Specific PPAR gamma agonists may have different effects on cancer incidence

We read with interest the recent article by Kao et al. where they demonstrate an increased incidence of cancer in diabetic patients compared with non-diabetics [hazard ratio (HR) 1.20, 95% CI 1.11–1.29] [1]. They also analyzed the diabetic cohort to assess whether the use of PPARγ agonist thiazolidinediones (TZDs) had an effect on cancer incidence. Within this cohort, they did not find any significant difference in overall cancer incidence in TZD compared with non-TZD users. They did, however, find that the spectrum of cancer incidence differed between these two groups in keeping with prior observations that modulation of the PPARγ pathway can have contrasting effects on carcinogenesis depending on the biological microenvironment [2].

With respect to bladder cancer, Kao et al. report a numerically increased risk of bladder cancer in TZD users with a HR of 1.48, but this was not statistically significant. This is in contrast with a recently published meta-analysis by Colmers et al., which found a statistically significant increased risk of bladder cancer in TZD users (risk ratio 1.15, 95% CI 1.04–1.26) [3]. This study analyzed over 2 million diabetic patients compared with 22,910 in the current study which explains its statistically significant result despite the smaller magnitude of effect. Notably however, Colmers et al. found that the risk was limited to pioglitazone users (risk ratio 1.22, 95% CI 1.07–1.39) with no increased risk in rosiglitazone users. Whether the observed increased incidence of bladder cancer is the result of chance, PPARγ pathway modulation or drug-specific off-target effects remains to be determined.

We would be interested to know whether the authors of the present study had recorded the specific TZD prescribed to patients. Notwithstanding the relatively small number of patients, analysis of these data may shed further light on whether specific TZDs differentially affect cancer incidence.

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references

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