Published in final edited form as:

Curr Opin Oncol. 2012 September ; 24(5): 531–536. doi:10.1097/CCO.0b013e3283560697.

Impact of highly effective antiretroviral therapy on the risk for Hodgkin lymphoma among people with human immunodeficiency virus infection

James J. Goedert^a and Mark Bower^b

^aInfections and Immunoepidemiology Branch, Division of Cancer Epidemiology and Genetics, National Cancer Institute, Rockville, Maryland, USA

^bNational HIV Oncology Centre, Chelsea & Westminster Hospital, London, UK

Abstract

Purpose of review—To estimate the impact of highly effective antiretroviral therapy (ART) on the incidence and prognosis of Hodgkin lymphoma among people with human immunodeficiency virus infection or AIDS (PWH).

Recent findings—Age-adjusted incidence of Hodgkin lymphoma in PWH is unchanged and is still five-fold to fifteen-fold higher than in the general population. Aging of the PWH population with ART may account for increasing numbers of Hodgkin lymphoma cases. CD4 cell count has a complex relationship to Hodgkin lymphoma risk in PWH. Depending on the time of measurement, Hodgkin lymphoma risk is highest with 50–249 CD4cells/μl, and falling CD4 count on ART may be a harbinger of Hodgkin lymphoma onset. HIV load appears irrelevant to Hodgkin lymphoma. For obscure reasons, Hodgkin lymphoma risk may be elevated soon after starting ART, but the risk is probably modestly reduced with 6 or more months on ART. For PWH who develop Hodgkin lymphoma, ART and ABVD chemotherapy can be administered safely, with one recent study demonstrating equivalent outcomes for HIV-positive and HIV-negative Hodgkin lymphoma patients.

Summary—Vigilance for Hodgkin lymphoma is needed for immune-deficient PWH, including those on ART. ART with opportunistic infection prophylaxis enables the delivery of effective chemotherapy for Hodgkin lymphoma, leading to a good prognosis.

Keywords

acquired immunodeficiency syndrome; antiretroviral therapy; cancer chemotherapy; CD4 count; Hodgkin lymphoma; human immunodeficiency virus

INTRODUCTION

For over a decade, it has been recognized that the incidence of Hodgkin lymphoma is 5–15 times higher among people with HIV and AIDS (PWH) compared to the general population [1•, 2•, 3–6], and that it has become a more frequent cause of morbidity in recent years as antiretroviral therapy (ART) has become more widely available and more

© 2012 Wolters Kluwer Health | Lippincott Williams & Wilkins

Correspondence to James J. Goedert, MD, Infections and Immunoepidemiology Branch, Division of Cancer Epidemiology and Genetics, National Cancer Institute, 6120 Executive Boulevard, Room 7068, Rockville, MD 20852, USA. goedertj@mail.nih.gov.

Conflicts of interest

There are no conflicts of interest.

effective. In the first decade after the introduction of combination ART in 1996, Hodgkin lymphoma was the third most frequent non-AIDS defining malignancy in the United States after lung and anal cancers. During 1991–1995 AIDS defining non-Hodgkin lymphoma (NHL) was 30 times more frequent than Hodgkin lymphoma, but by the 2001–2005 period the NHL:Hodgkin lymphoma ratio had fallen to 7 : 1 [1••]. The immune reconstitution and improving survival attributable to ART, as well as changes in the demographics of PWHAs and possible direct effects of ART, have all been postulated to contribute to these recent changes in the incidence of Hodgkin lymphoma and AIDS-NHL.

HODGKIN LYMPHOMA IN THE GENERAL POPULATION

To understand the changing risk of Hodgkin lymphoma among PWHAs, one starts with the basic epidemiology of Hodgkin lymphoma in the general population. Almost uniquely among cancers (one other exception is osteosarcoma), the age-specific incidence of Hodgkin lymphoma is strikingly bimodal, with peak risks for young and elderly adults, and relatively low risk between the ages of 40 and 59 years (Fig. 1). One possible explanation for this bimodal distribution is that Hodgkin lymphoma in the general population may be two or more distinct diseases [7]. This hypothesis is partly supported by the association of some but not all cases of Hodgkin lymphoma with Epstein-Barr virus (EBV) infection and indeed with infectious mononucleosis, an association that predates the discovery of EBV [8]. However, this association between EBV and Hodgkin lymphoma depends upon numerous factors including the country of residence, Hodgkin lymphoma histological subtype, sex and ethnicity as well as age. EBV is more commonly found in Hodgkin lymphoma in children and the elderly [9]. The age distributions of Hodgkin lymphoma and NHL in the general population yield two notable observations, both of which are illustrated in Fig. 1. First, like most malignancies, the risk of NHL increases steeply with advancing age. Second, the incidence of Hodgkin lymphoma exceeds NHL incidence before age 30, but NHL incidence is 10-fold to 20-fold greater than Hodgkin lymphoma incidence after the age of 50.

