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

Zachariah DeFilipp,[1] Laura Fox,[2] Tobias A.W. Holderried,[3] Varun Mehra,[4] David Michonneau,[5] Andy Ingram,[6] Alex Pashley,[7] Andrei Karlsson,[8] Dennis Dong Hwan Kim[9]

Objectives

To evaluate the clinical efficacy and safety of extracorporeal photopheresis for the treatment of steroid-refractory chronic graft-versus-host disease.

Background

- Chronic graft-versus-host disease (cGvHD) is associated with substantial morbidity and non-relapse mortality in hematopoietic cell transplant (HCT) recipients.[1]
- Extracorporeal photopheresis (ECP), which mediates an anti-GvHD effect via immunomodulation, is recommended as a treatment option for steroid refractory cGvHD (SR-cGvHD).[2–4]

Methods

- A systematic literature review (SLR) was conducted according to PRISMA guidelines.
- MEDLINE, Embase, Cochrane, DARE and relevant conference proceedings were searched to 19 October 2022 for studies of patients with SR-cGvHD receiving ECP and reporting on efficacy, safety or health-related quality of life (HRQoL) outcomes.
- A feasibility assessment (FA) was conducted to assess sources of potential between-study heterogeneity in the meta-analyses (MA).
- Random-effects MAs were performed for long- and short-term efficacy outcomes including overall survival (OS) and failure-free survival (FFS), and overall response rate (ORR) and skin-specific response, respectively.
- Timepoint windows were used for ORR (Months 3–4 and Months 6–8) and skin-specific response (Months 2–3 and Months 4–6).
- Insufficient safety and HRQoL data precluded further analysis.
- A subgroup analysis for ORR only was conducted to explore the effect of outcome assessment criteria (National Institutes of Health [NIH] vs non-NIH/unknown).

ABBREVIATIONS: CI: confidence interval; **cGvHD:** chronic graft-versus-host disease; **ECP:** extracorporeal photopheresis; **FA:** feasibility assessment; **FFS:** failure-free survival; **HCT:** hematopoietic cell transplantation; **HRQoL:** health-related quality of life; **MA:** meta-analyses; **NIH:** National Institutes of Health; **ORR:** overall response rate; **OS:** overall survival; **SLR:** systematic literature review; **SR-cGvHD:** steroid refractory cGvHD.

INSTITUTIONS: [1]Massachusetts General Hospital, Boston, US; [2]Vall d'Hebron University Hospital, Barcelona, Spain; [3]University Hospital Bonn, Bonn, Germany; [4]Kings College Hospital London, London, UK; [5]Hôpital Saint-Louis, Paris, Assistance Publique des Hôpitaux de Paris, Université Paris Cité, Paris, France; [6]Mallinckrodt Pharmaceuticals, Surrey, UK; [7]Costello Medical, Cambridge, UK; [8]Costello Medical, London, UK; [9] Princess Margaret Cancer Centre, University Hospital Toronto, Toronto, Canada.

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Summary

An **SLR** and **MA** was conducted to evaluate the **clinical efficacy** of **ECP** used in the treatment of **SR-cGvHD**

The SLR identified **621 records**, of which **47 unique studies** reporting on Therakos ECP machines were included

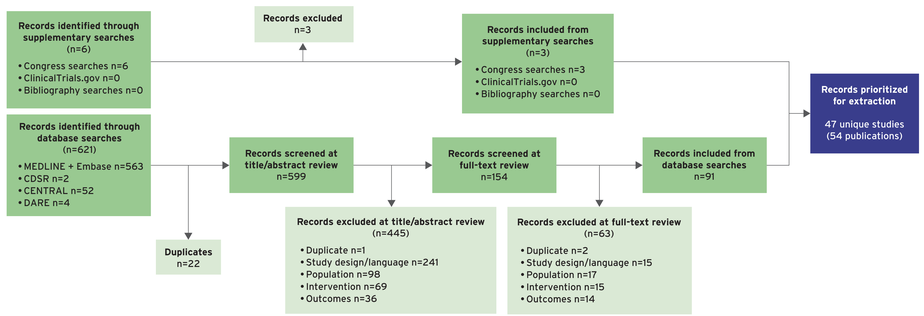
The MA found **favorable outcomes with ECP** in SR-cGvHD, including OS, FFS and ORR

Pooled **OS** rate at **Month 12**: 83.97%

Pooled **FFS** rate at **Month 12**: 60.79%

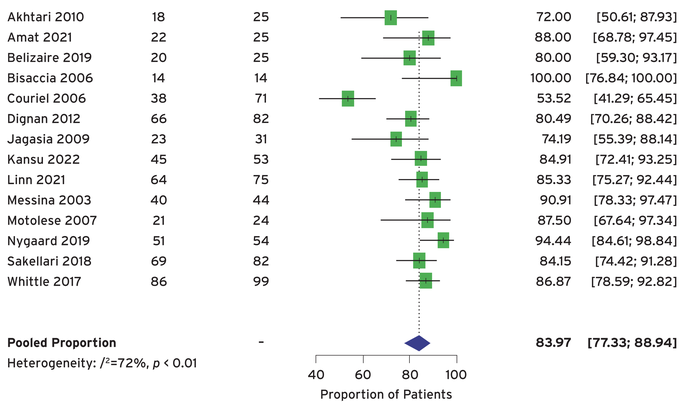
Pooled **ORR** rate at **Months 6–8**: 58.23%

