PLENARY SESSION 1
EMERGING TRENDS IN CANCER-ASSOCIATED THROMBOSIS (PART I)

OC-01

IMMUNE CHECKPOINT BLOCKADE PROMOTES THROMBOSIS VIA T-CELL AND NEUTROPHIL ACTIVATION, AND TUMOR-CELL ASSOCIATED TISSUE FACTOR IN A MURINE MODEL OF COLORECTAL CANCER

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Introduction: The use of immune checkpoint inhibitors (ICI) to treat cancer is associated with several immune-related adverse events (irAE), including venous thrombosis.
Aim: To define mechanisms of ICI-associated thrombosis (IAT), we used a mouse model of colorectal cancer in which ICI stimulates the development of venous thrombi.
Materials and Methods: Mice bearing CT26 mouse colorectal tumors were treated with ICI (aPD-1+aCTLA4). Levels of circulating nucleosomes (Nu.Q H3.1), neutrophil extracellular traps (NETs), neutrophil-platelet aggregates, thrombin-antithrombin (TAT) complexes, and tumor and extracellular vesicle (EV) tissue factor (TF) were measured before and after ICI. Tumor cytokines were also profiled. The role of tumor-derived TF in IAT was determined using mice bearing CT26 cells in which TF was deleted using CRISPR/Cas9 (TFKO cells).
Results: ICI treated tumor-bearing mice developed larger thrombi than mice treated with control IgG and demonstrated elevated levels of circulating nucleosomes (114 *vs* 82 ng/ml), NETs (15.8 *vs* 6.8%), platelet-neutrophil aggregates (44.8 *vs* 22.3%), and TAT complexes (12.6 *vs* 7.9 ng/ml). TF expression was increased in tumor extracts from ICI-treated mice. Tumors from ICI-treated mice expressed increased levels of IFNɣ (2-fold) and TNFα (5-fold) and CXCL11 (6.8-fold). To assess the role of IFNɣ on tumor cell TF expression, CT26 cells were incubated with IFNɣ, which increased TF expression in a concentration dependent manner. Increased TF expression was associated with phosphorylation of STAT1 at Tyr701 and STAT3 at Tyr705, along with increased IRF-1 expression, a downstream target of STAT1, that was blocked by a JAK1/2 inhibitor, baricitinib. While the quantity of large EV remained constant, treatment with IFN-γ enhanced release of small EVs, accompanied by upregulation of Rab27a, a small GTPase that initiates release of small EVs.
Conclusions: IFN-γ, potentially originating from activated T cells induced by ICI, contributes to increased TF expression in tumor cells via the JAK-STAT pathway. Through upregulation of Rab27a, IFNɣ may also contribute to the release of TF+ EV. TF KO in CT26 cells resulted in reduced tumor and EV-associated TF and was associated with a decrease in IVC thrombus size after ICI treatment (24.2 *vs* 20.5 mg; P=0.047). Neutrophil and platelet activation, and tumor-associated TF may contribute to ICI-associated thrombosis.

OC-02

NAVIGATING THE INTERPLAY OF CANCER, HEMOSTASIS, AND THROMBOSIS: INVESTIGATING TISSUE FACTOR IN COLORECTAL CANCER (CALGB/SWOG 80405)

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Introduction: Cancer induces hypercoagulability. Tissue factor (TF) plays a crucial role in the coagulation cascade as a transmembrane receptor and cofactor for factor VII/VIIa. The TF-VIIa complex activates PAR2, leading to intracellular signaling. Elevated TF expression (exp) in malignancy correlates with cell proliferation, angiogenesis, and metastasis. In colorectal cancer (CRC), TF holds a pivotal role and is associated with oncogenic alterations (KRAS, BRAF, HER2).
Aim: This study investigates TF's prognostic and predictive relevance in CRC. TF-targeted antibody-drug conjugates are under investigation in solid tumors.
Materials and Methods: 433 metastatic CRC patients (pts) treated with bevacizumab (VEGFRi, n=226) or cetuximab (EGFRi, n=207) in combination with first-line chemotherapy were analyzed from the CALGB/SWOG 80405 trial. TF and PAR2 RNA from formalin-fixed, paraffin-embedded (FFPE) tumor samples were sequenced on the HiSeq 2500 (Illumina). Overall survival (OS) was compared by tertiles of TF exp (high *vs* mid *vs* low). Logrank p-values describe differences without pt characteristic adjustment. Transcriptome-wide gene association analysis used linear regression, adjusting for multiple factors. Gene Ontology enrichment analysis used the top 100 TF-associated genes.
Results: TF exp correlates with genes maintaining epithelial integrity, cell adhesion, migration, extracellular matrix structure, antigen processing, glycosylation, Wnt pathway regulation, cytokine production, and MAP kinase pathways. High TF exp associates with shorter median OS in the entire cohort (25.2 *vs* 30.9 *vs* 35.4 months, p=0.0051), FOLFOX-treated (22.4 *vs* 30.9 *vs* 33.4, p=0.0044), and EGFRi-treated pts (22.4 *vs* 30.9 *vs* 33.4, p=0.0044). This impact is notable in EGFRi-treated pts with liver metastases (23.6 *vs* 29.9 *vs* 35.1 months, p=0.016). TF exp lacks predictive value for OS in FOLFIRI or VEGFRi-treated pts. PAR2 exp levels do not correlate with survival outcomes.
Conclusions: TF exp is a prognostic marker in CRC and is predictive of OS in FOLFOX and EGFRi-treated pts, especially

those with liver metastases, possibly through PAR2-independent mechanisms. Further investigation into its association with EGFR is crucial. These findings underscore the significance of exploring TF and related thrombosis-associated genes in CRC.
Support: U10CA180821; U10CA180888, UG1CA180830, U24CA196175 (SWOG); https://acknowledgments.alliancefound.org.Lilly; Genentech; Pfizer; Clinicaltrials.gov Id#: NCT00265850.

PLENARY SESSION 2
EMERGING TRENDS IN CANCER-ASSOCIATED THROMBOSIS (PART II)

OC-03

PREDICTION OF CLINICALLY SIGNIFICANT BLEEDING IN PATIENTS ANTICOAGULATED FOR CANCER-ASSOCIATED VENOUS THROMBOEMBOLISM: VALIDATION OF THE B-CAT SCORE IN A COHORT OF PATIENTS FROM THE TESEO STUDY

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Introduction: No validated score is currently available for prediction of clinically significant bleeding in patients anticoagulated for cancer-associated venous thromboembolism (Ca-VTE).
Aim: The objective of this study was to validate the B-CAT score, a new tool designed to classify the risk of bleeding in oncology patients receiving anticoagulation.
Materials and Methods: Data came from the TESEO study, a national, multicenter and prospective registry that documents patients with Ca-VTE. Patients anticoagulated for any type of VTE were included and observed over a period of 180 days for major or clinically relevant bleeding. The variables of the B-CAT score (tumor location, presence of metastasis, history of major or clinically relevant bleeding, anaemia, coagulopathies, and cerebrovascular and gastrointestinal disease) were selected, except for minor trauma, and minor surgery and clinically relevant bleeding not requiring hospitalization after Ca-VTE, as these were not available. Patients were classified according to bleeding risk into three categories, and a multivariate logistic regression model was developed using these variables to estimate the risk of bleeding.
Results: The study cohort comprised 2301 patients with Ca-VTE receiving anticoagulation. After an observation period equivalent to 848 person-years, 157 significant bleeding events were identified (6.8%; 18.5 per 100 person-years): 63 major bleeding events (40.1%; 7.4 per 100 person-years) and 94 clinically relevant bleeding events (59.9%, 11.1 per 100 person-years). Patients classified as low (47.8%), medium (59.5%), and high (1.7%) risk as determinated by B-CAT score had different 6-month significant bleeding rates: 11.4, 24.4, and 100 per 100 person-years, respectively ($p<0.001$). The predictive model showed adequate calibration (Hosmer-Lemeshow test: $p=0.886$) and discrimination, evidenced by C-statistic index for significant bleeding, major bleeding, and clinically relevant bleeding of 0.63 (95% confidence interval: 0.58-0.67), 0.61 (0.53-0.69), and 0.63 (0.57-0.69), respectively, as shown in Figure 1.
Conclusions: We have validated the bleeding risk score B-CAT in patients with Ca-VTE receiving anticoagulation. This model can contribute to standardizing decision-making in a context where quality evidence is limited.

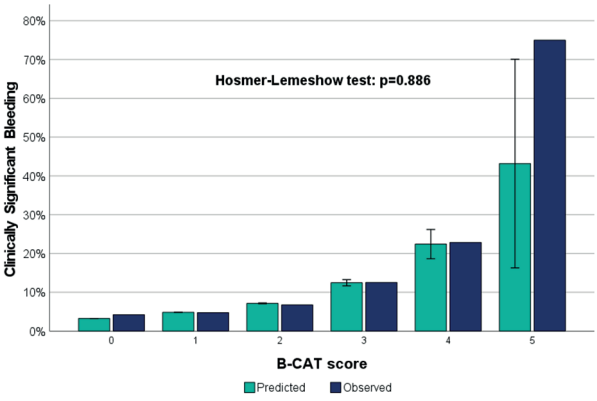

Figure 1. Observed and predicted rates of clinically significant bleeding for several values of the B-CAT score.

OC-04

TISSUE FACTOR PATHWAY-RELATED BIOMARKERS IN PANCREATIC CANCER: PLASMA LEVELS OF ACTIVATED FACTOR VII-ANTITHROMBIN COMPLEX MAY PREDICT VENOUS THROMBOEMBOLISM

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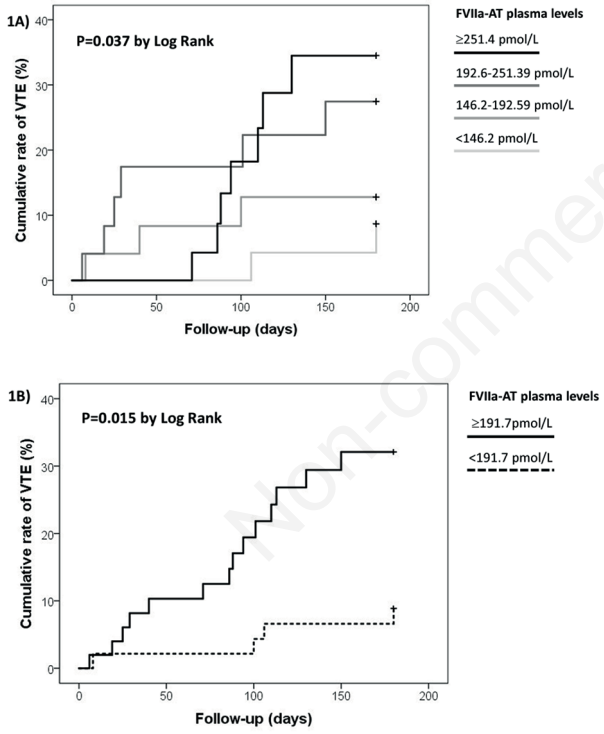
Introduction: Tissue factor (TF), the main initiator of the coagulation cascade, is well recognized to play a key role in pancreatic cancer-associated thrombosis. However, the laboratory evaluation of the transmembrane protein TF is hampered by multiple factors. The soluble activated factor VII–antithrombin complex (FVIIa-AT) is considered an indirect marker of TF exposure by reflecting TF-FVIIa interaction.

Aim: To evaluate plasma levels of FVIIa-AT and other TF pathway-related biomarkers, like tissue factor pathway inhibitor (TFPI), in a cohort of patients with pancreatic cancer and to analyze their association with subsequent VTE risk during a 6-month follow-up.

Materials and Methods: Patients with advanced pancreatic cancer planned for a new chemotherapy regimen were prospectively enrolled in 4 centers in The Netherlands and Italy between January 2019 and September 2021. Blood was drawn at baseline and patients were followed for 6 months for the occurrence of venous thromboembolism (VTE), including splanchnic vein thrombosis. FVIIa-AT, FVII Antigen (FVII Ag), and total TFPI were determined by ELISA.



Cumulative rate of venous thromboembolism (VTE) during the follow-up in the pancreatic cancer cohort (n=98) stratified on the basis of FVII-AT plasma concentration: **A)** according to the levels of quartile distribution and **B)** according to the threshold value defined by ROC curve analysis, i.e. 191.7 pmol/L (at level of 48° percentile).

Figure 1.

Results: Ninety-eight patients with pancreatic cancer (50% females, mean age 66.5±9.0) were included. During a 6-month follow-up, 24 subjects (24.5%) died and 19 subjects (19.4%) developed VTE. Subjects with VTE had a higher baseline plasma concentration of FVIIa-AT as compared to those without VTE (240.3 [188.0-309.1] pmol/L *versus* 183.6 [166.1-202.9 pmol/L], P=0.023), while no significant difference was found for either FVII Ag or TFPI levels. Stratifying the study population on the basis of FVIIa-AT plasma levels, Kaplan-Meier curves showed a progressively increased rate of VTE from the lowest to the highest quartile (8.3%, 12.0%, 24.0%, 33.3%, respectively, log-rank P=0.037, Figure 1A). The ROC curve analysis defined a cut-point value at 191.7 pmol/L (48th percentile, Figure 1B). Subjects with high FVIIa-AT levels above this threshold value (≥191.7 pmol/L) had a more than three-fold increased risk of VTE as compared to those with low FVIIa-AT levels (HR 3.63 with 95%CI 1.20-11.04). This association was confirmed after adjustment for sex, age, BMI, FVII Ag, and TFPI by Cox regression models (HR 3.44 with 95%CI 1.08-10.98).

Conclusions: High plasma levels of FVIIa-AT predict an increased risk of VTE in the setting of advanced pancreatic cancer, thereby demonstrating the potential clinically meaningful role of TF pathway-related biomarkers to include identify high-risk patients.

PLENARY SESSION 3
ANTICOAGULATION IN HEMATOLOGICAL CANCER PATIENTS

OC-05

THE RISK OF THROMBOEMBOLIC RECURRENCE OUTWEIGHS THE RISK OF MAJOR BLEEDING IN CANCER PATIENTS TREATED WITH TINZAPARIN, EVEN IN PATIENTS WITH FRAGILITY CRITERIA. META-ANALYSIS OF PROSPECTIVE STUDIES INVOLVING 1413 INDIVIDUAL PATIENTS' DATA

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Introduction: On anticoagulant therapy, patients treated for Cancer Associated Thrombosis (CAT) remain at high risk of both venous thromboembolic recurrence (rVTE) and major bleeding (MB). In practice, fragile patients are particularly concerned by the risk of bleeding. Whether the risk of recurrence and the risk

of bleeding under anticoagulant therapy are higher in patients with criteria of fragility remains poorly assessed, as these patients are under-represented in randomized clinical trials.

Aim: We estimated the rate of rVTE and MB at 6 months according to patient characteristics from prospective cohorts and randomized studies involving CAT patients on tinzaparin, using a meta-analysis on individual patient data.

Materials and Methods: Eligible studies for this meta-analysis (PROSPERO registration CRD42019119907) had to include a central adjudication committee for study outcomes. Main outcomes were cumulative incidences of rVTE and MB at 6 months. The cumulative incidences were estimated using the Kalbfleisch and Prentice method considering the competing risk of death for rVTE and MB. Patients were considered "with fragility characteristics" when they had at least one of the following: age ≥75, body weight (BW) ≤50 kg, creatinine clearance (CrCl) <50 ml/min or ECOG ≥2.

Results: Three prospective cohort studies (AXA - NCT02898051, N=308; PREDICARE - N=409 (1); TICAT - N=247 (2) and the tinzaparin arm of the CATCH study (N=449 (3)) were included. The 6-months cumulative incidences of rVTE and MB of the entire population of 1413 patients were 6.2% [95% CI: 5.0%; 7.7%], and 3.4% [2.7%; 4.5%] respectively. Among these patients, 21.3% were over 75 years, 9.3% had a BW ≤50 kg, 13.9% a CrCl <50 ml/min and 30.2% an ECOG ≥2. In all situations (presence or absence of each fragility criterion), the risk of rVTE under treatment was found to be higher than the risk of MB (Figure1).

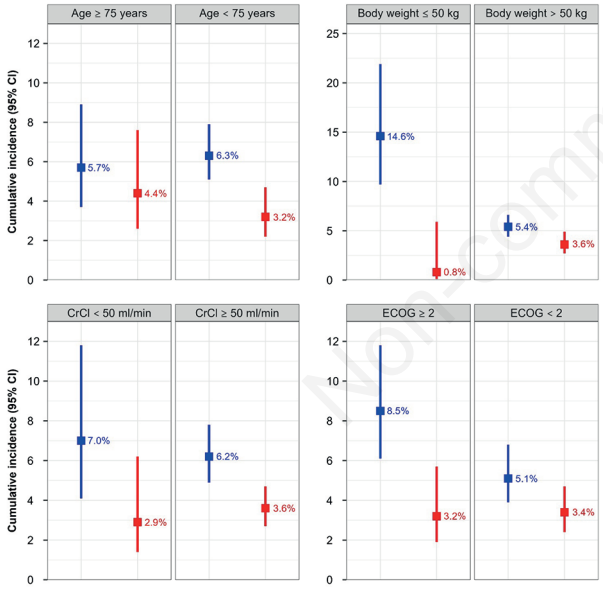

Figure 1. Risk of recurrent venous thromboembolism and major bleeding by 6 months in CAT patients treated with tinzaparin,according to patients' fragility characteristics Recurrent VTE (Blue), Major Bleeding (Red).

Conclusions: In CAT patients receiving tinzaparin for up to 6 months, the risk of rVTE is always greater than the risk of MB, but the rVTE to MB risk ratio is increased in fragile patients, often exceeding 2. This finding supports maintaining the recommended tinzaparin dose in fragile patients with CAT.

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OC-06

RAPID EXCLUSION OF CLINICALLY RELEVANT PLASMA LEVELS OF DIRECT ORAL ANTICOAGULANTS IN PATIENTS USING THE DOAC DIPSTICK IN VARIOUS INDICATIONS

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Introduction: Accurate and rapid detection of DOACs in the circulation remains a major challenge in patients presenting with major bleeding or with thrombotic events during treatment, or requiring urgent surgery or an invasive procedure. Rapid methods for assessing plasma concentrations of DOACs such as hemostatic assays, rotational thrombelastography using global or specific activators for blood clotting, require blood sampling, transportation of sample to the laboratory, centrifugation, coagulation platforms and coagulation specific reagents. A urine dipstick method contains one in all reagents and can be readily used as near patient test.

Aim: DOAC Dipstick (DOASENSE, Heidelberg, Germany) is a point-of-care test that uses a disposable test strip to detect DOACs in urine and to determines qualitatively for presence or absence dabigatran and factor Xa inhibitor (FXa) DOACs.

Methods and Results: Some recent investigations and studies have demonstrated the performance of DOAC Dipstick on urine at a threshold of >30 ng/mL plasma. A pooled analysis of 5 published studies calculated the following performance values (Thromb Haemost 2024). The proposed algorithm enhances medical decision-making in acute care indications useful primarily in hospitals not having readily available quantitative tests and 24/7. Another recently published pilot study, a plasma threshold of 100 and 120 ng/mL was compared to the results of the dipstick test for deciding on fibrinolytic or mechanical treatment in patients with acute ischaemic stroke or transient ischaemic attack. The sensitivity and specificity for FXA inhibitors were 83% and 93% of the still ongoing study (Front Neurol. 2023). The high sensitivity and NPV of the dipstick were also confirmed in a study in preoperative medicine using

a plasma threshold of >30 ng/mL determined by liquid mass spectrometry (Table 1). The receiver operating curve for the dipstick was 0.92 (95%CI 0.85 - 1.00) (submitted for publication).
Conclusions: The data confirm the ability of the DOAC Dipstick to exclude clinically significant levels at a plasma threshold of >30ng/mL of DOACs. An algorithm suggests quantitative method if dipstick results are positive if available within am adequality short time frame. As plasma threshold values have not yet been established for the various indications, further studies are performed.

Table 1.

	FXa DOACs Mean (95% CI)	Dabigatran Mean (95% CI)
Sensitivity	97.8 (95.6 – 99.0)	98.3 (91.0 – 100)
NPV	86.6 (76.0 – 93.7)	99.6 (97.7 – 100)
PPV	87.2 (83.7 – 90.1)	73.4 (63.7 – 83.2)
Specificity	50.0 (40.2 – 59.0)	91.8 (87.7 – 94 .9)

PLENARY SESSION 4
EXPLORING THE RELATIONSHIP BETWEEN HEMOSTASIS AND CANCER: NEW INSIGHTS

OC-07

INVESTIGATING A PROPOSED ANTI-CANCER IMMUNITY EFFECT OF RIVAROXABAN IN BREAST CANCER

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Introduction: Immune Checkpoint Inhibitors (ICI) are now licensed in the early and metastatic breast cancer setting. However, most cancer patients do not derive long-term benefit attributed to an intrinsic or acquired resistance. Myeloid cell-synthesized Factor Xa impedes anti-tumour immunity in the tumour microenvironment via the activation of PAR2, promoting tumour progression independent of coagulation. The Factor Xa inhibitor Rivaroxaban abrogates this tumour stimulatory effect. Improved response and survival is seen in melanoma patients on Factor Xa inhibitors (*e.g.*, for VTE prophylaxis) receiving ICI. We have recently completed a multi-centre phase II pre-operative 'Window-of Opportunity' randomised controlled trial of the oral Factor Xa inhibitor Rivaroxaban compared to no treatment in ER negative, stage I-III early breast cancer patients, the TIP Trial (n=88 patients). Patients were randomised 1:1 (Rivaroxaban 20mg od: no treatment) and received 14 (+/-3) days of treatment in the window between diagnosis and surgery or commencement of neoadjuvant chemotherapy.
Aim: The Factor Xa inhibitor Rivaroxaban promotes an anti-cancer tumour microenvironment in early breast cancer patients.
Materials and Methods: Using the PhenoCycler technology we shall comprehensively profile the immune microenvironment of TIP Trial FFPE tissue samples following transcriptome analysis of breast tissue cores collected into RNAlater. In work up experiments, we cultured the monocyte cell lines THP-1 and U937 and differentiated them into macrophages using PMA. We assessed expression of the macrophage marker CD68 and Factor X by Western Blot and tested Rivaroxaban-treated macrophage conditioned media by cytokine array.
Results: PMA-treated THP-1 and U937 expressed CD68 indicating successful differentiation into macrophages and expressed Factor X albeit at low levels, indicating they were suitable models for FXa-producing myeloid cells. In response to Rivaroxaban, both models showed a decrease in immune cell chemotactic cytokines such as CCL7 and CCL20. The highest increasing cytokines for THP-1 and U937 macrophages were FGF-7 and TGF-B2 respectively that have established roles in cancer cell migration.
Conclusions: The decrease in CCL7 and CCL20 cytokine levels may provide another mechanism by which FXa-producing myeloid cells effect the immune microenvironment. This provides preliminary data for the TIP Trial tissue analysis that should be complete by the 12th ICTHIC conference.

OC-08

TUMOR PLATELET TRANSCRIPTOME CHANGES AFFECTED BY MICRO METASTASIS

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Introduction: It is known that tumors induce profound alterations in platelet transcriptomes but modifiers and specific underlying mechanisms of platelet tumor education are incompletely understood. Thrombin is the major platelet activator through protease activated receptor (PAR) 4 in mice; and coagulation activation and thrombin generation is a hallmark of various cancers. We hypothesized that thrombin-PAR4 induced platelet hyperreactivity contributes to platelet transcriptome changes in tumor bearing mice.
Aim: We determined platelet transcriptomes of tumor free and tumor bearing WT and hyper-thrombotic thrombomodulin mutated TM^{Pro} mice. In hyper-thrombotic mice, we also deleted PAR4 to assess the role of thrombin signaling in platelets. We also prevented other thrombin signaling effects by crossing TM^{Pro} mice with a thrombin insensitive PAR1 point mutation ($PAR1^{R41Q}$) mouse.

Materials and Methods: We used the B16F10 transplantable tumor model, characterized tumor cell expressed and exosome released genes as well as platelet transcriptomes by RNA-seq.
Results: TM^{Pro} mice showed increased tumor growth, dependent on PAR signaling, and showed markedly lower platelet counts relative to tumor-bearing WT mice, indicating a profound intravascular prothrombotic state in this tumor model. Increased consumption of platelets in tumor-bearing hyper-thrombotic TM^{Pro} mice was reversed by PAR4, but not PAR1 signaling deficiency. Despite these variations in platelet counts, platelets from all genotypes showed very similar platelet transcriptome changes that overlapped to >80% with transcripts expressed in tumor cells and tumor cell-derived exosomes. Although hyper-thrombotic TM^{Pro} mice display increased metastasis to the lungs in various tumor models, spontaneous micro metastases were very low and not different between the different strains carrying B16F10 tumors. In contrast, bone marrow metastasis was indicated by increased abundance of tumor cell transcripts; and these were also highly enriched in the platelet transcriptomes of the tumor bearing mice.
Conclusions: Platelet transcriptome changes can be traced to tumor cell transcripts, as well as tumor-cell derived exosomes, and occur independent of thrombin-induced alterations of platelet hyperreactivity and platelet half-life in tumor bearing mice. In contrast, tumor platelet education is closely correlated with the degree of micro metastasis in bone marrow, indicating a transfer of tumor derived RNA and exosomes to megakaryocytes.

PLENARY SESSION 6
NOVEL BIOMARKERS FOR PREDICTING CLINICAL OUTCOMES IN CANCER PATIENTS

OC-09

GROWTH DIFFERENTIATION FACTOR-15 IS ASSOCIATED WITH RISK OF MAJOR BLEEDING IN CANCER PATIENTS WITHOUT ANTICOAGULATION: RESULTS FROM A PROSPECTIVE COHORT STUDY

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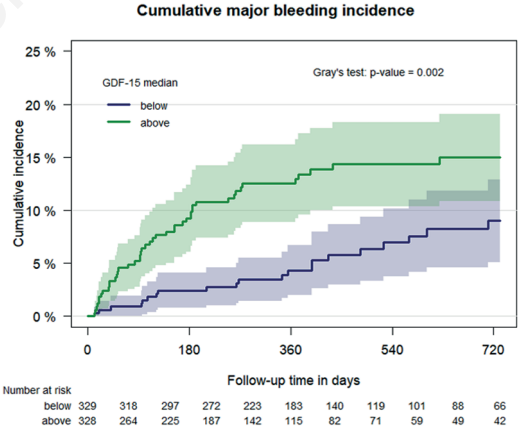
Introduction: Hemostatic imbalances are frequent in patients with cancer. Despite extensive knowledge of venous thromboembolism risk, there is limited understanding of bleeding risk, risk factors, and biomarkers predictive for bleeding in cancer patients without anticoagulation. Prior research indicates that growth differentiation factor-15 (GDF-15), a stress-response protein of the transforming growth factor-ß superfamily, holds promise as a predictive biomarker for bleeding risk in various patient populations, including a previous analysis in patients with cancer receiving anticoagulation.
Aim: We aimed to investigate the association between GDF-15 and bleeding risk in a novel cohort of patients with cancer initiating systemic anti-cancer therapies who did not receive anticoagulation.
Materials and Methods: Major bleeding (MB) was defined according to the ISTH recommendation. Measurements were performed in serum samples drawn before initiation of anti-cancer treatments with the Elecsys® GDF-15 assay (Roche Diagnostics, Rotkreuz, Switzerland). The association between GDF-15 and MB was analyzed in a Fine and Gray model accounting for all cause-mortality as competing risk.
Results: In total, 670 patients (49% women) were included in this analysis (median age: 61, interquartile range [IQR]: 53-69). During a median follow-up of 18 months (IQR: 11-28), 67 patients (10.0%) experienced a MB (12-month cumulative incidence: 8.3%, 95% confidence interval [CI]: 6.1-10.4). The median GDF-15 level was 1739.5 ng/L (IQR: 996.5-3437). Elevated GDF-15 levels were significantly associated with an increased risk of MB (SHR per doubling: 1.41 [95% CI: 1.20-1.66]), also when adjusting for sex, age, BMI, tumor type and stage, albumin, and hemoglobin (SHR: 1.28, 95% CI: 1.02-1.61). The cumulative incidence of MB was higher in patients with GDF-15 levels above the median (>1739.5 ng/L) than in those with levels below the median (≤1739.5 ng/L) (12-month cumulative incidence [95% CI]: 12.5% [8.9-16.2] *versus* 4.3% [2.0-6.7], p=0.002, Figure 1).
Conclusions: In patients with cancer without anticoagulation, elevated GDF-15 levels were significantly associated with an increased risk of major bleeding. Therefore, GDF-15 is a promising candidate biomarker for bleeding risk prediction in patients with cancer without anticoagulation.



Cumulative incidence of major bleeding in patients with GDF-15 levels below (n=335, blue line) (≤1739.5 ng/L) versus above the median (n=335, green line) (>1739.5 ng/L). Patients were divided according to their GDF-15 level and the group with levels below 1739.5 ng/L (≤median) was compared to the group with levels above 1739.5 ng/L (>median) within a Fine and Gray subdistribution hazard model (p=0.002).

Figure 1.

OC-10

PREDICTIVE VALUE OF ACTIVATED FXI-ANTITHROMBIN COMPLEX IN CANCER-ASSOCIATED THROMBOSIS (CAT): A PROSPECTIVE COHORT STUDY IN LUNG CANCER PATIENTS

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Introduction: Patients with lung cancer are particularly vulnerable to thrombosis, especially when undergoing chemotherapy. Activated factor XI (FXIa) plays a significant role in the contact system, which contributes to the pathophysiology of CAT. However, further extensive research is still necessary to fully understand the role of the contact system in lung cancer-related thrombosis.
Aim: In a prospective cohort of newly diagnosed non-small cell lung cancer (NSCLC) patients enrolled in the HYPERCAN study, we measured the levels of biomarkers of contact activation to assess whether they can help predict venous thromboembolism (VTE) within 6 months after starting chemotherapy.
Materials and Methods: Prechemotherapy plasma samples were tested by ELISA for *in vivo* complexes of contact pathway activation (*i.e.*, plasma kallikrein:C1-esterase inhibitor [PKa:C1Inh], FXIa:antithrombin [FXIa:AT], FXIa:C1Inh, FIXa:AT, and thrombin generation (*i.e.*, prothrombin fragment 1+2 [F1+2], thrombin-antithrombin complex [TAT]). Clinical data and VTE were recorded prospectively.
Results: A total of 719 (489M/230F, median age: 66 years) NSCLC patients (568 metastatic and 151 locally advanced) were studied. The 6-month cumulative incidence of VTE was 10%, with a higher incidence in the metastatic group (12%) compared to the locally advanced group (4%). A total of 68 patients developed VTE, and they were found to have significantly higher ($p<0.001$) levels of FXIa:AT complex, F1+2, and TAT before receiving chemotherapy compared to those who did not develop VTE. This finding remained significant even after correcting for age and gender. The results of a multivariable analysis revealed that FXIa:AT [HR 1.18 (95%CI 1.02-1.39)] and TAT [HR 1.30 (95%CI 1.08-1.57)] are independent risk factors for VTE during chemotherapy. Additionally, patients with FXIa:AT and TAT values above the highest quartile had a significantly higher incidence of VTE than those with values below the 3rd quartile. The difference was significant, with the former group exhibiting 23% incidence as opposed to the latter group's 8% incidence (log-rank <0.001), as shown by KM analysis.
Conclusions Patients with NSCLC who developed VTE showed increased activation of their contact system pathway. Furthermore, a scoring system based on both FXIa:AT and TAT was developed to identify patients who have a higher chance of developing VTE. These findings support the use of FXIa inhibitors in the prevention and treatment of CAT.

PLENARY SESSION 7
ANTICOAGULATION IN CANCER PATIENTS

OC-11

MANAGING A CANCER-ASSOCIATED THROMBOSIS CLINIC - OPPORTUNITIES AND CHALLENGES

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Introduction: Cancer-associated thrombosis (CAT) remains the number one cause of death during chemotherapy and the second-leading cause of all cancer deaths (1, 2). CAT is associated with a high risk of recurrent thrombosis, bleeding, and mortality (3). Cancer patients are estimated to have a 2-20-fold higher risk of developing venous thromboembolism (VTE) (4). Treatment of CAT is challenging, and the introduction of direct oral anticoagulants (DOACs) has made treatment decisions complex. Expert groups of clinicians across the world have defined various consensus guidelines (5). Despite evidence based guidelines, implementation remains unpredictable (6). A dedicated CAT service may improve overall standards of care in this setting. This is viewed positively both among patients and clinicians (1). Establishing a dedicated CAT clinic model for cancer patients with or at risk of VTE would help to reduce mortality and cut down financial cost (2).
Aim: To address these challenges, a dedicated CAT service has the potential to improve patient care by addressing various aspects of unmet needs.
Materials and Methods: A new dedicated thrombosis service was launched for cancer patients at University Hospitals of North Midlands (UHNM) in the UK. This presentation encapsulates recent developments in this area in light of the experience gained in running the CAT service for the last two years.
Results: A total of 2266 new patients were referred to anticoagulant management service within a year, from Dec. 2022 to Dec 2023, of which 282 were CAT patients. A significant number of them continued as follow-up cases but some of them were discharged back to the primary care. CAT service carries a multidisciplinary team that meets weekly. The comprehensive management of CAT requires a multidisciplinary approach that integrates anticoagulant therapy, cancer treatment, prophylaxis, bleeding management, and supportive care. This approach involves a diverse panel of specialists, including oncologists, haematologists, pharmacists, and clinical nurse specialists. The overarching goal is to minimize the risk of recurrent thrombosis, mitigate bleeding risks, and ultimately improve patient outcomes and satisfaction. The other aspects include addressing prophylaxis, supporting patients, research, education, and training.
Conclusions: In the pursuit of enhancing clinic access for patients grappling with CAT, seeking consultation with healthcare providers well-versed in thrombosis in cancer patients is crucial. Proposing a CAT service, aims to provide a specialized care, improve communication, offer support, and foster research and training in this field.

