ESOT®
Leading the way
in transplantation

EXTRACORPOREAL PHOTOPHERESIS (ECP)

A collaboration between ESOT and Therakos

Report

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esot.org

TOGETHER, LEADING organ transplantation

Partnerships with industry and academic organisations are central to the ESOT vision! They represent flexible, impactful models for collaborations to drive progress in the transplantation field, while balancing the interests of both corporate and non-profit entities.

ESOT calls on industry, academic institutions, foundations, and other organisations sharing its mission to propose collaborative initiatives aimed at advancing transplantation, ultimately benefiting patients, families, researchers, and healthcare professionals.

With the support of expert committees and a dedicated team, ESOT offers partners a comprehensive range of activities designed to align with their objectives: these include advancing education, supporting research initiatives, engaging in advocacy, facilitating post-transplant follow-up, informing policymakers, and developing medical guidelines.

Partnering with ESOT means:

Share the vision of a leading, international society

Aligning with our commitment to promote research and excellence in organ transplantation, with the goal of enhancing patient outcomes worldwide.

Engage with experts across Europe and worldwide

Connecting with our international network of researchers, clinicians, organ transplantation specialists, and experts dedicated to patient welfare.

Amplify your impact by connecting with the right audience

Enhancing visibility within the transplant field through collaborations and active participation in advancing organ transplantation research and clinical practice.

Let's explore how together we can scale impact on organ transplantation care.

https://esot.org/partnerships-v2/

Executive summary

Allograft rejection remains a major challenge in solid organ transplantation: immunosuppressive therapies, while improving post-transplant outcomes, are associated with significant long-term adverse effects, highlighting the need for safer, more targeted approaches to immune regulation.

Extracorporeal photopheresis (ECP) is an established immunomodulatory therapy that offers targeted immune regulation rather than generalised immunosuppression. Currently recommended as an adjunctive therapy in heart and lung transplantation, and increasingly explored in kidney and liver transplantation, ECP shows promise in reducing rejection, infections, and chronic allograft dysfunction. Nonetheless, its wider adoption is limited by gaps in awareness, lack of standardised protocols, incomplete mechanistic understanding, limited high-quality trial data, and unequal access.

To address these challenges, ESOT, in collaboration with Therakos, launched an initiative to advance ECP as a standardised therapy, ultimately improving long-term outcomes for transplant recipients; this comprehensive effort focuses on educational programs, research funding, and the development of evidence-based resources.

This partnership demonstrates how strategic collaborations between biomedical societies and industry can significantly advance the field of transplantation.

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Introduction

Allograft rejection remains one of the most significant challenges in solid organ transplantation (SOT), contributing to both short- and long-term morbidity and mortality.

Immunosuppressive regimens, administered as induction therapy, maintenance treatment, or management of active rejection, are essential in improving graft and patients' survival. Nevertheless, immunosuppression is a double-edged sword as it is associated with significant adverse effects, including increased susceptibility to infections, malignancy, cardiovascular complications, and nephrotoxicity. This highlights a significant unmet clinical need, emphasising the importance of developing safer approaches to prevent and manage graft rejection.

In the effort to balance optimal immunosuppression and minimal side effects, **extracorporeal photopheresis (ECP)** (recognised as an effective treatment option for various conditions, including cutaneous T-cell lymphoma, graft-versus-host disease, and autoimmune disorders), **emerges as a promising approach for targeted immunomodulation as opposed to generalised immunosuppression**, thereby potentially reducing reliance on conventional immunosuppressive regimens in SOT. Currently, international guidelines recommend ECP as an adjunctive therapy for the prevention and management of organ rejection, particularly in heart and lung transplant recipients. Evidence also supports its role in kidney and liver transplantation.

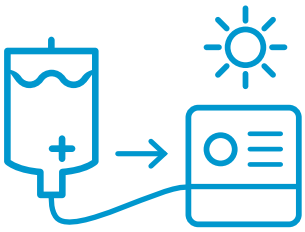
To address the urgent challenge of graft failure and rejection, the European Society for Organ Transplantation (ESOT) and Therakos have launched a joint project focused on ECP. The initiative aims to bridge the healthcare providers' knowledge gap, support education, advance research on the effects of ECP immunomodulation in SOT, gather evidence for ECP applications in SOT through standardised protocols and interdisciplinary exchanges, and address inequities in patient access to ECP treatments.

Extracorporeal photopheresis project	
Area	**Goal**
Education	Update clinical knowledge of ECP among transplant professionals.
Research	Support studies on ECP immunomodulation in SOT.
Expert interdisciplinary collaboration	Promote cross-speciality knowledge exchange to expand ECP clinical applications beyond current preferred settings.
Clinical practice	Establish standardised ECP protocols for SOT.

