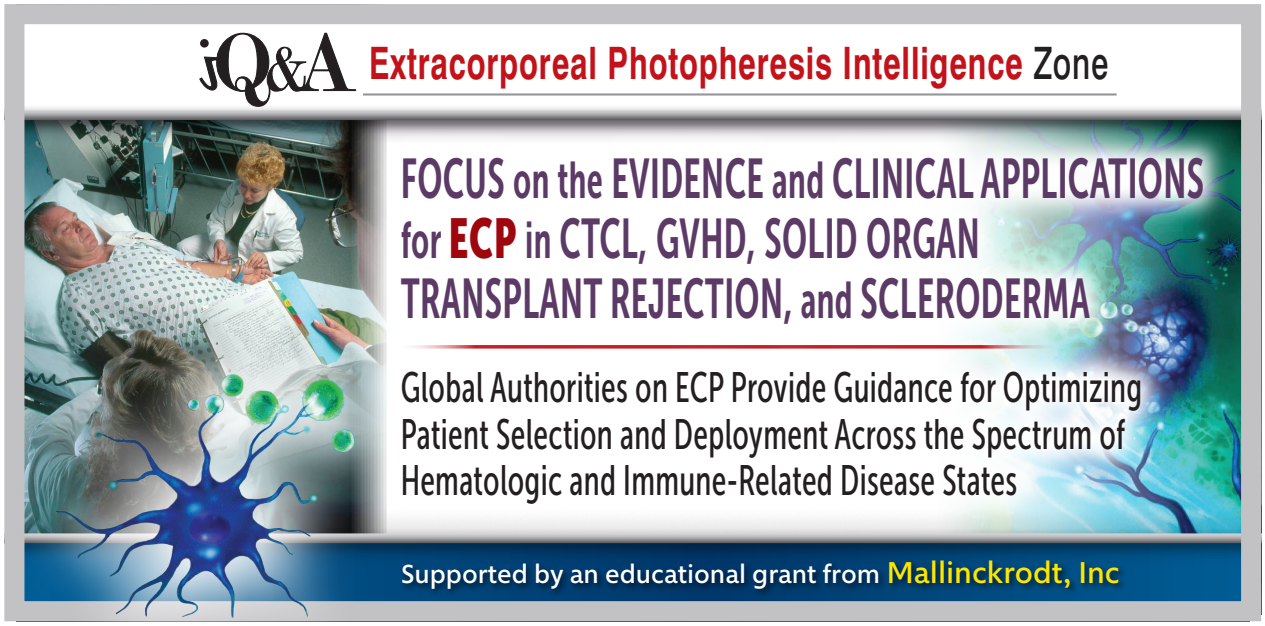
iQ&A Extracorporeal Photopheresis (ECP) Intelligence Zone

FOCUS on the EVIDENCE and CLINICAL APPLICATIONS for CTCL, GVHD, SOLID ORGAN TRANSPLANT REJECTION, and SCLERODERMA

Global Authorities on **Extracorporeal Photopheresis** Provide Expert- and Evidence-Based Guidance for Optimizing Patient Selection and Safe and Effective Deployment of ECP Across the Spectrum of Hematologic and Immune-Related Disease States



A Year 2019 Best Practice, Case-Based and Guideline-Driven Update for the Hematologist, Transplant Surgeon, Dermatologist, Immunologist, Rheumatologists, Oncologist, and Related Specialist

CMEducation Resources, LLC
A Medical Education Company

Richard Edelson, MD

Aaron B. and Marguerite Lerner Professor of Dermatology
Chair and Professor
Department of Dermatology
Yale School of Medicine

QUESTION #1: As a pioneer in the field of extracorporeal photopheresis (ECP) can you provide some background and history on how this therapeutic strategy was developed and for what challenging conditions, in particular, in CTCL?

QUESTION #2: Can you discuss, from both a translational and biological perspective what is unique about ECP and why this therapy provides an acceptable balance of efficacy and safety for malignant conditions as well as related conditions? And, the implications of ECP as both an immunizing and tolerizing factor for T-cells across a spectrum of disease states?