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OC-12

PROGNOSTIC FACTORS ASSOCIATED WITH RECURRENT VENOUS THROMBOEMBOLISM IN PATIENTS WITH CANCER-ASSOCIATED VENOUS THROMBOEMBOLISM: SYSTEMATIC REVIEW AND META-ANALYSIS

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Introduction: Recurrent venous thromboembolism (VTE) is frequent in cancer patients. Understanding the factors associated with an increased or decreased rate of recurrent VTE is essential for developing evidence-based tools to guide decisions regarding optimal duration and intensity of anticoagulation in this patient population.

Aim: To determine the association between prognostic factors and recurrent VTE in patients with cancer-associated VTE.

Materials and Methods: We searched MEDLINE, Embase, and the Cochrane Library (from inception to February 2024) for randomized controlled trials and cohort studies that examined factors associated with recurrent VTE in patients with cancer-associated VTE. We also obtained additional data from the Hokusai VTE Cancer, CLOT, CATCH, and SELECT-D randomized trials. For the primary analysis, we only pooled prognostic factors that were derived from a multivariable model which included at least age, sex, cancer site or cancer stage, and reported in at least two studies.

Results: Of 4587 citations, 26 studies (51,594 patients) met inclusion criteria for this review. Most of the studies were observational cohorts of cancer patients with VTE receiving anticoagulation for six months. Factors associated with an increased rate of recurrent VTE included a history of VTE (adjusted hazard ratio [aHR] 1.50 [95% confidence interval [CI] 1.08 to 2.09]), Eastern Cooperative Oncology Group performance status ≥1 (aHR 1.88 [1.44 to 2.46]), advanced cancer (aHR 1.43 [1.17 to 1.75]), lung cancer (aHR 2.19 [1.29 to 3.74]), genitourinary cancers (aHR 1.38 [1.10 to 1.74]), pancreatic cancer (aHR 6.06 [2.04 to 12.08]), elevated C-reactive protein (aHR 3.62 [1.27 to 9.58]), elevated D-dimer (aHR 2.93 [1.70 to 5.03]), and elevated soluble P-selectin (aHR 4.98 [2.00 to 12.40] (Table 1). Conversely, female sex (aHR 0.89 [0.79 to 0.99]) and recent surgery (aHR 0.56 [0.40 to 0.76]) were associated with a decreased rate of recurrent VTE (Table 1).

Conclusions: This systematic review and meta-analysis summarizes the association between several prognostic factors and recurrent VTE in patients with cancer-associated VTE. These factors should be carefully considered in risk stratification frameworks to help make clinical decisions regarding management of patients with cancer-associated VTE.

Table 1.

Prognostic Factors Associated with Recurrent Venous Thromboembolism.

Prognostic Factors	Studies	Adjusted Hazard Ratio (95% CI)	P	I^2(%)
Patient Factors				
Female sex	12	0.89 (0.79 to 0.99)	0.038	4
Older age	9	0.97 (0.95 to 1.00)	0.017	71
History of VTE	6	1.50 (1.08 to 2.09)	0.015	15
Renal insufficiency	4	1.09 (1.00 to 1.18)	0.061	72
Recent surgery	2	0.56 (0.40 to 0.76)	0.0003	0
Initial VTE				
DVT alone	9	1.25 (0.82 to 1.91)	0.292	70
Proximal DVT	3	0.98 (0.56 to 1.74)	0.956	22
Symptomatic VTE	3	1.36 (0.56 to 3.31)	0.502	52
Residual vein obstruction[a]	2	3.68 (0.69 to 19.7)	0.127	83
ECOG performance status ≥1	6	1.88 (1.44 to 2.46)	<0.0001	0
Cancer Factors				
Advanced cancer	13	1.43 (1.17 to 1.75)	0.0006	46
Chemotherapy	5	1.08 (0.86 to 1.37)	0.499	50
Cancer site				
Brain	3	1.38 (0.62 to 3.08)	0.429	84
Breast	5	0.46 (0.19 to 1.11)	0.084	87
Lung	6	2.19 (1.29 to 3.74)	0.004	83
Gastrointestinal	3	1.01 (0.46 to 2.22)	0.977	73
Genitourinary	3	1.38 (1.10 to 1.74)	0.006	0
Hepatobiliary	2	2.03 (0.19 to 21.27)	0.555	75
Pancreas	2	6.06 (2.04 to 12.08)	<0.0001	0
Biomarkers				
Elevated C-reactive protein	3	3.62 (1.27 to 9.58)	0.010	51
Elevated D-dimer	4	2.93 (1.70 to 5.03)	0.0001	57
Elevated P-selectin	2	4.98 (2.00 to 12.40)	0.0006	0

ECOG=Eastern cooperative oncology group; DVT= deep vein thrombosis; VTE=venous thromboembolism
[a]In patients who discontinued anticoagulation.

POSTER SESSION 1
BIOMARKERS/ HYPERCOAGULABILITY I

PO-01

ALTERED WHOLE BLOOD THROMBIN GENERATION AND HYPERRESPONSIVE PLATELETS ASSOCIATE WITH THROMBOEMBOLIC EVENTS IN PATIENTS WITH PANCREATIC DUCTAL ADENOCARCINOMA

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Introduction: Thromboembolic disease is a major complication in pancreatic ductal adenocarcinoma (PDAC) patients. Patients with PDAC often have altered blood cell counts, which associate with incident thrombosis. The high thrombotic risk in patients with PDAC may be partially explained by the effects of pro-coagulant blood cells.
Aim: 1. To compare blood cell dependent coagulation and fibrinolysis between PDAC patients and controls matched for age and sex. 2. To explore whether blood cell dependent coagulation associates with incident thrombosis in PDAC patients
Materials and Methods: Patients with locally advanced and metastatic PDAC and controls matched for age and sex were included. Thrombin generation (TG) was measured in whole blood (WB) and plasma. Platelet granule release capacity (PGRC) was measured in WB. Patients were followed for the occurrence of thromboembolic events during 6-months.
Results: At first, we tested differences in TG between patients (n=18) and controls (n=18). Patients (n=18) showed an increased endogenous thrombin potential (ETP) in WB, compared to controls (n=18; 2714 *vs* 2905, p=0.003). This was in contrast to plasma TG, as no difference in ETP was found in plasma when comparing patients to controls. For both plasma and WB the lag time was longer in patients compared to controls, respectively 10.5 *vs* 8.9 minutes (p=0.013) for WB and 7.6 *vs* 6.2 (p=0.006) for plasma. Secondly, the capacity of platelets to release granules was tested. Patients had hyperresponsive platelets, with a shorter time to maximum platelet granule release (43 *vs* 62 seconds, p=0.008). Of the 18 patients with PDAC, five patients developed thromboembolic events (28%). A shorter lag time in WB (HR=0.475, 95%-CI=(0.228-0.988)), not in plasma, and an increased PGRC (HR=1.148, 95%-CI=(1.007- 1.309)) were associated with thromboembolic events.
Conclusions: Patients with PDAC have an increased and delayed WB-TG coagulation profile compared to controls. The increase in coagulation was not found in plasma, implying blood-cell dependent procoagulant effects. Blood cell dependent coagulation seems to associate with incident thromboembolic events in patients with PDAC and platelets appear to play a key role. Hemostasis measurement in WB is likely to further improve thrombosis risk estimation in PDAC patients.

PO-02

THROMBO-HEMORRHAGIC EVENTS AND TISSUE FACTOR EXPRESSION IN NEWLY DIAGNOSED PATIENTS WITH ACUTE PROMYELOCYTIC LEUKEMIA RECEIVING INDUCTION THERAPY

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Introduction: Acute promyelocytic leukemia (APL) is characterized by a life-threatening coagulopathy, secondary to TF-mediated clotting activation. Current protocols including arsenic trioxide (ATO) and all trans retinoic acid (ATRA) have exhibited beneficial effects on the hemostatic derangement, particularly downregulating cellular TF expression. Given the still relevant rate of lethal thrombo-hemorrhagic events (THE) in APL, characterizing the coagulopathy and identifying predictive markers remains a critical issue.
Aim: We prospectively recorded THE occurrence in the first month after APL diagnosis, and monitored the circulating hypercoagulation markers and the molecular expression of TF, before and during induction therapy.
Materials and Methods: Sixty-five consecutive APL patients receiving ATRA+Idarubicin (n=60, GIMEMA AIDA2000) or ATRA+ATO (n=5, GIMEMA APL0406) for remission induction were enrolled in 2 Italian Centers (2005-2015). Blood samples were obtained from 35 patients at diagnosis before therapy (D0), and during induction on days (D)7, 14 and 28, and tested for Tissue Factor mRNA (TF mRNA) expression by peripheral mononuclear cells and for plasma levels of FVII-Antithrombin Complex (FVIIa-AT), a parameter of TF activity, together with markers of thrombin generation (TAT) and fibrinolysis (D-dimer).
Results: At D0, 12 patients (18%) presented with THE: 8 major bleeding (3 fatal intracranial and 5 non-fatal major bleedings (MB)) and 4 thrombosis (1 fatal). Within 3 days of ATRA, 2 additional fatal intracranial bleedings occurred, ac-

counting for 9% early deaths. In the next 20 days, 3 non-fatal MB and 2 non-fatal thrombosis developed. Laboratory study showed APL TF mRNA significantly higher than controls at D0, which progressively decreased by 68%, 70%, and 90%, at D7, D14 and D28, respectively. TAT and D-dimer levels, initially elevated, significantly decreased at D7, and were lowest at D28, while FVIIa-AT dropped significantly only at D28. Statistically significant correlations were found between the decrease in TF mRNA and the decrease in FVIIa-AT levels during induction therapy.
Conclusions: Our data show a significant rate of severe thrombo-hemorrhagic events in our cohort of APL patients (19/65, 29%), including 6 early fatal events. Laboratory data demonstrate the TF mRNA downregulation under induction therapy, which parallels hypercoagulation markers decrease. Persistent high TF-dependent clotting activation (FVIIa-AT) might explain post-ATRA THE.

PO-03

PLASMA MARKERS OF HEMOSTATIC ACTIVATION AND FIBRINOLYSIS IN PATIENTS WITH NON-METASTATIC CASTRATION-RESISTANT PROSTATE CANCER BEFORE AND AFTER SECONDARY HORMONAL THERAPY AND ANTI-PSMA RADIOIMMUNOTHERAPY

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Introduction: The number of venous and arterial thrombotic events in patients with prostate cancer (PCa) is amongst the most common across cancers, likely due to the prevalence of PCa. Events are related to stage as well as treatment. Multiple classes of therapeutic agents have improved outcomes for patients with PCa. While hormonal therapy has been utilized long-term, targeted radionuclides are newer. The effect of hormonal manipulation and radionuclides on the hemostatic and fibrinolytic system is under-studied. We previously described differences in plasma markers related to stage.
Aim: Here we report preliminarily results in a prospective, randomized study, for the first time assessing the effect of therapeutic radionuclides as well as hormonal therapy.
Materials and Methods: Patients with high-risk "non-metastatic" (CT and bone scan negative) castration-resistant prostate cancer (M0 CRPC) were enrolled in a multicenter study (NCT00859781). Treatment included a 1-month run-in period of open-label secondary hormonal therapy (ketoconazole and hydrocortisone) followed by addition of radioimmunotherapy (RIT) with radiolabeled anti-PSMA antibody J591 (blinded to receive the therapeutic beta/gamma emitter 177Lu *vs* the diagnostic gamma/auger emitter 111In in 2:1 ratio). Plasma was collected for analysis of markers of hemostatic activation, fibrinolysis, and angiogenesis at baseline, after 1 month of hormonal therapy, and 1 month after radionuclide. ELISA was performed for D-dimer, thrombin-antithrombin complex (TAT), tissue factor (TF), IL-6, IL-8, and VEGF.
Results: As previously reported, baseline pre-treatment levels of plasma markers appear to be overall higher in this M0 CRPC population compared to historical controls of untreated clinically localized disease. Median levels of plasma markers were not significantly different after 1 month of secondary hormonal therapy. However, after radiolabeled J591, D-dimer increased (median 4-fold) while TAT appeared to decrease. Full analysis of unblinded data is ongoing; it appears that the D-dimer increase is driven by changes after 177Lu as opposed to 111In and this may be similar for TAT.
Conclusions: Plasma markers of hemostatic activation and fibrinolysis appear to be affected by radioimmunotherapy. As there may be a relationship to cancer status in addition to treatment effects, analysis with relationship to PSA response, the development of metastatic disease, and thrombotic/bleeding events is ongoing.

PO-04

ALTERED PLASMIN GENERATION IN PATIENTS WITH PANCREATIC DUCTAL ADENOCARCINOMA

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Introduction: Thromboembolic disease is an important complication in pancreatic ductal adenocarcinoma (PDAC) patients. Fibrin degradation plays a role in the occurrence of a thrombus. However, assays studying fibrinolysis kinetics are unexplored. A recently developed assay to measure plasmin generation kinetics offers promising avenues for exploring potential alterations in the fibrinolytic system.
Aim: To study fibrinolysis phenotype in PDAC patients, using a case-control approach.
Materials and Methods: 18 patients with locally advanced and metastatic PDAC, before and 8 weeks after chemotherapy, and 18 controls with the same age and sex distribution, were included. Plasmin generation (PG), thrombin generation (TG) and clot lysis time (CLT) were measured in platelet-poor plasma (PPP). The relation between fibrinolysis parameters and PDAC prevalence was studied using a case-control analysis.
Results: In PDAC patients before and after chemotherapy, we observed significant changes in endogenous plasmin potential (EPP) and plasmin peak levels compared to controls (Figure 1). Specifically, patients exhibited higher EPP (116.1% & 110% *vs* 95.08%, p=0.008 & p=0.004) and plasmin peak levels (98.96% & 105.9% *vs* 93.57%, p=0.1 & p=0.006), expressed as median % relative to normal pooled plasma. Additionally, patients showed prolonged lag time (2.50 & 2.67 *vs* 2.33 min, p=0.26 & p=0.021) and ttPeak (5.33 & 5.53 *vs* 4.67 min, p=0.002 & p=0.0002) compared to controls. In contrast, profiles of patients before and after chemotherapy and controls were similar in terms of TG and CLT, with the exception of prolonged TG lag

time (3.67 *vs* 2.9 min, p=0.009) observed in patients before chemotherapy. In the presence of thrombomodulin (TM), patients showed less inhibition of EPP by TM (41.93% & 37.80% *vs* 55.14%, p=0.017 & p=0.001) and less inhibition of plasmin peak levels (26.14% & 31.61% *vs* 39.82%, p=0.003 & p=0.028) compared to controls.

Conclusions: PDAC patients exhibit an elevated plasmin generation compared to controls. Additionally, both PG and TG are delayed in PDAC patients. The observed delay in thrombin formation and fibrinolysis among PDAC patients may contribute to thrombus formation and increase the risk of venous thromboembolism (VTE). Strikingly, PDAC patients exhibit reduced sensitivity to the inhibitory effect of TM on PG.

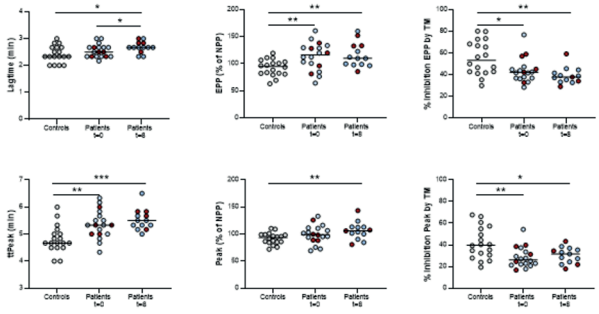

Figure 1. Plasmin generation in patients with PDAC and healthy controls.

Plasmin generation parameters in patients with PDAC before chemotherapy and 8 weeks after the start of chemotherapy and matched controls. Plasmin generation was triggered with 1.25 µg/mL tPA and 5 pM TF in the presence or absence of TM in platelet poor plasma. Medians are presented as error bar. Patients before chemotherapy (t=0) are indicated in light blue, patients during chemotherapy (t=8) are indicated in dark blue, healthy controls are indicated in grey. Patients that developed a thromboembolic event, either venous or arterial, are indicated in purple. Wilcoxon rank sum tests or Mann-Whitney U tests were performed to compare the groups. EPP: Endogenous plasmin potential, min: minutes; TF: Tissue Factor; TM: Thrombomodulin; t_0: first blood withdrawal before chemotherapy; t_8: second blood withdrawal 8 weeks after the start of chemotherapy. *P <0.05, **P<0.01, ***P<0.001.

PO-05

AN MRI RADIOMICS APPROACH TO PREDICT THE HYPERCOAGULABLE STATUS OF GLIOMAS

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Introduction: Venous thromboembolic events are frequent complications of Glioblastoma Multiforme (GBM) and Low-Grade Gliomas (LGG). The overexpression of the Tissue Factor (TF) plays an essential role in the local hypercoagulable phenotype that underlies these complications. Magnetic Resonance Imaging (MRI) plays a key role in the diagnosis and follow-up of LGG/GBM. It also allows for a powerful and non-invasive exploration of many facets of the biology of these tumors using a radiomics strategy, *i.e.* the extraction of features related to tumor morphology and texture. The possibility of using MRI radiomics to explore the local hypercoagulable status of LGG/GBM has not yet been tested.

Aim: Our aim was to build an MRI radiomics model for the non-invasive exploration of the hypercoagulable status of LGG/GBM.

Materials and Methods: Radiogenomics data available from two cohorts were used: TCGA (The Cancer Genome Atlas) and REMBRANDT (Repository for molecular BRAin Neoplasia DaTa) (n=136 and n=39 LGG/GBM patients, used as training and validation cohorts, respectively). We retrieved 120 tumor radiomics features and RNA expression levels of F3, encoding TF. The seven most contributive MRI radiomics features from LGG/GBM linked to high TF were identified in TCGA using Least Absolute Shrinkage and Selection Operator (LASSO) regression. A logistic regression model (Radscore) was built in order to identify the top-20% F3-expressing tumors, considered to be at high thromboembolic risk.

Results: This model had good performance in TCGA/training and REMBRANDT/validation cohorts: AUC=0.87 [CI95: 0.81-0.94, p<0.0001] and AUC=0.78 [CI95: 0.56-1.00, p=0.02], respectively. In agreement with the key role of the coagulation cascade in gliomas, LGG patients with a high Radscore had lower overall and disease-free survival. The Radscore was linked to the presence of specific genomic alterations, the composition of the tumor coagulome and the tumor immune infiltrate.

Conclusions: Our findings suggest that a non-invasive assessment of the hypercoagulable status of LGG/GBM is possible with MRI radiomics.

PO-06

ANTIPHOSPHOLIPID ANTIBODIES IN WOMEN WITH ENDOMETRIAL AND CERVICAL CANCER

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Introduction: Current generally accepted clinical and laboratory criteria for antiphospholipid syndrome are well known and include vascular thrombosis and pregnancy complications in patients with circulating antiphospholipid antibodies (aPLA). However, in the last few years, aPL have become a common finding in patients with malignancy.

Aim: The aim of our work was to understand the role of aPLA in patients with endometrial and cervical cancer.

Materials and Methods: The study included 96 cancer patients Grade 1 and Grade 2 aged 28 to 49 years with a verified histomorphological diagnosis of adenocarcinoma: endometrial cancer (group I, n=73) and cervical cancer (group II, n=23). The control group consisted of 60 healthy women. Plasma samples from all study participants were tested for the presence of lupus anticoagulant and IgG, IgM isotypes of antibodies to cardiolipin (aCL), β2-glycoprotein 1 (anti-β2-GP1), annexin V and anti-phos-

phatidylserine-prothrombin complex antibodies (anti-PS-PT) by enzyme immunoassay.

Results: Statistically significant differences were found in the assessment of aCL IgG/IgM, anti-b2-GPI IgG, anti- annexin V, IgM, anti- PS-PT, IgG, depending on the group of women with cancer and the control group (p=0.041, p=0.017, p=0.004, p=0.001, p=0.044, respectively). When comparing aPLA depending on Grade 1 or 2, we got the following results (Table 1). Statistically significant differences were revealed for aCL IgM (p <0.001 and p=0.008, respectively) for I and II groups. Anti-b2-GpI IgM prevailed in patients of both groups, IgG – in women with cervical cancer Grade 2. Antibodies to annexin V IgG, IgM prevailed in both groups in women with Grade 2 (p <0.001). Analyzing Grade 1/2, depending on the increased level of anti-PS-PT, IgM, it was not possible to establish statistically significant differences (p=0.597 for the IgG isotype, p=0.143 for IgM). Based on the data obtained, when evaluating antibodies to PS-PT, IgG, depending on Grade 1/2, we identified statistically significant differences (p <0.001).

Conclusions: We found a statistically significant increase in the aPLA titer in patients with endometrial and cervical cancer compared with the control group of healthy women. However, when comparing the antibody titer depending on Grade 1 or 2, we found a significant relationship between the high antibody titer in Grade 2 cancer patients compared to Grade 1. Further studies are needed to establish whether aPLA can be used as a diagnostic tool in oncogynecological cencer to identify patients at risk of disease progression and cancer recurrence.

Table 1. aPLA in cancer patients depending on Grade 1 and Grade 2.

Parameter	Category	**aCL, IgG** (IU/ml)			p
		Me	$Q_1 – Q_3$	n	
Endometrial cancer	Grade 1	4,60	2,23 – 5,68	41	0,829
	Grade 2	4,60	2,72 – 6,42	31	
Cervical cancer	Grade 1	5,01	4,62 – 5,99	13	0,750
	Grade 2	4,68	4,60 – 6,07	11	
Parameter	Category	**aCL, IgM** (IU/ml)			p
		Me	$Q_1 – Q_3$	n	
Endometrial cancer	Grade 1	2,10	1,80 – 3,17	41	< 0,001*
	Grade 2	5,50	3,51 – 6,27	31	
Cervical cancer	Grade 1	2,60	1,06 – 3,17	13	0,008*
	Grade 2	5,24	4,38 – 6,41	11	
Parameter	Category	anti-b2GpI, IgG (IU/ml)			p
		Me	$Q_1 – Q_3$	n	
Endometrial cancer	Grade 1	3,20	1,69 – 7,01	41	0,909
	Grade 2	4,74	1,66 – 6,76	31	
Cervical cancer	Grade 1	1,80	1,20 – 2,62	13	0,001*
	Grade 2	6,89	6,00 – 7,71	11	
Parameter	Category	anti-b2GpI, IgM (IU/ml)			p
		Me	$Q_1 – Q_3$	n	
Endometrial cancer	Grade 1	1,96	1,20 – 3,40	41	< 0,001*
	Grade 2	6,43	5,59 – 7,63	32	$p_{P3\ Grade\ 2 – P3\ Grade\ 1}$ < 0,001
Cervical cancer	Grade 1	0,73	0,43 – 2,10	12	$p_{PIIIM\ Grade\ 2 – P3\ Grade\ 1}$ < 0,001
	Grade 2	7,20	6,49 – 25,95	11	$p_{PIIIM\ Grade\ 1 – P3\ Grade\ 2}$ < 0,001
					$p_{PIIIM\ Grade\ 2 – PIIIM\ Grade\ 1}$ < 0,001
Parameter	Category	anti-ANX V, IgG (IU/ml)			p
		Me	$Q_1 – Q_3$	n	
Endometrial cancer	Grade 1	1,80	1,12 – 3,10	41	< 0,001*
	Grade 2	4,26	3,98 – 4,90	32	$p_{P3\ Grade\ 2 – P3\ Grade\ 1}$ < 0,001
Cervical cancer	Grade 1	1,55	0,87 – 2,64	12	$p_{PIIIM\ Grade\ 2 – P3\ Grade\ 1}$ = 0,001
	Grade 2	4,12	4,00 – 8,54	11	$p_{PIIIM\ Grade\ 1 – P3\ Grade\ 2}$ < 0,001
					$p_{PIIIM\ Grade\ 2 – PIIIM\ Grade\ 1}$ = 0,001
Parameter	Category	anti-ANX V, IgM (IU/ml)			p
		Me	$Q_1 – Q_3$	n	
Endometrial cancer	Grade 1	1,80	1,30 – 3,70	41	< 0,001*
	Grade 2	4,20	3,47 – 4,93	32	$p_{P3\ Grade\ 2 – P3\ Grade\ 1}$ = 0,001
Cervical cancer	Grade 1	1,64	0,08 – 2,19	12	$p_{PIIIM\ Grade\ 2 – P3\ Grade\ 1}$ = 0,004
	Grade 2	4,70	4,17 – 4,83	11	$p_{PIIIM\ Grade\ 1 – P3\ Grade\ 2}$ < 0,001
					$p_{PIIIM\ Grade\ 2 – PIIIM\ Grade\ 1}$ < 0,001
Parameter	Category	anti-PS-PT, IgG (IU/ml)			p
		Me	$Q_1 – Q_3$	n	
Endometrial cancer	Grade 1	2,90	2,10 – 4,80	41	< 0,001*
	Grade 2	8,06	2,55 – 8,90	32	$p_{P3\ Grade\ 2 – P3\ Grade\ 1}$ = 0,002
Cervical cancer	Grade 1	3,10	1,90 – 4,12	12	$p_{PIIIM\ Grade\ 2 – P3\ Grade\ 1}$ = 0,026
	Grade 2	7,80	4,65 – 8,91	11	$p_{PIIIM\ Grade\ 1 – P3\ Grade\ 2}$ = 0,026
					$p_{PIIIM\ Grade\ 2 – PIIIM\ Grade\ 1}$ = 0,036
Parameter	Category	anti-PS-PT, IgM (IU/ml)			p
		Me	$Q_1 – Q_3$	n	
Endometrial cancer	Grade 1	2,88	2,14 – 5,69	41	0,402
	Grade 2	3,25	2,61 – 5,69	32	
Cervical cancer	Grade 1	4,76	2,47 – 6,22	12	
	Grade 2	6,38	3,93 – 8,09	11	

* – differences are statistically significant (p <0.05).

PO-07

RAPID AND EFFECTIVE ISOLATION OF HUMAN PLATELETS FROM WHOLE BLOOD: MAXIMIZING PURITY FOR EVALUATING PROTEOMICS METHODS IN CLINICAL STUDIES FOR CANCER PATIENTS

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Introduction: Platelets are tiny, disc-shaped anucleate cells found in the blood that play a pivotal role in hemostasis and have emerged as key players in various physiological and pathological processes. To understand platelets function in cancer progression and their potential as biomarkers in cancer research and clinical studies, it is vital to gain insights into their proteomic profile. Isolating high-purity platelets from whole blood is crucial for accurate proteomic analysis. In this study, we present a rapid and effective protocol for the isolation of human platelets, maximizing purity.

Aim: We evaluate this protocol using various proteomic methods, aiming to determine the most suitable proteomics pipeline for analyzing platelets in cancer patients.

Materials and Methods: Blood samples were collected in ACD anticoagulant solution tubes to prevent platelet activation. The samples were then treated according to protocol and stored in -20 C for subsequent analysis. The platelets, red blood cells and white blood cells were counted in an automated cell counter at the laboratory clinic at Haukeland Hospital, Bergen. To validate the efficiency of the isolation protocol, we conducted proteomics analysis using Data Dependent Acquisition (DDA), Data Independent Acquisition (DIA), and Tandem Mass Tag (TMT) labeling.

Results: The protocol with our optimized centrifugation time exhibited minimal contamination from other blood components. The scatter plot controls showed positive correlation with no activation of platelets. The results from DDA, DIA and TMT demonstrated a notable and novel identification of platelet-specific proteins, facilitating a more accurate and detailed characterization of the platelet proteome.

Conclusions: Our rapid and effective platelet isolation protocol enhances the purity of isolated platelets and demonstrates its applicability for robust downstream proteomic analyses. DIA demonstrated slightly better coverage and sensitivity in identifying platelet proteins and would be the preferable choice.

PO-08

FACTOR VIIIC IMPROVES PREDICTION OF VTE BY THE THROMBOGYN SCORE

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Introduction: Venous thromboembolism (VTE) is a significant cause of morbidity and mortality in patients with gynaecological

cancer. Guidelines recommend prophylaxis following risk assessment with validated risk assessment tools. The Thrombogyn score is a risk model for gynaecological cancer patients developed and validated by our group which identifies patients at low and high risk for VTE[1]. Previous work has shown that Factor VIIIc (FVIIIC) is a predictive biomarker for VTE in cancer patients. Recent data has suggested that combining risk models with biomarkers for VTE can improve prediction of VTE in cancer patients.

Aim: To evaluate the ability of FVIIIC when combined with the Thrombogyn score and the Khorana score to predict VTE in a population of gynaecological cancer patients.

Materials and Methods: Gynaecological cancer patients who donated blood samples to the TCD gynaecological cancer bioresource between 2017-2020 were included in the study. All patients gave full and informed consent. Patients were followed up for a minimum of one year. All blood samples were collected before surgery. The Thrombogyn and Khorana scores were calculated for each patient and objectively diagnosed VTE was recorded during follow-up. FVIIIC levels were measured by chromogenic substrate assay. 1 point for FVIIIC above a prespecified cutoff (199.8%) was added to Thrombogyn and Khorana scores to create the extended Thrombogyn+FVIIIC and Khorana+FVIIIC scores respectively.

Results: 302 cancer patients were included in the study (Ovarian n=116, Endometrial n=124, Cervical n=37, Vulval n=25). The majority of patients were treatment naive (88.4%) at sampling. 22 patients developed VTE during follow-up. FVIIIC levels were significantly increased in patients who developed VTE compared with patients who were thrombosis free during follow-up(P=0.008). 2.6% of patients in the Thrombogyn low risk group (Thrombogyn score <1) developed VTE compared with 10.1% in the intermediate/high risk group(P=0.038). 6.6% of patients classified by the Khorana score as low risk (Khorana score<2) developed VTE during follow-up compared with 9.7% in the intermediate/high risk group(P=0.39). Cox regression analysis showed that the FVIIIC+Thrombogyn high risk group had a13.4 fold (95%CI1.47-117.8) increased risk of VTE and a cumulative incidence of VTE of 18.1% after 6 months compared with 1.5% in the low-risk group and 7.5% in the intermediate risk group. There was no significant difference in VTE risk between the risk groups with the FVIIIC+Khorana score. Overall survival was lower in the Thrombogyn+FVIIIC high risk group compared with the low-risk group (P=0.008).

Conclusions: Addition of FVIIIC data to the Thrombogyn score increases the ability of the score to predict VTE. In contrast, the Khorana score did not predict VTE in these patients either with or without FVIIIC. FVIIIC is an easily available assay in hospital laboratories and may be useful as an aid to prediction of VTE in gynaecological cancer patients. Further studies are required to determine the utility of the Thrombogyn+FVIIIC score to guide prophylaxis in gynaecological cancer patients post-surgery.

Reference

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POSTER SESSION 2
THROMBOHEMORRHAGIC COMPLICATIONS

PO-09

ASSOCIATION BETWEEN ANTICOAGULATION-RELATED BLEEDING AND MORTALITY IN PATIENTS WITH HEMATOLOGICAL MALIGNANCIES AND CANCER-ASSOCIATED VENOUS THROMBOEMBOLISM

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Introduction: Patients with hematological malignancies are at an increased risk of venous thromboembolism (VTE) requiring anticoagulation (AC), but they are also at higher risk of bleeding, both of which can be associated with morbidity and mortality. The association between AC-related bleeding and death in these patients is unclear.

Aim: To evaluate the association between AC-related bleeding and mortality in patients with hematological malignancies and cancer-associated VTE on AC.

