Transplant for ALL

The 4th Worldwide Network for Blood and Marrow Transplantation (WBMT) Workshop and Symposium
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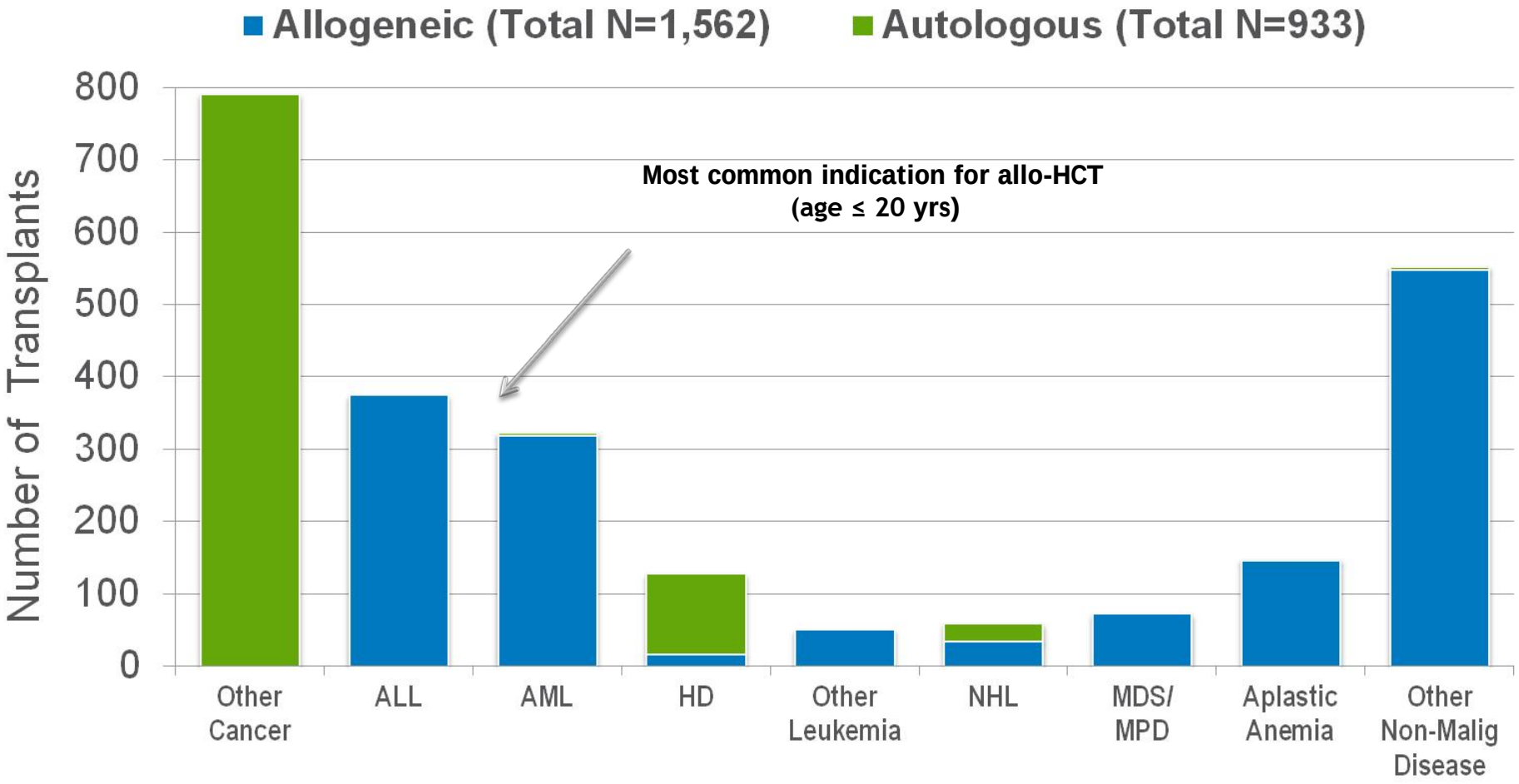
Disclosure

- Nothing to disclose

Outline

- Introduction
- HCT in the era of adult type chemotherapy
- HCT in the era of pediatric inspired chemotherapy
- Take home messages

Indications for Hematopoietic Stem Cell Transplants for Age ≤ 20 years, in the US, 2011



