Anti-thrombotics in patients with thrombocytopenia (and cancer)

MUMC+ Vascular Rounds, Roermond, Nov 2017

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- Hematology Institute, Rabin Medical Center, Petah Tikva, Israel
Disclosure potential conflicts of interest:  Avi Leader

<table>
<thead>
<tr>
<th>Geen (potentiële) belangenverstrengeling</th>
<th>I have no conflicts of interest to declare</th>
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<td>Voor bijeenkomst mogelijk relevante relaties:</td>
<td>Bedrijfsnamen</td>
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<tr>
<td>• Sponsoring of onderzoeksgeld</td>
<td>NA</td>
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<td>• Honorarium of andere (financiële) vergoeding</td>
<td>NA</td>
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<td>• Aandeelhouder</td>
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<td>• Andere relatie, namelijk ...</td>
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Agenda

• Background
  – Bleeding Risk Factors in Thrombocytopenic Cancer Patients (but no AC)
  – Anticoagulation in non-thrombocytopenic cancer patients

• Antithrombotic medication in thrombocytopenic patients
  – Management guidelines
  – Literature review
  – Knowledge gaps
  – Why do we do what we do?
    • Results of a multinational decision-making analysis

• Ongoing research: MATTER study (multinational registry)

• Take Home Messages
Laboratory predictors of bleeding and the effect of platelet and RBC transfusions on bleeding outcomes in the PLADO trial

• Degree of (severe) TCP is not clearly associated with bleeding
  – Other factors may contribute: *cause of TCP, medications, infection*

• Bleeding risk may be related to low HCT and coagulation abnormalities.

• Platelet transfusion (<10 x 10^9/L) are used prophylactically to *reduce clinically significant* bleeding

• **Secondary (Post-hoc) analysis of patients enrolled in the PLADO trial**
  – >1200 patients with TCP d/t chemotherapy for malignancy or stem cell transplant
  – PLADO = RCT assessing different prophylactic (PLT<10) platelet transfusion doses.
  – Daily monitoring of **WHO bleeding, Daily HCT, Hb, Platelet count**
  – aPTT, INR and fibrinogen at baseline and whenever else taken
  – **Follow-up 30 days** after first transfusion.

*Uhl, Blood 2017*
Association between morning platelet count and grade ≥2A bleeding by stratum
Result Summary

- The following lab parameters were associated with increased bleeding:
  - PLT < 5 \times 10^9/L (≥2A; but not ≥grade 3) – compared to >80
  - HCT < 25% (both) – compared to HCT >29%
  - INR > 1.2 (both)
  - aPTT > 30 seconds (≥2A; but not ≥grade 3)

- Platelet count, HCT and treatment stratum remained significant predictors of bleeding (≥2A) in a multi-predictor model (1).
  - Only HCT<25% associated with grade ≥3

- In model 2, INR and aPTT are added: only stratum, aPTT and INR are significant.

- More bleeding with ALLO than AUTO / CHEMO
- Platelet and RBC transfusions on days of bleeding were not sufficient to change bleeding outcomes the next day.
Discussion

• Observation of <HCT and bleeding is consistent with animal models
  – Interpret with care as RBC transfusion qualifies as grade 3 bleeding.

• Findings support investigating a risk adapted approach.

• Limitations:
  – Limited clinical data (i.e. confounders)
  – No effect of RBC and PLT Tx on bleeding could be because of **confounding by indication**.
  – **Timing of bleeding events not recorded** – don’t know if before or after transfusion
  – **Limited numbers of grade 3-4 bleeding**
  – No coagulation tests required after enrollment. May explain why findings of coagulation contradict the ATHENA findings (estcourt BJH, 2014).
    • The association between physician ordered tests and bleeding may simply reflect the team’s assessment of current bleeding which led to the test being done.
Anticoagulation in non-TCP cancer patients with VTE

LMWH is standard of care. WHY?

