台灣血栓暨止血學會

112 年度 Post-Ash 會後研討會

Highlights of ASH 2023 Post-ASH

2023

TSTH 台灣血栓暨止血學會

FEBURUARY 11, 2023
臺灣大學醫學院 104 講堂
Room 104, National Taiwan University
College of Medicine (NTUCM)

台灣血栓暨止血學會 Post-ASH 會後研討會
Highlights of ASH 2023 Post-ASH

時間 :112 年 02 月 11 日 (週六)12:30~17:00
地點 : 台灣大學醫學院 104 講堂 (台北市中正區仁愛路一段 1 號)
大會主席 : 彭慶添理事長

時間	題目	演講者
12:20~12:30	註冊	
12:30~12:35	開幕致詞	彭慶添 理事長
12:35~12:40		Moderator: 林東燦教授
12:40~13:10	Disorders of coagulation or fibrinolysis: looking forward-novel therapy and diagnostic modality for bleeding disorders (I)	張家堯 醫師 北醫附醫
13:10~13:15	討論	
13:15~13:45	Disorders of coagulation or fibrinolysis: looking forward-novel therapy and diagnostic modality for bleeding disorders (II)	黃鼎煥 醫師 新竹馬偕
13:45~13:50	討論	
13:50~14:20	Gene therapy for hemophilia	周聖傑 醫師 台大醫院
14:20~14:25	討論	
14:25~14:55	Disorders of platelet number or Function-Clinical and Epidemiological	王建得 醫師 台中榮總
14:55~15:00	討論	
15:00~15:10	Coffee Break	
15:10~15:15		Moderator: 邱世欣教授
15:15~15:45	Disorders of coagulation or fibrinolysis: von Willebrand and other congenital and acquired bleeding disorders	翁德甫 醫師 中山附醫
15:45~15:50	討論	
15:50~16:20	Thrombosis and anti-coagulation: controversies in anticoagulation and venous thromboembolism	林炫聿 醫師 彰化基督教醫院
16:20~16:25	討論	
16:25~16:55	Thrombosis and anti-coagulation: cancer associated thrombosis (including ASH guideline on VTE prevention and treatment in patients with cancer)	劉嘉仁 醫師 台北榮總
16:55~17:00	討論	
17:00~17:05	閉幕致詞	沈銘鏡榮譽理事長

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獲獎
東亞血友病論壇 (EAHF) 口頭發表：旅行獎 (2015 日本東京)
國際血栓止血學會大會 (ISTH congress) 口頭發表：世界展望獎 (2017 德國柏林)
亞太血栓止血學會大會 (APSTH) 口頭報告：研究論文獎 (2021 韓國光州線上會議)

Disorders of coagulation or fibrinolysis: looking forward-novel therapy and diagnostic modality for bleeding disorders (I)

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In decades, there has been great advancement in hemophilia care. In the recent years, more and more data of long half life clotting factor concentrates (eg: Efanesoctocog Alfa), non-factor therapy (eg: Emicizumab, Fitusiran, Concizumab, etc), and gene therapy for people with hemophilia A (PwHA) and B (PwHB) have been addressed every year. In this section, we will focus on the update of Efan and Fitusiran. Meanwhile, we will also take a look at the update of joint health of non-severe hemophilia patients. The following are some summaries from the abstract of hemophilia updated in ASH 2022.

With regard to Efanesoctocog Alfa, the first one is the study on “A population pharmacokinetic (PopPK) model to characterize Efanesoctocog Alfa FVIII activity levels in patients with severe hemophilia A”(Poster 3788), in which the authors developed a popPK model to characterize FVIII:C, identify intrinsic and extrinsic factors affecting PK, and assess PK variability. Interestingly, clearance rate of Efanesoctocog Alfa in Asians was 10.4% lower than in non-Asians. Baseline VWF level was not identified as a statistically significant covariate in the final popPK model, consistent with prior studies that demonstrate that the PK of efanesoctocog alfa is VWF-independent. Simulations for perioperative management during major surgery and treatment of major bleeds showed that a loading dose of 50 IU/kg, followed by 30 IU/kg every 3 days in the postoperative period.