FIGURE 1. PRISMA Diagram



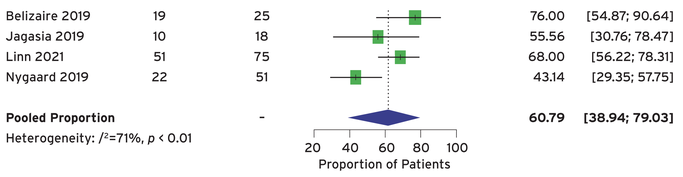
CDSR: Cochrane Database of Systematic Reviews; **CENTRAL:** The Cochrane Central Register of Controlled Trials; **DARE:** Database of Abstracts of Reviews of Effect.

FIGURE 2. Pooled OS rate at Month 12



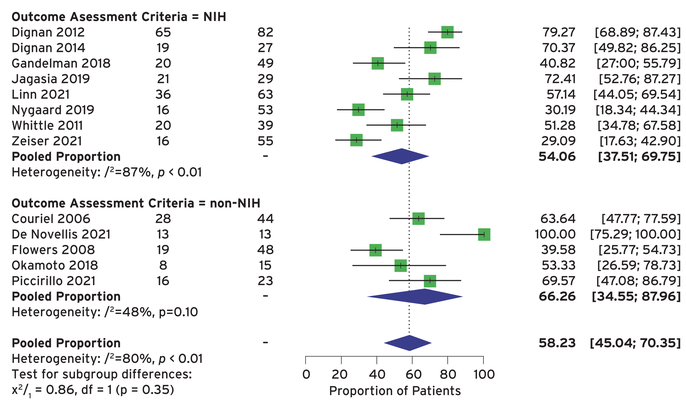
CI: confidence interval; **OS:** overall survival.

FIGURE 3. Pooled FFS rate at Month 12



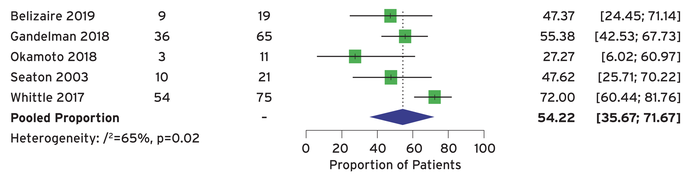
CI: confidence interval; **FFS:** failure-free survival.

FIGURE 4. Pooled ORR at Months 6–8



CI: confidence interval; **NIH:** National Institutes of Health; **ORR:** overall response rate.

FIGURE 5. Pooled skin-specific response at Months 4–6



CI: confidence interval.

Results

- The SLR identified 621 records, of which 47 unique studies reporting on Therakos ECP machines (inline; CELLEX™ or UVAR-XTS™) were included; **Figure 1**.
- In general, reporting of study characteristics and outcomes was inconsistent.
  - The majority of studies (n=28) reported on adult only populations (≥18 years). Lines of therapy were poorly reported (n=15) and ranged from 0 to ≥4 lines of previous treatment. Most studies (n=27) used a retrospective case series study design.
- For long-term efficacy, the pooled OS rate at Month 12 was 83.97% (95% confidence interval [CI]: 77.33–88.94; 14 studies, 704 patients; **Figure 2**).
- At Month 60, the pooled OS rate was 57.96% (95% CI: 35.48–77.56; 8 studies, 431 patients).
- Results from four studies (169 patients) indicated a pooled FFS rate of 60.79% at Month 12 (95% CI: 38.94–79.03; **Figure 3**).
- For short-term efficacy, the pooled ORR was 45.34% (95% CI: 26.64–65.45) at Months 3–4 (7 studies; 293 patients) and 58.23% (95% CI: 45.04–70.35) at Months 6–8 (13 studies; 540 patients; **Figure 4**).
  - Subgroup analyses showed no significant difference in ORR between studies utilizing NIH criteria and those utilizing non-NIH criteria.
- The pooled skin-specific response was 34.86% (95% CI: 13.26–65.21) at Months 2–3 and 54.22% (95% CI: 35.67–71.67) at Months 4–6; **Figure 5**.
- There was considerable heterogeneity across all analyses, with I^2 values ranging from 65% to 91%.

Discussion

- An important limitation of this study was the inconsistency of reporting across the literature which resulted in high heterogeneity.
- This highlights the need for consistent study reporting in the field; future primary research should aim to harmonize diagnostic and outcome criteria, including timepoints for response measurement, as well as consistency in reporting baseline characteristics of patients.
- However, due to the relative rarity of cGvHD, patient recruitment can be challenging, limiting the size and quality of potential studies.

Conclusion

This recent systematic review and MA indicated that ECP results in favorable clincial outcomes in SR-cGvHD, including OS, FFS and ORR.

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