Chemotherapy Treatment Costs of AIDS-Related Malignancies

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ABSTRACT

The costs of medications used to treat human immunodeficiency virus (HIV) disease and its associated opportunistic infections continues to rise as new and improved drug therapies are introduced. The purpose of this study was to determine the oncology drug cost delivered to the HIV-infected patient population and to characterize the use of chemotherapeutic regimens according to protocols for each tumor grouping. We reviewed 165 patient charts of patients with AIDS-related cancers diagnosed between 1984 and June 1996 at the provincial cancer institution. Full acquisition costs of chemotherapy consisting of the cost of anti-neoplastic drugs and anti-emetic drugs were calculated. Adjusted costs with consideration to a price capping program of α-interferon were determined. Protocols for specific diagnosis of AIDS-related malignancies were also summarized. The total cost of chemotherapy invested in the treatment of 175 AIDS-associated cancers between 1984 and 1996 was $642,015 with an average cost of $4,196 per course of treatment. The total adjusted cost was $569,761 with an average cost of $3,724. Total anti-emetic drug cost was $9,612 with an average cost of $160 per patient. An appreciation of the malignancy treatment costs is important in determining the full cost of illness for HIV infection.

Key Words: AIDS-related malignancies, chemotherapeutic regimens, cost

RÉSUMÉ

Le coût des médicaments utilisés pour traiter les affections causées par le virus de l'immunodéficience humaine (VIH) et les infections à germes opportunistes qui y sont associées, continue de grimper avec l'arrivée des nouveaux médicaments plus puissants. Le but de cette étude était de déterminer le coût des médicaments anticancéreux administrés à une population de patients infectés par le VIH et de caractériser l'usage des traitements chimiothérapeutiques selon les protocoles pour chaque groupe de tumeurs. Nous avons passé en revue 175 dossiers médicaux de patients atteints de cancers liés au SIDA qui ont été diagnostiqués entre 1984 et juin 1996 dans le centre provincial du cancer. Les coûts d'acquisition totaux des traitements chimiothérapeutiques, soit le coût des médicaments antinéoplasiques et des médicaments antiémétiques, ont été calculés. Les coûts ajustés en tenant compte du programme de plafonnement des prix de l'-interféron ont été déterminés. Un résumé des protocoles relatifs au diagnostic des tumeurs malignes liées au SIDA a aussi été publié. Le coût total des traitements chimiothérapeutiques ayant servi au traitement des 175 cas de cancers liés au SIDA entre 1984-1996 était de 642 015 $, pour un coût moyen de 4 196 $ par séance thérapeutique. Le coût total ajusté était de 569 761 $ pour un coût moyen de 3 724 $. Le coût total des antiémétiques était de 9 612 $, pour un coût moyen de 160 $ par patient. Il est important de prendre connaissance des coûts des traitements des tumeurs malignes dans l'établissement du coût total des affections associées à l'infection au VIH.*

MOTS CLÉS : coûts, traitements chimiothérapeutiques, tumeurs malignes liées au SIDA.

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INTRODUCTION

Since the first reported cases of the acquired immune deficiency syndrome (AIDS) in 1981, AIDS has come to be the most important epidemic infectious disease of our time.[1] Moreover, human immunodeficiency virus (HIV) infection is associated with an increased rate of developing secondary malignancies.[1] The most common neoplasms are Kaposi's sarcoma, non-Hodgkin's lymphoma, and primary central nervous system (CNS) lymphoma which, in the presence of HIV infection, are AIDS-defining.[1] Development of other cancers such as Hodgkin's lymphoma, squamous cell carcinomas of various sites, testicular, lung and gastric carcinomas associated with AIDS have also been reported.[2]

Advances in antiviral therapy and treatment or prophylaxis against opportunistic infections have resulted in the prolonged survival of AIDS patients. As a result, such prolongation of life has potentially exposed them to a greater risk of developing AIDS-related cancers which

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often occur late in the course of AIDS.[3] As the overall survival in AIDS patients has improved, non-Hodgkin's lymphoma and Kaposi's sarcoma have become limiting factors in the life expectancy of these patients.

Over the past 14 years, a variety of cytotoxic drugs have been used to manage these AIDS-related malignancies. Biological response modifiers such as interferon and cytokines have also been proven to have some therapeutic influence on tumors at the cellular level.[4] A number of different treatment regimens have been designed for the management of cancers. Unfortunately, intensive chemotherapy often presents drug tolerance problems for AIDS-patients because of their advanced immune deficiency. The therapies of choice for Kaposi's sarcoma and non-Hodgkin's lymphoma are still poorly defined.[1] Chemotherapy regimens often need to be tailored to the specific patient situation. As the number of AIDS-related cancers rises, so have the associated costs of their treatment. The purpose of this study was to identify and classify oncology pharmaceuticals into protocols for HIV patients with malignancies in Alberta and to determine the approximate acquisition cost of oncology drugs delivered to this patient population.

