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Treatment of Systemic Sclerosis with Extracorporeal Photochemotherapy: Results of a Multicenter Trial

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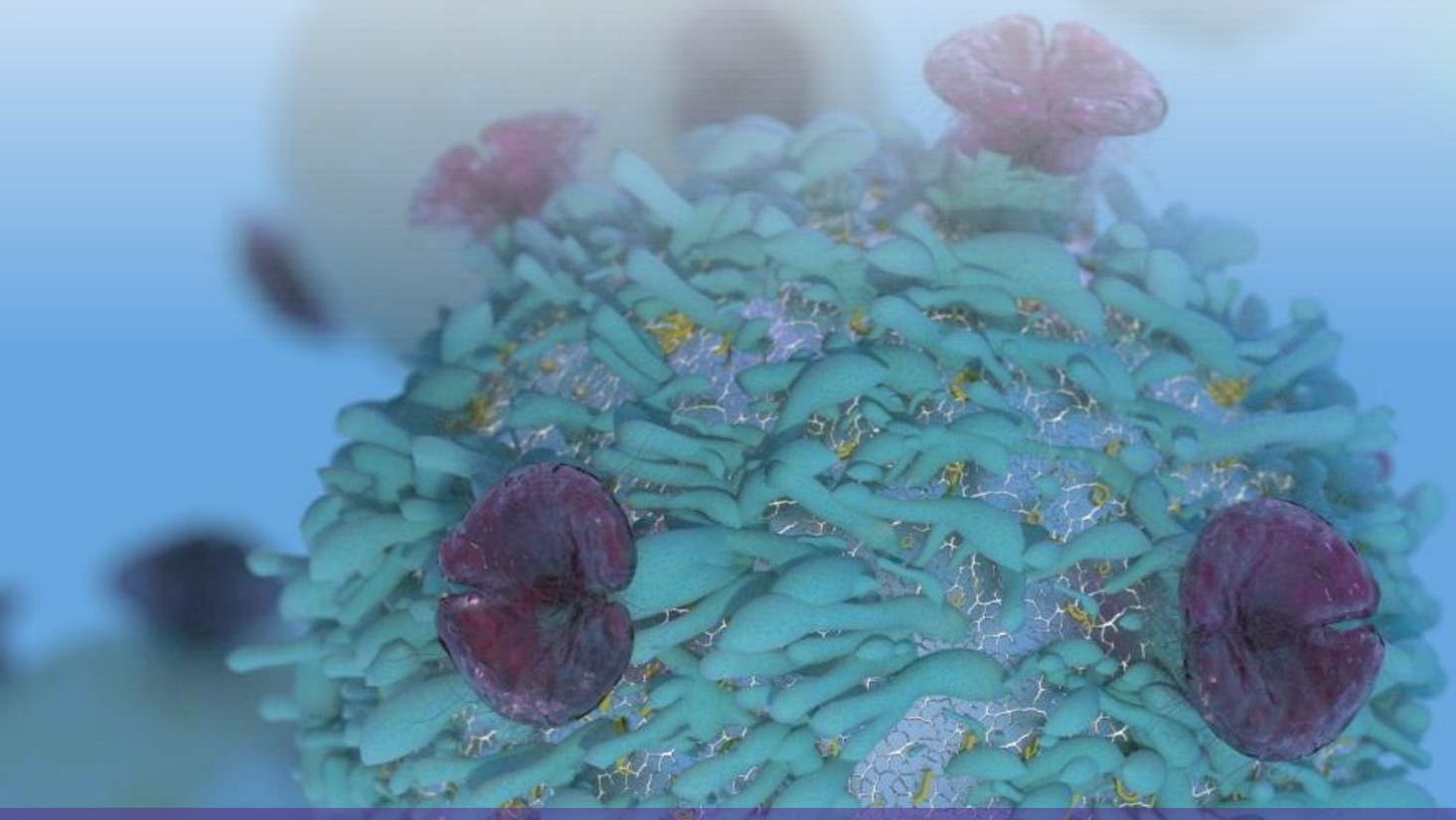
Arch Dermatol. 1992;128:337-346

A summary of the findings on the efficacy of extracorporeal photochemotherapy in the treatment of patients with systemic sclerosis (scleroderma).*



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This work was supported by Therakos, Inc, Hazelwood MO.

During the course of this study Dr. Edelson served as a paid consultant for Therakos on the broad subject matter of photopheresis.

*The specific instrument model used for this study, the Therakos UVAR, is no longer manufactured or supported, and has been replaced by the Therakos CELLEX photopheresis system.