Materials and Methods: In a nationwide cohort of US Veterans (2012-2020), we identified patients with active hematological malignancies and cancer-associated VTE who initiated AC within 30 days of VTE diagnosis. Patients were excluded if they had any outpatient AC prescriptions within 6 months prior to VTE. Bleeding events were identified by previously validated algorithms using ICD codes. We evaluated the association between bleeding and death within 12 months of AC initiation by multivariate Cox regression models, accounting into multiple potential confounders. The occurrence of bleeding events was analyzed as a time-variant variable.

Results: The cohort included 1825 patients, 123 (6.7%) had bleeding events within 12 months of starting AC (Table 1), while 162 (8.9%) patients died. Patients with bleeding events were more likely to have anemia, history of bleeding, aspirin use, chemotherapy use, and frailty (Table 1). Multivariable analysis showed that any episode of AC-related bleeding was associated with an increased risk of death (HR 3.1, 95% CI 1.9-5.2). In addition, increasing age, increasing frailty, and liver disease are other independent risk factors for death. Body mass index (BMI) was protective (*i.e.* higher BMI was associated with lower mortality). When further stratified by bleeding site, intracranial bleeding was associated with the highest risk of death (HR 17.0, 95% CI 5.9-49.5), followed by gastrointestinal bleeding (HR 4.03, 95% CI 2.2-7.4). Bleeding at other sites including the genitourinary track was not significantly associated with death.

Conclusions: In this cohort of patients with hematological malignancies and VTE initiated on AC, bleeding was associated

with a significantly increased risk of death within 12 months, with even higher risks when bleeding occurred in intracranial or gastrointestinal sites. AC-related bleeding events carry a substantial risk of mortality and future investigations focusing on strategies to reduce these complications are essential.

Table 1.

Variables	Yes (n = 123)	No (n = 1702)	p value
Age, median (Standard Deviation)	68 (10.1)	68 (9.8)	0.08
Alcohol Abuse % (n)	6.5 (8)	4.7 (80)	0.37
Anemia (HGB <10g/dL OR HCT <30%) % (n)	64.2 (79)	52.3 (890)	0.01
Anticoagulant Type			0.24
DOAC % (n)	37.4 (46)	39.1 (666)	
LMWH % (n)	43.1 (53)	36.1 (615)	
Warfarin % (n)	19.5 (24)	24.7 (421)	
AntiPLT Therapy			
Aspirin % (n)	24.4 (30)	15.6 (265)	0.01
Clopidogrel OR Ticagrelor % (n)	7.3 (9)	4.8 (82)	0.22
Aspirin + Clopidogrel or Ticagrelor % (n)	3.3 (4)	1.6 (27)	0.17
Bleeding History % (n)	17.9 (22)	8.0 (136)	0.0002
Cancer Type			
Leukemia % (n)	53.7 (7)	5.5 (94)	0.94
Lymphoma % (n)	49.6 (61)	53.8 (915)	0.38
MDS % (n)	17.1 (21)	13.7 (233)	0.3
Myeloma % (n)	27.6 (34)	26.1 (44)	0.7
Chemotherapy Tx % (n)	61.8 976)	49.2 (837)	0.007
Chemotherapy subtype			
BTK Inhibitor % (n)	1.6 (2)	3.9 (66)	0.21
Hydroxyurea % (n)	4.1 (5)	2.6 (45)	0.35
VEGF Inhibitor % (n)	0.8 (1)	0.2 (4)	0.24
VEGF TKI % (n)	0.8 (1)	0.3 (5)	0.33
eGFR Category			0.16
<30 % (n)	45.5 (56)	36.8 (627)	
30 to <60 % (n)	20.3 (25)	24.0 (409)	
>=60 % (n)	34.2 (42)	39.1 (666)	
Fall History/Predisposition % (n)	39.8 (49)	37.1 (632)	0.55
Liver Disease % (n)	2.4 (3)	3.4 (57)	0.58
Race Category			0.76
Black % (n)	25.2 (31)	22.6 (385)	
Other % (n)	2.4 (3)	2.1 (35)	
White % (n)	72.4 (89)	75.3 (1282)	
Stroke History % (n)	6.5 (8)	5.6 (95)	0.67
Thrombocytopenia <50,000 % (n)	8.1 (10)	9.6 (164)	0.58
Uncontrolled HTN % (n)	49.6 (61)	41.7 (710)	0.09
Frailty			0.001
Non-Frail % (n)	8.9 (11)	13.1 (223)	
Pre-Frail % (n)	3.3 (15)	25.6 (436)	
Mild Frail % (n)	28.5 (35)	26.8 (456)	
Moderate Frail % (n)	27.6 (34)	19.7 (335)	
Severe Frail % (n)	22.8 (28)	14.8 (252)	

PO-10

ASSOCIATION BETWEEN ANTICOAGULATION-RELATED BLEEDING AND MORTALITY IN PERSONS WITH SOLID TUMORS

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Introduction: Balancing the high risk of venous thromboembolism (VTE) recurrence against anticoagulant (AC)-related bleeding in patients with cancer-associated VTE presents a significant clinical challenge. Limited data exist regarding the risk that AC-related bleeding confers on survival in patients with cancer and delineating this risk could inform duration of AC therapy.

Aim: We aimed to quantify the association between AC-related bleeding and death in solid tumor patients with newly diagnosed cancer-associated VTE starting AC therapy.

Materials and Methods: Using a nationwide cohort of US Veterans (2012-2020), we identified solid tumor patients with cancer-associated VTE who initiated AC within 30 days of VTE diagnosis. Patients with outpatient AC prescriptions within 6 months preceding VTE were excluded. Utilizing Cox regression, we assessed the association between AC-related bleeding & death within 12 months of AC therapy initiation. Time-varying adjustment for AC-related bleeding events accounted for immortal time bias.

Results: We identified 9,326 patients with newly diagnosed VTE and active solid tumors starting AC therapy, of which 746 (8.0%) developed bleeding within 12 months. Patients with bleeding were more likely to have a history of alcohol abuse, anemia, previous bleeding, stroke, kidney or liver disease, metastatic disease, thrombocytopenia, uncontrolled hypertension & frailty. Bleeding occurred more often in gastrointestinal (GI) (22.1%), genitourinary (17.4%), & brain tumors (2.4%). Most patients received AC therapy with LMWH (52.8%), with lower DOAC use in the bleeding group (19.7% *vs* 24.4%). There was a total of 2,003 deaths at 12 months post-AC initiation. In the multivariable Cox regression, AC-related bleeding was associated with a 2.86-fold (95% CI 2.44-3.35) increased risk of mortality at 12 months. When stratified by bleeding sites, intracranial hemorrhage had the highest association with mortality (hazard ratio [HR] 5.68) followed by GI (HR 2.73), & other bleeding sites (HR 1.89) (Figure 1).

Conclusions: AC-related bleeding in patients with solid tumors and VTE is associated with increased mortality, with ICH & GI bleeding conferring the highest risk. These findings highlight the importance of careful risk assessment & monitoring in cancer-associated VTE patients receiving AC therapy.

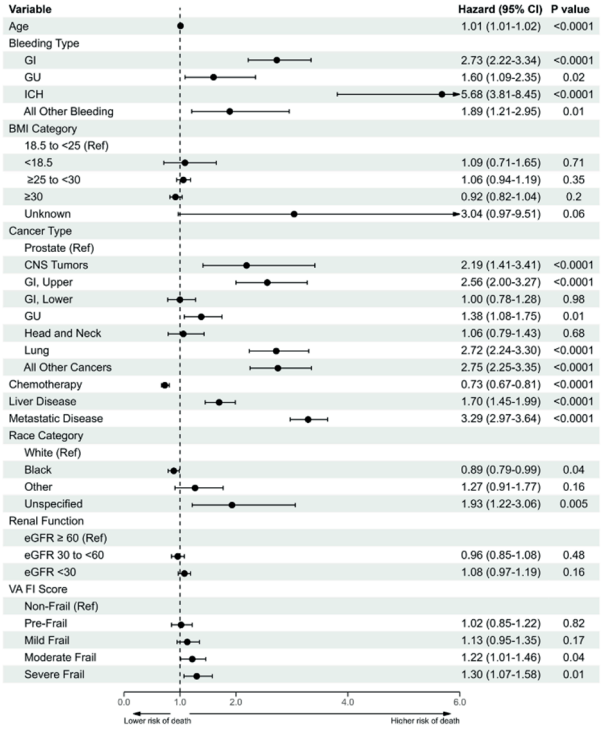

Figure 1.

PO-11

CANCER-ASSOCIATED VENOUS THROMBOEMBOLISM: A CASE OF A POSSIBLE RESISTANCE TO DOAC

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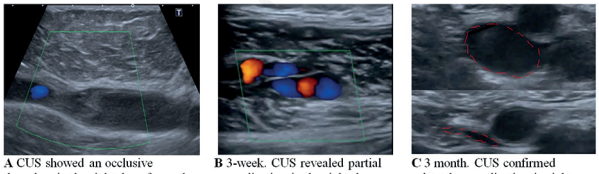
Introduction: Cancer-associated thrombosis is one of the major complications during cancer treatment, and the second most common cause of mortality in cancer patients. About 20% of patients develop a recurrence within 12 months despite optimal anticoagulation.
Aim: To discuss a real clinical practice case of a patient with VTE recurrence that was resistant to rivaroxaban.
Case presentation: A 56-year-old woman, with diffuse large B-cell lymphoma was referred to Cardio-Oncology Center. After 4 courses of R-CHOP chemotherapy, she complained of pain in the right hip that was ongoing for 1 week. She had a 1-point risk of VTE as per Khorana's score before the start of the cancer therapy. Lower-limb CUS showed an occlusive thrombus in the right femoral vein. Anticoagulation with rivaroxaban 15 mg BID was started. After a 3-week, the patient's condition continued to deteriorate: dyspnea, chest pain, and edema of the legs. ECG showed sinus tachycardia with HR 104 bpm. TTE demonstrated a slightly dilated right ventricular with mildly reduced systolic function and LVEF was 54%. Troponin I level was normal, while D-dimer elevated at 5800 ng/ml. Pneumonia signs and left pleural effusion were detected at the X-ray. PE was suspected. CTPA showed thrombi in the segmental and sub-segmental branches of the right and left pulmonary arteries. Lower-limbs CUS revealed partial recanalization in the right deep femoral vein. PE of intermediate-low risk and DVT were diagnosed. DOAC-resistant VTE was suspected, and enoxaparin 1 mg/kg BID was started. Non-compliance, interruption of therapy, inadequate dosing, cancer progression, and thrombophilia (protein C, protein S, antithrombin deficiency, and Factor V Leiden mutation) were excluded as the reasons for VTE recurrence. In 1-month FU no PE signs on CT, partial (70%) recanalization of DVT was confirmed by CUS, and the patient was switched to apixaban 5 mg BID. In 3 months CUS confirmed subtotal recanalization (Figure 1).
Conclusions: In this case, the patient had VTE recurrence and resistance to DOAC (rivaroxaban). After successful recanalization on LMWH, the patient was re-switched to another DOAC - apixaban. Future studies are needed to confirm our hypothesis.



A CUS showed an occlusive thrombus in the right deep femoral vein.
B 3-week. CUS revealed partial recanalization in the right deep femoral vein.
C 3 month. CUS confirmed subtotal recanalization in right deep femoral vein.

Figure 1.

PO-12

RISK OF RETHROMBOSIS AND MAJOR BLEEDING IN WOMEN WITH CANCER INCLUDED IN THE TESEO-SEOM REGISTRY

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Introduction: Patients with cancer have a higher risk of rethrombosis and bleeding during anticoagulantion than patients without cancer. Several factors including location of primary tumor, stage, oncological treatment, duration of anticoagulant therapy and sex may influence these risks.
Aim: We analyzed the risk of rethrombosis and major bleeding in women included in TESEO according to primary tumor location.
Materials and Methods: TESEO is an observational, non-interventional and prospective registry promoted by the Spanish Society of Medical Oncology (SEOM), with the collaboration of 52 Spanish 2 Portuguese centers, that recruit consecutive cases of cancer-associated thrombosis.
Results: A total of 2823 patients were recruited for the registry between July 2018 and December 2022, with 48% consisting of women (n=1351). Most common primary cancer in women were: breast cancer (BC) (n=282; 20.9%); colorectal (CRC) (223; 16.5%), lung (LC) (223; 16.5%) gynecological (GC) (200; 14.8%) and non-colorectal gastrointestinal cancer (non-CRC GI) (176; 13.0%). Pulmonary embolism was the most frequent thromboembolic event, regardless of the primary tumor location (BC 51.2%, CRC 57.4%, LC 65.9%, GC 56.5% and non-CRC GI 41.5%). Most of catheter-associated thromboses occurred in women with BC (59/156; 38%), followed by CRC (32/156; 21%). Median follow-up for all women was 7.4 months (IQR 2.1-16.7): 12.8 months (3.2-24.9) for BC patients, 9.5 (2.9-20.2) for CRC, 5.0 (1.4-11.8) for LC, 8.5 (2.6-19.5) for GC and 4.4 (1.3-10.8) non-CRC GI. The cumulative incidence of rethrombosis at 6 months, 12 months and end of follow-up was: 1.4%, 3.2% and 6.1% respectively for BC; 2.3%, 4.5% and 8.1% for CRC; 1.3%, 2.2% and 3.1% for LC; 3.0%, 4.0% and 6.1% for GC; 5.8%, 8.1% and 10.4% for non-CRC GI. The cumulative incidence of major bleeding at 6 months, 12 months and the end of follow up was: 2.1%, 3.2% and 3.9% respectively for BC; 1.4%, 1.4% and 1.8% for CRC; 0.9%, 1.3% and 1.3% for LC; 0%, 0% and 1.0% for GC; 0.6%, 0.6% and 1.2% for non-CRC GI. The percentage of patients with a duration of anticoagulant treatment greater than 12 months was: 32% (n=92) of BC, 28% (n=61) of CRC, 21% (n= 46) of LC, 28% of GC, 17% (n=30) of non-CRC GI.
Conclusions: In female cancer patients, the cumulative incidence of rethrombosis and bleeding varies depending on the location of the primary tumor. This information should be considered when deciding the duration of anticoagulant treatment.

PO-13

RISK OF CAR T-CELL THERAPY-RELATED THROMBOSIS AND BLEEDING: PRELIMINARY RESULTS OF THE MULTICENTER 'FOLLOW THAT CAR' REGISTRY

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Introduction: Chimeric antigen receptor T-cell (CAR-T) therapy has dramatically changed treatment and survival rates for patients with hematological malignancies. Reports on thrombosis and bleeding complications after CAR-T are emerging, but their relevance remains unclear because of large heterogeneity between studies.
Aim: To assess incidence of thrombosis and bleeding in a homogenous cohort of adults with lymphoma undergoing CAR-T therapy, and evaluate anticoagulation use in this population.
Materials and Methods: We used the 'Follow that CAR' registry, a retrospective multicenter cohort including adults with relapsed/refractory lymphoma receiving CAR-T therapy in the Netherlands between 2020-2022. Patients were monitored from start of lymphodepleting chemotherapy before CAR-T until 1 year after infusion. We recorded all venous and arterial thrombosis, major bleeding (according to ISTH definition) and death events during follow-up.
Results: 58 patients treated in Erasmus MC were included in this analysis (baseline characteristics; Table 1).

Table 1.

Patient characteristics	N = 58
Median age at baseline, years (IQR)	64 (55.8-69.0)
Sex, n (%)	
Male	39 (67.2%)
Female	19 (32.8%)
Diagnosis, n (%)	
Diffuse large B cell lymphoma (DLBCL)	33 (56.9%)
Transformed follicular lymphoma	14 (24.1%)
Mantle cell lymphoma	5 (8.6%)
T cell/histiocyte-rich large B cell lymphoma	3 (5.2%)
Other	3 (5.2%)
Previous lines of therapy, median (range)	2 (1-5)
History of autologous SCT, n (%)	18 (31.0%)
Bridging therapy, n (%)	39 (67.2%)
Lymphodepleting chemotherapy, n (%)	
Fludarabine/ Cyclophosphamide	58 (100.0%)
CAR-T cell product, n (%)	
Axicabtagene ciloleucel	41 (70.7%)
Lisocabtagene maraleucel	11 (19.0%)
Brexucabtagene autocel	5 (8.6%)
Zamtocabtagene autocel	1 (1.7%)
Median LDH levels at baseline, U/L (IQR)	246 (198.5-312.8)
Median platelet levels at baseline, x10^9/L (IQR)	188 (141.2-222.8)
History of thrombosis, n (%)	15 (25.9%)
Venous	12 (20.7%)
Arterial	3 (5.2%)
Cardiovascular comorbidity, n (%)	12 (20.7%)
Atrial fibrillation	8 (13.8%)
Antithrombotic therapy at baseline, n (%)	
No	27 (46.6%)
Yes	31 (53.4%)
LMWH	28 (48.3%)
Prophylactic dose	17 (29.3%)
Therapeutic dose	11 (19.0%)
Atrial fibrillation	3
Pulmonary embolism	3
Deep venous thromboembolism	3*
Cerebral vascular accident	1
Other VTE	1
DOAC	0 (0.0%)
Antiplatelet therapy	3 (5.2%)
Padua score at baseline, median (range)	4 (3-11)
Cytokine release syndrome (CRS) after infusion, n (%)	
Any	46 (79.3%)
Grade 1	16
Grade 2	24
Grade 3	6
Neurotoxicity (ICANS) after infusion, n (%)	
Any	28 (48.3%)
Grade 1	10
Grade 2	6
Grade 3	6
Grade 4	6

*Patient characteristics at baseline (upon admission before lymphodepleting chemotherapy) and during or after CAR-T infusion. CRS = cytokine release syndrome; DOAC = direct oral anticoagulant; ICANS = immune effector cell-associated neurotoxicity syndrome; IQR = interquartile range; LDH = lactate dehydrogenase; LMWH = low-molecular-weight heparin; SCT = stem cell transplantation; VTE = venous thromboembolism; * including 1 splanchnic vein thrombosis with concurrent atrial fibrillation.*

After median follow-up of 372 days, 5 patients experienced thrombosis (incidence rate 11.6% [95% CI, 3.76-27.02] per person-year); 3 had venous (all in upper extremity after central venous catheters) and 2 arterial thrombosis (1 myocardial infarction, 1 peripheral artery disease-related limb event). 4 patients experienced major bleeding (incidence rate 8.7% [95% CI, 2.38-22.37] per person-year). Median time to thrombosis and major bleeding was 55 and 22.5 days, respectively. 17 patients (29.3%) received thromboprophylaxis during CAR-T infusion, 12 (20.7%) therapeutic anticoagulation. One patient received therapeutic anticoagulation at time of major bleeding, all other thrombosis or bleeding occurred in patients without prophylactic or therapeutic anticoagulation. 17 (29.3%) patients had died after 1 year follow-up, mostly due to progression of underlying disease.
Conclusions: This homogeneous cohort confirms that patients are at considerable risk of thrombosis and bleeding in the first year after CAR-T therapy. These preliminary results will be completed with data from other Dutch centers, but justify further research on the relevance and prevention of these complications.

PO-14

ESTIMATING RISK OF BLEEDING AND THROMBOSIS FOR THROMBOCYTOPENIA IN CANCER-ASSOCIATED SPLANCHNIC VEIN THROMBOSIS: A TIME-VARYING ANALYSIS

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Introduction: Thrombosis and thrombocytopenia are common in patients with cancer, making decisions regarding anticoagulation challenging. We previously observed that thrombocytopenia at the time of diagnosis of cancer-associated splanchnic vein thrombosis (CA-SpVT) is not associated with risk of thrombosis recurrence and bleeding over the subsequent year. It is unclear, however, whether the risk of recurrence and bleeding varies with thrombocytopenia over time.
Aim: We analyzed risk of SpVT recurrence and bleeding with thrombocytopenia as a time-varying exposure in patients with CA-SpVT, adjusting for important covariates.
Materials and Methods: We performed a retrospective analysis of patients with CA-SpVT at our institution between 2010-2021. We excluded patients with myeloproliferative neoplasms and squamous and basal cell carcinoma and those without available platelet counts. We analyzed clinically-relevant bleeding (CRB; composite of major bleeding and clinically-relevant non-major bleeding) and SpVT progression or recurrence. Outcomes were analyzed using Cox proportional hazards models to calculate adjusted hazard ratios (aHR) and 95% confidence intervals (CI) and thrombocytopenia (<100x10^3/μL) and severe thrombocytopenia (<75x10^3/μL) as a time-varying exposure adjusting for age 65 or more years, sex, prior major bleed, comorbid chronic kidney disease, and use of antiplatelets or anticoagulants at baseline.

Results: We included 512 patients with CA- SpVT with median age 64.5 (IQR: 57.2-71.4); 62.3% male, and 57.8% with cirrhosis. Nearly 40% of patients (39.5%) had any thrombocytopenia, with 26.8% having severe thrombocytopenia. The most common cancer types were hepatobiliary (54.1%) and pancreatic (22.3%); 41.7% had metastatic disease. In adjusted time-varying analyses, periods of any thrombocytopenia were not associated with risk of CRB (aHR: 0.89, 95% CI: 0.55-1.45), but severe thrombocytopenia was associated with increased risk of CRB (aHR: 1.93, 95% CI: 1.19-3.15). Periods of any thrombocytopenia were associated with significantly increased risk of SpVT recurrence or progression (aHR: 1.96, 95% CI: 1.18-3.24). Severe thrombocytopenia was associated with a non-significantly increased risk (HR: 1.48, 95% CI: 0.81-2.70) (Table 1).
Conclusions: Thrombocytopenia, when analyzed as a time-varying exposure modulates risk of bleeding and SpVT recurrence/progression in patients with CA-SpVT. Clinicians should consider these competing risks when treating patients with anticoagulation.

Table 1. Risk of clinically-relevant bleeding (composite of major bleeding and clinically-relevant non-major bleeding) among those with varying degrees of thrombocytopenia at the most recent blood draw relative to those without thrombocytopenia in an adjusted time-varying analysis for patients with cancer associated splanchnic vein thrombosis.

Characteristic	Any thrombocytopenia (<100 x10^3/µL) HR (95% CI)	Severe thrombocytopenia (<75 x10^3/µL) HR (95% CI)	Most severe thrombocytopenia (<50 x10^3/µL) HR (95% CI)
Thrombocytopenia	0.85 (0.45-1.60)	2.06 (1.21-3.50)	1.79 (0.86-3.75)
Age <65 years vs. >65 years	1.31 (0.77-2.23)	1.04 (0.66-1.63)	1.06 (0.67-1.66)
Female vs. male sex	0.45 (0.24-0.86)	0.44 (0.25-0.76)	0.44 (0.25-0.77)
Cirrhosis vs. none	0.95 (0.53-1.68)	0.93 (0.58-1.50)	1.06 (0.68-1.67)
Abdominal surgery in past 3 months	1.43 (0.62-3.29)	1.32 (0.61-2.82)	1.26 (0.59-2.69)
Prior major bleed	1.43 (0.70-2.92)	1.24 (0.67-2.29)	1.29 (0.70-2.38)
Baseline creatinine >1.0	1.28 (0.79-2.08)	1.26 (0.78-2.04)	1.23 (0.76-2.00)
Recent systemic therapy	0.76 (0.35-1.63)	0.93 (0.52-1.68)	0.90 0.50-1.61)
Anticoagulation vs. none	1.85 (0.72-4.79)	1.01 (0.40-2.54)	1.04 (0.41-2.63)
Tumor vs. bland/mixed thrombus	0.97 (0.55-1.72)	0.98 (0.56-1.74)	0.99 (0.56-1.75)
Completely vs. partially-occlusive thrombus	1.41 (0.85-2.36)	1.51 (0.90-2.52)	1.49 (0.89-2.49)
Single vs. multiple vessels involved	1.38 (0.73-2.62)	1.29 (0.73-2.28)	1.27 (0.72-2.22)

PO-15

THROMBOTIC THROMBOCYTOPENIC PURPURA ASSOCIATED WITH NIVOLUMAB AND IPILIMUMAB IMMUNOTHERAPY IN METASTATIC MELANOMA: A CASE REPORT

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Introduction: Thrombotic Thrombocytopenic Purpura (TTP) is a rare auto-immune disorder characterized by thrombotic microangiopathy with hemolytic anemia, thrombocytopenia and organe failure. TTP is idiopathic or secondary to other conditions, for example systemic lupus or drugs. Anticancer immunotherapy is an emerging cause of TTP. We report the case of a patient presenting an acquired immune TTP 24 hours after the administration of a first cycle of Nivolumab and Ipilimumab in treatment of a metastatic melanoma.
Aim: The aim of this case report is to highlight the risk of TTP in patients receiving anticancer immunotherapy
Case Presentation: We report the case of a 51 year old female surgically treated for a melanoma in may 2021. Unfortunately, the patient experienced a relapse with brain metastasis in december 2022 treated by surgical excision and stereotaxic radiotherapy. An adjuvant immunotherapy with Nivolumab and Ipilimumab was started 03 march 2023. One day later, the patient was admitted in hospital for abdominal pain, vomiting and confusion. Blood test showed grade 4 thrombocytopenia, acute renal failure and elevated CRP. The first diagnosis was urinary sepsis and the patient was admitted in intensive care unit and treated by platelet transfusion and Piperacillin-Tazobactam. Despite this treatement, evolution was unfavourable and a TTP was suspected based on features of microangiopathye (hemolytic anemia, thrombocytopenia, organ failure, presence of schizocytes on blood semar) and confirmed by very low ADAMTS13 level (undosable activity inferior to 0.2% for a normal between 60.6 and 130.6%) and presence of anti-ADAMTS13 IgG antibodies. A diagnosis of acquired immune TTP was made and the patient received corticosteroids, Rituximab, Caplacizumab and plasma exchanges. Unfortunately, the TPP was refractory to this first line treatment and the patient died 2 days after a first dose of second line treament with Bortezomib.
Conclusions: TTP is a rare but fatal complication of anticancer immunotherapy and oncologists should be aware of this conditon. A prompt diagnosis can avoid platelet transfusion not recommended in TTP and permit the rapid initiation of a treatment by plasma exchange, corticosteroids, Rituximab and Caplacizumab. More data are needed to better understand and characterize TTP associated with anticancer immunotherapy (evolution, prognosis and safety of Caplacizumab).

PO-16

FURTHER PROOF THAT THE OTTAWA SCORE FAILS TO PREDICT RECURRENT VTE IN CANCER PATIENTS. META-ANALYSIS OF INDIVIDUAL PATIENT DATA

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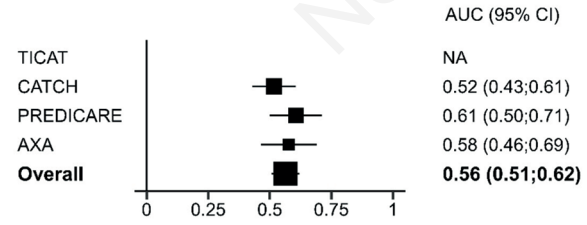
Introduction: The risk of venous thromboembolism (VTE) recurrence remains high in patients with cancer-associated thrombosis (CAT) despite therapeutic anticoagulation. The original Ottawa score, which was designed to stratify the risk of recurrent VTE in patients with CAT, has performed poorly. This may be due to the small sample sizes as well as the heterogeneity of statistical analyses and treatments used among the validation studies.
Aim: To overcome these sources of noise, we performed a meta-analysis using individual patient-level data to assess the performance of the Ottawa score in predicting VTE recurrence in CAT patients who were treated with the same therapy, tinzaparin, for at least 3 months.
Materials and Methods: Prospective studies of CAT patients treated with tinzaparin initially for at least 3 months and for which the clinical events of interest had been assessed by an independent central adjudication committee were eligible (PROSPERO: CRD42019119907). When eligible, the study sponsor was asked to provide individual patient data for each trial. The area under the receiver operating characteristic (ROC) curve, estimated risk and performance parameters were calculated with 95% confidence intervals (95% CI).
Results: Three prospective cohort studies and 1 randomised controlled trial were eligible (1413 patients) and the Ottawa score could be calculated for 1088 patients. For the patients considered at high risk of recurrence (Ottawa score ≥1, 59.4% of patients), the 6-month cumulative incidence of recurrent VTE was estimated to be 8.5% (95% CI, 6.6 to 10.8) compared with 5.0% (3.2 to 7.8) in the Ottawa low-risk group. The area under the ROC curve was 0.56 (0.51 to 0.62) with consistent results across studies (Figure 1). Using the recommended cut-off (score <or ≥1), the best parameter is the negative predictive value: the probability of a score <1 identifying patient without recurrent VTE is equal to 95.3% (93.3 to 97.4%). The other parameters were sensitivity 72.8% (62.6 to 83.0%), specificity 41.9% (37.8 to 45.9), and positive predictive value 8.6% (6.4 to 10.8).

Forest plot of area under the curve associated with the model including the Ottawa score variables in each study and in the overall meta-analysis population.



AUC (95% CI): area under the curve (95% confidence interval); NA: not available

Figure 1.

Conclusions: Despite the large number of patients and the standardisation of both treatment and dosage, the performance of the Ottawa score failed to accurately predict VTE recurrence in CAT patients treated with tinzaparin. In fact, the score mainly identifies low-risk patients.

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PO-17

USUAL-SITE VENOUS THROMBOEMBOLISM IN PATIENTS WITH CANCER-ASSOCIATED SPLANCHNIC VEIN THROMBOSIS

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Introduction: Venous thromboembolism in patients with cancer usually occurs in the deep veins (DVT)and pulmonary embolism (PE), but it may occur in atypical sites, such as the splanchnic veins (SpVT). It is unclear whether patients with cancer-associated (CA-SpVT) are at increased risk of usual-site VTE (Us-VTE), what the risk factors for US-VTE are, and how anticoagulation (AC) modulates this risk.
Aim: We analyzed US-VTE incidence and associated factors in patients diagnosed with CA-SpVT.
Materials and Methods: We performed a retrospective study of patients with CA-SpVT at our institution between 2010 and 2021. Outcomes included US-VTE (upper/lower-extremity DVT, PE) up to 1 year following initial SpVT. Medical records were manually reviewed to determine baseline clinical data, treatments, and outcomes. We performed log-binomial regression to identify independent risk factors for US-VTE including age (continuous), sex, cirrhosis, creatinine (continuous), recent systemic chemotherapy, tumor type (tumor *vs* mixed/bland), thrombocytopenia (platelet count <100x10^3/uL), and use of antiplatelets or anticoagulants.
Results: We identified 581 patients with CA-SpVT, with a mean age of 64 years, 36.4% male and 82.5% gastrointestinal malignancy; 39.2% were treated with AC. A total of 27 (4.6%) patients had a history of US-VTE prior to the diagnosis of SpVT and 23 (4.0%) presented with US-VTE concurrently with SpVT. The cumulative incidence of US-VTE at 1 year after diagnosis of SpVT in patients without prior or concomitant VTE was 5.4% (95% CI: 3.6-7.7) with death as a competing risk. Of these 27 US-VTE events in the follow up period, 14 were limb DVT and 13 were PE. Thrombocytopenia (<100x10^3/uL) occurred in 39.5% of patients and was not associated with US-VTE (P=0.70). There was no significant difference in US-VTE rates in patients that were treated with AC compared to those not receiving AC (6.3% *vs* 5.7%; P=0.70). Progression of SpVT was not associated with US-VTE (7.5% *vs* 5.4%, P=0.44) Multivariate regression did not identify any independent predictors of US-VTE (Table 1).

Conclusions: We observed US-VTE in patients with CA-SpVT concurrently and subsequent to SpVT, but was not associated with SpVT recurrence, thrombocytopenia or AC. More research is required to understand the interplay of SpVT and US-VTE in patients with cancer.

Table 1. Risk factors for usual-site venous thromboembolism in patients with cancer-associated splanchnic vein thrombosis.

