keenova™

Mallinckrodt Presents Data on Real-World Outcomes with THERAKOS™ CELLEX™ Photopheresis System Treatment at the 2024 Tandem Meetings

February 21, 2024

– Analysis of published studies of extracorporeal photopheresis (ECP) treatment for steroid-refractory chronic graft-versus-host disease (SR-cGvHD) assessed that THERAKOS ECP can improve short- and long-term patient outcomes[1] –

THIS INFORMATION IS INTENDED FOR EUROPEAN AUDIENCES ONLY

DUBLIN, Feb. 21, 2024 /PRNewswire/ -- Mallinckrodt plc, a global specialty pharmaceutical company, today announced a poster presentation of findings from a systematic literature review and meta-analysis of the safety, efficacy, and real-world outcomes of extracorporeal photopheresis (ECP) treatment for patients with steroid-refractory chronic graft-versus-host disease (SR-cGvHD).[1] An analysis of 47 studies reporting on the THERAKOS™ CELLEX™ Photopheresis System showed that treatmen of SR-cGvHD with ECP was associated with improvements in patients' overall survival (OS), failure-free survival (FFS), and overall response rate (ORR).[1] The results will be shared in a poster presentation at the 2024 Tandem Meetings, the combined Transplantation & Cellular Therapy Meetings of the American Society of Transplantation and Cellular Therapy (ASTCT) and the Center for International Blood and Marrow Transplant Research (CIBMTR) taking place February 21-24, 2024 in San Antonio, TX.

A systematic review of literature available through October 19, 2022 was first conducted to identify and analyze studies of patients receiving ECP for SR-cGvHD that reported on efficacy, safety, or health-related quality of life (HRQoL) outcomes.[1] The literature review identified 47 studies which uniquely reported on THERAKOS ECP treatment with a sample size ≥ 10 patients, comprising a total of 2,361 patients.[1] Lines of therapy were poorly reported (n=15) and ranged from 0-≥4 lines of previous treatment.[1] Most clinical studies (n=27) used a retrospective case series design.[1]

Using the studies identified from the systematic literature review, random effects meta-analyses were then performed for short- and long-term efficacy outcomes including ORR and skin-specific response, and OS and FFS, respectively.[1] A subgroup analysis was also conducted to explore the effect of outcome assessment criteria from the National Institutes of Health (NIH) vs. non-NIH/unknown criteria.[1] Safety and HRQoL outcomes were poorly reported in the existing clinical literature and therefore were not suitable for the meta-analysis.[1]

"We are pleased to share this important analysis of real-world data supporting THERAKOS ECP's efficacy, safety, and associated improvements to short- and long-term outcomes – such as overall survival, failure-free survival, and overall response rate – for patients with steroid-refractory chronic graft-versus-host-disease,[1]" said **Zachariah DeFilipp, MD, Hematopoietic Cell Transplant and Cellular Therapy Program, Massachusetts General Hospital, MA.** "This analysis not only builds upon the growing body of evidence supporting ECP's utility in treating patients with this condition, but also reflects the importance of supporting clinicians with treatment options for managing patients who do not respond to other types of therapy, such as steroids.[1]"

In assessing the short-term efficacy of THERAKOS ECP, this meta-analysis found[1]:

- The ORR (7 studies; 293 patients) at Months 3-4 and at Months 6-8 (13 studies; 540 patients) were 45.34% (95% CI: 26.64 – 65.45) and 58.23% (95% CI: 45.04-70.35), respectively.
- No significant difference in ORR between studies utilizing NIH criteria vs. non-NIH criteria, per the subgroup analysis.
- Skin-specific response at Months 2-3 and at Months 4-6 were 34.86% (95% CI: 13.26-65.21) and 54.22% (95% CI: 35.67-71.67), respectively.

In assessing the long-term efficacy of THERAKOS ECP, this meta-analysis found[1]:

- The pooled OS rate (14 studies; 704 patients) at Month 12 was 83.97% (95% CI: 77.33-88.94).
- The OS rate (8 studies; 431 patients) at Month 60 was 57.96% (95% CI: 35.48-77.56).
- The FFS rate (4 studies; 169 patients) at Month 12 was 60.79% (95% CI: 38.94-79.03).