**CLOT study:** benefit with LMWH over warfarin in VTE

- RCT of dalteparin vs VKA for 6 months
  - Patients with solid tumors and VTE
    - Reduced recurrent VTE in dalteparin group (primary EP)
      - 9% vs 17% at 6 months (0.48; P=0.002)
    - Bleeding similar
    - Initial 6 mo. Analysis for all subgroups showed similar results

Lee, NEJM 2003
CATCH RCT: tinzaparin vs warfarin

- Full dose tinzaparin throughout study
- Included ~10% hematologic malignancies
- rec VTE in 7.2% of LMWH, and 10.5% of warfarin (p=0.07)

Bleeding
- Same major bleeding
- Less minor with tinzaparin (HR 0.58)
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• Take Home Messages
• **ISTH SSC**\(^1\) GL’s for cancer associated thrombosis (CAT)
  
  • 50% **dose-reduction** or prophylactic doses of LMWH when PLT < 50 \( \times \) \(10^9\)/L but > 25 \( \times \) \(10^9\)/L

• **Discontinuation** of AC when PLT < 25 \( \times \) \(10^9\)/L

• **In the acute setting:** **platelet transfusions** to enable full-dose anticoagulation. IVC filters may be considered

• Data (and guidelines\(^1,2\)) strictly on LMWH (mostly) in the VTE setting

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1. **Common problem in cancer patients**
   - 45% (!!) of 197 thrombocytopenic cancer patients were receiving antiplatelet and/or anticoagulant therapy in a prospective cohort.\(^1\)

2. **Prolonged chemoRx-induced thrombocytopenia does not provide protection** against VTE.\(^2\)
   - 34% of VTEs occurred with PLT $< 50K$.
   - 13% when PLT $< 20K$.

3. **Bleeding is a problem**
   - In HSCT, VTE is 3-fold less common than clinically significant bleeding.\(^3\)

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Antithrombotic Rx in Thrombocytopenia & Cancer

• Complex and uncertain management
  Anticoagulation
  – Practice guidelines (venous thromboembolism) based on expert opinion
  – Variance in reported practice\(^2,^3\) (e.g. platelet tranfusion; holding/reducing dose)
  – Suggestive supportive data on safety of dose reduction\(^4,^5\) and withholding Rx\(^6\)

Antiplatelet medication
  – Continuing aspirin in acute myocardial infarction and thrombocytopenia was associated with improved survival\(^7\).

• What are the management strategies?
• What is the risk of bleeding / thrombosis with each strategy?

\(^2\)Samuelson, Thromb Res 2016; \(^3\)Chayaler, Transfusion 2014; \(^4\)Khanal ; Am J Hem, 2016; \(^5\)Mantha, J Thromb Thrombolysis, 2017; \(^6\)Li, Blood Adv 2017; \(^7\)Feher, Oncologist 2017
### Table 1: Summary of estimates of bleeding and thrombosis in thrombocytopenic (Plt<50K) cancer patients receiving anticoagulation

<table>
<thead>
<tr>
<th>Population</th>
<th>AC management</th>
<th>Bleeding</th>
<th>Recurrent Thrombosis</th>
</tr>
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<tbody>
<tr>
<td></td>
<td></td>
<td>Major</td>
<td>Clinically Relevant</td>
</tr>
<tr>
<td>HM^2 and acute or prior VTE^a (N=78)</td>
<td></td>
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<tr>
<td><strong>Composite</strong> bleeding and thrombosis was 29% (13/45) if AC Continued, vs. 18% (6/33) if stopped. (IRR 1.83, 95% CI 0.65–5.86) at 100 days from TCP.</td>
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</table>

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<tr>
<td><strong>HM^2 and acute or prior VTE^a (N=47)^c</strong></td>
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<td></td>
<td>19%</td>
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<tr>
<td></td>
<td>18%</td>
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<td></td>
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<tr>
<td>Any cancer, prior VTE and at least 7 days Plt&lt;50K (n=140)^d</td>
<td>77%</td>
<td></td>
<td></td>
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<tr>
<td></td>
<td>18%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Leukemia &amp; ac. VTE (n=74)^e</td>
<td>31%</td>
<td></td>
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</tr>
</tbody>
</table>

Platelet transfusions not without risk in these patients

- 83 patients with acute VTE and plt < 50 x 10^9 (or transfused for ≥ 50x10^9) within 30 days
  - Retrospective chart review | 30 day follow-up.
  - 88% had a platelet transfusion threshold of ≥ 50x10^9

- 9% new/progressive thrombosis | 37% bleeding events (grade 2 or more) | 11% grade 3-4
- **13% had transfusion reactions. 37% volume overload** requiring diuretics or dialysis.

