Cancer Risk and Use of PI or NNRTI-based Combination Antiretroviral Therapy (cART): The D:A:D Study

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BACKGROUND

The potential effects of cART on cancer risk, especially regimens including protease inhibitors (PI) and non-nucleoside reverse transcriptase inhibitors (NNRTI), are unclear [1-4]. The aim of this study was to assess the relationship between cancer risk and cART, PI and NNRTI use.

METHODS

D:A:D participants were followed from the latest of D:A:D Study entry or 1/1/2004 (start of prospective cancer data collection) until the earliest of a first incident cancer diagnosis (any type, excluding pre-cancer stages), 1/1/2012, death, or 6 months after last visit. Poisson regression models assessed associations between the incidence of cancer and cumulative (per year) use of either CART or PI and NNRTI.

RESULTS

41,762 persons were included in the analysis, contributing 239,832 person-years (PY) of follow-up. Baseline characteristics are displayed in Table 1. During a median follow-up of 6.4 years (interquartile range [IQR] 3.7-8.1), a total of 2,242 cancers were diagnosed (incidence rate [IR]: 0.93/100PY [95% confidence interval (CI): 0.90-0.97]), 1,151 ADC (IR: 0.48/100PY; 95%CI: 0.45-0.51) and 1,091 NAD (IR: 0.45/100PY; 95%CI: 0.43-0.48). The most frequent AIDS-defining and non-AIDS-defining cancers were cervical cancer (496 cases, IR: 0.21/100PY; 95%CI: 0.19-0.22) and lung cancer (194 cases, IR: 0.08/100PY; 95%CI: 0.07-0.092), respectively.

According to the duration of cART exposure, NADCr increased from 0.24/100PY (95%CI: 0.19-0.30) among unexposed patients to 0.73/100PY (95%CI: 0.60-0.86) after >12 years of cART exposure, Figure 1. ADCIr decreased from 0.81/100PY (95%CI: 0.72-0.91) among unexposed patients to 0.11/100PY (95%CI: 0.07-0.17) after >12 years of cART exposure, Figure 1. Longer exposure to cART was associated with a lower risk of cancer overall (adjusted rate ratio [aRR]: 0.98/year; 95%CI: 0.97-1.00; p=0.009). No association was seen between PI use and risk of cancer overall (aRR: 1.01/year; 95%CI: 0.99-1.02), whereas longer NNRTI use was associated with a lower risk (aRR: 0.97/year; 95%CI: 0.95-0.99; p=0.0009), Figure 2.

LIMITATIONS

Residual confounding cannot be ruled out in this observational study.

CONCLUSION

Cumulative use of any CART was associated with reduced ADC, but increased NADCr risk. Both PI and NNRTI use appeared to be protective for the development of ADC, while the increased risk of NADCr associated with cART appeared to be restricted to PI use (3% higher risk per year). Biological mechanisms for the latter association possibly indicative of an adverse effect of PI merit further investigation.

REFERENCE

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