10th Anniversary
THE BANGKOK MEDICAL JOURNAL
For Better HealthCare



From Bangkok Hematology Center to

# BDMS Center of Excellence for Hematology

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**The Bangkok Hematopoietic Stem Cell Transplant Center** was established in January 2009 under the auspices of Professor Dr. Voravit Ratanatharathorn, Karmanos Cancer Institute, Wayne State University, USA. Later on Professor Voravit asked me to be a consultant for the program. However, the number of referred patients for transplant was small. **Bangkok Hematology Center** was then established under the recommendation of Dr. Chatree Duangnet and the opening ceremony was held on August 20, 2010. The objectives of the Center are to cure patients with blood disorders by offering prompt diagnosis and quick and appropriate treatment. Moreover, we provide education to patients and relatives regarding the disease pathogenesis, symptoms, early diagnosis and treatment. Our motto of the center is to support not only a "good body" but also a "good mind". We also emphasize novel targeted therapy and hematopoietic stem cell transplantation (HSCT). We celebrated the 5th anniversary of Bangkok Hematology Center on August 19, 2015 with the success of the center for the treatment of hematologic malignancies and hematologic disorders.

The most prestigious event was the occasion we announced becoming one of the sister institutions of MD Anderson Cancer Center, University of Texas, USA together with Faculty of Medicine Siriraj Hospital, Mahidol University, Thailand. As sister institutions we share education and research findings; MD Anderson Cancer Center collaborates with other cancer institutions and government health authorities across the world on advancing initiatives in population health, public policy, and translational and clinical research. With the sister institution program, we are provided with the best opportunity to advance the knowledge in the field. Thanks to Professor Dr. Borje Andersson and Associate Professor Dr. Simrit Parmar from MD Anderson Cancer Center who have been kind enough in helping and supporting us to be a sister institution. I also would like to thank Major General Dr. Niwat Boonyuen, Dr Chatree Duangnet and the President Dr. Prasert Prasarttong-Osoth for supporting this project. The signing ceremony between MD Anderson Cancer Center with BDMS and Faculty of Medicine Siriraj Hospital was held on August 19, 2015 at Nailert Park Hotel.

## Patient Care

Hematologic or blood disorders are common worldwide. There is a trend towards the increasing incidence of hematologic malignancies particularly in Asia. With regard to hematologic disorders, thalassemia and hemoglobinopathies are common and are considered to be a hallmark of South-East Asia. Among them, homozygous beta thalassemia and double heterozygosity between Hb E and beta-thalassemia so called Hb E / beta-thal as well as Hb H disease are common thalassemia syndromes in this region. Other than thalassemia, other hematologic disorders including aplastic anemia, iron deficiency anemia, autoimmune hemolytic anemia, paroxysmal nocturnal hemoglobinuria and idiopathic thrombocytopenic purpura are frequently found in Thailand.


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Hematologic malignancies comprise acute leukemia, malignant lymphoma and multiple myeloma.

Acute leukemia is the most severe hematologic malignancy. It is caused by neoplastic proliferation of white blood cells precursors without further differentiation, leading to clinical manifestations of bone marrow failure namely anemia, infection and thrombocytopenic bleeding. The etiology of acute leukemia is unknown but may be related to inherited disorders such as Down's syndrome, or exposure to chemicals like benzene. The diagnosis of acute leukemia is based on its clinical manifestations, presenting through CBC, bone marrow smear, biopsy, flow cytometry and cytogenetic study. Treatments include induction of complete remission with chemotherapy and prevention of relapse with post remission, therapy and HSCT.

Malignant lymphoma is the malignant neoplasm of lymph nodes and other lymphoid organs. It is the most common hematologic malignancy. Patients may manifest with enlarged lymph node, spleen, superior vena cava syndrome, (edema of face and neck due to compression of superior vena cava); fever, weight loss and night sweat are common symptoms. Lymphoma is divided into Hodgkin lymphoma and non-Hodgkin lymphoma based on histopathology. Appropriate investigations include CBC, lymph node biopsy, PET/CT scan. Treatments of lymphoma depend on histopathology which include chemotherapy and targeted therapy.

Multiple myeloma is one of the common hematologic malignancies. It is the neoplasm of plasma cells in the bone marrow, manifested by chronic anemia, bone pain, renal failure, and pathological fracture. Diagnosis can be made by blood chemistry, albumin, globulin, bone marrow smear, immunofixation and serum free light chain. Treatments are given with targeted therapy including proteasome inhibitor, immunomodulating agents and chemotherapy, followed by autologous hematopoietic stem cell transplantation.



## Hematopoietic stem cell transplantation (HSCT)

HSCT is the curative treatment for hematopoietic malignancies and hematologic disorders. It is indicated in hematologic malignancies including leukemia, lymphoma, multiple myeloma and myelodysplastic syndrome and hematologic disorders such as thalassemia, aplastic anemia.