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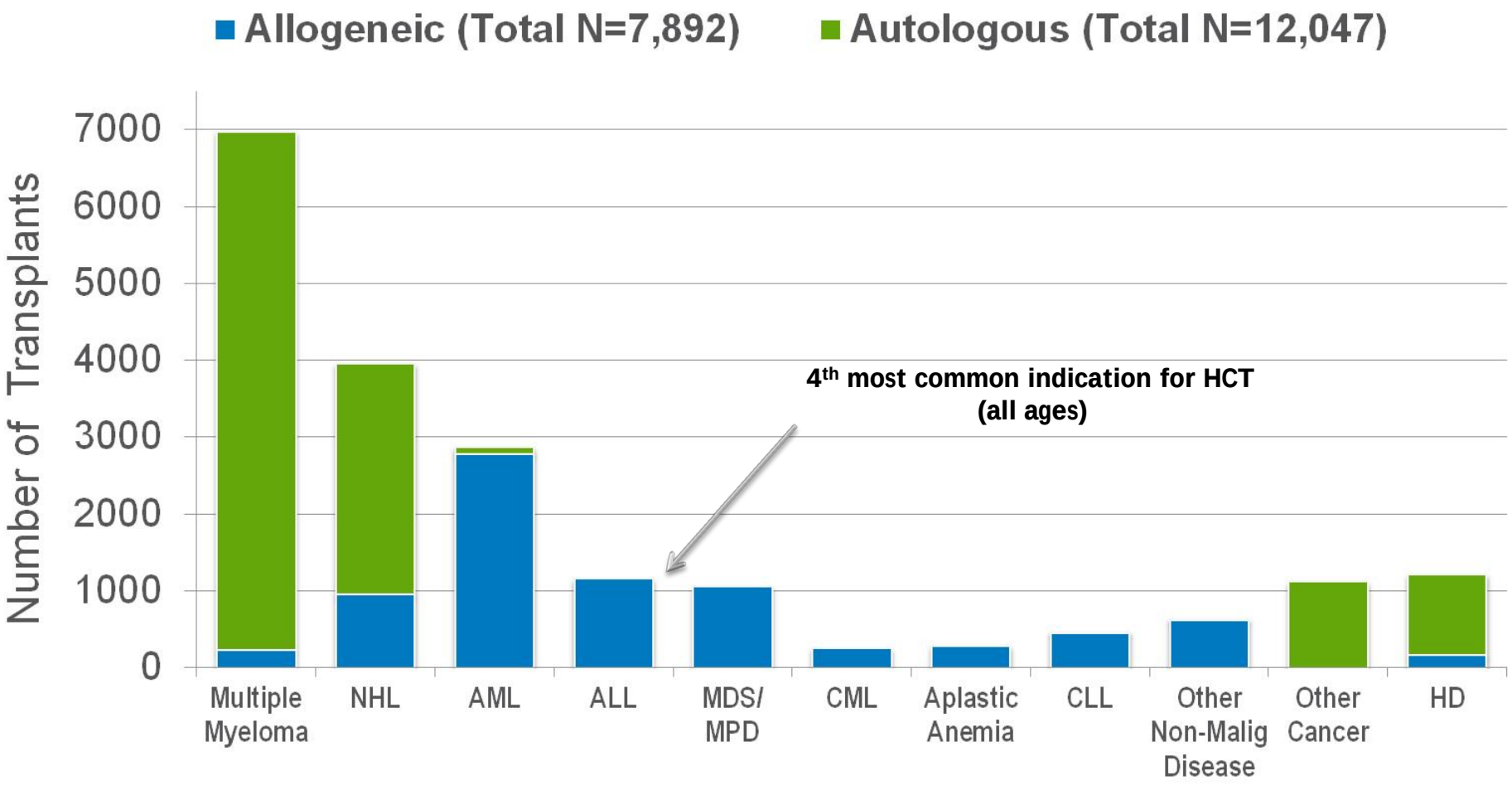
Indications for Hematopoietic Stem Cell Transplants in the US, 2011



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ALL

- Rare disease of the young
- Remarkable success in kids (CR 90%, survival 80%)
- Same CR in adults 90%, but long survival < 40-45%
- Survival rate after relapse in adults < 10%
- Risk-oriented consolidation therapy (chemotherapy, autologous or allogeneic transplant) is the key to improve survival in adults

Case

46 yo male with newly diagnosed PH-neg Pre B ALL, achieved remission 3 weeks after starting an adult ALL protocol, his MRD was negative at 12 weeks post induction. He has no matched donor

- Do you offer HCT? CR1 or beyond?
- Allo-HCT? Auto-HCT?
- Conditioning?
- Donor?