HODGKIN LYMPHOMA AND NONHODGKIN LYMPHOMA INCIDENCE TRENDS

The incidence of NHL in the general population is rising at approximately 0.4% per year, as illustrated in Fig. 2a. The higher frequency of NHL among PWHAs has had relatively little impact on this trend. At its peak in the mid-1990s, AIDS accounted for approximately 10% of NHL cases in the United States, decreasing steeply to approximately 4% by the early 2000s (Fig. 2a) [10•].

In contrast to NHL, the age-adjusted incidence of Hodgkin lymphoma has remained steady at approximately 2.8 per 100 000 person-years (<http://seer.cancer.gov>). Among people with AIDS in the United States, the number of Hodgkin lymphoma cases increased significantly from the early 1990s to the early 2000s (Fig. 2b). Despite increasing case numbers in most studies [1••, 2•, 3–5, 11, 12], but not all [6,13], a concomitant increase in the age-adjusted incidence of Hodgkin lymphoma with AIDS has not been seen (Fig. 2b) [1••]. Thus, one might speculate that aging of the HIV and AIDS population may contribute to the increasing number of Hodgkin lymphoma cases. However, this hypothesis would have to confront a paradox that the HIV and AIDS population has increased most at ages between 40 and 59 years [14], when Hodgkin lymphoma risk in the general population is relatively low (Fig. 1).

CD4 COUNT AND HODGKIN LYMPHOMA RISK

The risk of NHL in PWHAs rises as the CD4 cell count falls, but the risk of Hodgkin lymphoma does not have a simple relationship to CD4 cell count. In a study of 173 Hodgkin

lymphoma cases that occurred 4–27 months after first being registered with an AIDS-defining illness, when the CD4 count was measured, Biggar *et al.* [6] noted that the risk of Hodgkin lymphoma was highest with 225–249 CD4cells/ μ l. Subsequent studies have generally confirmed these findings. In the large Collaboration of Observational HIV Epidemiological Research Europe (COHERE) consortium that examined 78 Hodgkin lymphoma cases, the risk was highest with a baseline CD4 cell count of 100–199 CD4cells/ μ l and with a nadir CD4 count of 50–99 CD4cells/ μ l [15••]. When CD4 count was measured within a few months of the Hodgkin lymphoma diagnosis in 149 cases in the French hospital database cohort, the risk was about 70% higher with a CD4 cell count of 50–99/ μ l than with a CD4 count below 50/ μ l. The CD4 cell count at entry into the Swiss HIV Cohort Study tended to be inversely related to Hodgkin lymphoma risk, although this was based on only 47 Hodgkin lymphoma cases [5].

Only one study has examined the effect of CD4 count on the risk of Hodgkin lymphoma by histologic subtype [6]. The risk of nodular sclerosing Hodgkin lymphoma was significantly lower at extremely low CD4 cell counts. Indeed, there were no cases of nodular sclerosing Hodgkin lymphoma presenting with a CD4 count below 50 cells/ μ l. They proposed two possible explanations. First, clinical manifestation of nodular sclerosing and perhaps other subtypes of Hodgkin lymphoma may require a cellular immune response that is lost at very low CD4 counts. Or second, lymphomas that do manifest at very low CD4 counts shift from a Hodgkin lymphoma to an NHL phenotype, a diagnostic misclassification that may be difficult to detect with the large excess of NHL among PWHA.

CURRENT USE OF ANTIRETROVIRAL THERAPY AND HODGKIN LYMPHOMA RISK

Only five published studies have examined the relationship between Hodgkin lymphoma and current use of ART [2•, 5, 13, 15••, 16]. Powles *et al.* [13] identified 35 Hodgkin lymphoma cases in their hospital-based cohort in London, UK, and they reported that Hodgkin lymphoma risk was increased three-fold (95% confidence interval 1.4–6.7) with current use of ART. Adjustment for concurrent CD4 cell count attenuated the risk associated with ART to 2.7-fold [13]. The elevated Hodgkin lymphoma risk was associated with the use of nonnucleoside reverse transcriptase inhibitors [13]. In the Swiss HIV Cohort Study, with 47 Hodgkin lymphoma cases, current ART use was not related to Hodgkin lymphoma risk, but there was a trend toward lower risk (odds ratio 0.7, 95% confidence interval 0.3–1.7) with more than 5 years on ART [5]. In COHERE, current use of ART was not associated with Hodgkin lymphoma risk, based on 61 cases currently taking and 17 not currently taking ART [15••].