HSCT can be divided into autologous and allogeneic. Autologous HSCT is indicated in lymphoma and multiple myeloma. Allogeneic HSCT is used for acute leukemia, thalassemia and aplastic anemia.

Allogeneic HSCT can be performed by using donor e.g. matched sibling, matched unrelated, or haploidentical donor. HSCT procedure includes conditioning, stem cell infusion, GVHD prophylaxis. Allogeneic HSCT may be complicated by acute and chronic graft versus host disease.





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So far, 168 patients underwent HSCT at Wattanosoth Hospital, 24 of them were children and 144 were adult. Of 144 adult patients, 66 received autologous, 41 matched sibling donor HSCT, and 37 haploidentical transplant. 79 out of 144 (55%) were Thais and 45 (45%) were foreigners. It is of interest to note that 21 patients (15%) were from Myanmar.

The detail of allogeneic HSCT at Wattanosoth Hospital is shown in Table 1. The outcome of haploidentical HSCT is more or less similar to matched sibling HSCT, although 30% of patients in haplo HSCT are relapse / refractory patients

Haploidentical HSCT offers the opportunity to perform transplants in all eligible patients whereas only 25% of patients can have an HLA matched sibling as a donor.

**Table 1:** Allogeneic Stem Cell Transplantation at Wattanosoth Hospital

| | Matched sibling Donor HSCT | Haploidentical HSCT |
|---|---|---|
| Number | 41 | 37 |
| Age median (range) | 51 (17 - 66) | 45 (23 - 72) |
| Sex M : F | 19 : 22 | 30 : 7 |
| Relapse / Refractory (%) | 1 (0.2 %) | 11 (30 %) |
| Disease | | |
| AML | 22 (54 %) | 23 (62 %) |
| ALL | 5 (12 %) | 8 (22 %) |
| Others | 14 (34 %) | 6 (16 %) |
| Outcome | | |
| Alive | 28 (68 %) | 23 (62 %) |
| Death | 13 (32 %) | 14 (38 %) |

## Education, Training and Networking

Patient education for hematologic disorders and hematologic malignancies is critical. Information helps patients and relatives to understand the disease, symptoms, investigations for diagnosis and selection of the appropriate treatment. Table 2 shows patient seminar activity during the past years.

Another activity is self-help group meetings. This activity provides the opportunity for newly diagnosed patients to learn from the experiences of other patients who have been successfully treated and to meet with their physicians. This is a meeting between physicians, newly diagnosed and previously treated patients. The details of activities are shown in Table 3.

Training and education is of tremendous importance to hematologists. We have established the BDMS network academy to provide an opportunity for hematologists to update the knowledge in the field as well as to meet experts and discuss case problems. This forum can be either a 1-2 hours' session or a whole day meeting. The details are depicted in Tables 4 and 5. Moreover, networking may facilitate patient referral for further treatment.

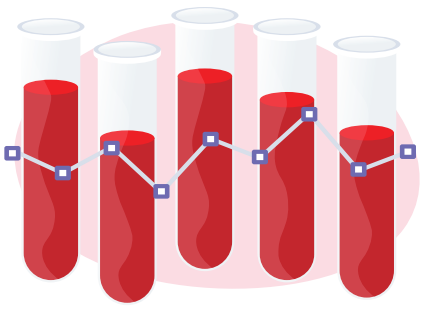
With regard to international conferences and meetings, we have organized an "Annual Update on Breakthrough in Hematology" (AUBH) and BTG 2015. The international meetings provide opportunities for our hematologists to meet and discuss with international experts from the USA, China, Japan, Singapore, South Korea and other countries. The details are in Table 6.

**Table 2:** Patient Seminar Activities

| Dates | Topics |
|---|---|
| Jun 4, 2011 | • Malignant Lymphoma |
| Mar 24, 2012 | • Leukemia |
| Jul 6, 2013 | • Malignant Lymphoma |
| Aug 31, 2013 | • Hematopoietic Stem Cell Transplantation |
| Sep 1, 2013 | • Hematologic Malignancies I |
| Feb 15, 2014 | • Hematologic Malignancies II |
| Feb 4, 2015 | • Hematologic Malignancies III |
| | • World Cancer Day 2015 |
| Aug 30, 2015 | • Hematologic Malignancies |
| Feb 24, 2016 | • Hematologic Malignancies |
| Aug 27, 2016 | • Cancer..... Curable |

**Table 3:** Self Help Group Activities

| Dates | Place |
|---|---|
| Jul 17-18, 2010 | • Budharaksa Hotel, Hua Hin |
| Mar 7-8, 2015 | • Maregesh Hotel, Hua Hin |
| Mar 26-27, 2016 | • Serene Sands Health Resort, Chon Buri |
| Mar 11-12, 2017 | • Worabura Resort&Spa, Hua Hin |
| Mar 17-18, 2018 | • Renaissance Pattaya Resort & Spa, Pattaya |