	Unadjusted RR (95% CI)	Adjusted* RR (95% CI)
Age at time of SpVT >65 years	0.92 (0.47-1.79)	1.01 (0.93-1.09)
Male gender	1.15 (0.57-2.32)	0.98 (0.89-1.08)
Cirrhosis	0.13 (0.04-0.41)	1.06 (0.84-1.35)
Baseline creatinine >1.0	0.22 (0.05-0.92)	1.02 (0.88-1.19)
Recent systemic chemotherapy	1.08 (0.48-2.42)	1.00 (0.90-1.12)
Use of antiplatelets at baseline	1.55 (0.74-3.25)	0.97 (0.85-1.10)
Tumor vs. bland/mixed thrombus	1.50 (0.71-3.15)	0.99 (0.89-1.10)
Anticoagulation vs. no anticoagulation	1.11 (0.28-4.42)	0.99 (0.83-1.18)
Thrombocytopenia		
None	Ref	Ref
Platelets <100x10³/uL	0.32 (0.12 - 0.82)	1.0 0.86-1.17)

RR, risk ratio; CI, Confidence Interval

PO-18

DEEP VEIN THROMBOSIS AS AN INITIAL SYMPTOM OF PROSTATAE CANCER: A CASE REPORT

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Introduction: Prostate cancer does not belong to the high-risk entities for VTE as gastric and pancreas cancer. The initial incidence rate ratio (IRR) for prostate cancer is 3.25 (2.56 - 4.13). However, there have been reported cases of cancer that suffered VTE as an initial symptom of malignancy. The incidence of VTE has been shown to be the highest within the first few months after diagnosis of cancer.
Aim: In this abstract, we report the diagnosis of deep vein thrombosis that discovered prostate cancer in an 77-year-old man, presented for the first time with acute urinary retention and left leg swelling.
Case presentation: On clinical examination,there was a painful, hot and very swelling of the entire left leg with a positive sign of Homans. The diagnosis was confirmed by laboratory data (PT, aPTT, and D-Dimer test) and Doppler ultrasound.Because of the urinary retention he was sent to a urologist where, after the tests, he was diagnosed with adenocarcinoma of the prostate with metastasis in an inguinal lymph node. The coagulation tests shows very high results of D-Dimers (9500ng/ml), a sign of secondary activated fibrinolysis,other coagulation tests were normal.Dopller ultrasound showed the presence of an extensive acute deep venous thrombosis of the left sural vein extended to the popliteal and to the homolateral deep femora veinl. The patient was treated with effective anticoagulation therapy with LMWH and analgesics 7 days, and then he continue the treatment with 15 mg of Rivaroxaban twice daily for 21 days, followed by 20 mg of Rivaroxaban once daily. During the treatment laboratory values,clotting times, D-Dimer levels, and the Doppler ultrasound were repeated and showed signs of improvement. He was referred to urology for the surgical management of the prostate.
Conclusions: This case highlights the importance of screening for a cause of the thromboembolic event in patients. The existence of active cancer in a patient is a known risk factor for VTE and, conversely, the discovery of a first episode of deep vein thrombosis (DVT) may be the first clinical manifestation of cancer. Routine pelvic examination and an examination by a urologist especially in older patients with an unknown cause of urinary retention and deep vein thrombosis of the lower limbs can help in the early diagnosis of prostate cancer.

POSTER SESSION 3
EPIDEMIOLOGY

PO-19

PROGNOSTIC VALUE OF HULL SCORE 0 *VERSUS* SUBSEGMENTAL UNSUSPECTED PULMONARY EMBOLISM IN CANCER PATIENTS: A COMPARATIVE ANALYSIS

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Introduction: The significance of subsegmental pulmonary embolism (SSPE) and its impact on cancer patient outcomes is still under debate, with conflicting findings regarding its association with mortality risk or the existence of symptoms. The HULL score CPR (HS-CPR) stratifies ambulatory cancer patients with UPE and can identify truly asymptomatic, clinically unimpaired UPE patients with low-risk HULL Score 0 (HS 0) for proximate mortality (1-3).
Aim: This study aims to assess the anatomical distribution of PE among HULL Score 0 (HS 0) patients and to evaluate the predictive capacity of SSPE *vs* HS 0 for mortality outcomes.
Materials and Methods: 521 consecutive patients managed under the UPE-acute oncology service in HUTH NHS trust from February 2010 to April 2020 were included. These patients were evaluated and managed using the UPE pathway and prospectively categorised by the (HS-CPR) into low (HS 0), intermediate (HS 1-2), and high (HS 3-4) risk levels. 100% received anticoagulant treatment as per guidelines. CT reports were reviewed retrospectively to verify PE distribution. Survival outcomes were analysed using Kaplan Meier (univariate) methods and compared using the log-rank test.
Results: Among the cohort, 12.9% (67 patients) had only SSPE distribution, and 25.7% (134 patients) were classified as low-risk, HS 0. Over half of the SSPE patients (55.2%) fell into the intermediate or high-risk HS-CPR categories. The anatomical distribution of PE in the HS-0 patients was central (11.2%), lobar (26.1%), segmental (41%) and subsegmental (21.6%) PE. The median follow-up for the group was 12.1 months (ranging from 0.13 to 126.7 months). The median overall survival (OS) for UPE patients with SSPE was 14.7 months, with a 95% confidence interval (CI) of 10.8 to 18.6 months, compared to 26.3 months, with a 95% CI of 16.2 to 36.4 months, for those categorised as HS 0, p <.001 (Figure 1).
Conclusions: Hull Score 0, or truly asymptomatic UPE, does not correspond with the subsegmental distribution of PE. Indeed, several patients had central emboli (including one saddle embolus). Our study reveals that low-risk UPE patients, as identified by the HULL Score 0, demonstrate a significantly better survival

outcome than those with SSPE. Factors relating to the underlying malignancy likely have a greater impact on mortality.

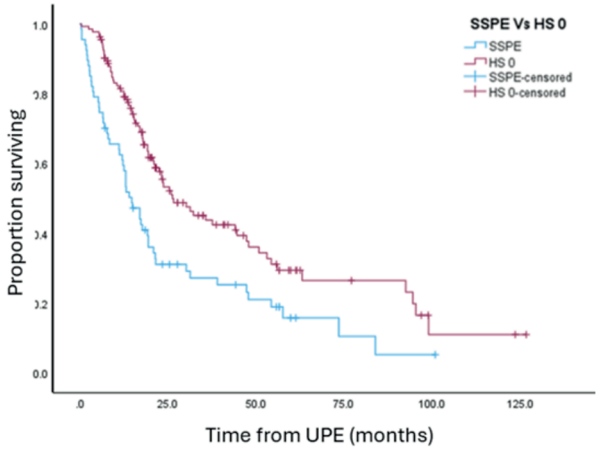

Figure 1. Survival (Kaplan Meier) for the HULL score 0 *vs* SSPE ($p<0.001$).

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PO-20

VENOUS THROMBOEMBOLISM AND RISK OF CANCER IN PATIENTS WITH STROKE: A POPULATION-BASED COHORT STUDY

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Introduction: Stroke is associated with an increased risk of venous thromboembolism (VTE), particularly in the initial months after stroke. It is a long-standing observation that VTE may be a marker of occult cancer. However, it is unclear whether VTE in patients with stroke is a marker of cancer.
Aim: To examine the risk of cancer after VTE in patients with stroke, compared to the expected risk of cancer, based on national cancer incidence rates.
Materials and Methods: We used Danish health registries to identify all patients with a first-time hospital diagnosis of VTE and a stroke prior to this date from 1996 to 2021. Follow-up started from the date of VTE diagnosis until either a cancer diagnosis, death, emigration, or end of study period, whichever came first. We calculated the absolute risk of cancer and standardized incidence ratios (SIRs) of cancer based on national cancer incidence for the first year after VTE and 1-15 years follow-up. Analyses were stratified based on stroke subtype and time from stroke to VTE.
Results: During the study period, we identified 9535 patients with stroke and a subsequent VTE, and within this group, 1085 cancer cases were observed. The median age at the time of the VTE was 76 years, with equal sex distribution. During the first year of follow-up, the absolute risk of cancer was 4.7%, with a SIR of 3.20 (95% confidence interval (CI): 2.91-3.52). Looking at the 1-15 years of follow-up, the overall SIR decreased to 1.15 (95% CI: 1.07-1.25). Within the first year, SIR according to stroke subtype were similar, with slightly higher SIR for subarachnoid hemorrhage [SIR 3.89 (95% CI: 2.51-5.74)], followed by ischemic stroke [SIR 3.19 (95% CI: 2.88-3.52)], and intracerebral hemorrhage [SIR 3.00 (95% CI: 2.08-4.20)]. For all three stroke subtypes, SIR decreased markedly for 1-15 years follow-up, but an increased risk remained among those with subarachnoid hemorrhage [SIR 1.32 (0.97-1.77)] and ischemic stroke [SIR 1.16 (1.07-1.26)]. The risk pattern varied minimally with the time from stroke to VTE when examining the first year for follow-up. However, for 1-15 years follow-up, increased risk notably persisted for VTEs more than twelve months after stroke with a SIR of 1.24 (95% CI: 1.13-1.35).
Conclusions: Venous thromboembolism may be a marker of undiagnosed cancer in patients with stroke.

PO-21

VENOUS THROMBOEMBOLISM AND RISK OF CANCER IN PATIENTS WITH A HISTORY OF MIGRAINE: A POPULATION-BASED COHORT STUDY

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Introduction: Migraine is associated with an elevated risk of venous thromboembolism (VTE). It is well established that VTE may be a marker of occult cancer, but it is unclear whether VTE in patients with migraine is a marker of cancer.
Aim: To examine cancer risk following VTE in patients with a history of migraine, compared to the expected cancer risk, based on national cancer incidence rates.
Materials and Methods: We used Danish health registries to identify patients with a first-time hospital diagnosis of VTE and a history of migraine from 1996 to 2021. Follow-up started from the date of VTE diagnosis until either a cancer diagnosis, death, emigration, or end of the study period, whichever came first. We calculated the absolute cancer risk and standardized incidence ratios (SIRs) based on national cancer incidence divided into the first year after VTE and 1-15 years follow-up to measure the relative cancer risk after VTE.
Results: We identified 9190 patients with VTE and a history of migraine and observed 1010 cancer cases. The median age at the time of the VTE diagnosis was 56 years, and 78% of the patients were females. During the first year after VTE diagnosis, absolute cancer risk was 3.6%, with a SIR of 4.08 (95% confidence interval (CI): 3.65-4.55). During 1-15 years of follow-up, the SIR of cancer remained elevated but decreased to 1.16 (95% CI: 1.07-1.25). During the first year, SIRs were 4.36 (95% CI: 3.50-5.36) for males and 3.99 (95% CI: 3.50-4.53) for females. For the 1-15 years follow-up, SIRs were 1.17 (95% CI: 1.00-1.36) for males

and 1.16 (95% CI: 1.06-1.26) for females. All cancer groups showed an increased SIR during the first year of follow-up. Further, a persistently increased risk during the 1-15 years follow-up was observed for cancers of neurological origin [1.46 (95% CI: 1.04-1.99)], hematologic cancers [1.41 (95% CI: 1.08-1.81)], hormone-related cancers [1.22 (95% CI: 1.07-1.38)], and smoking-related cancers 1.19 (95% CI: 1.02-1.38).
Conclusions: Venous thromboembolism is a marker of occult cancer in patients with a history of migraine.

PO-22

SENSITIVITY AND POSITIVE PREDICTIVE VALUE OF CANCER-ASSOCIATED VENOUS THROMBOEMBOLISM DIAGNOSES IN THE DANISH NATIONAL PATIENT REGISTER

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Introduction: Hospital discharge diagnoses from administrative health registries are commonly used in epidemiological studies of cancer-associated venous thromboembolism. Yet, the validity of International Classification of Diseases (ICD) codes for identifying such events remains uncertain.
Aim: To explore the positive predictive value (PPV) and sensitivity of using ICD-10 discharge codes to identify cancer-associated venous thromboembolism within the Danish National Patient Register.
Materials and Methods: The PPV was estimated from a random sample of 370 ICD codes registered from 2017-2021 in the North Denmark Region. The PPV was calculated as the number of cases confirmed after manual search of the electronic health record divided by the total sample count. Sensitivity was determined by identifying of 100 patients with documented cancer-associated venous thromboembolism identified via use of therapeutic doses of low-molecular-weight heparin, who were sampled without knowledge of their ICD discharge diagnosis status. Sensitivity was calculated by dividing the number of patients with a concomitantly registered ICD code with the total number of patients with documented venous thromboembolism.
Results: The overall PPV of an ICD-10 diagnosis of cancer-associated venous thromboembolism was 75.9% (95% confidence interval: 71.3-80.0). Subgroup analysis (see Table 1) demonstrated particularly low PPVs for recurrent venous thromboembolism (44.2%), secondary position diagnosis (55.7%), outpatient diagnoses (65.3%), and for diagnoses given at surgical (66.7%), emergency wards (48.4%), or by palliative team or at hospices (0%). Overall sensitivity was 68.0% (95 CI: 58.3-76.3), meaning 32% of patients diagnosed in a hospital setting with cancer-associated venous thromboembolism were discharged without any registered ICD-code for venous thromboembolism.
Conclusions: The PPV of an ICD-10 discharge diagnosis of cancer-associated venous thromboembolism in the Danish Patient Register was 75.9%, but with notable variation across subgroups. The sensitivity of using ICD-codes to identify events was limited, as one in three patients with venous thromboembolism were discharged without any relevant ICD-code. Although the overall PPV may be adequate for research purposes, cautious interpretation of incidence of cancer-associated venous thromboembolism based on administrative register-based data is warranted.

Table 1.

Positive predictive values of ICD-10 discharge diagnoses for cancer-associated venous thromboembolism in the Danish National Patient Register in prespecified subgroups

	ICD-10 diagnoses, *n*	Positive predictive value (95% confidence interval)*
Venous thromboembolism subtype		
Deep vein thrombosis	147	71.4 (63.7-78.1)
Pulmonary embolism	223	78.9 (73.1-83.8)
Incident or recurrent event		
Incident	275	86.9 (82.4-90.4)
Recurrent	95	44.2 (34.6-54.2)
Underlying malignancy		
Haematological	172	80.8 (74.3-86.0)
Oncological	198	71.7 (65.1-77.5)
Diagnosis position		
Primary	239	87.0 (82.2-90.7)
Secondary	131	55.7 (47.2-63.9)
Inpatient or outpatient		
Inpatient	246	81.3 (76.0-85.7)
Outpatient	124	65.3 (56.6-73.1)
Registering department		
Oncology	52	88.5 (77.0-94.6)
Haematology	80	95.0 (87.8-98.0)
Other internal medicine	157	85.4 (79.0-90.0)
Surgical	15	66.7 (41.7-84.8)
Emergency ward	31	48.4 (32.0-65.2)
Hospice/palliative department	35	0.0 (N/A)

* Confidence intervals calculated using the Wilson score method.

PO-23

VENOUS THROMBOEMBOLISM IN CANCER PATIENTS AND SELF-RATED HEALTH: A CROSS-SECTIONAL STUDY

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Introduction: Cancer is a strong risk factor for venous thromboembolism (VTE), and cancer patients have a nine-fold higher VTE risk than the general population, as well as significantly higher rates of bleeding and recurrence during anticoagulant treatment than VTE patients without cancer. The occurrence of VTE is associated with interruption of cancer treatment, and increased morbidity and high mortality. Cancer patients with VTE have shorter survival than cancer patients without VTE. However, little is known about self-rated health (SRH) and quality of life in cancer patients with VTE.
Aim: Our objective was to assess the prevalence of poor SRH in cancer patients with VTE compared to two groups: patients with VTE only and patients with cancer only.
Materials and Methods: We conducted a cross-sectional study using data from the Better Health in Late Life cohort. Danish residents aged 50-65 years in the period 2021-2022 completed an online questionnaire covering lifestyle, stress, physical health, and mental health. The 12-Item Short Form Health Survey was used to measure SRH based on the question: "How do you find your

overall health?". Information regarding VTE, cancer, and comorbidities were retrieved from the Danish National Patient Registry. We estimated prevalence proportion ratios (PR) and 95% confidence intervals, adjusting for age, sex, and educational level, to compare poor SRH in patients with cancer and VTE to the comparison groups. Furthermore, we investigated this association across various levels of stress and comorbidity.

Results: We identified 231 persons with both cancer and VTE, 2236 persons with VTE only, and 9729 persons with cancer only. Overall, 46.3% of cancer patients with VTE reported poor SRH. The proportion of poor SRH in cancer patients and VTE patients was 30.9% and 24.3%, respectively. The difference in poor SRH was more pronounced in patients with low perceived stress, PR 2.14 (95% CI: 1.55-2.96) and PR 2.70 (95% CI: 2.01-3.64) compared to patients with VTE only and cancer only, respectively. The difference was smaller in participants with a high level of comorbidity, PR 1.11 (95% CI: 0.83-1.50) and PR 1.26 (95% CI: 0.95-1.68) compared to patients with VTE only and cancer only, respectively.

Conclusions: Cancer patients with VTE had a higher prevalence of poor SRH compared to patients with only cancer or VTE. However, the difference varied across levels of comorbidity and stress.

PO-24

POLY (ADP-RIBOSE) POLYMERASE INHIBITORS (PARPI) – ASSOCIATED THROMBOSIS IN PATIENTS WITH OVARIAN CANCER: A STUDY OF THE SPANISH SOCIETY OF MEDICAL ONCOLOGY (SEOM) THROMBOSIS AND CANCER GROUP

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Introduction: Although clinical trials with PARP inhibitors (PARPi) have shown a low incidence of venous and arterial thromboembolic disease (VTE/AT), we lack information on patients in routine clinical practice.

Aim: The objective was to evaluate the incidence and characterize VTE/AT in ovarian cancer patients treated with PARPi.

Materials and Methods: Retrospective, multicenter study promoted by the Spanish Society of Medical Oncology (SEOM). Individuals with ovarian cancer who initiated PARPi between 2015 and 2022 were recruited. Minimum follow-up was 6 months (except in cases of demise). We performed a descriptive analysis, analyzed the impact of VTE/AT on survival and determined predictor variables using multivariate logistic regression.

Results: 329 patients were recruited, whose baseline characteristics are shown in Table1.

Table 1. Baseline characteristics of the patients.

	Total (n = 329)	VTE/AT (n = 16)	No VTE/AT (n = 313)
Age – median (IQR)	62 (55-71)	60 (57-68)	62 (55-71)
ECOG PS – n (%)			
0	154 (46.8%)	6 (37.5%)	148 (47.3%)
1	147 (44.7%)	9 (56.3%)	138 (44.1%)
2	24 (7.3%)	1 (6.3%)	23 (7.3%)
3	4 (1.2%)	0 (0%)	4 (1.3%)
Stage – n (%)			
III	161 (49.2%)	5 (31.3%)	156 (50.2%)
IV	166 (50.8%)	11 (68.8%)	155 (49.8%)
Khorana Score – n (%)			
1	251 (76.3%)	10 (62.5%)	241 (77%)
2	71 (21.6%)	5 (31.3%)	66 (21.1%)
3	7 (2.1%)	1 (6.3%)	6 (1.9%)
Oncological situation at the start of PARPi - n (%)			
Complete response	92 (28.2%)	5 (31.3%)	87 (28.1%)
Partial response	149 (45.7%)	7 (43.8%)	142 (45.8%)
Stable disease	56 (17.2%)	4 (25%)	52 (16.8%)
Tumor progression	29 (8.9%)	0 (0%)	29 (9.4%)
Homologous Recombination Deficiency – n (%)			
No	151 (45.9%)	4 (25%)	147 (47%)
Yes	168 (51.1%)	12 (75%)	156 (49.8%)
Not determined/Unknown	10 (3%)	0 (0%)	10 (3.2%)
BRCA mutation – n (%)			
No	175 (53.2%)	6 (37.5%)	169 (54%)
Yes, BRCA1	74 (22.5%)	1 (6.3%)	73 (23.3%)
Yes, BRCA2	69 (21%)	9 (56.3%)	60 (19.2%)
Yes, BRCA 1 and 2	1 (0.3%)	0 (0%)	1 (0.3%)
Not determined/Unknown	10 (3%)	0 (0%)	10 (3.2%)
BRCA mutation type – n (%)			
Somatic	35 (24.3%)	1 (10%)	34 (25.4%)
Germinal	100 (69.4%)	8 (80%)	92 (68.7%)
Unknown	9 (6.3%)	1 (10%)	8 (6%)
Treatment modality – n (%)			
Maintenance after 1st line of mts disease	149 (45.4%)	8 (53.3%)	141 (45%)
Maintenance after 2nd line of mts disease	132 (40.2%)	5 (33.3%)	127 (40.6%)
Maintenance after 3rd or more lines of mts disease	41 (12.5%)	2 (13.3%)	39 (12.5%)
2nd line of mts disease	1 (0.3%)	0 (0%)	1 (0.3%)
3rd or later lines of mts disease	5 (1.5%)	0 (0%)	5 (1.6%)
PARPi type – n (%)			
Olaparib	160 (48.6%)	10 (62.5%)	150 (47.9%)
Niraparib	151 (45.9%)	6 (37.5%)	145 (46.3%)
Rucaparib	18 (5.5%)	0 (0%)	18 (5.8%)
Concomitant treatment with PARPi – n (%)			
No	315 (95.7%)	14 (87.5%)	301 (96.2%)
Bevacizumab	11 (3.3%)	0 (0%)	11 (3.5%)
Other	3 (0.9%)	2 (12.6%)	1 (0.3%)

ECOG PS: Eastern Cooperative Oncology Group Performance Status. IQR: interquartile range. Mts: metastatic. PARPi: poly ADP-ribose polymerase inhibitor. VTE/AT: venous and arterial thromboembolic disease.

After an observation period equivalent to 489 person-years, 16 thrombotic events were identified (4.9%; 3.3 events per 100 person-years). The form of presentation was: 31.3% deep vein thrombosis (DVT), 25% pulmonary embolism (PE), 18.8% visceral thrombosis, 12.5% catheter-associated thrombosis, 6.3% other forms of venous thrombosis, and 6.3% mixed event (venous and arterial). Concurrent with the diagnosis of thrombosis, 25% (n=4) were in progression. The median time between start of PARPi and VTE/AT was 4 months (interquartile range: 2–14.3 months). 62.5% of events were incidentally diagnosed and 75% in the outpatient setting. No patient experienced recurrence or bleeding as a complication. A higher proportion of thrombotic events was observed with olaparib (6.3%) compared to niraparib (4%) and rucaparib (0%), but the differences were not statistically significant (p=0.398). The most frequent presentation of VTE/AT associated with olaparib was DVT (40%), while in patients who received niraparib it was PE (50%), without a significant association being observed (p=0.2). Median overall survival was 33 months (95% CI 28.8-37.2) in the subgroup without VTE/AT, while in patients with VTE/AT it was 44 months (95% CI 22.5-65.5) (log-rank test=0.12). Multivariate

analysis revealed that combination treatment (PARPi+another agent) was associated with a lower risk of VTE/AT (OR 0.127, 95% CI 0.017-0.963) compared to PARPi alone.
Conclusions: The risk of VTE/AT associated with PARPi in patients with ovarian cancer is low, consistent with that has been described in clinical trials. VTE/AT associated with these drugs did not impact survival.

PO-25

IMPACT OF THROMBOEMBOLIC EVENTS ACROSS THE SPAN OF BREAST CANCER SURVIVORSHIP: DATA FROM A LARGE OBSERVATIONAL STUDY ON LONG-TERM BREAST CANCER SURVIVORS

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Introduction: Breast cancer (BC) patients comprise the main group of cancer survivors. There are several factors influencing the risk of venous thromboembolic events (VTE) in these patients, but we are unaware of previous studies that have evaluated the incidence of VTE in unselected series of long-term BC survivors.
Aim: Evaluation of the cumulated incidence and features of VTE in a large cohort of long-term BC survivors.
Materials and Methods: Ambispective observational study (ILL-CAR 2018-01). Approved by the Regional Ethics Board. All patients signed the informed consent for the study. Entry criteria included BC patients with a follow-up of at least 10 years from the time of their first therapy. Detailed clinical data were retrieved from a comprehensive electronic medical record, comprising all the information on hospital and primary care in our regional health system.
Results: 2,847 patients (p.) were included and are available for full analysis. Median time of follow-up from first therapy of BC: 18.7 years (10-55.3). 183 VTE were diagnosed in 152/2,847 p (5.3%). Median age at diagnosis of VTE: 71.7 years (37.5-97.5). Median interval from first therapy of BC to the diagnosis of VTE: 15.2 years (0.0-55.6). VTE were 96 deep-vein thromboses (DVT), 70 pulmonary embolisms (PE) and 17 PE with concurrent DVT. DVT (alone or with PE) were diagnosed in the lower limb (71), upper limb (23), splanchnic (8), cranial sinuses (2), other (9). VTE occurred with active metastatic BC (30 VTE), during adjuvant drug, surgical or radiation therapy of nonactive BC or during follow-up after adjuvant therapy (116 VTE), or associated to late second non BC neoplasms (37 VTE; 33 solid, 4 hematologic). Predisposing factors for VTE were active cancer and/or cancer therapy (117 VTE), medical conditions (40 VTE, including COVID-19 in 7), surgical procedures and/or traumatic lesions (13 VTE). No predisposing factors were found in 13 p. VTE evolved to chronic thromboembolism in 14 p.
Conclusions: The cumulated incidence of VTE remained low for BC survivors in this cohort with real world data, even after a long follow-up. This may be related to the generalized use of prophylaxis in medical and surgical settings and to advances in the clinical care of the patients. Secondary neoplasms are related to a substantial proportion of VTE in long-term survivors, and this may be a confounding factor for observational studies.

PO-26

VENOUS THROMBOEMBOLISM AND RISK OF CANCER IN PATIENTS WITH ATOPIC DERMATITIS

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Introduction: It is well established that venous thromboembolism (VTE) may be a marker of occult cancer in patients with unprovoked VTE. There is also increasing evidence that atopic dermatitis is a risk factor of VTE, but it is unclear whether VTE in atopic dermatitis patients is a marker of occult cancer.
Aim: To examine the risk of cancer after VTE in patients with a hospital diagnosis of atopic dermatitis in a nationwide cohort in Denmark
Materials and Methods: For 1980-2021 we used Danish health registries to identify all patients with and in- or outpatient clinic diagnosis of VTE, who were also recorded as having a previous or concurrent diagnosis of atopic dermatitis. Patients were followed from the date of VTE to first incident cancer, death, emigration, or December 31, 2021, whichever came first. To estimate possible increases in cancer risks we calculated age-, sex- and calendar period standardized incidence ratios (SIRs) using Danish national cancer rates to compare the observed cancer incidence among patients with atopic dermatitis and VTE to the one expected.
Results: In a cohort of 64,001 patients with a hospital-based diagnoses of atopic dermatitis, 435 patients (57% female) developed VTE. At the time of thromboembolic admission or during first year of follow-up, the cumulative incidence of all cancer types was 1.16% (95% confidence interval (CI): 0.44-2.57). The median age at VTE diagnosis was 46 years (interquartile range (IQR): 32-61) and the median follow-up time was 5.2 years (IQR: 2.0-11.2). A total of 27 cancers were observed during the study period. During the first year of follow-up five patients were diagnosed with cancer yielding a SIR of 1.8 (95% CI: 0.6-4.3). The overall SIR during the subsequent years of follow-up was 1.1 (95% CI: 0.7-1.7).
Conclusions: At the time of VTE or in the first year afterwards, we found an increased cancer risk in atopic dermatitis patients. In subsequent years a 10% increase in risk remained. These findings indicate that occult cancers promote thrombosis in atopic dermatitis patients. However, estimates were imprecise and diagnostic bias cannot be excluded.

PO-27

EPIDEMIOLOGIC STUDY OF PATIENTS WITH THROMBOTIC EVENTS REFERRED TO A TERTIARY HOSPITAL IN SOUTHERN IRAN

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Introduction: Thromboembolic events mainly occur in older age is related with high morbidity and mortality, and considerable health-care costs particularly in developing countries. Both

arterial and venous thromboembolism has known risk factors such as hyperlipidemia, obesity, diabetes, cancer, major surgery, central catheter.
Aim: We aimed to evaluate the occurrence of thrombotic events and related risk factors in a group of Iranian patients.
Materials and Methods: In this cross-sectional study, all patients (n=99) who were complicated by thrombotic events referred to the Hematology Research Center of Shiraz University of Medical Sciences were investigated from 2015 to 2017, in Shiraz, Southern Iran. Data were collected from their medical records by a designed data gathering form.
Results: The median age of the occurrence of thrombosis was 51 (IQR: 31) years. From all thrombotic events 52.5% occurred in females. Venous thrombosis was more prevalent than arterial (61.6% *vs* 38.4%). Hypertension, diabetes mellitus and ischemic heart disease were the most associated disease with thrombosis. Most of the patients (79.8%) had no episodes of relapse and the occurrence of relapse had no significant relationship with thrombophilia and underlying disease. Acceptable response rate for warfarin therapy was achieved in 46.5% with 5 mg and 43.4% with 5-7.5 mg.
Conclusions: Knowing the frequency and risk factors for thrombotic events lead to timely diagnosis and management of thrombosis. Atrial fibrillation and valvular rheumatic heart disease are the most common risk factors of thrombosis in our study showing prophylaxis is necessary in high-risk patients.

PO-28

RATES OF VENOUS THROMBOEMBOLISM DURING NEOADJUVANT CHEMOTHERAPY FOR OVARIAN CANCER: A NATIONAL STUDY OF UK GYNAECOLOGICAL CANCER CENTRES

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Introduction and Aim: This study aimed to determine the incidence of venous thromboembolism (VTE) in patients with advanced epithelial ovarian cancer undergoing neoadjuvant chemotherapy (NACT) before debulking surgery in gynaecological cancer centres across the UK. Patients generally receive 3 x 3 weekly cycles of combination chemotherapy before surgery. Secondary outcomes included overall incidence and timing of VTE since cancer presentation, VTE presentation (symptomatic/incidental), impact on cancer treatment and mortality.
Materials and Methods: All UK gynaecological cancer centres were invited, through the British Gynaecological Cancer Society network, to participate in this multicentre retrospective study. A bespoke data collection tool was developed, and peer reviewed. Data was captured on all patients undergoing NACT for FIGO stage III/IV epithelial ovarian cancer within a (centre-defined) 12-month period within 2021-2022. We excluded all patients on anticoagulation prior to ovarian cancer presentation. We excluded patients who developed VTE prior to commencing NACT from analysis of our primary outcome.
Results: Fourteen UK gynaecological cancer centres returned data on 660 eligible patients. The median age was 67.0 years. In total, 132/660 (20.0%) patients were diagnosed with a VTE from presentation with ovarian cancer until discharge following cytoreductive surgery. Excluding those who developed VTE prior to NACT, 66/594 (11.1%) patients developed VTE from start of NACT until discharge following cytoreductive surgery (median 11.3%, IQR 5.9-11.3), with no significant difference across centres (p=0.47). Of these 66, 45 (68%) developed pulmonary embolism and 30 (46%) developed deep vein thrombosis (9 had both), including in major abdominal/pelvic vessels. 37 (56%) presented symptomatically and 29 (44%) were incidentally diagnosed on imaging. VTE resulted in mortality in 3 patients (5%); delays/cancellation of treatment in 17 (26%); and need for inferior vena cava filter in 3 cases (4.5%).
Conclusions: Across a large, representative sample of UK gynaecological cancer centres, 1 in 9 patients undergoing NACT for advanced ovarian cancer developed a potentially preventable VTE. This led to adverse clinical consequences for one third. This unacceptably high VTE rate, and the limitations of existing risk-stratification tools in this cohort, justify consideration of a national protocol for thromboprophylaxis in this patient group.

POSTER SESSION 4
THROMBOPROPHYLAXIS IN CANCER

PO-29

ELECTRONIC HEALTH RECORD (EHR) INTEGRATION OF THROMBOEMBOLISM RISK STRATIFICATION MODEL IN PATIENTS WITH CANCER

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Introduction: Despite multiple risk models validated for venous thromboembolism (VTE) prediction in patients with cancer, the overall implementation rate is low.
Aim: We aimed to design and test a clinical decision support (CDS) tool to automatically calculate VTE risk at time of new treatment initiation in Epic, the most used electronic health record (EHR) in the US.
Materials and Methods: We designed a SQL algorithm in Epic Clarity data warehouse to 1) extract 11 variables to calculate the modified Khorana score (EHR-CAT, Li JCO 2023) at each new systemic therapy (cancer type, stage, treatment, body mass index,

blood count, history of VTE, paralysis, recent hospitalization, and Asian); and 2) identify clinical trial exclusions, including existing anticoagulation (AC), non-aspirin antiplatelet (AP), CYP3A4/P-glycoprotein inducer/inhibitor, abnormality in platelet, creatinine, bilirubin, alanine aminotransferase, weight <40 kg, acute leukemia, or primary/metastatic brain cancer. Finally, we designed a large language model natural language processing (NLP) algorithm to extract new VTE events. We tested the algorithm on patients with cancer and treatment plans at Harris Health System, TX in 1/2017-1/2023 and verified with chart reviews. Competing risk regressions were used to estimate the VTE incidence to account for cancer deaths.

Results: A total of 14,151 treatment plans from 7,640 patients with cancers were identified over 6 years. Clinical trial exclusion criteria removed 21.9% patients (26.6% plans). The most common reason for exclusion was AC for prior VTE (9.6%), brain metastasis (5.9%), and acute leukemia (4.4%). The final list included 10,264 treatment plans (73.7% chemotherapy) from 5,915 patients. After random sampling to create one plan per patient, the index plan count was 1st, 2nd, and 3rd+ in 67.3%, 22.2%, 10.5% of patients, respectively. The cumulative incidence of VTE at 6 months was 1.7%, 4.3%, 5.8%, 6.0%, 8.6%, and 14.7%, respectively, for scores 0-5 (time-dependent c index of 0.67). The original Khorana score resulted in c index of 0.61 (Figure 1).