A pair of analyses from the French hospital database are the largest studies to date. In the first of these, there were 149 Hodgkin lymphoma cases among 52 278PWHA[16]. Adjusted for currentCD4 count, receiving ART for at least 6 months was associated with a nonsignificantly reduced risk of Hodgkin lymphoma. The second series included 187 Hodgkin lymphoma cases among 64 368 PWHA [2•]. In this study, use of ART for at least 6 months was associated with a marginally reduced risk of Hodgkin lymphoma (odds ratio 0.8, 95% confidence interval 0.6–1.2), and adjustment for CD4 count and HIV viral load had little effect on this estimate.

ANTIRETROVIRAL THERAPY INITIATION AND CD4 COUNT INTERACTIONS

The French hospital database study further attempted to examine the temporal effects of ART on the risk of Hodgkin lymphoma and, in particular, whether ART had a short-term effect on this risk. Restricting the analysis to the period since 1996 when ART became

widely available, they found that there was a 2.6-fold rise (95% confidence interval 1.4–4.7) in the Hodgkin lymphoma risk during the first 3 months on ART. This raised risk subsequently declined to 1.4-fold after 4–6 months on ART, and then to 0.8-fold with more than 6 months on ART [2•]. Unlike in the UK study [13], the risk for Hodgkin lymphoma in the French study was unrelated to the ART regimen [2•]. Adjustment for contemporaneous CD4 cell count attenuated the risk during the first 3 months on ART to 1.4-fold. One possible mechanism postulated for this early rise in the risk of Hodgkin lymphoma after starting ART is an immune reconstitution inflammatory syndrome (IRIS) phenomenon. Of note, however, during the first 3 months on ART only 15 Hodgkin lymphoma cases occurred, and the rate of rise of their CD4 cell counts resembled the slopes of noncases during ART initiation [2•].

The COHERE team conducted two matched case–control analyses of CD4 cell counts and slopes related to ART initiation [15••]. The rise in CD4 cell counts during the first 18 months after starting ART did not differ between 61 Hodgkin lymphoma cases and 1652 matched controls. These findings appear to make an IRIS-like phenomenon unlikely to be the mechanism of the early increase in Hodgkin lymphoma risk following initiation of ART. A further intriguing clinical observation is that the mean CD4 cell count in patients established on ART fell during the year prior to Hodgkin lymphoma diagnosis by 98 cells/ μ l compared to a mean rise of 35 cells/ μ l in the controls controls ($P=0.0001$). Likewise, at diagnosis mean CD4 count was significantly lower in Hodgkin lymphoma cases than controls (193 versus 383 cells/ μ l, $P=0.0001$) [15••]. Clinicians should be wary that Hodgkin lymphoma appears to be among the several causes for a declining CD4 cell count in PWH on ART. In other words, declining CD4 counts may indicate an increasing risk for developing Hodgkin lymphoma in patients on fully suppressive ART.

HIV LOAD

Only three studies, with overlapping populations, have examined the relationship of plasma HIV load to Hodgkin lymphoma risk. Bohlius *et al.* [15••] found that during the first 1.5 years on ART, the area-under-the-curve of HIV load was marginally higher among Hodgkin lymphoma cases than controls. In contrast, once current CD4 count and ART use were considered, HIV load was unrelated to Hodgkin lymphoma risk in the French hospital database analyses [2•, 16]. These findings would suggest that HIV per se is not directly implicated in the pathogenesis of Hodgkin lymphoma in PWH.

SEX, RACE AND HIV RISK GROUP

In the general population, Hodgkin lymphoma overall occurs more frequently in men than women and in whites than blacks. The sex bias toward men has also been found in PWH in Italy and France [2•, 4]. In particular, men have a higher risk of the mixed cellularity subtype of Hodgkin lymphoma (<http://seer.cancer.gov>), and it is this histological subtype that is most common among PWH [3, 4, 6]. In the Swiss cohort study, sex did not alter the risk of Hodgkin lymphoma, but men who have sex with men (MSM) were at more than two-fold higher risk of Hodgkin lymphoma compared to injection drug users [15••]. A final demographic observation from the French PWH cohorts was that the risk of Hodgkin lymphoma was higher in French natives than sub-Saharan African natives [2•].