QUESTION #3: Can you explain the biological and clinical importance of the fact that ECP provides dual or bifurcated effects on immune modulation, i.e., it both has the capacity to potentiate immune response against malignancies such as CTCL, and to tolerize immune response in such conditions as graft vs. host disease (GVHD)? How can ECP address, in ambidextrous fashion, both sides of the "immune response coin?"

QUESTION #4: Once you and colleagues in the field had determined that dendritic presenting cells (DPCs) were critical mediators of the therapeutic effects of ECP, how did you determine the actual mechanism by which ECP activated DPCs? And what is the role of monocyte activation and antigen processing in this immune-modulating cascade?

QUESTION #5: What explains the bi-directional immunomodulatory and therapeutic effects of ECP, and what are the practical implications of its deployment against a broad spectrum of disease states?

QUESTION #6: Can you discuss the findings, implications, consensus agreements, and recommendations issued by the American Council of Extracorporeal Photopheresis (ACE), which was commissioned by ASFA?

QUESTION #7: What are the key immunological criteria and/or clinical factors that must be met in order to identify patients with advanced CTCL who are likely to respond to ECP? Can you provide a systematic approach—including assessment of CD8 T-cell count—for screening these individuals?

QUESTION #8: Can you be specific about how you interpret the results of the CD4/CD8 T-cell ratios in order to determine suitability for ECP therapy? And what is the role of anti-T-cell antibodies for patient screening?

QUESTION #9: From a practical, clinical perspective, how do you sequence therapies for patients with CTCL? What is the initial modality, and why, and when and in whom does ECP represent an evidence-based approach to treating CTCL? How many ECP treatments and at what frequency do you employ them?

QUESTION #10: How enduring is the response to ECP in appropriately selected patients with CTCL? What percentage of CTCL patients who have failed initial therapy can be expected to respond? And what are the characteristics of the dose-response curve?

QUESTION #11: Can you summarize the mechanistic underpinnings of ECP and its role in anti-cancer therapy and future applications?

Daniel R. Couriel, MD, MS

Professor of Internal Medicine
Director, Huntsman Cancer Institute (HCI) Blood and Marrow Transplant Program
University of Utah School of Medicine
Salt Lake City, UT

QUESTION #12: Although corticosteroids are the established standard first-line therapy for chronic cGVHD (Graft Versus Host Disease), and multiple second-line treatments have been or are being evaluated for patients who are steroid-refractory or steroid-intolerant, what potential role does ECP play in this disease state?

QUESTION #13: Are there specific variants or clinical signatures of chronic cGVHD that respond better to ECP therapy than others? What other second line therapies, including ibrutinib, have been evaluated and/or FDA-approved? Has ECP been shown to have a steroid-sparing or tapering effect? What is the expected timing and kinetics of response for acute vs chronic GVHD?

QUESTION #14: In what specific patient populations/ disease states is allogeneic hematopoietic cell transplantation (HCT) an important therapeutic option?

QUESTION #15: Can you characterize the signs, symptoms, and complications of allogeneic cell transplant, in particular acute and chronic GVHD? Can you distinguish between these two forms of GVHD? What were the classifications provided by the NIH consensus?

QUESTION #16: What is the difference between acute and chronic GVHD? And how is the diagnosis of GVHD made? How is each condition treated? What is the role of steroids as current SOC and what percentage of patients are steroid refractory and, therefore, will potentially require ECP?

QUESTION #17: What is the role of ECP in steroid refractory patients with GVHD? And what is the evidence confirming acceptable response rates and safety of ECP in these patient populations?

QUESTION #18: From a practical implementation perspective, what kind of ports are available for ECP and what is the recommended schedule for deploying ECP in both acute and chronic GVHD? On what basis was this schedule determined?

QUESTION #19: Once you have made the decision to deploy ECP as your second-line therapy for steroid-refractory aGVHD or cGVHD, what practical considerations should clinicians be knowledgeable of when considering ECP treatment?