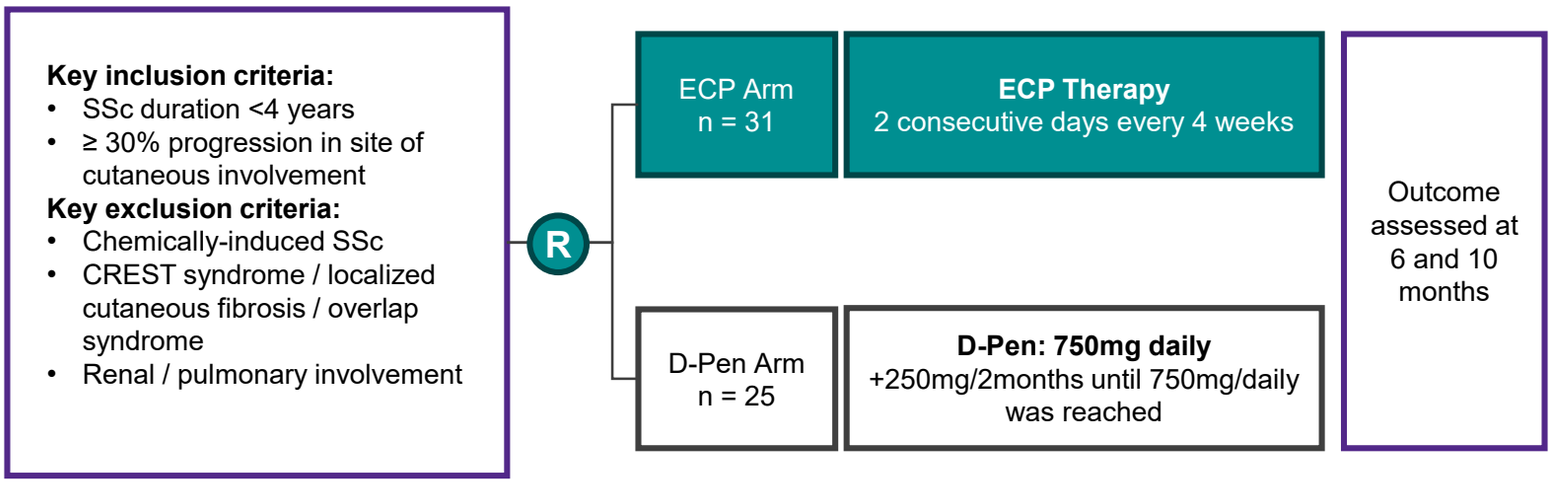
Systemic sclerosis intervention with THERAKOS™ ECP resulted in significant improvement in skin severity and joint involvement

Background:

Availability of therapeutic agents that can block fibrosis progression are essential, as diffuse skin involvement extending to the trunk within one year of onset may be associated with poor prognosis. To compare the efficacy of photopheresis treatment with D-Pen treatment in patients with SSc, a 10-month randomized, single-blind, controlled trial was performed in patients with recent onset SSc.

Methods:

- 56 patients received Therakos™ ECP* (n=31) via the UVAR XTS™ or D-Pen (n=25) for a minimum duration of 6 months.
- Parallel treatment with pharmacological agents that reduce collagen production, such as steroids, colchicine, potassium aminobenozate, were not permitted for the treatment of Raynaud's phenomenon.



Outcome Measures:

Assessed monthly for 6 months:

- Skin score was assessed by rating the thickness of the skin on a 0 to 3 scale in 15 areas of the body. Possible skin severity scores ranged from 0 to 45.
- Joints were assessed by standardized measurements of the change in oral aperture and right and left hand closure.
- Skin biopsies at baseline, 6 month and 12 month followup
- Adverse effects were recorded monthly

Limitations:

- Single-blinded study
- Small sample size**
- Disproportional number of patients within the two arms at 10 months as several patients were not available to follow up. Therefore the 10 month comparison may not be accurate.

Abbreviations: SSc- Systemic Sclerosis, ECP-extracorporeal photopheresis; D-Pen-D-penicillamine
**The specific instrument used for this study has been replaced by Therakos CELLEX™ photopheresis system, and is no longer manufactured or supported
**Results are not generalizable to larger patient populations due to the small sample size

BASELINE CHARACTERISTICS

Clinical and demographic characteristics of the patient population studies

Characteristic	D-Penicillamine	ECP
No. of patients	25	31
Age (y) at first treatment **Mean** **Median** **Range**	 44.12 42.0 21-73	 43.55 44.0 21-74
Sex (male/female)	7/18	6/25
Disease duration (y) **Mean ± SD** **Median**	 1.9 ± 1.9* 1.2	 1.8 ± 1.1 1.7
Skin severity score (mean ± SD)**	21.7 ± 9.3*	21.4 ± 9.1
% Skin involvement (mean ± SD)**	29.6 ± 22.6*	28.5 ± 23.7