Conventional RF

- CNS involvement
- Hypodiploidy/near triploidy on karyotype or DNA index
- Resistance to steroid pre-phase
- Poor early bone marrow (BM) blast clearance
- Delayed remission
- Ig/TCR MRD positivity after the first induction
- Elevated WBC
- Age
- MLL gene rearrangement
- t(1;19) or E2A-PBX1 gene fusion
- Complex karyotype
- Immature immunophenotype
- PH pos

Allo in CR1

	Number	TRM	LFS	OS	Notes
LALA 87	257	19.5%v3.4%	39%v14% at 5 yrs	44%v20% at 5 yrs	Stat sig only in high risk
LALA 94	259	18% for both at 5 yrs	45%v23% at 5 yrs	51%v29 for auto and 21 for chemo	Only HR offered allo
EORTC	184	6 yrs Death in cr 23% vs 7%	56v38%	41% vs 39% at 6 yrs	Included lymphoma pts
HOVON	138	16%v3%	60v42%	61v47% in all 69v49% in SR	53v41% but not stat sig in HR
GOELAL02	156	15.4%V6.9%	75%V31% at 6 yrs	75%v39% at 6 yrs for HR	Allo vs Auto in HR
MRC/ECOG	562	35.8% in HRv19.5% in standard risk	Double relapse rate in the no donor group	53V45% for all but only sig in standard risk	NRM abrogated the OS benefits in HR

Meta analysis

	Number	OS	Note
Yanada	1274	OS in HR	OS in all risk but more pronounced in HR
Ram	2225	OS in SR	Not stat sig in HR
Pidala	3157	OS in SR	
Gupta	2962	No diff	< 35 benefit

SUMMARY

- DFS in favor of allo-HCT as compared to chemotherapy or auto-HCT, at a price of higher NRM
- OS benefit in all risk groups but sometimes not stat sig
- No MRD

Donor

- Safety of alternate donor has improved
- MUD=MSD
  - Dahlke et al. BBMT 2006
  - Lee et al. BBMT 2007
  - Ringden et al. Blood 2009
  - Kiehl et al. JCO 2014
  - Dhedin et al. Blood 2015

Conditioning

- Cy/TBI is the most widely used regimen
- 12 gray TBI given in six fractions and 120 mg/kg Cy
- NRM at 2 years ranges from 20-40%
  - In pediatrics, Bu was inferior to TBI (RCT: Bunin et al. BBMT 2003, retro CIBMTR, Blood 2006) (CIBMTR review in kids showed more relapse in non xrt)
  - Bu/Flu (with pharmacokinetics) showed very good results in a retrospective review by Kunter et al. BMT 2014 (65 pts, 2 yrs OS, LFS, RR, NRM 65, 61, 26, and 14% respectively)
  - VP16/TBI (Marks et al. BBMT 2006, 502 patients all have ALL)
  - Addition of VP 16 to standard Cy/TBI increased TRM and did not decrease relapse for children an adolescents (CIBMTR data, Tracey et al. BBMT 2012)
  - For adults however Japanese published very good outcomes with medium dose VP 16 addition (Shigematsu et al. BBMT 2008)

RIC

- Cause less tissue damage, reduce incidence and severity of GVHD and thus decrease NRM
- There are no RCT comparing RIC and MAC in ALL patients transplanted in CR1
- Retrospective reports
  - CIBMTR (Marks et al. blood 2010)
  - EBMT (Mohty et al. blood 2010)
  - JSHCT (Tanaka et al. BMT 2013)

Auto-SCT

- No GVL
- Graft contamination
- In the MRC/ECOG trial 456 patients were randomized to chemo vs auto, chemo showed better OS in all risk groups (37 vs 31 % in HR, 56 vs 46 % in SR)
- In metaanalysis (Gupta, Yanada): not better than chemo

Philadelphia positive

- Before TKI long term survival ~ 25% (154 patients on LALA94, 267 on MRC/ECOG…)
  - Of the 267 patients on MRC/ECOG, 76 received SCT, 5 yr OS was 34% with a sibling donor and 25% without a sibling donor
- TKI->higher remission rates, improved depth of remissions, auto became an attractive option
- EBMT Giebel et al. European Journal of Cancer 2014: retrospective review of 177 ph pos patients.3 yrs OS increased from 16% for transplants performed between 1996 and 2001 to 48% between 2002 and 2006 and 57% between 2007 and 2010

