"A NEW GENETIC RISK SCORE FOR PREDICTING VTE EVENTS IN CANCER PATIENTS RECEIVING CHEMOTHERAPY"

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BACKGROUND
Venous thromboembolism (VTE) is a common event in cancer patients and one of the major causes of cancer-associated mortality and a leading cause of morbidity. Nowadays a majority of VTE occur in the outpatient setting and the risk of VTE varies notably between cancer patients. Khorana score is a multivariable clinical risk assessment model (RAM) for VTE that includes site of tumour, BMI and some haematology values. It has been developed and internally and externally validated in ambulatory patients with cancer receiving chemotherapy. It is important to note that genetic factors are essential to evaluate thrombotic risk since thrombosis is a multifactorial disease resulting from the interaction of genetic and environmental factors, with an estimated heritability of about 60%. However, Khorana and all available VTE RAMs ignore the substantial genetic risk in these patients. In April 2013 we launched ONCOTHROMB12-01, a translational study to optimize risk assessment of VTE in cancer patients receiving chemotherapy in ambulatory setting.

MATERIALS AND METHODS
ONCOTHROMB12-01 is a prospective, translational, observational study that includes 400 patients diagnosed with locally advanced or metastatic cancer (colon, stomach, pancreas and lung) receiving systemic outpatient chemotherapy. In this preliminary report we included 207 patients with the first follow-up at 6 months. Demographic and clinical data have been obtained from each patient as well as Khorana’s score and the Thrombo inCode score (TIC score). TIC score is based on a combination of genetic and clinical risk factor for thromboembolic disease. The genetic factor including in TIC are: F5 rs6025/rs118203906/rs118203905, F2 rs1799963, F12 rs1801020, F13 rs5985, SERPINC1 rs121909548, SERPIN A10 rs2232698, plus A1 blood group (rs8176719, rs7853998, rs1187643, rs8176750) and risk factor such as age, sex, family history of VTE, BMI, smoking and diabetes. We constructed different predictive models based on: a) Khorana score; b) TIC score; c) Khorana score plus cancer disease status and d) TIC score plus site of tumour and cancer disease status. Each model is based on Support Vector Machine (SVM) classification algorithm that matches the predictor variables to the response variable (whether the patient has thrombosis or not). The predictive capacity of each model was defined in terms of the discrimination capacity of the different VTE risk functions expressed as the area under the receiver-operating characteristic (ROC) curve (AUC).

RESULTS
Clinical characteristics and Khorana score are shown in table 1 and 2, respectively. Among the first 207 patients with a first follow-up in 6 months, 47 suffered a thromboembolic event. As shown in Figure 1, the predictive model based on KS showed an AUC of 56.9 and the TIC score 41.2. The same approach was used to assess the validity and predictive capacity improvement of the different score models with the addition of cancer disease status. The results in Figure 1 indicate that both models predict better with the addition of cancer disease status (CDS); being the TIC score better (66.2 for KS approach) than the Khorana score (56.9).

CONCLUSIONS
Our results showed TIC score plus CDS and ST improves VTE risk predictive capacity compared to KS alone and KS plus CDS.

REFERENCES