Annual Report 2015

Pediatric Hematology-Oncology and Stem Cell Transplantation

Mervi Taskinen, MD
Jaana Vettenranta, RN
Kim Vettenranta, MD (Editor-in-Chief)

CONTENTS

ABBREVIATIONS

ALL	acute lymphoblastic leukemia
AML	acute myeloid leukemia
CNS	brain tumors
NOPHO	Nordic Organization for Pediatric Hematology and Oncology
allogeneic	from a healthy donor
autologous	transplantation with the patient's own cells
CML	chronic myeloid leukemia
MDS	myelodysplastic syndrome
NBL	neuroblastoma
NHL	non-Hodgkin lymphoma
SIB	HLA identical sibling
SAA	severe aplastic anemia
URD	unrelated HLA matched donor
TRM	transplant-related mortality, deaths related to recurrence of the disease excluded

Cover photo Kim Vettenranta on leukemic cells.
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UNIT INTRODUCTION

The Pediatric Hematology, Oncology and Stem Cell Transplantation Unit is Finland's largest unit specialized in pediatric cancer care and hematological diseases, as well as allogeneic stem cell transplantation for children. The unit comprises the Pediatric Cancer Ward, a day hospital unit, a procedure unit, and an outpatient clinic.

The unit is responsible for the diagnosis and treatment of pediatric cancers and hematological diseases in its area. Additionally, the unit carries out all of Finland's pediatric allogeneic bone marrow transplantations, and the respective training as part of physician´s specialization in pediatric hematology-oncology and stem cell transplantation. The unit also bears the key national responsibility for international cooperation in pediatric hematology-oncology as well as stem cell transplantation.

The unit treats all pediatric patients receiving stem cell transplantation, provides intravenous chemotherapy for pediatric cancer patients, and treats patients with benign hematological diseases as well as conducts research in the field.

Staff at the unit includes six consultants in pediatric hematology-oncology and stem cell transplantation (and one 50% time consultant position), a fellow in pediatric hematology-oncology as well as a pediatric anesthesiology consultant, a pediatric resident, more than 60 nurses, five ward clerks, as well as supportive staff including ward pharmacists, physiotherapists, a rehabilitation coordinator, dietician, consultant in adolescent psychiatry, psychologist, social worker, kindergarten teacher, teacher, hospital pastor, instrument technician and ward domestics. All the consulatnts have an MD as well as a PhD degree, and three have a docent's competence (equivalent to Assistant Professor) in pediatric hematology and oncology. In addition, at least three of the consultants will receive a docent's competence in 2016.

The hospital sees approximately 5,000 in-patient days, 1,200 day clinic visits and 1,300 procedures that require anesthesia annually. There are approximately 4,000 outpatient clinic visits and around 1,000 home visits each year.

International/Nordic research and treatment PROTOCOLS in which we already participate, or we will be joining in 2016

Treatment protocols in which we are participating in at the end of 2015:

- Ewing's sarcoma: Ewing 2008, Ewing-relapses (rEECur)
- Neuroblastoma: SIOPEN-HR-NBL 1.7
- Leukemias: Nopho-ALL-2008, Nopho-AML-2012, Interfant-06, IntReALL2010-SR
- Brain tumors: Angiocomb
- Allogeneic stem cell transplantation ALL SCTped FORUM 2012

Treatment protocol in which we will join in 2016:

- Brain tumors: PNET5 MB

CONVENTIONAL CANCER THERAPY

KEY FIGURES

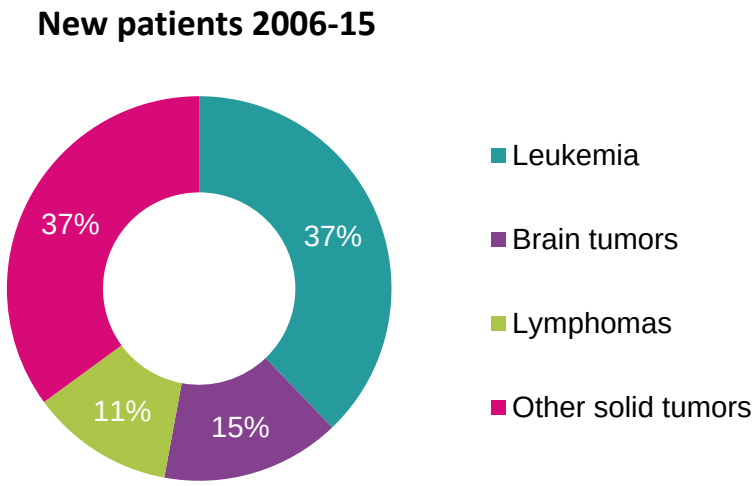


Figure 1. Diagnosis distribution of new pediatric cancer cases in the years 2006–15. In 2015, 41 new patients were admitted, 14 of whom had leukemia.