Conclusions: We demonstrated the feasibility of a CDS design for VTE risk stratification in patients with cancer. Nearly 1 in 4 patients would be excluded based on trial exclusions due to potential bleeding risk. In the remaining eligible patients, EHR-CAT scores could be estimated using standard SQL algorithms and the resulting risk strata had similar observed VTE event rates as the original model. Future work on CDS implementation may lead to improved guideline-concordant thromboprophylaxis.

Structured Data SQL extraction for baseline variables & exclusion

7,640 patients (14,151 treatment plans) at HHS in 1/2017-1/2023 [EPIC BEACON]

- 533 patients (1355 plans) on anticoagulant (AC) prescription
- 113 patients (188 plans) on P2Y12 antiplatelet prescription
- 135 patients (277 plans) on CYP3A4/P-GP strong inducer/inhibitor prescription
- 235 patients (479 plans) with abnormal labs (Plt, Cr, Bili, ALT) or low weight
- 237 patients (629 plans) with acute leukemia diagnosis
- 417 patients (835 plans) with primary/metastatic brain cancer diagnosis

Free-Text Notes NLP transformer for VTE prediction

5,970 patients (10,388 treatment plans)

- 55 patients (124 plans) with recent VTE last 6 mo but not on AC

5,915 patients (10,264 treatment plans => randomly select 1 plan per patient)

Algorithm Performance Comparison

Khorana score	VTE at 6 mo	Cut-Off	EHR-CAT score	VTE at 6 mo	Cut-Off
		Cut-off 2+ treats **2,182** correct **10.1%** captures **52%** of all VTE events AUC = **0.61 (0.58-0.63)**	0- = 749 (12.7%)	12 (1.7%)	Cut-off 3+ treats **3,090** correct **9.7%** captures **72%** of all VTE events AUC = **0.67 (0.64-0.70)**
0 = 1,776 (30.0%)	85 (5.0%)		1 = 1,027 (17.4%)	42 (4.3%)	
1 = 1,957 (33.1%)	104 (5.6%)		2 = 1,049 (17.7%)	59 (5.8%)	
2 = 1,401 (23.7%)	108 (8.2%)		3 = 1,070 (18.1%)	61 (6.0%)	
3+ = 781 (13.2%)	100 (13.5%)		4 = 1,005 (17.0%)	80 (8.6%)	
			5+ = 1,015 (17.2%)	143 (14.7%)	

Figure 1.

PO-30

APIXABAN THROMBOPROPHYLAXIS IN MULTIPLE MYELOMA (MM) PATIENTS RECEIVING CHEMOTHERAPY: A COHORT STUDY

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Introduction: There are not yet sufficient data to recommend a particular myeloma VTE risk assessment model (RAM) or thromboprophylactic agent in clinical practice. We previously reported on low dose apixaban as thromboprophylaxis in high VTE risk MM patients on chemotherapy.

Aim: This cohort study aimed further to assess safety and efficacy of an apixaban-based thromboprophylactic strategy in MM patients in a regional cancer centre.

Materials and Methods: Data was systematically collected from electronic records for sequential MM patients receiving outpatient chemotherapy 1/11/2021-1/5/2023. Exclusion criteria included anticoagulation for other indications. Data collected included VTE history, thromboprophylaxis, 6 month VTE & bleeding event rate. Patients were risk assessed with an adapted International Myeloma Working Group (IMWG) RAM, received apixaban 2.5mg bd if high risk, and aspirin 75mg od or no thromboprophylaxis if low risk (Figure 1).

Results: 122 patients, 75M(61.5%) median age 63.9y & median BMI 26.6, were included. 4/122(3.3%) patients had prior VTE, all catheter-associated. Treatment regimens included lenalidomide in 68/122(55.7%), pomalidomide in 25(20.5%) & thalidomide in 9(7.4%). 15/122 (12.3%) had newly diagnosed MM. 57/122 (46.7%) patients received apixaban 2.5mg bd, 41 (33.6%) aspirin, 2 (1.6%) clopidogrel (1 aspirin allergy, 1 for cardiac ischaemia) & 22 (18%) did not receive thromboprophylaxis. 98/122 (80.3%) of thromboprophylaxis decisions were in accordance with local guideline. Newly diagnosed VTE occurred in 1/122 (0.8%), with lower limb DVT 1 month after starting DVRD. Patient received aspirin but prophylactic LMWH indicated (apixaban contraindicated as abnormal liver function). The patient was stratified as low thrombotic risk by SAVED & intermediate risk by IMPEDE RAM. 2/122 (1.6%) patients had clinically relevant non-major bleeding: 1 hematuria on aspirin–no cause found;1 rectal bleed during autograft–off anticoagulation as thrombocytopaenic. No major bleeding events occurred.

Conclusions: Use of apixaban 2.5mg bd in MM patients with high VTE risk, and aspirin in low VTE risk, had low thrombotic and bleeding rates in this cohort risk-stratified using modified IMWG criteria. The VTE rate compares favourably to published cohorts using IMWG RAM with LMWH for high risk patients eg Myeloma XI VTE rates >10%. Our study adds to the growing body of real world data supporting use of low dose apixaban as part of the thromboprophylactic strategy in MM.

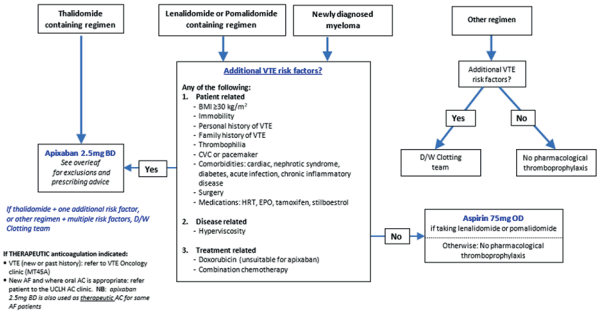

Figure 1. Thromboprophylactic strategy for MM patients introduced 2019 in our regional centre (Sayar *et al.*, 2022).

PO-31

TINZAPARIN PROPHYLAXIS IN PATIENTS WITH METASTATIC COLORECTAL CANCER (PROTINCOL)

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F.J. Pelegrín Mateo[9], E. Jiménez[10], J. Sastre[11], E. Martínez De Castro[12], E. Coma[13], L. París Bouzas[14], A.I. Ferrer Pérez[15] Y. De Miguel[16], E. Mompradé Olivé[17], L. Robles Díaz[18], J.M. Soria[19], M. Salgado[4]

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Introduction: Colorectal cancer (CRC) is the third most commonly diagnosed cancer worldwide. CRC leads to increased activation of the clotting system. Since CRC patients present a higher rate of bleeding, careful evaluation of the risk/benefits of anticoagulant prophylaxis is necessary.
Aim: To evaluate low molecular weight heparin (LMWH) *versus* no treatment for primary thromboprophylaxis in metastatic CRC outpatients receiving first-line systemic cancer therapy
Materials and Methods: PROTINCOL (NCT05625932) is a randomised, open-label (PROBE), multicentre study (Figure 1). Patients will receive tinzaparin (75 IU/kg) or no treatment for 4 months and will be stratified based on: BRAF/RAS mutation, primary resection tumour and antiangiogenic therapy. Subsequently, two months of post-treatment follow-up will be carried out. The study outcomes will be assessed by a blinded central independent adjudication committee. The primary efficacy endpoints will include the cumulative incidence of any venous thromboembolism (VTE) event (symptomatic or incidental) including symptomatic central venous catheter VTE. Secondary variables will be clinically relevant bleedings, health-related quality of life and the predictive value of validated risk assessment scales of VTE, as well as a risk assessment of VTE based on a validated clinical-genetic model. A further 18 months of follow-up by telephone could be carried out at the end of the study to monitor for progression and survival. Our hypothesis is that prophylactic LMWH will reduce the 55% relative risk to an estimated VTE incidence of 13.5%. A total of 526 patients will be required.
Conclusions: Risk prediction of chemotherapy-associated VTE is a compelling challenge in oncology, as VTE may result in treatment delays, impaired quality of life, and increased mortality. Patients with a single type of metastatic cancer with a high risk of VTE will be selected for study inclusion. For the first time in ambulatory prophylaxis of cancer-associated thrombosis, a precision medicine approach will be used in a randomised clinical trial. If the individualization of antithrombotic prophylaxis can reduce the complications of outpatient cancer treatment and be cost effective, it would be of great value in the future care of patients with metastatic CRC.

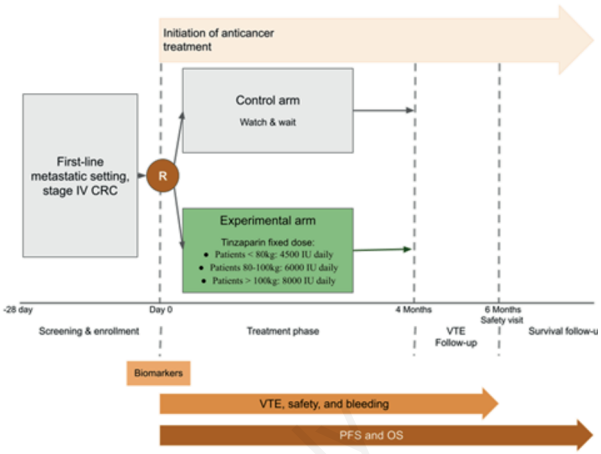

Figure 1. Study design.

PO-32

COMPARATIVE ANALYSIS OF RISK PREDICTION SCORES INCLUDING ALL TYPE OF CANCER ASSOCIATED THROMBOSIS.

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Introduction: Classically, only symptomatic deep vein thrombosis (DVT) and pulmonary embolism (PE) have been included in the predictive risk scores. However, visceral vein thrombosis (VVT) and central venous catheter–related thrombosis (CRT) as well as incidental events have clinical and economic implications in cancer patients.
Aim: The aim of the study is to conduct a comparative analysis of the different predictive risk scores in assessing all types of thrombotic events.
Materials and Methods: We evaluated and compared the performance of the Khorana, PROTECHT, CONKO, modified VIENA-CATS (without P-selectin value) and MICA-CATS risk scores in the second cohort of the multicenter, prospective ONCOTHROMB12-01 study. Data of 391 patients receiving ambulatory systemic therapy from 11 Spanish hospitals between 2018 to 2021 were analyzed. Clinical data associated with the risk of venous thromboembolism (VTE) were collected at the time of diagnosis. The primary outcome was confirmed incidental or symptomatic VTE including DVT, PE, VVT and CRT during a 12 month follow up period. Area under Receiver Operating Characteristics (AUROC) and area under Precision-Recall curve

(AUPRC) were used to compare the score's performance. The cutoff for considering high-risk patients in MICA-CATS score was 10%.

Results: Out of 391 patients (p), 229 men (58.6%) and 162 women (41.4%) with a median age of 64.7 years, 91 p (24.4%) developed a thrombotic event. The most common malignancy was pancreatic cancer (28.7%, n=112), followed by colorectal (26.4%, n=106) and lung cancer (19.2%, n=75). Most p were metastatic (53.3%, n=202), having 118 p locally advanced disease (31.3%) and 59p (15.5%) localized disease. The performance of the predictive scores is detailed in Table 1. Our findings show that MICA-CATS score demonstrates the best predictive capacity according to both AUROC (0.61, 95% CI 0.54-0.67) and AUPRC (0.38, 95% CI 0.30-0.46). For symptomatic events only MICA-CATS score seems to be predictive (0.60 [95% CI 0.5003-0.711]). Regarding incidental events, both PROTECHT and MICA-CATS score seems to be useful (HR 0.62 [95% CI 0.55-0.68] and HR 0.60 [95% CI 0.513-0.6813]).

Conclusions: The score that has the best predictive capacity for all types of events, including incidental and symptomatic VTE, is the MICA-CATS score. New models need to be developed in order to improve this outcome and consequently the patients who would benefit from thromboprophylaxis.

Table 1. Comparative AUROC and AUPRC among different scores.

Scores	AUROC	AUPRC
Khorana risk score	0.5453 [0.4768-0.6096]	0.2543 [0.2222-0.2973]
Incidental VTE	0.5522 [0.4813-0.6244]	0.1652 [0.1408-0.2008]
Symptomatic VTE	0.5191[0.4323-0.6188]	0.0902 [0.0734-0.1280]
PROTECHT	0.5819[0.5220-0.6395]	0.2651[0.2353-0.3049]
Incidental VTE	0.6242[0.5578-0.6878]	0.1855 [0.1591-0.2201]
Symptomatic VTE	0.4868[0.3870-0.5744]	0.0846 [0.0674-0.1290]
CONKO	0.5633 [0.5030-0.6236]	0.2617 [0.2307-0.3062]
Incidental VTE	0.5678 [0.4937-0.6405]	0.1721 [0.1455-0.2098]
Symptomatic VTE	0.5348 [0.4459-0.6162]	0.0914 [0.0746-0.1206]
VIENA-CATS	0.5870 [0.5309-0.6430]	0.2837 [0.2484-0.3361]
Incidental VTE	0.5687 [0.4914-0.6402]	0.1714 [0.1437-0.2116]
Symptomatic VTE	0.5869 [0.4928-0.6786]	0.1159 [0.086-0.1813]
VIENA MICA-CATS	0.6174 [0.5469-0.6767]	0.3803 [0.3055-0.4601]
Incidental VTE	0.6017 [0.5130-0.6813]	0.2044 [0.162-0.2819]
Symptomatic VTE	0.6029 [0.5003-0.7110]	0.2152 [0.1192-0.3651]

PO-33

DIRECT ORAL ANTICOAGULANTS FOR THE PREVENTION OF VENOUS THROMBOEMBOLISM AFTER CANCER SURGERY: A SYSTEMATIC REVIEW AND NETWORK META-ANALYSIS

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Introduction: Data on the role of direct oral anticoagulants (DOACs) for post-operative prophylaxis of venous thromboembolism (VTE) after cancer surgery are awaited.

Aim: We performed a systematic review and network meta-analysis (NMA) to evaluate the efficacy/effectiveness and safety of DOACs for VTE prophylaxis after cancer surgery.

Materials and Methods: PubMed, EMBASE and Cochrane Library were searched for eligible studies. Randomized controlled trials (RCTs) and non-randomized studies (NRSs) reporting on VTE events and/or bleeding complications in patient receiving DOACs for VTE prophylaxis after cancer surgery were included. A frequentist NMA using random-effects model was conducted to estimate the pooled odds ratios (ORs) and corresponding 95% confidence intervals (CIs), including direct and indirect evidence. P-scores were used to rank the treatment for all possible prophylactic strategies.

Results: Five RCTs (1694 patients) and 6 NRSs (2042 patients) were included in the analysis. When all the studies were considered regardless of the timing from surgery to the starting of DOACs, prophylaxis with apixaban (OR 0.12, 95% CI 0.02-0.73) or rivaroxaban (OR 0.26, 95% CI 0.07-1.04) and not with LMWH (OR 0.38, 95% CI 0.08-1.76) was associated with reduction in the risk of VTE at 30 days from surgery compared with placebo/no treatment. Prophylaxis with apixaban (OR 0.31, 95% CI 0.11-0.84) and not with rivaroxaban (OR 0.69, 95% CI 0.35-1.34) was associated with significant reduction in VTE at 30 days in comparison to LMWH. No significant difference in 30-day VTE was found with apixaban *vs* rivaroxaban (OR 0.45, 95% CI 0.13-1.49). Compared to placebo/no treatment, antithrombotic prophylaxis was associated with increased rates of clinically relevant bleeding at 30 days (apixaban OR 6.13, 95% CI 1.02-36.74; LMWH OR 7.29, 95% CI 1.18-44.94; dabigatran OR 3.95, 95% CI 0.10-151.4; rivaroxaban OR 2.62, 95% CI 0.58-11.91) (Table 1).

Conclusions: Our study in post-operative prophylaxis of VTE after cancer surgery support apixaban and rivaroxaban as promising alternative to LMWH, despite further high-quality data are needed in specific surgical settings.

Table 1.

Effect estimates and 95% confidence intervals table (random effect model) – VTE at 30 days from surgery

	DIRECT ESTIMATE			
NETWORK ESTIMATE	Api	.	0.31 (0.11; 0.84)	.
	0.45 (0.13; 1.49)	Riva	0.69 (0.35; 1.34)	0.26 (0.07; 1.04)
	0.31 (0.11; 0.84)	0.69 (0.35; 1.34)	LMWH	.
	0.12 (0.02; 0.73)	0.26 (0.07; 1.04)	0.38 (0.08; 1.76)	Placebo/no treat

PO-34

BARRIERS TO VTE PREVENTION IN AMBULATORY ONCOLOGY PRACTICE: A CLINICIAN-BASED SURVEY

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Introduction: Prior studies have shown underuse of evidence-based recommendations for venous thromboembolism (VTE) prevention in ambulatory oncology practice and have identified barriers such as clinicians' lack of knowledge and resource limitations.

Aim: We sought to evaluate use of and barriers to using VTE prevention by different clinician groups in a safety-net cancer clinic with limited healthcare resources.

Materials and Methods: From December, 2023 to February, 2024, we conducted an anonymous clinician survey at a safety-

net hospital system that primarily services uninsured and underinsured patients from low socioeconomic backgrounds. The survey assessed knowledge and awareness, current practice and attitudes towards, and barriers to using VTE prevention guidelines, and to solicit recommendations. We analyzed results based on years of medical experience (fellows <5 years *vs* senior clinicians >5 years) (Table 1).

Results: We received 35 responses from 46 distributed surveys (76% response rate) from 13 attending physicians, 15 fellows, and 3 NPs, where 55% of respondents had <5 years of oncology experience. There are similarities in both experience groups, and >80% of all clinicians would not prescribe anticoagulant (AC) prophylaxis in scenarios of high-risk cancer patients, despite 60% responding that it is "quite a bit" important to address VTE in oncology practice, and nearly all respondents (96%) felt "quite a bit" or "somewhat" comfortable prescribing/managing AC. Regarding knowledge, 54% responded "not at all" or "a little bit" familiar with guideline recommendations and VTE risk-assessment scores, and 50% were "not at all" or "a little bit" familiar with data from clinical trials. There are also notable differences. For example, 54% senior clinicians *vs* 80% fellows responded "never" or "rarely" use validated risk scores. The most frequent barriers identified by senior clinicians were not being convinced of evidence (38%), unfamiliarity with evidence (38%), and workflow limitations (38%); whereas fellows identified lack of unfamiliarity with evidence as the most significant barrier (90%) followed by workflow limitations (53%).

Conclusions: Recommended VTE prevention strategies are infrequently used in our resource-limited oncology practice. Similar barriers exist to those previously reported, including lack of knowledge and familiarity with evidence. We show that barriers may be different among senior clinicians *vs* fellows. While incorporating a clinical decision support tool addresses the workflow, we should focus on education of existing literature for fellows and generation of more convincing and targeted risk-stratified data for senior clinicians which may help to inform targeted implementation strategies.

Table 1.

Less experienced clinicians (0-5 years clinical experience) - Fellows and NPs		Experienced clinicians (5- >10 years clinical experience) - Attendings and NPs	
Areas assessed	**Comments/ opinions/ summary of responses**	**Areas assessed**	**Comments/ opinions/ summary of responses**
Knowledge Check	Apprehension in prescribing anticoagulants in demonstrated high-risk patients	Knowledge Check	Less apprehension in prescribing anticoagulants in demonstrated high-risk patients when compared to fellows
Awareness of Guidelines	Lack of familiarity with the guidelines (43.8% - not at all; 37.5% - a little bit)	Awareness of Guidelines	Some familiarity with the guidelines (57.1% - somewhat; 28.6% - a little bit; 14.3% not at all)
	Lack of familiarity with the RCTs conducted to demonstrate pro/cons of thromboprophylaxis (52.9% - not at all; 29.4% - a little bit)		Some familiarity with the RCTs conducted to demonstrate pro/cons of thromboprophylaxis (64.3% - somewhat; 14.3% - a little bit)
	Lack of familiarity with validated risk scores like Khorana score (50% - not at all, 31.3% a little bit)		Some familiarity with validate risk scores like Khorana score (21.4% quite a bit, 35.7% somewhat and 28.6% a little bit)
Importance of VTE assessment	Indicate importance of carrying out assessments (58.8%) but do not do so in practice (62.5%).	Importance of VTE assessment	Indicate importance of carrying out assessments (78.6%) and carry it out sometimes (57.1%) or usually (42.9%) depending on the specialty.
Barrier Assessment (Can choose multiple responses)	Not familiar with evidence behind prophylactic anticoagulation in cancer patients (94.1%)	Barrier Assessment (Can choose multiple responses)	Not familiar with evidence behind prophylactic anticoagulation in cancer patients (42.9%)
	Not able to due to workflow limitations (e.g. busy clinic) (52.9%)		Not able to due to workflow limitations (e.g. busy clinic) (35.7%)
	Not able to due to patient specific barrier (e.g. education/language) (29.4%)		Not convinced on the benefits of prophylactic anticoagulation in cancer patients (35.7%)
	Not convinced on the benefits of prophylactic anticoagulation in cancer patients (23.5%)		
	Not comfortable assessing VTE risk in cancer patients (e.g. high vs. low risk) (23.5%)		Not comfortable prescribing and managing anticoagulation in cancer patients (e.g. drug drug interaction, duration) (21.4%)
	Not comfortable prescribing and managing anticoagulation in cancer patients (e.g. drug drug interaction, duration) (17.6%)		
Recommendations (Free text response)	Multidisciplinary decision to prescribe anticoagulants	Recommendations	Risk assessment scores
	Built-in Epic tool/ optional EMR tool		Multidisciplinary action to prescribe anticoagulants/ Using tumor board presentations
	Evaluate bleeding risk before prescribing anticoagulant		Optional Epic tool with automated calculation

PO-35

EXPLORING THE IMPACT OF KRAS MUTATION TYPE ON THE THROMBOTIC RISK

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Introduction: Thrombotic complications are common in patients (pts) with cancer, and an important cause of morbidity and mortality. The management of this complication is particularly challenging and routine thromboprophylaxis is not recommended. Risk prediction scores have a disappointing clinical utility and the majority of these scores don't take in account specific genetic pathogenic variants, ignoring the presence of certain molecular aberrations in a variety of different cancers, namely lung tumors, that have been associated with an increased risk of venous thromboembolism (VTE) and arterial thrombotic events (ATE), such as ALK and ROS1 rearrangements and KRAS mutations, the latter with a 16.1% to 54% VTE incidence (a 2.6-fold increase).

Aim: Our study aims to determine VTE and ATE incidence in our population and to explore the impact different RAS mutations may have on the thrombotic risk.

Materials and Methods: Retrospective analysis of pts at a Portuguese tertiary center with histologically confirmed metastatic or locally advanced lung adenocarcinoma, who were tested for KRAS mutations with Next-generation sequencing between January 1st 2017 and December 31st 2022. Data cut-off was December 31st 2023. Data was obtained from pts clinical files, collected in an anonymous registry and analyzed with SPSS.

Results: 101 pts were identified, with a median age of 66 years old and 29 were female. 66 had metastatic disease and 35 had locally advanced disease. Concerning the mutational profile, the most frequent mutation was KRAS G12C (38 pts), followed by G12V (23 pts), G12D (14 PTS), G12A (7 pts) and G13C (5 patients). There were 12 events in 11 patients, corresponding to an overall incidence of VTE of 6.9% and ETA of 4.9%. Regarding the incidence according to specific mutations, the overall incidence in G12V was 17.4%, with VTE incidence of 13.1% and ETA 8.7%; G12D overall incidence was of 14.3%, VTE 7.1%, and ETA 7.1%. G12C overall incidence of 5.3%, VTE 2.6%, and ETA 2.6%. Noteworthy, G13C had a TVE incidence of 40% (2 events in 5 patients).

Conclusions: The use of thromboprophylaxis rests on suboptimal clinical models. Specific molecular aberrations in driver genes may drive the thrombotic risk, as we observed in our data that G12V and G13C KRAS mutations had higher incidence of VTE. The integration of this genetic information in future clinical models may improve its reliability. More research in expanded databases is required to validate these findings.

PO-36

ANTITHROMBOTIC AND ANTI-LEUKEMIC EFFECTS OF *RICINUS COMMUNIS* IN BENZENE–INDUCED LEUKEMIC WISTAR RATS

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Introduction: The use of medicinal plant is very wide spread in many parts of the world because it is commonly considered that herbal drugs are cheaper and safer as compared to synthetic drugs and may be used without or minimum side effects.

Aim: This study was designed to assess the efficacy of some herbal extract in the management of leukemia and their mode of actions.

Materials and Methods: Leukemia was experimentally induced in wistar rats by Benzene chromosolv at 0.2ml at 1:10 dilution water 1/2 – propanol 50/50 v/v in water daily via tail vein for 4 weeks. The Rats were divided into 6 main groups consisting of 6 rats per group. They were administered with the extracts of four different plants viz: *Ricinus communis, Rosy periwinkle,*

Psorospernum febrifugum, and Azadirachta indica separately after the determination of the LD50 for 4 weeks after induction. The LD50 of each of the extracts are *Ricinus communis* 340mg/kg, *Azadirachta indica* 40mg/kg, *Psorospermum febrifungum* 548mg/kg and *Rosy Periwinkle* 30mg/kg. The animal were thereafter weighed and sacrificed, blood samples were collected into appropriate containers for laboratory analysis of complete Blood Counts and coagulation profiles as well as BCL-2 gene expression using standard methodologies.
Results: We observed a statistically significant decrease in final weight in all groups (pre and post treated with the extracts and a statistically significant increase in WBC count in benzene induced rats ($p<0.05$, respectively) compared with non-induced controls. The induced leukaemia was the lymphocytic type. These values reduced significantly with the post treated animals especially with *Ricinus communis* ($P<0.05$, respectively). Also, there was a statistical significant increase in PTTK with concomitant decreases in the values of D-dimer, Protein C and S in the post-treated animals with all the 4 extracts ($P<0.05$, respectively) when compared with controls. Finally, the BCL-2 gene was significantly up-regulated in the animals treated *Ricinus communis* and *Psorospernum febrifugum* but with a higher value exhibited by the latter.
Conclusions: *Ricinus communis* exhibited a significant efficacy in the management of leukemia and its thrombotic complications over the other three extracts. A further pharmacologic potential of this extract is hereby indicated.

PO-37

CANCER ASSOCIATED THROMBOSIS (CAT): OPTIMIZING VTE PREVENTION AND IMPROVING PATIENT CARE EXPERIENCE

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Introduction: The University Health Network (UHN) Thrombosis and Hemostasis Program provides outpatient management for venous thrombosis (VTE). Currently treating more than 10,000 patients/year, greater than 5,000 CAT patients, this clinic is one of the largest in North America. The Clinic is notable for its innovative model of Nurse Practitioner (NP) led care delivery. VTE including CAT is associated with substantial morbidity, mortality, and health care expenditures. Cancer patients with higher Khorana score have an estimated risk of thrombosis of 10% during the first six months of diagnosis. The emotional distress caused by cancer associated thrombosis (CAT) and lack of understanding of CAT risk are well documented. Clinical practice guidelines underscorethe need to educate patients and prescribe VTE prophylaxis for patients at high risk for CAT. There is strong evidence-based data to direct best management for treatment and prophylaxis of CAT. While there is excellent data on the prevention of VTE with prophylaxis in the high-risk cancer population by more than 50% there is a substantial care gap in at risk cancer patients receiving this cost-effective intervention resulting in increased CAT and health care expenditures.
Aim: To evaluate a dedicated satellite Princess Margaret Hospital CAT clinic to expand CAT management to also manage CAT thromboprophylaxis better optimize and improve health care outcomes, patient well-being and decrease costs including emergency visits.
Materials and Methods: Develop and implement a QIRC approved quality improvement initiative to: 1. Establish program inclusion/exclusion criteria and standards of practice. 2. Develop patient decision and patient education tools. 3. Create database to enroll and track patient outcomes (bleeding, thrombosis, ER avoidance). 4. Promote patient awareness of CAT (how). 5. Evaluate impact of patient education and management for experience and satisfaction.
Results: Outcomes for 24 months since implementation in 2022: - ER avoidance:650 encounters (opportunity cost savings $250 K CDN). - Successful implementation of cancer prophylaxis program (60 high risk patients enrolled). - Metrics for provider and patient experience and satisfaction are very high.
Conclusions: The CAT clinic has resulted in ER avoidance, enhanced patient, and provider satisfaction with thrombosis management. We have established a VTE prophylaxis program that is meeting with growing interest and patient acceptance.

PO-38

CANCER ASSOCIATED THROMBOSIS: SURVEYING PATIENTS' AWARENESS AND EDUCATION NEEDS

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Introduction: Cancer-associated thrombosis (CAT) is a significant cause of morbidity and mortality. Despite guidelines suggesting the use of primary thromboprophylaxis in high-risk patients with cancer, patient awareness of risk and risk-reduction strategies are key to successful implementation.
Aim: Our goal was to understand gaps in patients' awareness of CAT and education about VTE prevention.
Materials and Methods: A questionnaire was designed for individuals with history of cancer or active cancer by a multidisciplinary expert group including patient advocates, pilot tested and electronically circulated through non-profit patient advocacy groups for thrombosis and cancer. Survey domains included: 1) risk factor awareness 2) clinical presentation/diagnosis 3) treatment 4) prevention. Response rate could not be calculated.
Results: There were 95 respondents, including 44% receiving active treatment for their disease (surgery, radiation, or chemotherapy within the last 3 months). Most respondents (89%) were women aged 50 or older. Breast cancer was the most common diagnosis (50%); 40% of respondents reported prior venous thromboembolism (VTE). Forty percent of respondents were unaware that cancer increased VTE risk. 57% of respondents were unaware that certain types of cancer can increase

VTE risk, 51% were unaware certain types of chemotherapy can increase VTE risk, and 41% were unaware that surgery increased VTE risk. One third of respondents had not received any information regarding the risk of VTE in patients with cancer. Only 30% reported hearing about this risk from their clinician, however the majority (80%) would like to receive additional information from their clinician. Sixty percent of respondents had not discussed thromboprophylaxis with their clinician, though 70% stated they would consider the use of thromboprophylaxis if discussed. Compared to patients with prior VTE, patients without prior VTE were more likely to perceive that a VTE diagnosis would affect coping with cancer and quality of life (Table 1).

Conclusions: Patients' awareness of CAT risk remains low. Clinicians are an important source of desired information about CAT. Discussion of thromboprophylaxis remains low, though patients are receptive to thromboprophylaxis as there is a high perceived impact on cancer treatment and survivorship. This study demonstrates patient education will be an important component of efforts to improve guideline implementation.

Table 1.

Domain	Prior VTE N = 35 n (%)	No Prior VTE N=56 n (%)	p-value[1]
Cancer Treatment			0.07
There was/would be an impact	14 (40)	34 (60)	
Coping			0.02*
There was/would be an impact	12 (35)	35 (63)	
Quality of Life			0.02*
There was/would be an impact	18 (51)	43 (76)	

[1]Chi-Square Test, (*) denotes significance

Real and Expected Impacts of VTE on patients with and without prior VTE. Patients with and without prior VTE responses to questions regarding the real or perceived effect on various domains of cancer treatment.

POSTER SESSION 5
TREATMENT OF THROMBOSIS IN CANCER

PO-39

USE OF TINZAPARIN IN THE TREATMENT OF PICC-RELATED THROMBOSIS IN CANCER PATIENTS

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Introduction: In recent years, the need for central venous catheters in oncology has increased. The ease of placement and management as well as the lower economic cost have given peripherally inserted central catheters (PICCs) absolute prominence. However, an increase in the rate of thrombosis associated with PICCs has been observed. Some studies have evaluated several risk factors for PICC-related thrombosis (PRT), but the results have been contradictory and are, thus, unclear. For the treatment of symptomatic catheter-related thrombosis in cancer patients, anticoagulant treatment with LMWH (low molecular weight heparin) is recommended for a minimum of 3 months.

Aim: To describe the characteristics and clinical variables of cancer patients with PRT and evaluate the effectiveness and safety of tinzaparin in the treatment of this complication.

Materials and Methods: This was a prospective, multicentre, observational study including cancer patients in whom a PICC was placed at the Catalan Institute of Oncology from November 2020 to February 2022. Patients were followed for 6 months and the incidence of PRT and associated variables were analysed. A sub-analysis of patients who presented PRT and were treated with tinzaparin was performed.

Results: 801 patients with PICC were included, 52 of whom presented symptomatic PRT (6.5%). All patients with PRT treated with tinzaparin were analysed (24); 62% were men with a mean body mass index of 26.3. 54% received onco-specific treatment with curative intention. Table 1 shows the distribution of patients according to the type of primary tumour. 16 (67%) patients had metastasis or locally advanced stages. Regarding the characteristics of the catheters, most were placed in the basilic vein (22-91.6%) and 2 in the brachial vein; 12 (50%) were inserted in the right arm; and in 14 (58%) patients the catheter began to be used on the same day of placement. For the treatment of PRT, patients received a dose of 175 IU/Kg/day of tinzaparin while the catheter was in placeand for 3 months after its removal. There were no cases of thrombosis recurrence or bleeding 6 months after initiating treatment.

