

Supplement for

Changing incidence and risk factors for Kaposi sarcoma by time since starting antiretroviral therapy: Collaborative analysis of 21 European cohort studies

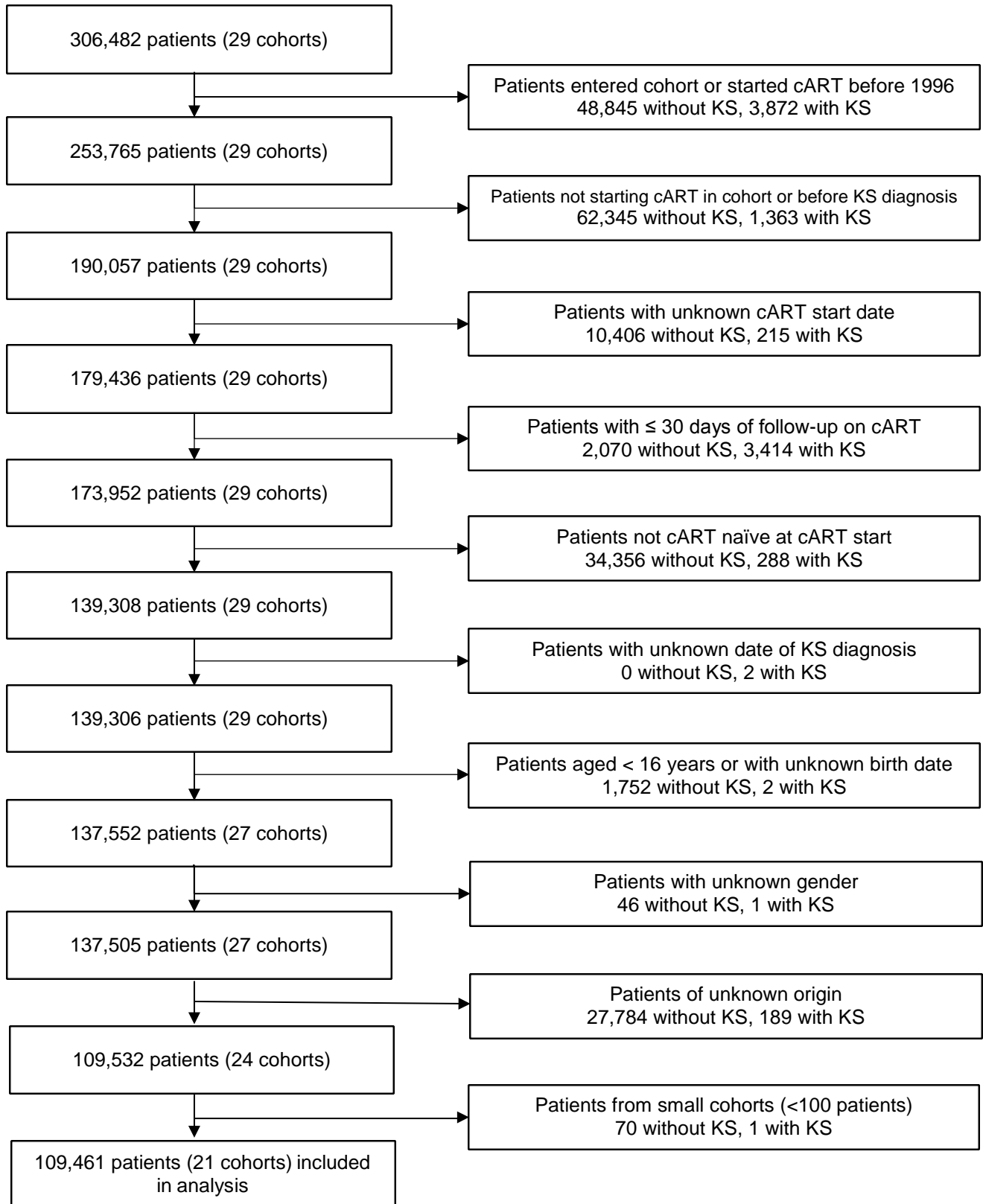
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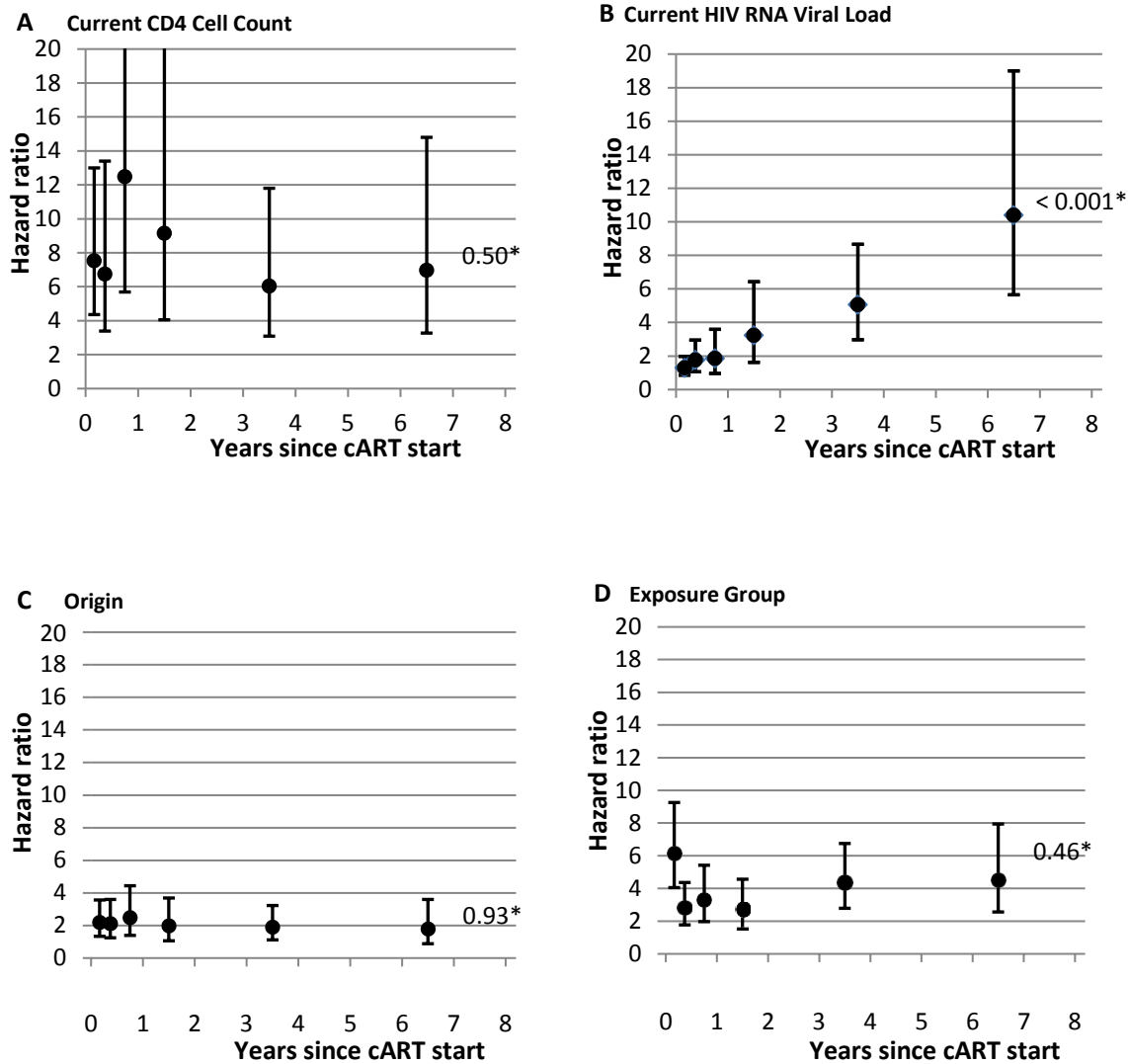
¹A list of the writing group members is provided in the acknowledgments.

