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Completion of and early response to chemoradiation among HIV-positive and HIV-negative patients with locally advanced cervical carcinoma in South Africa:

A retrospective cohort study

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Abstract

Background—Very few published studies have dealt with the management of locally advanced cervix carcinoma among HIV-positive patients. The objective was to compare the clinical characteristics, radiation and chemotherapy treatments, and outcomes in a cohort of HIV-positive and –negative women with cervical cancer.

Methods—We reviewed the charts of 59 HIV-positive patients and 324 HIV-negative patients with stage IBI – IIIB cervical carcinoma, who received radiation therapy. We compared demographic and clinical characteristics at diagnosis and radiation dose, chemotherapy cycles, and response at time of brachytherapy and six-week follow-up. We developed logistic regression models of response to treatment.

Results—49 (88.1%) of the HIV-positive patients but only 213 (65.7%) HIV-negative patients presented with stage IIIB disease ($p=0.009$). 47 (79.7%) HIV-positive patients and 291 (89.8%) HIV-negative patients completed the equivalent radiation dose of 68Gy EBRT and HDR brachytherapy ($p=0.03$). Of the 333 patients who commenced concurrent chemotherapy, 26 (53.1%) HIV-positive patients and 212 (74.6%) HIV-negative patients completed four or more weekly cycles of platinum-based treatment. Follow-up was censored at six weeks. In models that included age, stage, HIV status, and treatment, poor response at six weeks was associated only

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with having stage IIIB disease (OR=2.39, 95% CI 1.45 – 3.96) and receiving less than 68Gy EQD₂ radiation (OR=3.14, 95% CI 1.24 – 7.94).

Conclusions—HIV-positive patients fared worse than HIV-negative patients due to later presentation and a decreased likelihood of completion of treatment. Our findings emphasise the importance of completing irradiation therapy. Further studies will address the association of these variables with survival.

Keywords

cervical cancer; HIV-positive; AIDS-defining malignancy; radiation; chemoradiation

Introduction

Cervical cancer is the second most common cancer in women worldwide and the most common malignancy in young women in sub-Saharan Africa. In South Africa, women have a 4 percent lifetime risk of developing the disease¹. One out of six women of reproductive age in the Western Cape in South Africa is living with HIV². HIV-positive patients have a greater persistence of the human papillomavirus (HPV), a greater likelihood of developing high-grade cervical intraepithelial neoplasia, and ultimately a more rapid progression to invasive cervical carcinoma than women without HIV³. Highly effective anti-retroviral therapy (HAART) prolongs survival among women with HIV, but does not appear to prevent them from developing cervical carcinoma; therefore, the increasing availability of HAART is paradoxically likely to lead to a rise in the incidence of cervical carcinoma⁴.

Most cervical carcinoma patients in South Africa present at an advanced stage precluding the use of surgery. In 1999, several studies reported that chemoradiation was superior to radiation alone, the prior standard of care for women with locally advanced cervical carcinoma⁵⁻⁸. A meta-analysis confirmed that the combination of chemotherapy and radiation therapy was associated with improved survival for patients with stage IB2-IVA cervical cancer⁹. Chemoradiation is now the standard of care, where resource constraints allow, in South Africa.

However, no published studies have focused on the management of HIV-positive patients treated with chemoradiation for locally advanced cervical carcinoma. The randomized trials of chemoradiation reported to date have excluded women with HIV. Randomized studies currently under way are intended to address this question. The potential risks of treating HIV-positive patients with chemoradiation include the additional risk of infectious morbidity due to immunosuppression and drug interactions between HAART and chemotherapy including gastrointestinal toxicities and severe skin reactions.

Although data regarding the tolerance of chemoradiation are lacking for HIV-positive women with cervical cancer, chemotherapy has now been incorporated into their treatment. The objective of our study was to compare the clinical characteristics, treatments, and outcomes of HIV-positive and –negative women with advanced cervical cancer.