PATIENTS AND METHODS

A chart review of HIV-positive patients diagnosed with AIDS-related malignancies between 1984 and 1996 was conducted at the Cross Cancer Institute in Edmonton and the Tom Baker Cancer Centre in Calgary, which are the primary cancer institutions providing treatment for all malignancies in Alberta. Data were collected by reviewing patient charts between May and June of 1996.

Demographic and clinical details such as HIV seropositivity, severity of immune deficiency (CD4 count), presence of opportunistic infections, tumor type, and date of diagnosis were recorded. Patients were classified into tumor diagnostic groups. Kaposi's sarcoma patients were separated into two Kaposi's sarcoma subsets according to the classification system proposed by Krown.[5] This system subdivided Kaposi's sarcoma groups into "good risk/prognosis" and "poor risk/prognosis" based on the extent of the tumor, the status of patient's immunity in terms of CD4 count, and the involvement of tumor in the systemic illness. The remaining diagnostic cancer groups included primary CNS lymphoma, non-Hodgkin's lymphoma and other non-AIDS defining cancers.

Data collection concerning cancer treatment consisted of treatment type and year, chemotherapy regimen selected, dose, number of cycles or doses received, and usage of concurrent anti-emetic medications were noted and analyzed along with the evaluation of chemotherapy outcomes. Response to treatment was defined with either a noticeable decrease or stabilization of malignancy as stated in patient charts. Progression of malignancy, discontinuation of treatment due to treatment-induced toxicity, or death from malignancy were considered failures to respond to chemotherapy.

The cost of chemotherapy included the acquisition cost of anti-neoplastic and anti-emetic drugs. The calculation of cost was based on the year of treatment and the actual historical price for each drug during that year paid by the Cross Cancer Institute. The final estimated costs of chemotherapy were expressed as the cost per treatment cycle, the cost per course of treatment for each treated patient, and the total chemotherapy cost of all patients who have been treated between 1984 and June 1996. The cost of chemotherapy was also adjusted according to the price capping program for α-interferon in Alberta. This capping program limited the cost of α-interferon to a maximum of $12,000 per patient per year. When the amount of α-interferon needed by a patient exceeded this limit, the rest of the drug was donated by pharmaceutical companies. Thus, the actual cost charged to the pharmacy at Alberta Cancer Board did not exceed $12,000 per patient per year for α-interferon therapy. Drug costs were rounded to the nearest dollar. Other costs, including pharmacy preparation costs, drug administration costs, nursing and other health professional salary costs, the cost of surgery or radiotherapy, and hospital hotel costs were not included in the study.

RESULTS

Tumor Diagnostic Groups

The charts of 165 HIV positive patients with malignancies were reviewed. Of the 165 patients, 155 were identified with a single case of an AIDS-defining or other malignancy while the remaining 10 patients were diagnosed with 2 malignancies. Of these 10 patients with 2 malignancies, 4 patients had Kaposi's sarcoma and non-Hodgkin's lymphoma, 1 patient had CNS lymphoma and a second non-Hodgkin's lymphoma at a different site, and 5 patients had AIDS-related malignancies with another incidental cancer. In total, there were 175 AIDS-related malignancies in a pool of 165 HIV patients. The majority of AIDS-related cancers (153 of 175), occurred in homosexual male patients followed by homosexual male intravenous drug users (7 of 175) as displayed in Table I. Among 175 AIDS cancers, 47 were presented as the first clinical manifestations of AIDS, 113 followed other AIDS symptoms and the relationship of the remaining 15 to AIDS was unknown. Table I shows the distribution of AIDS-related cancers by cancer type and gender. Of the 175 AIDS-related malignancies, there were a total number of 118 cases of Kaposi's sarcoma. Seventy out of 118 Kaposi's sarcoma malignancies belonged to the good prognosis group and 48 out of 118 were classified as a poor prognosis. In 49 cases of

AIDS-defining malignant lymphomas, 9 were primary CNS lymphoma and 40 were non-Hodgkin's lymphoma. Other incidental cancers comprised of 2 Hodgkin's lymphoma, 2 squamous cell, 1 testicular, 1 gastric, and 1 lung carcinomas were also found. The proportion of Kaposi's sarcoma relative to the reported HIV cases in Alberta between 1984 and 1995 fluctuated, whereas, the incidence of non-Hodgkin's lymphoma appears to rise (Figure 1), although this trend is not significant.

Treatment Modalities

Various therapeutic approaches have been used for the management of AIDS-defining neoplasms (Table II). Of the 175 cases, 135 cases were treated with chemotherapy or α-interferon therapy while 44 received neither chemotherapy nor α-interferon therapy. Patients who did not receive any treatment had either one or more of the following reasons: 1) no medical intervention was necessary at the time of diagnosis as disease was quiescent; 2) death occurred before a treatment is initiated; or 3) treatment was not established due to neutropenia. The most common treatment, if any was given, for Kaposi's sarcoma with a

