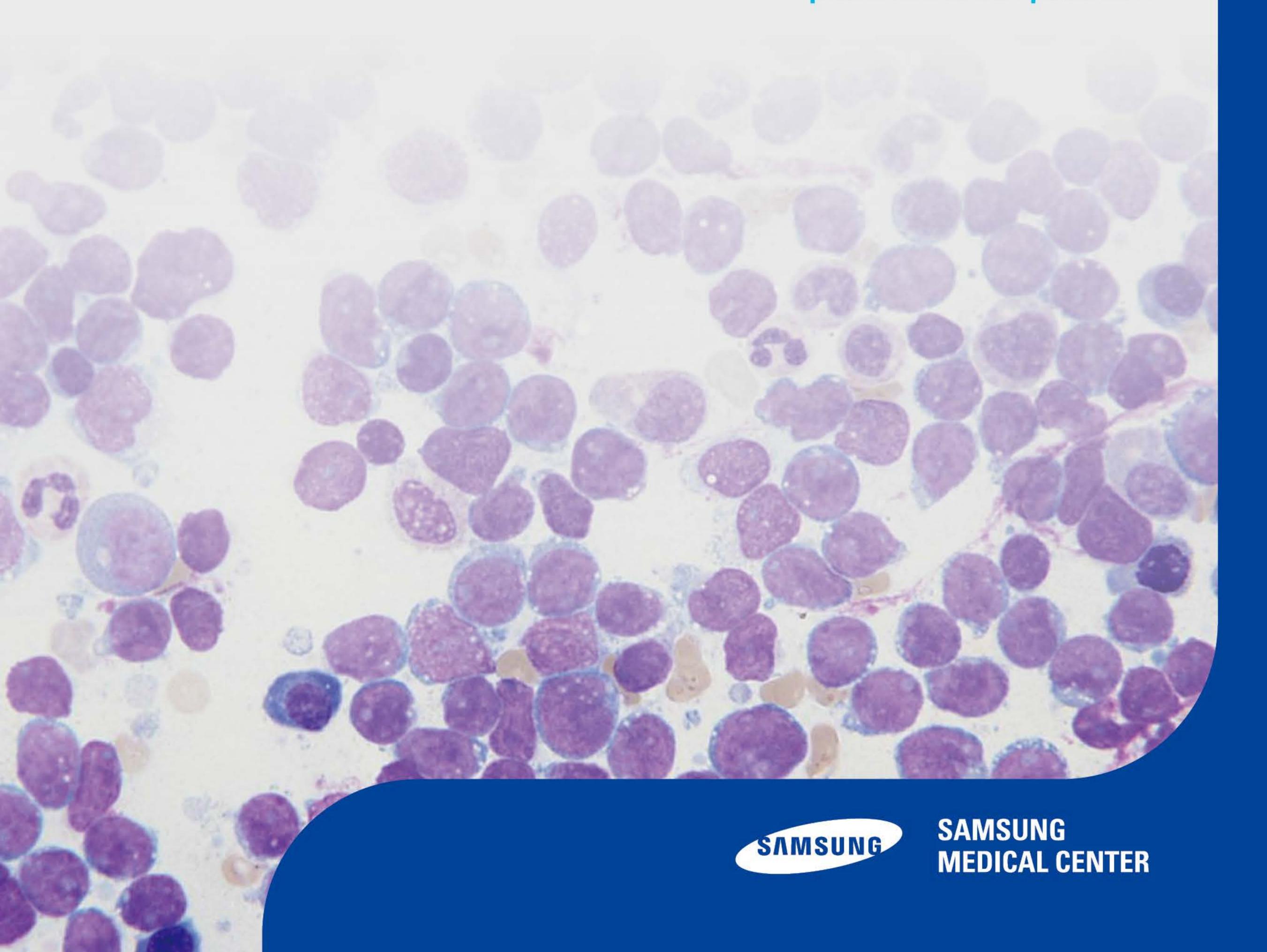
# Pediatric Cancer Treatment

New hope for refractory pediatric cancer patients

With creation and innovation, we make the new standard for refractory pediatric cancer patients!