- Patients who experienced a platelet count below 50,000 for > 5 days had higher rates of minor (Grade 2) bleeding, but not major bleeding.
  - Most Grade 2-4 bleeding occurred with counts above 50 (median 54)

- Negative effects potentially related to transfusions
  - Transfusion reactions and volume overload
  - Early discontinuation of AC due to difficulty adhering to goal.

Samuelson Bannow, J Thr Thrombolysis, 2017
Antiplatelet Rx & thrombocytopenia

- Retrospective review of records at MSKCC (2015-2014)
  - Hematological malignancy with AMI

- Two groups based on counts at 1 wk after index AMI
  - Plt > 50K vs Plt < 50 K
  - Plt < 50K subdivided according to aspirin administration profiles

- N = 118. 49% had severe thrombocytopenia (sTP, plt<50K)
  - sTP pts were younger and had myeloid leukemia more often
  - CV risk profile and medication was similar
  - sTP pts were tachycardic, lower Hb, higher troponin
  - sTP less likely to receive aspirin (43% vs 83%, p<0.001), thienopyridines and statins
  - sTP had Higher proportion of platelet transfusions (79% vs 13%)
Patients with sTP who received aspirin had a **median survival of 96 days**, compared with **17.5 days** in patients who did not receive aspirin (HR, 0.44; 95% CI, 0.24–0.81).
Among patients with acute leukemia, acute MI and Plt<50K:

- **Bleeding:**
  - 19% (11/58) major bleeding (BARC 3a-c) overall.
    - 16% (4/25) with aspirin and 21% (7/33) without.
    - Median FU = 3.7 yrs !!!

- **Thrombotic risk**
  - 6.9% (4/58) chance of recurrent MI
    - 8% with aspirin vs. 6.1% without
Antiplatelet Rx & thrombocytopenia

- sTP patients have worse clinical outcomes as previously shown

- The concerns for bleeding at these plt counts are not supported by scientific evidence, here and previously.  
  
  Friedmann, Transfus Med Rev 2002

- We don’t know how the platelet transfusions affected this and what the threshold should be

- Most patients had Plt > 30K.
  - Results not valid for lower counts

Conclusion

- Treatment of AMI with aspirin in patients with hematologic malignancies and sTP is associated with improved survival without increase in major bleeding
Anti-thrombotics in TCP: No practicing changing data, but:

- Maybe OK to withhold AC in patients with remote VTE (>3 months to be on safe side) who have thrombocytopenia post autoHSCT

- Risk of rec. thrombosis & maj. bleeding is from 0% to 15% & > 20%, respectively.
  - Data difficult to comprehend. But definitely there is a clinical problem.

- Relationship between bleeding, platelet count and AC is complex and nonlinear.
  - Platelet threshold/count were not predictive of bleeding in AutoSCT (Cr, bilirubin and PT were)
  - High rate of AEs associated with a platelet transfusion threshold of $50 \times 10^9$/L i.

- Continue using your institutional platelet transfusion thresholds
  - but use clinical logic and remember evidence is weak

- Should tend to continue aspirin in acute Mi
  - Data mainly for plt > $30 \times 10^9$

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a) Li, Blood advances 2017; b) Samuelson-Bannow, J Thr thrombolysis 2017; c) Feher, Oncologist 2017
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- **Ongoing research**: MATTER study (multinational registry)

- **Take Home Messages**
Knowledge gaps for anti-thrombotics in TCP

• Many of the previous studies are not longitudinal and don’t give you insight into the dynamics of management – measure lab parameters only during bleeding or at diagnosis

• No data on antiplatelet drugs, non-LMWH anticoagulation or non-VTE anticoagulation indications