Materials and Methods

Tygerberg Hospital is a state-funded public hospital in the Western Cape. It provides state oncology services to patients from the remote and rural areas of the province, urban Cape Town, and the suburban area close to the hospital. Most patients seen at the hospital have little education, limited incomes, difficulties accessing care, and co-morbidities. The hospital's oncology resources for cervical carcinoma patients are comparable to those of many tertiary care facilities in Europe and the United States; they include a full surgical

gynaecological oncology unit, access to chemotherapy and modern radiation machines with CT planning and conformal techniques. Since 2007, HAART has been widely available in the province, and HIV-positive patients have access to medication and expertise from the infectious diseases department.

Patient records

We performed a retrospective study of all women diagnosed with invasive cervical cancer between June 2007 and December 2010. Patients included in the study were those who were diagnosed with histologically confirmed cervical cancer FIGO Stage IBi to IIIB and were treated with curative intent. Patients with early-stage disease who underwent primary surgery were excluded.

Approval for the study was obtained from the Stellenbosch University ethics committee.

Patients were stratified into two cohorts based on HIV status: HIV-positive and HIV-negative. Clinical and demographic characteristics were extracted from institutional databases. Among HIV-positive patients, prior use of HAART and CD4 cell counts at the start of treatment were documented. Disease characteristics included tumor histology; evidence of hydronephrosis; nodal involvement as detected by abdominal ultrasound or computed tomography (CT); stage; and chemoradiation treatment regimen. Treatment variables included external beam radiation therapy (EBRT) dose and fractionation; number of chemotherapy cycles; high dose rate brachytherapy (HDR) or external beam boost dose and fractionation; and overall treatment time for those who completed prescribed EBRT and HDR radiation. The total dose of EBRT and HDR radiation received was calculated using EQD₂ equations¹⁰. Reasons for incomplete radiation and/or chemotherapy were noted, when available. Response data were collected at time of examination under anaesthetic (EUA) for brachytherapy planning, and at clinical examination at six-week follow-up in the clinic.

Treatment

The standard treatment protocol at our institution for patients with locally advanced Stage IB2 to IIIB cervical carcinoma is 46-50Gy in 23-25 fractions of EBRT delivered to the pelvis, with concurrent weekly cisplatin chemotherapy at a dose of 40mg/m² for four to six cycles, and HDR brachytherapy 20-26Gy in four to five fractions starting in week five of EBRT¹¹. The cervix, uterus, parametrium and pelvic lymph nodes up to, and including, the common iliacs are delineated on a planning CT scan following the guidelines of Taylor et al¹². The para-aortic nodes (PAN) are delineated up to the renal hilum if the common iliacs or lower para-aortic nodes are involved on imaging. This volume is then conformally planned on the XiO planning system. The department protocol is EBRT 2Gy per fraction five days a week, or alternatively 1.8Gy per fraction if the patient has a history of abdominal surgery, is HIV-positive, or has a PAN field. The PAN field receives 45Gy and the pelvic field receives 50.4Gy. Patients who have a poor performance status or very advanced local disease with bilateral hydronephrosis or renal compromise are prescribed 40.05Gy in 15 fractions at 2.67Gy per fraction. Treatment is delivered on an 18MV linear accelerator with multi-leaf shielding capabilities. During or after the fifth week of EBRT, each patient is examined under anaesthetic (EUA) and her cancer is categorized as having a complete response, CR or a partial response, PR. A smit sleeve is then placed in the cervical os, and high-dose rate (HDR) brachytherapy is planned; with a standard plan straight source to a total dose of 20 to 26Gy in four to five fractions¹³. The dose is delivered on a Varian GammaMed machine. Overall treatment time recommended is 55 days or less as per the American Brachytherapy Society (ABS)¹¹.