# What are differences between pediatric cancers and adult cancers, and how are they diagnosed?

Pediatric cancer is cancer that occurs in pediatric population (generally, up to 18 years old), but it is fundamentally different from adult cancer. In adults, commonly known cancers such as lung cancer, liver cancer, colon cancer, etc. occur frequently, but in children, such cancers rarely occur. Unlike adults, blood cancer is the most common one, and diseases such as neuroblastoma, rhabdomyosarcoma whose names are not even familiar take the majority. Therefore, the cancer pathogenesis and pathophysiology as well as the age of onset are different from those of adult cancers. Moreover, in most pediatric cancers, the role of chemotherapy is very important and the complete cure, not an extension of life, is the goal. For pediatric patients, the post-management of complications is much more important than for adult patients because any serious sequelae caused by treatment would remain for the rest of their lives.

Sustained fever without cause	Severe tiredness, pallor, and easy bruisibility	Sustained bone pain
Swelling of abdomen or palpable mass	Lymph node enlargement	Vomiting, headache, or double vision

<sup>\*</sup>Diagnosis of pediatric cancer

Pediatric cancers usually occur in blood or other organs so that no symptoms manifest until they progress much. Also, unlike adults having health checkups, there are few opportunities to discover cancer early. For diagnosis of pediatric cancers, radiologic tests such as ultrasound, CT, MRI, etc. and nuclear medicine tests (PET, MIBG, SCAN) are performed in addition to blood test as the basic test, and the bone marrow exam is performed for confirmation if needed. By analyzing all test results together, the most appropriate treatment method is selected based on the severity of cancer. Recently, the targeted therapy is performed as well if the molecular genetic anlaysis of cancer cells is possible after the blood test or biopsy.

Blood Test

Ultrasonography

CT, MRI, PET

Bone Marrow Exam

# What treatment methods are available for pediatric cancer?

Like adult cancers, three treatment methods (i.e. surgery, radiation and drug) are basic methods, and the pediatric cancer treatment result is better than that of adult cancer so that the cure rate is about 70 - 80%. For some high-risk blood cancers or refractory solid tumors, allogeneic hematopoietic stem cell transplantation or high-dose chemotherapy followed by autologous stem cell transplantation, targeted therapy, immunotherapy, etc. can be performed to increase the survival rate.

## Treatment methods performed in Samsung Medical Center

# Hematopoietic Stem Cell Transplantation



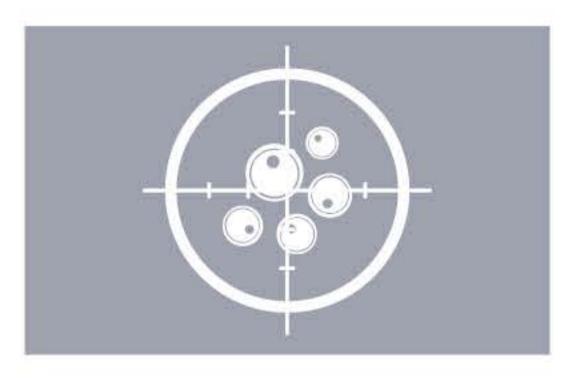
- Allogeneic: In this treatment method, after removing tumor cells and bone marrow of the patient using the high-dose anticancer agent with or without total body irradiation, healthy hematopoietic stem cells of another person whose histocompatibility antigens (HLA) are identical are infused through blood vessels to make the bone marrow function normal. Tranplantation between persons with HLA-matched related bone marrow or peripheral blood stem cells, HLA-matched unrelated bone marrow or peripheral stem cells, cord blood tranplantation, histocompatibility mismatch tranplantation, transplantation between family members with haploidentical type, etc. are all possible. This method is performed for treatment of various diseases such as leukemia, severe aplastic anemia, congenital immune deficiency, various hemoglobinopathy, other genetic diseases, etc.
- Autologous: In this treatment method, after removing tumor cells as much as possible using the high-dose anticancer treatment and systemic radiation therapy, precollected autologous hematopoietic stem cells are infused through blood vessels to recover the function of the bone marrow that is damaged during the cancer treatment. Especially, for children with high-risk solid tumors, the survival rate is much improved by performing the tandem high-dose chemotherapy and autologous stem cell transplantation (HDCT/autoSCT).

