Oncology
and Radiotherapy ©
17 (6) 2023: 241-243 • RESEARCH ARTICLE

Paclitaxel as first or second line treatment for Kaposi's sarcomas: A retrospective study from the north-east of Morocco

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ABSTRACT

Introduction: Paclitaxel has recently been approved for AIDS-related Kaposi's Sarcoma (KS) and there is much interest also in HIV-negative KS. In our study we aimed to report the activity and safety data of paclitaxel from a cohort of patients from the north east of Morocco.

Patients and Methods: A retrospective analysis of our departmental database from January 2010 to December 2018 was performed. Histologically proven KS cases were recorded. Patients, tumour characteristics, treatment and outcome were analysed.

Results: 16 patients were identified. KS represents 0,13% of all oncology admissions. The mean age at diagnosis was 67 years (+/-17,8) with a sex ration of 3:1. Among these patients 14 had a classic KS, and 2 were HIV-positive. The most common primary site was the lower limbs (50%). The involvement of lymph nodes, mucosa, and/or visceral organs has been registered in 31, 25%, 12,5%, and 37,5% respectively. There were 13 disseminated stage IV patients and 3 stage III. 4 patients underwent radiotherapy. 6 patients received intravenous paclitaxel 100 mg weekly as first-line treatment, whereas 3 received paclitaxel as second line treatment after failure of other regimens (Bleomycin (B), doxorubicin (A), or ABV (V=Vinblastine). Most common side effects were grade 1-2 neutropenia, anaemia, and asthenia. 8/9 patients were evaluable, 6/8 patients achieved a PR, one CR, and one SD. No PD was observed under paclitaxel after a median follow-up of 27 months, while 40 % of patients treated with other regimens relapsed after a mean of 11,5 (+/- 7,85) months.

Conclusion: KS is a very rare disease in the north east of Morocco. Classic type is the most common. Low dose weekly Paclitaxel seems to be effective as a first line chemotherapy and second line as well, for both classic and HIV- positive form, with a very good toxicity profile.

Key words: paclitaxel, kaposi, sarcoma, retrospective study

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Word count: 2152 **Tables:** 02 **Figures:** 00 **References:** 19

Received:- 25 May, 2023, Manuscript No. OAR-23-99951

Editor assigned: - 28 May, 2023, Pre-QC No. OAR-23-99951 (PQ)

Reviewed:- 19 June, 2023, QC No. OAR-23-99951 (Q)

Revised: - 22 June, 2023, Manuscript No. OAR-23-99951 (R)

Published: - 25 June, 2023, Invoice No. J-99951

INTRODUCTION

Kaposi's Sarcoma (KS) is an angio-proliferative disease, defined as a neoplasm of blood or lymph vessels with nodules in the skin or other organs [1]. There are four epidemiological forms of KS: AIDS-Associated KS, classic KS affecting typically elderly men of Mediterranean origin, the endemic presence in Southern Africa, and the Iatrogenic form observed in the organ transplant receivers [1-4]. Cytotoxic chemotherapy is effective in treating patients with Kaposi Sarcoma; it is generally warranted for disseminated, symptomatic or progressive KS. Several cytotoxic agents have been approved, among them; Taxanes have been used for their antiproliferative activity. Paclitaxel has recently been approved for AIDS-related Kaposi's Sarcoma (KS) and there is much interest also in HIV-negative KS [5-10]. In our study we aimed to report the activity and safety data of paclitaxel from a cohort of patients from the north east of Morocco.

PATIENTS AND METHODS

Clinical and histopathological data of a total of 16 patients diagnosed with Kaposi sarcoma, at the medical oncology department of Hassan II university hospital, between January 2010 and December 2018, were retrospectively analysed.

Patient's age, gender, tumour localization, secondary sites, therapy administered, follow up time and side effects were recorded based on patients' medical files.

Patients were divided into paclitaxel users and non-paclitaxel users whether as first or second line therapy.

The staging of the disease was based on Brambilla et al. classification (Table 1) [11].

RESULTS

16 patients were identified which represent 0,13% of all medical oncology admissions.

The mean age at diagnosis was 67 years (+/-17,8). 12 patients were men (75%) and 4 were women (25%) with a sex ration of 3:1. Among these patients 14 had a classic KS (87,5%), and 2 were HIV-positive (12,5%).

There were 13 disseminated stage IV patients, 2 stage III, and one patient was stage II.

The most common primary site at diagnostic was the lower limbs

Tab. 1. Staging of Kaposi sarcoma

Stage	Prevalent skin lesion	Behavior	Evolution	Complications
I Macular/nodular	Macules and/or nodules	Non aggressive (mostly limbs)	Slow (A)	Lymphoedema
			Rapid (B)	Lymphoerrhoea
II Infiltrative (± V)	Infiltrative plaques	Locally aggressive (mostly limbs)	Slow (A)	Hemorrhage
			Rapid (B)	Pain
III Florid (± V)	Angiomatous nodules and plaques	Locally aggressive (mostly limbs)	Slow (A)	Ulceration
			Rapid (B)	Functional Impairment
IV Generalized (± V)	Angiomatous nodules and plaques	Disseminated agressive	Slow (A)	No
			Rapid (B)	No

(50%). 3 patients had lesions localized in the upper extremities (18,75%). 2 patients had lesions on the trunk while one other patient had lesions located in the penis.

