Therakos®
ECP Immunomodulation

Clinical Summary in SSc

Trial 1 – Rook *et al.*[1]*

	D-Penicillamine (n=25)†	THERAKOS® ECP (n=31)†
Disease duration in years (mean ± SD)	1.9 ± 1.9	1.8 ± 1.1
Baseline skin severity score (mean ± SD)	21.7 ± 9.3	21.4 ± 9.1
Primary Endpoint: Skin Improvement Patients with ≥15% improvement in skin severity score		
6 months	32%	68% (*p*=0.02 vs. D-Pen)
10 months	50%	69% (*p*=NS vs. D-Pen)
Joint Assessment: Oral aperture Mean change from baseline (mm)		
6 months	-0.98 (*p*=NS)	+1.60 (*p*=0.010)
10 months	-0.81 (*p*=NS)	+2.07 (*p*=0.018)
Joint Assessment: Left hand closure Mean change from baseline (mm)		
6 months	+0.94 (*p*=NS)	-2.45 (*p*=NS)
10 months	-2.44 (*p*=NS)	-6.45 (*p*=0.013)
Joint Assessment: Right hand closure Mean change from baseline (mm)		
6 months	+2.22 (*p*=NS)	-3.21 (*p*=NS)
10 months	-3.31 (*p*=NS)	-6.81 (*p*=0.008)

There was a disproportional number of patients within the 2 arms at 10 months as several patients were not available for follow-up. Therefore, the 10-month comparison may not be accurate. Results are not generalizable to larger patient populations due to the study's small sample size.[1]

Trial 2 – Knobler *et al.*[2‡]

	Sham ECP (n=30)	THERAKOS® ECP (n=27)
Disease duration in years (mean ± SD)	1.2 ± 0.4	1.0 ± 0.5
Baseline skin severity score (mean ± SD)	34.9 ± 10.4	34.7 ± 10.8
Primary Endpoint: Skin Improvement Baseline-adjusted change in skin score		
6 months	-0.1 (*p*=NS)	-3.2 (*p*=0.024)
12 months	-2.0 (*p*=NS)	-5.6 (*p*=0.008)
Secondary Endpoint: Joint Involvement Involved joints from baseline (mean)		
6 months	6.9	11.7
12 months	7.2	9.0
Secondary Endpoint: Joint Involvement New joints involved from baseline (mean)		
6 months	6.5	2.8
12 months	7.9	2.5

Only patients with recent-onset SSc were included; however, time from disease onset may not be a valuable criterion for selecting patients most likely to have progressive disease. The comparison of skin scores between the two study arms did not achieve statistical significance because of the small sample size of the study arms.[2]

SSc=systemic sclerosis; ECP=extracorporeal photopheresis; SD=standard deviation; NS=not significant.

* A 10-month randomized, single-blind, controlled trial in patients with recent-onset SSc (<4 years) and ≥30% progression in site of cutaneous involvement. Patients were randomized 1:1 to receive THERAKOS ECP via the UVAR XTS for 2 consecutive days every 4 weeks or D-penicillamine +250 mg/2 months until 750 mg daily was reached, for ≥6 months. Patients were assessed monthly for ≥6 months. Only stable doses of calcium channel blockers were permitted for the treatment of Raynaud's phenomenon; collagen production-reducing pharmacologic agents were not permitted.

† At the 10-month timepoint, the D-penicillamine arm included 18 patients, whereas the THERAKOS ECP arm included 29 patients.

‡ A 12-month randomized, double-blind, placebo-controlled trial in patients with diffuse SSc (<2 years). Patients were randomized 1:1 to receive THERAKOS ECP via the UVAR XTS or sham ECP for 2 consecutive days every 4 weeks. Patients were assessed monthly for 12 months. Collagen production-reducing pharmacologic agents were not permitted.

See Indication and Important Safety Information on back page.

Important Safety Information for THERAKOS® CELLEX® 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 CELLEX 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 CELLEX 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 CELLEX 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, 37.7–38.9ºC (100–102ºF), 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 AND 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

See 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 health-products.canada.ca/dpd-bdpp/ or by calling us at 1-833-223-4ECP (1-833-223-4327).

References: 1. Rook AH, et al. *Arch Dermatol*. 1992;128(3):337-346. **2.** Knobler RM, et al. *J Am Acad Dermatol*. 2006;54(5):793-799.

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