Kaposi sarcoma incidence in the Swiss HIV Cohort Study before and after highly active antiretroviral therapy

S Franceschi1,2, L Dal Maso1, M Rickenbach3, J Polesel2, B Hirschi4, M Cavassini5, A Bordoni6, L Elzi7, S Ess8, G Jundt9, N Mueller10, GM Clifford11 and the Swiss HIV Cohort Study11

1International Agency for Research on Cancer, 150 cours Albert Thomas, 69372 Lyon cedex 08, France; 2Epidemiology and Biostatistics Unit, Aviano Cancer Center, Via Franco Gallini 2, 33081 Aviano, Italy; 3Coordination and Data Center, Swiss HIV Cohort Study, Mont-Pa¨ssible 16, CH-UV, 1011 Lausanne, Switzerland; 4Division of Infectious Diseases, Department of Internal Medicine, University Hospital of Geneva, Rue Michel-du-Grest 24, CH-1211 Geneva 14, Switzerland; 5Division of Infectious Diseases, Department of Medicine 2, CHUV Lausanne, Lausanne 1011, Switzerland; 6Division of Infectious Diseases and Hospital Epidemiology, University Hospital Basel, Petersgraben 4, CH-4031 Basel, Switzerland; 7Cancer Registry of the Canton of Ticino, Via in Selva 24, CH-6600 Locarno, Switzerland; 8Division of Infectious Diseases and Hospital Epidemiology, University Hospital Basel, Petersgraben 4, CH-4031 Basel, Switzerland; 9Cancer Registry of Basel, Schœ{"o}nbeinstrasse 40, CH-4003 Basel, Switzerland; 10Division of Infectious Diseases and Hospital Epidemiology, Department of Medicine, University Hospital Zurich, Rämistrasse 100, CH-8091 Zurich, Switzerland

Between 1984 and 2006, 12,959 people with HIV/AIDS (PWHA) in the Swiss HIV Cohort Study contributed a total of 73,412 person-years (py) of follow-up. 35.5% of which derived from PWHA treated with highly active antiretroviral therapy (HAART). Five hundred and ninety-seven incident Kaposi sarcoma (KS) cases were identified of whom 52 were among HAART users. Cox regression was used to estimate hazard ratios (HR) and corresponding 95% confidence intervals (CI). Kaposi sarcoma incidence fell abruptly in 1996–1998 to reach a plateau at 1.4 per 1000 py afterwards. Men having sex with men and birth in Africa or the Middle East were associated with KS in both non-users and users of HAART but the risk pattern by CD4 cell count differed. Only very low CD4 cell count (<50 cells µl−1) at enrolment or at HAART initiation were significantly associated with KS among HAART users. The HR for KS declined steeply in the first months after HAART initiation and continued to be low 7–10 years afterwards (HR, 0.06; 95% CI, 0.02–0.17). Thirty-three out of 52 (63.5%) KS cases among HAART users arose among PWHA who had stopped treatment or used HAART for less than 6 months.

British Journal of Cancer (2008) 99, 800–804. doi:10.1038/sj.bjc.6604520 www.bjcancer.com

Keywords: HIV; AIDS; Kaposi sarcoma; antiretroviral drugs; Swiss HIV cohort study

At the beginning of the HIV epidemic, Kaposi sarcoma (KS) was one of the most common manifestations of AIDS (Dal Maso et al., 1995; Biggar et al., 1996), present during the mid-1980s in 25% of individuals at the time of AIDS diagnosis in the United States, but decreased steadily through the late 1980s and mid-1990s, down to 2% after the advent and widespread use of highly active antiretroviral therapy (HAART) in 1996 (Engels et al., 2006).

A similar temporal pattern was observed for KS in Australia (Grulich et al., 2001) and in European countries (Dal Maso et al., 1995; Rezza et al., 2000; Franceschi et al., 2003; Mocroft et al., 2004; Clifford et al., 2005), but detailed data on the long-term trends of KS incidence in Europe are limited. We therefore took advantage of the more than 20 years of follow-up data available from the Swiss HIV Cohort Study (SHCS) to assess changes in the incidence of and risk factors for KS before and after HAART use.