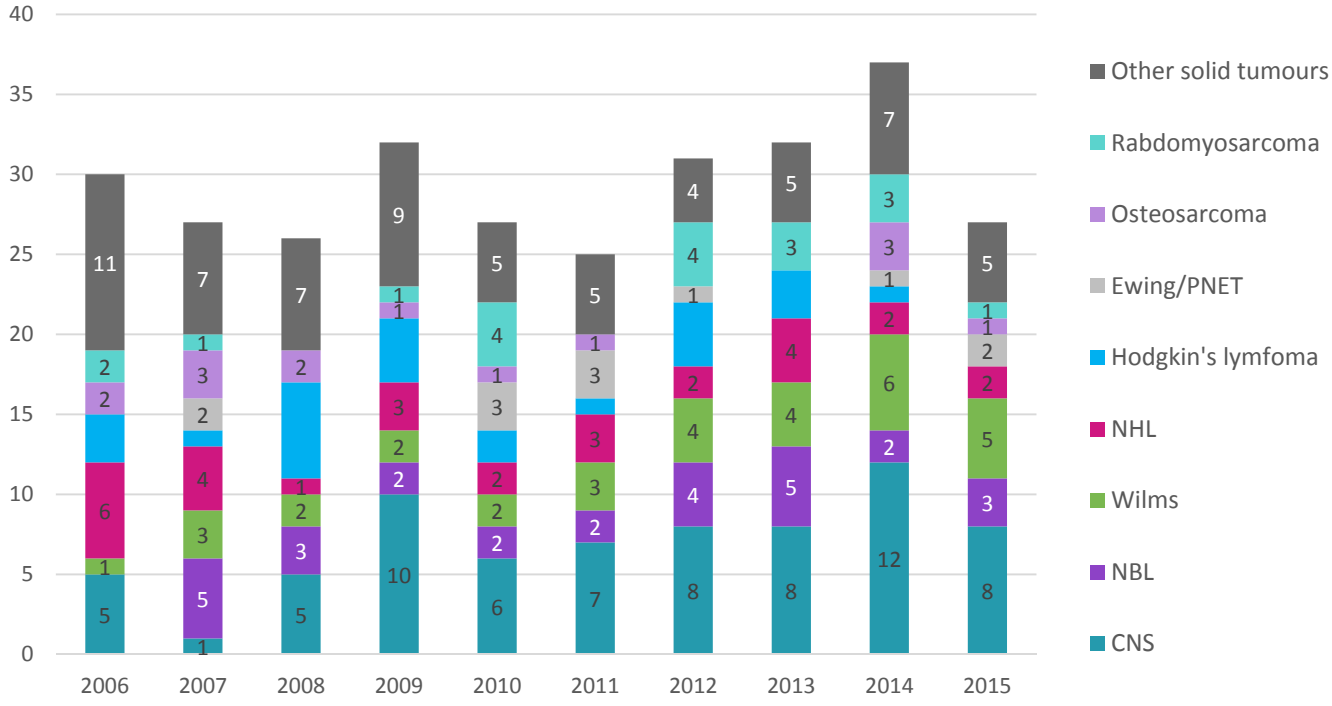


Figure 2. Distribution of diagnoses in solid tumors in 2006-2015.

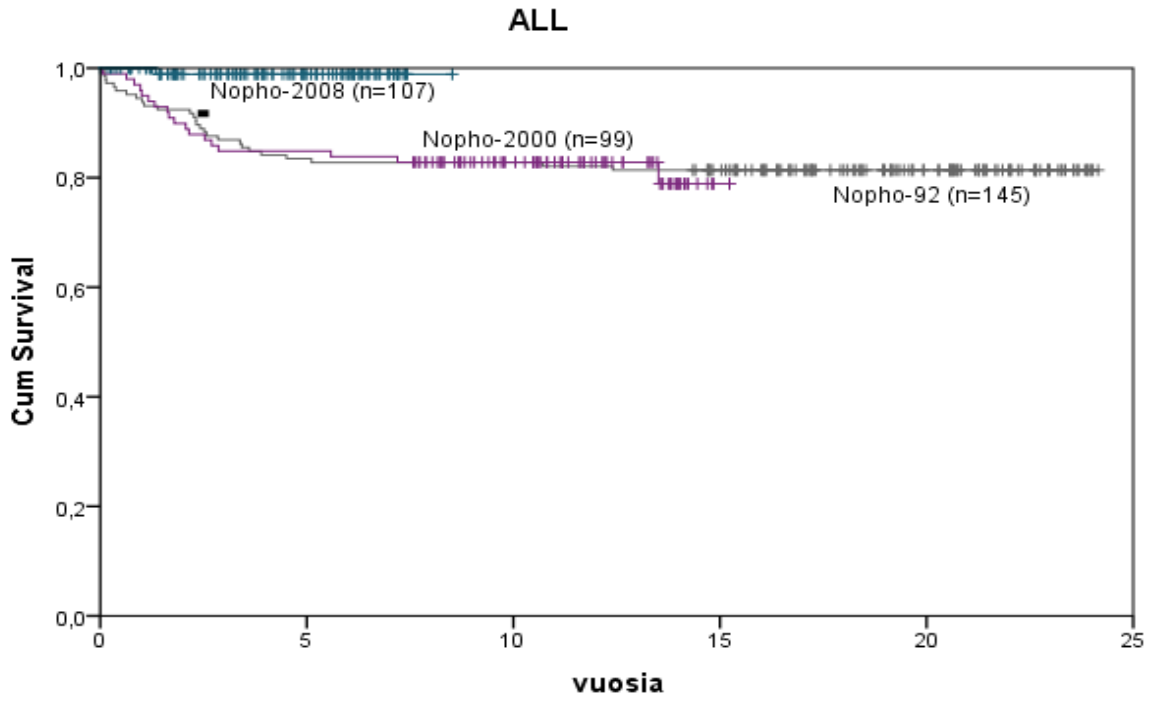


Figure 3. Treatment results in pediatric ALL and their development (Kaplan-Meier analysis). The figure also shows the positive development of the prognosis in the NOPHO-ALL-2008 treatment protocol currently in use. The rectangle at 5 years shows the respective, combined NOPHO result.