The second one is the study on “Efficacy of Efanesoctocog Alfa on physical functioning from the XTEND-1 phase 3 clinical trial in previously treated PwHA”(Poster 2468). Totally 159 PwHA were included in the XTEND-1 trial. Physical functioning was assessed as a secondary endpoint using Haem-A-QoL (patients aged ≥ 17 years), Patient-Reported Outcomes Measurement Information System (PROMIS)-Short Form v2.0 physical function (PF; patients aged ≥ 18 years), and as exploratory endpoints using HAL (patients aged ≥ 18 years), and EuroQol- 5 Dimension-5 Level (EQ-5D-5L; mobility and usual activities domains). Exit interviews, ActiGraph Activity Monitors (worn for 8 consecutive days at intervals throughout the study period), and post-hoc analysis (including psychometric analyses) were also used to evaluate physical functioning. The mean change from baseline to Week 52 in Haem-A-QoL Physical Health (PH) score, PROMIS PF 6b T-score, and HAL overall score. The result showed once-weekly prophylaxis with efanesoctocog alfa resulted in improvement in physical functioning in PwHA, positively impacting daily living activities, in patients who were on prior standard of care FVIII prophylaxis.

The third one is the study on “Efficacy of efanesoctocog alfa on pain in PwHA from the XTEND-1 phase 3 clinical trial.” (Poster 2474) Pain was assessed as a secondary endpoint using the Patient-Reported Outcomes Measurement Information System (PROMIS)-Short Form (SF) v1.0 pain intensity 3a first question (item, pain intensity at its worst in the past 7 days), and as exploratory endpoints using the PROMIS-SF v1.0 pain intensity 3a total T-score, PROMIS-SF v1.0 pain interference 6a T-score (in patients ≥ 18 years of age), and EuroQol- 5 Dimension 5-level (EQ-5D-5L) pain/discomfort domain. Pain was further assessed in post-hoc analyses (including psychometric analyses) of PROMIS-SF Pain Intensity 3a and during exit interviews. Pain medication usage was also evaluated. The result showed once-weekly prophylaxis with efanesoctocog alfa resulted in improvement in reduction of pain in patients with severe hemophilia A, when switching from prophylaxis with standard of care FVIII therapies to efanesoctocog alfa.

With regard to Fitusiran, the first one is the study on "Development of a quantitative systems pharmacology model to explore hemostatic equivalency of Antithrombin lowering."(Poster 2472) The aim was to better understand the hemostatic equivalency of fitusiran prophylaxis (i.e., AT lowering), a quantitative systems pharmacology (QSP) model was developed to investigate thrombin generation in PwHA and PwHB in the context of AT lowering. QSP modeling is a mechanistic approach that integrates clinical and nonclinical data of the coagulation pathway to simulate the results of multiple in vitro coagulation assays, including the thrombin generation assay (TGA) and to mechanistically understand the readouts of these assays. The result showed that by considering the impact of α-2-macroglobulin, the QSP model provides a mechanistic representation of thrombin generation under conditions of AT lowering, consistent with internal TGA data from donor-derived spiked plasma and clinical TGA data from both PwHA and PwHB. The VP analysis of fitusiran prophylaxis provided hemostatic equivalency with FVIII in a representative population of severe PwHA, with a targeted therapeutic range of AT of 15-35% resulting in a thrombin peak profile which was comparable to 10-20 IU/kg FVIII.

The second one is the study on "Fitusiran prophylaxis improves health-related quality of life of PwHA and PwHB with or without inhibitors from ATLAS-ppx study." (Poster 3559) The study assessed HRQoL at Month -6, Day 1 (baseline) and Month 7, during factor/BPA prophylaxis and during treatment with fitusiran using the following questionnaires: Hemophilia Quality of Life Questionnaire (Haem-A-QoL & Haemo-QoL; lower scores = improved HRQoL), Hemophilia Activity List (HAL & PedHal; range 0–100, higher scores = improved HRQoL), EuroQoL-5 Dimension 5-Level (EQ-5D-5L; index score ranges 0–1, higher scores = improved HRQoL), Treatment Satisfaction Questionnaire for Medication (TSQM-9), and the Hemophilia Joint Health Score (HJHS). The result showed that associated with a marked ABR reduction, PwHA/B with or without inhibitors on fitusiran prophylaxis consistently improved all HRQoL endpoints, demonstrating added value in PwHA/B beyond the improvement in bleeding phenotype.

The third one is the study on “Fitusiran reaches people’s with hemophilia and their caregivers’ treatment expectations: interviews of Participants of ATLAS-OLE trial” (Poster 3565). Qualitative insights from this study provides encouraging and positive interim insights into the experiences of PwHA/B, with or without inhibitors, and their caregivers, with fitusiran prophylaxis. Fitusiran treatment demonstrated added value in PwHA/B, irrespective of inhibitor status, particularly resulting in improving joint health, decreasing bleeds, improving joint mobility, and an overall reduction of treatment and disease burden.