• Retrospective

Unmet need for knowledge on management of antithrombotic therapy and associated bleeding and thrombosis outcomes among cancer patients with thrombocytopenia.
Factors Influencing Management of Anticoagulation in Thrombocytopenic Patients with Hematological Malignancy

• Leader A, ten Cate V, ten Cate-Hoek A, Beckers E, Spectre G, Raanani P, Schouten H, Falanga A, ten Cate H.
• ASH annual conference 2017, Poster presentation #1106

Objectives

1) Identify the patient and physician characteristics associated with anticoagulation (AC) management strategies in TCP patients with hematological malignancy

2) Evaluate whether a physician assessment of bleeding and thrombotic risk is associated with AC management.
Methods (1)

• Case vignette study in a multinational and multicenter setting

1. **Semi-structured interviews** with 11 hematologists and thrombosis & hemostasis (T&H) specialists in Israel and the Netherlands
   – “Which patient variables influence management of AC in this scenario?”

2. **Patient variables were refined** based upon the number of interviewees selecting a given option

3. **5 selected attributes with 2-5 levels each** were then entered into an algorithm creating a balanced & reduced design from a full factorial model
<table>
<thead>
<tr>
<th>Attribute (i.e. Risk factor category)</th>
<th>Level 1</th>
<th>Level 2</th>
<th>Level 3</th>
<th>Level 4</th>
<th>Level 5</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hematological malignancy and treatment²</td>
<td>• Diffuse large B cell lymphoma • R-CHOP treatment</td>
<td>• ALL • Asparaginase-based intensive chemotherapy</td>
<td>• AML • High dose Cytarabine consolidation</td>
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</tr>
<tr>
<td>Depth of Thrombocytopenia</td>
<td>40,000/μL</td>
<td>20,000/μL</td>
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<tr>
<td>Indication and type of antithrombotic regimen³</td>
<td>• Atrial fibrillation; CHA₂DS₂-VASC = 2 • AC only</td>
<td>• Atrial fibrillation; CHA₂DS₂-VASC = 6 • AC only</td>
<td>• Symptomatic upper extremity catheter-related DVT • AC only</td>
<td>• Symptomatic PE • AC only</td>
<td>• Symptomatic PE • AC • Aspirin treatment (due ischemic stroke 4 months earlier)</td>
</tr>
<tr>
<td>Time since the antithrombotic indication-defining event</td>
<td>6 months</td>
<td>2 months</td>
<td>2 weeks</td>
<td></td>
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</tr>
<tr>
<td>Major GI bleeding from an unidentified source (no bleeding since)</td>
<td>Never</td>
<td>4 months earlier</td>
<td>3 weeks earlier</td>
<td></td>
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<tr>
<td>Case constants which are identical in all case vignettes</td>
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<tr>
<td>Age</td>
<td>50 years</td>
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<td>Sex</td>
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<td>Renal Function</td>
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<td>DIC</td>
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</tr>
<tr>
<td>Surgery</td>
<td>None</td>
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<tr>
<td>AC dose</td>
<td>Full dose</td>
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<tr>
<td>Indication for antithrombotic treatment upon revision?</td>
<td>Yes</td>
<td></td>
<td></td>
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</tbody>
</table>

¹ Anticoagulation only or anticoagulation combined with aspirin
² This risk factor links 2 other risk factors: 1) Duration of thrombocytopenia, represented by type of disease and treatment; 2) Additional thrombotic risk with certain drugs
³ This risk factor links 2 other risk factors: 1) Type of antithrombotic treatment; 2) Indication for antithrombotic treatment

AC, anticoagulation; ALL, Acute lymphoblastic leukemia; AML, Acute myeloid leukemia; DIC, Disseminated intravascular coagulation; DVT, deep vein thrombosis; GI, gastrointestinal; PE, pulmonary embolism; R-CHOP, rituximab cyclophosphamide doxorubicin vincristine prednisone; STEMI, ST-Elevation myocardial infarction
4. The model generated **30 clinical cases of TCP patients with different patient variable combinations**

5. **Each responder received 5 AC case vignettes** and had to choose:

   1) no change in AC
   2) no change in AC but transfuse platelets
   3) hold AC
   4) modify AC (i.e. AC class/dose).