MATERIALS AND METHODS

The SHCS is an ongoing study that has been enrolling people with HIV/AIDS (PWHA) over 16 years of age since 1988, with some retrospective enrolment going back to 1984, from seven large hospitals in Swiss cities (Basel, Bern, Geneva, Lausanne, Lugano, St Gallen, and Zurich) (www.shcs.ch). Follow-up visits take place every 6 months and all AIDS-defining events, including KS diagnosis and death, are recorded. The present study included PWHA enrolled up to 30 September 2005, and information recorded in the SHCS database up to 31 March 2006. People with HIV/AIDS were excluded from the present study if they (1) did not have information on date of birth, gender, or HIV transmission category (number (n) = 54), (2) were diagnosed with KS at
enrollment or earlier (n = 568), or (3) had no follow-up visits (n = 131). A total of 597 KS cases were included in our present study: 545 were identified from the SHCS database, and 52 through record linkage with eight Swiss Cantonal Cancer Registries (Clifford et al., 2005). Six of these cancer registries (Basel, Geneva, Ticino, St Gallen and Appenzell, Vaud, and Zurich) overlap directly with six of the seven cantons covered by SHCS hospitals (all except Bern). The Neuchâtel and Valais Cancer Registries do not directly overlap with SHCS hospitals, but some residents of these cantons are followed in a neighbouring SHCS hospital. Places of birth were classified as Europe (Switzerland and the rest of Europe, 87.1% of PWHA) and Africa or the Middle East (8.1%). The few PWHA previously born outside Europe, but in countries where KS is not endemic (e.g., the Americas and Asia; Hengge et al., 2002), were included in the Europe category. Conversely, the few PWHA born in the Caribbean were included in the Africa/Middle East category. Histological confirmation was mentioned in the majority of KS cases, but presentation site (i.e., skin only vs other) was available only for 382 (64%) KS cases.

Highly active antiretroviral therapy was defined as a combination of at least three drugs, including a protease inhibitor or a non-nucleoside transcriptase inhibitor, or three nucleosides including abacavir. Individuals who had used HAART for more than 1 month were classified as users. Treatment interruption was defined as in a previous report from the SHCS (Taffe et al., 2002), as absence of any antiretroviral drug in PWHA who were previously receiving HAART. Taffe et al. (2002) evaluated the impact of interruptions of less than 3 months on the progression of HIV infection, whereas we focused on the impact of interruptions of 3 months or more on KS incidence. CD4 cell counts at enrolment were excluded in the SHCS and, among HAART users, at, or within 6 months before HAART initiation were retrieved.

For each participant, person-years (py) at risk were calculated between enrolment and KS diagnosis, death, or last follow-up visit, whichever occurred first. Incidence rates per 1000 py were standardised for gender and age based on the enrolled population in the overall study period, using the direct method (Breslow and Day, 1987). Ninety-five percent confidence intervals (CI) of incidence were computed according to the Poisson distribution (Breslow and Day, 1987). The effect of various risk factors on KS incidence were computed according to the Poisson distribution (Breslow and Day, 1987). Ninety-five percent confidence intervals (CI) of standardised incidence rates per 1000 py were calculated (95% CI, 0.08–1.14). Among non-users of HAART, intravenous drug users (HR, 0.09; 95% CI, 0.06–0.13), and heterosexuals and other HIV transmission categories (HR, 0.27; 95% CI, 0.20–0.36) showed a lower KS incidence than MSM. The HR for KS was increased among PWHA older than 35 years (HR, 1.53; 95% CI, 1.29–1.82) and those born in Africa/Middle East (HR, 1.84; 95% CI, 1.10–3.06). Kaposi sarcoma risks among non-users of HAART steeply increased with decreasing CD4 cell count (HR for < 50 vs ≥ 350 cells μl⁻¹, 12.85; 95% CI, 9.59–17.23). These associations were also present, but were weaker, among HAART users with the exception of the association with place of birth that became stronger (HR for Africa/Middle East vs Europe among HAART users, 6.49; 95% CI, 2.79–15.11). In contrast with non-users, no change in the HR for KS was seen among HAART users with CD4 cell counts in the range of 50–350 cells μl⁻¹ and the only significant risk increase was found for CD4 cell count less than 50 cells μl⁻¹ at enrolment (HR, 3.26; 95% CI, 1.53–6.91). On account of the rarity of KS among non-users of HAART, incidence rates were standardised (direct method) on age and gender, based on Swiss HIV Cohort Study participants. Vertical bars represent 95% CI. MSM: men having sex with men.