Figure S1. Flow Diagram for Selection of Study Population



Abbreviations: cART, combination antiretroviral therapy; KS, Kaposi sarcoma

Figure S2. Hazard Ratios for the Risk of Developing KS by Time Periods Since Starting Combination Antiretroviral Therapy.



*p-value for change over time since cART start from test for interaction

The graphs show the hazard ratios of high risk versus low risk groups for different risk factors. Panel A: current CD4 cell count < 50 cells/ μ L versus 350-500ells/ μ L, panel B: current HIV RNA viral loads >100,000 coples/ml versus <500 copies /mL; panel C: sub-Saharan Africa versus European origin, and panel D: Men who have sex with men versus heterosexual men. Hazard ratios are adjusted for exposure group, origin, current age, current CD4 cell counts, current HIV RNA viral loads, first-line cART regimen, calendar period of enrolment; and stratified by cohort. Error bars correspond to 95% confidence interval.

Abbreviations: cART, combination antiretroviral therapy; KS, Kaposi sarcoma.

Table S2. Risk Factors for Developing Kaposi Sarcoma by Time Periods Since Starting Combination Antiretroviral Therapy. Results from Univariable Cox Regression Models.[#]

	30-90 days		91-180 days		6-12 months		1-2 years		2-5 years		5-8 years		P-value [§]
	HR	95% CI	HR	95% CI	HR	95% CI	HR	95% CI	HR	95% CI	HR	95% CI	
Exposure group	(249 KS/103170 patients) (143 KS/99973 patients) (121 KS/96225 patients) (101 KS/89522 patients) (163 KS/77361 patients) (95 KS/48963 patients)												0.21
MSM	3.03	(2.18-4.21)	1.56	(1.07-2.29)	1.82	(1.18-2.80)	1.70	(1.08-2.68)	2.45	(1.67-3.60)	2.82	(1.71-4.64)	
Other men	1.00	-	1.00	-	1.00	-	1.00	-	1.00	-	1.00	-	
Women	0.58	(0.36-0.95)	0.48	(0.28-0.82)	0.57	(0.32-1.03)	0.52	(0.28-0.97)	0.60	(0.36-1.02)	0.39	(0.17-0.88)	
Origin	(269 KS/109461 patients) (149 KS/105990 patients) (123 KS/101944 patients) (106 KS/94762 patients) (168 KS/81776 patients) (101 KS/51674 patients)												0.81
European	1.00	-	1.00	-	1.00	-	1.00	-	1.00	-	1.00	-	
African	0.84	(0.58-1.21)	1.17	(0.77-1.79)	1.22	(0.76-1.96)	1.07	(0.64-1.80)	0.94	(0.61-1.44)	0.71	(0.39-1.29)	
Other	0.72	(0.44-1.19)	1.16	(0.65-2.09)	0.59	(0.26-1.37)	0.87	(0.37-2.02)	0.95	(0.51-1.77)	0.57	(0.20-1.57)	
Age group [years]*	(269 KS/109461 patients) (149 KS/105990 patients) (123 KS/101944 patients) (106 KS/94762 patients) (168 KS/81776 patients) (101 KS/51674 patients)												<0.01
16-30	1.00	-	1.00	-	1.00	-	1.00	-	1.00	-	1.00	-	
31-40	1.33	(0.91-1.95)	2.25	(1.26-4.01)	1.53	(0.86-2.73)	1.61	(0.78-3.32)	0.94	(0.56-1.60)	0.60	(0.30-1.19)	
41-50	1.74	(1.18-2.57)	1.95	(1.06-3.60)	1.32	(0.71-2.45)	1.98	(0.95-4.14)	0.87	(0.51-1.49)	0.28	(0.13-0.58)	
>50	1.89	(1.23-2.90)	2.66	(1.41-5.02)	2.01	(1.06-3.79)	2.57	(1.20-5.52)	1.04	(0.59-1.84)	0.40	(0.19-0.85)	
CD4 cell count start cART [cells/ μ l]	(237 KS/97660 patients) (134 KS/94573 patients) (108 KS/90954 patients) (97 KS/84564 patients) (151 KS/73054 patients) (94 KS/46108 patients)												<0.001
<50	6.22	(3.82-10.1)	6.45	(3.14-13.2)	6.39	(2.81-14.6)	2.06	(1.05-4.01)	1.23	(0.64-2.36)	0.60	(0.29-1.24)	
50-99	4.17	(2.44-7.15)	4.68	(2.14-10.2)	3.21	(1.24-8.32)	0.95	(0.38-2.35)	1.55	(0.78-3.07)	0.70	(0.32-1.54)	
100-199	1.80	(1.04-3.11)	2.37	(1.10-5.12)	3.42	(1.47-7.94)	1.58	(0.82-3.05)	1.48	(0.82-2.66)	0.44	(0.22-0.91)	
200-349	1.14	(0.67-1.93)	1.84	(0.88-3.85)	2.03	(0.89-4.65)	0.70	(0.35-1.38)	1.02	(0.58-1.81)	0.58	(0.32-1.05)	
350-499	1.00	-	1.00	-	1.00	-	1.00	-	1.00	-	1.00	-	
>500	0.15	(0.03-0.64)	0.68	(0.21-2.21)	0.85	(0.25-2.92)	0.87	(0.36-2.07)	2.26	(1.23-4.15)	1.07	(0.56-2.05)	