The below sections present an overview of the ECP procedure, its underlying mechanisms of action, and the main challenges encountered in implementing this treatment within the transplantation field, followed by a detailed description of all activities launched through the ESOT and Therakos collaboration.

Extracorporeal photopheresis in organ transplantation: current status

What is ECP and how is it performed?



"ECP is a technique sometimes described to the lay audience as dialysis for the immune system."

Andrew John Fisher,
ESOT webinar "The science of ECP in transplantation"

ECP, also referred to as photochemotherapy or photoimmunotherapy, is a therapeutic procedure in which whole blood is withdrawn from the patient via a cubital vein, or a permanently implanted catheter, and centrifuged to separate erythrocytes (red blood cells) and plasma (the blood liquid component) from leukocytes, the white blood cells involved in graft rejection. While erythrocytes and plasma are returned to the patient without any additional processing, the isolated leukocyte fraction (the buffy coat) is treated outside of the body with the photosensitising agent 8-methoxypsoralen (8-MOP) and subsequently exposed to ultraviolet A (UVA) irradiation for 8-MOP activation, before being reinfused. Once activated, 8-MOP intercalates into the DNA of leukocytes and forms cross-links preventing proliferation and mediating gradual apoptotic cell death.

Several closed and open devices are currently available for clinical use: ECP can be performed using an offline approach where blood is drawn from the patient, processed in a laboratory, and then reinfused, or via an automated in-line closed-circuit system, a one-step method where blood cell separation, drug photoactivation, and reinfusion are fully integrated and automated processes, with the entire procedure typically lasting about two hours, maintaining continuous patient connection to the device throughout.

Each course of treatment represents a cycle, and a treatment cycle generally consists of two individual sessions administered on consecutive days, with different regimens defined according to the total number of cycles and the frequency of treatments.

ECP treatments are generally well tolerated, with few notable adverse effects observed.

ECP's **safety profile and tolerability** make it a valuable **therapeutic treatment**.

What are the clinical indications for ECP?

ECP has been in clinical use for more than thirty years for the treatment of T-cell-mediated conditions, initially approved for the management of Sézary syndrome, a variant of cutaneous T-cell lymphoma.

Since its introduction, **the indications for ECP have expanded to include** graft-versus-host disease, autoimmune diseases, inflammatory conditions, and **solid organ transplantation**.

ECP in solid organ transplantation

Although immunosuppressive therapies have significantly evolved in recent years, SOT continues to face major concerns, including the reduced efficacy of standard immunosuppressive treatments and their significant side effects.

ECP represents a promising approach to overcoming these challenges, offering immuno-modulatory benefits that can help reduce the need for standard immunosuppressive drugs.

The level of evidence supporting its use in SOT differs considerably across organ types, with the most comprehensive data currently available for cardiothoracic transplantation, and comparatively less data for kidney and liver transplantation. Recent guidelines from the International Society for Heart and Lung Transplantation and other scientific societies recommend ECP as an adjunctive therapy for rejection prophylaxis, treatment of recurrent or resistant acute cellular rejection and refractory antibody-mediated rejection in heart transplant, as well as Chronic Lung Allograft Dysfunction (CLAD) following lung transplantation. There is currently no established guideline recommendation for ECP use in kidney or liver transplant rejection.

Heart	In the context of **heart transplantation**, the use of ECP is suggested as prophylaxis against rejection. Additionally, it is recommended for the treatment of chronic or resistant acute cellular rejection and refractory antibody-mediated rejection.
Lung	CLAD is a major risk to long-term survival after **lung transplantation**. The most common CLAD phenotype is bronchiolitis obliterans syndrome (BOS). Evidence indicates that ECP can stabilise lung function in patients with CLAD/BOS. In addition, ECP has been used in patients with acute recurrent cellular rejection, though evidence is limited to small studies. Prospective, randomised controlled trials are needed to clarify its role in this context. Early prophylactic ECP is not currently recommended for lung transplantation, but research is ongoing.
Kidney	Data on the use of ECP for the treatment of rejection in **kidney transplantation** are limited, and studies often include only a small number of patients, which does not enable the assessment of clinical impact. Overall, available evidence suggests that ECP may have an adjunctive role in acute rejection, particularly in patients who do not tolerate high-dose immunosuppressive drugs.

Liver 	Current evidence for the use of ECP in **liver transplantation** comes from small case series, pilot studies and anecdotal reports, with no randomised controlled trials confirming its effectiveness for rejection prevention or treatment.