# **Chemo Therapy**



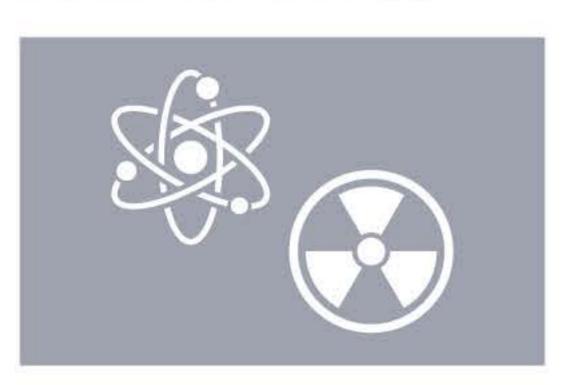
- In children, it is characteristic that the weight of chemotherapy using anticancer agents is comparatively larger than that of adult cancers. Much of treatment of blood cancers such as leukemia, etc. relies on chemotherapy, and even for most of solid tumors, chemotherapy is used before or after surgery for the purpose of maximizing treatment effects such as reducing the tumor size, suppressing the recurrence, etc.
- For acute lymphoblastic leukemia which is the most common pediatric cancer, unlike adult cancers, the anticancer treatment schedule is very complex so that the customized treatment based on the cancer characteristics at the time of diagnosis and response to the treatment is provided.

# Targeted Therapy



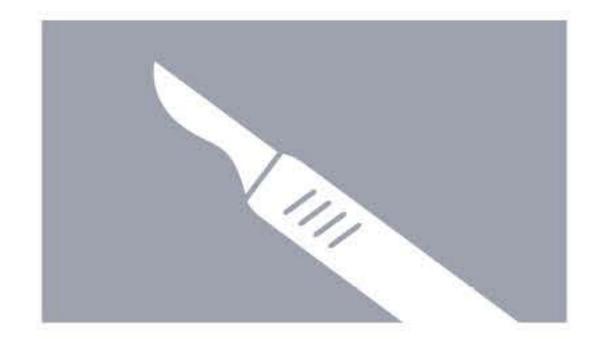
In this treatment method, the genetic information of cancer cells is analyzed comprehensively to discover the mutant gene that only exists in the particular cancer and administer the drug that targets the mutant gene.

# Proton therapy Radiation therapy



- Radiation therapy: In this treatment method, cancer cells in the human body are destroyed and their growth is prevented using radiation or radioactive isotopes.
- Proton therapy: The proton beam passes through the body and transfers maximum energy to the cancer tissues and subsequently annihilates to minimize radiation exposure to the normal tissues. This process is composed of physical characteristics called, "Bragg peak," which achieves effective treatment results while decreasing the risks associated to side effects in comparison to the existing radiotherapy methods. Especially, the proton therapy has been much applied to patients with pediatric cancer (brain tumor) who still have many years to live by minimizing the adverse effect of radiation and risk of secondary cancer occurrence.