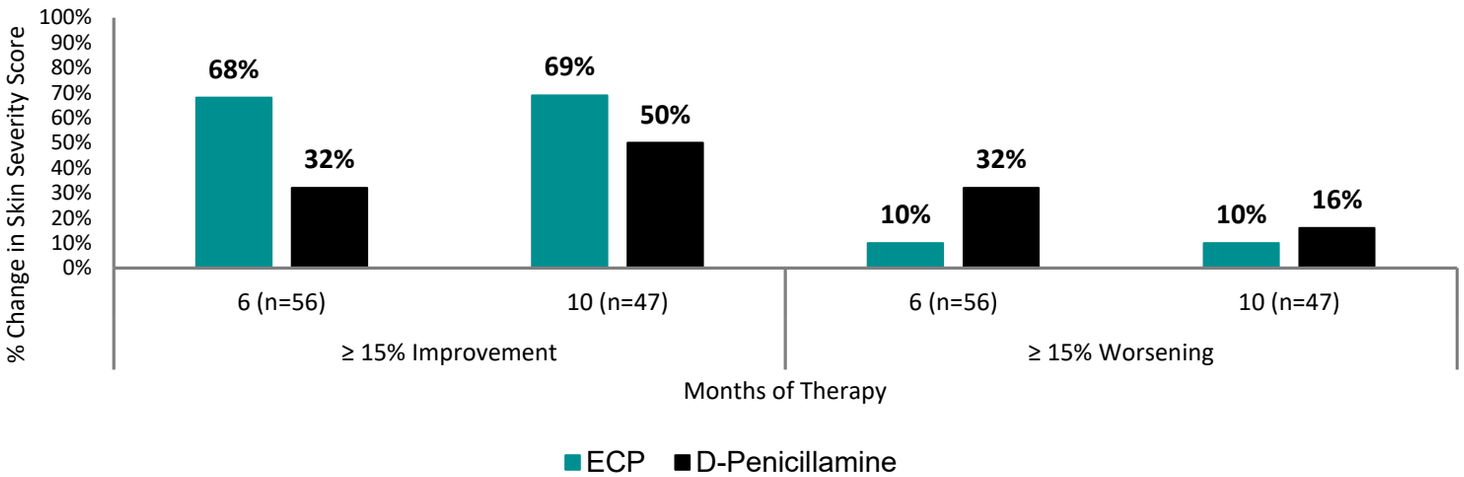
ECP, Extracorporeal photopheresis; *SD*, standard deviation.
*Indicates that the two groups are not significantly different
**Assessed as described in the Materials and Methods section of the Rook 1992 paper.

TRIAL RESULTS

SKIN INVOLVEMENT IN 15 AREAS OF THE BODY: SKIN SEVERITY SCORES

Therakos™ Photopheresis patients experienced statistically significant improvement *(P=0.02)* in skin score compared to D-Pen-treated patients after 6 months*

Greater percentage of ECP patients had ≥15% improvement in skin severity scores and lesser percentage of ECP patients had ≥15% worsening in skin severity scores compared to D-Pen patients**



*No significant improvement in skin score of ECP compared to D-Pen-treated patients was observed at 10 months
**A change in the skin score during treatment was considered to be clinically relevant if it differed by at least 15% from baseline.

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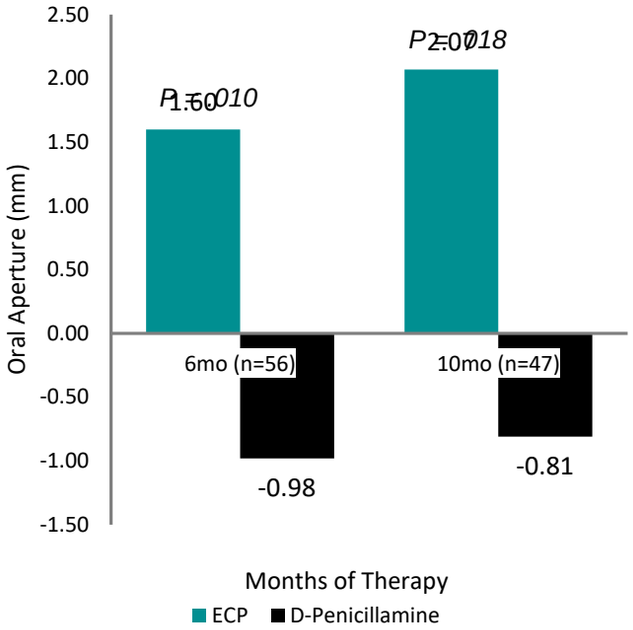
TRIAL RESULTS

