

## EXTRACORPOREAL PHOTOPHERESIS FOR SYSTEMIC SCLEROSIS – WHY, HOW AND WHEN?

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**Introduction.** The therapeutic options in systemic sclerosis (SSc) are limited mainly to the management of complications, and halting fibrosis and preventing disease progression are still great challenges. Extracorporeal photopheresis (ECP) is one of the promising therapeutic strategies in SSc, nevertheless, there is no consensus on the ideal timing and frequency of treatment cycles. In the present study, we evaluated the long-term effects of consecutive ECP treatments, and the durability of clinical and laboratory improvements after the last cycle of ECP.

**Methods.** We enrolled 9 patients with diffuse cutaneous SSc and performed 12 ECP cycles (24 ECP treatments) per capita in total. ECP cycles were carried out once in every six weeks, each cycle consisted of 2 procedures. Skin involvement was assessed by modified Rodnan skin score (MRSS) and high-resolution ultrasonography. Visceral organ involvements were also determined. Laboratory tests were carried out prior to the beginning of the therapy and after each ECP cycles. Samples were also obtained from 16 healthy controls. By flow cytometry, we quantified peripheral NK, NKT, early- and late-activated T, Th1, Th2, Th17, Tr1 and CD4+ CD25+ Treg cells. Levels of complements were measured by nephelometry, certain cytokines (IL-10, TGF-beta), anti-nuclear antibodies and anti-endothelial cell antibodies were determined by ELISA technique.

**Results.** Following the 6<sup>th</sup> cycle of ECP, we continued the therapy and observed further significant improvement in MRSS, which was confirmed by the ultrasonography results as well. Organ involvements did not show amelioration or deterioration. After the 2<sup>nd</sup> ECP cycle, values of Tr1 and CD4+CD25+ Treg cells elevated significantly, however, Tr1 cell percentages remained under the healthy control values until the 10<sup>th</sup> cycle. Frequency and absolute number of peripheral Th17 cells decreased, while the other investigated lymphocyte subpopulations did not show measurable quantitative changes. During the follow-up, 12 months after the last treatment we did not observed significant deterioration in the clinical state, however, improvements in laboratory parameters diminished after 6 months.

**Conclusions.** If the first 6 ECP cycles are effective for an SSc patient, uninterrupted continuation of treatment should be considered, which may lead to the normalization of Tr1 cell values along with further clinical improvement. Based on our laboratory observations, reminder ECP cycles are recommended in every year for the best therapeutic outcomes.

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