## Surgery



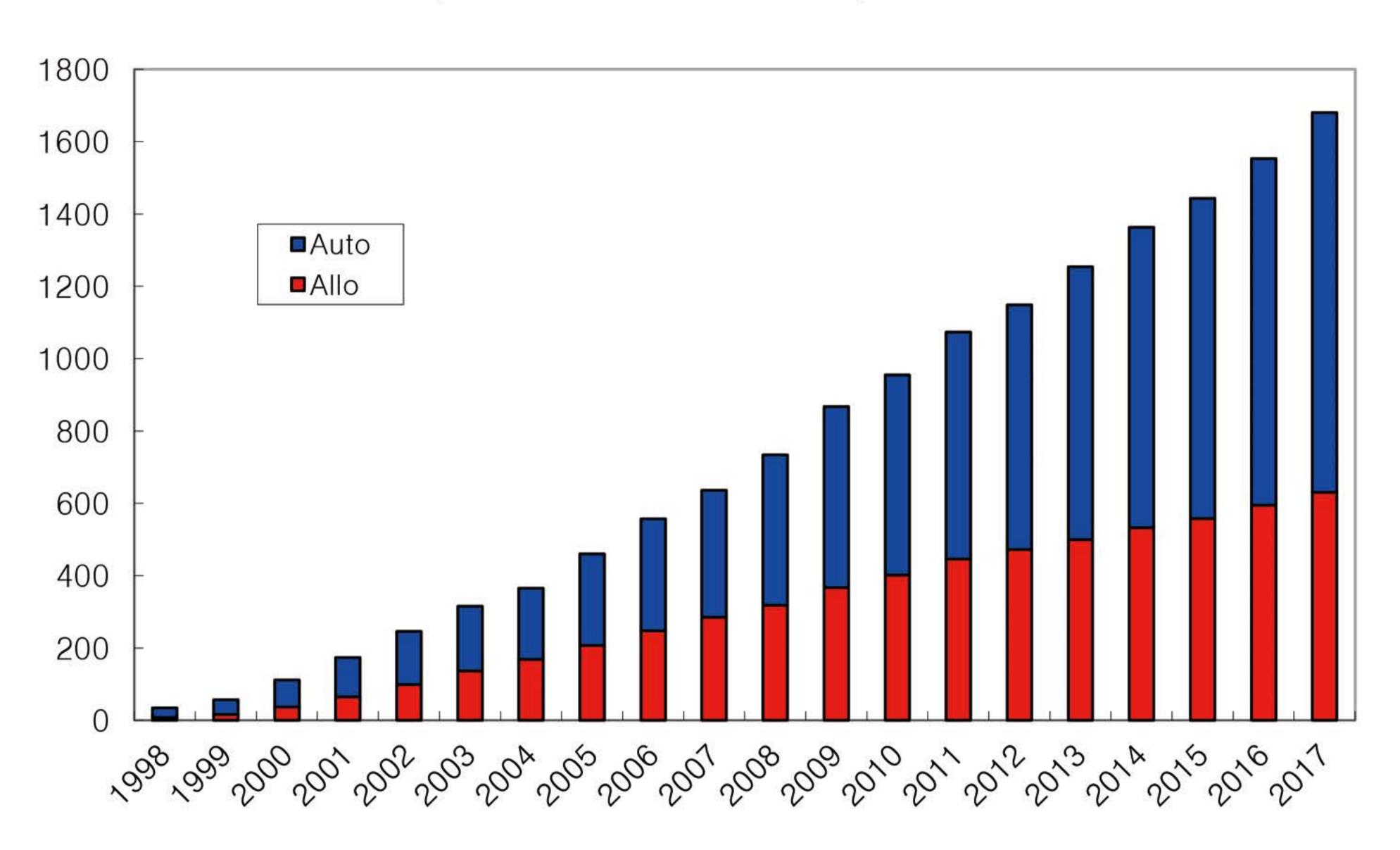
Surgeries are performed by surgeons who are specialized in pediatric patients

# What distinguishes the Pediatric Cancer Center of Samsung Medical Center from others?

# Indeed, we are performing the most number of pediatric hematopoietic stem cell transplantation in South Korea as ranked No. 1

Since the highest risk group at diagnosis that includes certain types of acute leukemia, high-risk neuroblastoma, high-risk brain tumor, other high-risk solid tumors or some recurrent tumors, etc. has low survival rate with conventional chemotherapy, we improve the complete cure rate by performing hematopoietic stem cell transplantation. The medical staff of Samsung Medical Center is most actively performing hematopoietic stem cell transplantation in South Korea, and in June 2011, we reached 1,000 cases of pediatric hematopoietic stem cell transplantation for the first time in South Korea so that, based on the accumulated experiences in hematopoietic stem cell transplantation, we are producing the treatment results whose results are better than those of advanced countries. For pediatric patients who do not have appropriate donors, we perform cord blood transplantation successfully so that the survival rate that is similar to that of transplantation between siblings or unrelated persons is secured, and transplantation between haploidentical types is also performed for therapeutic effect depending on diseases.