Finally, regarding joint health of non-severe hemophilia (nSH) patients from Spain’s report (Poster 1156), they evaluated the joint disease (JD) in nSH patients as well as the correlation between JD, basal FVIII/FIX levels, age and global hemostatic capacity (GHC) evaluated by thrombin generation test (TGT) or thromboelastometry (ROTEM®). Another aim was to determine the degree of discrepancy between FVIII-chrom and FVIII-coag values in this group of patients. Totally 56 patients: 6 moderate hemophilia (MoH) and 50 mild hemophilia (MiH) patients were included. The results showed that patients with nSH may present JD. Neither basal FVIII/FIX levels, nor GHC, nor age correlated in the study with the degree of JD though wider studies are needed to confirm these findings. Although correlation between basal levels of FVIII/FIX and GHC was observed, none of these variables were able to explain the degree of JD. Target joints can be observed in patients with MiH, therefore additional studies are necessary to clarify the need of new therapeutic intervention in this group of patients. Future studies should address the relationship between degree of JD (values of HEAD-US) and patients' quality of life (QoL) to stablish cutoff values of HEAD-US score that may affect the QoL. The study reminded us: Do NOT neglect the joint health of non-severe hemophilia (nSH) patients and scheduled musculoskeletal assessment might be needed. The unexpected high % of nSH patients with JD urges the need for larger studies on JD in this population to clarify the need of new type of therapeutic intervention in this group of patients.

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著作

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3. Liu H-C, Yeh T-C, Hou J-Y, Chen K-H, Huang T-H, Chang C-Y, Liang D-C. Triple intrathecal therapy alone with omission of cranial radiation in children wth acute lymphoblastic leukemia. Journal of Clinical Oncology. 2014; 32: 1825-1829.
4. Yeh T-C, Liu H-C, Hou J-Y Chen K-H, Huang T-H, Chang C-Y, Liang D-C. Severe Infections in Children With Acute Leukemia Undergoing Intensive Chemotherapy Can Successfully Be Prevented by Ciprofloxacin, Voriconazole, or Micafungin Prophylaxis. Cancer. 2014; 120: 1255-1562.

Disorders of coagulation or fibrinolysis: looking forward-novel therapy and diagnostic modality for bleeding disorders (II)

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This oral session in 64th ASH focused on novel therapies and diagnostic modalities for Hemophilia A and B. The topics related to pharmacotherapy included: interim analysis of HAVEN 7 and safety analyses from the European Haemophilia Safety Surveillance (EUHASS) database for Emicizumab, comparing hemorrhagic and thrombotic adverse events with Emicizumab and extended half-life FVIII From EudraVigilance surveillance database, results of phase 3 explorer7 trial of Concizumab, and the first-in-Human Study of serpinpc.

HAVEN 7 (NCT04431726) is a Phase IIIb, multi-center, open-label study, aiming to evaluate the efficacy, safety, pharmacokinetics (PK) and pharmacodynamics (PD) of emicizumab in infants ≤ 12 months with severe HA without FVIII inhibitors. Participants receive subcutaneous emicizumab 3mg/kg weekly for 4 weeks, then 3mg/kg every 2 weeks for 52 weeks; at Week 53, participants can continue with this regimen or switch to 1.5mg/kg weekly or 6mg/kg every 4 weeks for the 7-year long-term follow-up period. There were total 54 participants with the median emicizumab treatment duration was 42.1 (1–60) weeks in this interim reports. Overall, 77 bleeds were reported in 31 participants (57.4%): 88.3% traumatic; 5.2% procedural/surgical; 6.5% spontaneous. In total, 14 treated bleeds, all traumatic, were reported in 12 participants (22.2%). No intracranial hemorrhage occurred, and no participant experienced >2 treated bleeds. Mean model-based ABR for treated bleeds was 0.4 (0.23–0.65); it was 1.9 (95% CI: 1.35–2.68) and 0.1 (95% CI: 0.01–0.22) for all bleeds and treated joint bleeds, respectively. Zero treated bleeds were reported in 77.8% of participants (n=42), while 42.6% of participants (n=23) had no bleeds at all. Fifty participants (92.6%) had ≥ 1 AE and nine (16.7%) had ≥ 1 emicizumab-related AE (all injection-site reactions). No AE leaded to treatment withdrawal/modification/interruption. Eight participants reported 12 serious AEs (SAEs); none was considered emicizumab related. There were no deaths, TEs or TMAs at the time of this interim analysis.