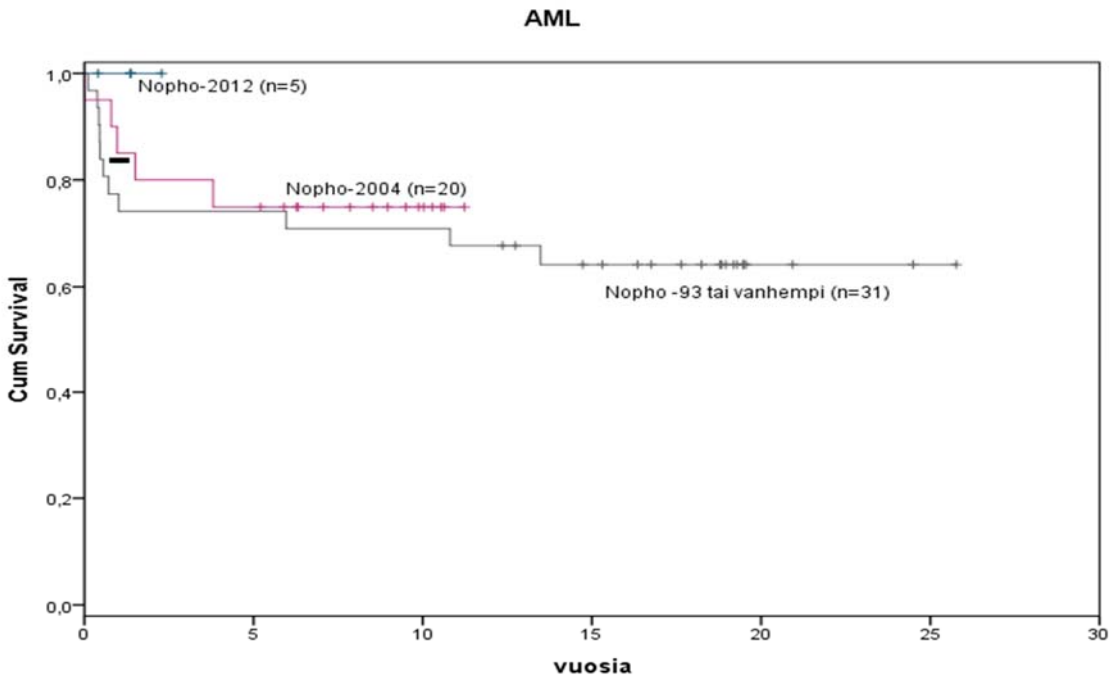


Figure 4. Treatment results in pediatric AML do not attain the level of those in ALL even on the international level, but in our unit are excellent. The new AML treatment protocol (AML-NBH-2012) has been launched at in all the Nordic nations in 2013. The rectangle at 5 years gives the respective, combined estimated prognosis for survival in all treated patients at 30 months.

SOLID TUMORS

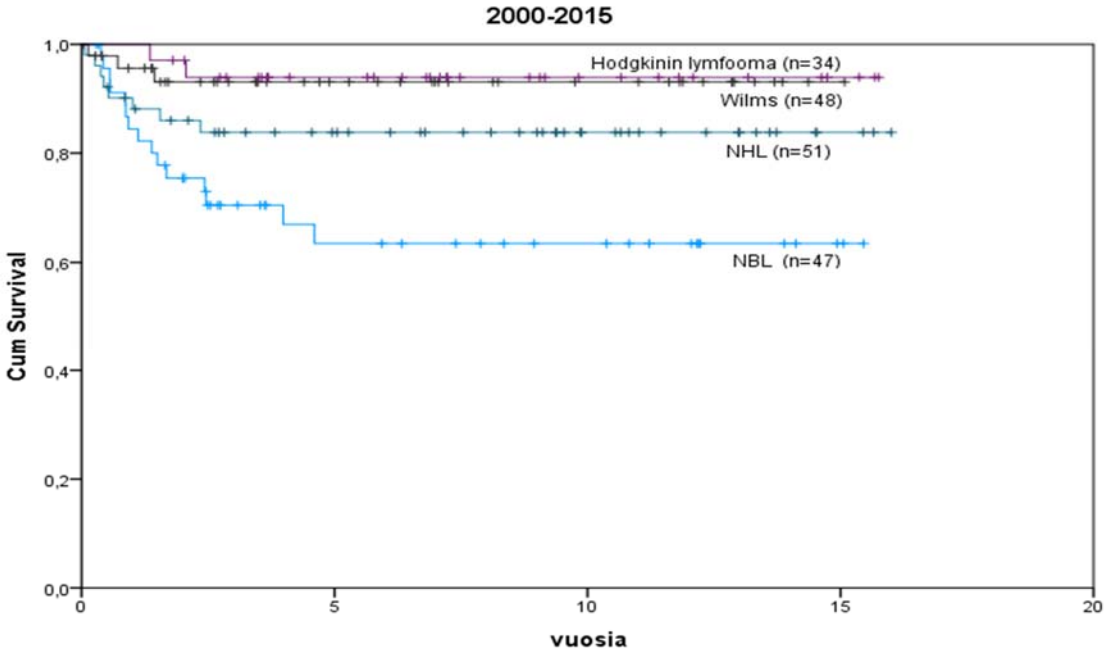


Figure 5. Cumulative survival for patients treated in four key diagnostic groups.