Chemotherapy is prescribed based on evaluation of renal function prior to treatment. The creatinine clearance (cGFR) is calculated using the Cockcroft Gault formula, or when available an EDTA-GFR. If the cGFR or EDTA-GFR is 60ml/min or more, weekly cisplatin 40mg/m² for a minimum of four cycles is prescribed; if 50-60ml/min, the dose is reduced by 25% per cycle, and if <50ml/min, cisplatin is not given. If the GFR is 30-50ml/min, carboplatin weekly at a dose of AUC2 is given as an alternative. The regimen consists of pre-chemotherapy anti-emetics, cisplatin diluted in 250ml normal saline given over 15 minutes, followed by 1000ml of normal saline over two hours, and 20mg of oral furosemide. In 2009, an additional 1000ml of pre-hydration was added to the regimen. Chemotherapy is delayed if the neutrophil count falls below 1,000/ μ L; the platelet count falls below 75,000/ μ L; or the patient develops grade III gastrointestinal (GIT) toxicity. Chemotherapy is discontinued if the cGFR falls below 50ml/min or increases by >50%; the neutrophil or platelet count does not recover; or the patient develops persistent grade III GIT toxicity. Patients on hypofractionated radiation schedules and patients who have serious medical comorbidities (e.g., active tuberculosis) do not receive chemotherapy.

At the time of diagnosis, patients who have never been tested for HIV or who have not been tested recently are referred for testing and counselling. HIV-positive patients are referred expeditiously for infectious disease consultation so that they can begin prophylaxis with co-trimoxazole and those not already receiving it can commence antiretroviral therapy. Before April 2010, the standard HAART protocol included stavudine, lamivudine and efavirenz. Thereafter, tenofovir was substituted for stavudine at the discretion of the infectious disease specialist.

HIV-positive patients receive the same treatment for their cervical cancer as HIV-negative patients, but the dose per fraction is reduced to 1.8Gy, and if the CD4 count is less than 200 cells/ μ L, chemotherapy is omitted. Patients whose CD4 count is less than 150 cells/ μ L may not tolerate a long course of radiation; some are treated with a shortened regimen dependent on performance status.

Statistics

The outcome variables were total dose of external beam radiation (45 Gy, <45 Gy); total dose of HDR (18 Gy, <18 Gy); total radiation dose expressed as EQD₂ (68Gy, <68Gy) (equivalent to 45Gy in 25 fractions EBRT and 18Gy in three fractions HDR); total overall treatment time (55 days, >55 days); number of cycles of chemotherapy (4 cycles, <4 cycles); and clinical response (complete vs partial), at EUA during or after the fifth week of chemoradiation, and six weeks post-treatment. We compared the demographic and clinical characteristics of HIV-positive and -negative patients, using t-tests for normally distributed continuous variables and chi-square tests for categorical variables. We then developed multivariable logistic regression models to analyze the risk of adverse outcomes, controlling for HIV status, age, stage and completion of treatment. Results are expressed as odds ratios (OR) with 95% confidence intervals (CI). All tests were two-sided and p<0.05 was considered significant. We used SPSS Statistics Version 18.0

RESULTS

Patient characteristics

A total of 461 patients with Stage IB1 – IIIB cervical carcinoma who met inclusion criteria were identified. Twenty-four patients were lost to follow up or declined treatment. A further 41 patients (9.7%) received palliative external beam radiotherapy alone ranging from 8Gy to 40.05Gy, due to either poor performance status or comorbidities. These patients were also excluded from the analysis.

A total of 383 patients initiated curative intent treatment and were included in the analysis. (Figure 1) They included 59 HIV-positive patients (15.4%), 19 (32.2%) of whom were taking HAART at the time of their initial evaluation. The median CD4 count of the HIV-positive patients was 354 cells/ μ L (range 33-1249). 88.1% of all HIV positive patients had a CD4 count above 200 cells/ μ L. The HIV-positive patients were younger than the HIV-negative patients (median age 41 vs 50 years, $p<0.001$).