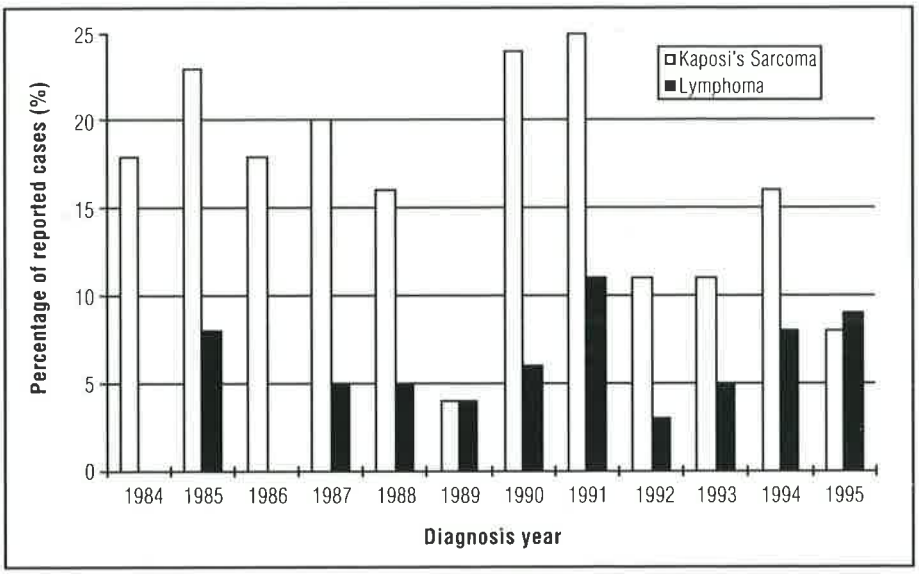

Figure 1. Proportion of AIDS-related Malignancies in the HIV-positive Population of Alberta from 1984 to 1995. Each percentage was calculated by dividing the number of Kaposi's sarcoma or lymphoma patients diagnosed in that particular year in Alberta by the total number of all known HIV-positive individuals in Alberta in the same year. Open bars represent cases of Kaposi's sarcoma and closed bars represent cases of lymphoma.

Table I. Patients and AIDS-related Malignancies Characteristics

Characteristics		Kaposi's sarcoma (Good Risk)	Kaposi's sarcoma (Poor Risk)	Primary CNS lymphoma	Non-Hodgkin's lymphoma	Incidental cancers	Total no. of AIDS-related cancer cases
Sex	Male	70	48	9	39	8	174
	Female	-	-	-	1	-	1
Location	Northern Alberta	23	17	2	11	5	58
	Southern Alberta	47	31	7	29	3	117
Mean age (range)		38 (18 - 60)	37 (20 - 52)	33 (26 - 45)	40 (23 - 67)	39 (24 - 59)	38 (18 - 67)
Risk Group	Homosexual	65	44	8	30	6	153
	Heterosexual	-	-	1	3	2	6
	IVDU*	-	1	-	1	-	2
	Blood transfusion recipient	1	-	-	3	-	4
	Homosexual + IVDU	4	1	-	2	-	7
	Heterosexual + IVDU	-	1	-	-	-	1
	Unknown	-	1	-	1	-	2
Immune status at diagnosis	Asymptomatic	19	13	2	9	4	47
	AIDS prior to diagnosis	43	32	6	30	2	113
	Unknown	8	3	1	1	2	15
Vital Status	Alive	26	11	-	14	4	55
	Deceased	44	37	9	26	4	120

* IVDU = Intravenous Drug Users

Table II. Treatment Overview for 175 Cases of AIDS-related Cancers

Treatment type	Kaposi's sarcoma (Good Risk)	Kaposi's sarcoma (Poor Risk)	Primary CNS lymphoma	Non-Hodgkin's Imphoma	Incidental cancers	Total
No treatment	23	5	3	10	3	44
Chemotherapy alone	-	5	1	13	2	21
Interferon therapy alone	13	8	-	-	-	21
Radiotherapy alone	16	1	3	3	-	23
Surgery alone	-	-	2	-	1	3
Chemotherapy + interferon therapy	3	5	-	1	-	9
Chemotherapy + radiotherapy	2	4	-	7	1	14
Interferon therapy + radiotherapy	10	9	-	-	-	19
Chemotherapy + surgery	-	-	-	5	1	6
Chemotherapy + interferon therapy + radiotherapy	3	11	-	1	-	15
Total	70	48	9	40	8	175

good prognosis was radiotherapy alone followed by α-interferon therapy. Patients with a poor prognosis for Kaposi's sarcoma were mainly treated with a combination of radiotherapy, chemotherapy and α-interferon therapy. Treatment choices for CNS lymphoma included no treatment (3 patients), radiotherapy (3 patients), surgery (2 patients), and chemotherapy alone (1 patient). The most common treatment of non-Hodgkin's lymphoma was chemotherapy alone (13 of 40 patients) or chemotherapy in conjunction with radiotherapy, interferon or surgery (14 of 40 patients).