CD4 cell count [cells/ μ l]*	(242 KS/101742 patients) (142 KS/101335 patients) (119 KS/99024 patients) (103 KS/93051 patients) (164 KS/81135 patients) (100 KS/51448 patients)												<0.01
<50	5.93	(3.75-9.38)	7.42	(4.11-13.4)	12.92	(6.51-25.7)	14.11	(7.15-27.9)	13.73	(8.00-23.6)	20.20	(10.5-38.8)	
50-99	3.95	(2.39-6.55)	5.15	(2.81-9.41)	3.85	(1.72-8.60)	6.11	(2.88-13.0)	6.87	(3.66-12.9)	5.64	(2.24-14.2)	
100-199	2.60	(1.63-4.15)	2.44	(1.37-4.36)	3.65	(1.95-6.80)	1.84	(0.91-3.70)	2.53	(1.46-4.39)	4.28	(2.22-8.27)	
200-349	1.52	(0.96-2.40)	1.39	(0.78-2.46)	1.65	(0.87-3.13)	0.99	(0.51-1.93)	1.47	(0.92-2.36)	1.37	(0.71-2.64)	
350-499	1.00	-	1.00	-	1.00	-	1.00	-	1.00	-	1.00	-	
>500	0.37	(0.17-0.81)	0.68	(0.33-1.40)	1.13	(0.58-2.21)	1.04	(0.57-1.89)	0.58	(0.36-0.93)	0.53	(0.29-0.98)	
HIV RNA at start cART [copies/mL]	(269 KS/109461 patients) (149 KS/105990 patients) (123 KS/101944 patients) (106 KS/94762 patients) (168 KS/81776 patients) (101 KS/51674 patients)												<0.001
≥100,000	6.65	(3.12-14.2)	5.92	(2.40-14.6)	3.81	(1.53-9.49)	2.15	(0.97-4.77)	1.80	(1.00-3.25)	0.94	(0.49-1.79)	
10,001-99,999	2.45	(1.11-5.41)	2.30	(0.89-5.92)	2.60	(1.02-6.63)	1.73	(0.76-3.91)	1.28	(0.69-2.37)	1.11	(0.58-2.12)	
501-9,999	1.00	-	1.00	-	1.00	-	1.00	-	1.00	-	1.00	-	
≤500	1.15	(0.24-5.55)	2.10	(0.50-8.81)	0.78	(0.09-6.65)	1.04	(0.22-5.04)	0.31	(0.04-2.39)	-	-	
HIV RNA [copies/mL]*	(222 KS/98458 patients) (134 KS/98557 patients) (122 KS/96769 patients) (98 KS/91286 patients) (162 KS/79992 patients) (101 KS/51255 patients)												<0.001
≥100,000	2.58	(1.78-3.72)	3.12	(1.96-4.95)	3.84	(2.22-6.65)	7.01	(4.10-12.0)	12.06	(7.93-18.4)	26.03	(16.4-41.3)	
10,001-99,999	1.12	(0.71-1.76)	0.86	(0.43-1.75)	2.06	(1.13-3.76)	2.74	(1.51-4.96)	5.42	(3.57-8.22)	4.03	(2.14-7.57)	
501-9,999	1.30	(0.91-1.88)	1.13	(0.72-1.78)	1.50	(0.90-2.51)	1.10	(0.57-2.12)	2.59	(1.63-4.12)	2.87	(1.52-5.41)	
≤500	1.00	-	1.00	-	1.00	-	1.00	-	1.00	-	1.00	-	
Late presentation	(262 KS/103729 patients) (143 KS/100444 patients) (118 KS/96605 patients) (102 KS/89838 patients) (157 KS/77630 patients) (98 KS/48973 patients)												<0.001
No	1.00	-	1.00	-	1.00	-	1.00	-	1.00	-	1.00	-	
Yes	4.18	(2.95-5.93)	2.73	(1.80-4.13)	1.81	(1.20-2.74)	1.16	(0.77-1.75)	1.05	(0.75-1.46)	0.69	(0.46-1.03)	
First-line cART regimen	(269 KS/109461 patients) (149 KS/105990 patients) (123 KS/101944 patients) (106 KS/94762 patients) (168 KS/81776 patients) (101 KS/51674 patients)												0.10
Nonboosted PIs	0.63	(0.44-0.88)	1.13	(0.73-1.74)	1.37	(0.85-2.20)	1.31	(0.81-2.10)	1.20	(0.82-1.75)	1.40	(0.85-2.29)	
Boosted PIs	1.00	-	1.00	-	1.00	-	1.00	-	1.00	-	1.00	-	
NNRTI without PIs	0.56	(0.42-0.73)	0.92	(0.62-1.36)	0.93	(0.60-1.44)	0.88	(0.55-1.42)	0.85	(0.58-1.25)	0.64	(0.35-1.16)	
Other	0.38	(0.19-0.78)	1.03	(0.52-2.03)	0.90	(0.38-2.12)	0.41	(0.13-1.33)	0.41	(0.16-1.04)	0.47	(0.16-1.36)	
Calendar year of enrolment	(269 KS/109461 patients) (149 KS/105990 patients) (123 KS/101944 patients) (106 KS/94762 patients) (168 KS/81776 patients) (101 KS/51674 patients)												0.17
1996-2000	1.00	-	1.00	-	1.00	-	1.00	-	1.00	-	1.00	-	
2001-2005	1.23	(0.89-1.68)	0.80	(0.54-1.18)	1.13	(0.72-1.76)	0.62	(0.39-0.96)	0.85	(0.61-1.18)	0.60	(0.39-0.91)	
2006-2010	0.95	(0.67-1.34)	0.66	(0.43-1.02)	0.91	(0.56-1.48)	0.68	(0.42-1.10)	0.56	(0.35-0.90)	0.39	(0.09-1.64)	
2011-2014	1.70	(1.12-2.58)	0.91	(0.47-1.74)	0.75	(0.31-1.83)	-	-	-	-	-	-	

[#] All cases including those having missing values for other covariates have been used in this cox-regression model.

Abbreviations: cART, combination antiretroviral therapy; KS, Kaposi Sarcoma; CDC, United States Centers for Disease Control; NNRTI, Non-nucleoside reverse-transcriptase inhibitors; PI, Protease inhibitors; MSM, men having sex with men.