# Pediatric HSCT(Cumulative number) - 1680 as of 2017



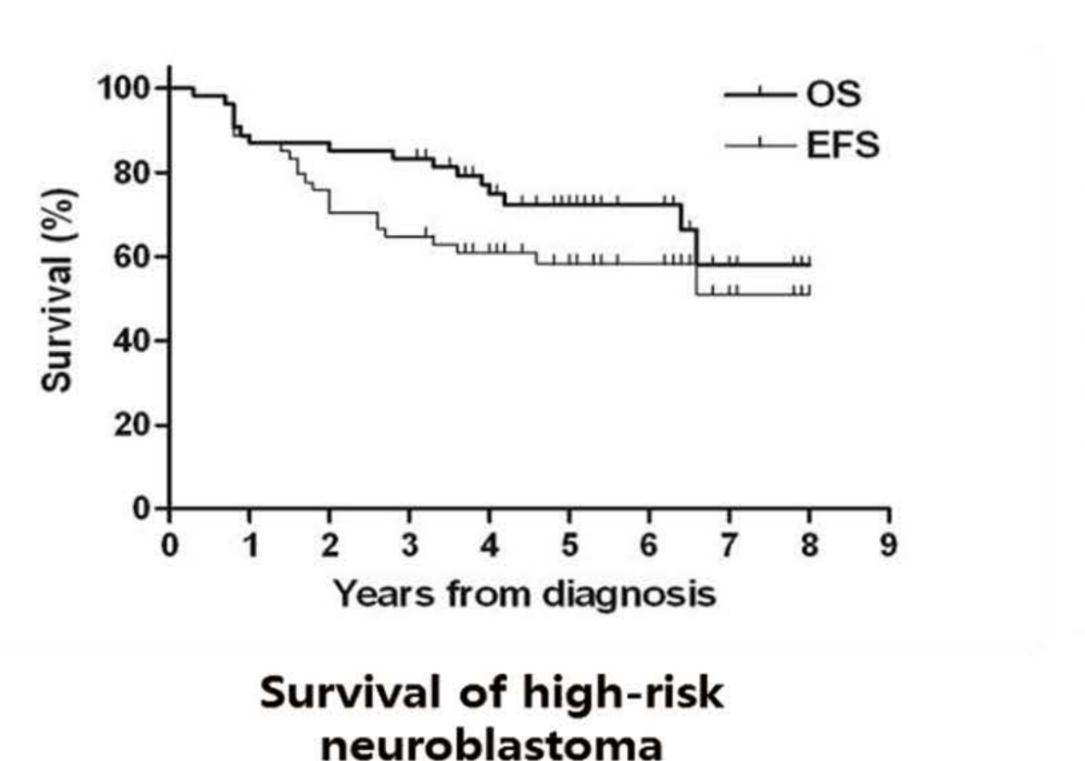
# We are producing the high survival rate with the new treatment strategy in pediatric acute myeloid leukemia.

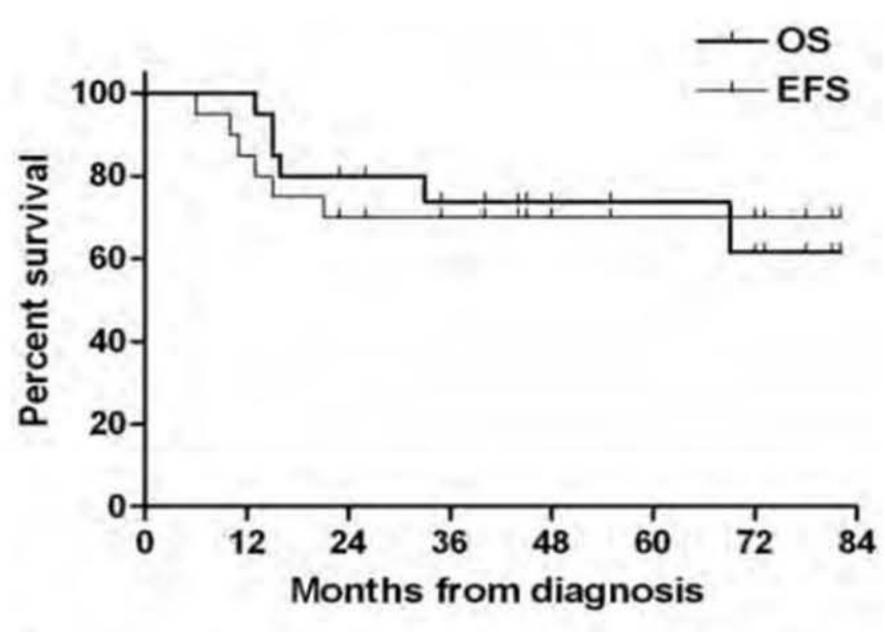
Unlike pediatric acute lymphoblastic leukemia whose survival rate is 85 - 90%, the five-year survival rate of pediatric acute myeloid leukemia is only about 60 - 70% even in Western advanced countries. The medical staff of Samsung Medical Center has been developing the unique anticancer protocol since 2012, and prognosis groups are classified based on molecular and cytogenetic characteristics at diagnosis to apply differentiated treatment strategies based on each prognosis. For Favorable Prognosis Group, there are only a total of six courses of chemotherapy. For Poor Prognosis Group, allogeneic hematopoietic stem cell transplantation is performed after four to five courses of chemotherapy. For Intermediate Prognosis Group, allogeneic hematopoietic stem cell transplantation with reduced intensity conditioning is performed when HLA-identical donor is available. As the result of applying such unique treatment strategies, we have achieved the surprising performance of the five-year survival rate, 78%.