CD4-lymphocyte Count

The T helper lymphocyte (CD4) count, which is a measure of HIV-positive patient's immune status, has been used in the past as a clinical indicator for predicting therapy outcomes.[3] In 130 patients, the CD4-lymphocyte count was available at the time of malignancy diagnosis. As displayed in Table III, 97 patients of 130 were severely immune deficient having a CD4 count which ranged from 4 cells/mm^3 to 200 cells/mm^3. Twenty-two were considered moderately immune deficient with a CD4 count between

Table III. Predictive Effect of CD4 Count on the Outcomes of Chemotherapy

Diagnosis	Outcomes of chemotherapy	CD4 count (X 10 ^6 cells/L)			
		<50	50-200	200-500	>500
		n (%)	n (%)	n (%)	n (%)
Kaposi's sarcoma - Good risk	Responding to chemotherapy	8 (36%)	7 (54%)	5 (50%)	2 (50%)
	Ongoing therapy	-	1 (8%)	1 (10%)	-
	Treatment failure*	8 (36%)	4 (31%)	2 (20%)	-
	No necessary medical intervention †	6 (27%)	1 (8%)	2 (20%)	2 (50%)
	Total (n = 49)	22	13	10	4
Kaposi's sarcoma - Poor risk	Responding to chemotherapy	2 (18%)	6 (24%)	1 (33%)	3 (75%)
	Ongoing therapy	-	1 (4%)	-	-
	Treatment failure	9 (82%)	17 (68%)	2 (67%)	1 (25%)
	No necessary medical intervention	-	1 (4%)	-	-
	Total (n = 43)	11	25	3	4
Primary CNS Lymphoma	Responding to chemotherapy	1	1 (25%)	-	-
	Treatment failure	-	2 (50%)	-	-
	No necessary medical intervention	-	1 (25%)	-	-
	Total (n = 5)	1	4	-	-
Non-Hodgkin's Lymphoma	Responding to chemotherapy	3 (38%)	8 (62%)	5 (71%)	2
	Treatment failure	2 (25%)	3 (23%)	1 (14%)	-
	No necessary medical intervention	3 (38%)	2 (15%)	1 (14%)	-
	Total (n = 30)	8	13	7	2
Incidental Cancers	Responding to chemotherapy	-	-	2	-
	Ongoing therapy	-	1	-	-
	Total (n = 3)	-	1	2	-

* Treatment failure is due to unfavourable prognosis factors such as progression of illness, discontinuation of treatment due to treatment-induced toxicity, treatment not established because of neutropenia and treatment termination due to death from malignancies.

† No necessary medical intervention consists of no immediate medical intervention (no chemotherapy) is necessary at the time of diagnosis as disease was quiescent, on going consultations and assessment only.

200 cells/mm^3 and 500 cells/mm^3. The remaining 10 patients had a CD4 count greater than 500 cells/mm^3.

Treatment failure occurred in 67-82% of Kaposi's sarcoma patients with a poor prognosis and a severe immune deficit (CD4 counts of less than 500 cells/mm^3), whereas, only 25% of Kaposi's sarcoma patients with a CD4 count greater than 500 cells/mm^3 experienced treatment failure (Table III). In Kaposi's sarcoma patients with a CD4 count of greater than 500 cells/mm^3, treatment failures occurred less than 36% of the time. Patients diagnosed with primary CNS lymphoma were all severely immune deficient. Only one of the 9 CNS lymphoma patients that was treated with chemotherapy had a response. Patients with non-Hodgkin's lymphoma and a CD4 count between 50 cells/mm^3 and 200 cells/mm^3 were observed to have response rates between 62 - 71 % following chemotherapy (Table III).

Chemotherapy Costs

Cytotoxic drugs were all administered on an outpatient basis. Twenty-nine different chemotherapy regimens used for the management of AIDS-related cancers at Cross Cancer Institute and Tom Baker Cancer Centre are listed in Appendix A. For these regimens, the average cost per patient for each single dose or cycle and the average cost for each effective course of chemotherapy is summarized in Table IV. The total

Table IV. Cost of Chemotherapeutic Regimens in the Management of AIDS-defining Malignancies

