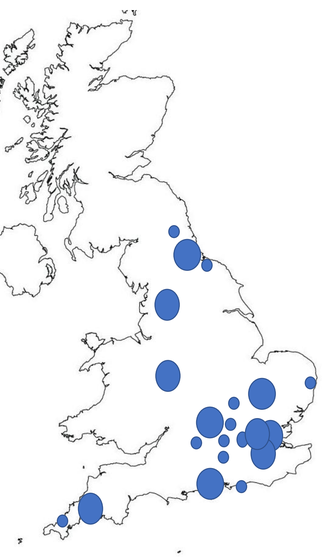
CAVEaT a multicentre audit of venous thrombosis in patients with haematological malignancy and thrombocytopenia.

Authors: S. Booth[1], The HaemSTAR Network[2], J. Grant-Casey[3],M. Desborough[4], H. Emms[5], N. Curry[1], S. Stanworth[6],[7]
[1] Dept. Haematology, Oxford University Hospitals, Oxford; [2]The HaemSTAR Network, UK; [3]National Comparative Audit of Blood Transfusion, NHS Blood and Transplant, Oxford; [4] Dept. Haematology, Guy's and St Thomas's NHS Foundation Trust; [5]St George's University Hospitals NHS Foundation Trust, London; [6]NHS Blood and Transplant; [7]Radcliffe Department of Medicine, University of Oxford, Oxford, UK
Correspondence: CAEVaT@nhsbt.nhs.uk Further information: http://haemstar.org/caveat

Venous Thrombosis (VTE) in patients with malignancy and thrombocytopenia is uncommon but presents a complex management situation with high rates of thrombosis recurrence and risk of bleeding[1]. There is highly variable use of platelet transfusion. The British Society for Haematology and International Society on Thrombosis and Haemostasis (ISTH) have issued guidance, whilst accepting very limited data to inform optimal management[2,3]. In order to better document UK practice, the CAVEaT (**C**ancer **A**ssociated **V**enous thrombosis **a**nd **T**hrombocytopenia) multicentre audit has been established in collaboration with the HaemSTAR network of Haematology trainees and NHS Blood and Transplant (fFig1). We present interim data from the first 16 months.

Fig 1: Centres participating in CAVEaT



Methods

Consecutive patients with haematological malignancy, platelets < 50 x 10^9/L and VTE within 28 days were identified prospectively by the local haematology team at participating sites. Anonymised and routinely available data were collected at entry, 4 weeks and 12 weeks from VTE. Prompts to confirm the numbers of cases were issued every fortnight in view of the low incidence.

Key outcomes included the percentage of patients managed according to strategies recommended by the ISTH or BSH, or other strategies; mortality; bleeding (major bleeding or clinically relevant non-major bleeding); Thrombosis progression or recurrence; platelet transfusions given; number of inpatient days; and IVC filter placement.
Participating sites are required to register the project through local clinical governance processes before submitting cases.

Results:

Baseline characteristics

Key baseline characteristics are shown in Table 2. 64 were symptomatic and 14 incidentally diagnosed thromboses. 41 of the thromboses with catheter associated. 2 patients had a history of COVID-19 infection, 8 patients had received asparaginase and 14 had recent bleeding which was judged to affect the management of the thrombosis.

Table 2: Baseline Characteristics (N = 78)

Median age		64 years	Setting at diagnosis:		
Gender:	Male	N = 45	Inpatient		64
	Female	N = 33	Outpatient		14
Median platelet count:		34 x 10^9/L	Site of Thrombosis:		
Haematological malignancy:				Pulmonary Embolus	18
	Acute Leukaemia / MDS	48		Proximal Lower Limb DVT	12
	MPD/CML	2		Internal Jugular Vein	2
	Aggressive NHL	13		Upper Limb	35
	Indolent NHL / CLL	10		Subsegmental PE	4
	Myeloma	5		Other	7

Management strategies

Acute thrombosis management strategies were reviewed and categorised as shown in Table 1. Approaches were: 1 – as per BSH guidance or ISTH guidance for high risk thrombosis (all thrombosis excluding line associated upper limb and subsegmental pulmonary embolism (PE)); 2 – similar to (1) but with a less stringent platelet transfusion threshold of 25 - 30 x 10^9/L; 3 – as per ISTH guidance for low risk thromboses (catheter-associated upper limb or subsegmental PE; Unfractionated heparin; DOACs; No anticoagulant.

Table1: Anticoagulation and Platelet transfusion strategy groups.