Conclusions: PRT is a relatively frequent complication in cancer patients. Tinzaparin has shown to be effective and safe for preventing the recurrence of thrombosis in patients with PRT.

Table 1.

Patients distribution according to primary tumour

Primary Tumour	N
Breast	4
Germ cell	3
Pancreas	3
ENT	2
Ovary	2
Urothelial	2
Lung	1
Unknown origin	1
Colon	1
Endometrium	1
Gastroesophageal	1
Muscle	1
Bile	1
Other	1

PO-40

DIRECT ORAL ANTICOAGULANTS ARE ASSOCIATED WITH LOWER CIRCULATING LEVELS OF PROCOAGULANT EXTRACELLULAR VESICLES COMPARED TO LOW MOLECULAR WEIGHT HEPARIN TREATMENT IN PATIENTS WITH CANCER ASSOCIATED THROMBOSIS

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Introduction: Cancer Associated Thrombosis (CAT) affects up to 1 in 10 cancer patients and is a leading cause of death in this population. The mechanisms underlying thrombosis risk are varied but include the effects of pro-coagulant extracellular vesicles on plasma hypercoagulability. Low molecular weight heparins (LMWH) were previously considered to be the gold standard for anti-thrombotic therapy in cancer and are known to exhibit anti-inflammatory and other biological properties. Recently, Direct Oral Anticoagulants (DOAC) have emerged as alternatives to LMWH in this CAT cohort, however it remains unclear if these agents exhibit equivalent effects on EV pro-coagulant activity.
Aim: The EXPECT Study aims to characterise the small, large and procoagulant extracellular vesicles as well as plasma and EV cargo proteomic signatures upon treatment with DOAC compared to LMWH in CAT patients.
Materials and Methods: Patients with active cancer newly presenting with a DVT or PE to the Mater Misericordiae University Hospital treated with either DOAC or LMWH anticoagulation were recruited to the EXPECT Study with a baseline blood draw at point of VTE diagnosis and a follow up blood sample 2-9 weeks post-treatment. Small and large EVs were characterised using Nanoparticle Tracking Analysis (NTA) and flow cytometry respectively, quantifying the size, concentration and procoagulant profiles of EVs between treatment arms. Proteomic profiles of the soluble plasma proteins and EV cargo were quantified using tandem mass spectrometry and O-Link analysis.
Results: Small and large EV size and concentration were not significantly altered upon anticoagulant treatment, remaining unchanged between DOAC and LMWH treatment arms. Platelet-derived along with tissue factor and podoplanin expressing circulating EVs were attenuated in the DOAC arm to the same degree as LMWH anticoagulation, highlighting the comparable effects of these anticoagulants at reducing potent procoagulant circulating EVs. Proteomic signatures between the two treatment arms revealed intriguing insights into potential pleiotropic mechanisms at play, with a shift in inflammatory markers between groups.
Conclusions: No significant difference in procoagulant EV profiles were observed with DOAC therapy compared to LMWH, suggesting that both influence this pro-thrombotic mechanism in cancer to a similar extent.

PO-41

ANTITHROMBOTIC THERAPY DECISION-MAKING IN ADVANCED CANCER: KEY FACILITATORS AND BARRIERS

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Introduction: The decision to continue or stop antithrombotic therapy (ATT) in patients with cancer at the end of life is complex. SERENITY is a pan-European study aiming to develop and evaluate a shared decision-making support tool to facilitate ATT management; it is important to understand decisions for ATT.
Aim: To explore facilitators and barriers to ATT decision-making in advanced cancer.
Materials and Methods: Semi-structured interviews with patients and clinicians were conducted in from April 2023 to March 2024 across four countries (Denmark, France, Spain, UK). Data are being analysed using Framework Analysis, informed by concomitant SERENITY work packages, interview summaries and patient and public representatives.
Results: Sixty patients and 77 clinicians were interviewed (Table 1). The prioritisation of other medications and conditions is at the core of the barriers and facilitators for ATT decision-making. Patients had multiple comorbidities, with cancer taking precedence over other health concerns, relegating ATT to a low priority, which resulted in more passive decision-making. ATT indications were in the periphery when managing these patients. Clinicians described a culture of continuing and showed preference for exploring alternative options rather than deprescribing; this was coupled with clinicians not feeling it was their role to take on ATT decisions. Clinicians described the decision as complex, requiring knowledge and expertise from multiple specialties to guide it. However, clinicians also faced challenges with the lack of evidence to support the decision. Patient knowledge about their ATT, including the indication rationale, varied widely. Patients expressed more concern about the reason for being on ATT than that of its side effects, preferring alternative ATT options over deprescribing. Certain patients expressed a need for receiving additional information, indicating that the more information they received, the better. The importance of being informed about the decision and the options was emphasised by patients. This, alongside deferring to the clinicians' expertise, resulted in confidence in the decision that was made.
Conclusions: Barriers and facilitators were identified across various domains, spanning organisational, resource allocation, clinical practice, cultural considerations, and individual factors.

These must be taken into consideration in the development of the shared decision-making support tool.

Table 1.

Characteristic	Patients n=60	Characteristic	Clinicians n = 77
Male, n (%)	28 (47)	**Male, n (%)**	41 (53)
ATT indication		**Antithrombotic affiliated specialists, n (%)**	28 (36)
CAT	26 (44)	Cardiology	7 (9)
Atrial fibrillation	6 (10)	Neurology	4 (6)
Ischaemic heart disease	11 (18)	Vascular medicine/surgeon	8 (10)
Stroke (+/- AF)	3 (5)	Respiratory/Pneumologist	6 (8)
Heart Valve	2 (3)	Internal medicine	3 (4)
Multiple ATT indications	12 (20)		
Age		**Cancer specialists, n (%)**	14 (18)
45-54	6 (10)	Oncology	8 (10)
55-64	9 (15)	Haematology	6 (8)
65-74	24 (40)		
75-84	17 (28)		
85+	4 (7)	**Advanced disease care, n (%)**	35 (46)
		Palliative	10 (13)
ATT		Palliative nurse	8 (10)
DOAC	24 (40)	General Practitioner	10 (13)
LMWH	17 (28)	Geriatrician	7 (9)
Antiplatelets	16 (27)		
VKA	1(2)		
Dual antithrombotic therapy	2 (3)		

ATT: Antithrombotic therapy

PO-42

EFFECTS OF TINZAPARIN ON THE PRESENCE OF RESIDUAL THROMBUS IN PATIENTS WITH CANCER-ASSOCIATED THROMBOSIS

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Introduction: Residual thrombosis (RT) assessed by computed tomography (CT) in patients with venous thromboembolism (VTE) was reported to be 23% (C. Becattini *et al.* JTH 2019). However, information on RT is scarce in patients with cancer-associated thrombosis (CAT).
Aim: The objectives of this study were to assess the presence or absence of RT and to identify variables associated with RT in patients with CAT treated with tinzaparin.
Materials and Methods: Consecutive cohort of CAT patients from January 2008 to June 2022. During their neoplasm follow-up, all patients underwent follow-up CT, and the presence of RT was evaluated. Within VTE, we included patients with deep vein thrombosis (DVT), pulmonary embolism (PE), and unusual thrombosis locations.
Results: The study included 511 CAT patients treated with tinzaparin who underwent at least one follow-up CT. The mean age was 63.1 +/- 13.2 years, with a slight male predominance (52%). Regarding VTE location: PE (38.4%), DVT (35.6%), DVT and PE (16.4%), and atypical VTE (9.6%). During a median follow-up of 17.6 months (p25-75: 7.9-34) and a median anticoagulation duration of 5.7 months (p25-75: 3.1-12.9), 35.8% of patients (n=183) had RT. Multivariate analysis using Cox regression identified that variables associated with residual thrombosis were metastasis (HR: 1.9; 95% CI: 1.4-2.6), ECOG performance status >1 (HR: 2.4; 95% CI 1.6-3.6), and tumor locations (pancreatic and gynecological *vs* others) (HR: 1.6; 95% CI 1.1-2.3).
Conclusions: One-third of cancer-associated VTE patients treated with tinzaparin have residual thrombosis, with identified variables associated with residual thrombosis.

PO-43

A SINGLE-CENTER EXPERIENCE WITH THE USE OF TINZAPARIN FOR THE TREATMENT OF VENOUS THROMBOEMBOLIC EVENTS IN BREAST CANCER PATIENTS ON THERAPY WITH TARGETED DRUG AGENTS

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Introduction: Targeted therapy (TT) has a major impact on the care of patients with breast cancer (BC). Monoclonal antibodies (MoAbs), antibody-drug conjugates (ADC) and kinase inhibitors (KI) are the main agents for TT in BC. Some of these agents, like the cyclin-dependent kinase inhibitors (CDKI), increase the risk of venous thromboembolic events (VTE), and there are some concerns on potential interactions and adverse events of anticoagulant therapy in this context, but published evidence about this topic is limited.
Aims: Review of tinzaparin use for BC patients on TT in a single academic center (2016-2023).
Materials and Methods: Retrospective observational analysis on BC patients treated with TT who received treatment with tinzaparin (TZP). Full data were retrieved from the electronic medical record, covering all the information from hospital and primary care in our regional health service.
Results: 28 patients (p.) received TZP concurrently with TT with antiHer2 monoclonal antibodies, antibody-drug conjugates and/or kinase inhibitors. Median age at the start of TZP: 55.4 years (34.2-83.5). VTE were 11 pulmonary embolisms (PE), 3 PE plus concurrent deep vein thromboses (DVT) and 14 DVT (9 upper limb, 4 lower limb, 1 renal). Therapy setting was adjuvant for early disease in 7 p. and noncurative for metastatic disease in 21 p. Dominant sites of metastatic disease: 11 visceral, 5 bone, 3 soft tissues, 2 brain. TT included KI as follows: palbociclib (10 p.), palbociclib followed by alpelisib (1 p.), abemaciclib (1 p.) and everolimus (1 p). MoAbs included several schemes with trastuzumab (10 p.) and pertuzumab plus trastuzumab (2 p.). ADC included sacituzumab govitecan (2 p.) and trastuzumab deruxtecan (1 p.). Duration of TZP was dependent on the setting, and 17 p. received TZP for more than 6 months, with 9 p. reaching 1 year of TZP or even longer. 8/28 p. continued therapy with direct oral anticoagulants and 1 p. changed to other low-molecular- weight heparin. 7 p. continued TZP in palliative care. 21/28 p. had total resolution of the VTE during TZP, 2 p. had residual disease, and 5 were not fully evaluated. Major bleedings were absent and tolerance was good. 1 p. stopped TZP after developing an itching abdominal rash.
Conclusions: TZP had a good pattern of tolerance and displayed a high activity for event resolution and prevention of new episodes and complications from VTE in BC patients under therapy with KI, MoAbs and ADCs.

PO-44

TREATMENT OF CANCER ASSOCIATED VENOUS THROMBOSIS WITH EDOXABAN IN PATIENTS RECEIVING CONCOMITANT ENZALUTAMIDE

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Introduction: Enzalutamide is a second-generation androgen receptor inhibitor licensed for treatment of metastatic hormone sensitive prostate cancer and high risk non-metastatic castration-resistant prostate cancer. Primarily eliminated by hepatic metabolism, renal excretion provides an insignificant elimination pathway for enzalutamide and its active metabolite. Enzalutamide is a strong inducer of CYP 3A4 and is transported via P-glycoprotein (P-gp). The cytochrome P450 enzymes (CYP3A4 and 2D6) are responsible for the metabolism of the Anti-factor Xa Direct Oral Anticoagulants (DOAC), apixaban and rivaroxaban. Edoxaban is an oral direct factor Xa inhibitor not metabolised by the cytochrome p450 pathway but does undergo P-gp transportation.
Aim: Effect of enzalutamide treatment on anticoagulant efficacy and safety of edoxaban treatment of cancer associated venous thromboembolism (CAT) and atrial fibrillation (AF).
Materials and Methods: Consecutive patients referred to a regional CAT service (with an indication for anticoagulation) who were receiving enzalutamide and DOAC, apixaban or rivaroxaban, were switched to edoxaban. Steady state plasma trough level measurement (24hours after last dose) of edoxaban was completed for all patients. All patients were followed up for a period of 12 months (or until death, whichever occurred earlier) to describe any recurrent thrombotic and/or bleeding episodes.
Results: 13 patients (8 VTE and 5 AF) received concomitant edoxaban and enzalutamide and had 15 trough edoxaban levels taken. Patients were all male with a median age of 74yrs (range 64-84). The median edoxaban plasma level was 27ng/ml (range 22.5-43.4ng/ml). No major or clinically significant non-major bleeds were recorded. No patients in the cohort experienced on-treatment recurrence of VTE or stroke within the monitoring period (Table 1).
Conclusions: There was no evidence of clinically significant drug-drug interaction between enzalutamide and edoxaban. There were no edoxaban levels above the expected steady state level when administered with enzalutamide. Co-administration of enzalutamide and edoxaban patients treated for CAT / AF in this patient group did not result in on-treatment recurrence of VTE or stroke within the monitoring period.

Table 1.

Age	Weight (kg)	Crcl(ml/min)	Indication for anticoagulation	Edoxaban dose	Edoxaban Trough Level (ng/ml)*	Major bleeding	On treatment recurrent venous thrombosis / stroke
76	82	102	Popliteal DVT	60mg OD	34.9	No	No
71	102	93	Upper Limb DVT	60mg OD	30.7	No	No
72	123	99	Ilio Femoral DVT	60mg OD	24.9	No	No
84	73	61	Femoral DVT	60mg OD	22.7	No	No
77	91	89	Fem-pop DVT	60mg OD	37.6	No	No
77	96	94	PE	60mg OD	41.9	No	No
77	96	94	PE	60mg OD	26.6	No	No
69	104	107	PE	60mg OD	27	No	No
71	79	62	PE	60mg OD	43.4	No	No
76	102	66	AF	60mg OD	42.8	No	No
72	114	111	AF	60mg OD	24.1	No	No
78	100	93	AF	60mg OD	22.5	No	No
74	113	105	AF	60mg OD	32.7	No	No
72	117	174	AF	60mg OD	26	No	No
72	117	146	AF	60mg OD	23.3	No	No

PO-45

CHEMOTHERAPY ASSOCIATED CEREBRAL VENOUS SINUS THROMBOSIS (CVST)-EXPERIENCE FROM A TERTIARY CANCER CENTRE

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Introduction: Cancer patients area at increased risk of venous thromboembolism. The risk is further increased by chemotherapy. The diagnosis and management of CVST is challenging in cancer patients receiving chemotherapy.
Aim: To study the clinical profile and outcome of patients with CVST post chemotherapy
Materials and Methods: This is a retrospective study of cancer patients with chemotherapy associated CVST registered at the cancer thrombosis clinic of a tertiary referral cancer centre in the period 2018 to 2022. The details of cancer, chemotherapy, details of CVST, its treatment and related complications were recorded. The data was analysed using IBM SPSS statistics 25 software. The study is approved by the Institute ethics committee.
Results: 25 patients with chemotherapy associated CVST were registered in the study period. Females were predominant (60%). The median age was 31 years (range 16-71). 56% had hematolymphoid malignancy, all had received l asparaginase prior to CVST and further l asparaginase was discontinued. 44% patients had solid tumors of these 72% developed CVST after cisplatin based chemotherapy and cisplatin was discontinued in all except 1. Seizures was the commonest presentation (60%). The CVST was diagnosed by CECT brain in 72% and MRI brain in 28%. Cerebral Infarcts were seen in 8 patients (7 were hemorrhagic). All except one patient received therapeutic anticoagulation. All patients were started on Low molecular weight heparin (LMWH). After initial treatment with LMWH 5 patients were shifted to oral anticoagulation (Rivaroxaban-4, warfarin-1), in rest LMWH was continued. Chemotherapy induced thrombocytopenia (CIT) occurred in 13/14 patients of hematologic malignancy, requiring interruption of LMWH in 6 patients. In 8/11 patients with solid tumor, chemotherapy was continued of whom only 1 patients developed CIT. 18 patients received anti epileptic drugs. Bleeding complications (non neurologic) were seen in 2 patients and 2 developed recurrent CVST. The median duration of anticoagulation was 6 months (range 1-18 months).11/14 patients showed complete recanalization on follow up neuroimaging.
Conclusions: The commonest chemotherapeutic drugs associated with CVST are l asparaginase and cisplatin. LMWH was the anticoagulation of choice and was well tolerated with good clinical outcome. CIT is a common challenge in management of CVST patients with hematolymphoid malignancy.

PO-46

DURATION OF ANTICOAGULATION IN CANCER ASSOCIATED THROMBOSIS WHAT IS IDEAL

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Introduction: Cancer associated thrombosis (CAT) has been increasing in prevalence and is the second common cause of death after cancer itself. Both, deep venous thrombosis and pulmonary thromboembolism are prevalent, more common than in the general population. Despite this, the optimal duration and intensity of anticoagulation remain unclear.
Aim: We describe and analyze a case of cancer associated thrombosis and discuss the evidence (or the lack of it) in areas of management and then subsequently areas where further direction and guidelines are essential.
Materials and Methods: An elderly lady presented to the clinic for symptomatic right lower limb proximal deep vein thrombosis. She had 2 weeks ago, undergone surgery for adenocarcinoma of

the right colon, status post, hemicolectomy and was now awaiting neoadjuvant chemotherapy. In view of the proximal DVT, she was started on tablet Apixaban, after discussing the risk benefit ratio and other options available (Low molecular weight heparin). For the next 6 months, she continued her anticoagulation as well as her chemotherapy, often interrupting oral anticoagulation for minor, but clinically significant bleeding, which caused great distress to herself and her family. Further scans and colonoscopy revealed recurrence of tumor, for which she was advised to undergo further chemotherapy. In the interim, the deep vein thrombosis had resolved and a repeat scan of the right leg did not even show a residual thrombosis.

Results: In such an instance, what should be the strategy for anticoagulation? A) Continue therapeutic anticoagulation in view of tumor recurrence and the fact she had had no major bleeding while on anticoagulation. B) Continue prophylactic anticoagulation, at a reduced dose, in order to minimize the risk of bleeding but at the same time trying to offer some level of protection from recurrence of venous thromboembolism. C) Withhold further anticoagulation in view of the fact that she has no VTE. D) Consider changing the anticoagulant to low molecular weight heparin in view of better tolerability and lesser risk of bleeding.

Conclusions: We discuss in our presentation, the pros and cons as well as the evidence behind each of the options.

PO-47

WHAT IS THE IDEAL ANTICOAGULANT?

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Introduction: With the advent of Novel Oral Anticoagulants (NOAC), they remain the choice for anticoagulation in most clinical circumstances, except when there is renal impairment, significant valvular heart disease, pregnancy and lactation, mechanical heart valve and significant drug interaction. Despite safety and data for more than 10 years, cost remains a significant issue and some patients who are adjusted with Warfarin, are keen to continue rather than switch over to NOAC.

Aim: We describe a clinical scenario where it calls upon choosing the right anticoagulant for a patient with multiple comorbidities.

Materials and Methods: An elderly lady was admitted to the hospital for bleeding per rectal (PR). Amongst other comorbidities, she had atrial fibrillation, CHADS2 Vasc score of 4, on Warfarin with a target International Normalised Ratio (INR) of 2-3, and obesity (BMI 27). Due to the PR bleed, Warfarin was withheld and she underwent a colonoscopy, which showed a rectal adenocarcinoma, for which she was advised surgery. In view of PR bleeding and requirement of 2 pints of blood, her anticoagulation was withheld and she was given compression stockings as well as pneumatic compression devices for VTE prevention. While awaiting work up for the major surgery, she developed a right lower limb swelling, which was diagnosed to be a proximal deep vein thrombosis. Surgeons planned to do a hemicolectomy and since there was a localized cancer, did not offer any further chemo/radiotherapy.

Results: In such an instance, what should be the strategy for long term anticoagulation? A) Continue therapeutic anticoagulation with Warfarin, insert an Inferior vena cava (IVC) filter in the perioperative period, remove it post operatively and resume anticoagulation with Warfarin. B) Stop Warfarin, and change to NOAC in the long term. C) Continue Warfarin and there is no need to change to NOAC since the risk factors in this case were obesity, immobility and hospitalization; with no prophylactic anticoagulation.

Conclusions: We discuss in our presentation, the pros and cons of choosing between Warfarin and NOAC (and if so, the particular NOAC) in this scenario with multiple confounding factors, which play out in real life.

PO-48

A 44 KILOS UTERINE FIBROID RESECTION COMPLICATED BY EXTENDED VENOUS THROMBOEMBOLISM NOT SOLVED BY FULL DOSE EDOXABAN. A CLINICAL CASE

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Introduction: 44 y-o woman, without cardiovascular risk factors, in levothyroxine therapy after thyroidectomy due to cancer, reported a marked abdominal enlargement (Figure 1) in the last year. Thus, being addressed to bariatric surgery, she started further examinations. An abdominal ultrasound detected an exceptionally large pelvic mass severely compressing the great abdominal vessels, confirmed by a CT scan to be solid and non-homogeneous (60 x 50 cm), that was completely not suspected at the initial clinical evaluation of the bariatric surgeon.

Aim: At this time, she was admitted to our institution at the oncological gynecological unit. During her stay, a 44 Kg uterine fibroid was resected, but 1 day after surgery she complained with pain and swelling of the right leg without dyspnea or chest pain.

Materials and Methods: An ultrasound of the lower limbs showed an extended right superficial femoral deep vein thrombosis (DVT). A CT scan detected an incidental subsegmental bilateral pulmonary embolism (PE), bilateral ovarian DVT and right internal iliac DVT. D-dimers: 6081 ng/mL, troponin: 48.4 ng/L. The patient was hemodynamically stable. An echocardiogram was performed: no signs of right ventricular dysfunction with normal ejection fraction (58%). sPESI score was 0 (low-risk PE). She started enoxaparin 1 mg/Kgx2/die (weight: 67 Kg) replaced after 1 week with edoxaban 60 mg/die. After 3 months she came back to our institution to follow up and was completely asymptomatic. A CT scan showed resolution of PE but persistence of the ovarian and iliac DVT. An ultrasound detected a partial resolution of the femoral DVT.

Results: Due to subsequent complaints of the patient for epistaxis (Hemoglobin: 10 g/dL), to the absence of malignant disease and to the chronic nature of the venous thrombotic events mostly incidentally detected, we decided to proceed with the anticoagulant treatment reducing edoxaban dose (30 mg/die).

Conclusions: Abdominal and pelvic major surgery is strongly associated with venous thromboembolism. In this clinical case, an extremely large uterine fibroid (44 Kg), although not malignant,

heavily compressed the abdominal vessels and may have caused soon after surgery the development of incidental PE and symptomatic DVT. Due to DVT persistence and to the complaints of the patient for clinically relevant non-major bleedings, we decided to reduce the edoxaban dose and check the patient clinical conditions with frequent follow up visits.

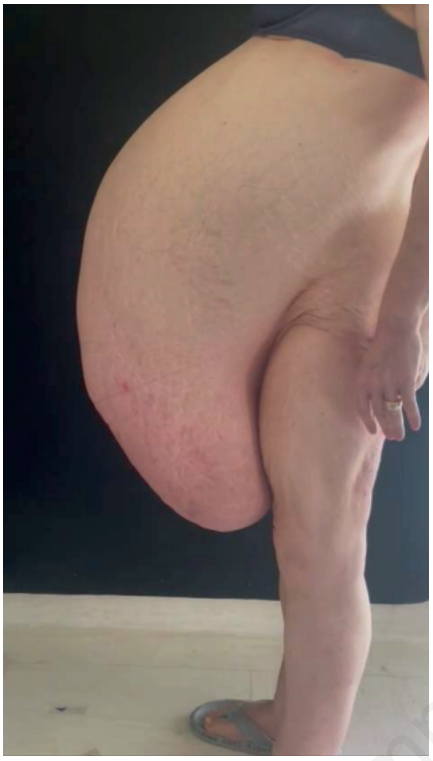

Figure 1.

POSTER SESSION 6
HEMOSTATIC PROTEINS AND CANCER BIOLOGY

PO-49

ANTI-PROLIFERATIVE, ANTI-ANGIOGENIC AND ANTI-INVASIVE EFFECT OF ANTITHROMBIN IN GLIOBLASTOMA MULTIFORME

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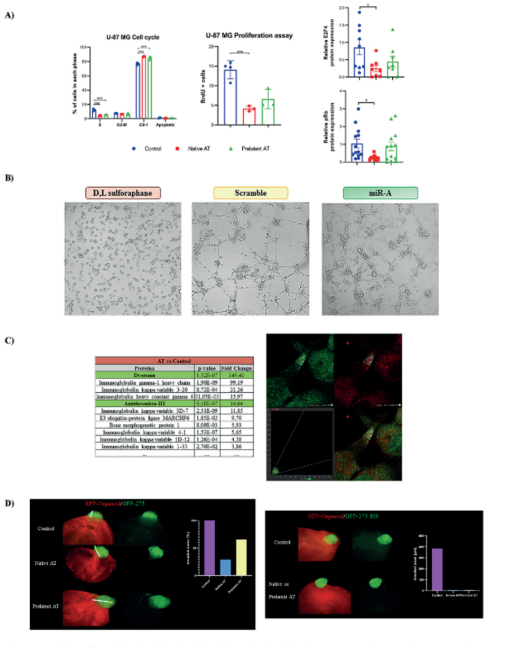
Introduction: Antithrombin (AT) has other functions beyond hemostasis. We have demonstrated that native and prelatent AT reduce migration and invasion as well as the expression and phosphorylation of VEGFA, STAT3, and ERK1/2 in U87 glioblastoma multiforme (GBM) cells. Regarding GBM, it is the most lethal primary malignant tumor of the central nervous system in adults, and the median survival is 12-15 months after diagnosis.

Aim: 1) Investigate the role of AT on other pro-tumor pathways using *in vitro* and preclinical models of GBM; 2) identify the potential receptor of AT in GBM.

Materials and Methods: Native and prelatent AT were purified from healthy donor's plasma. Prior to each experiment, U87 cells were treated with 2.16 µM of native, prelatent AT or PBS. A microarray analysis was performed on U87 (Human Clariom D). Differences were validated by western blot. Cell cycle and proliferation were assessed by flow cytometry. Three microRNAs (miR-A/B/C) with altered expression in GBM were transfected into U87 cells, and angiogenesis was evaluated by co-culture with endothelial cells. The receptor was determined by crosslinking and immunoprecipitation, followed by quantitative proteomics and confocal microscopy. Healthy human brain RFP-organoids were generated from iPSCs, and neurospheres from the biopsy of one GMB patient, at diagnosis (GFP-275) and at relapse (GFP-275-BIS). Anti-invasive AT effect was validated through organoids and neurospheres co-culture.

Results: AT treatment reduced the expression of cell cycle-related genes (FC, p-value): CDK4 (-1.64, 2.60-5), CCNE2 (-2.06, 2.65-6), RB1 (-1.58, 1.37-6) and E2F4 (-2.03, 1.09-7). Native AT reduced U87 S-phase and proliferation as well as E2F4 and pRb expression (Figure 1A). Moreover, AT increased miR-A expression (FC 1.61), and our results preliminarily suggest that miR-A reduces angiogenesis (Figure 1B). We identified dystonin as the receptor of AT on U87, and confocal microscopy images show small regions of colocalisation in U87 between dystonin and AT (Figure 1C). Interestingly, native and prelatent AT partially reduced invasion of 275 neurospheres (100% *vs* 28.89%, 100% *vs* 65.64%, respectively), and completely reduced 275-BIS neurospheres invasion of the brain-organoids (Figure 1D).

Conclusions: AT has surprising and versatile anti-tumor properties on GBM. Our results support its potential therapeutic usefulness in GBM, a tumor in which new treatments are urgently needed.



Antitumor role of AT on GBM. A) Antiproliferative effect. Cell cycle and proliferation were assessed by measuring 7-AAD and BrdU incorporation by flow cytometry (n=3/group) after treating U87 cells with 2.16 µM native or prelatent AT or PBS (control) for 12h. **B) MiRNA control of angiogenesis on endothelial cells.** Representative images of the angiogenesis assay after transfecting U87 cells with miR-A, and in comparison with a scramble and D,L sulforaphane controls. **C) Identification of the receptor: Dystonin.** Left panel: results from quantitative proteomic. Right panel: dystonin (green) and AT (red) co-localization by confocal microscopy. Potential areas of co-localization are visualized in white. **D) Anti-invasive effect on a 3D model of invasion.** GFP-275 (top) or GFP-275 BIS (bottom) neurospheres (green) were obtained from the biopsy at diagnosis or relapse of a GBM patient, respectively. Human brain organoids (red) were generated from induced pluripotent stem cells. Representative fluorescence images of the results are shown on the left. On the right is the percentage of invasion of each neurosphere. * AT: antithrombin; GBM: glioblastoma; GFP or RFP: Green or Red Fluorescence Protein, respectively.

Figure 1.

PO-50

RIVAROXABAN COMPARED TO NO TREATMENT IN EARLY BREAST CANCER PATIENTS (THE TIP TRIAL, EUDRACT 2014-004909-33): EFFECT ON EPCAM SERUM CONCENTRATIONS AS A SURROGATE FOR CIRCULATING TUMOUR CELLS (CTCS)

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Introduction: The TIP Trial is a multi-centre phase II pre-operative 'Window-of Opportunity' RCT of Rivaroxaban (Factor Xa inhibitor) *vs* no treatment in ER negative, stage I-III early breast cancer patients (n=88). Patients were randomised 1:1 (Rivaroxaban 20mg od: no treatment) and received 14 (+/-3) days of treatment in the window between diagnosis and surgery/start of neoadjuvant chemotherapy. We hypothesised that TF-FXa inhibition would reduce tumour growth and metastases. A secondary outcome was circulating tumour cell (CTC) enumeration in response to Rivaroxaban/control. Unfortunately, an Institute fire disrupted the time-critical CTC analysis. EpCAM (Epithelial cell adhesion molecule) is expressed by CTCs and is therefore a potential surrogate marker.

Aims and Methods: In early breast cancer, to determine if: 1. Serum EpCAM decreases in response to Rivaroxaban. 2. EpCAM correlates with plasma thrombin-antithrombin III (TAT), Tissue Factor (TF) and D-dimer, at baseline, and with tumour Ki67. 3. Change in EpCAM correlates with change in TAT, TF, D-dimer, and Ki67 in response to Rivaroxaban. EpCAM, TAT and TF were measured by ELISA, D-dimer by immunoturbidimetry and Ki67 by IHC 'pre' Rivaroxaban/Control and 'post' treatment.

Results: Of 77 patients with serum pre and post treatment, 21 (27%) had detectable EpCAM at baseline (8 of 40 controls; 13 of 37 Rivaroxaban). All 8 controls (+ 2 additional) had EpCAM at 'post' treatment. All 13 Rivaroxaban (+ 0) had EpCAM at 'post' treatment. When dichotomised as EpCAM+ (n=44) and EpCAM- (n=110), TAT (but not Ki67, D-dimer or TF) was higher in EpCAM+ (Table 1). Change in EpCAM from baseline to 'post' treatment was lower in Rivaroxaban *vs* controls (mean 0.95 (95% CI 0.86-1.03) *vs* 1.06 (0.98-1.14), p=0.04). However, (despite randomised allocation), pre-treatment EpCAM were lower in controls (mean 208 (95% CI 133-282) *vs* 374 (298-491) pg/ml, p=0.003). EpCAM did not correlate with Ki67, TAT, TF or D-dimer at baseline. In the Rivaroxaban (but not control) arm, changes in EpCAM and TF correlated (Pearson r=0.61, n=12, p=0.04). Change in EpCAM did not correlate with TAT, Ki67 or D-dimer change.

Conclusions: There appears to be a small but significant decrease in EpCAM in response to Rivaroxaban in early breast cancer. EpCAM+ patients have higher plasma TAT, which could indicate increased coagulation caused by CTCs. The correlation between EpCAM and TF in the Rivaroxaban group warrants further investigation.

Table 1.

Marker	EpCAM+ (Mean, 95% CI)	EpCAM- (Mean, 95% CI)	p-value (Mann-Whitney)
TAT (ng/ml)	8.5 (5.1-12.0)	6.3 (4.5-8.2)	0.01
Ki67 (%)	31 (24-39)	24 (21-28)	0.08
D-dimer (ng/ml FEU)	478 (352-604)	469 (377-560)	0.9
TF (pg/ml)	44 (40-49)	41 (39-42)	0.15

PO-51

CHARACTERISATION OF PROCOAGULANT FIBROBLASTS IN THE EARLY BREAST CANCER MICROENVIRONMENT THROUGH *EX VIVO* CULTURE

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Introduction: Mammographic density, reflecting increased fibroblast activity, is a strong independent risk factor for breast cancer. Both cancer-associated fibroblasts (CAFs) and high-density breast tissue have increased alpha smooth muscle actin (α-SMA) and secrete elevated levels of cytokine TGFβ1. Tissue factor (TF) is overexpressed in breast cancer and is correlated with a worse prognosis. We have previously found higher levels of TF expression in DCIS (pre-cancer) fibroblasts compared to normal breast fibroblasts, and even higher TF expression in invasive breast cancer (IBC) fibroblasts.