Diagnosis	Chemotherapy protocols.	Average cost ($) per single dose or cycle		Average cost ($) per effective course of chemotherapy		
		n †	Average cost ($) (range)	n ∞	No. of doses or cycles (range)	Average cost ($) (range)
Kaposi's Sarcoma - Good Risk	α-IFN (low dose)	32	51 (6 - 168)	15	98 (24 - 147)	4,868 (469 - 15,201)
	α-IFN (high dose)	10	145 (92 - 209) 118 (62 - 209) §	9	104 (33 - 193)	15,056 (4,455 - 34,054) 10,139 (4,455 - 12,000) §
	ABV	4	333 (314 - 366)	3	3 (2 - 5)	1,102 (641 - 1,568)
	BV	1	200	1	10	1,997
	BV-Vb	1	331	1	3	993
	Vb-VP	2	122 (78 - 165)	-	-	-
Kaposi's Sarcoma - Poor Risk	α-IFN (low dose)	34	45 (2 - 91)	8	245 (84 - 539)	6,010 (939 - 11,354)
	α-IFN (high dose)	5	182 (104 - 412) 110 (92 - 152) §	1	85	35,020 12,000 §
	ABV	11	285 (197 - 410)	3	8 (5 - 14)	2,668 (1,248 - 5,007)
	Doxorubicin	1	119	-	-	-
	AVb	1	207	-	-	-
	A-VP	3	411 (285 - 595)	1	4	1,140
	AV-VP	2	252 (225 - 279)	-	-	-
	AVb-VP	1	1,882	-	-	-
	BVb	1	201	1	7	1,409
	AB-VP	4	404 (321 - 451)	2	6 (5 - 7)	2,595 (2,257 - 2,934)
	M-VP	2	245 (199 - 291)	1	3	597
	VVb	2	49 (30 - 67)	-	-	-
	AV-Vb	1	206	-	-	-
	Etoposide	1	83	-	-	-
Primary CNS lymphoma	CHOP+ I.T.	1	388	1	1	388
Non-Hodgkin's Lymphoma	Cyclophosphamide	1	1	-	-	-
	CHOP	11	231 (26 - 349)	9	5 (3 - 7)	1,015 (132 - 2,370)
	CNOP	3	322 (281 - 389)	2	5 (4 - 6)	1,622 (1,558 - 1,686)
	CNOP+ I.T.	1	375	1	6	2,251
	VACOBP	3	376 (352 - 383)	1	13 (12 - 13)	4,843 (4,596 - 5,090)
	VACOBP + I.T.	1	435	1	12	S,223
	VACOBP-VP (modified) + I.T.	1	313	1	12	3,756
	MACOP-B	5	304 (224 - 530)	5	9 (2 - 15)	2,577 (520 - 3,361)
	MACOP-B+ I.T.	1	290	1	5	1,449
	CEPP - Bleomycin	1	405	1	2	811
	COMP + I.T.	1	115	1	19	2,187

* Chemotherapeutic agents and dosage ranges used in protocols are listed in Appendix A.
† Denotes number of chemotherapies used to treat malignancies.
∞ Denotes number of malignancies responding to drug therapy.
§ Denotes the adjusted cost of chemotherapy with the price capping program of α-interferon.

cost of chemotherapy based treatment for AIDS-related cancers treated at Alberta Cancer Board between 1984 and June 1996 was calculated to be $642,015 (Table VI) and averaged $4,196 for each patient (Table V). When the price capping program of α-interferon in Alberta was taken into account, the total cost was $569,761 with an average cost of $3,724 per patient (Table V). In addition, Table V shows a gradual, but consistent decline in the average chemotherapy cost since 1988.

Antiemetic Drug Costs

Most patients receiving chemotherapy experience unpleasant side effects of nausea and vomiting.[6] Antiemetic drugs were often administered prior to chemotherapy as well as following chemotherapy. Antiemetic drugs used were dexamethasone, metoclopramide HCL, ondansetron, and prochlorperazine mesylate. The total antiemetic drug cost for these 165 patients between 1984 and 1996 was $9,612 (Table VI). The average cost per patient was $160 (Table V). These costs were included as they are considered an intrinsic component to the chemotherapy in the treatment of these malignancies.

DISCUSSION

Tumor Diagnostic Groups

In the cohort of patients with AIDS-related malignancies, Kaposi's sarcoma and non-Hodgkin's lymphoma were found to be the most frequent neoplasms. Of 175 cases of AIDS-related cancers, 67% were Kaposi's sarcoma and 28% were non-Hodgkin's lymphomas of CNS and various other sites. Both Kaposi's sarcoma and non-Hodgkin's lymphomas had been recognized as the first clinical manifestations of AIDS in 47 out of 175 AIDS-related tumor cases.[6] The remaining 5% of cancers encountered in the AIDS population comprised of Hodgkin's lymphoma, squamous cell, testicular, lung, and gastric carcinomas. Unlike Kaposi's sarcoma and non-Hodgkin's lymphoma, the frequency of these malignancies was not found to be higher in the HIV-positive population than the normal population. As a result, they are not considered as AIDS-defining illness.[2]

In the present study, the incidence of AIDS-related malignancies appeared to fluctuate with the dynamic change in the HIV positive population. As the life expectancy of AIDS patients is prolonged, more cases of AIDS-related malignancies are presenting and requiring effective management.[3] Unfortunately, specific treatment

Table V. Average Cost of Chemotherapy and Antiemetic Drugs between 1984 and 1996.