European Haemophilia Safety Surveillance (EUHASS) is an investigator-led pharmacovigilance program collecting real-world safety data on treatments for inherited bleeding disorders from >90 centers in >25 countries. From Jan 1, 2020 — Dec 31, 2020, data from 985 people who received emicizumab were reported to EUHASS. In 2020, a 26-year-old male who received emicizumab alone had FVIII inhibitor recurrence. Two males (40 years and 55 years of age) who received emicizumab alone had an allergic or other acute reaction (rash). Across ≥ 985 people spanning 4 years from 2017–2020, four TEs occurred. Two occurred in 78-year-old males who received emicizumab and another hemophilia treatment: one received emicizumab, rFVIIa, and a FVIII product and had a thrombosis in his port-a-cath; the other received emicizumab and aPCC and had a myocardial infarction (Shang et al. Blood 2020). Two TEs occurred in males (32 years and 53 years of age) who received emicizumab alone: an MI and a superior mesenteric artery thrombus, respectively.

EudraVigilance is the pharmacovigilance database to manage the collection and analysis of suspected adverse reactions to medicines authorised in the European Economic Area. Total ADR reported during treatment with emicizumab or with EHL FVIII products retrieved from January 1 to December 31, 2021 from EudraVigilance database were collected to comparing the proportional reporting ratios (PRR) and reporting odds ratio (ROR) of event of interest. Total 406 ADR for emicizumab and 376 for EHL FVIII products were retrieved. Overall, 232 and 275 hemorrhagic ADR were reported for emicizumab and for EHL FVIII products, respectively. Thrombotic ADR were 24 for emicizumab and 9 for EHL FVIII products. On the whole, about 25% of thrombotic ADR were reported in concomitance with eptacog alfa. The reporting odds of hemorrhagic ADR was smaller for emicizumab than for EHL FVIII products, with a ROR of 0.49 (95% CI 0.36-0.66). On the other hand, the reporting odds of thrombotic ADR was higher in emicizumab than in EHL products, with a ROR of 2,56 (95%CI 1,18-5,59).

Explorer7 Trial (NCT04083781) is a phase 3 trial to assess efficacy and safety of daily concizumab prophylaxis versus no prophylaxis for patients with hemophilia with inhibitors. Patients were randomized 1:2 to no prophylaxis (arm 1; ≥ 24 weeks) or concizumab prophylaxis (arm 2; ≥ 32 weeks), or assigned to concizumab prophylaxis (arms 3 & 4). Patients received a 1.0 mg/kg concizumab loading dose on Day 1, followed by an initial 0.20 mg/kg daily dose starting Day 2, with potential adjustment to 0.15 or 0.25 mg/kg based on measured plasma concizumab concentration level after week 4. Of 133 patients in the trial, 52 patients were randomized to concizumab prophylaxis (arm 2: HAwI, n=18; HBwI, n=15) or no prophylaxis (arm 1: HAwI, n=9; HBwI, n=10). The remaining 81 patients were assigned to concizumab prophylaxis (non-randomized arms 3 & 4). The estimated mean ABR for treated spontaneous and traumatic bleeding episodes in patients with HAwI was 1.6 (95% CI, 0.9–2.8) for concizumab prophylaxis versus 18.3 (95% CI, 10.2–32.9) for no prophylaxis (ABR ratio, 0.09 [95% CI, 0.04–0.18]). The estimated mean ABR in patients with HBwI was 2.2 (95% CI, 0.8–6.5) for concizumab prophylaxis versus 7.2 (95% CI, 2.6–20.1) for no prophylaxis (ABR ratio, 0.31 [95% CI, 0.07–1.36]). The overall median ABR on concizumab prophylaxis was 0.0 in both the HAwI and HBwI subgroups (arms 1 to 4). Following the treatment restart, no thromboembolic events were reported while on concizumab treatment in patients with either HAwI or HBwI.

SerpinPC is a recombinant serine protease inhibitor (SERPIN) designed to increase the amount of thrombin at sites of tissue damage by reducing the activity level of circulating activated protein C (APC) and thereby prolong the activity of prothrombinase. AP-0101 is an ongoing first in human open label multicenter study to investigate the safety, tolerability and pharmacokinetics of subcutaneous doses of SerpinPC in participants with severe hemophilia. AP-0101 consists of 5 parts: Part 1 was a Single Ascending Dose Study. Part 2 enrolled 23 male PwH (19 HemA and 4 HemB) who were not on factor prophylaxis to receive SerpinPC at 0.3, 0.6 or 1.2 mg/kg, administered as a subcutaneous injection every 4 weeks over a 24-week period (6 total doses). In Part 3, subjects who completed Part 2 receive a flat dose of 60mg every 4 weeks for 48 weeks. Part 4 is a further extension in which subjects who completed Part 3 receive 1.2mg/kg of SerpinPC every 2 weeks for 24 weeks. Part 5 is an additional extension in which subjects who complete Part 4 receive 1.2mg/kg of SerpinPC every 2 weeks for a further 52 weeks. In Part 2, one subject discontinued treatment due to an injection site reaction. No other treatment-related adverse events were observed. Two subjects had anti-drug antibodies and remained on treatment without apparent impact on ABRs. In the highest dose cohort, SerpinPC reduced the self-reported 'all bleeds ABR' and spontaneous joint bleeds ABR by by 88% and 94%, respectively. In Part 3 and 4, no treatment related adverse events observed. Two subject discontinued treatment due to emigration to another country and rectosigmoid cancer, respectively. In Part 3, SerpinPC reduced the self-reported 'all bleeds ABR' and spontaneous joint bleeds ABR by by 83% and 86%, respectively. In Part 4, the reduction of 'all bleeds ABR' and spontaneous joint bleeds ABR were both 93%. The all bleed median ABR was 2.2 in part 4.

