Annals of Oncology 26 (Supplement 6): vi36–vi52, 2015
doi:10.1093/annonc/mdv340.30

Session E. Gastrointestinal (colorectal) cancer

E30 KRAS status and risk of venous thromboembolic events in patients with metastatic colorectal cancer: a case-control study

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Background: Cancer patients are at increased risk of venous thrombotic events (VTE). Tissue factor (TF) is the primary initiator of blood coagulation and preclinical data suggest that its expression is also controlled by KRAS. Higher levels of TF seem to be associated with mutations of KRAS; the latter therefore might be a plausible link to hypercoagulability and increased VTE risk for metastatic colorectal cancer (mCRC) patients (pts).

Patients and methods: A retrospective case-control study was conducted. Cases had VTE (deep vein thrombosis (DVT), pulmonary embolism (PE), and/or migratory superficial thrombophlebitis) occurring after diagnosis of metastatic disease. Controls were pts with mCRC without VTE, matched for age, sex, year of diagnosis of metastatic disease, and presence of a central venous access device. Cases and controls were identified from the electronic health records of the Department of Oncology, Udine, and of the Department of Oncology, Pisa. Formalin-fixed, paraffin-embedded samples were reviewed and tested by pyrosequencing for KRAS status (codons 12, 13, 61 and 146). Estimating that about 40% of mCRC harbor a KRAS mutation and with a cases/controls ratio of 1:2, the sample size needed to determine a significant odds ratio (OR) of 2.5 was approximately 77 cases and 154 controls, with $\alpha = 0.05$ and a power of 80%.

Results: Between January 2008 and December 2014 a total of 68 cases with VTE and 177 controls without VTE were included. Thirty-four of the cases had DVT, 34 had PE. Of note, 6 patients had both thrombotic events. When VTE occurred, 37% of pts were receiving a bevacizumab-containing regimen. Among the controls, 38% received bevacizumab. Fifty-three (78%) of the cases and 137 (77%) of the controls had a central venous access device. The OR for thrombosis in KRAS mutated (codon 12, 13, 61 and 146) mCRC pts was 1.34 (95%CI 0.77-2.36, $p = 0.303$).

Conclusions: Despite the trend towards an increased risk of VTE for pts with KRAS-mutant mCRC, our results were not statistically significant and did not confirm the findings of a similar retrospective study conducted in pts with mCRC [Ades S, et al. J Thromb Haemost 2015]. Whether tumor genetic profile may contribute to the thrombotic risk assessment of CRC cancer pts remains uncertain.