Single-center experience of using pegylated liposomal doxorubicin as maintenance therapy in mycosis fungoides

Daniel Falkenhain-López, Jon Fulgencio-Barbarin, Mario Puerta-Peña, Alba Sánchez-Velázquez, Pablo Luis Ortiz-Romero
Department of Dermatology, Hospital Universitario 12 de Octubre, Madrid, Spain

Primary cutaneous T-cell lymphomas (CTCL) are characterized by a clonal accumulation of T cells in the skin. Mycosis fungoides (MF) is the most common subtype. **Advanced forms** of MF lead to a decrease of the patients 5-year overall survivor. Consequently, more aggressive systemic therapies are needed for a better control of advanced disease and **maintenance strategies** seem to be advisable for a good management of these patients.

Doxorubicin is an anthracycline with antineoplastic activity in patients with non-Hodgkin lymphoma. **We report our experience using pegylated-doxorubicin (Caelyx®) as a maintenance strategy for advanced-stage MF, describing 18 patients** from our centre who continued to receive doxorubicin following the initial response (partial/total) in at least one compartment: skin, visceral, nodal involvement and/or blood. 18 patients (12 men, 6 women) were treated with pegylated liposomal **doxorubicin 20mg/m^2**, tipically biweekly (in maintenance prolonged to every 3 and 4 weeks in some patients) receiving **between 15 and 37 infusions**.

All the patients were previously treated with at least one systemic therapy (oral/intravenous drugs and/or total radiotherapy) due to advanced MF. Patients' characteristics and response to treatment are shown in **Table 1**.

Skin disease improvement was achieved in 77% of patients. Regarding the patients with nodal (N3) and blood involvement, a response was observed in 2/4 and 3/5 cases respectively. The **median (interquartile range) of response parameters** in weeks were:
- Time to response: 12 (21-7=14)
- Time to best response: 24 (29-11=18)
- Response duration: 47.5 (65-34=31)
- Time to next treatment: 55 (70-36=34)
- Survival: 160 (182-61=121)

Caelyx® was well tolerated, without relevant cardiotoxicity or other adverse events. **Lymphopenia** was the most common adverse effect (n: 8), leading to doxorubicin interruption only in one case

Sex, age (Caelyx® onset), comorbidities	Disease, stage (Caelyx® onset)	Response				Number of infusions, TIT	TTR (w)	TTBR (w)	Response duration (w)	TTNT (w)	Survival (m)	AE	Discontinuation
		T	N	M	B								
Male, 72	MF IVB (T3N0M1B0)	SD	NI	PR	NI	29, 87w	30	30	54	ND	25	Lower limbs edema	Yes (skin PD)
Male, 73	MF IVA.1 (T4N2M0B2)	PR	NI	NI	SD	25, 50w	20	28	32	-	8	Cytopenias	Yes (decease)
Male, 70. CKD, COPD	SS IVA.1 (T4N0M0B2)	SD	NI	NI	SD	22, 45w	-	-	-	52	36	Lymphopenia	Yes (severe lymphopenia)
Male, 34	MF IVA.2 (T3N3M0B0)	CR	CR	NI	NI	22, 54w	6	10	49	55	>42	-	Yes (CR)
Male, 52. Melanoma	MF IIB (T3N0M0B0)	PR	NI	NI	NI	29, 71w	26	33	70	ND	17	Disgeusia	Yes (melanoma metastasis)
Male, 81. CKD	MF IIB (T3N1M0B0)	SD	NI	NI	NI	17, 34w	-	-	-	12	42	-	Yes (SD)
Male, 44	MF IIB (T3N0M0B0)	PR	NI	NI	NI	26, 62w	10	22	>52	>62	>13	Lymphopenia	No
Male, 34	MF IIB (T3N1M0B0)	CR	NI	NI	NI	15, 40w	10	17	46	41	13	-	Yes (CR)
Female, 65	MF IVA.2 (T2bN3M0B2)	PR	CR	NI	PR	30, 61w	16	26	>45	>61	>14	-	No
Female, 36	MF IIB (T3N1M0B0)	PR	PD	NI	NI	27, 69w	10	10	36	55	47	-	Yes (nodal PD)
Female, 57	MF IIB (T3N0M0B0)	PR	NI	NI	NI	17, 35w	8	14	22	32	41	Lymphopenia	Yes (skin PD)
Female, 73	MF IVA.1 (T4N0M0B2)	SD	PD	NI	PR	18, 54w	4	4	60	70	43	Lymphopenia	Yes (nodal PD)
Male, 33	MF IIA (T2bN1M0B0)	PR	PD	NI	NI	18, 36w	4	12	28	36	24	Erythrodysestesia	Yes (nodal PD)
Male, 54. Aortic stenosis	MF IIB (T3N0M0B0)	CR	NI	NI	NI	19, 38w	22	32	44	59	38	Erythrodysestesia	Yes (skin PD)
Male, 70. ET	MF IIB (T3N0M0B0)	CR	NI	NI	NI	22, 44w	14	26	76	143	>58	Erythrodysestesia Lymphopenia	Yes (CR)
Male, 66	MF IVA.2 (T4N3M0B0)	CR	SD	NI	NI	17, 34w	22	28	108	138	>41	Lymphopenia	Yes (skin CR)
Female, 44	MF IVA.2 (T3N3M0B2)	PR	SD	NI	PR	15, 32w	6	10	22	28	5	Lymphopenia, infusion reaction	Yes (skin PD)
Female, 69	MF IIIA (T4N0M0B0)	CR	NI	NI	NI	37, 196w	32	44	>152	>196	>56	Low-grade neutropenia	No