* Time-updated data; [§] P-value for change over time from test of interaction

Table S3. Risk Factors for Developing Kaposi Sarcoma by Time Periods Since Starting Combination Antiretroviral Therapy. Results from Univariable Cox Regression Model of Complete Cases.[#]

	30-90 days (201 KS/90789 patients)		91-180 days (130 KS/91646 patients)		6-12 months (116 KS/90511 patients)		1-2 years (93 KS/85735 patients)		2-5 years (156 KS/75503 patients)		5-8 years (94 KS/48498 patients)		p-value [§]
	HR	95% CI	HR	95% CI	HR	95% CI	HR	95% CI	HR	95% CI	HR	95% CI	
Exposure group													
MSM	3.37	(2.30-4.94)	1.55	(1.04-2.31)	1.74	(1.12-2.71)	1.73	(1.07-2.78)	2.39	(1.62-3.52)	2.92	(1.76-4.84)	0.20
Other men	1.00	-	1.00	-	1.00	-	1.00	-	1.00	-	1.00	-	
Women	0.75	(0.44-1.27)	0.44	(0.25-0.77)	0.55	(0.30-1.01)	0.54	(0.28-1.04)	0.59	(0.35-1.01)	0.41	(0.18-0.92)	
Origin													
European	1.00	-	1.00	-	1.00	-	1.00	-	1.00	-	1.00	-	0.77
African	0.81	(0.53-1.25)	1.09	(0.69-1.72)	1.21	(0.74-1.96)	1.10	(0.64-1.91)	0.93	(0.60-1.45)	0.67	(0.36-1.25)	
Other	0.77	(0.44-1.34)	1.34	(0.74-2.42)	0.62	(0.27-1.44)	1.00	(0.43-2.33)	0.93	(0.48-1.80)	0.60	(0.22-1.66)	
Age group [years]*													
16-30	1.00	-	1.00	-	1.00	-	1.00	-	1.00	-	1.00	-	<0.01
31-40	1.29	(0.83-2.02)	2.54	(1.33-4.84)	1.60	(0.88-2.90)	1.45	(0.70-3.03)	0.97	(0.56-1.66)	0.61	(0.29-1.26)	
41-50	1.76	(1.12-2.77)	2.16	(1.09-4.27)	1.31	(0.69-2.49)	1.72	(0.81-3.64)	0.85	(0.49-1.49)	0.29	(0.13-0.63)	
>50	2.05	(1.26-3.35)	3.31	(1.65-6.66)	2.16	(1.12-4.15)	2.23	(1.02-4.88)	1.06	(0.59-1.91)	0.47	(0.22-1.02)	
CD4 cell count at start cART [cells/μl]													
<50	6.95	(3.97-12.2)	5.98	(2.90-12.4)	6.37	(2.79-14.5)	2.37	(1.17-4.82)	1.28	(0.65-2.51)	0.60	(0.29-1.27)	<0.001
50-99	5.03	(2.74-9.24)	4.07	(1.83-9.07)	3.28	(1.26-8.50)	0.97	(0.36-2.60)	1.69	(0.84-3.39)	0.75	(0.34-1.67)	
100-199	2.10	(1.14-3.90)	2.05	(0.93-4.52)	3.17	(1.35-7.41)	1.57	(0.77-3.20)	1.44	(0.79-2.65)	0.47	(0.23-0.97)	
200-349	1.27	(0.70-2.32)	1.72	(0.82-3.61)	2.02	(0.88-4.63)	0.77	(0.37-1.59)	1.06	(0.59-1.91)	0.59	(0.32-1.08)	
350-499	1.00	-	1.00	-	1.00	-	1.00	-	1.00	-	1.00	-	
> 500	0.20	(0.05-0.88)	0.69	(0.21-2.24)	0.86	(0.25-2.94)	1.02	(0.42-2.50)	2.41	(1.30-4.47)	1.07	(0.55-2.08)	
CD4 cell count [cells/μl]*													
<50	6.13	(3.64-10.3)	7.39	(3.93-13.9)	13.93	(7.02-27.7)	16.14	(8.09-32.2)	13.94	(7.96-24.4)	20.54	(10.5-40.3)	<0.01