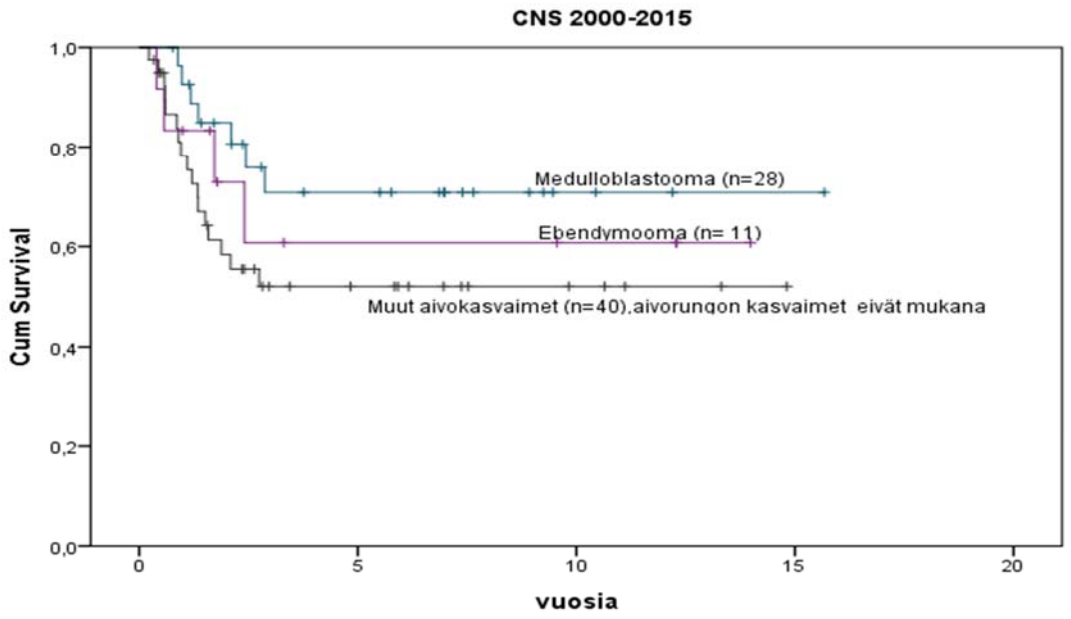
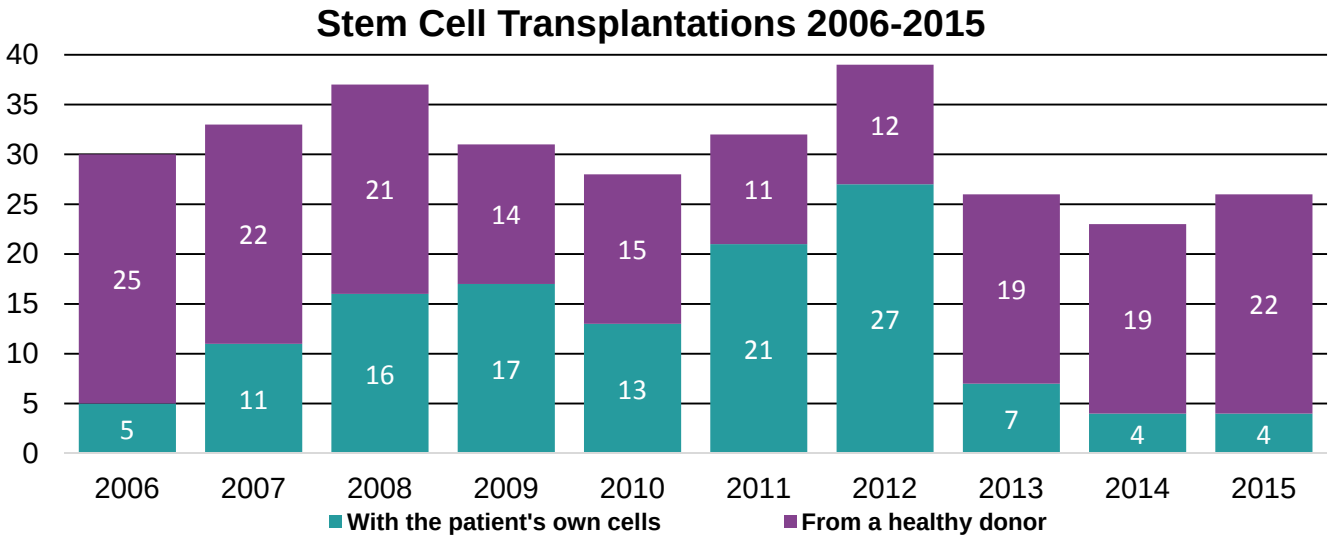


Figure 6. Cumulative survival for patients in three key brain tumor groups.