A total of 49 (88.1%) HIV-positive patients but only 213 (65.7%) of the 324 HIV-negative patients presented with stage IIIB disease ($p=0.009$). HIV status was not associated with histological subtype (more than 90% of both HIV-positive and -negative patients had squamous cell carcinoma), hydronephrosis, or nodal disease. (Table 1)

Treatment

Radical radiotherapy—A total of 291 (89.8%) HIV-negative patients and 47 (79.7%) HIV-positive patients received a dose of 68Gy EQD₂ of radiation ($p=0.03$). Table 2 provides details of radiation received. Of note, six out of the seven patients with a CD4 count less than 200 cells/ μ L completed 68Gy EQD₂. 27 patients who received extended field radiotherapy, 25 completed 45Gy. The two patients that did not complete the intended PAN treatment were HIV-positive. Two HIV-negative patients had missing data on treatment time. The overall treatment time for those who completed both the EBRT and HDR component was 55 days or less for all HIV-positive patients, and only one patient in the HIV-negative group was treated longer than 55 days. Mean overall treatment time for the HIV-positive patients was 44 days compared to 41 days in the HIV-negative group ($p<0.01$) (Table 2). Reasons for incomplete EBRT (<45 Gy) included hypofractionated regimens, poor attendance, refusal to complete, renal failure, neutropaenia, grade III gastrointestinal toxicities, and development of metastatic disease (Table 2).

Concurrent chemotherapy—Of 284 HIV-negative patients who began platinum-based chemotherapy, 212 (74.6%) completed 4 or more cycles. Of the 49 HIV-positive patients who commenced chemotherapy, only 26 (53.1%) completed four or more cycles of platinum-based chemotherapy ($p=0.01$) (Table 3). Eight of 19 patients on HAART (42.1%) and 18 of 40 patients not on HAART (45.0%) managed to complete adequate chemotherapy. Those who completed chemotherapy had higher median CD4 counts than those who did not (416 vs 311, $p=0.02$).

Fifty patients (40 HIV-negative, 10 HIV-positive) received no chemotherapy, due to poor renal function, poor performance status, CD4 <200 , active pulmonary tuberculosis, or hypofractionated radiotherapy. Renal dysfunction was the most common reason why chemotherapy was not completed. Other contributing factors were poor compliance, incomplete EBRT, discovery of active PTB, discovery of a positive HIV test and subsequent low CD4 count, haematological toxicity, persistent grade III GIT toxicity, and a diagnosis of small-cell carcinoma in one patient, who therefore received a different regimen (Table 4).

Completion of ≥ 45 Gy EBRT/ ≥ 18 Gy HDR/4 Cycles of chemotherapy—Among the 49 HIV-positive and 284 HIV-negative patients who initiated curative intent chemoradiation, 22 HIV-positive patients (44.9%) and 199 HIV-negative patients (70.4%) completed treatment ($p=0.001$) (Table 3).

Response to treatment—By the time of EUA and six-week follow-up, the numbers of patients available for evaluation were reduced due to incomplete treatment, loss to follow up, referral back to distant medical centres and death. Of the 383 patients analyzed, 370 patients (309 HIV-negative and 51 HIV-positive patients) had EUA prior to initiation of

brachytherapy; 108 HIV-negative patients (35.0%) but only 10 (19.6%) HIV-positive patients had a complete response ($p=0.008$) (Table 4).

At six weeks, only 326 patients (279 HIV negative and 47 HIV positive) presented for follow-up. Of those, 160 HIV-negative patients (57.3%) but only 18 HIV-positive patients (38.3%) had a documented CR ($p=0.02$) (Table 4). In logistic regression models, adjusting for age, HIV status, stage, and completion of treatment, the factors associated with an incomplete response were stage IIIB disease (Odds Ratio=2.39, 95% CI 1.45-3.96) and receiving less than 68Gy EQD₂ (Odds Ratio=3.14, 95% CI 1.24-7.94). Table 5 details each component of treatment. CD4 count was not included in the model as 52 out of 59 HIV positive patients had a count greater than 200 cells/ μ L.