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**Table 4:** BDMS Network Academy: Hematology Forum

| Dates | Topics | Speaker |
|---|---|---|
| Mar 28, 2019 | • Myeloma Updates | Dr. Archrob Khuhapinant |
| May 2, 2019 | • Meet the Expert: MCL Treatment in novel agent era | Prof. Mats Jerkeman Lund, Sweden |
| Aug 27, 2020 | • Myeloma Updates | Dr. Nuchanan Areethamsirikul<br>Dr. Jiranuch Tantirakrot |
| Oct 16, 2020 | • Lymphoma: Advances in treating indolent non HD lymphoma and CLL | Dr. Archrob Khuhapinant<br>Dr. Jiranuch Tantirakrot |
| Nov 13, 2020 | • BDMS Nurses & Pharmacists education | Dr. Pattariya Chantarasap<br>Ms. Pakawan Promrueng |
| Sep 3, 2021 | • State of the Art : Management in chronic lymphocytic leukemia | Prof. John Gribben, London |

**Table 5:** BDMS Network Academy: Hematology Forum

| Dates | Topics | Venue |
|---|---|---|
| May 20, 2017<br>9.00-15.45 | • Multiple Myeloma | InterContinental Hotel |
| Jul 22, 2017<br>9.00-15.15 | • Lymphoma | Pullman Bangkok<br>King Power Hotel |
| Sep 9, 2018<br>8.30-16.30 | • Best patient care in hematologic malignancies | Renaissance Hotel |

**Table 6:** International Conferences and Meetings

| Dates | Conference / Meeting |
|---|---|
| Sep 2 - 3, 2011 | 1st AUBH 2011 |
| Aug 31 - Sep 1, 2012 | 2nd AUBH 2012 |
| Aug 30 - 31 , 2013 | 3rd AUBH 2013 |
| Aug 30 - 31, 2014 | 4th AUBH 2014 |
| Aug 28 - 29, 2015 | 5th AUBHO 2015 |
| Aug 25 - 27, 2016 | 6th AUBHO 2016 |
| Feb 2 - 3, 2015 | Satellite Meeting, BTG 2015 |
| Jan 21 - 23, 2017 | BTG 2017 |

AUBH (O): Annual Update on Breakthrough in Hematology (and Oncology)
BTG: The International Hematologic Malignancies Conference: Bridging the Gap

## Research Activities

Research activities and publications are the most important indicator for academic excellence. Our goal is to promote research activities not only clinical research but also basic science. Over the past few years, 16 of 23 publications under Wattanosoth Hospital have been from our group. We are collaborating with Siriraj Center of Excellence for Stem Cell Research (SiSCR) to perform basic research on stem cells in general and hematopoietic stem cell in particular. The areas of interest include embryonic stem cell, induced pluripotent stem cell, mesenchymal stem cell and hematopoietic stem cell. The ultimate objectives of the research projects are to promote large scale production of red blood cells and platelets from stem cells for clinical use. Moreover, basic research on control and regulation of stem cell self-renewal and differentiation are being investigated.

Both clinical trials and clinical research are also being launched in collaboration with the Division of Hematology, Department of Medicine, Faculty of Medicine Siriraj Hospital, Mahidol University. There are several ongoing clinical trials on novel drugs for the treatment of hematologic malignancies.

## List of Publications


1. YAP as a key regulator of adipo-osteogenic differentiation in human MSCs. Lorthongpanich C, Thumanu K, Tangkiettrakul K, Jiamvoraphong N, Laowtammathron C, Damkham N, U-Pratya Y, **Issaragrisil S.** *Stem Cell Res Ther* 2019;10(1):402. doi: 10.1186/s13287-019-1494-4.
2. Generation of a serine/threonine-protein kinase LATS1 gene-edited iPSC MUSIi012-A-3. Lorthongpanich C, Laowtammathron C, Jiamvoraphong N, Srisook P, Chingsuwanrote P, Klaihmon 1, Waeteekul S, U-Pratya Y, **Issaragrisil S.** *Stem Cell Res.* 2020. 48:101950. doi: 10.1016/j.scr.2020.101950
3. YAP-depleted iPSC MUSIi012-A-2 maintained all normal stem cell characteristics. Lorthongpanich C, Laowtammathron C, Jiamvoraphong N, Srisook P, Chingsuwanrote P, Klaihmon P, Damkham N, Terbto P, Waeteekul S, U-Pratya Y, **Issaragrisil S.** *Stem Cell Res* 2020;43:101723. doi: 10.1016/j.scr.2020.101723.
4. Effect of YAP/TAZ on megakaryocyte differentiation and platelet production. Lorthongpanich C, Jiamvoraphong N, Klaihmon P, Lueangamornnara U, U-Pratya Y, Laowtammathron C, **Issaragrisil S.** *Biosci Rep* 2020: 40(8):BSR20201780. doi: 10.1042/BSR20201780.
5. Matched sibling donor hematopoietic stem cell transplantation for thalassemia. **Issaragrisil S**, Kunacheewa C. *Curr Opin Hematol* 2016;23(6):508-14. doi: 10.1097/MOH.0000000000000286.
6. Derivation of a MUSIi012-A iPSCs from mobilized peripheral blood stem cells. Laowtammathron C, Srisook P, Chingsuwanrote P, Jiamvoraphong N, Waeteekul S, Terbto P, U-Pratya Y, Lorthongpanich C, **Issaragrisil S.** *Stem Cell Res* 2019;41:101597. doi: 10.1016/j.scr.2019.101597.