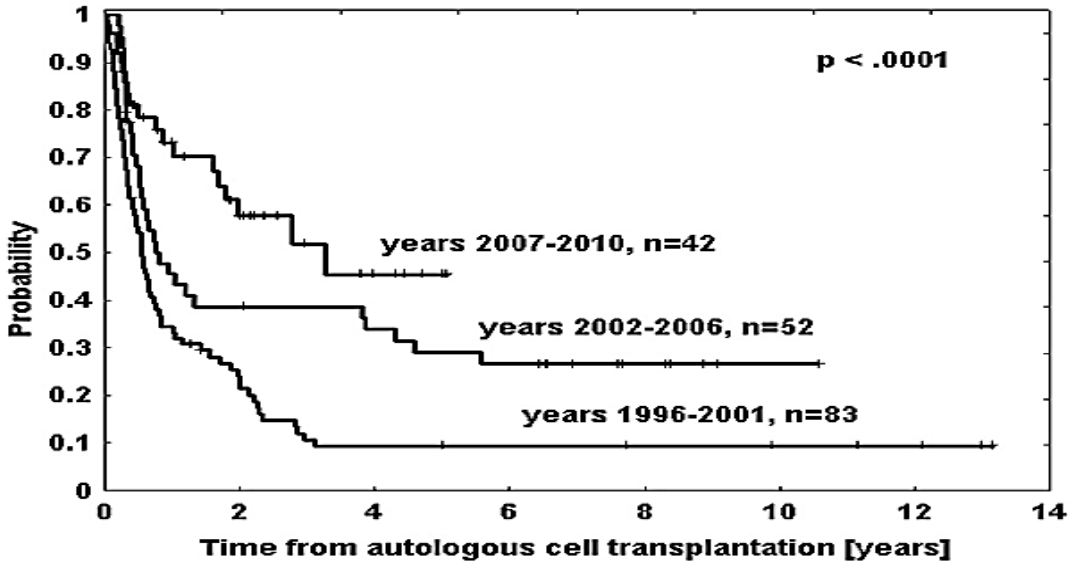

Fig. 1. Leukaemia-free survival after autologous stem cell transplantation in adults with Philadelphia-positive acute lymphoblastic leukaemia according to year of transplantation.

Auto for Ph pos

- GRAAPH 2003 Tanguy-Schmidt et al. BBMT 2013: 45 pt, 4 yrs OS 52% (50% after allo, 80% after auto, 33% with chemo)
- CALGB Wetzler et al. Haematologica 2014: 58 patients; 19 underwent autologous and 15 underwent allogeneic, similar median OS and median DFS
- GRALL Chalandon et al. blood 2015:268 Ph pos patients, 161 underwent allo 5 yrs OS 56.7% RFS 48.3%. 35 patients underwent auto 5 yrs OS 55.1% RFS 46.1%

KFSHRC

- Phase II trial
- Weekly VCR, weekly dexamethasone, plus ponatinib 30 mg daily
- Autologous HCT for patients who achieve more than MmolR at 4-6 months of therapy
- Allogeneic HCT for persistently positive transcripts

Beyond CR1

- CR after salvage range from 40% to 45%
- 421 with relapsed ALL on the LALA 94
  - 5-year OS 7%
  - 5-year OS after SCT 25%
- 609 with relapsed ALL on the MRC/ECOG
  - 5-year OS 7%
  - 5-year OS after SCT ranged from 15% to 23% (15% auto, 16% MUD, 23% MSD)
  - 5-year OS with chemotherapy 4%
- 263 with relapsed ALL on the PETHEMA
  - Best 5-year OS (38%) was seen in patients younger than 30, and had a long CR1 and transplanted in CR2

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JOURNAL OF CLINICAL ONCOLOGY

ORIGINAL REPORT

Hematopoietic Stem-Cell Transplantation for Acute Leukemia in Relapse or Primary Induction Failure

Michel Duval, John P. Klein, Wensheng He, Jean-Yves Cahn, Mitchell Cairo, Bruce M. Camitta, Rammurti Kamble, Edward Copelan, Marcos de Lima, Vikas Gupta, Armand Keating, Hillard M. Lazarus, Mark R. Litzow, David I. Marks, Richard T. Maziarz, David A. Rizzieri, Gary Schiller, Kirk R. Schultz, Martin S.Tallman, and Daniel Weisdorf

