

Supplemental Table 3 Risk of malignancies in patients using insulin glargine or other insulin analogues in comparison with those using human insulin (fixed analysis)

Covariables ^a included in the model	Insulin glargine		Other insulin analogues	
	HR	95% CI	HR	95% CI
None	0.73	0.69, 0.77	0.80	0.77, 0.82
Stratified for dose of first insulin prescription				
< Median	0.67	0.52, 0.88	0.87	0.76, 0.99
Median	0.73	0.67, 0.78	0.76	0.73, 0.80
> Median	0.63	0.56, 0.71	0.87	0.83, 0.92
Age, sex	0.74	0.70, 0.78	0.80	0.78, 0.83
Full model: age, sex, calendar time, hospitalisations, unique drugs	0.77	0.73, 0.82	0.85	0.82, 0.88
Full model adjusted for time since cessation ^b	0.73	0.69, 0.78	0.83	0.80, 0.86
Full model adjusted for days of prior OGLD use				
< 1 year OGLD use	0.75	0.64, 0.89	0.81	0.75, 0.88
> 1 year OGLD use	0.80	0.75, 0.86	0.88	0.86, 0.92
Full model, adjusted for use of OGLD (time-dependent)				
Biguanide	0.77	0.73, 0.82	0.85	0.82, 0.88
SU	0.77	0.73, 0.82	0.85	0.82, 0.88
Other OGLD	0.77	0.73, 0.82	0.85	0.82, 0.88
Full model adjusted for average DDD	0.77	0.72, 0.82	0.85	0.82, 0.88
Full model, stratified for dose of first insulin prescription				
< Median	0.65	0.49, 0.86	0.88	0.76, 1.02
Median	0.78	0.72, 0.84	0.81	0.77, 0.85
> Median	0.66	0.58, 0.75	0.93	0.88, 0.99
Full model including a latency time of 1 year ^c	0.75	0.70, 0.81	0.87	0.84, 0.91

^aCovariables: age, age at first insulin prescription; calendar time, time since inclusion of participant in PHARMO RLS; hospitalisations, number of hospitalisations in the year prior to start of insulin; unique drugs, number of unique drugs dispensed in the year prior to start of insulin; days of prior OGLD use, number of days of OGLD use as of January 1998; average DDD, dose calculated over all previous insulin prescriptions

^bTime since cessation of insulin glargine, other insulin analogues and/or human insulin in days

^cModel included a 1 year latency period: exposure was cumulated up till one year prior to the date of cancer diagnosis; incidence rate (no. of cancer diagnoses/1,000 patient years) for insulin glargine 7.20; for other insulin analogues 7.90 and for human insulin 9.23. SU, sulfonylurea derivative