Association between HMG-CoA reductase inhibitors (statins) use and cancer occurrence among HIV-1 treated patients

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IAS 2013 Kuala Lumpur June 30-July 3

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AUTHOR CONCLUSION

This study showed, in a large number of treated HIV-infected subjects, that the use of statins was associated with a 46% reduction in cancer occurrence over a 10-year follow-up; this effect appeared to be even stronger in relation to the AIDS-defining malignancies which were not observed.

BACKGROUND

Statin use has been recently associated with reduced cancer incidence and mortality both in general population and among HIV-infected subjects1-3. Based on these encouraging results, we hypothesized that statin use begun after the start of the antiretroviral therapy and before a cancer diagnosis would be associated with reduced cancer occurrence.

METHODS

Retrospective longitudinal study on HIV-infected patients recorded in IDD-HSR (database of the Infectious Diseases Department, San Raffaele Scientific Institute, Milan, Italy), not on treatment with statin at antiretroviral therapy (ARV) initiation, cancer-free at ARV initiation and also at statin initiation, followed until October 2012. Follow-up was calculated since ARV initiation (baseline) until the first cancer diagnosis or loss to follow-up or death or last available visit, whichever occurred first. According to CDC-1993 classification, malignancies were divided into AIDS-defining (ADM) and non-AIDS-defining malignancies (NADM). Results described as median (IQR). Cox proportional hazard model was used to examine the effect of statin use on the risk of cancer, adjusting for potential confounders: age, gender, body mass index, HCV serology, ARV exposure, use of statins, HIV-RNA, CD4 and CD8 cell count, total cholesterol, LDL-cholesterol, fasting glucose, triglycerides.

RESULTS

Five thousand three hundred and fifty-seven patients followed for 10.3 (4.8-15.1) years. Patients' distribution and characteristics are reported in Figure 1 and Table 1 respectively.
During 52663 person-years of follow-up (PYFU), 375 (7%) patients developed cancer [ADM: 194 (52%); NADM: 181 (48%)]. During follow-up 740 (14%) patients used statin [duration: 24.7 (10.4-42.6) months]. Distribution of the type of statin among statin users is shown in the Figure 2.
Overall the crude cancer incidence rate was 7.1 (95%CI: 6.4-7.9) per 1000 PYFU [Statin users: 12 events, 9420 PYFU, incidence rate =1.3 (95% CI: 0.6-2.0); Non-Statin users: 363 events, 43243 PYFU, incidence rate=8.4 (95% CI: 7.5-9.3)] **Cancer occurred in 12/740 (1.6%) statin users and in 363/4617 (7.9%) non-statin users (p<0.0001); all cancers among statin users were NADM**. Malignancies distribution in the overall sample and according to statin use is described in Table 2, while the time to cancer occurrence according to statin use is shown in Figure 3. Finally, the results from multivariate analysis on the risk of cancer occurrence are reported in the Figure 4.

