RESEARCH LETTER

Sustained Complete Remission in Sézary Syndrome using Extracorporeal Photopheresis: A Multicentric Case Series

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To the Editor,

Sézary syndrome (SS) is a cutaneous T-cell lymphoma (CTCL) characterized by erythroderma, blood involvement, and poor prognosis (1). Complete remission (CR) was previously only exceptionally reported in SS, e.g., after allogeneic stem cell transplantation (2). Extracorporeal photopheresis (ECP) is an established treatment option for CTCL recommended in various guidelines (3, 4). However, evidence concerning its efficacy is sparse. The objective of this study is to report on patients with SS who have achieved durable CR during ECP, using time-based clinical endpoints.

In this case series, we included patients with SS from Charité-Universitätsmedizin Berlin and University Medical Centre Mannheim who were treated with ECP and have achieved CR.

The patients received ECP as mono- or combination therapy. Clinical evaluations included flow cytometry following EORTC 2018 criteria (5).

Data collection from patients' records was retrospectively carried out from September 2022 to June 2023, followed by descriptive statistics. Missing data were not considered in the analysis. Response criteria were evaluated for skin and blood separately and globally, respecting definitions from Olsen et al. (1) with time to response (TTR), relapse-free survival (RFS), time to progression (TTP), and time to next treatment (TTNT).

Patient characteristics and time-based response criteria are presented in **Table I**.

Eight patients were identified with a female/male ratio of 1/3 and mean age of 59 years at diagnosis. Mean follow-up period was 71 months (22–124). Six patients

Table I. Clinical characteristics and time-based response criteria of patients with Sézary syndrome treated with extracorporeal photopheresis leading to durable complete remission

	Patients							
Parameters	1	2	3	4	5	6[a]	7	8
Sex	w	w	w	w	w	w	m	m
Age at diagnosis	38	46	54	66	68	79	53	71
Diagnostic latency (years)	14	3	–	1	10	5	9	1
TNMB at diagnosis	T4NXM0B2	T4N0M0B2	T4N2MXB2	T4bNXM0B2b	T4aN1aM0B2	T4N2M0B2	T4NXM0B0	T4N0M0B2
ISCL-/EORTC classification	IVA1	IVA1	IVA1	IVA2	IVA1	IVA2	IVA1	IVA1
Number of relapses	0	2	0	1	0	1	0	0
Follow-up (months)	97	124	120	76	33	33	22	62
First line	ECP	ECP	ECP	ECP[b]	ECP[b]	ECP	ECP, Methotrexate[b]	ECP[b]
Second line	ECP, IFN-alpha[b]	Bexarotene, ECP[b]	ECP, IFN-alpha	ECP, IFN-alpha	–	Bexarotene, ECP[b]	–	–
Third line	ECP	Bexarotene	Acitretin, ECP, IFN-alpha	–	–	–	–	–
Fourth line	–	Bexarotene, ECP	ECP, IFNa-alpha[b]	–	–	–	–	–
Fifth line	–	–	ECP	–	–	–	–	–
Subsequent treatments	–	Bexarotene, pegIFNa	–	Mogamulizumab	–	Mogamulizumab	–	–
Time to response (skin), months	67	3	–	61	2	8	3	3
Time to response (blood), months	93	21	56	31	3	10	1	29
Response duration, months	–	–	–	5	–	9	–	–
Relapse-free survival, months	–	86	–	3	–	9	–	–
Time to progression, months	–	–	–	66	–	24	–	–
Time to next treatment[c], months	67	18	22	70	30	11	20	60

The time-based criteria were assessed following recommendations from Olsen et al. (1).
[a]This patient died 33 months after both time of diagnosis and initiation of ECP. [b]This treatment line was the one to achieve complete remission in both skin and blood, resulting in global complete remission for the first time. [c]The depicted time to next treatment corresponds to the treatment line, after which complete remission in both skin and blood was assessed for the first time.
m: male; w: female; TNMB: tumour, node, metastasis, and blood for staging regarding disease involvement according to Olsen et al. (1) and Scarisbrick et al. (5); X: unknown status regarding TNMB stage; ISCL-/EORTC classification: International Society for Cutaneous Lymphomas/ European Organization for Research and Treatment of Cancer – classification regarding staging according to Olsen et al. (1); First line: First treatment line the patient received; Second line: Second treatment line the patient received; Third line: Third treatment line the patient received; Fourth line: Fourth treatment line the patient received; Fifth line: Fifth treatment line the patient received; ECP: extracorporeal photopheresis; IFN-alpha: interferon-alpha; pegIFN-a: pegylated interferon alpha-2a; –: not available, no event, or not possible to calculate due to missing data.

were initially staged with IVA1 and 2 with IVA2. Four patients received other treatment lines prior to ECP.

Both ECP mono- and combination therapy (with acitretin, bexarotene, or interferon-alpha), were applied. Patients were treated biweekly, expanded up to intervals of 8 weeks or longer as part of maintenance therapy (3). Five patients received combination therapy after ECP monotherapy. Subsequent therapies after ECP included mogamulizumab, bexarotene, and pegylated interferon alpha-2a. Five patients underwent continuous ECP with prolonged schemes as maintenance therapy.

TTR in skin was mean 21 months (standard deviation [SD] 30; range 2–67 months) and in blood 31 (31; range 1–93) months. Global TTR was 36 (31; range 1–93) months. ECP had a TTNT of 37 (24; range 11–70] months. RFS was 33 (46; range 3; 9; 86) months. TTP was 45 (30; range 24; 66) months.

During the disease course, 1 patient relapsed in both skin and blood, 1 in skin only, and 1 in blood only. One patient died 33 months after diagnosis and initiation of ECP.

To our knowledge, this is the first case series to report on durable complete remission after ECP in SS.

Studies have shown CR rates varying from 0 to 36% in SS (Table SI). Differences in these rates could be due to different study populations (6), varying definitions of SS (6), various assessment processes, different treatment schemes of ECP, and varying definitions of response criteria (1).

A limitation of this study is the retrospective nature. We purposely report on selected patients. Hence, we cannot describe the percentage of patients with CR among all patients with SS who underwent ECP.

We uniquely showed that patients not only have achieved CR, but also have sustained CR. These results are supported by other recent multicentric reports on TTNT and overall survival (7, 8).

This is the first report on the possibility of durable complete remission with long relapse-free survival, highlighting the importance of ECP. Based on time-based clinical endpoints, we consider ECP a substantial and potent treatment option for SS. We observed earlier complete remission in skin than in blood. These findings may support clinical decision-making and optimize patient information.

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Informed consent was obtained from all participants.

Conflict of interest disclosures: GD and JPN received speakers' honoraria from Mallinckrodt Therakos. The other authors have no conflicts of interest to declare.

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