50-99	4.37	(2.48-7.69)	5.17	(2.72-9.81)	4.04	(1.80-9.02)	5.65	(2.51-12.7)	7.03	(3.66-13.5)	4.06	(1.37-12.0)	
100-199	3.03	(1.81-5.09)	2.67	(1.46-4.88)	3.75	(2.01-7.00)	1.59	(0.74-3.41)	2.76	(1.58-4.82)	4.35	(2.21-8.57)	
200-349	1.74	(1.05-2.90)	1.45	(0.80-2.64)	1.54	(0.80-2.96)	1.07	(0.55-2.10)	1.51	(0.93-2.44)	1.47	(0.76-2.85)	
350-499	1.00	-	1.00	-	1.00	-	1.00	-	1.00	-	1.00	-	
> 500	0.41	(0.17-0.97)	0.77	(0.37-1.61)	1.07	(0.54-2.11)	0.93	(0.50-1.74)	0.60	(0.37-0.97)	0.54	(0.29-1.01)	
HIV RNA at start cART [copies/mL]													
≥100,000	7.06	(3.11-16.0)	5.82	(2.36-14.4)	3.72	(1.49-9.28)	2.47	(1.05-5.81)	1.93	(1.05-3.55)	1.10	(0.55-2.21)	<0.01
10,001-99,999	2.72	(1.16-6.37)	2.23	(0.87-5.75)	2.47	(0.97-6.30)	1.90	(0.79-4.55)	1.33	(0.71-2.52)	1.22	(0.61-2.47)	
501-9,999	1.00	-	1.00	-	1.00	-	1.00	-	1.00	-	1.00	-	
≤500	1.50	(0.30-7.43)	2.17	(0.52-9.11)	0.81	(0.09-6.97)	1.26	(0.25-6.24)	0.35	(0.05-2.67)	-	-	
HIV RNA [copies/mL]*													
≥100,000	2.65	(1.79-3.93)	3.18	(1.99-5.09)	3.86	(2.20-6.78)	7.72	(4.51-13.2)	12.38	(8.11-18.9)	26.37	(16.3-42.6)	<0.001
10,001-99,999	1.23	(0.77-1.98)	0.90	(0.44-1.81)	1.82	(0.96-3.48)	2.73	(1.48-5.04)	5.36	(3.51-8.19)	3.98	(2.06-7.67)	
501-9,999	1.50	(1.02-2.20)	1.17	(0.75-1.84)	1.45	(0.86-2.46)	1.06	(0.53-2.11)	2.32	(1.42-3.77)	2.86	(1.48-5.52)	
≤500	1.00	-	1.00	-	1.00	-	1.00	-	1.00	-	1.00	-	
Late presentation													
No	1.00	-	1.00	-	1.00	-	1.00	-	1.00	-	1.00	-	<0.001
Yes	3.78	(2.57-5.57)	2.43	(1.58-3.73)	1.78	(1.17-2.71)	1.23	(0.79-1.91)	1.01	(0.72-1.42)	0.66	(0.43-1.00)	
First-line cART regimen													
Nonboosted PI	0.52	(0.34-0.79)	1.11	(0.69-1.77)	1.36	(0.83-2.21)	1.39	(0.85-2.29)	1.20	(0.81-1.76)	1.36	(0.82-2.25)	<0.001
Boosted PI	1.00	-	1.00	-	1.00	-	1.00	-	1.00	-	1.00	-	
NNRTI without PIs	0.50	(0.37-0.69)	0.99	(0.65-1.50)	0.89	(0.57-1.40)	0.85	(0.51-1.42)	0.82	(0.55-1.22)	0.61	(0.33-1.13)	
Other	0.37	(0.16-0.85)	1.21	(0.60-2.40)	0.96	(0.40-2.28)	0.00	(0.00-0.00)	0.35	(0.13-0.97)	0.49	(0.17-1.44)	
Calendar year of enrolment													
1996-2000	1.00	-	1.00	-	1.00	-	1.00	-	1.00	-	1.00	-	0.07
2001-2005	1.47	(1.01-2.14)	0.83	(0.55-1.25)	1.15	(0.72-1.82)	0.54	(0.33-0.88)	0.87	(0.62-1.23)	0.58	(0.38-0.91)	
2006-2010	1.04	(0.69-1.57)	0.64	(0.40-1.03)	0.96	(0.58-1.60)	0.65	(0.39-1.08)	0.50	(0.30-0.85)	0.41	(0.10-1.72)	
2011-2014	1.62	(0.96-2.72)	1.00	(0.49-2.04)	0.82	(0.33-2.03)	-	-	-	-	-	-	