QUESTION #20: What length of time is typically required to determine whether ECP has been effective for cGVHD, and when might you consider discontinuation of ECP based on a clinical response to ECP? What is the accepted tapering schedule in responders?

QUESTION #21: What is the degree of steroid-sparing effect that can be anticipated when using ECP to treat GVHD? And what complications should be considered to be part of and ECP-dominant treatment strategy for GVHD?

QUESTION #22: What are the most important randomized studies that support ECP and what do we still need to know about ECP as a foundational, second-line treatment strategy for GVHD?

QUESTION #23: How do you taper corticosteroid therapy in acute and chronic GVHD?

Ian Odell, MD, PhD

Assistant Professor
Dermatology Director, Adult Primary Care Center
Scleroderma and Myositis Program
Yale University School of Medicine

QUESTION #24: Can you provide a brief review of scleroderma—systemic sclerosis—as a multisystem connective tissue disease characterized by humoral and cellular immune abnormalities and fibroblast activation?

QUESTION #25: Given the multiple clinical phenotypes and subtypes that are observed with systemic sclerosis, what therapeutic approaches are aligned with what forms of the disease? And what is the evidence-based role for ECP?

QUESTION #26: What findings of progressive skin involvement with scleroderma are sufficient clinical triggers to warrant consideration of ECP in the heterogeneous population of patients with this condition? What is the clinical trial data supporting the use of ECP in scleroderma?

QUESTION #27: Based on the clinical trial data, the benefit-to-risk equation, contraindications, and experience with ECP at your institution, which specific patients with scleroderma are you treating with ECP, and what practical strategies are your deploying to optimize outcomes?

QUESTION #28: What is the schedule—i.e. frequency of ECP treatments—that patients with scleroderma require, and what are the possible side effects that require monitoring?

QUESTION #29: Since you and others at Yale have treated a number of patients with scleroderma—and other conditions—with ECP, can you share your real world clinical experience with this treatment modality? And how measure clinical response to this therapy?

Dr. Julia Scarisbrick

Consultant Dermatologist & Cutaneous Lymphoma Lead at the University Hospital
Birmingham, UK

QUESTION #30: Can you provide an overview of the clinical and pathologic findings of CTCL?

QUESTION #31: What treatment modalities are currently used for CTCL prior to employing ECP?

QUESTION #32: What role does ECP play in patients with CTCL with progressive disease and/or those who have not responded to initial systemic, immune-modifying, or skin-directed therapy?

QUESTION #33: What did the initial trials show, efficacy- and safety-wise, in patients with CTCL who were treated with ECP?

QUESTION #34: What have your own meta-analyses, as well as others conducted in the UK, shown as far as response rates to ECP in patients with advanced CTCL?

QUESTION #35: Do you typically employ ECP in patients with CTCL as monotherapy, or in conjunction with other systemic, pharmacologic or immune-based treatments?

QUESTION #36: How do you identify patients with CTCL who are likely to be highly responsive to ECP?

QUESTION #37: What is the role of measuring T-cell counts when you employ ECP for CTCL?

QUESTION #38: At your institution, how long is each ECP treatment session, and how long do patients with CTCL typically require treatment? Within what period do you expect to see a treatment response?

QUESTION #39: What is the safety and adverse effect profile of ECP in your experience, and how often do they occur?

QUESTION #40: What are the contraindications to ECP?

QUESTION #41: Can you take us through a typical patient with CTCL that you would evaluate, treat, and finally, determine the evidence and suitability of this patient for treatment with ECP?

QUESTION #42: What is the approach to using ECP in a patient with erythroderma, and when in the time course of the natural history of CTCL do these patients usually present to you for consideration of ECP?

QUESTION #43: How do you manage patient expectations whom you are committing to ECP?

QUESTION #44: From a top-line perspective, what is the mechanism of ECP in the setting of CTCL?

QUESTION #45: Has access to the technology required for implementing ECP improved over the past years, and if so, why?