S56-5 Development of a new treatment for DIC, thrombomodulin alfa (genetical recombination) - focus on clinical development

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Thrombomodulin (TM) is a membrane glycoprotein expressed on the surface of endotherial cells that plays an important role in the regulation of intravascular coagulation. Drs. K.Suzuki, I.Maruyama, and Asahi Kasei Pharma have focused on TM as a candidate for a new anticoagulant and in 1987, succeeded in cloning the TM gene. Subsequently, we developed recombinant soluble TM, thrombomodulin alfa (TM-a), which comprises an extra cellular domain of TM including an active site. Disseminated intravascular coagulation (DIC) is a frequent complication of leukemia and infections such as sepsis. In these patients, coagulation activation leads to excess thrombin generation, fibrin deposition in microvessels, and bleeding symptoms. TM-a binds to thrombin and thrombin-TM-a complex activates protein C to produce activated protein C, which inactivates factors VIIIa and Va, and thereby inhibits further thrombin formation. DIC is expected to be treated by TM-a, and we started a clinical trial in 1992. We conducted a multi-center, double-blind, randomized, parallel-group trial to compare the efficacy and safety of TM-a to heparin for the treatment of DIC associated hematologic malignancy and infection. TM-a therapy has been shown to have the non-inferiority of DIC resolution rate with alleviate bleeding symptoms when compared to heparin therapy (J Thromb Haemost, 5:31-41, 2006). A new drug application was made in Japan in 2006. TM-a was approved as a treatment for DIC and the product “Recomodulin Inj. 12800” was launched by Asahi Kasei Pharma in 2008.