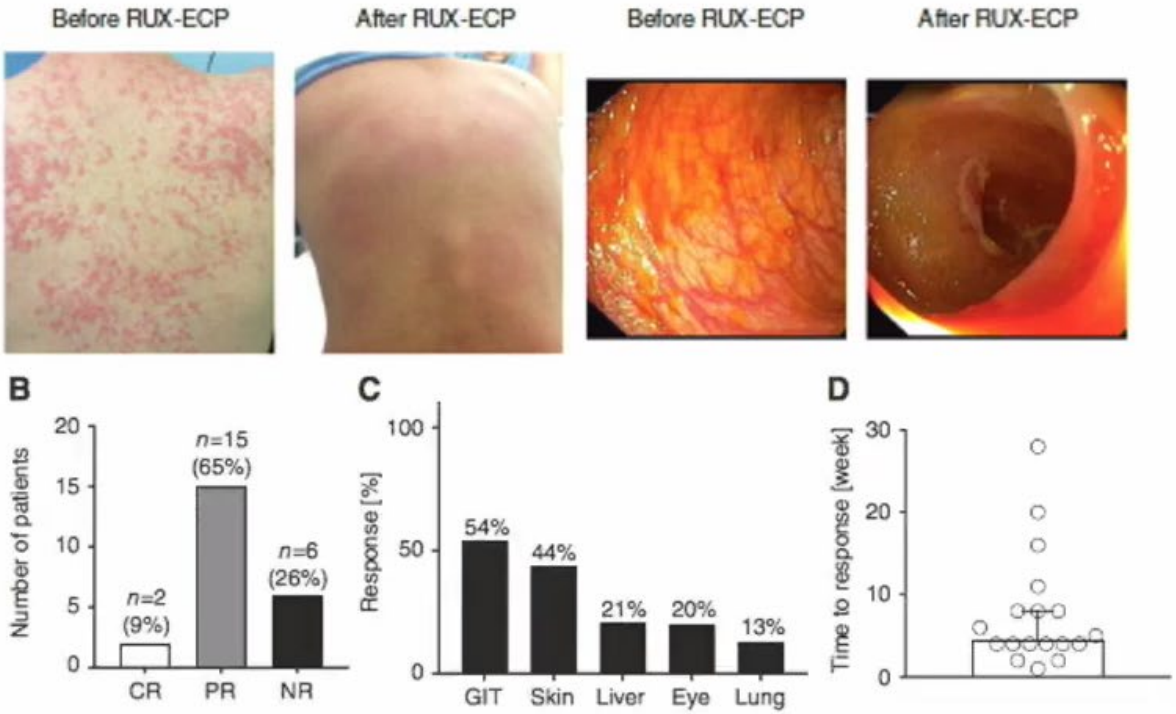
Responses per cGVHD affected organ:

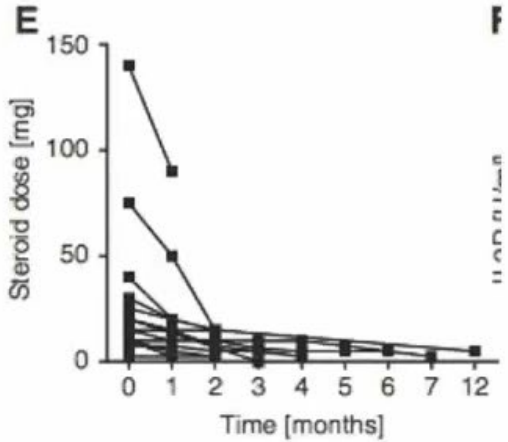
- GIT, 54%
- Skin, 44%
- Liver, 21%
- Eye, 20%
- Lung, 13%

- Steroid dose was reduced in 76% (13/17) of patients that responded to the RUX–ECP combination
- Serum levels of sIL-2R correlated with response
  - IL-2R levels declined once patients started RUX monotherapy (p=0.02)
  - IL-2R levels further declined after RUX-ECP combination therapy (p=0.046)