Ongoing research increasingly supports the effectiveness of ECP in minimising both acute and chronic rejection in transplant recipients. As a result, ECP is anticipated to play a larger role in SOT, particularly for patients who do not tolerate conventional immunosuppressive regimens.

Further investigation is required in this field to support evidence-based decision-making, especially in the context of kidney and liver transplantation.

What is the mechanism of action of ECP?

ECP demonstrates anti-tumour and anti-inflammatory properties, reduces antibody-mediated tissue injury, autoimmunity, and tissue fibrosis, increases immunological tolerance and may enable reduction of immunosuppression in organ transplantation. However, the mode of action by which treated cells exert this range of immunological effects remain unclear.

Initial theories suggested that using psoralen with UVA caused cell death in treated leukocytes, preventing them from attacking the graft. However, further observations revealed that ECP affects the immune system in ways that extend beyond inducing leukocytes apoptosis.

Transimmunization represents an alternative mode of action mediated by differentiation of immature dendritic cells, modification of the cytokine profile, and stimulation of several T-cell lineages (in particular regulatory T-cells).

Different pathways may contribute to the beneficial effects of ECP in different indications and the final role of the various immune cell components, including regulatory T cells, has yet to be definitively clarified.

Although ECP has been employed for more than thirty years, **the precise immunological mechanisms underlying its effects remain incompletely elucidated. Ongoing research aims to gain insights into the mode of action to expand its applications in SOT and optimize its use in established indications**.

Bridging the gap: challenges, future directions, and ESOT-Therakos initiatives in advancing ECP for transplantation

ESOT-Therakos educational collaboration (2022-2024)

Over three years, ESOT and Therakos worked together to create a comprehensive educational plan for the dissemination of knowledge on ECP, targeting a broad range of stakeholders, including HCPs, researchers, patients, and patient advocacy groups.

By bridging the knowledge gap and fostering effective exchange, the project sought to make a significant contribution to the wider acceptance and implementation of ECP in clinical practice.

This section outlines the initiatives undertaken as part of this collaboration.

Usage of ECP in solid organ transplantations in Europe: a narrative review

Transplant International

A survey conducted by ESOT addressed the significant challenges hindering the broader implementation of ECP in transplantation. The targeted responders were transplant clinicians across Europe. The results of this survey were published as a narrative review in *Transplant International* (Cashmore et al., 2025).

Below is a summary of the main barriers described in the review and possible strategies for advancing the integration of ECP as a therapeutic option in SOT.

Barriers	Future directions
Awareness Awareness of ECP is limited. Clinicians surveyed were less familiar with ECP for liver transplants compared to heart, lung, and kidney transplants.	**Expanding knowledge and clinical expertise** Increasing HCP awareness and expertise will promote broader implementation. Future initiatives should include targeted education and training workshops for transplant clinicians, nurses, and allied health professionals.
Lack of high-quality clinical trial data Limited robust clinical trial evidence remains a major barrier to expanding ECP use in SOT, as most available data comes from single-centre or case studies.	**Advancing evidence through randomised controlled trials** Large-scale randomised controlled clinical trials are required to evaluate the efficacy and safety of ECP in SOT, with particular emphasis on kidney and liver transplantation.

Barriers (cont.)	Future directions (cont.)
Lack of standardised protocols Protocols vary widely across centres and countries (e.g., treatment schedules, devices, and patient selection). ECP is recommended in international guidelines for heart and lung transplantation, but not for kidney and liver transplantation.	**Developing standardised, evidence-driven procedures** The development of evidence-based guidelines will help harmonise patient selection and treatment procedures, reduce practice variability, allow consistent data collection, improve evaluation of effectiveness and cost-efficiency, and enhance patient care. **Establishing large-scale multicentre registries** Establishing registries to collect real-world data will enable protocol comparison, evaluation of long-term outcomes, and informed policy and practice development.
Incomplete understanding of ECP mechanism of action The incomplete understanding of ECP mechanism of action limits the refinement of ECP protocols for specific transplant-related conditions and patient groups.	**Enhancing mechanistic understanding of ECP** Ongoing research aims to clarify the mechanism of action and immunological effects of ECP, with the goal of expanding its application in transplantation and optimising its use in existing indications.
Limited access ECP availability varies widely across Europe, with access largely confined to major urban transplant centres. Geographic and infrastructural disparities, lengthy treatment sessions, and the need for repeated visits contribute to unequal patient access, particularly in rural or underserved regions.	**Overcoming logistical and access barriers** Successful implementation of ECP in SOT requires coordinated efforts among transplant specialists, immunologists, policymakers, and industry. Interdisciplinary initiatives should focus on overcoming logistical challenges, standardising protocols, and ensuring equitable patient access across healthcare settings.
Costs High initial costs for ECP equipment, treatment sessions, trained staff, and infrastructure limit access, particularly in smaller or resource-limited centres. Variable reimbursement policies often fail to cover full expenses, further restricting availability in public healthcare systems and underfunded regions.	**Implementing cost-effectiveness analyses** Cost-effectiveness studies are needed to evaluate the economic impact of ECP in clinical practice. Robust economic analyses are currently lacking, representing a key research gap for future investigation.