Figure 1 shows the HR for KS in different periods after HAART initiation compared with non-users. The HR of KS was already reduced by 76% in the first 5 months of use and declined to 0.06 (95% CI, 0.02–0.17) in the subsequent 6 months of use. The

Figure 2 shows the HR for KS in different periods after HAART initiation compared with non-users. The HR of KS was already reduced by 76% in the first 5 months of use and declined to 0.06 (95% CI, 0.02–0.17) in the subsequent 6 months of use. The
TABLE 1 Incidence rates and HR of KS overall and by selected characteristics, and use of HAART

| KS | HAART non-users | HAART users |
|----|----------------|-------------|
|     | Incidence/1000 py (95% CI) | HR (95% CI) | Incidence/1000 py (95% CI) | HR (95% CI) |
| Overall | 545 | 37,861 | 15.0 (13.8–16.3) | 1 | 545 | 35,551 | 1.3 (1.0–1.7) | 0.11 (0.08–0.14) |
| HIV transmission category |
| MSM | 446 | 10,900 | 27.8 (25.3–30.5) | 1 | 35 | 12,216 | 1.6 (1.1–2.3) | 1 |
| Het/Oth | 62 | 10,183 | 8.9 (6.8–11.4) | 0.27 (0.20–0.36) | 16 | 13,796 | 1.2 (0.7–1.9) | 0.54 (0.27–1.10) |
| IDU | 37 | 16,778 | 2.1 (1.5–2.9) | 0.09 (0.06–0.13) | 1 | 9,559 | 0.0 (0.0–0.3) | 0.05 (0.01–0.37) |
| Age at enrolment (years) |
| <35 | 256 | 27,795 | 7.4 (6.5–8.4) | 1 | 25 | 20,136 | 0.9 (0.6–1.3) | 1 |
| ≥35 | 289 | 10,066 | 17.6 (15.7–19.8) | 1.53 (1.29–1.82) | 27 | 15,416 | 1.4 (1.0–2.1) | 1.07 (0.61–1.85) |
| Place of birth |
| Europe | 529 | 36,334 | 15.0 (13.8–16.4) | 1 | 43 | 32,495 | 1.0 (0.7–1.4) | 1 |
| African/Middle East | 16 | 1,527 | 12.5 (7.1–20.4) | 1.84 (1.10–3.06) | 9 | 3,057 | 2.4 (1.4–4.6) | 6.49 (2.79–15.11) |
| CD4 cell count at enrolment (cells µl⁻¹) |
| ≥350 | 128 | 20,988 | 6.7 (5.6–8.0) | 1 | 18 | 15,212 | 1.0 (0.6–1.6) | 1 |
| 200–349 | 93 | 6,126 | 15.3 (12.4–18.8) | 2.44 (1.86–3.20) | 9 | 8,382 | 0.9 (0.4–1.8) | 0.84 (0.38–1.88) |
| 50–199 | 133 | 3,883 | 33.6 (28.2–39.9) | 5.04 (3.90–6.51) | 7,556 | 1.1 (0.6–2.0) | 1.13 (0.53–2.44) |
| <50 | 94 | 1,119 | 77.1 (62.3–94.3) | 12.85 (9.99–17.23) | 1,302 | 4.8 (2.5–8.4) | 3.26 (2.79–15.11) |
| Unknown | 97 | 5,745 | 61.8 (47.4–79.1) | — | 2 | 1,381 | 0.7 (0.1–2.7) | — |
| Treatment interruption |
| No | — | — | — | — | 28 | 27,234 | 0.9 (0.6–1.2) | 1 |
| Yes | — | — | — | — | 24 | 8,317 | 2.8 (1.8–4.1) | 8.14 (4.01–16.54) |

