

## HEALTHCARE DELIVERY

# Kaposi's sarcoma: Good outcome with doxorubicin, bleomycin and vincristine sulphate (ABV) chemotherapy and highly active antiretroviral therapy

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There is little published information on effective treatment of Kaposi's sarcoma (KS) in children in low-income countries. We prospectively treated 12 patients with an institutional review board-approved protocol consisting of four monthly courses of doxorubicin (Adriamycin), bleomycin and vincristine sulphate (ABV), with highly active antiretroviral therapy (HAART) plus co-trimoxazole prophylaxis for those who were HIV-positive, with additional vincristine if remission was not achieved after 4 months. Maintenance HAART plus co-trimoxazole was given to all HIV-positive patients. A fine-needle aspirate and CD4+ count were done if possible, and staging was performed according to Mitsuyasu. Eight of ten HIV-positive patients with stage III - IVB disease, and both HIV-negative patients with stage I disease, were in remission after 473 - 1 490 (mean 939) days. One patient died after absconding during treatment, and one died from neutropenia-related pulmonary infection. ABV with or without HAART is an effective treatment option for children with KS.

*S Afr Med J* 2017;107(11):952-953. DOI:10.7196/SAMJ.2017.v107i11.12559

There is a memorandum of understanding between the Department of Paediatrics at Tygerberg Children's Hospital, Cape Town, South Africa (SA), and the Cameroon Baptist Hospitals in Cameroon to support the Cameroon Baptist Hospitals' paediatric oncology programme. A recent Cochrane review found a lack of information on the effective treatment of Kaposi's sarcoma (KS) in children with chemotherapy and highly active antiretroviral therapy (HAART).<sup>[1]</sup> Published treatment guidelines for the management of KS in resource-limited settings include chemotherapy with the single drugs etoposide, thalidomide and vincristine, with two drugs, namely vincristine and bleomycin, and with three drugs, namely doxorubicin (Adriamycin), bleomycin and vinblastine sulphate.<sup>[2]</sup> An SA multi-institutional review of HIV-positive children treated with HAART and unspecified chemotherapy schedules reported a 58% projected 5-year survival rate.<sup>[3]</sup> In Malawi the combination of vincristine plus bleomycin resulted in a 50% 1-year survival rate.<sup>[4]</sup> We report the outcome of a prospective study in children with KS in Cameroon treated with ABV, together with HAART for those who were HIV-positive. This combination of drugs was chosen because they have individual activity against KS, and because they were available in this resource-limited setting.

## Methods

All patients diagnosed with KS at Bango, Mbingo and Mutengene Baptist hospitals in north-west and south-west Cameroon between October 2011 and August 2015 were staged according to Mitsuyasu.<sup>[5]</sup> Treatment was with an institutional review board-approved protocol consisting of doxorubicin 10 mg/m<sup>2</sup>, bleomycin 15 IU/m<sup>2</sup> and vincristine 1.5 mg/m<sup>2</sup> intravenously (ABV) every 4 weeks for four cycles. Chemotherapy commenced 4 weeks after

the initiation of HAART, which was continued indefinitely in HIV-positive patients together with daily co-trimoxazole prophylaxis. HAART consisted of triple antiretrovirals adapted for age and weight according to World Health Organization guidelines. Chemotherapy was given at 4-week intervals to limit toxicity. Vincristine 1.5 mg/m<sup>2</sup> was continued every 4 weeks for four doses if remission was not achieved. A fine-needle aspirate (FNA) and CD4+ count were recommended investigations. Informed parental consent was obtained. Follow-up was achieved by outpatient visits, telephone calls and home visits. Treatment was free.

## Results

Twelve patients, 10 boys and 2 girls aged 2 - 11 (median 7) years, were treated. Two HIV-negative patients presented with a localised skin lesion and localised lymphadenopathy, respectively. The HIV-positive patients presented with stage III (*n*=3), IVA (*n*=3) and IVB (*n*=4) disease. An FNA was performed in 7 patients, and a CD4+ count in 7 (median 144 (range 11 - 946) cells/μL). One HIV-negative patient received additional vincristine. Two deaths occurred, both in HIV-positive patients. One died from febrile neutropenia and pulmonary disease on day 48, while the other did not return after two courses of ABV, his family deciding in favour of traditional medicine, and died of progressive KS on day 390. Both these patients had a CD4+ count of <100/μL. Eight HIV-positive patients were in remission after 1.5 - 50 (median 30) months' follow-up at the time of writing, and the 2 HIV-negative patients were in remission after 19 and 37 months' follow-up, respectively. Table 1 sets out details of age, sex, stage, FNA, CD4+ count, treatment and outcome (December 2016). No patients were lost to follow-up.

**Table 1. Clinical and laboratory findings in children with Kaposi's sarcoma**

Case	Age (yr), sex	Stage	HIV	CD4+ count (cells/μL)	FNA	Treatment	Status	Follow-up (mo)
1	7, M	I	-		KS	ABV	CR	37
2	6, M	IVB	+	240	KS	HAART/ABV	CR	44
3	7, M	IIIB	+	27	NT	HAART/ABV	CR	24
4	6, M	IVB	+	11	KS	HAART/ABV	Died	13
5	7, F	IIIB	+	144	KS	HAART/ABV	CR	49
6	2, M	IVB	+	NT	KS	HAART/ABV	CR	50
7	7, M	IVB	+	946	KS	HAART/ABV	CR	22
8	4, M	IVA	+	54	NS	HAART/ABV	Died	1.5
9	11, M	I	-		NT	ABV+	CR	19
10	9, M	IIIB	+	NT	NT	HAART/ABV	CR	49
11	12, M	IVB	+	NT	NT	HAART/ABV	CR	36
12	11, F	IVB	+	619	NT	HAART/ABV	CR	16

FNA = fine-needle aspirate; M = male; F = female; - = negative; + = positive; NT = not tested; NS = nonspecific; ABV = doxorubicin (Adriamycin), bleomycin and vincristine sulphate; HAART = highly active antiretroviral therapy; ABV+ = extended vincristine; CR = complete remission.

### Discussion

Although the incidence of KS in some African countries is decreasing because of HAART, it remains an important cause of childhood cancer.<sup>6]</sup> No effective chemotherapy for patients in low-income countries has been published to date. We used the above chemotherapy agents because of their individual efficacy and their availability. Although the number of patients is small, treatment with ABV with or without HAART achieved good medium-term survival in HIV-positive and HIV-negative patients, with one possible treatment-related death.

### Conclusion

Four cycles of ABV plus HAART in HIV-positive patients achieved good medium-term survival in patients with KS.

**Acknowledgements.** The authors thank research nurses Patience Nfor and Comfort Kimbi for data collection.

**Author contributions.** All the authors were actively involved in protocol design, patient diagnosis and management and the preparation of the manuscript.

**Funding.** Funding was received from the Swiss Cancer League, Beryl Thyer Memorial Africa Trust and World Child Cancer.

**Conflicts of interest.** None.

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Accepted 28 July 2017.