Aim: To test if: 1. Increased tumour fibroblast procoagulant marker expression and activity, promotes breast cancer progression. 2. High density breast reflects a wound-like stroma (more procoagulant fibroblasts) that promotes breast cancer development.

Materials and Methods: Primary fibroblasts were cultured from 144 fresh breast tissue samples from IBC (n=50), DCIS (n=12), risk reduction mastectomy (n=14) and reduction mammoplasty patients (n=10). Procoagulant (TF) and fibroblast activation marker (α-SMA) expression were assessed by immunocytochemistry. Procoagulant activity of fibroblasts and their conditioned media (CM) were quantified by modified prothrombin time. In fibroblast CM, TF activity and TGFβ1 levels by ELISA were quantified. Migration of MCF-7 breast cancer cells was measured by a migration scratch assay in the presence of fibroblast CM, with and without TF (10H10 antibody) and TGF-β Receptor (SB 431542) inhibitors. Breast density was assessed by BI-RADS.

Results: Fibroblasts were successfully cultured from 108 of 144 samples (75%). TF expression correlated with α-SMA (r=0.61, p=0.009) and procoagulant activity (r=-0.42, p=0.01). In CM, TF and TGFβ1 correlated with CM procoagulant activity (r=-0.51, p<0.0001; r=-0.41, p=0.0001). MCF-7 cell migration, in fibroblast CM, correlated with TF levels (r=0.52, p=0.01). Combined inhibition of both TF and TGF-β receptor inhibited migration and was more effective than either inhibitor alone. There was no difference in procoagulant or fibroblast activation markers between high (BI-RADS C/D) and low (A/B) density patients.

Conclusions: This study provides *ex vivo* functional results showing that fibroblast procoagulant phenotype correlates with fibroblast activation phenotype. Increased fibroblast TF and TGF-β secretion promotes breast cancer cell migration, with combined inhibition a potential therapeutic strategy.

PO-52

CANCER ASSOCIATED THROMBOSIS ALTERS NEUTROPHILS TO PROMOTE PANCREATIC DUCTAL ADENOCARCINOMA PROGRESSION

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Introduction: Cancer-associated thrombosis (CAT) is a marker of poor prognosis with disease progression and increased cancer-related morbidity and mortality. Neutrophils, the most abundant of the innate immune cells, are critical cellular determinants of venous thrombosis. Pancreatic ductal adenocarcinoma (PDAC) is a highly prothrombotic cancer with a poor prognosis.
Aim: Given the increasing appreciation for the role of the innate immune system in CAT as well as in tumor growth, we posited that the cells of the innate immune system, specifically neutrophils are altered in CAT and facilitate tumor growth.
Materials and Methods: C57BL/6J mice receive intra-pancreatic or subcutaneous injection with PAN02 cells to develop pancreatic tumors (PDAC). Venous thrombosis was achieved by (1) complete inferior vena cava (IVC) ligation for IVC thrombosis OR (2) pulmonary thrombosis by intravenous microbead (MB) injection. For cancer associated thrombosis or CAT, 48 hours after the injection of PAN02 cells, animals underwent either IVC ligation OR intravenous MB injection.
Results: 1. PDAC+CAT mice developed significantly larger tumors than only PDAC. 2. PDAC+CAT tumors showed decreased lymphocyte content (CD8 +T cells) in the TME. No difference was noted in neutrophil, macrophage content or angiogenesis. 3. Bone marrows showed decreased CD8+ T cells while spleen showed increase in neutrophils in PDAC+CAT as compared to PDAC mice. 4. Neutrophil depletion mitigated tumor growth in PDAC+CAT mice. Interestingly, tumors in the PDAC mice had increased tumor progression. Macrophage depletion did not alter tumor growth in either group. 5. Transcriptomic analysis of circulating neutrophils showed 210 DEG between PDAC only *versus* PDAC+CAT mice with significant alterations specifically in hypoxia and inflammatory pathways.
Conclusions: Our results are the first to demonstrate that CAT is associated with altered neutrophil activity that affects the TME and facilitates tumor growth. Additionally, CAT is associated with changes in the hematopoietic system evidenced by decreased CD8+ T cells in the bone marrow and increased neutrophil presence in the spleen. Tumor progression in CAT is neutrophil-dependent and is associated with an altered neutrophil transcriptome specifically in the inflammatory and hypoxia-mediated pathways. Ongoing studies are exploring the molecular mechanisms involved in CAT-directed neutrophil alterations and the cellular elements affecting the TME and tumor progression.

PO-53

GLUCOCORTICOIDS AS TRANSCRIPTIONAL REGULATORS OF THE TUMOR COAGULOME OF ORAL SQUAMOUS CELL CARCINOMAS

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Introduction: Oral Squamous Cell Carcinoma (OSCC) are the most frequent type of upper aerodigestive tumors. OSCC are characterized by a specific tumor coagulome, defined by the simultaneous high mRNA expression of the main regulators of coagulation (tissue factor, TF) and fibrinolysis (urokinase-type plasminogen activator, uPA). While the landscape of the human tumor coagulome has been rather well defined, studies adressing its regulation are lacking. Glucocorticoids are stress hormones that are used in clinics as anti-inflammatory drugs.
Aim: We explored the transcriptional regulation of the tumor coagulome of OSCC.
Materials and Methods: Two human OSCC cell lines (PE/CA PJ34 and PE/CA PJ41) were treated with dexamethasone and various agonists of the nuclear receptor family. Using immunoblotting and qPCR, we examined the expression of the core coagulome: TF, uPA and plasminogen activator inhibitor-1 (PAI-1). Data retrieved from The Cancer Genome Atlas (TCGA) and Gene Expression Omnibus (GSE159546, with chromatin immunoprecipitation and RNAseq data for lung cancer cell lines treated with hydrocortisone) were used to examine the effects of glucocorticoids. Functional assays measuring thrombin and uPA activation were also used *in vitro*.
Results: Dexamethasone, a potent agonist of the glucocorticoid receptor (GR), decreased uPA and TF expression, and activated PAI-1 expression. The decrease in uPA and TF expression is most likely explained by an anti-inflammatory signalling effect, as suggested in conditions of TNFα exposure. Conversely, PAI-1 induction was most likely the product of a direct, GR (*NR3C1*)-dependant transcriptional effect. Genomic data from GSE159546 allowed us to confirm and extend our conclusions to a larger array of coagulation-related genes (n=85 from KEGG). Our conclusions were independently validated with a functional analysis examining the activation of thrombin and uPA protease activity *in vitro* in OSCC cells. Finally, we examined the impact of direct PAI-1 regulation on the tumor microenvironment (TME) of OSCC. We observed a TME enriched in fibroblasts, endothelial cells and cells of the monocytic lineage, and a high TGF-β response.
Conclusions: Glucocorticoids exert potent, yet complex, regulatory effects on the expression of essential genes of the coagulome of OSCC. This regulation may be of importance for vascular complications in cancer patients, and it might also account for some of the effects of glucocorticoids on the TME.

PO-54

DESCRIPTION OF CLINICAL AND MOLECULAR FEATURES IN CANCER-ASSOCIATED VENOUS THROMBOEMBOLISM

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Introduction: Venous thromboembolism (VTE) stands as the second preventable cause of mortality in cancer patients and presents substantial challenges in the clinical management of cancer patients due to its impact on morbidity, mortality, and quality of life. Despite advances in understanding and preventing VTE in the cancer setting, gaps persist in our comprehension of this complication.

Aim: This study aims to describe the clinical, pathological, and molecular features of cancer patients with VTE, deepening our understanding of the cancer-thrombosis interplay. We aim to compare these features between VTE and non-VTE patients, identifying risk factors and predictive markers for this complication in oncology.
Matherials and Methods: We conducted a retrospective case-control study encompassing cancer patients diagnosed with VTE between 2022 and 2023 at Vall Hebron Hospital (cases) and cancer patients without VTE treated at the same center (controls). Clinical parameters, including cancer site, stage, pathological/ molecular profile, and treatment modalities, were documented. A univariate analysis was performed to compare cases and controls.
Results: A total of 123 cases and 100 controls were included in the analysis. The clinical characteristics described include age, sex, and Charlson and Khorana scores. According to the Khorana score, 75.41% of VTE cases were at intermediate or high risk for VTE. Female gender demonstrated an association with VTE. Cancer types are also described, with breast and pancreatic cancers exhibiting associations with VTE, while lung, colorectal, and gynecological cancers are not related. The distribution of cancer stages did not show differences between VTE cases and controls. Treatment modalities did not observe differences in cancer stage. Both chemotherapy and targeted therapies were associated with VTE. Regarding the molecular study, the most prevalent cancers among VTE patients were lung (predominantly adenocarcinomas; 13.6% EGFR mutated), breast (mostly invasive ductal carcinoma; 93.3% hormone receptor-positive and 40% HER2-positive), and colorectal cancer (all adenocarcinomas; 40% RAS/BRAF mutated, 13% with microsatellite instability).
Conclusions: The most prevalent cancers among VTE patients were lung (predominantly adenocarcinomas; 13.6% EGFR mutated), breast (mostly invasive ductal carcinoma; 93.3% hormone receptor-positive and 40% HER2-positive), and colorectal cancer (all adenocarcinomas; 40% RAS/BRAF mutated, 13% with microsatellite instability). Female gender, breast cancer, and pancreatic cancer were associated with VTE. Moreover, both chemotherapy and targeted therapies showed associations with VTE.

PO-55

MIR5683 PREDICTS VENOUS THROMBOEMBOLISM IN ADVANCED GASTRIC CANCER THROUGH REGULATION OF FIBRINOLYSIS AND ENDOTHELIAL TFPI EXPRESSION

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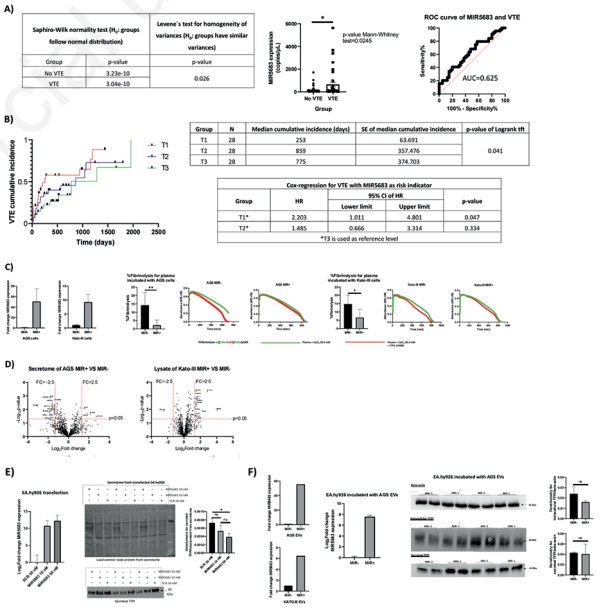
Introduction: Advanced gastric cancer (AGC) is one of the most thrombogenic neoplasms. Previously, we identified the microRNA MIR5683 overexpressed in AGC patients with venous thromboembolism (VTE) by transcriptomics (nested case-control [n=50 *vs* 50] study of patients selected from the AGAMENON registry [n=4000]).
Aim: To validate MIR5683 as a VTE biomarker in a new cohort and to explore the underlying mechanisms.
Materials and Methods: RNA purification from AGC biopsies (n=44 VTE patients *vs* 40 controls). Retrotranscription-preamplification-digital PCR for absolute quantification of MIR5683 expression. Correlation with VTE occurrence by Mann-Whitney test and ROC curve, and with VTE cumulative incidence by Cox-regression. Stable transfection of AGS and Kato-III cells with MIR5683/ empty vector (AGS-MIR+/MIR-, Kato-III-MIR+/MIR). Thrombin generation (TG) and fibrinolytic assays with platelet-poor plasma (PPP) previously incubated with cells. Quantitative proteomics of cell lines. Transient transfection of EA.hy926 cells with miR-5683 mimic and evaluation of TFPI (target according to TargetScanHuman) expression. Isolation of extracellular vesicles (EVs) from stably-transfected cells and incubation with EA.hy926.



Validation of MIR5683 expression as a biomarker for venous thromboembolism in advanced gastric cancer and study of the underlying mechanisms. A) Since the MIR5683 expression data of both patient groups did not follow a normal distribution and lacked homogeneity of variance, we compared MIR5683 expression between both groups of patients by Mann-Whitney test. We also checked the quality of MIR5683 expression as a venous thromboembolism biomarker by calculating the area under the ROC curve. **B)** To analyze the cumulative incidence of venous thromboembolism, we calculated tertiles according to MIR5683 expression data to divide patients into three groups: T1, or the 28 patients with the highest MIR5683 expression, T2, or the next 28 patients according to MIR5683 expression, and T3, or the 28 patients with the lowest MIR5683 expression. We also show the median cumulative incidence for the three groups and the p-value of Logrank test for trends. Finally, by Cox-regression, we obtained the hazard ratio expressing the differential risk of venous thromboembolism when comparing the T1 or T2 group with the T3 group, considered as the reference group for MIR5683 expression. **C)** Comparison of MIR5683 expression (U6 was used as loading control) between gastric cancer cells stably transfected with MIR5683 and empty vector. Fibrinolysis and thrombin generation in platelet-poor plasma incubated with these cells. In the fibrinolysis assay, for each plasma sample we analyze its coagulant or fibrinolytic activities by adding CaCl2 or CaCl2 and recombinant tissue plasminogen activator, respectively. Each graph with elapsed time corresponds to one representative replicate for each condition. **D)** Differentially expressed proteins between gastric cancer cells with MIR5683 and empty vector. From quantitative proteomics, we selected those proteins with |fold change|>2.5 and p-value<0.05. In blue we have highlighted the proteins related to fibrinolysis. We only show secretomes or lysates where we found differentially expressed proteins related to fibrinolysis. **E)** Effect of miR-5683 mimic on secreted TFPI from EA.hy296 cells. We performed transient transfection of two different concentrations of miR-5683 mimic in EA.hy926 cells and then measured secreted TFPI and total secreted protein as a loading control. **F)** Comparison of miR-5683 expression between extracellular vesicles from gastric cancer cells stably transfected with MIR5683 and empty vector. We also show effect of miR-5683 from extracellular vesicles derived from stably transfected AGS cells on TFPI from EA.hy926. We compared miR-5683 expression between EA.hy926 incubated with vesicles from AGS with MIR5683 vector and with vesicles from AGS with empty vector. We then measured secreted and intracellular TFPI from these endothelial cells, as well as beta-actin as a loading control. In all figure sections, the column graphs represent the mean and standard deviation of the different replicates. Significant statistical differences were calculated by unpaired t-test. H_0: null hypothesis; VTE: venous thromboembolism; copies/µL: unit for measuring quantitative expression by digital PCR; AUC: area under the curve; N: number of patients; SE: standard error; tft: test for trends; HR: hazard ratio; CI: confidence interval; MIR-:gastric cancer cells stably transfected with empty vector; MIR+:gastric cancer cells stably transfected with MIR5683 vector; ∑abs: sum of all absorbance points from time=0 to the time when the rTPA curve reaches absorbance=0; rTPA: recombinant tissue plasminogen activator; FC: fold change; p: p-value; SCR: scrambled mimic as negative control for transient transfection; EVs: extracellular vesicles; ns: not significant differences; *: p-value<0.05; **: p-value<0.01.

Figure 1.

Results: MIR5683 expression was significantly higher in VTE patients (p-value=0.025; ROC curve, AUC=0.625) (Figure 1A) and increased VTE risk with a significant hazard ratio (2.203, p-value=0.047) (Figure 1B). MIR5683 overexpression decreased fibrinolysis in PPP incubated with AGS and Kato-III (p-value<0.05) (Figure 1C). In AGS secretome, MIR5683 significantly downregulated MCP and SDC4, profibrinolytic proteins. In Kato-III lysate, MIR5683 significantly upregulated

TSP1, a plasmin inhibitor (Figure 1D). In EA.hy926, miR-5683 transfection reduced secreted TFPI (p-value=0.026) (Figure 1E). MIR-5683 levels were higher in EA.hy926 incubated with EVs from AGS-MIR+ *vs* EVs from AGS-MIR-, and increased miR-5683 levels reduced intracellular and secreted TFPI (Figure 1F). **Conclusions:** MIR5683 was validated as a novel VTE biomarker in AGC patients. These findings could be based on anti-fibrinolyitic effects of this miRNA, but also on its potential remote effect on endothelial TFPI.

PO-56

AAV-MOUSE DNASE I SUSTAINS LONG-TERM DNASE I EXPRESSION *IN VIVO* AND SUPPRESSES BREAST CANCER METASTASIS

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Introduction: Neutrophil extracellular traps (NETs) have been implicated in the pathology of various inflammatory conditions. In cancer, NETs have been demonstrated to induce systemic inflammation and thrombosis, impair peripheral vessel and organ function and promote metastasis. Administration of DNase I is one strategy to eliminate NETs but long-term treatment requires repeated injections and species-specific versions of the enzyme. In mouse models, this is currently limited by the availability of recombinant murine DNase I.
Aim: To enhance administration and therapeutic efficacy of DNase I and to enable long-term DNase I administration in murine cancer models to address potential effects on metastasis.
Materials and Methods: We have developed an adeno-associated virus (AAV) vector system for delivery of murine DNase I and addressed its potential to counteract cancer-associated pathology in the murine MMTV-PyMT model for metastatic mammary carcinoma. The AAV vector is comprised of capsid KP1 and an expression cassette encoding hyperactive murine DNase I (AAV-mDNase I) under the control of a liver-specific promotor.
Results: The AAV-mDNase I vector could support elevated expression and serum activity of murine DNase I over at least eight months. Neutrophil Gelatinase-Associated Lipocalin (NGAL), a biomarker for kidney hypoperfusion that is upregulated in urine from MMTV-PyMT mice, was suppressed in mice receiving AAV-mDNase I compared to an AAV-null control group. Furthermore, the proportion of mice that developed micro- and macro-metastasis was reduced in the AAV-mDNase I group. Moreover, we show that the plasma level of NETs is significantly higher in patients with metastatic breast cancer compared to those with local disease, or those that were considered cured at a 5-year follow-up, confirming NETs as interesting therapeutic targets in metastatic breast cancer.
Conclusions: Altogether, our data indicate that AAV-mDNase I has the potential to reduce cancer-associated impairment of renal function and development of metastasis. We conclude that AAV-mDNase I could represent a promising therapeutic strategy in metastatic breast cancer. We observed US-VTE in patients with CA-SpVT concurrently and subsequent to SpVT, but was not associated with SpVT recurrence, thrombocytopenia or AC. More research is required to understand the interplay of SpVT and US-VTE in patients with cancer.

POSTER SESSION 7
THERAPEUTIC CHALLENGES

PO-57

PERFORMANCE OF ESTABLISHED VTE RISK ASSESSMENT MODELS FOR THE PREDICTION OF ALL-CAUSE MORTALITY IN PATIENTS WITH CANCER – RESULTS FROM A PROSPECTIVE COHORT STUDY

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Introduction: Patients with cancer face a substantial risk of venous thromboembolism (VTE). VTE is also known to be associated with an increased mortality in patients with cancer. To identify patients with cancer at high risk of VTE and to implement effective thromboprophylaxis, several risk assessment models have been developed. Previously, some of them showed predictive ability for all-cause mortality in patients with cancer. However, this was not assessed in cohorts including patients with novel therapies, such as immune checkpoint inhibitors (ICI).
Aim: We aimed to assess the discriminatory performance of five established VTE risk assessment models in predicting all-cause mortality in a prospective observational cohort study including patients with cancer initiating systemic anti-cancer therapies, including ICI therapy.
Materials and Methods: The c-statistics for 6-months mortality risk discrimination of the Khorana, PROTECHT, CONKO, COMPASS-CAT, and the score by Ang Li *et al.* (J Clin Oncol. 2023;41(16):2926-2938.) were calculated.
Results: 625 patients (51% women) with a median age of 61 (interquartile range [IQR]: 52-69) years were included. The most common cancer types were lung (23.8%), breast (12.6%) and pancreatic (9.6%). Anti-cancer therapies initiated after study inclusion were chemotherapy (43.7%), combination of chemotherapy and ICI (17.6%), and ICI monotherapy (15%). At the time of inclusion, 390 (62.3%) patients had metastatic disease. During an observation period of 6 months, 64 patients died (6-month cumulative incidence: 8.9% 95% confidence interval [95% CI: 8.6-9.2]). The discriminatory performance of all five scores was moderate to poor, with the best c-statistic value seen with the Ang Li et al score, while the COMPASS-CAT score showed the lowest AUC value (c-statistics [95% CI]: Khorana: 0.58 [0.50-0.66], PROTECHT: 0.57 [0.49-0.65], CONKO: 0.60 [0.52-0.68], COMPASS-CAT: 0.54 [0.47-0.62], and Ang Li *et al.*: 0.64 [0.57-0.71]; Figure 1).

Conclusions: Five selected VTE risk assessment models showed a moderate to poor performance in predicting all-cause mortality in patients with cancer initiating systemic anti-cancer therapies.

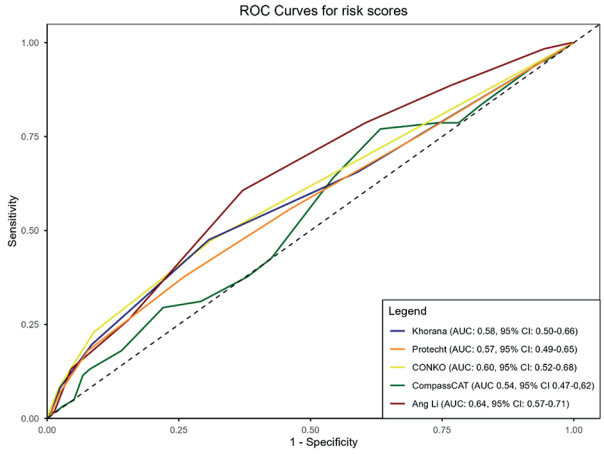

Figure 1.

PO-58

NOT PUBLISHED

PO-59

PATIENTS' EXPERIENCES, VALUES AND PERSPECTIVES ON ANTITHROMBOTIC THERAPY DECISION-MAKING IN ADVANCED CANCER

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Introduction: Patients' experiences, values and perspectives are essential to support decision-making on antithrombotic therapy (ATT) continuation or discontinuation in advanced cancer. However, patients' views remain largely unexplored. This study is a component of SERENITY, a pan-European project to develop a shared decision-making support tool (SDMST).

Aim: To explore patients with advanced cancers' experiences, values and perspectives of decisions about ATT continuation/discontinuation towards the end of life.

Materials and Methods: We conducted semi-structured interviews with patients with advanced cancer receiving ATT in the UK, Denmark, Spain and France. Data were analysed using Framework Analysis.

Results: Sixty patients were interviewed across the four countries (Table 1). Initial findings show that patient perspectives on their role in decision-making about their ATT differed. Some patients expressed a preference not to be involved or informed, while others expressed the decision should be shared, and placed importance on being informed about the decision the clinician has recommended; in addition, some felt they should have the ultimate authority over ATT decisions. Of note, there was little distinction between being informed about the decision and being involved in the decision, and patients had varying understandings of why they were on ATT, which could have affected their ability to engage in decision-making. Some patients expressed more concern about the reason for being on ATT over that of the medication itself, while others did not have a strong opinion about their ATT, deferring to their clinicians' expertise. For some there was a perception that there was no decision to make, either due to the complexities of the choice or that there was no circumstance in which ATT could be deprescribed, and they perceived their ATT as 'lifesaving'. Patients showed higher acceptance with continuing their ATT, either as normal, as a reduced dose, or changing to another ATT medication, over stopping ATT; they felt ATT medication was the "least of their troubles".

Conclusions: It is evident that patient views on decision-making about ATT varies and there are different influences on their ability to engage in the decision making. Development of an SDSMT could represent an opportunity to address patients' concerns about ATT indication and cater for the varied preferences and perspectives about involvement in decision-making.

Table 1.

Characteristic	Patients n=60
Male, n (%)	28 (47)
ATT, indication	
CAT	26 (44)
Atrial fibrillation	6 (10)
Ischaemic heart disease	11 (18)
Stroke (+/- AF)	3 (5)
Heart Valve	2 (3)
Multiple ATT indications	12 (20)
Age	
45-54	6 (10)
55-64	9 (15)
65-74	24 (40)
75-84	17 (28)
85+	4 (7)
Time on ATT	
Under 1 year	20 (33)
1-5 years	20 (33)
Over 5 years	20 (33)
ATT	
DOAC	24 (40)
LMWH	17 (28)
Antiplatelets	16 (27)
VKA	1(2)
Dual antithrombotic therapy	2 (3)

ATT: Antithrombotic therapy

PO-60

CLINICIANS' VIEWS AND EXPERIENCES OF ANTITHROMBOTIC THERAPY DECISION MAKING IN ADVANCED CANCER

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Introduction: The decision to continue or deprescribe antithrombotic therapy (ATT) in patients with advanced cancer is highly challenging, given the competing risks and benefits near the end of life. Clinicians' views and experiences of ATT decision making are essential for optimising ATT management. This study is a component of the pan-European SERENITY study, aimed at developing a shared decision-making support tool for ATT management.

Aim: To explore clinicians' experiences and perspectives of decisions about ATT continuation/deprescription in cancer patients near the end of life.

Materials and Methods: Semi-structured interviews were conducted with clinicians of varying specialties and fields of work, involved in ATT management across the UK, Denmark, Spain and France. Framework Analysis was used to analyse these data.

Results: Seventy-seven clinicians were interviewed across the 4 countries (Table 1). Clinicians' perceptions of roles (their own and others) in ATT decision making varied significantly. In the context of cancer and ATT near the end of life, participants revealed an extra layer of complexity in decision-making. This encompassed competing risk-benefit considerations and varying perceptions regarding responsibilities and appropriate timing for decision-making. Some medical specialties including palliative clinicians and general practitioners were more comfortable with taking on the decision of deprescribing ATT, while others were less prone to consider ATT deprescription as they were not the initial prescriber. Clinicians showed higher preference for considering medication adjustments to deprescribing ATT, including reducing doses and changing ATT medication. ATT deprescription was described as complex, with a variety of factors to consider, such as the specific ATT indication, the lack of evidence base to support the decision and difficulty establishing the optimal time for deprescription. Due to the complexity of the decision, clinicians placed significant value on the perspectives and preferences of patients in the decision-making process.

Conclusions: Clinicians' experiences and perspectives on ATT decision-making highlight the complex nature of ATT management. Understanding and clarifying roles and responsibilities is essential to ensuring active decisions about ATT management near the end of life. The multiple, competing factors influencing the decision in the context of cancer and ATT near the end of life is a significant challenge.

Table 1.

Characteristic	Clinicians n = 77
Male, n (%)	41 (53)
Antithrombotic affiliated specialists, n (%)	28 (36)
Cardiology	7 (9)
Neurology	4 (6)
Vascular medicine/surgeon	8 (10)
Respiratory/Pneumologist	6 (8)
Internal medicine	3 (4)
Cancer specialities, n (%)	14 (18)
Oncology	8 (10)
Haematology	6 (8)
Advanced disease care, n (%)	35 (46)
Palliative	10 (13)
Palliative nurse	8 (10)
General Practitioner (GP)	10 (13)
Geriatrician	7 (9)

ATT: Antithrombotic therapy

PO-61

LONG TERM VENOUS THROMBOEMBOLIC COMPLICATIONS IN CANCER PATIENTS WITH COVID-19 INFECTION

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Introduction: Several studies have highlighted the association between COVID-19 infection and venous thromboembolism (VTE). Nevertheless, limited research has been conducted on patients with active cancer and the impact of COVID infection on their long term venous thromboembolic risk.

Aim: Our objective was to identify clinical factors associated with VTE events following COVID-19 infection on patients with active cancer at MD Anderson Cancer Center.

Materials and Methods: A retrospective longitudinal study was conducted. The analyzed population included adults with active cancer and confirmed first COVID-19 infection (2020 through 2022) requiring hospital admission, and who were not taking any therapeutic anticoagulant therapy before. Demographic and clinical variables were reviewed: age, gender, ethnicity, race, body mass index (BMI), obesity status, COVID-19 vaccine status, cancer type, tumor stage, type of cancer therapy and its disease control before admission, Eastern Cooperative Oncology Group (ECOG) status, use of aspirin and remdesivir during hospital admission, prior lung and cardiovascular disease, and diabetes and

hypertension status. Additionally, admission to the Intensive Care Unit (ICU) and the use of mechanical ventilation during hospitalization were assessed. Clinical outcomes were deep venous thrombosis and pulmonary embolism within the following 6 months after admission for COVID-19 infection. Obtained data was further analyzed to determine the incidence of VTE and if there were correlations between VTE outcomes and clinical factors (Table 1).

Results: A total of 357 patients were included in the analysis. We found that the incidence of VTE within 6 months following admission was 6.7%. Amongst clinical factors, the history of hypertension showed significant association (p=0.02) with VTE outcome, however, it lost its significance (p=0.053) on multivariate analysis. Furthermore, the use of immune check point inhibitors for cancer (p=0.09) presented a tendency towards developing VTE.

Conclusions: Even though we only found hypertension as an associated factor to VTE, further investigation is needed to address the risk of VTE in cancer patients with severe illness from COVID-19 infection. Exploring other associated factors (*e.g.*, biomarkers) may help identify strategies to mitigate VTE risk in that population.

Table 1.

Characteristic	Categories	
Age (years)	Median, IQR	61, [52-72]
Sex	Female	158 (47.1)
Race	American Indian or Alaska Native	4 (1.1)
	Asian	17 (4.8)
	Black or African American	53 (14.8)
	White or Caucasian	220 (61.6)
	Other	59 (16.5)
	Unknown	4 (1.1)
Ethnicity	Hispanic or Latino	108 (30.3)
	Not Hispanic or Latino	241 (67.5)
	Unknown	8 (2.3)
Body mass index	Median, IQR	28.6, [25.2-38.9]
Obesity	Yes	137 (38.4)
COVID-19 Vaccine*	Yes	35 (9.8)
Chemotherapy before admission	Yes	137 (38.4)
Immunotherapy before admission	Yes	17 (4.8)
Tumor Type	Hematological	193 (54.1)
	Solid	163 (45.7)
	Both	1 (.3)
Metastatic disease¥	Yes	77 (21.6)
ECOG	0	83 (23.2)
	1	146 (40.9)
	2	63 (17.6)
	3	29 (8.1)
	4	6 (1.7)
Use of aspirin	Yes	113 (31.7)
Use of remdesivir	Yes	206 (57.7)
Prior Lung Disease	Yes	108 (30.3)
Prior Cardiovascular Disease	Yes	159 (44.5)
Diabetes	Yes	174 (48.7)
Hypertension	Yes	275 (77)
Mechanical ventilation	Yes	17 (4.8)
ICU	Yes	130 (36.4)

*COVID-19 vaccination received prior to date of hospital admission

PO-62

CATHETER-RELATED THROMBOSIS *VS* FIBROBLASTIC SLEEVE. INCIDENCE AND IMPACT IN ONCOLOGICAL AND HEMATOLOGICAL PATIENTS WITH PERIPHERALLY INSERTED CENTRAL CATHETER

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Introduction: Oncohematological patients often implant peripherally inserted central venous catheters (PICC). Associated complications are thrombosis and fibroblastic sleeve. Their correct discrimination can be difficult, as they are similar on ultrasound, but the management is completely different, with thrombosis alone requiring anticoagulant therapy. Few studies have investigated their incidence.

Aim: In a cohort of oncohematological patients with PICC, we evaluated the incidence of catheter-related thrombosis (CRT) and fibroblastic sleeve (FS) at 7-10 and 28-30 days.

Materials and Methods: We enrolled 45 patients. We also correlated the results with the type of oncological or hematologic disease.

Results: FS was identified in 11 patients (24.4%): 6 at 7-10 days (13.3%) and 5 at 28-30 days (11.1%); 5 patients (45.6%) had gastrointestinal cancer, 2 (18.1%) had airways cancer and 4 had breast cancer (36.3%). CRT was identified in 5 patients (11.1%): 3 at 7-10 days (60.0%) and 2 at 28-30 days (40.0%); 3 patients had gastrointestinal cancer (60.0%), 1 (20%) gynecological cancer and 1 (20%) onco-hematological disease. 3 thromboses were asymptomatic (60.0%). At the limits of significance (p-value 0.069) the relationship between vein diameter and development of fibroblastic sleeve/thrombosis (OR 5.29, 95% CI: 1.25 - 53.55). Statistically significant (p-value 0.039) the relationship between the timing of the complication and the platelets count (OR 1.03, 95% CI: 1.01 – 1.08).