Mass Bauer K et al, BMT 2021; 56: 909-916

- Ruxolitinib + ECP combination treatment in 23 patients for refractory severe cGvHD: ORR: 74% (CR, 9% and PR, 65%) and median time of treatment 6 months

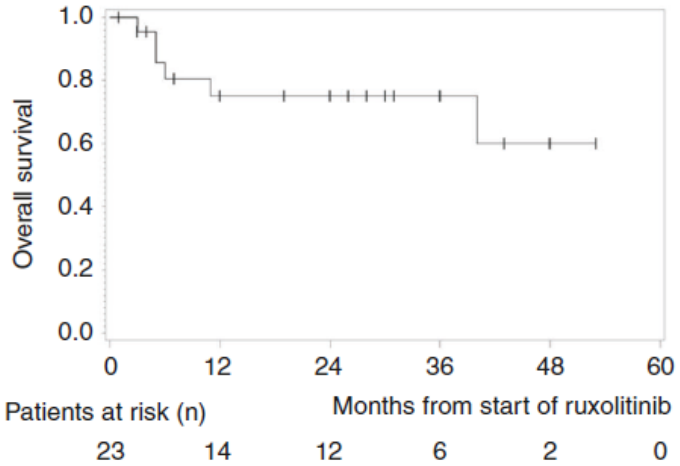




Mass Bauer K et al, BMT 2021; 56: 909-916

ECP+Ruxo for SR-cGvHD

Adverse event	n (%)
CMV reactivation	6 (26)
Cytopenia	
Mild cytopenia	3 (13)
Severe cytopenia	8 (35)
Cytopenia before ruxolitinib	6 (26)
Relapse of malignancy	0 (0)



Mass Bauer K et al, BMT 2021; 56: 909-916

Treatment of steroid-refractory acute/chronic graft versus host disease: A single-center real-world experience of ruxolitinib in combination with extracorporeal photopheresis in a high-risk population

SR-cGvHD	
Patients, N	27

ORR:
-at week +24 was 88%, including 12% CR and 76% PR.
-at week +48 was 94%, CR rate was 25%.

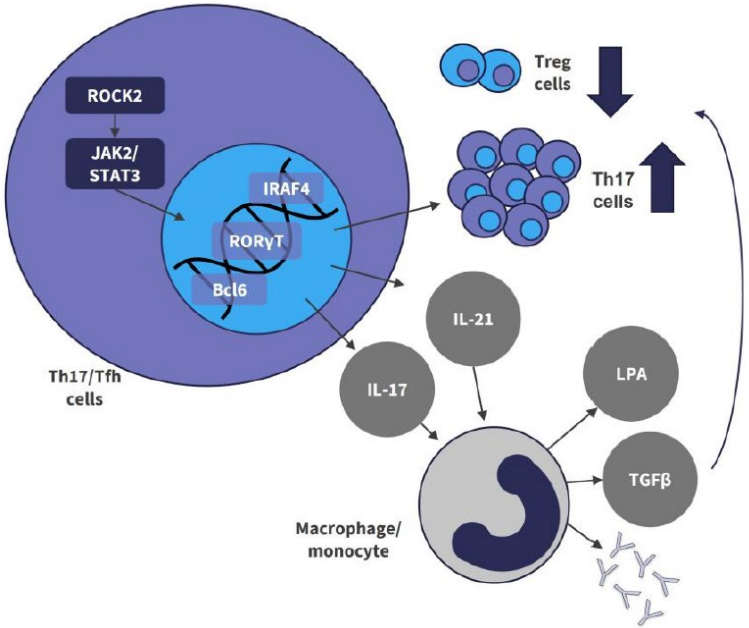
Patient with SR-cGvHD of the **skin had a higher response rate** as compared with patients with gastrointestinal involvement (ORR 83% and 78% at week 24, respectively).