# In treatment of refractory high-risk solid tumors among pediatric cancers, we are producing the high survival rate with the new treatment method.

For the high-risk group of neuroblastoma, brain tumor, etc. whose treatment results are not good among pediatric cancers, the survival rate and quality of life are improved through applying stratified treatment method per each disease stage. Especially, for the high-risk group of neuroblastoma, the targeted radiation therapy called metaiodobenzylguanidine (MIBG) is performed in combination with the high-dose anticancer therapy, and by this, we could report the world-class level of the survival rate, 70%, as the five-year treatment result.

For the treatment of medulloblastoma that is a common brain tumor in pediatric population, although the radiation therapy is one of standard therapies, there are adverse effects such as reduction of cognitive ability, growth impairment, etc. in pediatric patients. To avoid such problems, by introducing the tandem high-dose chemotherapy and method that reduces the radiation therapy, we reduced the adverse effects of the radiation therapy and increased the survival rate up to 70 - 80%, which is the world-class level. Besides, for brain tumors with poor prognosis, the high-dose chemotherapy is actively performed to improve the treatment results. Also, by introducing the proton therapy equipment recently, we have established the foundation that the post-complications such as secondary cancer, etc. can be reduced by performing proton therapy for patients with brain tumors.





Survival of high-risk medulloblastoma

\*EFS: Event Free Survival rate, OS: Overall Survival rate

# We are actively doing basic and translational research for treatment of refractory diseases.

At Samsung Medical Center Pediatric Cancer Center, we are making a lot of efforts in doing basic and translational research for continuously improving treatment results of patients as well as providing patients with the best care. To develop the new treatment method of graft-versus-host disease which is the biggest obstacle to successful allogeneic hematopoietic stem cell transplantation, we are doing research on mesenchymal stem cells, and the function of stem cells were able to be improved through a certain preconditioning method. We proved through animal experiments that the functionally augmented stem cells that are developed by the research team of Samsung Medical Center have much better treatment capability than those of naive stem cells. With such promising results, we will conduct clinical trials soon. Meanwhile, with cooperation with Samsung Genome Institute located in the medical center, the genetic information of cancer cells of refractory cancers is analyzed comprehensively, and we are doing genomic research on discovering mutant genes of those tumors. We are also currently conducting a clinical trial in which a mutant gene that exists according to the genomic test result is targeted with the selected drug. Based on the clinical and basic research, we have published 28 research papers with lead authors in international SCI academic journals for the last three years, and it is the highest number in this academic field in South Korea.

<sup>1.</sup> Lee JW, Lee S, Cho HW, Ma Y, Yoo KH, Sung KW, et al. Incorporation of high-dose 1311-metaiodobenzylguanidine treatment into tandem high-dose chemotherapy and autologous stem cell transplantation for high-risk neuroblastoma: results of the SMC NB-2009 study. J Hematol Oncol 2017;10:108.