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Gene therapy for hemophilia

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The main stay of current gene therapy of hemophilia, is using AAV vector to carry modified FIX gene (mostly FIX Padua) or modified FVIII gene (mostly B domain deleted FVIII) to achieve clinically effective level of coagulation factors. So far, the safety and efficacy are acceptable for several gene therapy products. Furthermore, one gene therapy for hemophilia B has been approved by FDA and EC, and another gene therapy for hemophilia A has been approved by EC. However, in its current form, there are several issues presented in this ASH.

1. Duration of effects:
Paper 2142/2141: These two posters showed the latest follow-up data of AMT-060, AMT-061, and HOPE-B clinical trials. Almost all participants had sustained FIX level across years and no significant decline has been observed. In the education program, Dr. Nathwani illustrated the latest data of the first successful gene therapy trial on hemophilia B, which also showed sustained expression. However, in recently published review of gene therapy, the decline of FVIII expression were almost universal among clinical trials of hemophilia A. What causes these differences is not yet elucidated.

2. Is there any better FVIII gene contract for gene therapy
Paper 784: This oral presentation showed a potential new version of FVIII gene construct “rhFVIII- △ 3-SD/PE” for gene therapy. With combination of canine type B domain and removal of furin cleavage recognition site, the rhFVIII- △ 3-SD/PE increases the expression efficiency by 3 to 5 folds. The construct was applied on mouse and dog models and could be the next generation of FVIII construct for gene therapy.

3. Non-viral vector that enables re-treatment

A problem of AAV-based gene therapy is anti-AAV neutralizing antibody. Some patients might be infected by AAV and had anti-AAV antibody which prevent them from receiving AAV-based gene therapy. And patients who had been treated AAV-based gene therapy is not possibly to receive re-treatment because the anti-AAV will be super high titer for a very long time.

Paper 400: This interesting paper illustrated a novel lipid nanoparticle (LNP) which can deliver gene construct to specific cells. With a RNA-based transposase and a rhFVIII gene in separated LNPs. Significant FVIII expression can be achieved and repeated treatment will increase FVIII level additionally. It could be the much better vector to apply in gene therapy.

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專長
1. 血友病及類血友病、先天性血栓症
2. 血小板低下症

Disorders of platelet number and functions: managing thrombocytopenia in challenging situations

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Abstract

Thrombocytopenia is one of the most common problem of hematology consultation. Some causes of thrombocytopenia, such as chemotherapy. chronic liver disease, and pregnant patient are frequently encountered and often challenging clinical situations, and optimal management in these situations can be elusive. New data for the use of thrombopoietin receptor agonists (TPO-RAs) in these patients in specific situations offers opportunities for updated and modernized treatment paradigms but also raise many questions. Chemotherapy-induced thrombocytopenia (CIT) is common, resulting in increased bleeding risk and chemotherapy delays, dose reduction, and treatment discontinuation, which can negatively affect oncologic outcomes. The availability of thrombopoietin receptor agonists has led to formal clinical trials describing efficacy in CIT. This review details the evidence to date for the management of TPO-RAs, discussing the efficacy data, the specific circumstances when treatment is warranted, and safety considerations.

There is also a concern for a non-pregnancy-specific etiology or an insufficient platelet count for the hemostatic challenges of delivery. The severity of thrombocytopenia and trimester of onset can help guide the differential diagnosis. Patients with chronic thrombocytopenic conditions, such as immune thrombocytopenia, should receive counseling on the safety and efficacy of various medications during pregnancy. The management of pregnant patients with chronic immune thrombocytopenia who are refractory to first-line treatments is an area that warrants further research. This review uses a case-based approach to discuss recent updates in diagnosing and managing thrombocytopenia in pregnancy.