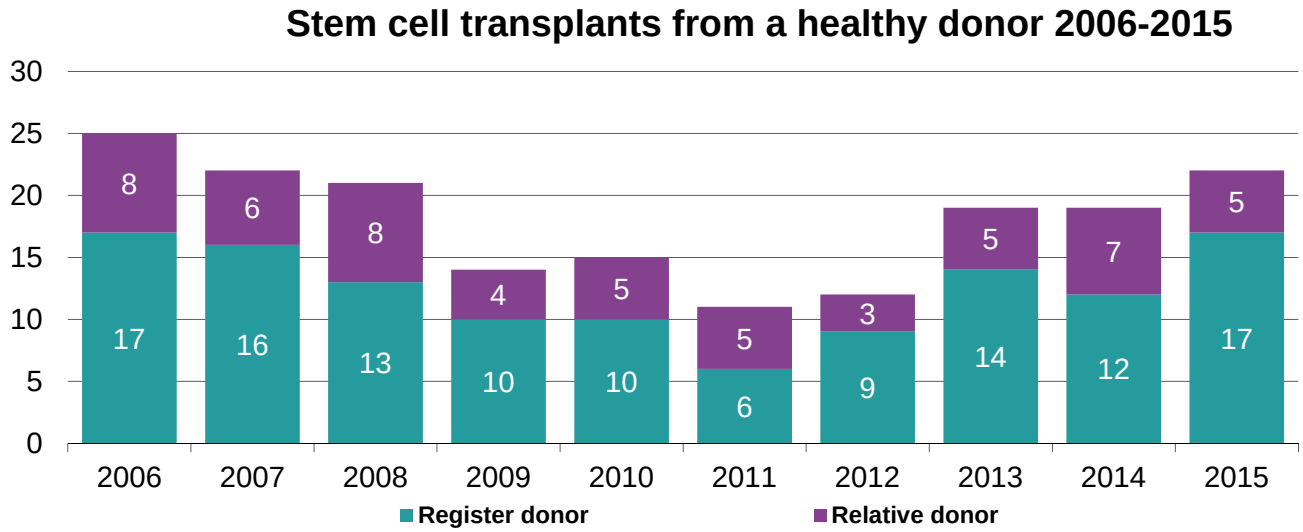
STEM CELL TRANSPLANTATION

KEY FIGURES

A total of 461 allogeneic bone marrow transplants had been conducted and 337 cases of intensive chemotherapy followed by autologous stem cell rescue carried out at the Children's Hospital by the end of 2015. This brings the total number of stem cell transplantations performed by the end of 2015 to 798, including a total of 41 cord blood stem cell transplantations.



ALLOGENEIC STEM CELL TRANSPLANTATIONS



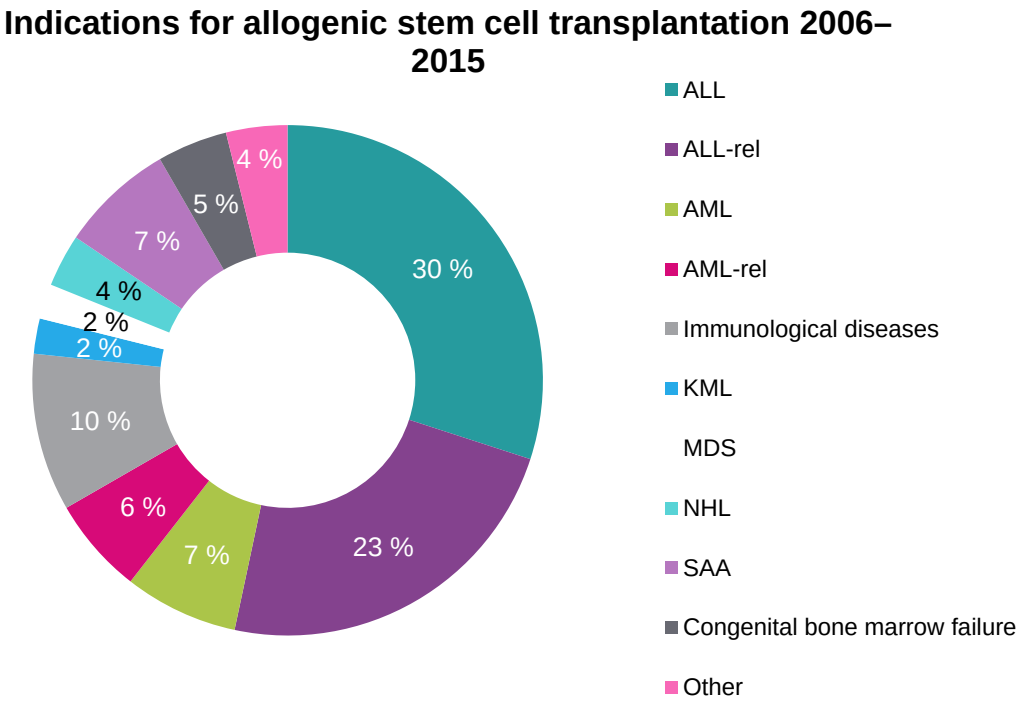


Figure 9. The indications for allogeneic transplantation in 2006-15 with leukemias constituting the largest single group.

AUTOLOGOUS STEM CELL RESCUE

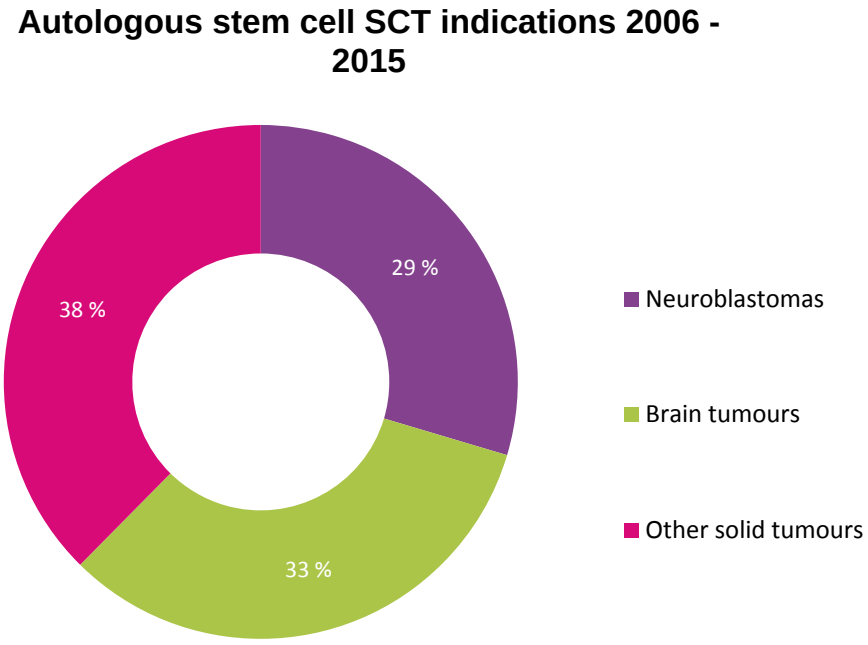


Figure 10. The diagnostic distribution of patients receiving autologous stem cell rescue with those with brain tumors constituting the largest single group.