[#]Only cases with no missing values for any of the covariates (complete cases) have been used in this cox-regression model.

Abbreviations: cART, combination antiretroviral therapy; KS, Kaposi Sarcoma; CDC, United States Centers for Disease Control; NNRTI, Non-nucleoside reverse-transcriptase inhibitors; PI, Protease inhibitors; MSM, men having sex with men.

* Time-updated data; [§] P-value for change over time from test of interaction

Table S4. Kaposi Sarcoma Incidence Rates per 100,000 Person-Years and Hazard Ratios for Univariable and Multivariable Cox Regression Models in the First Eight Years Since Starting Combination Antiretroviral Therapy.

	Incidence rate*			Univariable cox regression*			Univariable cox regression (Complete cases)*			Multivariable Cox Regression*		
	KS	pyrs	Rate (95% CI)	HR (95% CI)	p-value [§]	HR (95% CI)	p-value [§]	HR (95% CI)	p-value [§]	HR (95% CI)	p-value [§]	
				(916 KS/109461 patients)			(790 KS/100022 patients)			(790 KS/100022 patients)		
Total	916	501700	183 (171.1-194.8)	-	-	-	-	-	-	-	-	
Exposure group												
MSM	554	177000	313 (287.9-340.1)	2.24 (1.90-2.63)	<0.001	2.22 (1.86-2.65)	<0.001	4.02 (3.32-4.87)	<0.001			
Other men	211	155600	136 (118.5-155.2)	1.00	-	1.00	-	1.00	-			
Women	107	142200	75 (62.26-90.95)	0.54 (0.43-0.68)		0.53 (0.41-0.69)		0.63 (0.49-0.82)				
Origin												
European	713	391400	182 (169.3-196.1)	1.00	-	0.32	1.00	-	0.59	1.00	-	<0.01
African	146	74000	197 (167.8-232.2)	0.97 (0.81-1.17)		0.95 (0.77-1.16)		2.06 (1.64-2.59)				
Other	57	36400	157 (120.8-203.0)	0.81 (0.61-1.07)		0.85 (0.63-1.14)		0.98 (0.72-1.32)				
Age group [years]*												
16-30	102	56700	180 (148.2-218.5)	1.00	-	<0.001	1.00	-	<0.001	1.00	-	<0.01
31-40	358	187000	192 (172.6-212.4)	1.41 (1.13-1.76)		1.44 (1.12-1.85)		1.17 (0.92-1.49)				
41-50	265	162900	163 (144.2-183.5)	1.35 (1.07-1.70)		1.41 (1.09-1.82)		1.08 (0.83-1.39)				
>50	191	95200	201 (174.1-231.2)	1.70 (1.33-2.16)		1.88 (1.43-2.46)		1.53 (1.17-2.00)				
CD4 cell count at start cART [cells/μl]												
<50	224	61000	367 (322.0-418.4)	3.20 (2.49-4.10)	<0.001	3.20 (2.46-4.17)	<0.001	-	-	-	-	
50-99	105	40400	260 (214.6-314.6)	2.27 (1.71-3.02)		2.33 (1.73-3.15)		-	-	-	-	
100-199	155	85300	182 (155.3-212.8)	1.57 (1.21-2.05)		1.54 (1.17-2.04)		-	-	-	-	
200-349	188	145900	129 (111.7-148.7)	1.06 (0.83-1.37)		1.09 (0.84-1.43)		-	-	-	-	
350-499	87	67700	129 (104.1-158.5)	1.00	-	1.00	-	-	-	-	-	
> 500	62	47400	131 (101.9-167.7)	1.04 (0.75-1.45)		1.15 (0.82-1.60)		-	-	-	-	
CD4 cell count [cells/μl]*												
<50	164	8840	1855 (1592-2162)	9.42 (7.42-12.0)	<0.001	9.50 (7.34-12.3)	<0.001	7.90 (5.98-10.4)	<0.001			
50-99	100	11600	860 (706.5-1046)	5.05 (3.87-6.59)		5.07 (3.80-6.75)		4.72 (3.51-6.34)				
100-199	163	40900	398 (341.5-464.2)	2.81 (2.23-3.55)		2.83 (2.20-3.63)		2.86 (2.22-3.69)				
200-349	186	101400	183 (158.9-211.8)	1.46 (1.16-1.82)		1.46 (1.15-1.85)		1.48 (1.16-1.88)				
350-499	131	119500	110 (92.35-130.1)	1.00	-	1.00	-	1.00	-			
> 500	126	208800	60 (50.67-71.85)	0.65 (0.51-0.83)		0.61 (0.47-0.80)		0.61 (0.46-0.79)				
HIV RNA at cART start [copies/mL]												
≥100,000	460	186000	247 (225.7-271.0)	2.94 (2.19-3.95)	<0.001	3.10 (2.27-4.24)	<0.001	-	-	-	-	
10,001-99,999	236	160300	147 (129.6-167.3)	1.71 (1.26-2.33)		1.78 (1.29-2.46)		-	-	-	-	
501-9,999	49	54500	90 (67.95-119.0)	1.00	-	1.00	-	-	-	-	-	
≤500	9	12700	71 (36.99-136.6)	0.72 (0.35-1.46)		0.83 (0.41-1.70)		-	-	-	-	
HIV RNA [copies/mL]*												
≥100,000	204	21700	941 (820.7-1080)	5.87 (4.85-7.10)	<0.001	5.96 (4.87-7.30)	<0.001	2.76 (2.21-3.45)	<0.001			
10,001-99,999	113	37000	305 (253.9-367.1)	2.39 (1.92-2.97)		2.39 (1.90-3.02)		1.79 (1.41-2.28)				
501-9,999	158	60200	262 (224.5-306.6)	1.79 (1.48-2.18)		1.80 (1.46-2.21)		1.58 (1.28-1.95)				
≤500	364	366000	99 (89.75-110.2)	1.00	-	1.00	-	1.00	-			
Late presentation												
No	231	178100	130 (114.0-147.6)	1.00	-	<0.001	1.00	-	<0.01	-	-	
Yes	649	297500	218 (202.0-235.6)	1.79 (1.54-2.09)		1.64 (1.40-1.93)		-	-	-	-	
First-line cART regimen												
Nonboosted PI	253	134600	188 (166.1-212.6)	1.06 (0.89-1.25)	<0.001	1.05 (0.88-1.26)	<0.001	0.87 (0.69-1.08)	0.02			
Boosted PIs	334	148200	225 (202.5-250.9)	1.00	-	1.00	-	1.00	-			
NNRTI without PI	293	186900	157 (139.8-175.8)	0.74 (0.63-0.87)		0.72 (0.61-0.86)		0.82 (0.69-0.97)				
Other	36	32000	112 (81.09-155.8)	0.54 (0.38-0.77)		0.52 (0.36-0.76)		0.61 (0.42-0.89)				
Calendar year of enrolment												
1996-2000	336	188500	178 (160.2-198.4)	1.00	-	<0.01	1.00	-	<0.001	1.00	-	0.42
2001-2005	334	200100	167 (149.9-185.8)	0.87 (0.75-1.01)		0.89 (0.75-1.04)		1.06 (0.87-1.30)				
2006-2010	191	102900	186 (161.2-214.0)	0.72 (0.60-0.87)		0.71 (0.58-0.87)		0.92 (0.72-1.17)				
2011-2014	55	10200	537 (412.1-699.1)	1.03 (0.77-1.40)		0.94 (0.66-1.33)		1.16 (0.80-1.69)				