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專長
成人及兒童血友病與出血性疾病、血栓性疾病
各種血液病（各型地中海貧血、紅血球、白血球與血小板疾病）
兒童癌症（血液癌症與各種實體腫瘤）
兒童血管瘤及其他良性腫瘤
兒童骨髓移植及併發症（排斥、感染）治療

Disorders of coagulation or fibrinolysis: von Willebrand and other congenital and acquired bleeding disorders

翁德甫 醫師

中山醫學大學附設醫院　血液病中心

演講摘要

類血友病是最常見的出血性疾病，然而中、重度類血友病（Type 2, Type 3 或嚴重型的 type 1）在診斷上可利用類血友病因子檢驗或基因方式進行診斷，然而讓臨床醫師困擾的是輕度類血友病，尤其在最新的 ISTH/WFH/NFH 2019 Guideline 中定義 VWF<50% 搭配臨床出血症狀即可做為類血友病 Type 1 的診斷後，對於輕度類血友病的診斷與治療出現許多難題。因此載這次會議中，強調了臨床檢驗 VWF 在 30-50% 時，不同年齡、性別時，利用 Bleeding assessment tool (BAT) 來佐證病人的診斷，而且即使在兒童時期經由家族史或抽血報告，也必須在後續年齡持續追蹤患者的 BAT 分數，與是否在 bleeding challenge 後有出血的情形。若患者在隨著年齡成長後，VWF:Ag 恢復正常（>50%），仍必須以患者症狀為依歸，來做為輕度類血友病是否需要進行治療的標準，而非單純以 VWF:Ag 數值是否正常來診斷。

而在類血友病的出血表現，由於 angiodysplasia 引發的消化道出血也是此次大會重要的議題，由於缺少 VWF（尤其是 High molecular weight 的 VWF）導致 angiodysplasia 的發生，其 85% 會發生在消化道，而且以小腸最為常見，在臨床上遇到類血友病患者發生不明原因的消化道出血時，必須進行膠囊內視鏡檢查小腸是否有 angiodysplasia 的表現，而治療上，出血時可以使用較高劑量的凝血因子進行治療，對於 type 3 患者也可以考慮預防治療來避免出血，而在輔助治療上，atorvastain 與 thalidomide 等藥物，均可以抑制 angiogenesis 的發生，因此可抑制 angiodysplasia 的惡化。而在類血友病的女性出血表現上，這次大會針對類血友病患者的嚴重月經出血 (HMB) 進行仔細的討論，其包括了在家族中容易被誤以為正常的嚴重月經出血與對生活品質的傷害。由於隱私與文化上等原因，月經過多往往被避而不談，然而在研究中顯示月經出血影響了多數類血友病女性正常的求學、工作與競爭機會，由於病患本人、醫師與社會大眾對於類血友病的認知不足，往往影響了患者面對月經過多時所採取的處理方式。這是大會引入患者的意見，希望能夠進一步改善類血友病女性患者在多專科照護下的不足。

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血癌、淋巴瘤、貧血、不明原因的出血

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Thrombosis and anti-coagulation: controversies in anticoagulation and venous thromboembolism

林炫聿 醫師

Evidence on several controversial issues related to VTE as well as anticoagulants would be reviewed and discussed in today's talk. (1) Anticoagulant therapy for women: implications for menstruation, pregnancy, and lactation. (2) Should caplacizumab be used routinely in unselected patients with immune TTP? (3) DOAC usage among specific scenarios, including extreme obesity, renal injury, GI cancers, catheter-related thrombosis, and drug-drug interactions.

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主要研究
多發性骨髓瘤、癌症流行病學、基因分析、人工智慧

醫療專長
血液學、腫瘤內科學、貧血、惡性淋巴瘤 (淋巴癌)、多發性骨髓瘤、急性骨髓性白血病 (血癌)、血友病

證照
中華民國腫瘤內科專科醫師、中華民國血液病專科醫師、中華民國血液及骨髓移植專科醫師、中華民國內科專科醫師

代表著作 Original Article

(*corresponding author; 1equalcontribution)

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Thrombosis and anti-coagulation: cancer associated thrombosis (including ASH guideline on VTE prevention and treatment in patients with cancer)

劉嘉仁 醫師

Venous thromboembolism (VTE) is a common complication of cancer patients and contributes to their morbidity and mortality. We review the oral and poster presentations regarding the prevention and treatment of VTE in patients with cancer at the American Society of Hematology (ASH) Annual Meeting in 2022. The evidence-based guidelines of this field will also be addressed. In the ASH guidelines, the experts provide suggestions regarding mechanical and pharmacological prophylaxis in hospitalized medical patients with cancer. They also recommend the use of anticoagulation for the initial, short-term, and long-term treatment of VTE in patients with cancer. The oral presentations address apixaban for central venous catheter-associated upper extremity deep vein thrombosis in cancer patients, factor XI inhibition for the prevention of catheter-associated thrombosis in cancer patients undergoing central line placement, early dynamics of C-reactive protein predicting risk of venous thromboembolism in patients with cancer treated with immune checkpoint inhibitors, different thrombin generation affected by anticoagulants in patients with acute lymphoblastic leukemia, cardiovascular biomarkers for the prediction of adverse cardiovascular events and mortality in patients with cancer, and rivaroxaban versus apixaban for the treatment of cancer-associated venous thromboembolism.