From the Centre Hospitalier Universitaire Sainte-Justine, Universite de Montreal, Montreal; Princess Margaret Hospital, Ontario; and British Columbia's Children's Hospital, Vancouver, Canada; Center for International Blood and Marrow Transplant Research, Medical College of Wisconsin; and Children's Hospital of Wisconsin, Milwaukee, WI; Hospital A. Michallon, CHU de Grenoble, Grenoble, France; Morgan

ABSTRACT

Purpose

Patients with acute leukemia refractory to induction or reinduction chemotherapy have poor prognoses if they do not undergo hematopoietic stem-cell transplantation (HSCT). However, HSCT when a patient is not in complete remission (CR) is of uncertain benefit. We hypothesized that pretransplantation variables may define subgroups that have a better prognosis.

Patients and Methods

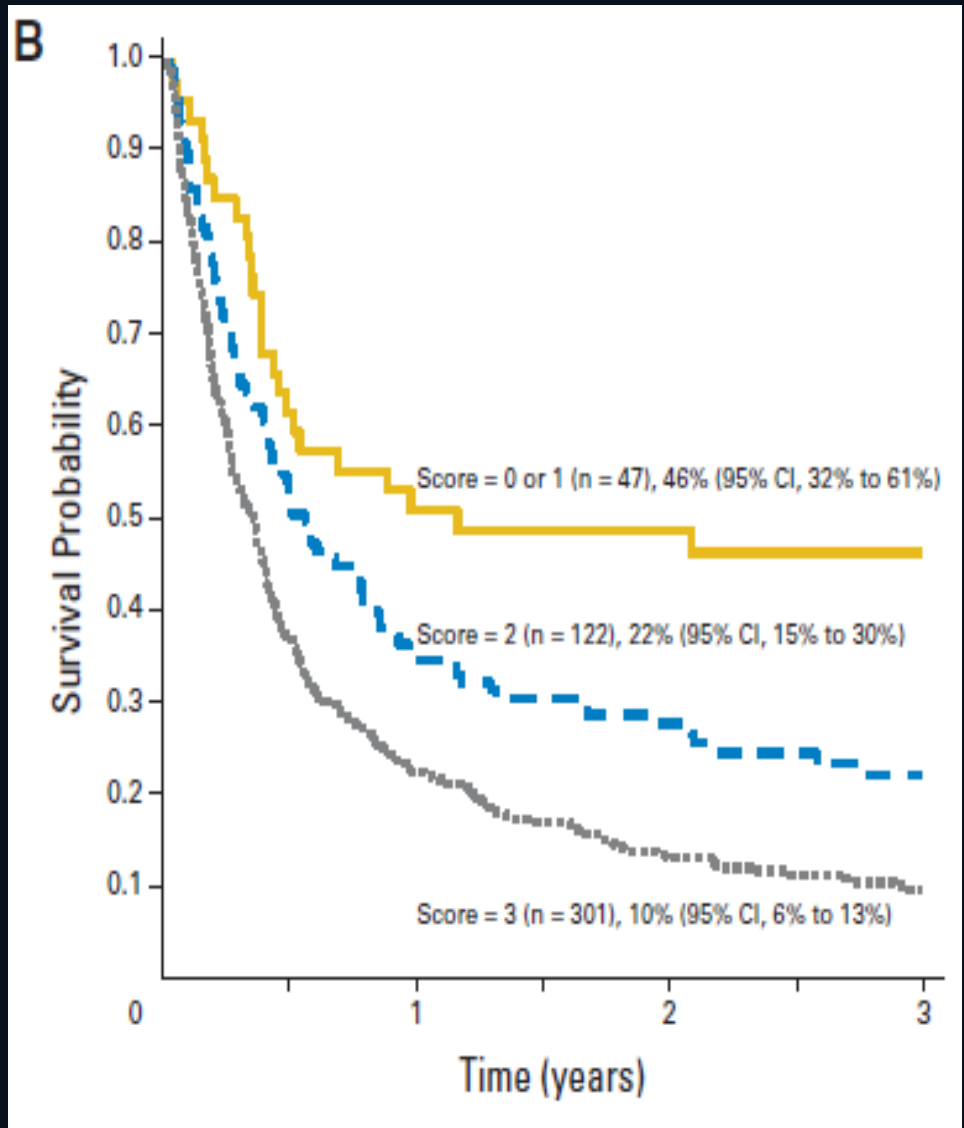
Overall, 2,255 patients who underwent transplantation for acute leukemia in relapse or with