	Kaposi's sarcoma (Good risk)		Kaposi's sarcoma (Poor risk)		Primary CNS lymphoma	Non-Hodgkin's lymphoma	Incidental cancers	Total average	
	Cost ($)	Adjusted cost ($)	Cost ($)	Adjusted cost ($)	Cost ($)	Cost ($)	Cost ($)	Cost ($)	Adjusted cost ($)
Chemotherapy									
Treatment year									
1984-85	-	-	558	558	-	2,187	-	965	965
1986-87	3,140	3,140	916	916	-	1,449	2,606	2,028	2,028
1988-89	11,081	8,199	11,995	6,240	-	3,344	4,546	9,858	6,786
1990-91	5,887	5,120	4,290	4,090	-	2,568	-	4,624	4,248
1992-93	4,413	4,225	3,954	3,954	388	1,816	239	3,566	3,519
1994-95	5,025	4,567	2,125	2,125	-	1,245	-	2,799	2,646
1996	-	-	1,601	1,601	-	-	1,949	1,775	1,775
Outcomes									
Responding to chemotherapy	7,407	5,882	5,849	4,495	388	2,109	2,463	5,036	4,127
Ongoing chemotherapy	8,896	8,896	1,601	1,601	-	-	1,949	4,149	4,149
Progression of illness *	4,081	4,081	3,368	3,270	-	702	-	3,381	3,315
Total average	6,106	5,222	3,954	3,548	388	1,867	2,335	4,196	3,724
Antiemetic drugs									
Pre-chemotherapy	34	-	95	-	1	63	141	76	-
Post-chemotherapy	2	-	296	-	-	161	-	211	-
Total average	27	-	219	-	1	135	189	160	-

* Signifies progression of illness, treatment-induced toxicity and treatment termination due to death from malignancies or other opportunistic infections.

Table VI. Total Cost of Chemotherapy and Antiemetic Drugs between 1984 and 1996

	Kaposi's sarcoma (Good risk)			Kaposi's sarcoma (Poor risk)			Primary CNS lymphoma		Non-Hodgkin's lymphoma		Incidental cancers		Total		
	n	Cost ($)	Adjusted cost ($)	n	Cost ($)	Adjusted cost ($)	n	Cost ($)	n	Cost ($)	n	Cost ($)	n	Cost ($)	Adjusted cost ($)
Chemotherapy															
Treatment year															
1984-85	-	-	-	3	1,674	1,674	-	-	1	2,187	-	-	4	3,861	3,861
1986-87	2	6,281	6,281	2	1,832	1,832	-	-	1	1,449	1	2,606	6	12,167	12,167
1988-89	8	88,651	65,591	4	47,981	24,961	-	-	2	6,688	1	4,546	15	147,866	101,786
1990-91	18	105,962	92,157	25	107,255	102,255	-	-	7	17,975	-	-	50	231,192	212,388
1992-93	10	44,134	42,253	22	86,978	86,978	1	388	6	10,894	1	239	40	142,633	140,751
1994-95	12	60,296	54,807	12	25,506	25,506	-	-	12	14,945	-	-	36	100,747	95,258
1996	-	-	-	1	1,601	1,601	-	-	-	-	1	1,949	2	3,550	3,550
Outcomes															
Responding to chemotherapy	29	214,799	170,565	17	99,440	76,420	1	388	24	50,626	3	7,390	74	372,643	305,389
Ongoing chemotherapy	1	8,896	8,896	1	1,601	1,601	-	-	-	-	-	-	3	12,446	12,446
Progression of illness*	20	81,628	81,628	51	171,786	166,786	-	-	5	3,512	1	1,949	76	256,926	251,926
Total	50	305,323	261,089	69	272,827	244,807	1	388	29	54,138	4	9,339	153	642,015	569,761
Antiemetic drugs															
Pre-chemotherapy	4	135	-	21	1,997	-	1	1	25	1,563	3	423	54	4,119	-
Post-chemotherapy	1	2	-	11	3,259	-	-	-	13	2,088	1	145	26	5,494	-
Total	5	136	-	24	5,257	-	1	1	27	3,651	3	568	60	9,612	-

* Signifies progression of illness, treatment-induced toxicity, treatment termination due to death from malignancies or other opportunistic infections.

regimens for AIDS-related cancers have not yet been defined. In general, response to various combination treatment regimens in AIDS patients is far inferior to that obtained from the normal population treated with the same combination chemotherapy.[2] Often, the presence of preceding or concomitant opportunistic infections, the immune compromised status of AIDS patients and the unusual histological presentation of AIDS-related tumors, as compared to the non HIV-infected population, impedes the administration of full doses of chemotherapy to AIDS patients.[1] Thus, the intensity and duration of treatment are frequently changed throughout the course of chemotherapy. In this study, several chemotherapy regimens were modified during the course of treatment in order to provide an effective and tolerable protocol with the most beneficial outcomes. The majority of these modifications consisted of delays in treatment administration, reductions in dosage, or the omission of a chemotherapeutic agent from the regimen due to either hematological treatment-related toxicity, progression of tumors, or complications by other opportunistic infections. Thus, in this study and in the treatment of AIDS related malignancies in general, a number of therapeutic alternatives are considered in the process of selecting a chemotherapy regimen designed to accommodate the specific needs of each patient.[6]