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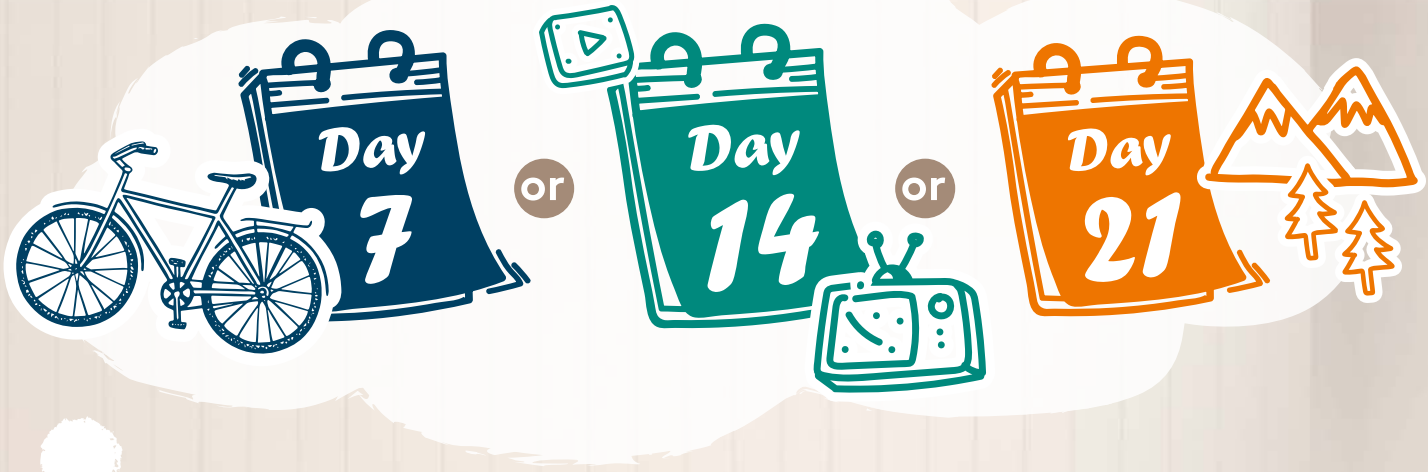

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警語：應告知病人過敏反應的早期症狀，包括蕁麻疹 (hives)、全身性蕁麻疹 (urticarial)、胸悶、喘鳴、低血壓和過敏性反應 (anaphylaxis)，若出現過敏症狀，建議病人應立即中止使用本藥品，並與其醫師聯繫。所有接受第九凝血因子藥品治療的病人應讓病患監測，以適當的臨床觀察和實驗室檢測是否形成抑制劑。患有肝臟疾病患者、手術後患者、新生嬰兒，或是有血栓或溶漫性血管內凝血 (DIC) 風險的患者使用本藥品時，應採取適當的生物檢驗，進行血栓及消耗性凝血病變早期徵象的臨床監視。如果需要放置中心靜脈導管裝置 (CVAD)，應考量 CVAD 相關併發症，包括局部感染、菌血症及導管部位血栓。如果使用最高劑量 (15 毫升 = 6000 IU)，本藥品每劑含鈉最多 25.8 毫克 (1.13 mmol)(體重 70 公斤)。對於控制鈉飲食的患者應列入考量。常見不良反應 (≥1%) 包括注射部位反應、頭痛。

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預防治療建議起始劑量：12歲以上：每次20-50 IU/kg，每週2至3次
未滿12歲：每次30-50 IU/kg，每週2至3次(兒童藥物清除率較高，可能需要更頻繁給藥或更高給藥劑量。)

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警語：應告知病人過敏反應的早期症狀，包括蕁麻疹(hives)、全身性蕁麻疹(urticaria)、胸悶、喘鳴、低血壓和過敏性反(anaphylaxis)，若出現過敏症狀，建議病人應立即中止使用本藥品，並與其醫師聯繫。所有接受第八凝血因子藥品治療的病人應該接受監測，以調查抗FVIII抑制劑和實驗室檢測是否形成抑制劑，本藥回溶後，含鈉量每毫升7毫克（0.3毫莫耳），常見不良反應(≥1%)包括過敏、頭暈、感覺異常、皮疹、發燒。