Limitations
Data collected in systematic literature reviews and meta-analyses may have errors or omissions. The studies included in the analysis are heterogeneous and use different patient populations, endpoints, interventions, and dosing.[1] There was considerable heterogeneity across analyses with I^2 values ranging from 65% to 91%.[1] Most studies included in the meta-analysis were retrospective analyses[1] and these observations may require further investigation in prospective, controlled trials. Statistical evaluations should be interpreted with caution. Outcomes may be influenced by therapies not evaluated in the study and the clinical/health economics outcomes may not be solely attributable to THERAKOS ECP.

This study was sponsored by Mallinckrodt Pharmaceuticals. Presentation details can be found below:

Abstract #340: Systematic Review and Meta-Analysis of Extracorporeal Photopheresis for the Treatment of Steroid-Refractory Chronic Graft-Versus-Host Disease[1]

- **Presenter:** Zachariah DeFilipp, MD, Hematopoietic Cell Transplant and Cellular Therapy Program, Massachusetts General Hospital, MA
- **Presentation Date:** Thursday, February 22, 2024; 6:45 – 7:45 p.m. CST
- **Location:** Exhibit Hall 4a (Street Level)

IMPORTANT SAFETY INFORMATION FOR THE THERAKOS™ PHOTOPHERESIS PROCEDURE

Indications
The THERAKOS™ CELLEX™ Photopheresis System is indicated for the administration of photopheresis. Please refer to the appropriate product labelling for a complete list of warnings and precautions.

Contraindications
THERAKOS™ Photopheresis is contraindicated in:

- Patients possessing a specific history of light sensitive disease
- Patients who cannot tolerate extracorporeal volume loss or who have white blood cell counts greater than 25,000 / mm^3
- Patients who have coagulation disorders or who have previously had a splenectomy

Warnings and 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. Safety in children has not been established.

- Do not expose the device to a magnetic resonance (MR) environment. The device may present a risk of protective injury, and thermal injury and burns may occur. The device may generate artifacts in the MR image, or may not function properly.
- Thromboembolic events, including pulmonary embolism and deep vein thrombosis, have been reported in the treatment of Graft versus Host Disease (GvHD). Special attention to adequate anticoagulation is advised when treating patients with GvHD.
- 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 Events

- Hypotension may occur during any treatment involving extracorporeal circulation. Closely monitor the patient during the entire treatment for hypotension.
- Transient pyretic reactions, 37.7–38.9 °C (100–102 °F), have been observed in some patients within six to eight hours of reinfusion of the photoactivated leukocyte-enriched blood. A temporary increase in erythroderma may accompany the pyretic reaction.
- Treatment frequency exceeding labelling recommendations may result in anaemia.
- Venous access carries a small risk of infection and pain.

Please refer to the THERAKOS™ CELLEX™ Photopheresis System Operator Manual for a complete list of warnings and precautions.

IMPORTANT SAFETY INFORMATION FOR METHOXSALEN USED IN CONJUNCTION WITH THERAKOS™ PHOTOPHERESIS

Contraindications
Methoxsalen is contraindicated in:

- Patients exhibiting idiosyncratic or hypersensitivity reactions to methoxsalen, psoralen compounds, or any of the excipients
- Patients with co-existing melanoma, basal cell or squamous cell skin carcinoma
- Patients who are pregnant, and sexually active men and women of childbearing potential unless adequate contraception is used during treatment
- Patients with aphakia because of the significantly increased risk of retinal damage to the absence of a lens

Warnings and Precautions

- Special care should be exercised in treating patients who are receiving concomitant therapy (either topically or systemically) with known photosynthesizing agents.
- Oral administration of methoxsalen followed by cutaneous UVA exposure (PUVA therapy) is carcinogenic**.**
- Patients should be told emphatically to wear UVA absorbing, wrap-around sunglasses for twenty-four (24) hours after methoxsalen treatment. They should wear these glasses anytime they are exposed to direct or indirect sunlight, whether

they are outdoors or exposed through a window.
- Safety in children has not been established.

Refer to the package insert for methoxsalen sterile solution (20 micrograms / mL) or the oral 8-methoxpsoralen dosage formulation for a list of all warnings and precautions.

Please refer to the THERAKOS™ CELLEX™ Photopheresis System Operator Manual for a complete list of warnings and precautions and adverse events.