Treatment Modalities

The treatment of Kaposi's sarcoma is palliative. The purpose of therapy is elimination or reduction of cosmetically unacceptable lesions, reduction of painful edema, and shrinkage of oral or other clinically significant lesions.[6] This study shows that radiotherapy and α-interferon therapy were the most common choice of therapy for Kaposi's sarcoma of good prognosis. In the case of disseminated Kaposi's sarcoma, a more aggressive therapeutic intervention is required such as a combination of radiotherapy, α-interferon therapy, and single or multiple agent chemotherapy regimens. The most common protocols used were low dose α-interferon, ABV combination, and high dose α- interferon, respectively. The remaining chemotherapy regimens were found only in a small number and have produced a lower rate of response in comparison to the combination of α-interferon therapy and ABV (Table IV). Intensive chemotherapy and radiotherapy protocols were the most frequent modality for non-Hodgkin's lymphoma. Chemotherapy regimens used in the management of AIDS-related lymphoma were similar to those in the general population.[1] CHOP and MACOP-B protocols were found to be most commonly prescribed and both are effective with 9/11 and 5/5 patients responding, respectively. Furthermore, CHOP is one of the least expensive chemotherapy protocols given

(Table IV). The rest of the protocols were less frequently prescribed to AIDS patients because of their myelotoxicity and their high cost (Table IV).

The success in treating primary CNS lymphoma is poor. Whether treated or not, the outcomes remain much the same.[6] Due to the secluded location of the tumor in the CNS sanctuary, most anti-neoplastic agents cannot cross the blood brain barrier to reach the target site. Few clinical trials have demonstrated the effectiveness of either chemotherapy or radiotherapy.[1] In this study, only 1 of the 9 patients diagnosed with primary CNS lymphoma was successfully treated and this patient received one cycle of intravenous CHOP and 4 doses of intrathecal methotrexate. The remaining CNS lymphoma patients received either radiotherapy, surgery or no treatment at all. Patients who did not receive any therapy generally died within a few months following diagnosis. Since the occurrence of CNS lymphoma takes place in the late stage of AIDS in which patients have already acquired other opportunistic infections, the cause of death is often not due to the CNS lymphoma but as a result of these opportunistic infections.[6]

CD4-lymphocyte Count

There is an inverse relationship between the absolute number of circulating T-helper cells and the development of cancers and opportunistic infections. As might be expected, the most extensive cancers are frequently associated with severe immune depression and this often limits patient tolerance for therapy.[7] Efficacy and tolerance of the chemotherapy regimen tend to be greater in patients with a CD4 count equal or greater than 500 cells/mm^3.

Chemotherapy and Antiemetic Drug Costs

The total acquisition cost for the treatment of AIDS-related malignancies between 1984 and June 1996 was $642,015 for anti-neoplastic drugs alone and an additional $9,162 was spent for antiemetics drugs in these patients. The average oncology drug cost for palliative treatment of Kaposi's sarcoma over the 12-year period was higher than the cost of treatment of any other AIDS-related malignancy. The cost of α-interferon therapy contributes most to this cost. If the price capping program of α-interferon in Alberta is considered, then the total cost and the average cost per patient is much lower. Furthermore, the average cost of chemotherapy per patient has declined since 1988 (Table V). This decline may be due to either the decrease in the price of some chemotherapeutic agents or a change in treatment strategy.

In summary, the purpose of our study was to determine the direct acquisition cost of anti-neoplastic and antiemetic drugs used in the treatment of AIDS-related malignancies from 1984 to 1996 in the HIV-infected population in Alberta. The drug cost presented in this study is only an estimation of the chemotherapy cost. It is noteworthy that several drug dosages were modified throughout the course of treatment to match the tolerance of the immune compromised HIV-positive patients while ensuring that the optimum results were obtained. Consequently, these deviations made exact costing difficult to determine.

It is beyond the scope of this study to determine the cost-effectiveness of all the chemotherapy regimens used. This study has succeeded in presenting all the chemotherapy regimens used in Alberta and their associated drug costs in the management of both the tumors and the treatment-related nausea and emesis. Further studies and research are required to compare the effectiveness of these identified protocols and to design a decision-making tree for the treatment of AIDS-associated cancers.[10,11] Hence, a better understanding of oncology treatment strategies for AIDS-related malignancies and their effects in improving patient's quality of life and prolonging overall survival will be attained.

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Appendix A. Chemotherapeutic Regimens used in the Management of AIDS-defining Cancers