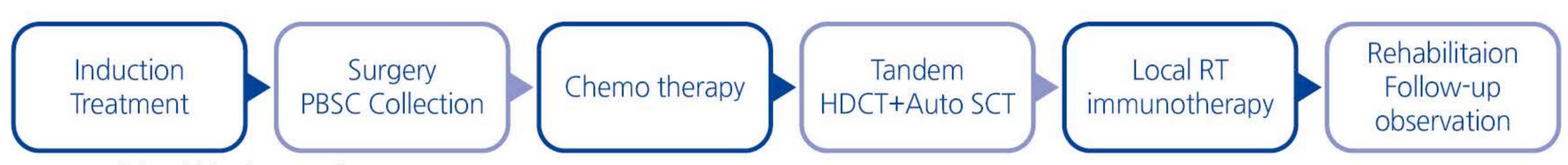
<sup>2.</sup> Sung KW, Lim DH, Son MH, Lee SH, Yoo KH, Koo HH, et al. Reduced-dose craniospinal radiotherapy followed by tandem high-dose chemotherapy and autologous stem cell transplantation in patients with high-risk medulloblastoma. Neuro Oncol 2013;15:352-9.

<sup>3.</sup> Sung KW, Lim DH, Yi ES, Choi YB, Lee JW, Yoo KH, et al. Tandem High-Dose Chemotherapy and Autologous Stem Cell Transplantation for Atypical Teratoid/Rhabdoid Tumor. Cancer Res Treat 2016;48:1408-19.

<sup>4.</sup> Lee JW, Lim DH, Sung KW, Lee HJ, Yi ES, Yoo KH, et al. Multimodal treatment including tandem high-dose chemotherapy and autologous stem cell transplantation in children with anaplastic ependymomas. Pediatr Transplant 2018;22:e13127