About Extracorporeal Photopheresis (ECP)
ECP, a blood based immunomodulatory therapy developed more than 30 years ago, is recommended by the International Society for Heart and Lung Transplantation (ISHLT)[2] and other clinical societies[3,4,5] as an adjunctive therapy for the prevention and treatment of ACR after heart transplantation. Additionally, ECP may be considered to treat AMR with or without donor specific antibodies.[6,7] In countries where it is approved, ECP is used to treat a range of immune-mediated diseases, including skin manifestations of cutaneous T-cell lymphoma (CTCL), graft-versus-host disease (GvHD), solid organ transplant rejection and other autoimmune diseases. During ECP treatment, a small amount of white blood cells is collected and treated with a drug that is activated by ultraviolet light.

ABOUT MALLINCKRODT
Mallinckrodt is a global business consisting of multiple wholly owned subsidiaries that develop, manufacture, market and distribute specialty pharmaceutical products and therapies. The company's Specialty Brands reportable segment's areas of focus include autoimmune and rare diseases in specialty areas like neurology, rheumatology, hepatology, nephrology, pulmonology, ophthalmology, and oncology; immunotherapy and neonatal respiratory critical care therapies; analgesics; and gastrointestinal products. Its Specialty Generics reportable segment includes specialty generic drugs and active pharmaceutical ingredients. To learn more about Mallinckrodt, visit www.mallinckrodt.com.

CAUTIONARY STATEMENTS RELATED TO FORWARD-LOOKING STATEMENTS
This release contains forward-looking statements, including with regard to THERAKOS ECP, its potential to improve health and treatment outcomes, its potential impact on patients, and the planned presentation regarding the THERAKOS ECP study results. The statements are based on assumptions about many important factors, including the following, which could cause actual results to differ materially from those in the forward-looking statements: the effects of Mallinckrodt's recent emergence from bankruptcy; satisfaction of, and compliance with, regulatory and other requirements; actions of regulatory bodies and other governmental authorities; changes in laws and regulations; issues with product quality, manufacturing or supply, or patient safety issues or adverse side effects or adverse reactions associated with THERAKOS ECP; and other risks identified and described in more detail in the "Risk Factors" section of Mallinckrodt's most recent Annual Report on Form 10-K and other filings with the SEC, all of which are available on its website. The forward-looking statements made herein speak only as of the date hereof and Mallinckrodt does not assume any obligation to update or revise any forward-looking statement, whether as a result of new information, future events and developments or otherwise, except as required by law.

CONTACT

Media Inquiries
Green Room Communications
908-577-4531
mediainquiries@grcomms.com

Investor Relations
Daniel J. Speciale
Senior Vice President, Finance and Chief Financial Officer, Specialty Generics
314-654-3638
daniel.speciale@mnk.com

Derek Belz
Vice President, Investor Relations
314-654-3950
derek.belz@mnk.com

References

[1] Data on File – Ref-07190. Mallinckrodt Pharmaceuticals.
[2] Costanzo MR, et al. The International Society of Heart and Lung Transplantation Guidelines for the care of heart transplant recipients. *J Heart Lung Trans*. 2010:29(8);914–956.

[3] Alfred et al. The role of extracorporeal photopheresis in the management of cutaneous T-cell lymphoma, graft-versus-host disease and organ transplant rejection: a consensus statement update from the UK Photopheresis Society. Br J Haematol. *2017*;177(2):287-310.

[4] Padmanabhan et al. Guidelines on the Use of Therapeutic Apheresis in Clinical Practice - Evidence-Based Approach from the Writing Committee of the American Society for Apheresis: The Eighth Special Issue. *J Clin Apher*. 2019;34:171–354.

[5] Knobler et al. European dermatology forum - updated guidelines on the use of extracorporeal photopheresis 2020 - part 2. *Eur Acad Dermatol Venereol*. 2021;35(1):27-49.

[6] Colvin et al. Antibody-mediated rejection in cardiac transplantation: emerging knowledge in diagnosis and management: a scientific statement from the American Heart Association. *Circulation*. 2015;131(18):1608-1639.

[7] Barten et al. The clinical impact of donor-specific antibodies in heart transplantation. *Transplant Rev (Orlando)*. 2018;32(4):207-217.

Logo - https://mma.prnewswire.com/media/167103/mallinckrodt_plc_logo.jpg