Venue: PYRAMID 1
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1515-1630 hr

Symposium 6B: Old problems, new solutions in Haematology

S6B-1. Molecular diagnosis of haemoglobin disorders

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Laboratory diagnoses of thalassemias and abnormal hemoglobins require a combination of tests including the measurement of red cell indices by automatic blood cell counter, hemoglobin (Hb) electrophoresis and quantitation of Hb A2 and Hb F by microcolumn or elution after Hb electrophoresis on soft cellulose membrane. The automatic HPLC system was developed to diagnose thalassemic diseases and the carriers in the last 15 years. This system gives both qualitative and quantitative analysis of hemoglobin components in the same run with good precision and reproducibility and help us to do both prenatal and postnatal diagnosis of thalassemia within the few minutes. The identity of the different globin chains can be identified accurately using TOFMS. The identity of the different thalassemia syndromes can be revealed by the ratio of intensities between / -globin chains and / -mRNA ratios. However, none of these tests can accurately diagnose specific thalassemia genotype. Specific thalassemia mutation can be carried out by DNA analysis. Many DNA techniques have been used for point mutation detection. For the last few years there is a development of DNA chip technology and DNA MassArray has been developed to address all these issues effectively, and will therefore play a key role in future genetic profiling. All of these techniques have some advantage and disadvantage. We highly recommend all service labs to use the technique(s) they are most familiar with and most economic one for their daily use.

S6B-2. Non-myeloablative cord blood transplantation in adults

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Cord blood is widely used as a third possible stem cell source for allogeneic transplantation following bone marrow and peripheral blood. CBT has unique characteristics such as allowing 2 loci mismatch and emergency use or ready to use transplantation. Reduced-intensity transplantation also has been widely accepted to offer opportunities for allogeneic transplant for older and poor overall status patients. We previously showed the feasibility of reduced-intensity cord blood transplantation (RI-CBT) in 30 patients with advanced hematological diseases. Then performed more than 300 times RI-CBT to those whom needed urgent transplantation without suitable HLA matched donors. We retrospectively analyzed medical records of 318 times and 287 cases of RI-CBT from 2004/1/1 to 2007/5/7 in Toranomon Hospital. Disease distribution of 287 studied patients was as follows; acute myeloblastic leukemia/myelodysplastic syndrome was 136 cases, malignant lymphoma 58, acute lymphoblastic leukemia 42, adult T cell leukemia/lymphoma 25, severe aplastic anemia 8 and others 18. A mean age was 56 ranging from 19 to 79 years old. The number of high risk and standard status patients were 243 and 44, respectively. High risk disease status is defined as residual uncontrollable

tumor cells despite of chemotherapy such as primary refractory and beyond CR1 and standard risk is as in remission in a meaning of tumor control. MDS and SAA patients who need frequent transfusions and intensive care for infection are defined as standard risk. Preparative regimen composed of fludarabine 25 mg/m^2 on days -7 to -3, melphalan 80 mg/m^2 on day -2, and 4 Gy total body irradiation on day -1. Graft-versus-host disease prophylaxis was composed of cyclosporine or tacrolimus alone. We analyzed the association of various factors on engraftment in possible 158 patients. Eighty eight % (95% CI, 83%-93%) of patients were engrafted on a median days of 20 (range, 11-55 days) after transplant. Multivariate analysis revealed 5 to 6 antigen match in GVH direction was a significant independent factor for engraftment as well as CD34 dose, while HLA in GVH direction did not significantly influence on engraftment. Three-year estimated overall survival (OS) in total 287 cases was 39.6% (95% CI: 33.5-45.8%). Standard risk patients (n=44) showed 3-year OS of 53.8% (95% CI: 38.3-69.2%) and high risk (n=243) was 26.3% (95% CI:20.2-32.5%). Tacrolimus GVHD prophylaxis group (n=159) had superior 3y-OS of 33.8% (95% CI: 25.9-41.8) to cyclosporine alone with 3yOS of 22.4 % (95% CI: 14.2-30.7). We previously reported pre-engraftment immune reaction characterized by high-grade fever and weight gain and developed on a median of day 9. More intensive immune suppression after RI-CBT using tacrolimus decreased the incidence and severity of PIR and increased OS. In conclusion, RI-CBT is a feasible approach for advanced hematological malignancies.

S6B-3. Cellular molecular imaging - the way forward

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The field of Molecular Imaging has developed rapidly in a short space of time with the advent of PET technology and various other modalities. The greater understanding of the molecular biology of disease provides new opportunities to develop new biological markers that may help diagnosis both *in vivo* as well as *in vitro*. Nuclear Medicine has been in the forefront of Molecular Imaging since its development following World War 2. Various physiological processes were able to be mapped out *in vivo* to aid in the diagnosis and management of various diseases. Measurement of physiological processes can be done in real time to detect pathologies at an early stage before anatomical and clinical changes have manifested. Although Nuclear Medicine techniques are highly sensitive, it lacks the specificity in that many disease and even normal physiological processes may appear relatively the same. This lack of specificity is the consequence of the choice of the molecular probe which has similar function in various pathological and physiological processes. This lack of certainty has caused Nuclear Medicine to earn a rather unfortunate moniker of being an "Un"clear Medicine in some quarters. The better understanding of the molecular processes that occur within the cell, from the DNA to the expression of the proteins that are embedded in the cell membranes and even intracellular organelles provides a unique opportunity to determine, with high degree of precision, various pathologies. The imaging of the cellular processes at the "lab bench" would include optical, nuclear and other imaging modalities but in the end what is learned from the "bench" would eventually have to be translated to the bedside. This is not only in the diagnosis of a disease but to choose appropriate therapy tailored to the patient's genotype and to monitor the disease progression. The way forward in cellular imaging therefore would incorporate genomics and proteonomics of cellular processes in the development of molecular probes that would enhance diagnosis *in vitro* in the lab and eventually *in vivo* by the bedside.