BLEEDING COMPLICATIONS OF TKIs

The receptor tyrosine kinase inhibitors (TKIs) sunitinib and sorafenib are used widely in the treatment of advanced cancer, including renal cell carcinoma. These agents have, however, been associated with bleeding complications in a number of trials and case reports. Now, a meta-analysis by researchers from the Dana-Farber Cancer Institute at Harvard Medical School has investigated the incidence of these adverse effects in patients who received TKIs for a range of indications.

A search of published articles and abstracts led the investigators to identify 23 trials with suitable data for analysis. Of these, 4 were phase III trials (2 sunitinib, 2 sorafenib), and 19 were phase II trials or expanded-access programs (9 sunitinib, 10 sorafenib). Overall, bleeding events of any grade were reported in 708 of 4,934 patients, and high-grade bleeding was seen in 100 of 6,597 patients; incidences calculated using a random effects model were 16.7% (95% CI 12.7–21.5%) and 2.4% (95% CI 1.6–3.9%), respectively. The incidence of bleeding of any grade was higher in patients with renal cell cancer than in those with other tumors (20.6% versus 7.6%). When the 4 randomized phase III studies were considered alone, use of a TKI conferred a two-fold increased risk of a bleeding event (relative risk 2.0, 95% CI 1.14–3.49). This risk seemed to be greater in patients with renal cell cancer than in those with non-renal tumors, although the difference was not significant.

The investigators conclude that the use of sunitinib and sorafenib increases the risk of bleeding; this increased risk might be especially apparent in patients who receive these agents for advanced renal cell carcinoma. Clinicians should be aware of these adverse effects when initiating and monitoring treatment with TKIs.

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Original article Je, Y. *et al.* Risk of bleeding with vascular endothelial growth factor receptor tyrosine-kinase inhibitors sunitinib and sorafenib: a systematic review and meta-analysis of clinical trials. *Lancet Oncol.* **10**, 967–974 (2009).