KEY DATA FOR 2015

1. **Five** allogeneic stem cell grafts were harvested
2. Autologous grafts were harvested in **13** sessions, **10** from bone marrow and **3** from peripheral blood.
3. A total of **18** donors were harvested
4. The engraftment: **B-neut > 0,5 E9/l**

Allogeneic
sib bm graft: median D +22 (min 15, max 26)
urd bm graft: median D +26.5 (min 19, max 49)
urd umbilical cord D +33
urd PBSC D +17 (min 12, max 46)
Autologous: median D +10.5 (min 8, max 14)

In 2015 a total of 22 allogeneic and 4 autologous stem cell transplantations were carried out.

Age and gender distribution of those receiving a transplantation

	0-5 years	**6-10 years**	**> 10 years**
Allogeneic boys 13, girls 9	14	4	4
Autologous: boys 2, girls 2		2	2

Indications for stem cell transplantation in 2013

	diagnosis	**number**
Allogeneic 19 cases	ALL 1. remission	3
	ALL ≥ 2. remission	5
	SAA	2
	Congenital erythroaplasia	1
	Red-cell aplasia	1
	CGD	1
	JMML	3
	SCID	1
	Beta-thalassemia	2
	HLH	3
Autologous: 4 cases	Brain tumor	1
	Nephroblastoma	1
	Ewing's sarcoma	1
	Rhabdoid tumor	1

Distribution of allogeneic stem cell transplantation patients according to university hospital district in 2015 and in 2006-15.

KEY RESULTS

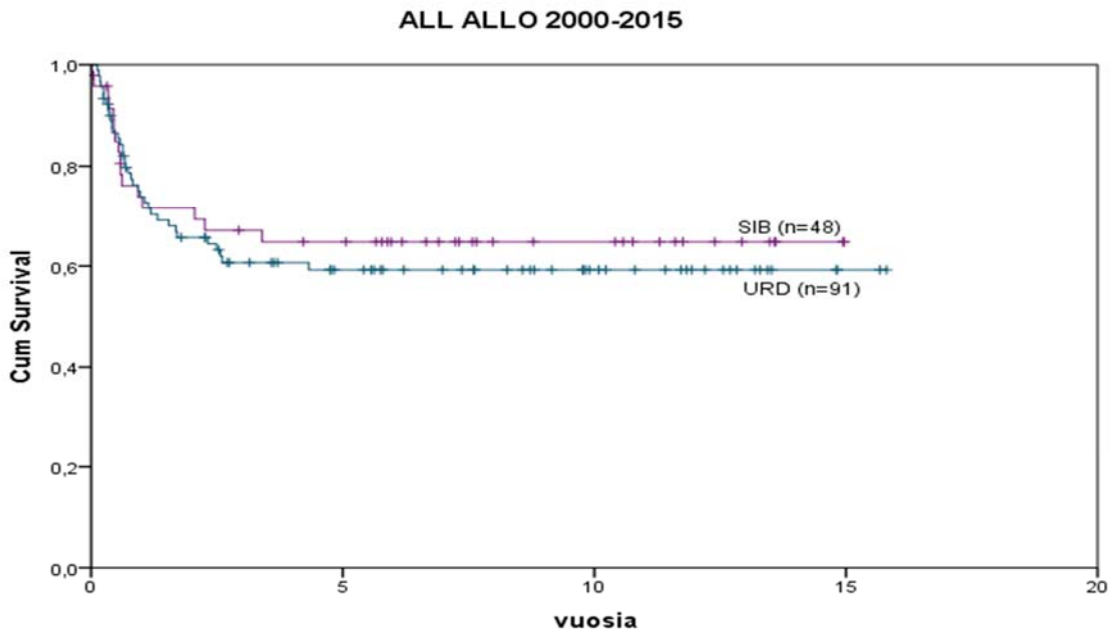


Figure 11. Cumulative survival in SIB or URD allogeneic transplantation for ALL by donor type.