EPSTEIN-BARR VIRUS

The epidemiological relationship between infectious mononucleosis and the presence of EBV in Hodgkin lymphoma tumor cells has led to the hypothesis that EBV is intimately related to the pathogenesis of at least some cases of Hodgkin lymphoma [7, 8]. Although the detection rate for EBV in Hodgkin lymphoma tumor cells varies depending upon the

technique used, EBV is present in around half of all Hodgkin lymphoma cases in the general population. EBV is more frequently present in Hodgkin lymphoma tumor cells in children and the elderly and is found more commonly in tumors in Africa and Asia than in North America and Western Europe [17]. EBV is almost universally present in Hodgkin lymphoma tumor cells in PWHAs [3].

Somatic immunoglobulin gene hypermutation in activated germinal center B cells in lymph nodes may result in crippling mutations and as a consequence these cells express no surface immunoglobulin and undergo apoptosis. The presence of EBV-derived oncogenes EBNA1 (EBV nuclear antigen 1) and LMP 2A (latent membrane protein 2A) is able to rescue these cells which appear to be the origin of Hodgkin lymphoma tumor cells [18]. Indeed, EBV contributes to several lymphoid malignancies in the context of immunodeficiency and the features vary markedly. In PWHAs, EBV not only is present in Hodgkin lymphoma tumor cells but also is invariably present in tumor cells in AIDS-defining primary cerebral lymphoma (PCL). This tumor is associated with very advanced immunosuppression and is becoming markedly less common since the introduction of ART [10, 19]. Similarly, EBV is present in the posttransplant lymphoproliferative disorders (PTLDs) that occur in allogeneic transplant recipients. These tumors may be polyclonal or monoclonal and polymorphic or monomorphic. Early polymorphic polyclonal PTLD may respond to reduction of iatrogenic immunosuppression alone, whereas more advanced PTLD may respond to adoptive immunotherapy using either autologous or HLA-matched allogeneic EBV-specific cytotoxic T-lymphocytes [20]. In both PCL and PTLD, there appears to be a more direct correlation between immunosuppression and the risk of disease, and alleviating immunodeficiency appears to be beneficial either by reducing the risk (PCL) or causing tumor regression (PTLD). Another aspect of the management of PTLD is the use of plasma EBV copy number as a monitor of disease activity and in some circumstances as a method of early detection of PTLD [21], comparable to the role of EBV viral load as a tumor marker in nasopharyngeal cancers [22]. It is possible that measurement of the EBV viral load in blood may provide a similar role in HIV-associated Hodgkin lymphoma.

TREATMENT IMPLICATIONS

Although it is clear that the epidemiological studies have yielded mixed messages, the outcomes of treatment for Hodgkin lymphoma in PWHAs have steadily improved. Indeed, a new multi-institutional study shows that the outcomes with ABVD combination chemotherapy are the same whether patients are HIV seropositive ($n=95$) or not ($n=131$) [23]. In this context, the impact of ART along with opportunistic infection prophylaxis may be the ability to deliver the chemotherapy without significant delays and dose reductions resulting in the improved response rate and overall survival reported in recent case series. In addition, the immune restoration afforded by ART has encouraged clinicians to aggressively treat patients who relapse with high-dose chemotherapy and progenitor cell rescue.

CONCLUSION

The risk of Hodgkin lymphoma is elevated in PWHAs, but this risk is not linearly related to CD4 cell count. The risk of Hodgkin lymphoma appears to be lower at very low CD4 counts than in patients with more modest immunosuppression. Moreover, the influence of ART on this risk appears uncertain, with both modest elevations and reductions in risk reported. Additionally in some studies the risk of Hodgkin lymphoma seems to be higher during the first few months after starting ART, although the reason for this remains obscure. It is tempting to hypothesize that the inability to control latent EBV infection of B lymphocytes recovers slowly or incompletely following the initiation of ART. Certainly this is supported

by the almost universal presence of EBV in Hodgkin lymphoma tumor cells in PWHA. Despite the relatively modest effects of ART on the epidemiology of Hodgkin lymphoma in PWHA, the use of ART and combination chemotherapy in this population has resulted in dramatically improved clinical responses and outcomes that should encourage both patients and clinicians.

Acknowledgments

The authors thank Dr Meredith Shiels for advice on and assistance with Fig. 2.