JOINT ASSESSMENT: ORAL APERTURE AND RIGHT AND LEFT HAND CLOSURE

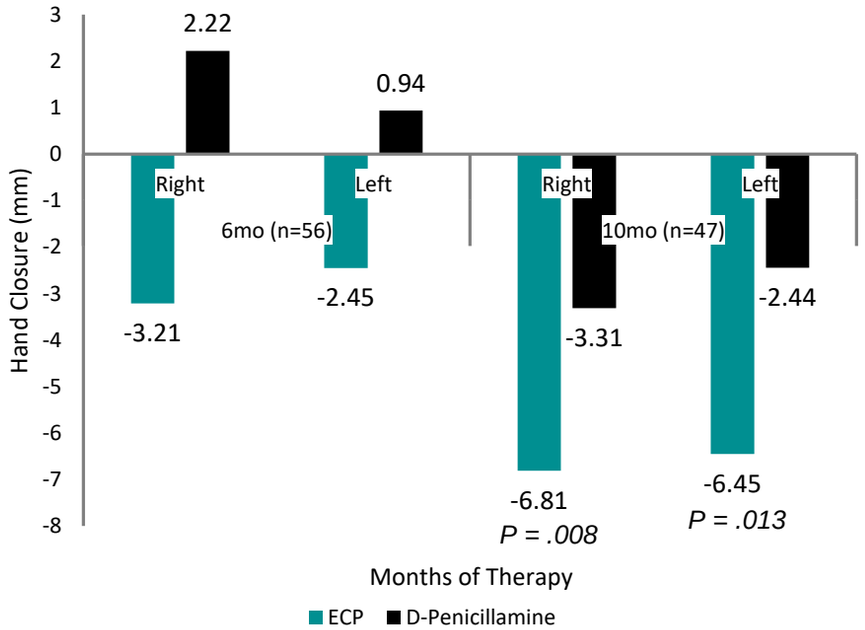
Therakos™ Photopheresis patients experienced significant improvement compared to baseline in oral aperture after 6 months and oral aperture and right/left hand closure after 10 months of treatment

Significant oral aperture improvement from baseline at 6 and 10 months for ECP arm*



*No significant improvement in oral aperture of D-Pen treated patients compared to baseline was observed.

Significant right and left hand closure improvement from baseline at 10 months for ECP arm*



*No significant improvement in hand closure of ECP treated patients compared to baseline was observed at 6 months. No significant improvement in hand closure of D-Pen treated patients compared to baseline was observed.

"In regard to the rapidity of the clinical response to treatment observed in this study, the majority of the patients who received extracorporeal photochemotherapy demonstrated significant clinical improvement of cutaneous features of disease after both 6 and 10 months of therapy. Furthermore, the mean 6-month and 10-month skin severity scores for the patients in this treatment arm were significantly lower than the baseline score.

By comparison, a smaller proportion of patients treated with D-penicillamine showed cutaneous improvement at the 6-month treatment interval. If D-penicillamine dropouts are excluded, the majority of whom experienced clinical worsening, mean skin severity scores were significantly improved in this group by the 10-month interval, but not at the 6-month interval."

TRIAL RESULTS

SAFETY AND TOLERABILITY

Therakos™ Photopheresis is a well tolerated treatment modality.

24% of D-penicillamine patients required permanent discontinuation of therapy due to serious adverse events. No serious adverse events were reported in ECP patients, however minor side effects were observed, such as difficulties in obtaining and maintaining vascular access.

Adverse Effects by Treatment Group	
Adverse Effect	Number of Patients* (%)
D-Penicillamine	
Myopathy	1 (4)
Proteinuria	4 (16)
Fever	1 (4)
Oral ulcers	2 (8)
Renal failure	1 (4)
Nausea	1 (4)
Elevated transaminase levels	1 (4)
ECP	
Nausea	2 (6)
Hemolysis	1 (3)
Hypotension	1 (3)
Vasovagal reaction	1 (3)
Clotted device	3 (10)
Thrombocyopenia	1 (3)

*Adverse experiences required permanent discontinuation of treatment in 6 patients receiving D-penicillamine and 0 cases in the ECP arm during 10 month of observation.

Conclusions:

THERAKOS™ ECP treatment demonstrated significant clinical improvement of cutaneous features of the disease after 6 and 10 months of therapy compared to baseline. ECP treatment resulted in significant improvement of skin scores after 6 months compared to D-penicillamine treated.