Figure 1. Patients' distribution

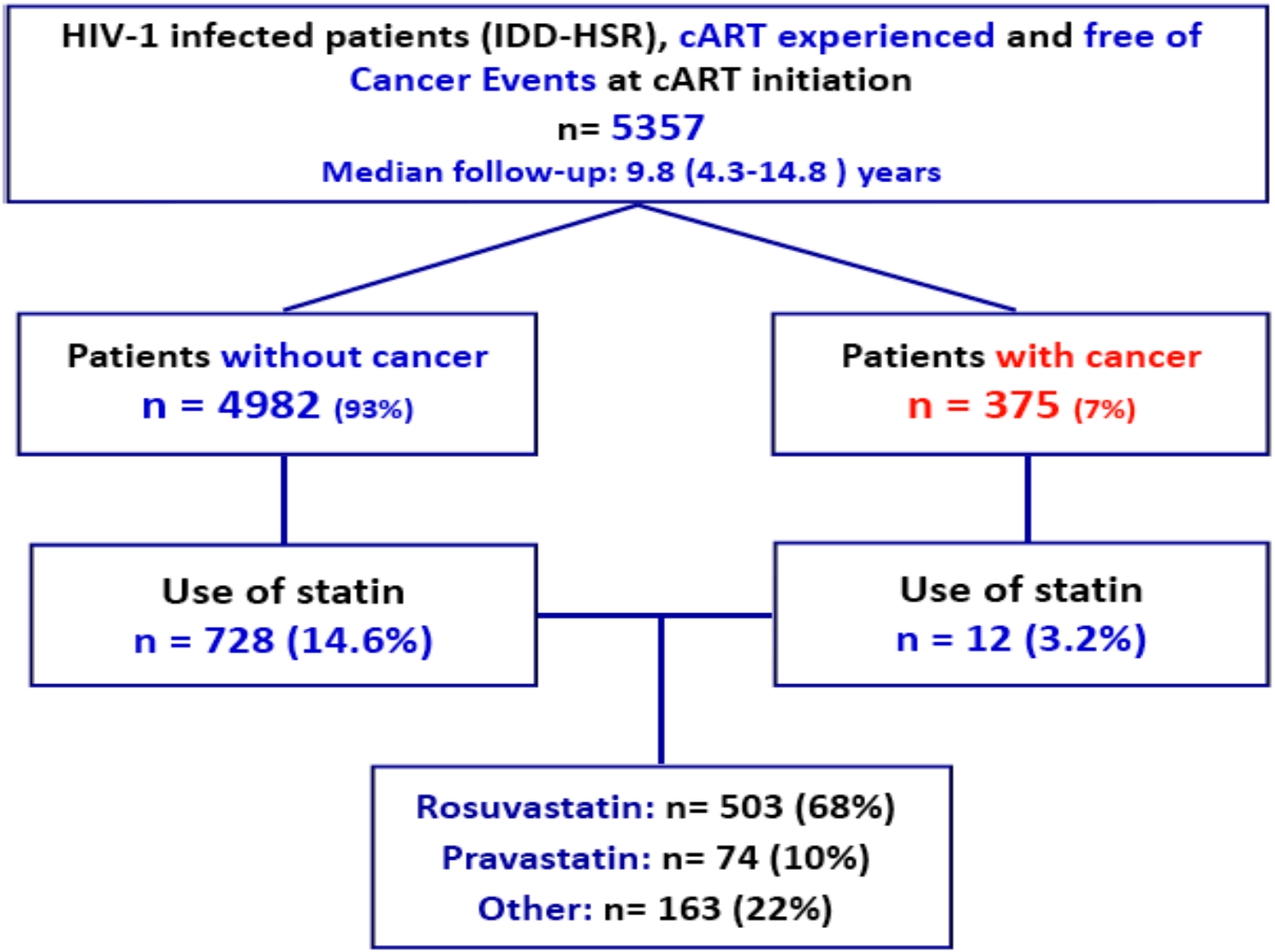


Table 2. Malignancies distribution

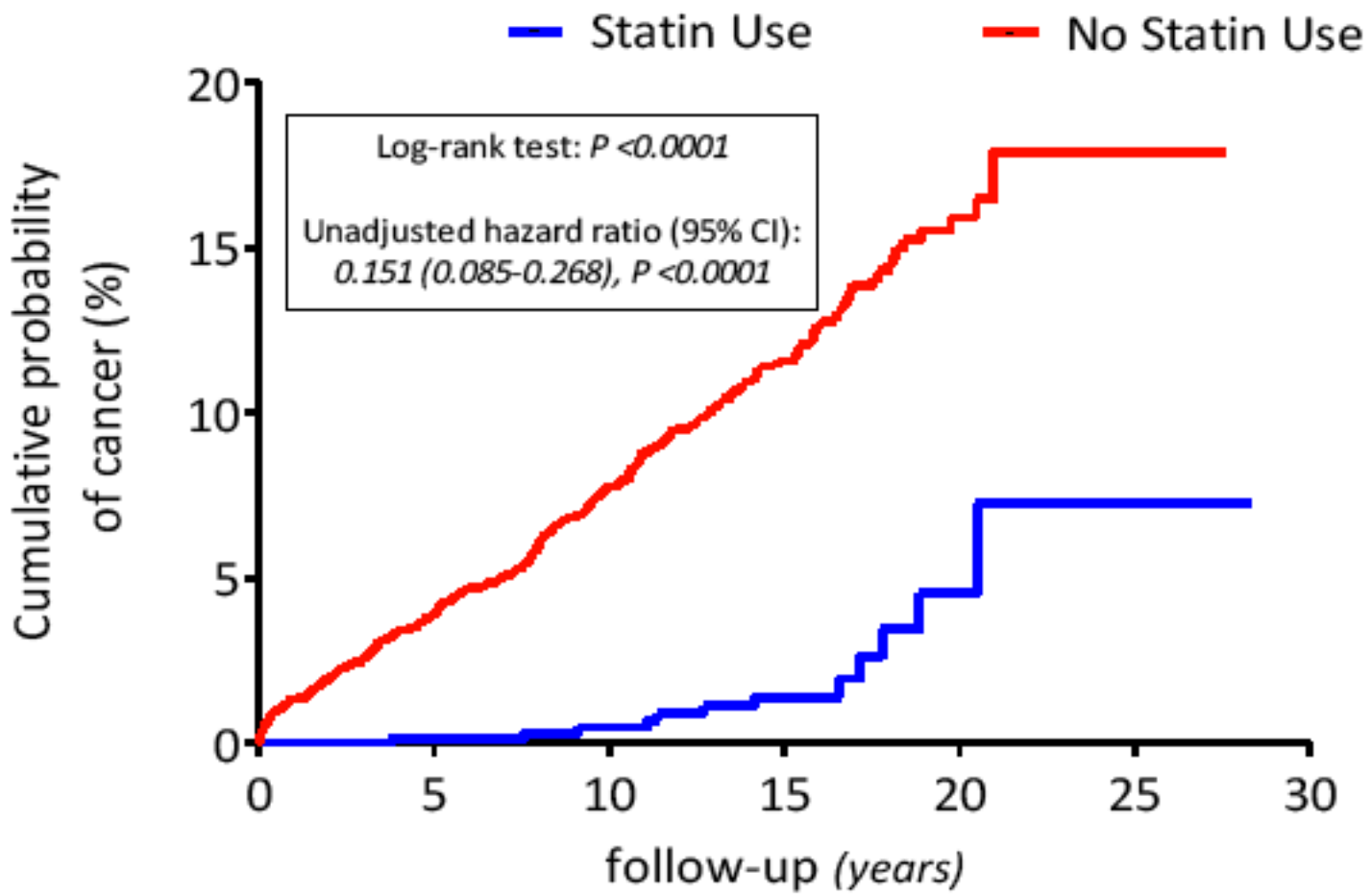
	All (N=375)	Statin Use (N=12)	No Statin Use (N=363)
ADM	**194 (52%)**	**0**	**194 (53%)**
Non Hodgkin Lynphoma	107 (29%)	0	107(30%)
Kaposi's Sarcoma	73 (20%)	0	73 (20%)
Uterine Cervical Cancer	14 (4%)	0	14 (4%)
NADM	**181 (48%)**	**12 (100%)**	**169 (47%)**
Hodgkin Lynphoma	44 (12%)	1 (8%)	43 (12%)
Hepatocarcinoma	19 (5%)	0	19 (5%)
Anal Cancer	23 (6%)	3 (25%)	20 (6%)
Lung Cancer	16 (4%)	0	16 (4%)
Skin Cancer	12 (3%)	1 (8%)	11 (3%)
Head and neck cancer	11 (3%)	2 (17%)	9 (2%)
Urinary tract	11 (35)	2 (17%)	9 (2%)
Solid Other[a]	34 (9%)	3 (25%)	31 (9%)
Other[b]	11 (3%)	0	11 (3%)

a. **Colon cancer (n=3), stomach cancer (n=2), esophagus cancer (n=2), pancreas cancer (n=3), breast cancer (n=8), prostate cancer (n=5), leiomyosarcoma (n=2), penile cancer (n=2),**

Table 1. Patients' characteristics according to statin use

Characteristic	All (n= 5357)	Statin Use (n= 740)	No Statin Use (n= 4617)	p-value