Abbreviations: pyrs, person-years; cART, combination antiretroviral therapy; KS, Kaposi Sarcoma; CI, Confidence Interval; NNRTI, Non-nucleoside reverse-transcriptase inhibitors; PI, Protease inhibitors; MSM, men having sex with men.

* Time-updated data [§]p-values from chi²-test; * Analysis is stratified by cohort, multivariable analysis adjusted for all covariates

Table S5. Additional Analysis including Baseline CD4 Cell Count. Risk Factors for Developing Kaposi Sarcoma by Time Periods Since Starting Combination Antiretroviral Therapy. Results from Multivariable Cox Regression Models.[#]

	30-90 days (197 KS/87178 patients)		91-180 days (122 KS/85832 patients)		6-12 months (105 KS/83518 patients)		1-2 years (88 KS/78327 patients)		2-5 years (145 KS/68311 patients)		5-8 years (90 KS/43670 patients)		p-value ^{&}
	HR	95% CI	HR	95% CI	HR	95% CI	HR	95% CI	HR	95% CI	HR	95% CI	
Exposure group													
MSM	6.11	(4.04-9.24)	2.70	(1.73-4.23)	3.24	(1.96-5.36)	2.70	(1.59-4.60)	4.17	(2.68-6.50)	4.33	(2.44-7.66)	0.28
Heterosexual men	1.00	-	1.00	-	1.00	-	1.00	-	1.00	-	1.00	-	
Women	0.87	(0.50-1.51)	0.54	(0.30-0.98)	0.53	(0.27-1.03)	0.66	(0.34-1.29)	0.58	(0.32-1.05)	0.40	(0.17-0.93)	
Origin													
European	1.00	-	1.00	-	1.00	-	1.00	-	1.00	-	1.00	-	0.96
African	2.12	(1.29-3.47)	2.10	(1.24-3.58)	2.49	(1.40-4.43)	2.10	(1.12-3.93)	1.93	(1.13-3.29)	1.93	(0.94-3.94)	
Other	0.87	(0.49-1.52)	1.50	(0.80-2.81)	0.65	(0.26-1.63)	1.10	(0.43-2.79)	1.04	(0.52-2.09)	0.82	(0.29-2.32)	
Age group [years]*													
16-30	1.00	-	1.00	-	1.00	-	1.00	-	1.00	-	1.00	-	0.19
31-40	0.97	(0.62-1.53)	2.20	(1.08-4.49)	1.46	(0.74-2.85)	1.27	(0.60-2.67)	1.08	(0.60-1.91)	0.62	(0.29-1.31)	
41-50	1.27	(0.80-2.01)	2.06	(0.98-4.35)	1.34	(0.65-2.72)	1.66	(0.77-3.59)	0.97	(0.53-1.78)	0.33	(0.15-0.75)	
>50	1.38	(0.84-2.29)	3.35	(1.56-7.19)	2.28	(1.09-4.75)	2.26	(1.00-5.11)	1.42	(0.74-2.69)	0.69	(0.31-1.55)	
CD4 cell count at start cART [cells/μl]													
<50	5.32	(2.15-13.2)	1.79	(0.62-5.21)	2.05	(0.68-6.14)	0.55	(0.21-1.42)	0.37	(0.17-0.79)	0.32	(0.14-0.73)	<0.001
50-99	3.74	(1.54-9.08)	1.54	(0.53-4.46)	1.73	(0.56-5.38)	0.35	(0.11-1.07)	0.66	(0.31-1.40)	0.55	(0.24-1.28)	
100-199	1.45	(0.62-3.40)	1.22	(0.46-3.22)	2.27	(0.85-6.06)	0.99	(0.44-2.24)	0.82	(0.43-1.57)	0.43	(0.20-0.92)	
200-349	0.94	(0.44-2.01)	1.59	(0.71-3.55)	2.00	(0.84-4.76)	0.69	(0.33-1.46)	0.92	(0.51-1.67)	0.65	(0.35-1.22)	
350-499	1.00	-	1.00	-	1.00	-	1.00	-	1.00	-	1.00	-	
> 500	0.30	(0.06-1.55)	0.75	(0.21-2.62)	0.82	(0.23-2.84)	1.11	(0.44-2.78)	2.50	(1.33-4.69)	1.06	(0.54-2.09)	
CD4 cell count [cells/μl]*													
<50	1.41	(0.59-3.40)	4.78	(1.70-13.4)	11.05	(3.88-31.4)	13.75	(4.95-38.2)	12.80	(6.14-26.7)	11.02	(4.93-24.6)	<0.01
50-99	1.29	(0.56-2.97)	4.27	(1.67-11.0)	3.51	(1.24-9.96)	6.40	(2.39-17.1)	7.55	(3.52-16.2)	2.57	(0.81-8.14)	
100-199	1.61	(0.76-3.41)	2.49	(1.09-5.67)	3.00	(1.33-6.74)	1.58	(0.65-3.85)	3.29	(1.76-6.14)	3.94	(1.90-8.16)	
200-349	1.51	(0.78-2.89)	1.14	(0.59-2.22)	1.40	(0.70-2.84)	1.13	(0.56-2.29)	1.77	(1.07-2.93)	1.28	(0.64-2.56)	
350-499	1.00	-	1.00	-	1.00	-	1.00	-	1.00	-	1.00	-	
> 500	0.61	(0.22-1.70)	0.92	(0.39-2.12)	1.37	(0.64-2.91)	0.66	(0.33-1.34)	0.43	(0.26-0.73)	0.49	(0.26-0.94)	
HIV RNA viral loads [copies/mL]*													
≥100,000	1.63	(1.06-2.49)	1.82	(1.07-3.10)	2.07	(1.07-4.02)	2.63	(1.30-5.34)	3.48	(2.00-6.04)	7.88	(4.19-14.8)	<0.01
10,001-99,999	1.18	(0.72-1.92)	0.78	(0.38-1.61)	1.43	(0.68-3.02)	1.98	(0.99-3.96)	2.72	(1.65-4.46)	1.97	(0.96-4.07)	
501-9,999	1.17	(0.79-1.73)	0.91	(0.55-1.51)	1.38	(0.76-2.52)	0.96	(0.46-2.00)	1.92	(1.14-3.25)	2.22	(1.11-4.45)	
≤500	1.00	-	1.00	-	1.00	-	1.00	-	1.00	-	1.00	-	
First-line cART regimen													
Nonboosted PI	0.53	(0.31-0.91)	0.75	(0.41-1.37)	1.46	(0.76-2.80)	0.87	(0.46-1.64)	1.11	(0.68-1.83)	0.85	(0.46-1.60)	0.18
Boosted PI	1.00	-	1.00	-	1.00	-	1.00	-	1.00	-	1.00	-	
NNRTI without PI	0.66	(0.47-0.92)	1.05	(0.68-1.63)	0.97	(0.60-1.56)	0.84	(0.49-1.44)	0.82	(0.53-1.27)	0.54	(0.28-1.03)	
Other	0.58	(0.25-1.34)	1.50	(0.74-3.05)	1.28	(0.53-3.09)	-	-	0.38	(0.13-1.06)	0.47	(0.16-1.40)	
Calendar year of enrolment													
1996-2000	1.00	-	1.00	-	1.00	-	1.00	-	1.00	-	1.00	-	0.49
2001-2005	1.18	(0.75-1.86)	0.82	(0.49-1.36)	1.79	(0.97-3.30)	0.58	(0.32-1.05)	1.39	(0.89-2.16)	1.06	(0.61-1.87)	
2006-2010	0.89	(0.54-1.47)	0.68	(0.38-1.23)	1.56	(0.77-3.13)	0.69	(0.36-1.33)	0.85	(0.46-1.59)	0.89	(0.20-3.96)	
2011-2014	1.23	(0.67-2.23)	0.98	(0.43-2.24)	1.32	(0.45-3.88)	-	-	-	-	-	-	

[#] Only cases with no missing values for any of the covariates have been used in this cox-regression model. Results are stratified by cohort.

Abbreviations: cART, combination antiretroviral therapy; KS, Kaposi Sarcoma; NNRTI, Non-nucleoside reverse-transcriptase inhibitors; PI, Protease inhibitors; MSM, men having sex with men.

* Time-updated data; [&] P-value for change over time from test of interaction

Table S6. Additional Analysis including Late Presentation. Risk Factors for Developing Kaposi Sarcoma by Time Periods Since Starting Combination Antiretroviral Therapy. Results from Multivariable Cox Regression Models.[#]