DISCUSSION

Among the cervical cancer patients in our study, those who were HIV-positive presented at a younger age and at more advanced stages than their HIV-negative counterparts. Most patients were able to complete adequate EBRT and HDR brachytherapy, but although the HIV-positive patients received less radiation and substantially less chemotherapy than the HIV-negative patients, disease stage and completing radiation were the only independent predictors of response. In particular, completion of brachytherapy was a vital component of treatment. The demographic and clinical differences we observed between HIV-positive and -negative patients with cervical carcinoma (e.g., younger age and more advanced disease at presentation) have been previously reported¹⁴. Few of our HIV-positive patients knew their HIV status prior to their cancer diagnosis, and few had commenced HAART prior to their first oncology visit. As the median CD4 count of the HIV-positive patients was 354 cells/ μ L, with the majority having a CD4 count over 200 cells/ μ L, immunocompetence did not appear to reduce the risk of cervical carcinoma as it does the risks of Kaposi's sarcoma and non-Hodgkin lymphoma.¹⁵

Our findings are similar to those of studies of tolerance for chemoradiation among HIV-positive patients with anal cancer^{16, 17}. Oehler-Janne et al found that significantly fewer HIV-positive (30%) than HIV-negative (64.2%) patients received the prescribed chemotherapy. Hammad et al also found that 89% of the HIV-negative patients, but only 45% of the HIV-positive patients, completed chemotherapy at the planned dose. What is clear is that the chemotherapy component is the most difficult aspect of chemoradiation therapy for HIV-positive patients to complete. In our study, we noted that patients who failed to complete chemotherapy had lower median CD4 counts than those who completed it. We were surprised to note that renal dysfunction, not myelosuppression or gastrointestinal toxicity, was the most common reason for HIV-positive patients to discontinue therapy. We may simply have a conservative and cautious approach to chemotherapy in choosing 50ml/min as the cut-off GFR for giving cisplatin. If cisplatin is commenced and renal function deteriorates, we do attempt to reduce the dose to either 25% or 50% of the planned dose in order to attempt to continue with weekly dosing. Some institutions use a lower standard dose of cisplatin upfront but the benefit of this approach has yet to be confirmed in prospective efficacy studies¹⁸. The benefit of chemotherapy in stage IIIB patients also is less than clear. The most recent meta-analysis of treatment for cervical cancer noted that among stage IIIB patients the incremental benefit of chemoradiation over radiation alone was only 3%⁹. The numbers of IIIB patients in these studies were small, however; further studies of such patients are awaited. In our cohort, completion of chemoradiation had no greater impact on response at six weeks than radiation alone. Because most of our HIV-positive and -negative patients had stage IIIB disease, it may be reasonable to omit chemotherapy; doing so may enable us to deliver a full dose of radiation in a timely manner.

The few studies of treatment and outcomes for HIV-positive patients undergoing radiotherapy for cervical carcinoma have reported variable results. Shrivastava et al described a cohort of 42 HIV-positive patients treated at the Tata Memorial Hospital in India¹⁹. Only 22 patients completed external beam radiation and only 50% had a complete response at six weeks. Moodley et al from KwaZulu/Natal, South Africa reported that only 53% of HIV-positive patients were able to complete treatment (including surgery or radiotherapy)²⁰, in part because of resource constraints in the region. Gichangi et al in Nairobi, Kenya, found that HIV-positive patients did not differ from HIV-negative patients in dose received but had significantly poorer outcomes at 4 and 7 months²¹. In the final analysis, 9 out of 24 patients had residual disease at follow up, with an adjusted risk ratio of 6.2 (95% CI 1.4-28.1). In our data, HIV-positive patients had worse responses than HIV-negative patients; however, in logistic regression models that adjusted for age, HIV status, stage, and completion of treatment, the only significant factors were advanced stage and completion of radiation. The model conveyed that the HIV-positive patients had poorer responses only because they were more likely to present with advanced disease and less likely to complete treatment than the HIV-negative patients.

