Guidance Proposal from SSC Malignancy and Haemostasis Subcommittee

“Prevention and treatment of venous thromboembolism in adults receiving asparaginase therapy”

Authors:

*Jeffrey Zwicker (Beth Israel Deaconess Medical Center/Harvard Medical School)
*Marc Carrier (University of Ottawa)
Daniel DeAngelo (Dana Farber Cancer Institute/Harvard Medical School)
Anna Falanga (University of Bergamo)
Tzu-Fei Wang (Ohio State University)
Mandy Lauw (University of Maastricht)
Gosia McMasters (Beth Israel Deaconess Medical Center/Harvard Medical School)
*SSC Malignancy and Haemostasis Subcommittee members

Background:

- Administration of asparaginase for the treatment of acute lymphoblastic leukemia is associated with high rates of venous thromboembolism complications
  - >30% in analyses of DFCI protocol (Grace et al. BJH 2011)
  - High rate of cerebral sinus venous thrombosis
- Asparaginase lowers levels of endogenous anticoagulants (antithrombin, protein C and S)
- Number of potential risk factors have been identified including number of doses, age, co-administration of steroids or anthracycline-based chemotherapy
- Approaches to thromboprophylaxis vary considerably across centers
  - Prophylactic strategies evaluated include prophylactic low molecular weight heparin and/or antithrombin concentrate
- Treatment and prevention of asparaginase-induced VTE not addressed in societal guidelines

Guidance document will address the following issues:

- Primary prophylaxis
  - Anticoagulation including which target populations and indications
  - Laboratory monitoring and repletion of antithrombin, fibrinogen, and platelets
  - Differential approaches for induction or consolidation
- Treatment of asparaginase-related VTE
  - Selection of anticoagulant
  - Role for antithrombin concentrate and monitoring levels
  - Management of central venous catheter
  - Implications for ongoing use of asparaginase
  - Duration of anticoagulation