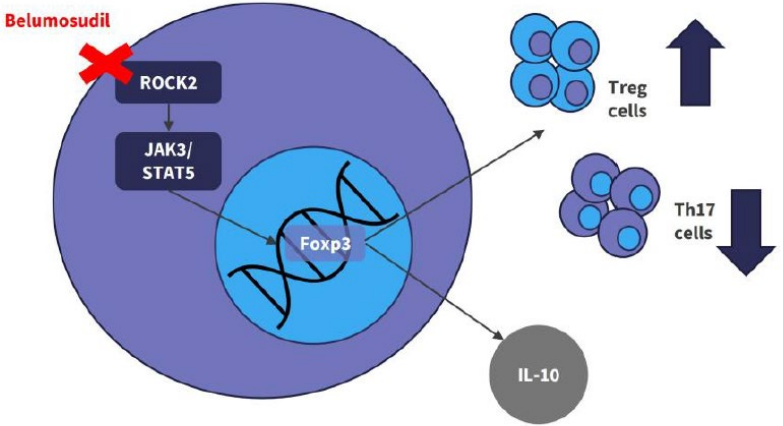
Discontinuation of steroid treatment was possible in **48%** of patients.
The median time of discontinuation of steroid treatment was 256 days after beginning of combination treatment (range 44–734 days).

The 12-month **OS** of patients with SR-cGvHD was **53%** (95% CI, 30–71%),
-for patients achieving a CR the 12-month OS was 76% (95% CI, 13–96%)
- 67% (95% CI, 34–86%) for patients achieving PR

Wais et al, Leukemia Research 147 (2024) 107611

Belumosudil: mechanism of action





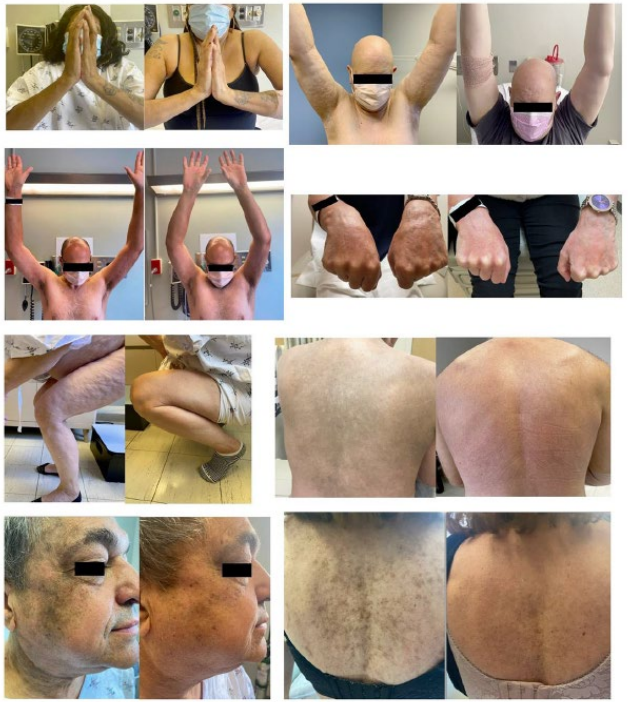
Cutler C et al, Blood 2021, 138, 2278–2289

Belu+ECP 13 cGVHD patients

At the start of treatment, the NIH cGVHD Global Severity scores included: 1 (8%) with mild disease
6 (46%) with moderate
6 (46%) with severe

By the NIH Clinical Response Scale at 4 months:
8 (**62%**) demonstrated PR
5 (38%) experienced stable disease

Of eight patients followed for 11 to 18 months:
6 (75%) demonstrated continuous improvement
1 experienced stable disease (13%)
1 experienced worsening (13%)



