Long-acting insulin analogs exposure and cancer specific mortality in patients with diabetes mellitus

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AIM

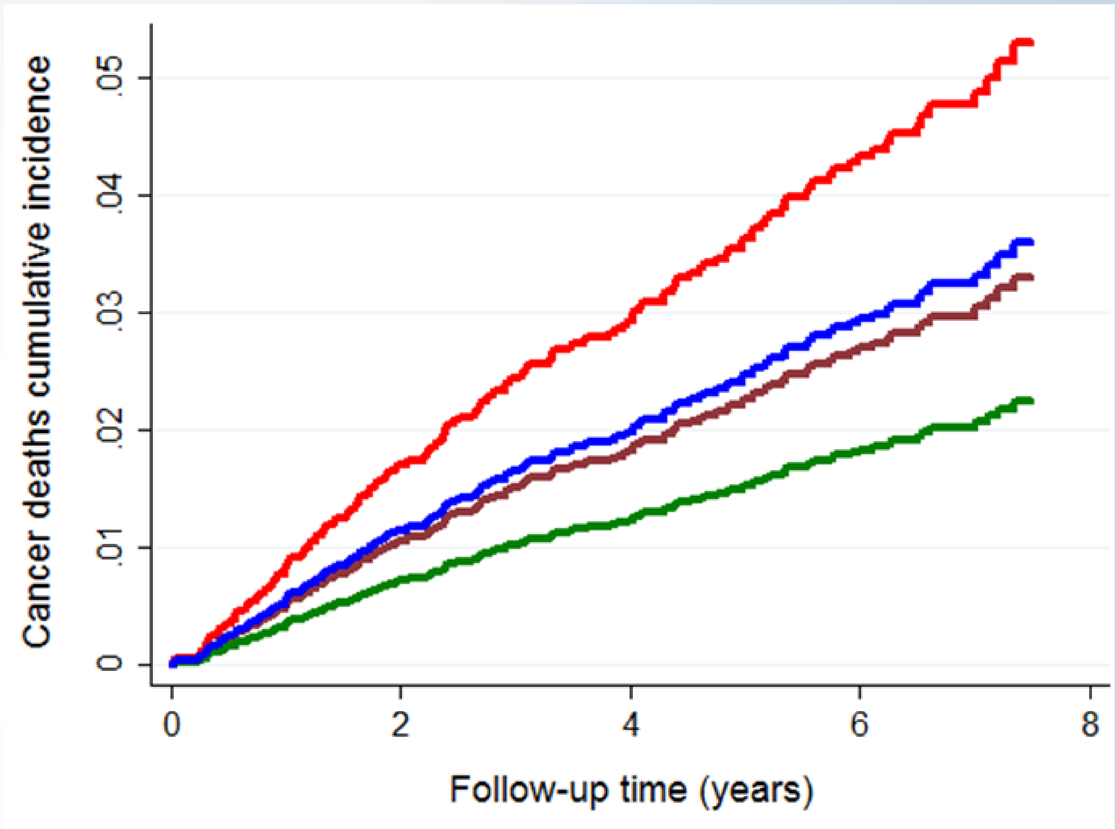
To test the hypothesis that exposure to insulin glargine might be associated with increased risk of cancer mortality compared with human basal insulin preparations.

MATERIALS AND METHODS

All consecutive diabetes patients aged over 40 years, residing in a major urban area were screened at their first diabetes outpatient visit between 01/01/2001-12/31/2008 (n=79869). Exclusion criteria were insulin treatment at screening (n=14752), no insulin treatment until 12/31/2008 (n=55795), <6 months of glucose-lowering treatment alone before insulin initiation (n=1154), insulin prescription before glargine became available (04/17/2003, n=1761), age <40 or ≥80 years at first insulin prescription (n=406), <6 months of insulin treatment following insulin initiation (n=1011). A total 4990 subjects were followed-up for death based on death certificate, until 12/31/2011, using data from National Institute of Statistics.

RESULTS II

Figure 1. Cancer deaths cumulative incidence functions. Green line, females exposed to glargine; maroon line, females unexposed to glargine; blue lines, males exposed to glargine; red line, males unexposed to glargine.



RESULTS I

Mean baseline age was 62±9 years, and follow-up 4.7±1.9 years. Glargine cumulative dose exposure significantly lowered cancer mortality risk, subhazard ratio (SHR) 0.94 (95% CI 0.89-0.99, p=0.033).

Table 1. Competing risk analysis of site-specific cancer mortality

Cancer site	Cumulative exposure SHR (CI 95%)	Cumulative dose SHR (CI 95%)
Lung (n=36)	1.008 (0.965-1.054)^{NS}	0.964 (0.897-1.036)^{NS}
Colorectal (n=20)	0.887 (0.657-1.197)^{NS}	0.913 (0.729-1.144)^{NS}
Female genital (n=18)	1.022 (0.895-1.167)^{NS}	0.956 (0.823-1.110)^{NS}
Liver (n=15)	0.985 (0.906-1.072)^{NS}	1.022 (0.950-1.099)^{NS}
Pancreatic (n=15)	$5*10^{-6}$ ($6*10^{-9}$-0.005)**	$9*10^{-5}$ ($1*10^{-7}$-0.058)**
Breast (n=13)	0.762 (0.663-0.877)**	0.849 (0.769-0.937)**
Urinary tract (n=11)	0.885 (0.761-1.030)^{NS}	0.933 (0.828-1.051)^{NS}

^{NS}not significant, *p<0.05, **p<0.01

CONCLUSIONS

- The cumulative dose exposure to insulin glargine was associated with a lower risk of cancer mortality in general, and of breast and pancreatic cancer in particular.
- No glargine associated "harm" was found even after additional "fixed" cohort or propensity score analyses were performed.

CONTACT INFORMATION

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