Age (years)	46.5 (40.6-51.6)	51.1 (47.0-58.8)	45.7 (40.0-50.6)	<.0001
Male **gender**	4093 (76%)	589 (80%)	3504 (76%)	0.028
HIV risk factor				
▪IDU	1233(23%)	76(10%)	1157(25%)	
▪MSM	1457 (27%)	257 (35%)	1200 (26%)	<.0001
▪Heterosex	1018 (19%)	169 (23%)	849 (18%)	
▪Unknown	1649 (31%)	238 (32%)	1411 (31%)	
Body Mass Index (kg/m^2)	23.4 (21.3-25.7)	24.2 (22.2-26.2)	23.2 (21.2-25.5)	<.0001
Years of **HIV-infection**	14.6 (8.3-20.4)	16.5 (10.4-20.7)	14.2 (7.9-20.2)	<.0001
Years of **cART**	10.3 (4.8-15.1)	14.2 (8.8-16.4)	9.6 (4.2-14.7)	<.0001
Nadir CD4+ (cells/µL)	214 (96-323)	231 (126-334)	211 (91-321)	0.002
Diagnosis of **AIDS before cART**	463 (8.6%)	61 (8.2%)	402 (8.7%)	0.725
Positive Ab-anti HCV	1587 (30%)	107 (15%)	1480 (32%)	<.0001
Baseline CD4+ (cells/µL)	293 (165-438)	291 (177-443)	293 (163-437)	0.516
Baseline CD8+ (cells/µL)	940 (640-1300)	963 (680-1318)	933 (636-1289)	0.224
Baseline HIV-RNA $\log_{10}$(cps/ml)	4.28 (1.90-5.00)	4.11 (1.69-4.93)	4.30(1.90-5.01)	0.016
Baseline Cholesterol (mg/dL)	170 (141-203)	204 (173-244)	165 (138-196)	<.0001