CI = confidence interval; HAART = highly active antiretroviral therapy; Het/Oth = heterosexuals and other; HR = hazard ratio; IDU = intravenous drug users; KS = Kaposi sarcoma; MSM = men having sex with men; py = person-years. *Individuals who were never treated with HAART and py before HAART among HAART users. **Rates are standardised (direct method) on age and/or gender based on all SHCS participants. †Adjusted for centre, age, gender, and HIV transmission category, when appropriate. ‡Reference category. §Absence of any antiretroviral drug for ≥3 months.

Figure 2 Hazard ratio of Kaposi sarcoma in patients receiving highly active antiretroviral therapy (HAART) following treatment initiation. Adjusted for centre, age, gender, HIV transmission category (men having sex with men, other), and CD4 cell count at enrolment. Vertical bars represent 95% confidence intervals. Reference category was defined as non-users of HAART.

| Month after HAART initiation | Hazard ratio |
|-----------------------------|-------------|
| 1–5                        | 0.5         |
| 6–11                       | 0.4         |
| 12–23                      | 0.3         |
| 24–35                      | 0.2         |
| 36–59                      | 0.1         |
| 60–83                      | 0.0         |
| 84–119                     | 0.0         |

DISCUSSION

Our study shows the dramatic decline of KS incidence in the SHCS following the advent of HAART. This expands an earlier report (Ledergerber et al, 1999) from this cohort showing that by 1998 the KS decline was at least as large as that seen for opportunistic infections. Similar reductions in the incidence of KS among PWHA were seen in many other studies (International Collaboration on HIV and Cancer, 2000) although the decrease started earlier (i.e., even before the introduction of HAART) in the United States (Biggar et al, 1996; Engels et al, 2006) and Australia (Grulich et al, 2001) than in Europe (Dal Maso et al, 1995). The prevalence of KS herpesvirus, the cause of KS (IARC, 1997), may have been especially high in the first wave of HIV infection in MSM in the United States and Australia (Osmond et al, 2002).

Highly active antiretroviral therapy became rapidly available to SHCS participants and, by 1997, 80% of them were using three antiretroviral drugs or more (www.shcs.ch). The proportion of SHCS participants with CD4 cell counts <350 cells µl⁻¹ who had never been treated was small (<3%) in 2006 in all HIV transmission categories. Despite the widespread use of HAART and the introduction after 1996 of successively more potent antiretroviral drugs, the decrease in KS incidence continued (Figure 2). Eighteen (34.6%) KS cases had not been taking any antiretroviral drug for 3 months or more, and in 10 instances for 12 months or longer. Recent initiation of HAART was identified in 15 KS cases, among whom five of the nine KS were from Africa/Middle East. Severe immunodeficiency was identified among 10 KS cases. Nine KS cases, all from the MSM transmission category, could not be assigned to any of the three categories above. Five of them (aged 35, 49, 52, 56, and 63 years) had a CD4 cell count ≥350 cells µl⁻¹ (i.e., 405, 440, 557, 596, 782) at KS diagnosis.