	30-90 days (199 KS/88373 patients)		91-180 days (125 KS/88496 patients)		6-12 months (111 KS/86898 patients)		1-2 years (90 KS/82046 patients)		2-5 years (146 KS/72054 patients)		5-8 years (92 KS/46152 patients)		p-value ^{&}
	HR	95% CI	HR	95% CI	HR	95% CI	HR	95% CI	HR	95% CI	HR	95% CI	
Exposure group													
MSM	6.13	(4.05-9.26)	3.10	(1.98-4.87)	3.41	(2.08-5.60)	3.24	(1.89-5.55)	4.46	(2.86-6.94)	4.16	(2.38-7.26)	0.53
Heterosexual men	1.00	-	1.00	-	1.00	-	1.00	-	1.00	-	1.00	-	
Women	0.89	(0.52-1.54)	0.59	(0.33-1.06)	0.63	(0.33-1.20)	0.72	(0.37-1.41)	0.63	(0.35-1.13)	0.39	(0.17-0.90)	
Origin													
European	1.00	-	1.00	-	1.00	-	1.00	-	1.00	-	1.00	-	0.93
African	1.95	(1.19-3.19)	2.17	(1.28-3.67)	2.21	(1.24-3.94)	2.37	(1.26-4.45)	2.26	(1.35-3.80)	1.84	(0.91-3.74)	
Other	0.85	(0.48-1.49)	1.57	(0.86-2.87)	0.70	(0.30-1.63)	1.29	(0.55-3.06)	1.14	(0.58-2.23)	0.72	(0.26-2.02)	
Age group [years]*													
16-30	1.00	-	1.00	-	1.00	-	1.00	-	1.00	-	1.00	-	0.09
31-40	1.03	(0.66-1.61)	2.08	(1.05-4.10)	1.54	(0.81-2.92)	1.29	(0.61-2.70)	0.86	(0.49-1.49)	0.59	(0.28-1.24)	
41-50	1.36	(0.86-2.15)	1.88	(0.92-3.85)	1.26	(0.63-2.51)	1.69	(0.79-3.62)	0.77	(0.43-1.38)	0.32	(0.14-0.71)	
>50	1.45	(0.88-2.40)	3.03	(1.45-6.32)	2.15	(1.05-4.39)	2.27	(1.00-5.12)	1.19	(0.65-2.21)	0.57	(0.25-1.29)	
Late presentation													
No	1.00	-	1.00	-	1.00	-	1.00	-	1.00	-	1.00	-	0.54
Yes	2.09	(1.33-3.29)	1.16	(0.69-1.97)	0.94	(0.55-1.60)	0.72	(0.42-1.24)	0.68	(0.46-1.01)	0.52	(0.33-0.83)	
CD4 cell count [cells/μl]*													
<50	4.73	(2.61-8.58)	7.52	(3.61-15.7)	14.85	(6.74-32.7)	11.12	(4.72-26.2)	6.69	(3.34-13.4)	8.34	(3.81-18.3)	<0.001
50-99	3.30	(1.78-6.13)	5.51	(2.69-11.3)	3.98	(1.64-9.63)	5.23	(2.13-12.8)	5.50	(2.70-11.2)	2.23	(0.71-6.98)	
100-199	2.41	(1.37-4.24)	2.80	(1.43-5.50)	3.65	(1.83-7.27)	1.74	(0.77-3.92)	2.53	(1.38-4.65)	3.72	(1.82-7.58)	
200-349	1.46	(0.86-2.48)	1.50	(0.79-2.83)	1.64	(0.84-3.20)	1.21	(0.60-2.44)	1.48	(0.89-2.46)	1.32	(0.67-2.62)	
350-499	1.00	-	1.00	-	1.00	-	1.00	-	1.00	-	1.00	-	
> 500	0.46	(0.19-1.09)	0.70	(0.32-1.57)	1.04	(0.52-2.09)	0.81	(0.42-1.59)	0.58	(0.35-0.95)	0.52	(0.27-0.98)	
HIV RNA viral loads [copies/mL]*													
≥100,000	1.45	(0.96-2.21)	1.61	(0.96-2.71)	1.62	(0.83-3.17)	3.03	(1.53-6.00)	4.45	(2.58-7.69)	8.64	(4.69-15.9)	<0.001
10,001-99,999	1.06	(0.66-1.72)	0.62	(0.29-1.33)	1.42	(0.70-2.86)	2.08	(1.06-4.09)	3.45	(2.12-5.60)	2.04	(1.00-4.15)	
501-9,999	1.22	(0.83-1.81)	0.93	(0.57-1.52)	1.51	(0.86-2.65)	0.99	(0.48-2.05)	2.27	(1.36-3.79)	2.19	(1.10-4.37)	
≤500	1.00	-	1.00	-	1.00	-	1.00	-	1.00	-	1.00	-	
First-line cART regimen													
Nonboosted PI	0.51	(0.30-0.88)	0.78	(0.43-1.42)	1.64	(0.87-3.09)	0.85	(0.45-1.62)	1.07	(0.65-1.77)	0.93	(0.50-1.74)	0.11
Boosted PI	1.00	-	1.00	-	1.00	-	1.00	-	1.00	-	1.00	-	
NNRTI without PI	0.60	(0.43-0.83)	1.04	(0.67-1.61)	0.99	(0.62-1.58)	0.79	(0.47-1.34)	0.98	(0.64-1.50)	0.59	(0.31-1.12)	
Other	0.51	(0.22-1.17)	1.47	(0.72-2.96)	1.22	(0.51-2.93)	-	-	0.40	(0.14-1.12)	0.49	(0.17-1.46)	
Calendar year of enrolment													
1996-2000	1.00	-	1.00	-	1.00	-	1.00	-	1.00	-	1.00	-	0.52
2001-2005	1.23	(0.78-1.94)	0.78	(0.47-1.29)	1.91	(1.05-3.45)	0.62	(0.34-1.11)	1.23	(0.80-1.90)	1.06	(0.61-1.85)	
2006-2010	0.86	(0.52-1.43)	0.69	(0.38-1.23)	1.60	(0.81-3.17)	0.67	(0.35-1.30)	0.79	(0.43-1.48)	0.88	(0.20-3.95)	
2011-2014	1.23	(0.68-2.23)	1.04	(0.47-2.31)	1.52	(0.55-4.16)	-	-	-	-	-	-	

[#] Only cases with no missing values for any of the covariates have been used in this cox-regression model. Results are stratified by cohort.

Abbreviations: cART, combination antiretroviral therapy; KS, Kaposi Sarcoma; NNRTI, Non-nucleoside reverse-transcriptase inhibitors; PI, Protease inhibitors; MSM, men having sex with men.

* Time-updated data; [&] P-value for change over time from test of interaction

Table S7. Kaposi Sarcoma Incidence Rates per 100,000 Person-Years by Time Periods Since Starting Combination Antiretroviral Therapy: Published Studies

Study	Cohort	Region	Calendar years	Patients receiving cART [n]	CD4 cell count at cART start [cells/ μ l]	up to 90 days	91-180 days	6-12 months	1-2 years	> 2 years	> 5 years
Yanik et al. 2013	CNICS	USA	1996-2011	11,485	202 (61–338)		1342 [#]	348	164 ⁺		
Mocroft et al. 2004	EuroSIDA	Europe	1994-2003	2,968	207 (98-328)		670 [#]	~300	~300	120	
Lodi et al. 2010	Cascade	Europe, Canada, Australia	1986-2006	4,199 ^{&}	NR		~650 ^{&}		~150 ^{&}	~250 ^{&}	~350 ^{&}
Current analysis	COHERE in EuroCoord	Europe	1996-2014	109,235	229 (108-343)	1472	582	247	120	85 ⁺⁺	82 ⁺⁺

[#] Cut off definition for incident KS cases not reported; [&] only MSM; ⁺ censored at 10 years after cART start; ⁺⁺ censored at 8 years after cART start

Abbreviations: CNICS, CFAR Network of Integrated Clinical Systems; COHERE in EuroCoord, Collaboration of Observational HIV Epidemiological Research Europe; MSM, men having s

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