Although our study is one of the largest to compare cervical cancer outcomes among HIV-positive and -negative women, it has a number of important limitations. It included all women with HIV from a region where the disease is endemic; however, its HIV-positive sample consisted of only 59 women. The study may therefore have been underpowered to detect differences in some characteristics and outcomes. Another limitation is that the data were collected retrospectively from the medical charts. However, all patients were treated according to the same treatment principles and guidelines.

We are currently conducting further analyses of treatment-associated toxicity and temporal trends in toxicity in our cohort. In addition, the goal of the current study was to report on completion of and short-term response to treatment. Data on overall survival are maturing and will be reported in future studies.

CONCLUSION

Despite the small numbers, our findings suggest that good medical care of HIV-positive patients can enable patients to complete treatment for locally advanced cervical cancer. They also highlight the importance of radiation therapy. As we await publication of the results of the randomised chemoradiation trials in progress among both FIGO stage IIIB disease and HIV patients, therefore, we will concentrate on enabling our patients to complete their radiation therapy.

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Condensed abstract

HIV-positive cervical cancer patients present at an earlier age, with more advanced disease. Early response in this sub-group of patients is dependent on stage of disease and completion of adequate radiation.

Figure 1.
Study population

Table 1

Demographic and clinical characteristics, by HIV status

		HIV-positive		HIV-negative		Total		
		N	%	N	%	N	%	P value
		59	15.4	324	84.6	383	100.0	
<i>Median age</i>		41		50				<0.001 *
<i>Age group</i>								<0.001 *
	<40	27	45.8	55	17.0	82	21.4	
	40-49	20	33.9	100	30.9	120	31.3	
	50-59	11	18.6	105	32.4	116	30.3	
	60+	1	1.7	64	19.8	65	17.0	
<i>Histology</i>								0.57
	Squamous	56	94.9	300	92.6	356	93.0	
	Adenocarcinoma	1	1.7	15	4.6	16	4.2	
	Other	2	3.4	9	2.8	11	2.9	
<i>Stage</i>	FIGO							0.009 *
	IB1	0	0	3	0.9	3	0.8	
	IB2	0	0	3	0.9	3	0.8	
	IIA	0	0	4	1.2	4	1	
	IIB	10	16.9	99	30.6	109	28.5	
	IIIA	0	0	2	0.6	2	0.5	
	IIIB	49	83.1	213	65.7	262	68.4	
<i>Hydronephrosis (IIIB only)</i>		9	15.3	31	9.6	40	10.4	0.51
<i>Nodes present</i>		15	25.4	61	18.8	76	19.8	0.28
	(Para-aortic/Common Iliac)	4	6.8	23	7.1	27	7.0	1.0

SD= standard deviation

* Significant p <0.05

Table 2

Completion of radiotherapy, by HIV status

	HIV positive		HIV negative		Total		P-value
	N	%	N	%	N	%	
	59	15.4	324	84.6	383	100	
<i>Mean EBRT dose Gy (SD)</i>	47.7	(4.6)	49.1	(6.7)			0.05*
45Gy EBRT	50	84.7	309	95.4	359	93.7	0.05*
18Gy HDR	47	79.7	293	90.4	340	88.8	0.051
45Gy EBRT + 18Gy HDR	45	76.3	284	87.7	329	85.9	0.026*
68Gy EQD ₂	47	79.7	291	89.8	338	88.3	0.026*
<i>Mean EQD₂ dose Gy (SD)</i>	72.4	(13.7)	75.1	(10.9)			0.094
<i>Mean overall treatment time in days (SD) ¶</i>	44	(3.60)	40	(3.83)			<0.01*
Reasons incomplete EBRT <45Gy							
	N	%	N	%	N	%	
	9	37.5	15	62.5	24	100	
Patient refused to complete	2	25.0	3	21.4	5	22.7	
Developed metastatic disease	2	25.0	-	-	2	9.1	
Infection	2	25.0	-	-	2	9.1	
Renal Failure	1	12.5	2	14.3	3	13.6	
Poor attender	-	-	2	14.3	2	9.1	
Persistent neutropaenia	-	-	1	7.1	1	4.5	
GIT toxicity Grade III/IV	-	-	2	14.3	2	9.1	
Hypofractionated RT	2	12.5	5	28.6	7	22.7	