No serious adverse events were observed

Archives of Dermatological Research (2025) 317:298

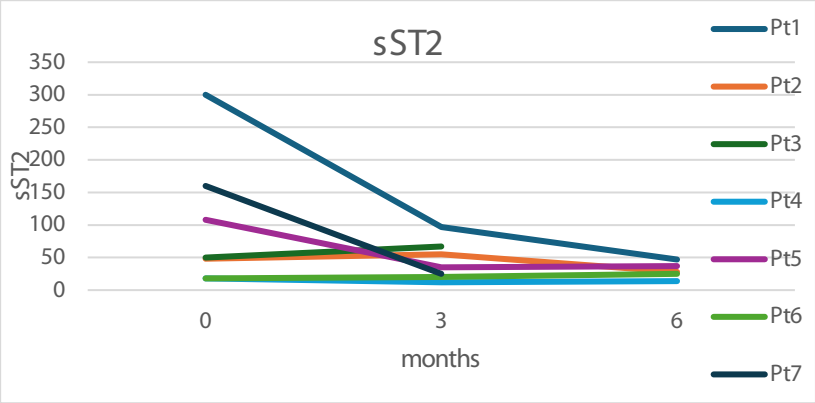
UCSC-monocentric experience: Belu+ECP

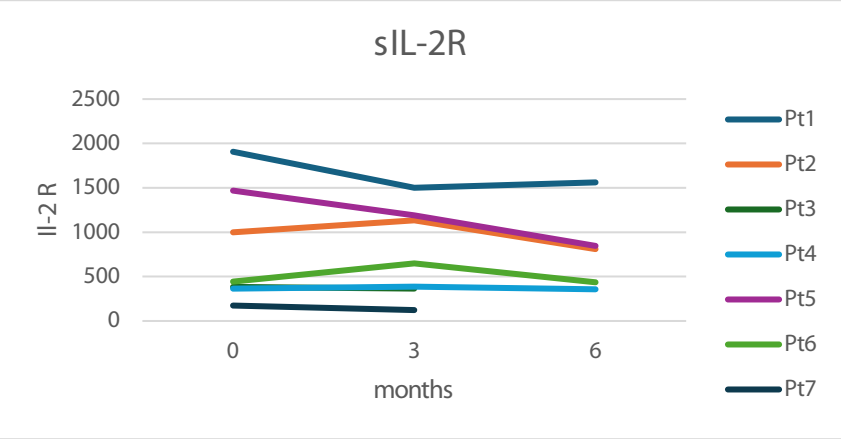
7 patients, 5 females and 2 males with age 41 (25-64)
At baseline 5 patients had severe and 2 had moderate cGVHD,
with treatment started for mainly pulmonary (n=4), intestinal (n=2), and cutaneous (n=1) involvement
Median treatment duration: 7 months (range 4-14)

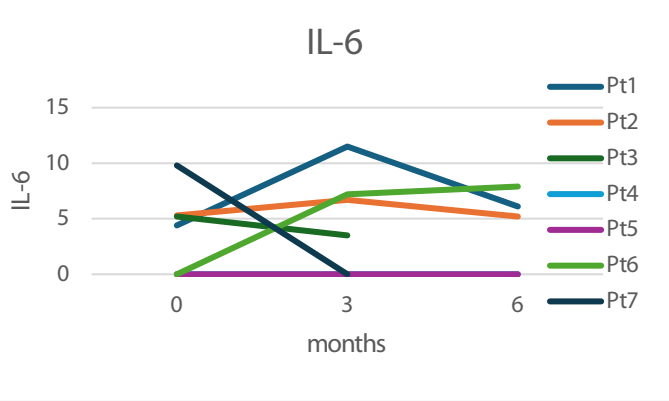
Steroid sparing in all patients

	Before Belu+ECP	Last F-Up	p
CD4/µl	179 (9-511)	396 (208-512)	p=0.006
CD8/µl	267 (41-449)	427 (237-1040)	p=0.017

Cytokines serum levels







Conclusions

- cGvHD has remained a serious complication of HCT.

- **ECP is an efficient, safe, well-tolerated, steroid-sparing treatment of cGvHD.**
- **ECP does not cause general immunosuppression.**
  Anti-infectious and anti-leukemic immune responses are not negatively affected.

- Severe cGvHD patients may need ECP therapy for longer duration to achieve maximum benefit.

- **Prospective studies of ECP in combination with novel drugs are warranted.**
  More rapid responses, faster reduction of steroids/other immunosuppressants
  Improved organ responses
  Longer duration of responses

Gemelli

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Università Cattolica del Sacro Cuore

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