Figure 3. Time to cancer occurrence according to statin use



Number of patients at risk

No statin use	***4617***	***3225***	***2120***	***994***	***193***	***3***
Statin use	***740***	***646***	***516***	***301***	***51***	***3***

Figure 2. Distribution of the type of statin among Statin users

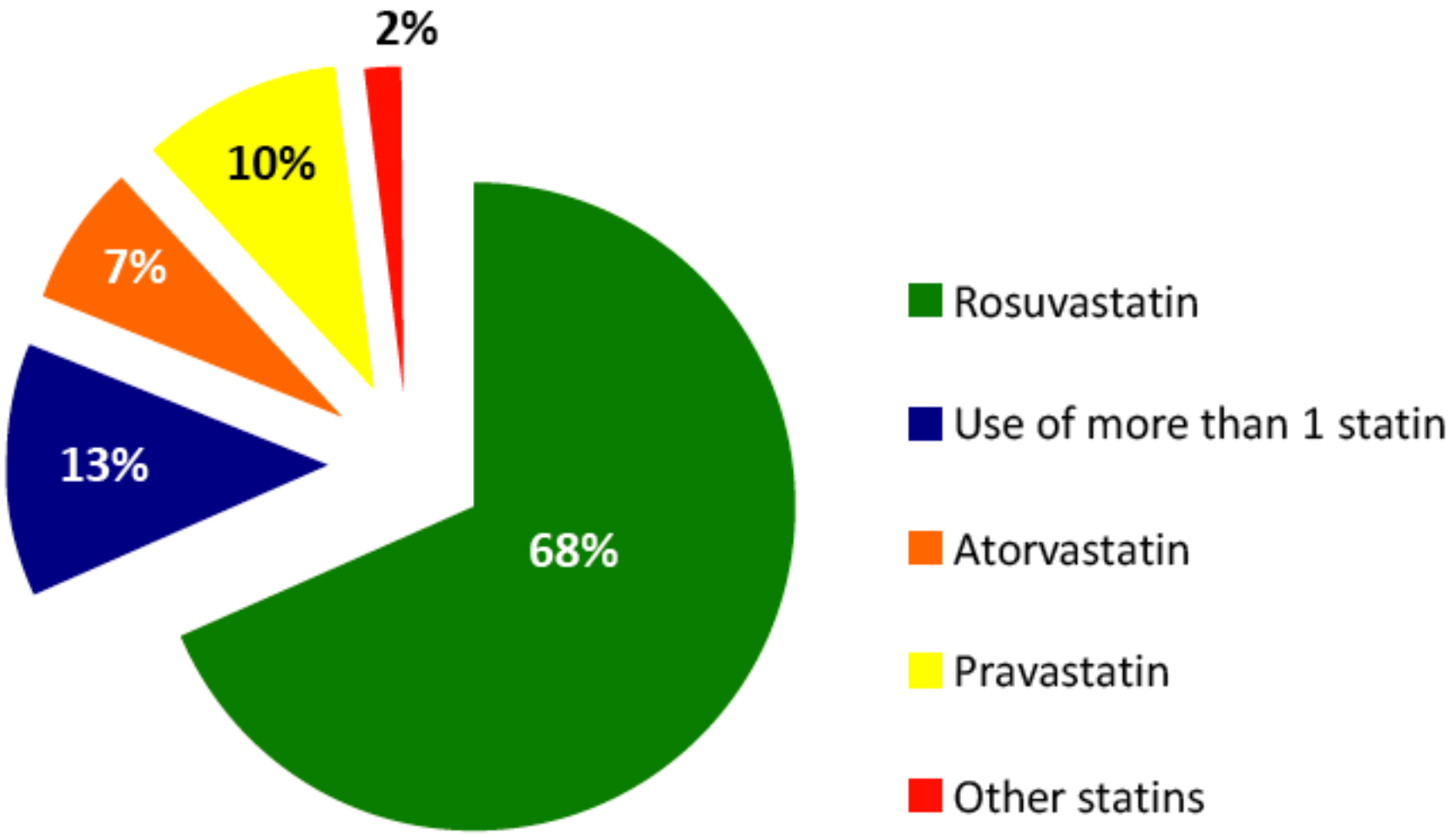
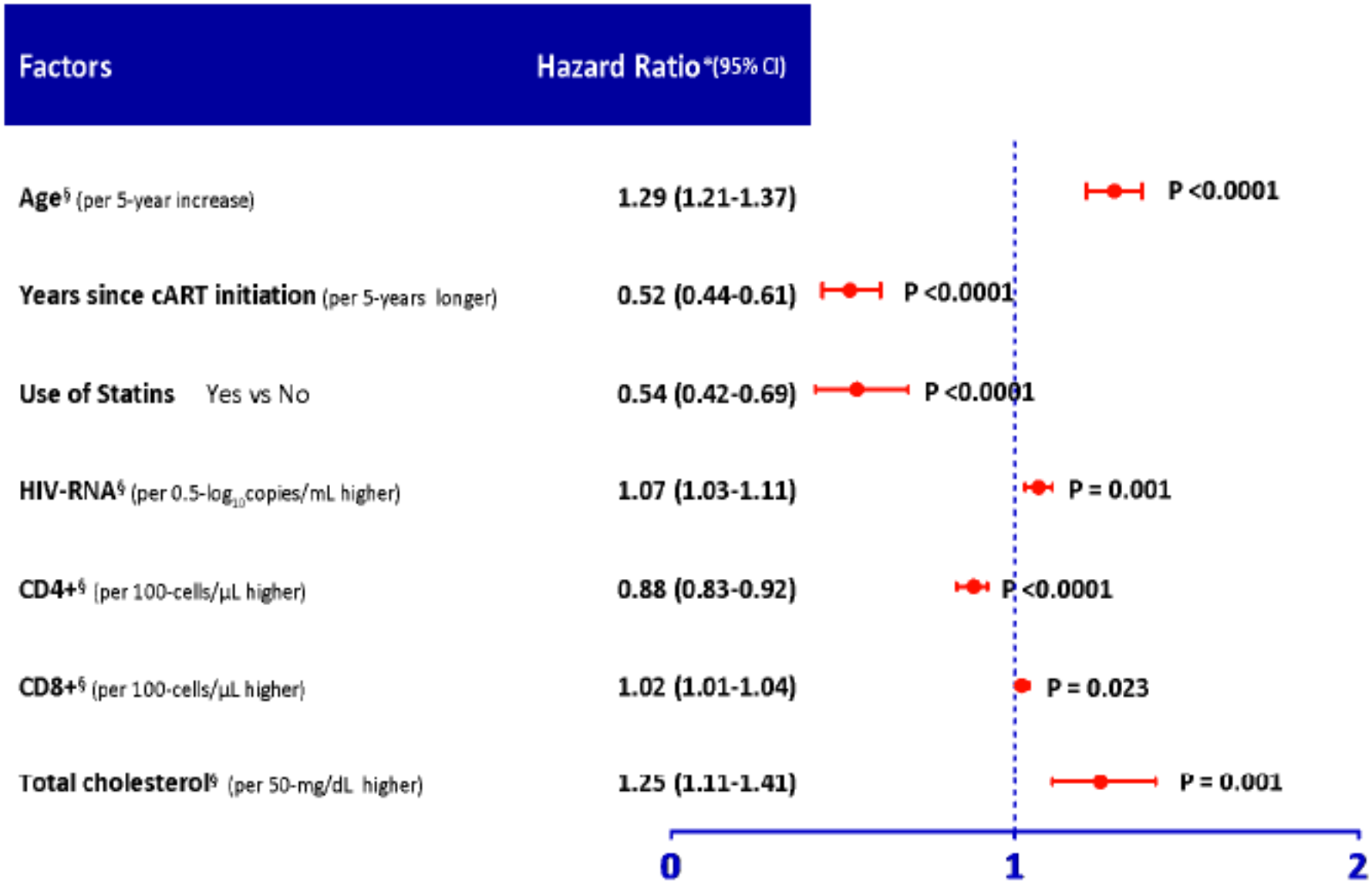


Figure 4. Multivariate analysis on the risk of cancer



*Adjusted for: gender, Body Mass Index, HCV, LDL cholesterol, fasting glucose, triglycerides

§ Time-updated covariate

References

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