EBRT=external beam radiation therapy; HDR=high dose rate brachytherapy; EQD₂= equivalent dose in 2Gy fractions

¶ For completed treatment 45Gy EBRT + 18Gy HDR

Table 3

Completion of Chemotherapy, by HIV status

	HIV positive		HIV negative		Total		P value
	N	%	N	%	N	%	
	59		324		383	100	
N who commenced chemotherapy	49	83.0	284	87.3	333	86.9	
4 cycles Cisplatin or Carboplatin	26	53.1	212	74.6	238	71.5	0.002*
(4 cycles Cisplatin)	23	46.9	191	67.2	214	57.3)	
0 cycles	10	16.9	40	12.7	50	13.1	
1 cycle	6	10.2	15	4.6	21	5.5	
2 cycles	11	18.6	26	8.3	37	9.7	
3 cycles	6	10.2	31	9.6	37	9.7	
4cycles chemo +45GyEBRT+18GyHDR	22	44.9	199	70.9	221	66.4	0.001*
Reasons incomplete platinum-based chemotherapy							
	N	%	N	%	N	%	
	23		72		95	100	
Renal Dysfunction	15	65.2	54	75.0	69	72.6	
Incomplete EBRT	3	13.0	5	6.9	8	8.4	
Active PTB #	1	4.3	-	-	1	1.1	
CD4<200 ¶	1	4.3	-	-	1	1.1	
Poor Compliance	-	-	2	2.8	2	2.1	
Haematological toxicity	2	8.7	4	5.5	6	6.3	
Gastrointestinal toxicity	-	-	4	5.5	4	4.2	
Alternate chemotherapy (small cell)	-	-	1	1.4	1	1.1	
Infection	1	4.3	2	2.8	3	3.2	

PTB= Pulmonary Tuberculosis diagnosed after treatment commenced

¶ HIV status only established after treatment commenced

Table 4

Response at EUA and six weeks, by HIV status

	HIV positive		HIV negative		Total		P-value
	N	%	N	%	N	%	
	59		324		383	100	
<i>Number undergoing EUA ¶</i>	<i>51</i>	<i>86.4</i>	<i>309</i>	<i>95.4</i>	<i>360</i>	<i>94.0</i>	
Complete response at EUA	10	19.6	108	35.0	118	32.8	0.036*
<i>Attendance at six weeks</i>	<i>47</i>	<i>79.7</i>	<i>279</i>	<i>86.1</i>	<i>326</i>	<i>85.1</i>	
Complete response at six weeks	18	38.3	160	57.3	178	54.6	0.018*

¶EUA= examination under anaesthesia

Table 5

Factors associated with partial vs complete response at six weeks

	OR[¶]	95% CI	P value
HIV status			
Negative	1.00	Referent	
Positive	1.71	0.85-3.36	0.135
FIGO Stage			
Ibi - IIIa	1.00	Referent	
IIIb	2.41	1.45-4.00*	0.001*
Age group			
<40	1.00	Referent	
40-49	0.87	0.44-1.69	0.67
50-59	0.68	0.35-1.33	0.26
60+	0.51	0.22-1.17	0.11
Completion of EBRT			
45Gy	1.00	Referent	
<45Gy	1.18	0.36-3.89	0.78
Completion of HDR			
18Gy	1.00	Referent	
<18Gy	3.13	1.28-7.61	0.012*
Completion of chemotherapy			
4 Cycles	1.00	Referent	
<4Cycles	0.62	0.36-1.06	0.08

[¶]OR= Odds ratio;

CI= Confidence intervals