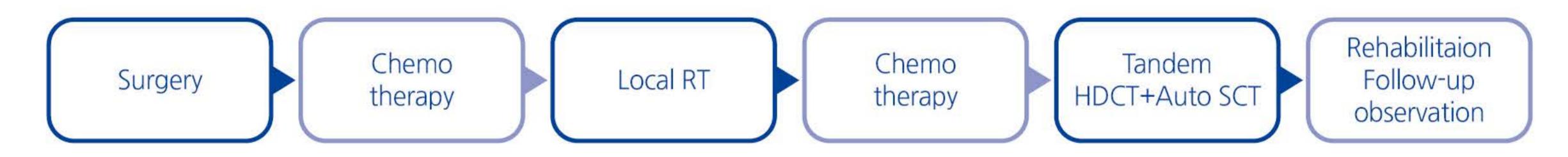
# Treatment procedure

## High-risk neuroblastoma

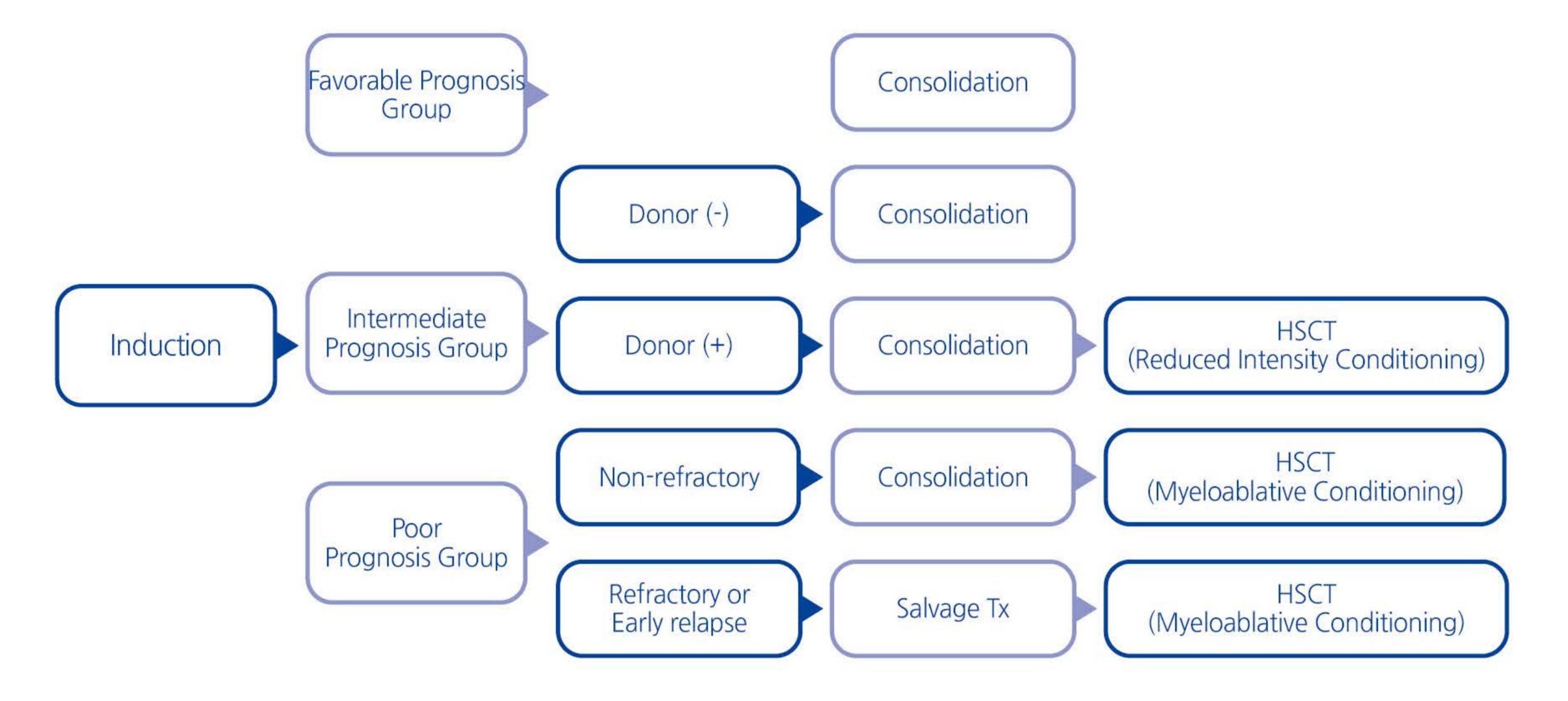


#### \*PBSC: peripheral blood stem cell

## High-risk brain tumor



# High-risk acute myeloid leukemia



# Very high-risk acute lymphoblastic leukemia



- This process applies to standard cases and the treatment plan may be changed depending on the patient's actual condition after the consultation and evaluation.
- For more information, please contact us via International Health Services at SMC.

# Best professors in pediatric cancer



Hong Hoe Koo M.D., Ph.D. Pediatric oncologist

Areas of Expertise:

Leukemia, Pediatric hematology, Pediatric Hematopoietic Stem Cell Transplantation



Ki Woong Sung M.D., Ph.D. Pediatric oncologist

Areas of Expertise:

Neuroblastoma, Brain tumor, Pediatric Hematopoietic Stem Cell Transplantation



Keon Hee Yoo, M.D., Ph.D.
Pediatric oncologist
Director of Children's Cancer Center

#### Areas of Expertise:

Pediatric leukemia, Aplastic anemia, Other benign hematology, Pediatric Allogeneic Hematopoietic Stem Cell Transplantation, Mesenchymal Stem Cells



Ji Won Lee, M.D., Ph.D. Pediatric oncologist

#### Areas of Expertise:

Pediatric solid tumor (Sarcoma, Wilms tumor, Other solid tumor), Cancer genomics.



Suk Koo Lee, M.D., Ph.D. Surgeon

#### Areas of Expertise:

Pediatric Surgery Transplantation Surgery



Hyung Jin Shin, M.D., Ph.D. Neurosurgeon

Areas of Expertise:

Pediatric brain tumor Medulloblastoma



Do Hoon Lim, M.D., Ph.D. Radiation Oncologist

#### Areas of Expertise:

Pediatric Cancer, Brain Tumor, Sarcoma, Hematologic Cancer, Stomach Cancer.



Jeong Yi Kwon, M.D., Ph.D. Pediatric Physiatrist

#### Areas of Expertise:

Pediatric Rehabilitation



Yoo Sook Joung, M.D., Ph.D. Psychiatrist

#### Areas of Expertise:

Child & Adolescent Psychiatry Developmental Disorder



Min Ki Baek, M.D., Ph.D. Surgeon

## Areas of Expertise:

Pediatric Urology



Sung Wook Seo, M.D., Ph.D. Orthopedic Surgeon

#### Areas of Expertise:

Bone Tumor and children fracture



Sang Hoon Lee, M.D., Ph.D. Surgeon

#### Areas of Expertise:

Pediatric and Transplant Surgery



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