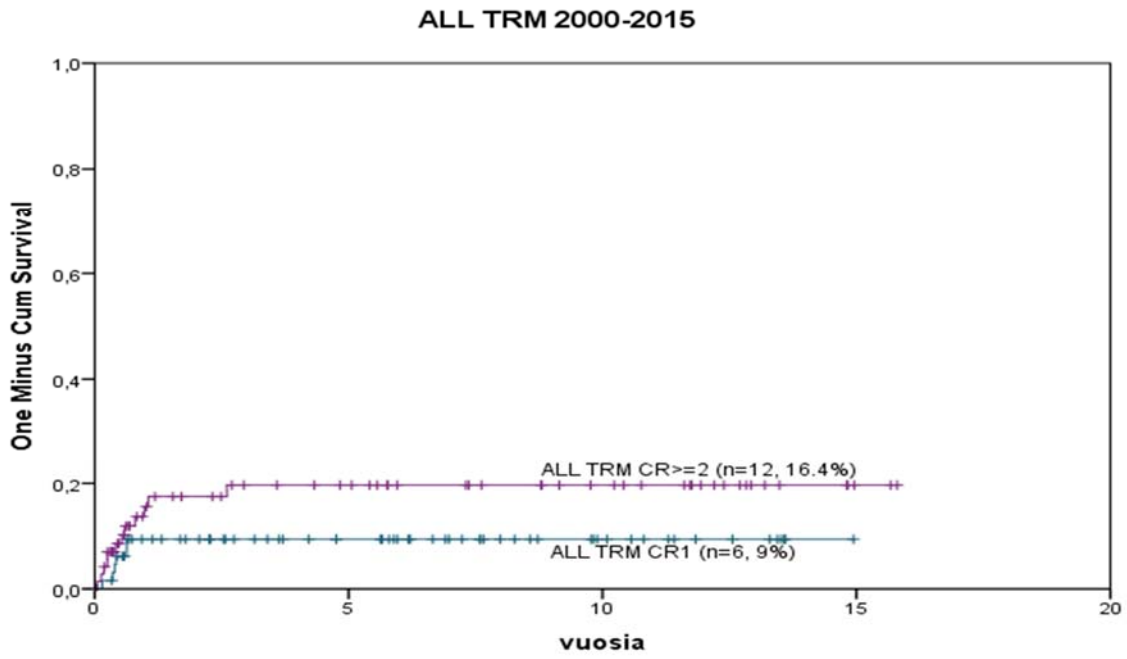


Figure 12. Transplant-related mortality (TRM) in ALL after allogeneic transplantation by donor type.

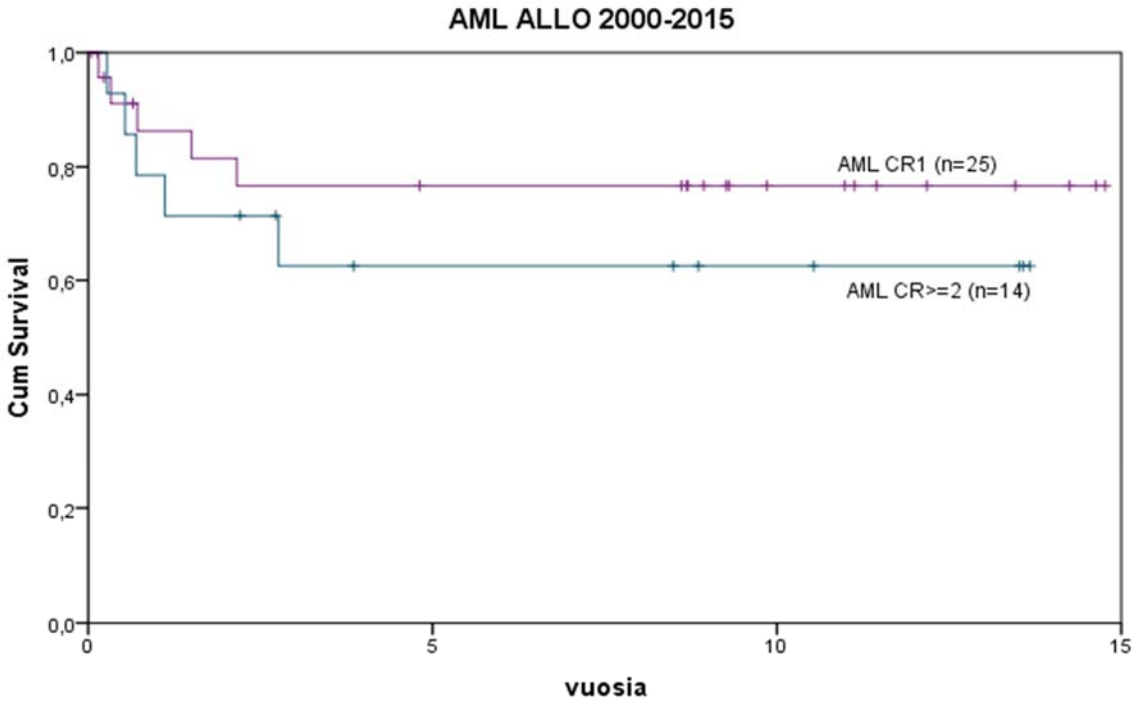


Figure 13. Cumulative survival in AML after allogeneic transplantation by remission status.