Table 1: Characteristics and demographics of patients under maintenance therapy with doxorubicin. CKD: chronic kidney disease; CPOD: chronic pulmonary obstructive disease; MF: mycosis fungoides; SS: Sézary syndrome; ET: essential thrombocytosis; CR: complete response; PR: partial response; SD: stable disease; PD: progression disease; TIT: time in treatment; NI: not involved; ND: no data; w: weeks; m: months; TTR: time to response; TTBR: time to best response; TTNT: time to next treatment; AE: adverse events.

In our experience, following the **good response in skin** (77%) and the **absence of severe adverse effects**, pegylated liposomal doxorubicin seems to be a **valuable and safe option in the maintenance treatment of primary CTCL**. Interestingly, seven patients have been on treatment for **more than 1 year**, being doxorubicin discontinued in four of them. The other three patients remain under treatment (13, 14 and 56 months at this moment, cumulative doses of 520, 600 and 740 mg/m^2), presenting good **disease control without adverse effects**.

We hope that our real-world clinical experience will contribute to a better characterization of the PEG-DOXO treatment in MF, although more studies are needed for a stronger definition of its role in the MF maintenance therapy.

Bibliography:
- Jawed SI, Myskowski PL, Horwitz S, Moskowitz A, Querfeld C. Primary cutaneous T-cell lymphoma (mycosis fungoides and Sézary syndrome): part II. Prognosis, management, and future directions. J Am Acad Dermatol. 2014 Feb;70(2):223.e1-17; quiz 240-2. doi: 10.1016/j.jaad.2013.08.033. PMID: 24438970.
- Stadler R, Scarisbrick JJ. Maintenance therapy in patients with mycosis fungoides or Sézary syndrome: A neglected topic. Eur J Cancer. 2021 Jan;142:38-47. doi: 10.1016/j.ejca.2020.10.007. Epub 2020 Nov 17. PMID: 33217680.
- Dummer R, Quaglino P, Becker JC, et al. Prospective international multicenter phase II trial of intravenous pegylated liposomal doxorubicin monochemotherapy in patients with stage IIB, IVA, or IVB advanced mycosis fungoides: final results from EORTC 21012. J Clin Oncol. 2012 Nov 20;30(33):4091-7. doi: 10.1200/JCO.2011.39.8065. Epub 2012 Oct 8. PMID: 23045580.
- Wollina U, Dummer R, Brockmeyer NH, et al. Multicenter study of pegylated liposomal doxorubicin in patients with cutaneous T-cell lymphoma. Cancer. 2003 Sep 1;98(5):993-1001. doi: 10.1002/cncr.11593. PMID: 12942567.