REFERENCES AND RECOMMENDED READING

Papers of particular interest, published within the annual period of review, have been highlighted as:

- of special interest
 - of outstanding interest
- Additional references related to this topic can also be found in the Current World Literature section in this issue (pp. 591–592).
- Shiels MS, Pfeiffer RM, Gail MH, et al. Cancer burden in the HIV-infected population in the United States. *J Natl Cancer Inst.* 2011; 103:753–762. [PubMed: 21483021] This is a comprehensive analysis of data representative of the United States that provides estimated total numbers of cases and incidence rates of 3 AIDS-defining and 30 non-AIDS-defining malignancies (including Hodgkin lymphoma) among people with AIDS (years 2001 – 2007) and among people with HIV without AIDS (years 2004 – 2007). It shows substantial increases in non-AIDS-defining malignancies, most of which were a consequence of growth and aging of the HIV and AIDS population.
 - Lanoy E, Rosenberg PS, Fily F, et al. HIV-associated Hodgkin lymphoma during the first months on combination antiretroviral therapy. *Blood.* 2011; 118:44–49. [PubMed: 21551234] This analysis of the French Hospital Database observed that the risk for developing Hodgkin lymphoma was increased three-fold during months 1 – 3 on ART, 1.6-fold during months 4 – 6 on ART, and not elevated with more than 6 months on ART. Risk was highest with a current CD4 count of 50 – 99 cells/ μ l. Adjustment for CD4 count partially accounted for the high risk during the first months on ART.
 - Glaser SL, Clarke CA, Gulley ML, et al. Population-based patterns of human immunodeficiency virus-related Hodgkin lymphoma in the Greater San Francisco Bay Area, 1988 – 1998. *Cancer.* 2003; 98:300–309. [PubMed: 12872349]
 - Dal Maso L, Polesel J, Serraino D, et al. Pattern of cancer risk in persons with AIDS in Italy in the HAART era. *Br J Cancer.* 2009; 100:840–847. [PubMed: 19223894]
 - Clifford GM, Rickenbach M, Lise M, et al. Hodgkin lymphoma in the Swiss HIV Cohort Study. *Blood.* 2009; 113:5737–5742. [PubMed: 19336755]
 - Biggar RJ, Jaffe ES, Goedert JJ, et al. Hodgkin lymphoma and immunodeficiency in persons with HIV/AIDS. *Blood.* 2006; 108:3786–3791. [PubMed: 16917006]
 - Hjalgrim H, Engels EA. Infectious aetiology of Hodgkin and non-Hodgkin lymphomas: a review of the epidemiological evidence. *J Intern Med.* 2008; 264:537–548. [PubMed: 19017178]
 - Rosdahl N, Larsen SO, Clemmesen J. Hodgkin's disease in patients with previous infectious mononucleosis: 30 years' experience. *Br Med J.* 1974; 2:253–256. [PubMed: 4406463]
 - Flavell KJ, Murray PG. Hodgkin's disease and the Epstein-Barr virus. *Mol Pathol.* 2000; 53:262–269. [PubMed: 11091850]
 - Shiels MS, Pfeiffer RM, Hall HI, et al. Proportions of Kaposi sarcoma, selected non-Hodgkin lymphomas, and cervical cancer in the United States occurring in persons with AIDS, 1980 – 2007. *JAMA.* 2011; 305:1450–1459. [PubMed: 21486978] This analysis of population-based data in the United States characterized the dramatic effects of the AIDS epidemic on the incidence of

Kaposi sarcoma, subtypes of non-Hodgkin lymphoma and cervical cancer over the course of the epidemic, 1980–2007.