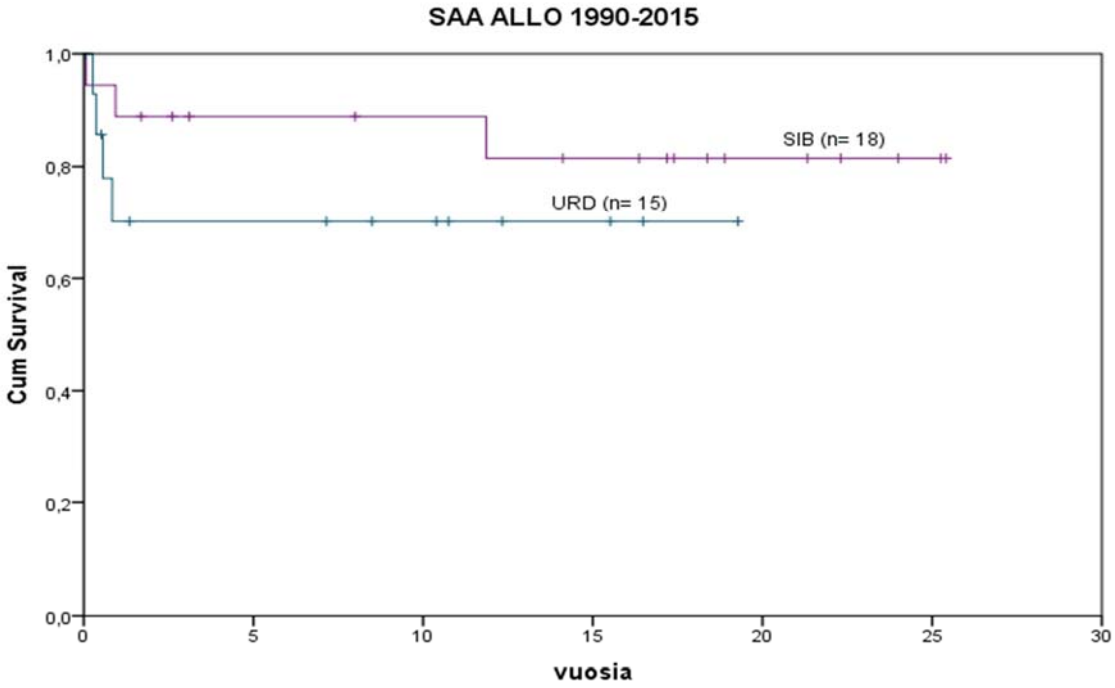


Figure 14. Cumulative survival after allogeneic transplantation in severe aplastic anemia by donor type.

SUMMARY

The Pediatric Hematology, Oncology and Stem Cell Transplantation Unit is Finland’s largest unit specialized in pediatric cancer care and hematological diseases, as well as allogeneic stem cell transplantation for children. The unit is in charge of approximately a third of all treatment for pediatric cancer and hematological diseases in Finland. The physicians at the Children's Hospital are primarily responsible for the Finnish contribution to international cooperation (NOPHO, EBMT, other collaborative efforts).

Our unit is one of the largest in the Nordic countries in stem cell transplant operations and mid-size on the European level. We are the first pediatric unit to receive JACIE accreditation for stem cell transplantation in the Nordic countries, and the only JACIE accredited pediatric unit in Finland. We initiated the use of cord blood stem cells in 1994, again as the first unit in the Nordic countries. With currently 41 cord blood transplants completed, the Children's Hospital has an unsurpassed experience in this field in the Nordic countries. In late 2015, a service to offer pediatric allogeneic bone marrow transplants to our international partners was initiated. During 2016 we will begin performing haploidentical stem cell transplants in cooperation with SPRV. An Estonian pediatric hematology specialist finished training at our ward in the spring of 2015 and another one will be trained in spring 2017.

The Pediatric Cancer Ward’s JACIE (Joint Accreditation Committee of ISCT and EBMT) accreditation was continued without any reprimand in the autumn of 2015. Our results for pediatric ALL and AML are on an internationally excellent level. The results even exceed those of the other Nordic centers (Figures 2 and 3). The new international ALL treatment protocol (NOPHO ALL-2016/ALLTogether) is being prepared and the new AML protocol (NOPHO-NBH-AML-2012) has already been employed. The ward is responsible for all pediatric allogeneic stem cell transplantations in Finland. For ALL, our stem cell transplantation results are good, and for AML our results are internationally excellent (Figures 8-12).With regard to solid tumors, our results are internationally excellent in lymphomas and nephroblastoma (Figure 4). For the treatment of pediatric neuroblastoma, we joined the comprehensive international SIOPEN-HR-NBL-1.5 treatment protocol in 2013, and thus justly expect a significant improvement in the treatment results. For other solid tumors, we will continue to increase our international cooperation in 2016 by joining European research and treatment protocols at least in lymphomas, soft tissue sarcomas and some brain tumors.

We also remain determined to develop our knowledge and skills: recently one of our consultants underwent further training in the treatment of congenital immune deficiencies with stem cell transplantation (Great Ormond St. Children´s Hospital, London, fall of 2013).). Another received further training in pediatric radiotherapy (HUS, fall-winter 2014-2015) and a third in haptoidentical transplantation for hemoglobinopathies (Ospedale Pediatrico Bambino Gesu, Rome, spring of 2015). Our nurses also actively participate in national and international pediatric oncology and stem cell transplantation collaboration and training. One of our consultants went through supplementary training in blood coagulation disorders in the HUH Coagulation Disorder Unit in the spring of 2015 and another will train there in the spring of 2016.

For the treatment of graft-versus-host reactions, we launched a new service involving extracorporeal photochemotherapy in the fall of 2014 as the first pediatric protocol of its kind within the Nordic countries. To maintain and develop our nursing expertise we also completed the fourth two-year Clinical Nurse Specialist training program for pediatric hematology and oncology and stem cell transplantation in 2015.

Furthermore, we are pursuing the international level of treatment in hemoglobinopathies in both conventional therapy and stem cell transplantation and are prepared for the treatment of these rare diseases to be nationally centralized to our unit.

In June 2015, the Pediatric Cancer Ward moved to a temporary location at HUH Triangle Hospital to await for the completion of the new Children´s Hospital in 2018.

Pediatric Hematology, Oncology and Stem Cell Transplantation Unit

K10 Pediatric Oncology Ward
Day hospital
Procedure unit
Outpatient clinic

HUH Children's Hospital

Street address Haartmaninkatu 4, Helsinki
Postal address: P.O. Box 372, 00029 FIN-00029 HUS
Phone: 09 4711
www.hus.fi/lastenklinikka