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A new day for hemophilia

EVERYDAY CONFIDENCE

【適應症】適用於帶有或未帶有第八凝血因子抗體的 A 型血友病 (先天性第八凝血因子缺乏) 病人之出血事件常規性預防。【劑量及用法】劑量：應於開始使用 Hemlibra 治療的前一天停止使用繞道治療劑 (如 aPCC 與 rFVIIa) 治療 (包括常規性預防治療)。建議劑量為於最初 4 週每週一次投予 3 mg/kg (負荷劑量)，之後改為每週一次投予 1.5 mg/kg (維持劑量)，並應皮下注射給藥。用法：Hemlibra 僅供皮下注射使用，且應採用適當的無菌技術投藥。僅限注射於建議的注射部位：腹部、上臂外側及大腿。將 Hemlibra 皮下注射劑注射於上臂外側時，應由照顧者或健康照護專業人員來進行。輪換注射部位可能有助於預防或減輕注射部位反應。Hemlibra 皮下注射劑不可注入皮膚有發紅、瘀傷、觸痛或硬化等現象的區域，或是有痣或疤痕的區域。【禁忌】對活性成分或 Hemlibra 賦形劑過敏。【警語及注意事項】可追溯性 (traceability)：為了提高生物醫藥產品的可追溯性，應清楚記錄所投予產品的名稱和批號。與 Hemlibra 及活化凝血酶原複合濃縮物 (aPCC) 相關的血栓性微血管病變：對接受 Hemlibra 預防性治療的病人投予 aPCC 時，應監視是否發生 TMA。如果出現與 TMA 相符合的臨床症狀及 / 或實驗室檢驗發現，醫師應立即停用 aPCC，中斷 Hemlibra 的治療，並視臨床需要進行處置。與 Hemlibra 及活化凝血酶原複合濃縮物相關的血栓栓塞：對接受 Hemlibra 預防性治療的病人投予 aPCC 時，應監視是否發生血栓栓塞。如果出現與血栓事件相符合的臨床症狀、造影檢查結果及/ 或實驗室檢驗發現，醫師應立即停用 aPCC，中斷 Hemlibra 的治療，並視臨床需要進行處置。接受 Hemlibra 預防性治療之病人的繞道治療劑使用指引：應於開始使用 Hemlibra 治療的前一天停止使用繞道治療劑。如果在進行 Hemlibra 預防性治療期間須使用繞道治療劑，醫師應向所有病人及 / 或照顧者說明準備使用之繞道治療劑的確切劑量與用藥時程。Hemlibra 會提高病人的凝血能力。因此，所需要的繞道治療劑劑量可能要低於未合併進行 Hemlibra 預防性治療之情況下所使用的劑量。使用繞道治療劑治療的劑量與療程須視出血的位置與程度及病人的臨床狀況而定。除非沒有其他的治療選擇 / 替代藥物，否則應避免使用 aPCC。Emicizumab 對凝血試驗的影響：Emicizumab 會彌補流失之活化態第八凝血因子 (FVIIIa) 的 tenase 輔因子活性。以內源性凝血 (包括活化凝血時間 [ACT]、活化部份凝血活酶時間 [如 aPTT]) 為基礎的凝血實驗室試驗可檢測總凝血時間，包括透過凝血酶 (thrombin) 將 FVIII 活化成 FVIIIa 所需要的時間。使用 emicizumab 時，這類以內源途徑為基礎的試驗就不須經過凝血酶的活化，因此會測得過度縮短的凝血時間。兒科族群：目前尚無任何用於 < 1 歲之幼童的資料。【不良反應】在 Hemlibra 的臨床試驗中所通報的最嚴重的藥物不良反應 (ADRs) 為血栓性微血管病變 (TMA) 與血栓事件，包括海綿竇血栓 (CST) 與表淺性靜脈血栓合併皮膚壞死。使用至少 1 劑 Hemlibra 之病人發生最常見且有 ≥ 10%通報的 ADRs 為：注射部位反應 (20%)、關節痛 (15%) 與頭痛 (14%)。

仿單版號：HEMLIBRA SmPC 201903　使用前詳閱說明書，警語及注意事項
北市衛藥廣字第 108120425 號

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HEMLIBRA® SC Injection 150 mg/mL
包裝：150 mg /1.0 mL、105 mg / 0.7 mL、60 mg / 0.4 mL
衛部菌疫輸字第001087 號

血甯博®皮下注射劑 30 毫克/ 毫升
HEMLIBRA® SC Injection 30 mg/mL
包裝：30 mg /1.0 mL
衛部菌疫輸字第001086 號

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Note

Highlights of ASH
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