The reduction in KS risk persisted unchanged up to 84–119 months after HAART initiation (HR, 0.06; 95% CI, 0.02–0.16) (Figure 2). Finally, the 52 HAART users who developed KS were individually reviewed and classified into the following groups: (1) no antiretroviral drug in the 3 months before KS diagnosis; (2) recent initiation of HAART (<6 months before KS diagnosis); (3) severe immunodeficiency (CD4 cell count <100 cells µl⁻¹) at KS onset while on HAART for ≥6 months; and (4) none of the above (data not shown).
antiretroviral drugs, KS incidence in the SHCS seems to have reached a plateau after 2001, as reported among AIDS patients in the United States (Engels et al., 2006). In addition to making KS a relatively rare event, HAART use has also diminished the variation in KS risk by host characteristics, including gender, age group, and to some extent, HIV transmission category and CD4 cell count at enrolment as compared with that found among non-users. Only a count <50 cells µL\(^{-1}\) at enrolment or HAART initiation was associated with an increased HR for KS. Reduced importance of CD4 cell count at enrolment in HAART users vs non-users was also seen in the SHCS for non-Hodgkin’s lymphoma, but the impact of HAART on non-Hodgkin’s lymphoma was weaker (HR, 0.26; 95% CI, 0.20 – 0.33) than on KS, and hence, non-Hodgkin’s lymphoma incidence (1.9; 95% CI, 1.6 – 2.6 per 1000 py) became higher than KS incidence among HAART users (Polesel et al., 2008).

Kaposi sarcoma risk was already reduced by over 90% after 1 year of HAART and it did not show any sign of increasing again for at least 10 years. The decline of non-Hodgkin’s lymphoma risk after HAART initiation was more gradual than for KS, but equally prolonged (Polesel et al., 2008). Approximately one-third of HAART users in the SHCS had one or more interruptions of antiretroviral treatment (Taffé et al., 2002) due in most cases either to intolerance to drugs, or social factors (i.e., being an intravenous drug user, poor education, etc.), and not to treatment failure. In our study, the absence of any antiretroviral treatment for 3 months or more was associated with an eight-fold increased KS risk, thus confirming the danger of treatment interruption already reported with respect to progression to AIDS or death (Holkmann et al., 2007). Significantly higher KS incidence among PWHA who were assigned to the CD4 cell-guided intermittent antiretroviral treatment arm than those assigned to the continuous treatment arm was also shown in a randomised clinical trial (Silverberg et al., 2007).

Of the 52 KS among HAART users, 23 arose among people who had either stopped using HAART at or had initiated treatment less than 6 months before KS diagnosis. Recent initiation of HAART in the SHCS seemed especially important among KS cases born in Africa/Middle East, suggesting possible delays in the diagnosis or treatment of HIV infection. Ten KS cases arose in PWHA whose CD4 cell count was very low despite concurrent HAART use whereas 5 MSM developed KS despite being on HAART and having CD4 cell counts at which AIDS-related KS is seldom seen (Biggar et al., 2007). The occurrence of KS cases in PWHA with high CD4 cell counts and undetectable viral loads has already been reported in the United States after 1996 (Maurer et al., 2007; Krown et al., 2008). It is possible that, with the ageing of PWHA, those who are co-infected with KS herpesvirus may develop KS despite good control of HIV infection.

Weaknesses of our study are the lack of information on year of HIV seroconversion and on the presence of KS herpesvirus co-infection. Furthermore, we evaluated HAART use by intention-to-treat, that is, without subtracting all periods where treatment had been stopped, so its efficacy may be underestimated. A major strength of our cohort study is that it is the largest ever reported with respect to the number of KS cases and the number of person-years of HAART use. Furthermore, the representativeness of the SHCS with respect to Swiss PWHA was especially good (i.e., inclusion of 49% of all HIV-positive people and 67% of all AIDS cases in the country, www.shcs.ch).

ACKNOWLEDGEMENTS

This study was performed within the framework of the Swiss HIV Cohort Study, supported by the Swiss National Science Foundation, and was funded by a grant from Oncosuisse (ICP OCS 01355-03-2003) and the Istituto Superiore di Sanità, Rome, Italy (Grant 20 G.3). We thank the staff of the Swiss Cantonal Cancer Registries, especially C Bouchardy (Geneva), D De Weck (Valais), N Probst-Hensch (Zurich), and F Levi (Vaud and Neuchâtel) for help with identification of KS cases and T Perdrix-Thoma for technical assistance.