No.	Regimen acronym	Chemotherapeutic agents	Dose (range)
1.	A-VP	Doxorubicin	50 - 90 mg I.V.
		Etoposide	200 - 300 mg I.V.
2.	AB-VP	Doxorubicin	25 - 45 mg I.V.
		Bleomycin	15 U I.V.
		Etoposide	100 - 200 mg I.V.
3.	ABV	Doxorubicin	25 - 40 mg I.V.
		Bleomycin	10 - 20 U I.V.
		Vincristine	1 - 2 mg I.V.
4.	AVb	Doxorubicin	50 - 75 mg I.V.
		Vinblastine	7.5-10 mg I.V.
5.	AV-VP	Doxorubicin	20 mg I.V.
		Vincristine	1 - 2 mg I.V.
		Etoposide	100 mg P.O.
6.	AVb-VP	Doxorubicin	50 mg I.V.
		Vinblastine	10 mg I.V.
		Etoposide	300 mg I.V.
7.	AV-Vb	Doxorubicin	30 - 50 mg I.V.
		Vincristine	2 mg I.V.
		Vinblastine	7 mg I.V.
8.	BV	Bleomycin	15 U I.V.
		Vincrlstine	2 mg I.V.
9.	BVb	Bleomycin	15 U I.V.
		Vinblastine	10 mg I.V.
10.	BVVb	Bleomycin	15 U I.V.
		Vincristine	2 mg I.V.
		Vinblastine	8 mg I.V.
11.	CEPP-Bleo	Cyclophosphamide	1000 mg I.V.
		Etoposide	120 mg I.V.
		Procarbazine	100 mg P.O.
		Prednisone	25 - 100 mg P.O.
		Bleomycin	25 U I.V.
12.	CHOP	Cyclophosphamide	50 - 1350 mg I.V.
		Doxorubicin	35 - 112 mg I.V.
		Vincristine	2 mg I.V.
		Prednisone	50 - 100 mg P.O.
13.	CHOP + I.T.	Cyclophosphamide	1000 mg I.V.
		Doxorubicin	75 mg I.V.
		Vincristine	2 mg I.V.
		Prednisone	50 mg P.O.
	PLUS	Intrathecal chemotherapy	
		Methotrexate	15 mg I.T.
14.	CNOP	Cyclophosphamide	1500 mg I.V.
		Mitoxantrone	20 mg I.V.
		Vincristine	2 mg I.V.
		Prednisone	100 mg P.O.
15.	CNOP + I.T.	Cyclophosphamide	190 - 1650 mg I.V.
		Mitoxantrone	14.5 - 20.0 mg I.V.
		Vincristine	2 mg I.V.
		Prednisone	100 mg P.O.
	PLUS	Intrathecal chemotherapy	
		Methotrexate	12 mg I.T.
		Cytarabine	30 mg I.T.
16.	COMP + I.T.	Cyclophosphamide	1.5 - 2.0 g I.V.
		Vincristine	2 mg I.V.
		Methotrexate	500 mg I.V.
		Prednisone	100 mg P.O.
	PLUS	Methotrexate	12 mg I.T.
17.	Cyclophosphamide	Cyclophosphamide	100 mg P.O.
18.	Doxorubicin	Doxorubicin	50 - 90 mg I.V.
19.	a - IFN (low dose)	Alpha-interferon	1 - 10 mu S.C.
20.	a - IFN (high dose)	Alpha-interferon	10 - 50 mu S.C.
21.	M-VP	Mitoxantrone	10 mg I.V.
		Etoposide	180 mg I.V.
22.	MACOP-B	Methotrexate	720 mg I.V.
		Doxorubicin	50 - 80 mg I.V.
		Cyclophosphamide	600 - 650 mg I.V.
		Vincristine	2 mg I.V.
		Bleomycin	15 U I.V.
		Prednisone	75 mg P.O.
23.	MACOP-B + I.T.	Methotrexate	720 mg I.V.
		Doxorubicin	75 - 90 mg I.V.
		Cyclophosphamide	500 - 650 mg I.V.
		Vincristine	2 mg I.V.
		Bleomycin	15 U I.V.
		Prednisone	75 mg P.O.
	PLUS	Intrathecal chemotherapy	
		Methotrexate	15 mg I.T.
		Cytarabine	30 mg I.T.
24.	Vb-VP	Vinblastine	10 mg I.V.
		Etoposide	100 mg I.V.
25.	VACOBP	Etoposide	90 - 100 mg I.V.
		Etoposide	150 - 200 mg P.O.
		Cisplatin	55 mg I.V.
		Doxorubicin	90 - 93 mg I.V.
		Cyclophosphamide	420 - 650 mg I.V.
		Vincristine	1 - 2.2 mg I.V.
		Bleomycin	15 - 20 U I.V.
		Prednisone	60 - 90 mg P.O.
26.	VACOBP + I.T.	Etoposide	100 mg I.V.
		Etoposide	200 mg P.O.
		Cisplatin	60 mg I.V.
		Doxorubicin	65 - 100 mg I.V.
		Cyclophosphamide	455- 700 mg I.V.
		Vincristine	2.0 - 2.4 mg I.V.
		Bleomycin	20 U I.V.
		Prednisone	100 mg P.O.
	PLUS	Intrathecal chemotherapy	
		Methotrexate	15 mg I.T.
		Cytarabine	30 mg I.T.
27.	VACOBP-VP + I.T. (modified)	Etoposide	170 mg I.V.
		Cisplatin	50 mg I.V.
		Doxorubicin	55 - 85 mg I.V.
		Cyclophosphamide	390- 600 mg I.V.
		Vincristine	2 mg I.V.
		Bleomycin	17 U I.V.
		Prednisone	75 mg P.O.
	PLUS	Intrathecal chemotherapy	
		Methotrexate	12 mg I.T.
		Cytarabine	50 mg I.T.
28.	VP16	Etoposide	100 mg I.V.
29.	VVb	Vincristine	2 mg I.V.
		Vinblastine	8 mg I.V.