Strategy label	Definition
ISTH High risk / BSH	Platelet transfusion threshold 40 - 50 x 10^9/L LMWH continued unless Platelets < 25 x 10^9/L LMWH either full dose or dose adjusted.
Platelet threshold 20-30	Platelet transfusion threshold 25 - 30 x 10^9/L LMWH continued unless Platelets < 25-30 x 10^9/L LMWH either full dose or dose adjusted.
ISTH Low risk	Platelet transfusion threshold ≤ 10^9/L LMWH dose reduced if Platelets ≤ 40 - 50 x 10^9/L LMWH withheld if Platelets ≤ 25 x 10^9/L
UFH	Platelet transfusion threshold 40 – 50 x 10^9/L Managed with UFH
DOAC	DOAC used Any Platelet transfusion threshold.
No anticoagulant	Thrombosis managed without anticoagulation

Follow up:

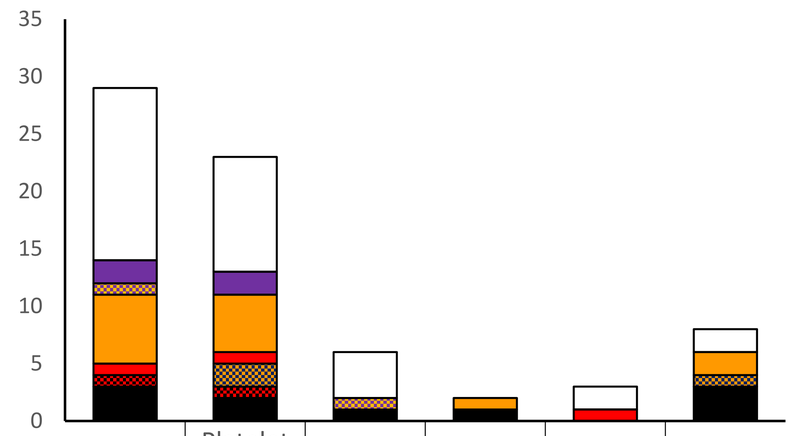
At the time of writing 78 patients were registered; one month follow up was available for 69 patients and 3 month follow up for 46.

Outcomes

Strategies recommended by the ISTH or BSH were used in 33 of 78 (42%) patients. Key clinical outcomes are presented in Figure 2 according to management strategy.

Fig 2: Clinical outcomes of thrombosis in patients with haematological malignancy and thrombocytopenia.

Definitions:
ISTH International Society for Haemostasis and Thrombosis; BSH British Society for Haematology; UFH unfractionated heparin; DOAC direct acting oral anticoagulant; CRNMB clinically relevant non-major bleeding



	ISTH High risk/BSH	Platelet transfusion threshold 25-30	ISTH Low risk	UFH	DOAC	No anti-coagulant
No events	15	10	4		2	2
Thrombosis Progression / Recurrence	2	2				
CRNMB and Thrombosis Progression / Recurrence	1		1			
CRNMB	6	5		1		2
Major Bleeding	1	1			1	
CRNMB and Death		2				1
Major Bleeding and Death	1	1				
Death	3	2	1	1		3

The median platelet units transfused in the first month was 6 (range 0-53), with lower platelet usage in the subsequent 2 months (median 1, range 0-20). Median inpatient days was 31%. IVC filters were placed in 2 patients: removal of both was planned but had not occurred.

The results demonstrate substantial variation in practice and high risks of adverse outcomes in this group with at least one of clinically relevant or major bleeding, thrombosis progression or recurrence or death affecting 52% of patients in the cohort.

Conclusion

These preliminary data from the CAVEaT audit project demonstrate substantial variation in practice, with significant morbidity and mortality in this group of patients with cancer associated thrombosis and thrombocytopenia. We plan to continue to a target of a total of 100 patients. This is clearly an area of need for research given the disappointing outcomes and our ambition is to establish a more formal registry as a platform for comparing intervention strategies.

Sites wishing to join the project as it continues should contact CAVEaT@nhsbt.nhs.uk.

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Contributors:

Cambridge University Hospitals: Mary Dunne; Barts Health Sophie Todd; Buckinghamshire Healthcare Renu Riat; Epsom & St Helier Corinne de Lord; Great Western Hospital Sarah Green; Guy's and St Thomas's Hospitals Andrew Doyle; Hampshire Hospitals Ana Carvalhosa; James Paget Hospital Ceclia Gyansah; King's College Hospital, Manu Wimalachandra; Milton Keynes University Hospital Sarah Davis; Newcastle Hospitals Lier Pickard, Alexander Langridge; Queen Alexandra Hospital, Portsmouth Maya Rajinder Raj; Royal Berkshire Hospital Ayesha Ejaz, Elissa Dhillon; Royal Cornwall Hospital, Sarah Challenor; Sunderland Royal Hospital Shika Chattree; University Hospitals Birmingham Pip Nicolson, Pip Nicolson, Raghav Syal, Gillian Lowe; Derriford Hospital, Nicky Crosbie, Kelly Holton; University Hospital Southampton Izabela James; Wexham Park Hospital John Willan, Nicky Gray Lakshmi Pillai.

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