Conflict of interest

The authors declare no conflict of interest.

REFERENCES

Biggar RJ, Chaturvedi AK, Goedert JJ, Engels EA (2007) AIDS-related cancer and severity of immunosuppression in persons with AIDS. J Natl Cancer Inst 99: 962 – 972

Biggar RJ, Rosenberg PS, Cote T (1996) Kaposi’s sarcoma and non-Hodgkin’s lymphoma following the diagnosis of AIDS. Multistate AIDS/Cancer Match Study Group. Int J Cancer 68: 754 – 758

Breslow NE, Day NE (1987) Statistical Methods in Cancer Research, Vol. II: The Design and Analysis of Cohort Studies IARC Scientific Publications No. 82 International Agency for Research on Cancer: Lyon

Clifford GM, Polese J, Rickenbach M, Dal Maso L, Keiser O, Kohler A, Rapiti E, Levi F, Jundt G, Fisch T, Bordoni A, De Weck D, Franceschi S (2005) Cancer risk in the Swiss HIV Cohort Study: associations with immunodeficiency, smoking, and highly active antiretroviral therapy. J Natl Cancer Inst 97: 425 – 432

Cox DR (1972) Regression models and life-time tables. J R Stat Soc B 34: 187 – 220

Dal Maso L, Franceschi S, Negri E, Serraino D, La Vecchia C, Ancelle-Park (2000) Statistical Methods in Cancer Research, Vol. II: Epidemiology

REFERENCES

Biggar RJ, Chaturvedi AK, Goedert JJ, Engels EA (2007) AIDS-related cancer and severity of immunosuppression in persons with AIDS. J Natl Cancer Inst 99: 962 – 972

Biggar RJ, Rosenberg PS, Cote T (1996) Kaposi’s sarcoma and non-Hodgkin’s lymphoma following the diagnosis of AIDS. Multistate AIDS/Cancer Match Study Group. Int J Cancer 68: 754 – 758

Breslow NE, Day NE (1987) Statistical Methods in Cancer Research, Vol. II: The Design and Analysis of Cohort Studies IARC Scientific Publications No. 82 International Agency for Research on Cancer: Lyon

Clifford GM, Polese J, Rickenbach M, Dal Maso L, Keiser O, Kohler A, Rapiti E, Levi F, Jundt G, Fisch T, Bordoni A, De Weck D, Franceschi S (2005) Cancer risk in the Swiss HIV Cohort Study: associations with immunodeficiency, smoking, and highly active antiretroviral therapy. J Natl Cancer Inst 97: 425 – 432

Cox DR (1972) Regression models and life-time tables. J R Stat Soc B 34: 187 – 220

Dal Maso L, Franceschi S, Negri E, Serraino D, La Vecchia C, Ancelle-Park RA (1995) Trends of AIDS incidence in Europe and the United States. Soz Praventivmed 40: 239 – 265

Engels EA, Pfeiffer RM, Goedert JJ, Virgo P, McNeel TS, Scoppa SM, Biggar RJ (2006) Trends in cancer risk among people with AIDS in the United States 1980 – 2002. AIDS 20: 1645 – 1654

Franceschi S, Dal Maso L, Pezzotti P, Polese J, Braga C, Piselli P, Serraino D, Tagliabue G, Federico M, Ferretti S, De Lisi V, La Rosa F, Conti E, Budroni M, Vicario G, Piffer S, Pannelli F, Giacomin A, Bellu F, Tumino R, Fusco M, Rezza G, for the Cancer and AIDS Registry Linkage Study (2003)

KS in the SHCS before and after HAART

5 Franceschi et al

Incidence of AIDS-defining cancers after AIDS diagnosis among people with AIDS in Italy, 1986 – 1998. J Acquir Immune Defic Syndr 34: 84 – 90