7. A novel TRPM7/O-GlcNAc axis mediates tumour cell motility and metastasis by stabilising c-Myc and caveolin-1 in lung carcinoma. Luanpitpong S, Rodboon N, Samart P, Vinayanuwattikun C, Klamkhlai S, Chanvorachote P, Rojanasakul Y, **Issaragrisil S.** *Br J Cancer* 2020;123(8):1289-301. doi: 10.1038/s41416-020-0991-7.
8. Generation of a WWTR1 mutation induced pluripotent stem cell line, MUSIi012-A-1, using CRISPR/Cas9. Lorthongpanich C, Jiamvoraphong N, Supakun P, Damkham N, Terbto P, Waeteekul S, U-Pratya Y, Laowtammathron C, **Issaragrisil S.** *Stem Cell Res* 2019;41:101634. doi: 10.1016/j.scr.2019.101634.
9. Generation of human induced pluripotent stem cell line carrying SCN5AC2204>T Brugada mutation (MUSli009-A-1) introduced by CRISPR/Cas9-mediated genome editing. Angsutararux P, Luanpitpong S, Chingsuwanrote P, Supraditaporn K, Waeteekul S, Terbto P, Lorthongpanich C, Laowtammathron C, U-Pratya Y, **Issaragrisil S.** *Stem Cell Res* 2019;41:101618. doi: 10.1016/j.scr.2019.101618.
10. Deciphering the Elevated Lipid via CD36 in Mantle Cell Lymphoma with Bortezomib Resistance Using Synchrotron-Based Fourier Transform Infrared Spectroscopy of Single Cells. Luanpitpong S, Janan M, Thumanu K, Poohadsuan J, Rodboon N, Klaihmon P, **Issaragrisil S.** *Cancers (Basel)* 2019;11(4):576. doi: 10.3390/cancers11040576.
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13. Metabolic sensor O-GlcNAcylation regulates megakaryopoiesis and thrombopoiesis through c-Myc stabilization and integrin perturbation. Luanpitpong S, Poohadsuan J, Klaihmon P, Kang X, Tangkiettrakul K, **Issaragrisil S.** *Stem Cells* 2021;39(6):787-802. doi: 10.1002/stem.3349.
14. Reactive oxygen species mediate cancer stem-like cells and determine bortezomib sensitivity via Mcl-1 and Zeb-1 in mantle cell lymphoma. Luanpitpong S, Poohadsuan J, Samart P, Kiratipaiboon C, Rojanasakul Y, **Issaragrisil S.** *Biochim Biophys Acta Mol Basis Dis* 2018;1864(11):3739-53. doi: 10.1016/j.bbadis.2018.09.010.
15. Inhibition of O-GlcNAcase Sensitizes Apoptosis and Reverses Bortezomib Resistance in Mantle Cell Lymphoma through Modification of Truncated Bid. Luanpitpong S, Chanthra N, Janan M, Poohadsuan J, Samart P, U-Pratya Y, Rojanasakul Y, **Issaragrisil S.** *Mol Cancer Ther* 2018;17(2): 484-96. doi: 10.1158/1535-7163.MCT-17-0390.
16. Selective Cytotoxicity of Single and Dual Anti-CD19 and Anti-CD138 Chimeric Antigen Receptor-Natural Killer Cells against Hematologic Malignancies. Luanpitpong S, Poohadsuan J, Klaihmon P, **Issaragrisil S.** *J Immunol Res* 2021;2021:5562630. doi: 10.1155/2021/5562630.

## Future Direction

Our strength is the experience and the success of haplo HSCT which can be undergone in all eligible patients. We therefore would like to strengthen our networking for patient referral both from BDMS hospitals and others from Thailand and overseas for HSCT. Our ultimate goal is to establish the **"South-East Asia Center for Haploidentical Stem Cell Transplant"** to be a referral center for haplo HSCT in the region.








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