11. Franceschi S, Lise M, Clifford GM, et al. Changing patterns of cancer incidence in the early- and late-HAART periods: the Swiss HIV Cohort Study. *Br J Cancer*. 2010; 103:416–422. [PubMed: 20588274]
12. Polesel J, Franceschi S, Suligoi B, et al. Cancer incidence in people with AIDS in Italy. *Int J Cancer*. 2010; 127:1437–1445. [PubMed: 20049835]
13. Powles T, Robinson D, Stebbing J, et al. Highly active antiretroviral therapy and the incidence of non-AIDS-defining cancers in people with HIV infection. *J Clin Oncol*. 2009; 27:884–890. [PubMed: 19114688]
14. Shiels MS, Pfeiffer RM, Engels EA. Age at cancer diagnosis among persons with AIDS in the United States. *Ann Intern Med*. 2010; 153:452–460. [PubMed: 20921544]
15. Bohlius J, Schmidlin K, Boue F, et al. HIV-1-related Hodgkin lymphoma in the era of combination antiretroviral therapy: incidence and evolution of CD4 T-cell lymphocytes. *Blood*. 2011; 117:6100–6108. [PubMed: 21368291] This analysis of data from 40 168 HIV-infected participants in 16 cohort studies in the Collaboration of Observational HIV Epidemiological Research Europe (COHERE) examined risk factors for Hodgkin lymphoma, focusing especially on CD4 count. Nearly all of the 78 Hodgkin lymphoma cases, as well as the other participants, were on ART. Hodgkin lymphoma cases had lower baseline and nadir CD4 counts, with highest risk at 100 – 199 and 50 – 99 cells/μl, respectively. During the year before Hodgkin lymphoma diagnosis, while on ART, cases lost 98 CD4cells/μl, whereas matched controls gained 35 cells/μl.
16. Guiguet M, Boue F, Cadranet J, et al. Effect of immunodeficiency, HIV viral load, and antiretroviral therapy on the risk of individual malignancies (FHDH-ANRS CO4): a prospective cohort study. *Lancet Oncol*. 2009; 10:1152–1159. [PubMed: 19818686]
17. Glaser SL, Lin RJ, Stewart SL, et al. Epstein-Barr virus-associated Hodgkin's disease: epidemiologic characteristics in international data. *Int J Cancer*. 1997; 70:375–382. [PubMed: 9033642]
18. Klein E, Kis LL, Klein G. Epstein-Barr virus infection in humans: from harmless to life endangering virus-lymphocyte interactions. *Oncogene*. 2007; 26:1297–1305. [PubMed: 17322915]
19. Biggar RJ, Chaturvedi AK, Goedert JJ, Engels EA. AIDS-related cancer and severity of immunosuppression in persons with AIDS. *J Natl Cancer Inst*. 2007; 99:962–972. [PubMed: 17565153]
20. Barker JN, Doubrovina E, Sauter C, et al. Successful treatment of EBV-associated posttransplantation lymphoma after cord blood transplantation using third-party EBV-specific cytotoxic T lymphocytes. *Blood*. 2010; 116:5045–5049. [PubMed: 20826724]
21. Wagner HJ, Cheng YC, Huls MH, et al. Prompt versus preemptive intervention for EBV lymphoproliferative disease. *Blood*. 2004; 103:3979–3981. [PubMed: 14751931]
22. Leung SF, Zee B, Ma BB, et al. Plasma Epstein-Barr viral deoxyribonucleic acid quantitation complements tumor-node-metastasis staging prognostication in nasopharyngeal carcinoma. *J Clin Oncol*. 2006; 24:5414–5418. [PubMed: 17135642]
23. Montoto S, Shaw K, Okosun J, et al. HIV status does not impact on outcome in patients with classical Hodgkin lymphoma treated with ABVD chemotherapy in the HAART era. *J Clin Oncol*. (in press). This study of 224 consecutive patients treated with ABVD chemotherapy for Hodgkin lymphoma (93 HIV-positive and 131 HIV-negative) shows that although more of the HIV-positive patients had high-risk disease by IPS criteria, there were no significant differences in response, event-free survival or overall survival rates between patients with and without HIV infection.

KEY POINTS

- Hodgkin lymphoma is a significant cause of mortality and morbidity in the post-HAART era.
- The incidence of Hodgkin lymphoma does not appear to be declining as dramatically as the incidence of AIDS defining malignancies.
- The outcome for patients with HIV-associated Hodgkin lymphoma appears to be similar to that in the general population.

Figure 1.

Age-specific incidence of Hodgkin lymphoma (solid line) and non-Hodgkin lymphoma (dashed line) in the United States, 1992–2008. From the Surveillance, Epidemiology and End Results Program, National Cancer Institute, National Institutes of Health (SEER 13, <http://seer.cancer.gov>).

Figure 2.

(a) Diffuse large B-cell lymphoma in the United States. Estimated number of cases (bars) by calendar year, 1980–2007. Dark bars and line indicate the proportion (%) of cases among people with AIDS, which peaked in 1993. Data from [10•]. (b) Hodgkin lymphoma among people with AIDS in the United States. Estimated number of cases (bars), and age-standardized and sex-standardized incidence rates (line) by calendar year, 1991–2005. Number of cases increased significantly, but incidence rate did not. Data from [1••].