Raising awareness: an educational strategy to overcome barriers to ECP use

The educational efforts put together by ESOT and Therakos targeted the improvement of awareness, which is a major barrier to ECP utilisation.

Webinars, national workshops conducted in multiple languages, and courses play a pivotal role in providing a thorough introduction to ECP. Leading experts presented the ECP technique, explored its underlying immunological mechanisms in transplant recipients, and highlighted its use across various SOT indications. Special emphasis has been placed on how ECP can be applied to prevent graft rejection, making these programs instrumental in advancing understanding of ECP among diverse audiences and across countries.

All recordings are available online on different platforms accessible via the ESOT website.

The ECP immunomodulation award in SOT

The ECP immunomodulation award in SOT provides a substantial educational grant of EUR 50'000. The award is intended to recognise and support investigators making significant contributions to advancing mechanistic and clinical understanding of ECP in SOT, thereby fostering innovation and addressing key evidence gaps in this evolving field.

ECP Awardee 2025 Anna Weijler 	**Single-cell transcriptomic analysis of immune modulation by extracorporeal photopheresis in lung transplant recipients** Supported by the award, **Anna Weijler** (Department of General Surgery, the Medical University of Vienna, Austria) **work addresses a critical mechanistic gap and investigates the transcriptional changes in individual immune subsets in lung transplant recipients receiving ECP compared to recipients without ECP treatment**, corroborating the hypothesis that ECP drives cell-specific immune remodelling, contributing to its well-known benefits including protection against infection, rejection and CLAD.
ECP Awardee 2023 Jordi Rovira 	**Deciphering the mechanism underlying ECP-induced immunomodulation in kidney transplantation** **Jordi Rovira** (Experimental Laboratory of Nephrology and Transplantation (LENIT), IDIBAPS, Barcelona, Spain) has been awarded for a project **assessing the mechanisms underlying ECP therapy in the context of kidney transplantation**, involving the analysis of biological samples from patients, characterization of peripheral mononuclear cells (PBMC) and the ECP cell product, and evaluation of the impact of ECP on the patients' T and B cell alloresponse as well as the transcriptomic profile of PBMCs.
ECP Awardee 2021 Johanne Hjort Baatrup 	**ECP treatment of chronic humoral rejection in cardiac transplantation: exploring immunomodulation by exosomes** Preliminary results indicate that ECP induces differential extra vesicles (EVs) generation in a leukocyte subset-specific pattern involving upregulation of CD9 and TGFβ-bearing exosomes in transplant patients. The project awarded to **Johanne Hjort Baatrup** (Department of Clinical Immunology, Aarhus University Hospital, Aarhus, Denmark) **aims to investigate and characterise the immunomodulatory effects of ECP in heart transplant recipients with donor-specific antibodies, with a focus on the role of EVs**.

Repository for ECP evidence

RECPE
Repository for Extracorporeal Photopheresis Evidence

The Repository for Extracorporeal Photopheresis Evidence (ESOT-RECPE) has been developed to provide centralised access to scientific articles on the use of ECP in SOT.

Concluding remarks

ECP represents an increasingly important immunomodulatory treatment in SOT, offering the potential to mitigate rejection while avoiding the burden of generalised immunosuppression. While clinical experience and emerging evidence highlight its therapeutic value, significant challenges remain, including limited high-quality trial data, incomplete mechanistic understanding, variability in clinical practice, and unequal patient access across healthcare systems.

Addressing these challenges requires coordinated, interdisciplinary collaboration among HCPs, researchers, industry partners, policymakers, and patient organisations. Such collaboration is essential to harmonise protocols, generate robust clinical and mechanistic evidence, improve cost-effectiveness assessments, and translate innovation into equitable clinical practice.

The partnership between ESOT and Therakos exemplifies how joint efforts between biomedical societies and industry can effectively drive progress in transplantation. By supporting education, research, and capacity building, this initiative has helped raise awareness of ECP, foster scientific exchange across disciplines, and stimulate research addressing key evidence gaps.

Through shared commitment, ECP can be further developed into a standardised, accessible, and evidence-based treatment in the transplant setting, ultimately improving long-term outcomes for transplant recipients worldwide.

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