6. The survey was then **re-piloted**, designed as a **website** and **distributed** via mailing lists to national hematology and T&H societies in **Israel, the Netherlands and Italy** (N=886).
Management was split into 3 steps, each with a choice between 2 options.

In multivariate analysis, mixed effects binomial logistic regression models:
- Calculated OR’s for using a specific strategy (over the other) for each patient / physician variable in comparison to their respective reference variables.

Random slopes were calculated for thrombosis risk perceived by each physician. (i.e. by-subject analysis to account for repeated measures)
- These were incorporated in the mixed effects model.
Results (1)

- **168 responders**, in Italy (59), Israel (52), the Netherlands (47) and other countries (10), answering **774 unique cases**.
  - 18% (158/886) of population directly contacted, **responded**.
  - Median **professional experience of 15 years** [IQR=17]
  - Estimated median of **5 patients** [IQR 8] with AC and TCP **per month**.

- **AC modification** was made by **84%** (141/168) of unique responders **at least once**.
  - AC was **held by 55%** (93/168)
  - No change **with** platelet transfusion = 37% (62/168)
  - 42% (71/168) no change **without** platelet transfusion
**22% HOLD (n=167)**

Lower platelets of 20,000/µL (vs. 40,000/µL); prior major GI bleeding (vs. none) and management (vs. fellow)

**78% CONTINUE (n=607)**

Higher risk AC indications (vs. AF; CHA2DS2-VASc = 2); more yrs of experience; expertise in transfusion medicine

**18% NO CHANGE (n=110)**

**24% No change but Transfuse PLTs (n=119)**

Lower platelet counts of 20,000/µL (vs. 40,000/µL); symptomatic PE, AC only (vs. AF; CHA2DS2-VASc = 2); Dutch physicians (vs. Israeli)

**82% INTERVENE (n=497)**

Lower platelet counts of 20,000/µL (vs. 40,000/µL); higher risk AC indications (vs. AF; CHA2DS2-VASc = 2)

**76% MODIFY (n=378)**

Italian physicians (vs. Israeli)

*Physician-assessed risk on a scale of 1-10 (1 = lowest risk; 10 = highest) for a given case.*
Conclusions on decision making analysis

- **Modifying** AC type or dose was the **most frequent** management action in TCP.
- **Physician-assessed bleeding risk is a universal driver** of management, at all 3 steps, while thrombotic risk only affects continuing AC over holding.

- **Degree of TCP** is the only variable pervasively associated with management, **in line with current guidelines**.
- **Prior major bleeding** and **various indications for AC** are variables not represented in current guidelines.
  - This could mean that physicians do not consider this component.

- **Significant variations in management** between individual physicians and countries.

- Suggests **oversimplification by current guidelines**, reflecting the need for high-quality prospective data on this high-risk group.

- **Current findings are hypothesis-generating**, and must be assessed in **prospective studies** evaluating the clinical relevance of these components of the decision making process.
  - If I were to plan a prospective study I would evaluate these factors.....
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• Take Home Messages
Management patterns of AntiThrombotics and outcomes in patients with hematological malignancy and Thrombocytopenia: a Prospective Registry

MATTER study

PI: Dr Avi Leader¹,²; Collaborators: Dr Erik Beckers¹, Prof dr Harry Schouten¹, Dr Yvonne Henskens¹, Prof. dr. Anna Falanga³, Dr Galia Spectre², Dr Arina ten Cate-Hoek¹, Prof. dr. Hugo ten Cate¹

¹ Maastricht University Medical Center, Maastricht, the Netherlands; ² Rabin Medical Center, Petah Tikva, Israel; ³ Hospital Papa Giovanni XXIII, Bergamo, Italy
MATTER registry: Study Design

**Objective:** Evaluate management and frequency of bleeding and thrombosis, in patients with hem malignancy, thrombocytopenia & antithrombotic Rx.