Conclusions: FS is frequent (24.4%), but asymptomatic, in oncological and hematological patients. Less frequent (11.1%), but with significant consequences, is CRT. Discrimination between them is clinically relevant as almost one in four patients could undergo unnecessary anticoagulant therapy, with consequent waste of resources and potential serious side effects. Incidence of asymptomatic thrombosis (4.4%) leads us to underline how about one patient out of twenty may undergo an unacknowledged venous thrombosis with significant consequences.

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PO-63

HEMOSTASIS AND THROMBOSIS CONSULTATIONS AT A CANCER DEDICATED INSTITUTION: A SIX-MONTH EXPERIENCE

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Introduction: Thrombosis and bleeding are common and undesirable occurrences in cancer patients. Around 10% of people with both solid tumors and hematologic neoplasms die due to bleeding and up to 20% develop thrombosis during follow-up, which represents the second cause of mortality in this population. Precise diagnosis of hemostasis disturbances can be complex, as well as the management of thrombosis in cancer patients, who possess at

the same time bleeding and recurrence risks. To face these challenges sometimes a multiprofessional team with expertise in thrombosis and hemostasis is needed.
Aim: The aim of this study is to describe the reasons and analyze the impact of specialized consultations on thrombosis and hemostasis at an institution dedicated to cancer care during 6 months.
Materials and Methods: Retrospective longitudinal cohort study. Data were collected from medical records at an electronic platform (TASY®). All requests of a specialized opinion received by the Hematology - Thrombosis and Hemostasis team (H-TH) from December 1, 2017 to May 5, 2018 were included. Criteria applied to analyze the consultations were: relationship between the number of requests to H-TH *versus* the total amount of requests to the Hematology team, specialty of origin, reason for the request, number of solved requests, completed diagnosis, treatment and additional recommendations.
Results: During the study interval, a total of 130 consultations were performed by the Hematology team at the institution, 71 (54,6%) by H-TH. The majority of them came from Oncology (23), the Emergency Department (13) and the Gastrointestinal Surgery team (8). Other requests came from Gynecology, Intensive Care Unit and Head and Neck Surgery teams (4 requests each one), Vascular Surgery, Orthopedics, Urology and Mastology (3 requests each one), Neurosurgery (2) and the Pain Control team (1). From 24 consultations requested to clarify the diagnosis (17 due to altered coagulation tests and 7 due to thrombocytopenia), 71,8% were successful. Regarding requests for treatment doubts (23 on coagulation management, 12 on thrombosis, 7 on perioperative management and 5 due to bleeding), 98,5% were clarified during the hospitalization period. Follow-up time varied from 1 to 25 days, (mean of 6 days) and more than 50% of the patients were referred to the outpatient clinic on Thrombosis and Hemostasis after discharge.
Conclusions: The amount of requests on thrombosis and hemostasis issues in cancer patients showed to be relevant compared to general hematological requests as well as resolutive. This can justify the presence of hemostasis and thrombosis experts in cancer hospitals.

PO-64

PATTERNS OF VENOUS THROMBOEMBOLIC EVENTS AND THEIR CLINICAL IMPLICATIONS IN PATIENTS WITH NEUROENDOCRINE NEOPLASMS

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Introduction: Venous thromboembolism (VTE) is a significant concern in oncology, but research on its incidence and management in neuroendocrine neoplasms (NENs) is limited. While some studies estimate the incidence of VTE in this population to be around 7.5%, the lack of evidence from large and representative datasets has left gaps in our understanding of this phenomenon.
Aim: To address this knowledge gap by comprehensively analyzing the incidence and treatment of VTE in patients with NENs. We conducted a detailed analysis of a cohort of consecutive patients with gastroenteropancreatic (GEP) and thoracic NENs treated at our institution from 2017 to 2022.
Materials and Methods: Consecutive patients with GEP and thoracic NENs treated at our institution during the aforementioned study period were selected to assess the incidence of cancer-related VTE. Thrombotic events were classified as visceral (splenic, portal, and mesenteric thrombosis) and non-visceral (pulmonary embolism, deep vein thrombosis, catheter-associated thrombosis, and other etiologies). Information on patients' clinical characteristics, follow-up, and VTE treatment was collected.
Results: A total of 771 patients were included in the analysis, with 72 episodes of cancer-related VTE reported, accounting for 9.3% of the cohort. Of these episodes, 42 (58.3%) were classified as visceral VTE, and 30 (41.6%) as non-visceral VTE. Significant differences in clinical characteristics between the two groups were observed, as detailed in the provided univariate analysis in Table 1. In the univariate analysis, patients with non-visceral VTE presented more symptomatic episodes (53.3% *vs* 0%; p 0.001), and higher proportion of lung primary NEN (16.7% *vs* 2.4%; p 0.031). On the other hand, patients with visceral VTE were asymptomatic (100% *vs* 46.7%; p 0.001), younger (60 *vs* 69 years; p 0.01), pancreatic primary (76.2% *vs* 43.3%; p 0.005) and did not start anticoagulant therapy (71.4% *vs* 6.7%; p 0.001). Additionally, a subset of patients with visceral VTE developed portal hypertension as a complication, especially in pancreatic tumors, underscoring the severity of these events (19% *vs* 0%; p 0.02, compared with non-visceral VTE).
Conclusions: In conclusion, this study highlights the clinical significance of VTE in patients with neuroendocrine neoplasms, with an incidence of 9.3%. The findings underscore the predominance of visceral VTE (58%), especially in pancreatic tumors, and suggest the need to consider anticoagulant therapy in all cases. These findings provide crucial insights for the understanding and optimal management of VTE in patients with NENs.

Table 1.

	All VTE (n=72)	Visceral VTE (n=42)	Non-visceral VTE (n=30)	Visceral vs Non-Visceral
Sex (male)	49 (68,1%)	27 (64,3%)	22 (73,3%)	P 0,417
Age	64,32	60,93	69,07	P 0,01
VTE	20 (27,8%)	-	20 (66,7%)	
TEP	3 (4,1%)	-	3 (10%)	
TVP	2 (2,8%)	-	2 (6,7%)	
Catheter	23 (31,9%)	23 (54,8%)	-	
Splenic	6 (8,3%)	6 (14,3%)	-	
Mesenteric	13 (18,1%)	13 (30,9%)	-	
Portal				
Symptoms	56 (77,8%)	42% (100%)	14 (46,7%)	P 0,001
Incidental	16 (22,2%)	0	16 (53,3%)	P 0,001
Symptomatic				
Anticoagulant therapy	37 (51,4%)	11 (26,2%)	26 (86,7%)	P 0,072
LMWH*	3 (4,2%)	1 (2,4%)	2 (6,7%)	P 0,417
Other	32 (44,4%)	30 (71,4%)	2 (6,7%)	P 0,001
No treatment				
Primary NEN	6 (8,3%)	2 (4,8%)	4 (13,3%)	P 0,195
Unknown	6 (8,3%)	1 (2,4%)	5 (16,7%)	P 0,031
Pulmonary	10 (13,9%)	4 (9,5%)	6 (20%)	P 0,205
Small intestine	45 (62,5%)	32 (76,2%)	13 (43,3%)	P 0,005
Pancreatic				
NEN Grade	37 (56,9%)	18 (47,7%)	19 (70,4%)	P 0,065
G1-G2	28 (43,1%)	20 (52,3%)	8 (29,6%)	P 0,064
NET G3-NEC				

PO-65

CANCER-ASSOCIATED THROMBOEMBOLISM (CAT) RISK FACTORS AS WELL AS FRAILTY PREDICT IMMUNOTHERAPY-ASSOCIATED VENOUS THROMBOEMBOLISM (IAT) IN PATIENTS WITH NON-SMALL CELL LUNG CANCER (NSCLC)

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Introduction: There is limited knowledge about specific risk factors predisposing to immune checkpoint inhibitor (ICI)-associated VTE, also among patients with lung cancer despite a decade of ICI FDA approvals.
Aim: Therefore, we assessed CAT risk factors and frailty to predict ICI-associated VTE (IAT).
Materials and Methods: The association of VTE (PE or DVT) with detailed a priori selected known CAT risk factors, baseline patient characteristics, Khorana Score, other laboratory values, as well as VA Frailty Index assessed in NSCLC diagnosed between 2015-2019 and starting ICI therapy in a well-curated, retrospective, observational cohort study in the Veterans Affairs healthcare system (VA). A new VTE diagnosis was assessed starting 72 hours after ICI start (index date) until 6 months post index date. VTE was defined either PE, DVT, or splanchnic VTE requiring anticoagulation, while excluding superficial VTE. Cancer therapy is categorized into ICI-only therapy (single ICI N=1073; or dual ICI therapy N=11) *versus* ICI-chemotherapy combinations (N=373). The association between risk factors and VTE was assessed in a Fine-Gray competing risk model to adjust for the competing risk of death.
Results: 77 (5.3%) patients experienced a VTE by 6-months. For the total population, median age was 69 (range 36-97); 1,398 (96%) men; 257 (18%) Black race; 1,167 (80.1) Caucasian; 33 (2.2%) other race or ethnicity. The competing risk VTE multivariable modeling identified the following independent risk factors (adjustment included Khorana Score): ICI-chemotherapy HR=1.80 (95% CI: 1.10-2.94) and severe frailty HR= 2.62 (95% CI: 1.19-5.77). Khorana Score, recent hospitalization, as well as non-VTE conditions requiring aspirin or anticoagulation use (DOAC, warfarin) were associated with a limited increased risk for VTE without statistical significance. In the absence of frailty adjustment, comorbidities also predict for IAT risk, likely contributing to frailty's predictive ability.
Conclusions: We confirmed the following risk factors for ICI-associated VTE (IAT) that are independent from Khorana Score in a large NSCLC cohort: ICI-chemotherapy combination therapy, and newly identified severe frailty. Confirmed VTE risk factors and associated prediction models improve personalized thromboprophylaxis strategies and may enable IAT prevention trials in higher-risk populations.

POSTER SESSION 8
BIOMARKERS/ HYPERCOAGULABILITY II

PO-66

PLASMA KININOGEN LEVELS PREDICT DEVELOPMENT OF VENOUS THROMBOSIS IN CANCER PATIENTS: ANALYSIS OF SAMPLES FROM THE CASSINI STUDY

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Introduction: The contact activation system is not required for normal hemostasis but may contribute to pathologic thrombosis. Cleaved kininogen (cHK) is a useful biomarker for activation of the contact system in plasma, and we have shown that elevated levels of cHK are present in most patients with cancer as well as in tumor-bearing mice.
Aim: To determine whether levels of plasma kininogen (HK) or cleaved kininogen predict thrombosis in prospectively collected plasma samples from patients in the Cassini study, which included 818 patients undergoing cancer therapy randomized to rivaroxaban or placebo.
Materials and Methods: Plasma samples from Cassini patients with a negative compression ultrasound and Khorana score ≥2 were collected prior to randomization. Levels of HK and cHK from patients who developed VTE during the study (n=61) were analyzed using a nested case-control design in which each VTE samples was time-matched to two samples from patients without VTE. Samples were also matched by sex, age group, and pancreatic or non-pancreatic cancer. Seven plasma samples from normal individuals without cancer were used as controls. Results were divided into quartiles and the Wilcoxon rank-sum test was used to compare the first, median and third quartiles in the VTE and no VTE groups compared to the normal plasma. HK and cHK levels were measured using the Protein Simple WES immunoassay system, using calibration standards for each run to assure reproducibility.
Results: There were no significant differences in age, sex, BMI, Khorana score, or percent of patients with pancreatic cancer in the VTE *vs* matched no VTE groups. When compared to the normal plasma samples, levels of HK in cancer patients (N=168) were significantly lower (P=0.034). Though there was not a significant difference in levels of cHK (P=0.240), the ratio of cHK/HK was significantly higher in patients with cancer (P=0.016). However, when analyzing time to development of VTE using a conditional logit approach with strata by match group to estimate VTE hazard ratios, only levels of HK showed a significant negative association with VTE risk (0.69 per SD increase, Z statistic -2.26, P=0.024).
Conclusions: Despite increased levels of cHK and increased cHK/HK ratio in cancer patients *versus* controls, using the WES analytical method, only low levels of HK were found to be predictive of VTE in the Cassini study.

PO-67

ERYTROCYTE-RELATED PARAMETERS IN RELATION TO CANCER DIAGNOSIS: A CASE-COHORT STUDY OF HEALTHY SUBJECTS

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Introduction: Abnormal erythrocyte parameters, *i.e.* red blood cell distribution width (RDW) and mean corpuscular volume (MCV), are associated with various diseases (*i.e.* ineffective erythropoiesis, cardiovascular disease, venous thromboembolism, inflammation and cancer).

Aim: In healthy subjects' Italian study, we wanted to evaluate the predictive value of MCV and RDW of cancer diagnosis and understand the possible influence of lifestyle habits on these parameters.
Materials and Methods: In a large prospective cohort of 10,261 blood donors of the HYPERCAN Study (enrolled 2012-2022), a case-cohort study was designed comparing 286 cancer cases with 848 randomly selected controls. A lifestyle questionnaire was administered at study entry (*i.e.* alcohol intake, smoking habits, and sport practice). Clinical, hematological, and biochemical data were collected together with blood samples at baseline and after 6-12 months. Analyses were performed with the SPSS Statistics version 21.0 software.
Results: In the whole cohort, MCV and RDW were in the normal range values, (MCV=87.3fL, range 81-94; RDW=13%, range 12-14). A multivariate analysis, controlled for age, gender, and lifestyle habits showed a negative correlation between MCV and RDW values (beta=-0.356, p <0.001). In the group of males, higher MCV values were significantly associated with smoking habit. Among cancer cases, the most common tumor site was prostate (25%) in males, and breast cancer (37%) in females. By multivariate regression analysis corrected for age and gender, both MCV (OR 1.083; 95% CI:1.008-1.164; p=0.029) and RDW (OR 1.378; 95% CI:1.132-1.676; p=0.001) were significantly associated with subsequent cancer diagnosis. In particular, having RDW >13.45% and MCV >87.75fL significantly predicted cancer diagnosis (OR 1.839; 95% CI:1.153-2.931; p=0.011). A multivariate analysis according to gender displayed a significant positive association between MCV and prostate cancer diagnosis (p=0.027), and between RDW and breast cancer diagnosis (p=0.014).
Conclusions: Our data suggest a potential utility of erythrocyte-related parameters in early cancer diagnosis. Furthermore, the positive association between MCV and smoking habits emphasizes the importance of healthy lifestyle in cancer prevention.

PO-68

NETS BIOMARKERS IN WOMEN WITH ENDOMETRIAL AND CERVICAL CANCER

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Introduction: Initially discovered as a mechanism to protect the host from pathogens and prevent the spread of infection from the inflammatory site, neutrophil extracellular traps (NETs) have been implicated in the progression of other conditions such as autoimmune diseases, diabetes and cancer.
Aim: The aim of our work was to establish the role of NETs in cancer patients, and to determine their effect on tumor progression and the risk of thrombosis in patients with endometrial and cancer cancer.
Materials and Methods: The study included 96 patients with endometrial cancer and cervical cancer Grade 1 and Grade 2 aged 28 to 49 years (average age 45 years) with a verified histomorphological diagnosis of adenocarcinoma: endometrial cancer (group I, n=73) and cervical cancer (group II, n=23). The control group consisted of 60 healthy women without a complicated gynecological, oncological and thrombotic history. All patients were tested for level of myeloperoxidase (MPO) and citrullinated histone (CitH3), the neutrophil/lymphocyte ratio (NLR), as well as for interleukin-1β (IL-1β).
Results: When analyzing NETs markers depending on Grade 1 or 2, significant differences were revealed for MPO level, IL-1β and NLR in group I (p <0.001, p <0.001, p=0.002, respectively) (Figure 1). No differences were found for CitH3. When analyzing the content of the MRO, IL-1β level in blood plasma depending on Grade 1 or 2 cervical cancer, we found statistically significant differences (p=0.007, p=0.003, respectively) (Figure 1). No differences were found for CitH3 and NLR.
Conclusions: The results of the study show that NETs components such as MPO, citH3, IL-1β and NLR reflect the potential role of inflammation and NETs in many aspects of cancer. Laboratory biomarkers such as MRO, IL-1β and NLR were significantly more often elevated in patients with Grade 2 oncological pathology compared with Grade 1.

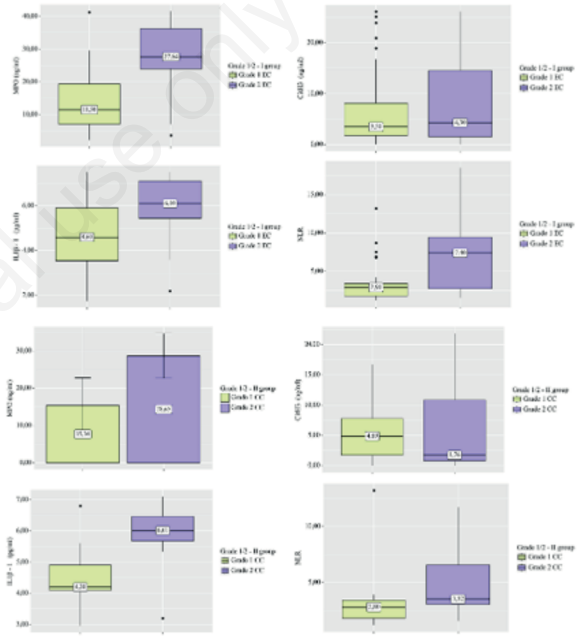

Figure 1. Boxplots for MPO, IL-1β, CitH3 and NLR in patients with endometrial cancer (EC) and cervical cancer (CC).

PO-69

MARKERS OF COAGULOPATHY IN MULTIPLE MYELOMA

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Introduction: Multiple myeloma (MM) is a plasma cell neoplasm characterized by clonal proliferation and accumulation of neoplastic cells and osteolytic skeletal involvement. Some of hemostasis disorders are attributed to M-Ig interactions with blood clotting factors (acquired von Willebrand's disease, acquired hemophilia A or deficits of other coagulation factors, circulating anticoagulant, hyperviscosity, amyloidosis and lupus anticoagulant) or with platelets (acquired thrombocytopathy), and also M-Ig-in-

dependent effects (thrombocytopenia, other thrombocytopathies, DIC, immobility and hypercalcaemia).
Aim: The aim of our work is to detect abnormalities of coagulation in patients in with newly diagnosed MM suitable for intensiv chemotherapy - depending on the activity of the disease, which predispose patients to thrombotic and bleeding complication, respectively, in MM. TGT is a global coagulation assai that measures the global capacity of blood plasma to form thrombin. Several clinical studies have shown that increased TG in platelet poor plasma (PPP) predicts an increased risk of (recurrent) VTE.
Materials and Methods: We included 189 patients with newly diagnosed multiple myeloma in this study. Patients with MM were examined by coagulation tests for detecting both bleeding and thrombotic tendency with following coagulation tests: PT, APTT, TT, fibrinogen, antithrombin, D-dimers, levels of coagulation factors (II, V, VII, X, VIII, IX, XI and XII), vWF, lupus anticoagulant, protein C, protein S, resistance to activated protein C and trombin generation assai modified with activated protein C. We also monitored plasma cell counts and serum M-Ig levels in these patients.
Results: We detected low level of vWF 25/189 (13,2%), high level of D-dimers 94/189 (49,7%), positive lupus antikoagulant 31/189 (16,2%), elevated level of FVIII 69/189 (36,5%). All markers were evaluated (average value, standard deviation) to the disease aktivity defined by the paraprotein level and a number of plasma cells (cytology analysis), respectively. A signifiant correlation was found between D-dimers and M-Ig quantity (p=0.0031), D-dimers and plasma cells number (p=0.0006), between vWF *vs* M-Ig quantity (p=0.0053). No correlation was found between vWF and plasma cells number (p=0.42), which is interesting. Correlations of vWF *vs* M-Ig quantity can predict bleeding conditions, however our ambition is to detect markers of thrombotic risk as well. For this purpose, we examined the modified TGT, which identified thrombotic pathology in eight cases (15%), while genetically determined thrombophilias were detected in only 3% of patients.
Conclusions: In newly diagnosed patients with MM, were commend increased attention to the level of D-dimers and vWF, especially in patients with higher disease activity according to M-Ig quantity in order to estimate possible bleeding or thrombotic complications and modified TGT for thrombotic complication, for which long term observation is needed.

PO-70

THROMBUS CHARACTERISTICS (COMPOSITION AND RESPONSE TO *IN VITRO* THROMBOLYSIS) AND PLASMA BIOMARKERS IN CANCER-RELATED ACUTE ISCHEMIC STROKE

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Introduction: Acute ischemic stroke (AIS) is a significant complication of cancer, often associated with a poor prognosis. AIS can also be the first manifestation of an occult cancer. The etiology of cancer-related AIS is frequently unknown, suggesting cancer-specific pathophysiological mechanisms that remain not clearly understood.
Aim: We aimed to identify the characteristics of thrombi from patients diagnosed with a cancer-related-AIS and to investigate plasma biomarkers associated with the presence of cancer during AIS.
Materials and Methods: AIS patients who underwent endovascular thrombectomy between January 2019 and December 2022 and who had both thrombus and citrate plasma samples available in the compoCLOT study were eligible. We retrospectively included patients with cancer-related-AIS (cancer group, n=11) with either nonbacterial thrombotic endocarditis (NBTE) or no other etiology identified. As a control group, we included patients without any history of cancer who experienced either cardio-embolic AIS (CE, n=23) or large artery atherosclerosis AIS (LAA, n=21), matched by age and sex to the cancer group.
Results: Thrombi were subjected to *ex vivo* thrombolysis in the presence of tissue-type plasminogen activator and plasminogen and analyzed by immunohistology or immunoassay to assess their composition. Thrombi from the cancer and CE groups were more resistant to lysis than thrombi from LAA group (median thrombus weight conservation 86 and 43 *vs* 8%, p=0.0006 and 0.006, respectively). Resistance to lysis was correlated positively with DNA content (r=0.75, p<0.0001) and negatively with red blood cell content (r=-0.66, p<0,0001). Within the cancer group, we identified a sub-group of white thrombi (n=5) that were poor in red blood cells but rich in platelets and Von Willebrand factor. Of note, all thrombi from NBTE (n=3) were in this sub-group. Plasma levels of D-dimer (D-Di), microvesicle-associated tissue factor (MV-TF) and myeloperoxidase (MPO) were higher in patients with cancer-related-AIS compared to patients without cancer, ie, patients pooled from CE and LAA groups (17350 *vs* 2040 ng/mL, 23 *vs* 9 fM and 48 *vs* 25pg/mL, p=0.02, 0.03 and 0.01, respectively). Levels of D-Di and MV-FT were especially elevated in plasma associated with white thrombi.
Conclusions: Thrombi from cancer-related AIS were more resistant to lysis, with an increased DNA content, when compared to LAA ones, but presented similar features (composition, sensitivity to lysis) to CE ones. The identification of a sub-group of white thrombi with similar characteristics, including all NBTE thrombi, suggests that the remaining thrombi within this group are associated with undiagnosed NBTE. Further prospective studies are required to assess the relevance of plasma biomarkers such as D-Di, MV-FT and MPO to identify patients with cancer- related AIS.

PO-71

CLINICAL SIGNIFICANCE OF IDENTIFYING ADAMTS13 AND VWF AS A HIGH-RISK FACTOR FOR THROMBOSIS IN GYNECOLOGICAL CANCER PATIENTS

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Introduction: A number of studies have shown that cancer patients have relatively higher levels of vWF and lower levels of ADAMTS13, and the dependence of this trend on the degree of cancer spread has been described. However, a clear relationship between the level and activity of ADAMTS13 and the risk of thrombotic complications has not been confirmed.
Aim: To substantiate the clinical significance of determining the level of ADAMTS13 and vWF in the blood in gynecological cancer patients with a high risk of developing thrombotic complications.
Materials and Methods: Group I consisted of 48 patients: 23

with ovarian cancer, 11 with adenocarcinoma of the cervical canal and 14 with breast cancer, who had a history of episodes of VTE. Group II consisted of 60 women: 20 with ovarian cancer, 20 with adenocarcinoma and 20 with breast cancer, in whom no clinically significant thrombotic complications were noted. The control group consisted of 25 women without malignant neoplasms. All patients had the level and activity of ADAMTS13 and vWF determined.

Results: In I group, the level of ADAMTS13 and its activity were significantly lower than those of II group and the control. During chemotherapy, there was a further decrease in both the level and activity of ADAMTS13. During polychemotherapy, the vWF level increased in both groups I and II and was significantly higher than the control group. In most patients, ADAMTS13 and vWF were within the reference values. For this purpose, an integral indicator was calculated - the ratio vWF/ADAMTS13. Noteworthy are the significant differences in the ratio of VWF and ADAMTS13 in groups I and II: 1.56 and 0.98, respectively, which significantly increased during chemotherapy: to 1.94 and 1.1, compared with the control group 0. 65.

Conclusions: The greatest prognostic significance for the development of thrombotic complications is the determination not of the activity of VWF or ADAMTS13 separately, but rather the ratio, which was confirmed in our study, VWF/ADAMTS13, which further increases during chemotherapy treatment. When vWF levels increase, even normal and subnormal ADAMTS13 levels and activity will not be able to sufficiently compensate for the increased vWF activity. It is the VWF/ADAMTS13 ratio, the imbalance of which occurs in cancer patients, that serves as one of the main prognostic factors for thrombotic complications.

PO-72

PLATELET PROTEOMIC PROFILING REVEALS MEDIATORS OF THROMBOSIS AND PROTEOSTASIS IN PATIENTS WITH MYELOPROLIFERATIVE NEOPLASMS

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Introduction: Myeloproliferative neoplasms (MPN) are characterised by myeloid proliferation and thrombocytosis. Patients with polycythemia vera (PV) and essential thrombocythemia (ET) have an increased risk of thrombosis and progression to myelofibrosis and/or acute leukaemia. While vascular risk is highest around the time of initial diagnosis, it remains elevated despite cytoreductive/anti-thrombotic therapy and represents the predominant source of early mortality and morbidity. There is emerging evidence that platelets are phenotypically distinct in multiple disease states, playing critical roles in a myriad of biological processes. However, the contribution of the platelet proteome to pathologic sequalae in MPN has yet to be fully elucidated.

Aim: We aimed to describe the untargeted platelet proteomic profile from a large clinical cohort of chronically treated ET and PV patients.

Materials and Methods: Platelet samples from patients with an established diagnosis of MPN (ET, n= 59; PV, n= 41) and healthy controls (n= 40) were recruited from the Mater Misericordiae University Hospital, Dublin, Ireland and the Papa Giovanni XXIII Hospital, Bergamo, Italy. Platelets were isolated from whole blood to generate platelet lysate. Differential proteomic signatures were established using label-free quantification (LFQ) mass spectrometry (MS). Identified peptides were searched using MaxQuant and bioinformatic analysis was performed using R.

Results: We evaluated the platelet proteome in 100 patients receiving treatment (anti-platelet/cytoreductive) for an established diagnosis of PV/ET and 40 healthy controls. 227 and 166 proteins significantly differentially expressed (false discovery rate <0.05; fold change >1.5) in ET & PV respectively. Mediators of inflammation were upregulated such as LGALS1 and MMP1. Effectors of platelet pro-coagulant activity were overexpressed in MPN including FcγRIIA and HSP47. Functional analysis of platelets using gene set enrichment demonstrated that proteins from the MTOR signalling pathway and unfolded protein response were enriched in PV & ET cohorts.

Conclusions: We describe the untargeted proteomic profile of platelets from a large clinical MPN cohort. In keeping with the observation that vascular risk remains elevated amongst chronically treated patients, we highlight the predominance of thromboinflammatory mediators in this group and demonstrate evidence of an altered platelet proteome despite standard therapy.

PO-73

NETOSIS IN GYNECOLOGICAL CANCER PATIENTS DURING ANTITUMOR THERAPY

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Introduction: Tumor cells secrete a large number of cytokines, which contribute to the development and maintenance of a chronic pro-inflammatory state and trigger the formation of extracellular neutrophil traps (NETs), which are part of the pathogenesis of both thrombosis and tumor growth. The dynamic changes in the formation of NETs during antitumor therapy, as well as the influence of anticoagulants and anti-inflammatory agents on them, have been poorly studied.

Aim: To determine the severity of NETosis reactions in gynecological cancer patients against the background of antitumor therapy, as well as the effect of LMWH and anti-inflammatory therapy (aspirin) on NETosis.

Materials and Methods: From 2019 to 2023, the study included 262 patients with neoplasms of the female reproductive system (uterine cancer (81), adenocarcinoma of the cervix (15), ovarian cancer (85) and breast cancer (81)), hospitalized for antitumor therapy. For all patients, blood was drawn four times: before the start of therapy, 14 days after surgery or the end of the 2nd course of chemotherapy, and also after the 4th and 6th courses. The studied parameters were NETosis markers (MPO antigen, Cit-H3 histone).
Results: The concentration of NETosis markers in cancer patients (citH3 1.78±1.03 ng/ml ($p<0.05$), MPO:Ag 15.97±11.83 ng/ml ($p<0.05$)) was initially significant increased compared to the control group. The severity of thromboinflammation before the start of therapy was higher, the higher the stage of the disease. 14 days after the 2nd course of chemotherapy, an increase in the concentration of both citH3 (2.46±1.24 ng/ml ($p=0.0001$)) and MPO:Ag (22.76±7.31 ng/ml ($p= 0.0001$)). 2 weeks after the 4th course of chemotherapy in the subgroup of patients (n=25) who used LMWH there was a significant decrease in the concentration of both markers of NETosis (CitH3 histone 1.35±0.36 ng/ml, MPO:Ag 17, 54±3.29 ng/ml, $p<0.05$). In the subgroup of patients taking LMWH+aspirin (n=28), a significant decrease in the concentration of NETosis markers was also noted (CitH3 1.15±0.36 ng/ml, MPO 15.12±4.28 ng/ml, p<0, 05).
Conclusions: Activation of NETosis occurs in all gynecological cancer patients at the start of antitumor therapy. Chemotherapy, compared to surgical treatment, leads to a more pronounced activation of NETosis. LMWH effectively reduces the severity of NETosis.

PO-74

AGEING AS SHARED RISK FACTOR FOR CANCER AND CARDIOVASCULAR DISEASE: THE IMPACT OF CANCER ON VASCULAR REMODELING

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Introduction: During (arterial) ageing, the risk of cancer and cardiovascular disease increases significantly. This is attributed to changes in vascular remodeling, *i.e.* changes in morphology, proliferation, and migration of vascular smooth muscle cells (VSMCs). This results in a reduction in elasticity of the vessel wall and an impaired ability to control blood flow and pressure. Furthermore, anti-cancer therapy is known to influence cardiovascular remodeling, while the direct effect of cancer itself is largely unknown.
Aim: To investigate the influence of human breast cancer cell conditioned media on ageing in iPSC induced-VSMCs (iVSMCs) phenotype.
Materials and Methods: iVSMCs were cultured as either young iVSMCs (P<13) or aged iVSMCs (P>30). For conditioned media, human breast cancer cells, BT474, were cultured in culture media (DMEM, 10% FBS, 1% P/S) for 24h. First, iVSMC phenotype was investigated by characterisation of several smooth muscle cells markers, including α-smooth muscle actin (α-SMA) and calponin. iVSMC proliferation and calcification was measured using impedance measurements (xCELLigence) and Biohybrid (Fetuin-A-AF546), respectively, after exposure to control or conditioned media (both at 1.8 and 4.8 mM Ca2+) over a period of 4 days.
Results: iVSMC phenotype was confirmed by characterization of smooth muscle markers α-SMA, p-myosin light chain (p-MLC), calponin, smooth muscle 22 α and S100A4. Aged iVSMCs show a significant decrease in α-SMA levels ($p=0.016$) and proliferation ($p=0.017$) compared to young iVSMCs. While young and aged iVSMCs exposed to conditioned media with 4.8 mM Ca2+ showed a significant decrease in proliferation (young iVSMCs $p=0.026$; aged iVSMCs $p=0.031$), vascular calcification was increased, as compared to control medium. Interestingly, aged iVSMCs exposed to conditioned media with 1.8 mM Ca2+ showed a lower proliferation rate ($p=0.001$) compared to young iVSMCs, while no difference could be detected for vascular calcification.
Conclusions: iVSMCs are a good model to investigate the effects of ageing on proliferation and vascular calcification *in vitro*. Furthermore, human breast cancer cells' conditioned media has a significant impact on ageing in iVSMCs, *i.e.* proliferation and vascular remodeling. Further research is needed to unravel the interactions between breast cancer and vascular remodeling.