Grulich AE, Li Y, McDonald AM, Correll PK, Law MG, Kaldor JM (2001) Decreasing rates of Kaposi’s sarcoma and non-Hodgkin’s lymphoma in the era of potent combination anti-retroviral therapy. AIDS 15: 629 – 633

Henggê UR, Ruzicka T, Tying SK, Stuschke M, Roggendorf M, Schwartz RA, Seeger S (2002) Update on Kaposi’s sarcoma and other HHV8 associated diseases. Part 1: epidemiology, environmental predispositions, and therapy. Lancet Infect Dis 2(2): 281 – 292

Holkmann OC, Mocroft A, Kirk O, Vella S, Blaxhult A, Clumeck N, Fisher M, Katlama C, Phillips AN, Lundgren JD (2007) Interruption of combination antiretroviral therapy and risk of clinical disease progression to AIDS or death. HIV Med 8: 96 – 104

IARC (1997) IARC Monographs on the Evaluation of Carcinogenic Risks to Humans. Volume 70: Epstein–Barr Virus and Kaposi’s Sarcoma

Herpesvirus/Epstein-Barr Virus and Kaposi’s Sarcoma Herpesvirus/Human Herpesvirus 8. IARC Press: Lyon

International Collaboration on HIV and Cancer (2000) Highly active antiretroviral therapy and incidence of cancer in human immunodeficiency virus-infected adults. J Natl Cancer Inst 92: 1823 – 1830

Krown SE, Lee JY, Dittmer DP (2008) More on HIV-associated Kaposi’s sarcoma. N Engl J Med 358: 535 – 536

Ledergerber B, Telenzi A, Egger M, for the Swiss HIV Cohort Study (1999) Risk of HIV related Kaposi’s sarcoma and non-Hodgkin’s lymphoma with potent antiretroviral therapy: prospective cohort study. BMJ 319: 23 – 24

Maurer T, Ponte M, Leslie K (2007) HIV-associated Kaposi’s sarcoma with a high CD4 count and a low viral load. N Engl J Med 357: 1352 – 1353
Mocroft A, Kirk O, Clumeck N, Gargalianos-Kakolyris P, Trocha H, Chentsova N, Antunes F, Stellbrink HJ, Phillips AN, Lundgren JD (2004) The changing pattern of Kaposi sarcoma in patients with HIV, 1994–2003: the EuroSIDA Study. Cancer 100: 2644–2654

Osmond DH, Buchbinder S, Cheng A, Graves A, Vittinghoff E, Cossen CK, Forghani B, Martin JN (2002) Prevalence of Kaposi sarcoma-associated herpesvirus infection in homosexual men at beginning of and during the HIV epidemic. JAMA 287: 221–225

Polesel J, Clifford GM, Rickenbach M, Dal Maso L, Battegay M, Bouchardy C, Furrer H, Hasse B, Levi F, Probst-Hensch NM, Schmid P, Franceschi S, the Swiss HIV Cohort Study (2008) Non-Hodgkin lymphoma incidence in the Swiss HIV Cohort Study before and after highly active antiretroviral therapy. AIDS 22: 301–306

Rezza G, Dorrucci M, Serraino D, Andreoni M, Giuliani M, Zerbini R, Sarmati L, Colangeli V, Salassa B, Monini P, Ensoli B, Pezzotti P (2000) Incidence of Kaposi’s sarcoma and HHV-8 seroprevalence among homosexual men with known dates of HIV seroconversion. Italian Seroconversion Study. AIDS 14: 1647–1653

Silverberg MJ, Neuhaus J, Bower M, Gey D, Hatzakis A, Henry K, Hidalgo J, Lourtau L, Neaton JD, Tambussi G, Abrams DI (2007) Risk of cancers during interrupted antiretroviral therapy in the SMART study. AIDS 21: 1957–1963

Taffé P, Rickenbach M, Hirschel B, Opravil M, Furrer H, Janin P, Bugnon F, Ledergerber B, Wagels T, Sudre P (2002) Impact of occasional short interruptions of HAART on the progression of HIV infection: results from a cohort study. AIDS 16: 747–775