**Main Study Questions**
1. What is the platelet threshold at which antithrombotic Rx is held or continued at baseline?

2. Calculate the RR of bleeding or thrombosis with continuing antithrombotic therapy vs. holding therapy

**Current Study Status:** Initiation in Dec 2017

**Design:** Prospective multinational cohort study (clinicaltrials.gov: NCT03288441)

**Study population:** Patients admitted to the inpatient hematology department or outpatient clinic
Study Concept

Risk Factors
- Bleeding
- Thrombosis
- General
- Outcome-specific

Antithrombotic Rx Management
- Physician characteristics
- Physician risk assessment
- Management decisions

Outcomes
- Arterial and Venous thrombosis
- Major bleeding
**Inclusion Criteria** (all three)

1. Hematological malignancies (including MDS)
   - With or without active treatment
   - Irrespective of treatment line and disease status
   - Both inpatients and outpatients

2. Current or predicted disease or treatment-related thrombocytopenia (<50 X 10⁹/L) of any duration.

3. Current antiplatelet and/or anticoagulant treatment
   - Any indication. Any Duration
   - At screening (even if stopped at that stage)

**Exclusion Criteria:**

1. Previous thrombocytopenia (<50 X 10⁹/L) with the current antithrombotic regimen;
2. HIT/TTP/ITP
**Data Collection Overview**

**At Inclusion¹:**
- Chronic (reference) antithrombotic medication and indications
- General clinical variables
- Malignancy-related data
- Bleeding-related variables

**At Study Index²:**
- *Record exposure* = Type of antithrombotic intervention
- Actual antithrombotic regimen at index
- Physician's reason for intervention choice
- Physician-related variables
- Physician assessment of bleeding & thrombotic risks
- Routine laboratory markers of bleeding and thrombosis
- ROTEM and peak anticoagulant activity

**Weekly during Follow-up³:**
- Monitor and record outcomes and other competing events (i.e., change in anticancer regimen; HIT, TTP)
- Record morning platelet counts, HCT and Hb
**Study Outcomes**

**Primary Composite Outcome:**
1. ISTH-defined **Major bleeding** events
   
   OR

2. Symptomatic or incidental deep or superficial **venous thromboembolism** or **arterial thromboembolism**

**Secondary Outcomes:**
1. Next management intervention
2. ISTH- defined Clinically Relevant non-Major Bleeding\(^1\)
3. Platelet Transfusions (number and adverse effects)
4. RBC transfusions (number)
5. Peak treatment intensity
   - Anti-Xa / Diluted thrombin time / INR / aPTT
6. Whole blood coagulation: ROTEM (Estcourt, BJH 2014)
7. Death

\(^1\)Kaatz, JTH 2015
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• **Take Home Messages**
Take home messages

• Platelet transfusion thresholds are not the holy grail
  – The relationship between bleeding, platelet count and AC is complex and nonlinear.
Antithrombotic Rx in Thrombocytopenia - DISCUSSION

• What do YOU do?
  – Dose reduction?
  – Transfusion thresholds
    • Anticoagulation and Antiplatelet

• Would you dare to perform an interventional study?
  – ...based on these data

• Questions?
hyperlinks
IF anti-coagulant HOLD, then WAS an IVC FILTER recommended? (n=167)

<table>
<thead>
<tr>
<th>Risk Scale* (mean±SD)</th>
<th>Thrombotic</th>
<th>Bleeding</th>
</tr>
</thead>
<tbody>
<tr>
<td>YES (8%)</td>
<td>6.46</td>
<td>7.31</td>
</tr>
<tr>
<td>NO (92%)</td>
<td>3.64</td>
<td>6.81</td>
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</tbody>
</table>

* Physician-assessed risk on a scale of 1-10 (1 = lowest risk; 10 = highest) for a given case

- Lower than the figures reported in a recent population based cohort in the USA.
  - 19.6% of 14,000 cancer pts had an IVCF placed (Ho, Thr Res 2015)
  - Only 21% had an obvious CI to AC!
- Main supportive evidence is for use during bleeding and not in “high risk” scenarios (White, Circulation 2016)
**Thrombotic Bleeding Risk Scale** (mean ± SD)

