SSC Subcommittee Project/Collaborative Project

NAME OF PROJECT:

Develop a consensus guideline on diagnosis of rare bleeding disorders caused by the impairment of fibrinolysis inhibitors

Subcommittee

Fibrinolysis

Person responsible (Chair / Principal Investigator): Tetsumei Urano

Description Abstract

State the application's broad, long-term objectives and specific aims, making reference to the health relatedness of the project. Suggested length is 2-3 paragraphs.

The impairment of fibrinolysis inhibitors causes lethal bleeding but their clinical features are not widely known. Such lack of knowledge makes it more difficult to identify those patients and to rescue them by providing proper treatment. At this moment, several families of α2-Antiplasmin (α2AP) deficiency (Ref 1), three families of plasminogen activator inhibitor type 1 (PAI-1) deficiency (Ref.2, 3 & 4), and one family of thrombomodulin abnormality which induces impaired function of thrombin activatable fibrinolysis inhibitor (TAFI) (Ref. 4). These patients need life-long medical support and Japanese Society of Thrombosis and Haemostasis (JSTH) started to develop a guideline for diagnosis which is required for the reliable diagnosis and financial support from our health insurance system. Taking this opportunity, we want to establish an international version of the guideline which contributes to increase the awareness these lethal diseases and to their better prognosis.

Design and methodology (Data expected to collect, sample size and statistical analysis):

Describe concisely the research design and methods for achieving these goals. Suggested length 2-3 paragraphs

In the SSC symposia in 2024, we invite three speakers who take care of these patients (One American family and two Japanese families of PAI-1 deficiency, and one abnormal TM Japanese family) in order to share the knowledge of these patients. We then try to establish a guide line based on the guide line to be made by JSTH as a group composed of co-chairs, recruited members and Yuko Suzuki who is responsible for making JSTH version guideline. The tentative guideline will be presented in ISTH SSC 2025. After getting public comments and proper revision, a guide line of ISTH version would be released.

Study population (Inclusion, exclusion, eligibility) (patient population; recruitment of participating institutions/physicians and subjects; minimum number needed; expected number):

Suggested length 2-3 paragraphs

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The project team will be composed of co-chairs, Dr. Yuko Suzuki, and those recruited from ISTH members. Physicians and those who were responsible for the identification of the existing patients would be also invited.

Expected timeline:

Project stage/set up: 2024 June
Launch: 2024 June
Duration: three years
Finalization/analysis: 2026
Reporting: 2026

Expected outcomes (ie. publications):

Publication type (SSC Communication, Guidance document or original article):

Guidance

Description of project set/up and management, needed infrastructure and resources (summary):

A project team is needed to develop a "consensus guideline on diagnosis of rare bleeding disorders caused by the impairment of fibrinolysis inhibitors".

Possible references:

1. Carpentersl and Mathew P. α2-Antiplasmin and its deficiency: fibrinolysis out of balance. Haemophilia (2008), 14, 1250–1254
2. Fay WP, Parker AC, Condrey LR, Shapiro AD. Human plasminogen activator inhibitor-1 (PAI-1) deficiency: characterization of a large kindred with a null mutation in the PAI-1 gene. Blood. 1997 Jul 1;90(1):204-8.
3. Iwaki T, Tanaka A, Miyawaki Y, Suzuki A, Kobayashi T, Takamatsu J, Matsushita T, Umemura K, Urano T, Kojima T, Terao T, Kanayama N. Life-threatening haemorrhage and prolonged wound healing are remarkable phenotypes manifested by complete PAI-1 deficiency in humans. Journal of Thrombosis and Haemostasis 9(6), 1200-1206, 2011
4. Iwaki T, Nagahashi K, Takano K, Suzuki-Inoue K, Kanayama N, Umemura K, Urano T. Mutation in a highly conserved glycine residue in strand 5B of plasminogen activator inhibitor 1 causes polymerization. Thromb Haemost 2017 117(5):860-869, DOI: 10.1160/TH16-07-0572
5. Masahiko Okada, Norio Tominaga, Goichi Honda, Junji Nishioka, Nobuyuki Akita, Tatsuya Hayashi, Koji Suzuki, and Hiroyuki Moriuchi. A case of thrombomodulin mutation causing

defective thrombin binding with absence of protein C and TAFI activation. Blood Advances 2020, DOI 10.1182/bloodadvances.2019001155