The involvement of lymph nodes, mucosa, and/or visceral organs has been registered in 31, 25%, 12, 5%, and 37,5% respectively.

14/16 patients underwent systemic therapy while active surveillance was indicated in 2 patients.

5 patients received intravenous 100 mg weekly Paclitaxel as first-line treatment, whereas 4 received paclitaxel as second line treatment after failure of other regimens (Bleomycin (B), doxorubicin (A), or ABV (V=Vinblastine).

In the Paclitaxel users subgroup, 8/9 patients were evaluable, 5/8 patients achieved a Partial Responses (PR), one Complete Response (CR), and two Stable Diseases (SD). No Progressive Disease (PD) was observed under paclitaxel after a median follow-up of 27 months, while 40% of patients treated with other regimens relapsed after a mean of 11,5 (+/- 7,85) months (Table 2).

Most common side effects were grade 1- grade 2 neutropenia, anaemia, and asthenia. In the non-Paclitaxel user's subgroup, three patients developed adverse events. We registered one Grade IV neutropenia under Doxorubicin, one Grade II anaemia under AV, and one patient developed a restrictive syndrome under bleomycin. While in the paclitaxel subgroup, there were 3 Grade I anaemias, 3 grade I neutropenia, and one patient developed a grade I neuropathy.

DISCUSSION

Cytotoxic chemotherapy is effective on Kaposi Sarcomas. It is generally warranted for disseminated, symptomatic or progressive KS [12].

It has been recently proved, by immune-histochemical analyses that Bcl-2, a proto-oncogene that antagonize apoptosis and prolongs cellular viability, is highly expressed in both classic and AIDS-associated KS [13].

Paclitaxel is a microtubule stabilizing drug, highly effective against several tumours, that is known to inhibit the anti-apoptotic activity of Bcl-2 [14]. It has been recently evaluated in the treatment of KS.

In 2002, a multi-centre phase II study, which enrolled 147 patients, evaluated the activity of low-dose Paclitaxel as second line in patients with advanced AIDS-related KS, it has shown that Paclitaxel induces major tumour regression in the majority of patients; this was associated with significant quality of life improvement and acceptable toxicity [8].

In 2006, Taxanes were tested in patients with non-AIDS-related KS. All patients improved after chemotherapy, with good tolerance except for 3 episodes of Grade 3 or 4 neutropenia and 1 episode of moderate myositis [15].

In a study published in 2008, which evaluated the clinical efficacy and tolerability of paclitaxel in a homogeneous group of 17 patients with advanced aggressive and refractory classic KS, Brambilla et al. showed that low dose Paclitaxel was effective and well tolerated.

A partial/complete response was achieved in 14 of 17 patients [16].

In 2010, a randomized trial compared Paclitaxel to liposomal Doxorubicin as first line chemotherapy in patients with AIDS associated KS. Both, Paclitaxel and pegylated liposomal doxorubicin appeared to be active first line agents, producing comparable clinical outcomes [7].

A case report published in 2012, showed a complete remission of a classic KS under first line paclitaxel, with no significant side effects [17].

A study published in 2015, which aimed to compare Paclitaxel to other chemotherapeutic regimens, in term of efficacy and side effects showed no significant difference in efficacy between Paclitaxel and other regimens, with borderline statistical significance in the occurrence of neuropathy [18].

In a recent guideline published in June 2019, written under the auspices of the European Dermatology Forum (EDF), the European Association of Dermato-Oncology (EADO), and the European Organization of Research and Treatment of Cancer (EORTC), the recommended first-line agents for aggressive, extensive and disseminated KS are pegylated liposomal doxorubicin and paclitaxel [19].

In our study, Paclitaxel have showed good tolerance and efficiency

Tab. 2. Disease control under paclitaxel and non-paclitaxel regimens

	First line		Second line	
	Paclitaxel	Other regimens	Paclitaxel	Other regimens
Stable Disease	1	4	1	1
Partial Response	3	3	2	0
Complete Response	1	0	0	0
Progressive Disease	0	4	0	0
Disease control rate	100%	63%	100%	100%
Clinical Benefit Rate	80%	27%	75%	0%

in our context.

No progressive disease was registered under Paclitaxel even as first or second line chemotherapy, while complete/partial response was achieved in 6 of 8 evaluable patients, with a clinical benefit rate of 80% and a disease control rate of 100% in first line, whereas, in second line, the disease control rate was 100% and the clinical benefit rate was 75%.

CONCLUSION

In conclusion, KS is a very rare disease in the north east of Morocco. Classic type is the most common. Low dose weekly Paclitaxel seems to be effective as a first line chemotherapy and second line as well, for both classic and HIV positive form, with a good toxicity profile.

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