In general, ECP was well tolerated with no serious side effects reported.

Please review the European Dermatology Forum (EDF) 2020 and American Society for Apheresis (ASFA) 2016 guidelines for recommendations on the use of ECP in systemic sclerosis.[1,2]

Please consult additional safety information and list of most common adverse events on page 6 of this reprint carrier.

1. Knobler R, et al. J Eur Acad Dermatol Venereol. 2020;10.1111/jdv.16989. 2. Schwartz J, et al. J Clinical Apheresis. 2016;31(3).

Important Safety Information for THERAKOS™ Photopheresis Procedure

INDICATION

The THERAKOS™ CELLEX™ Photopheresis System is indicated for use in the ultraviolet-A (UVA) irradiation, in the presence of the photoactive drug 8-methoxypsoralen (8-MOP), of extracorporeally circulating leukocyte-enriched blood, in the palliative treatment of the skin manifestations of cutaneous T-cell lymphoma (CTCL) and systemic sclerosis (SSc).

CONTRAINDICATIONS

Certain underlying medical conditions contraindicate THERAKOS Photopheresis, including:

- Patients who cannot tolerate extracorporeal volume loss during the leukocyte enrichment phase
- Patients exhibiting idiosyncratic or hypersensitivity reactions to 8-methoxypsoralen/psoralen compounds
- Patients with coagulation disorders or who have had previous splenectomy

WARNINGS & PRECAUTIONS

THERAKOS Photopheresis treatments should always be performed in locations where standard medical emergency equipment is available. Volume replacement fluids and/or volume expanders should be readily available throughout the procedure.

- **MR-Unsafe:** Do not expose the device to a magnetic resonance (MR) environment. The device may present a risk of projective injury, and thermal injury and burns may occur. The device may generate artifacts in the MR image, or may not function properly.
- **Thromboembolic Events:** Thromboembolic events, including pulmonary embolism and deep vein thrombosis, have been reported in the treatment of Graft versus Host Disease (GvHD, an indication not approved in Canada. Special attention to adequate anticoagulation is advised when treating patients with GvHD.
- **Concomitant Therapy:** When prescribing and administering THERAKOS Photopheresis for patients receiving concomitant therapy, exercise caution when changing treatment schedules to avoid increased disease activity that may be caused by abrupt withdrawal of previous therapy.

ADVERSE REACTIONS

Hypotension may occur during any treatment involving extracorporeal circulation. Monitor the patient closely during the entire treatment.

Transient pyretic reactions, 37.7-38.9o C (100-102o F), have been observed in some patients within 6-8 hours of reinfusion of the photoactivated leukocyte-enriched blood. A temporary increase in erythroderma may accompany the pyretic reaction.

Treatment frequency exceeding labeling recommendations may result in anemia.

Venous access carries a small risk of infection and pain.

Important Safety Information for Methoxsalen Sterile Solution Used in Conjunction with THERAKOS™ CELLEX Photopheresis System

CONTRAINDICATIONS

Methoxsalen Sterile Solution is contraindicated in:

- Patients exhibiting idiosyncratic reactions to psoralen compounds
- Patients with aphakia
- Patients possessing a specific history of a light-sensitive disease state

SERIOUS WARNINGS & PRECAUTIONS

- **Concomitant Therapy:** Exercise care in treating patients who are receiving concomitant therapy (either topically or systemically) with known photosensitizing agents.
- **Carcinogenicity:** Oral administration of methoxsalen followed by cutaneous UVA exposure (PUVA therapy) is carcinogenic. Patients exhibiting multiple basal cell carcinomas or having a history of basal cell carcinoma should be diligently observed and treated.
- **Teratogenicity:** Methoxsalen may cause fetal harm when given to a pregnant woman. Women undergoing photopheresis should be advised to avoid becoming pregnant.
- **Cataractogenicity:** Patients should be told emphatically to wear UVA absorbing, wrap-around sunglasses for twenty-four (24) hours after methoxsalen treatment, any time they are exposed to direct or indirect sunlight and whether they are outdoors or exposed through a window.
- Safety in children has not been established.

FOR MORE INFORMATION

Please consult the full product monograph for methoxsalen sterile solution (if used in conjunction with the THERAKOS™ CELLEX™ Photopheresis System) and the Operator's Manual for the CELLEX system at https://www.mallinckrodt.ca/products/therakos/, or by calling us at 1-877-566-9466.

Click Here
or access the URL below for the e-print of this study:

https://eorder.sheridan.com/3_0/app/orders/10410/article.php