**IF** anti-thrombotic **MODIFY**, then **HOW?**

[ scripture] sub-level of “level one (3)”

**42% LOWER DOSE by 50%**

(n=116)

**40% PROPHYLACTIC DOSES** (n=112)

Increasing thrombotic risk*;
Dutch physicians (vs. Israeli)

Lower platelet counts of 20,000/µL (vs. 40,000/µL)

* Physician-assessed risk on a scale of 1-10 (1 = lowest risk; 10 = highest) for a given case

**IF LMWH**

**13% CONTINUE NOAC at any dose** (n=37)

**87% CHANGE TO LMWH at any dose** (n=240)

**IF NOAC**

**5% CONTINUE VKA at any dose** (n=13)

**92% CHANGE TO LMWH at any dose** (n=255)

3% change to DOAC

**ANTI-COAGULANT CASES (without aspirin): LEVEL TWO (2)**
IF anti-coagulant NO CHANGE BUT TRANSFUSE PLATELETS, then HOW?
[sub-level of “level one (2)"

TRANSFUSION THRESHOLD?

30 x 10^9/L in 45% (n=54)

VS.

50 x 10^9/L in 48% (n=57)

IF PLATELET REFRACTORINESS develops and target not reached

15% CONTINUE without modification (n=18)

VS.

85% HOLD anti-platelet regimen OR LOWER INTENSITY (n=101)

* Physician-assessed risk on a scale of 1-10 (1 = lowest risk; 10 = highest) for a given case

Anti-Coagulant Cases (+/- aspirin): LEVEL TWO (3)
“BONUS” SLIDES (not presented)

• Detailed Study Questions:
  – Descriptive Pilot Phase
  – Outcome Analysis Phase
Antithrombotic Rx in Thrombocytopenia – Management study

- Variability in management of hematologic malignancy patients with venous thromboembolism and chemotherapy-induced thrombocytopenia
  - Samuelson B, Gernsheimer T, Estey E, Garcia D.

- Surveyed 24 physicians from 19 centers.
- Only focused on anticoagulation in the context of VTE.

1. What was the platelet count above which you would be comfortable with full/prophylactic dose anticoagulation?

2. Three case vignettes

Samuelson, Thrombosis Research, 2016
Variable Practice Patterns

A. Therapeutic dose anticoagulation

- Transfusion Medicine (n=7)
- Hematology (n=16)
- Total (n=23)

Threshold (platelets/μL)

Responses

20
18
16
14
12
10
8
6
4
2
0

25,000  50,000  75,000  100,000

Samuelson, Thrombosis Research, 2016
Clinical Scenarios – Acute Symptomatic VTE

• Withheld anticoagulation, pending platelet recovery, for catheter-associated thrombosis

• Would transfuse to a platelet threshold of 50,000/μL in order to administer therapeutic anticoagulation.

• Patient who can’t achieve a platelet count of 50,000/μL:
  • Most decrease the transfusion threshold to 20,000/μL rather than to decrease intensity of anticoagulation
    – Hold anticoagulation in favor of IVC filter placement
Antiplatelet Rx & thrombocytopenia

- **4-11% of pts with Acute MI** have thrombocytopenia
  - Plt < 100K is associated with early and late major CV events
  - Increased mortality

  *Hakim, Am Heart J, 2011*

- **One study showed benefit for aspirin in Plt < 100K**, but severe thrombocytopenia was under-represented.

  *Sarkiss, Cancer, 2007*

- Safety of aspirin in cancer pts with AMI and Plt <50K is unknown
  - **Underused in AMI and cancer – only 46%**

  *Yusuf, Clin Cardiol, 2012*

- **Aim:** Evaluate safety of benefit of aspirin in hematological malignancy patients with severe thrombocytopenia (<50K)

  *Feher, Oncologist 2017*
Antiplatelet Rx & thrombocytopenia

- No fatal bleeding
- Bleeding complications not associated with sTP or aspirin

Feher, Oncologist 2017