Transplanting R/R ALL

Prognostic Variables

ALL		
Disease group		
PIF or first untreated relapse	0	172
First refractory relapse	1	206
Second and additional relapse	2	92
Donor CMV		
Negative	0	235
Positive	1	235
Bone marrow blasts, %		
< 25	0	268
> 25	1	202
Age, years		
1-9	0	45
10-39	1	302
> 40	2	123

Duval JCO 2010



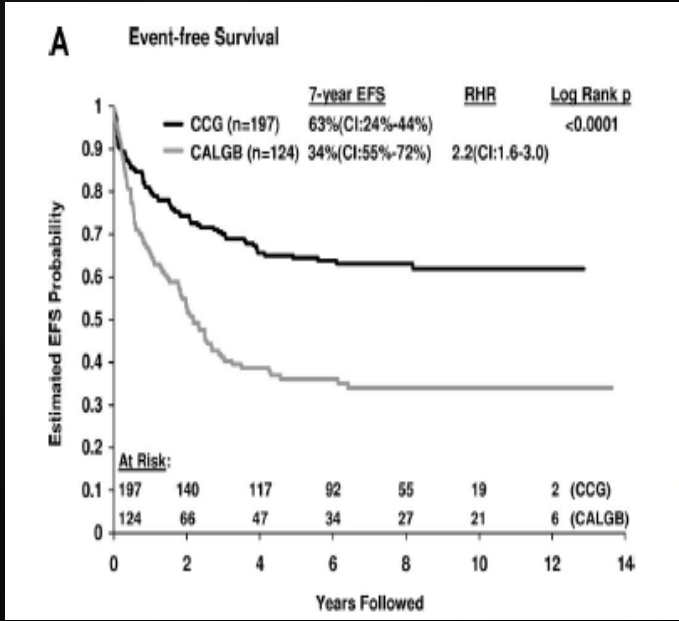
The new ERA Pediatric protocols

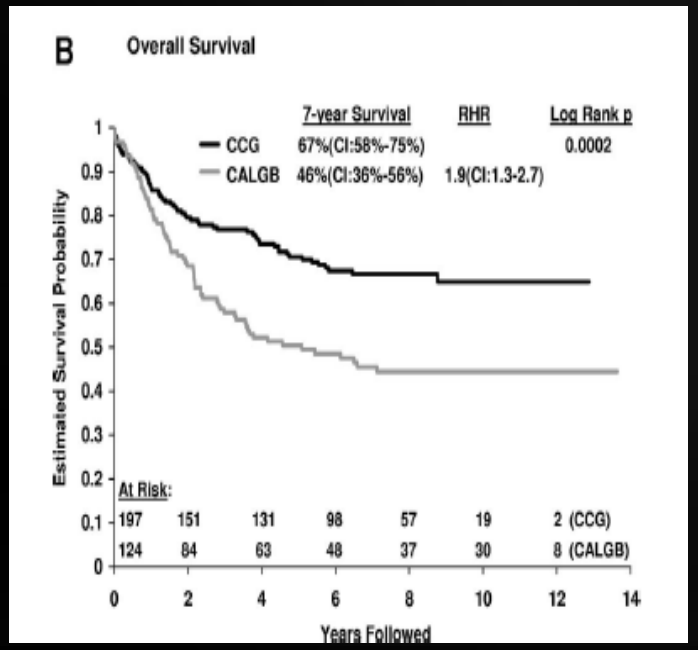
Pediatric protocols

- Several prospective trials suggest improved outcomes in young adults using pediatric, pediatric inspired or augmented regimens
  - ALL96: Ribera et al., JCO 2008
  - GRAALL -2003: Huguet et al. JCO 2009
  - Toronto Study: Storring et al BJH 2009
  - DFCI Consortium: DeAngelo et al., Leukemia 2015; DeAngelo ASH 2015
  - CALGB 10403: Stock et al., ASH 2014
  - Augmented-BFM: Ryttig et al., Cancer 2014

What determines the outcomes for adolescents and young adults with acute lymphoblastic leukemia treated on cooperative group protocols? A comparison of Children's Cancer Group and Cancer and Leukemia Group B studies

Wendy Stock,[1] Mei La,[2] Ben Sanford,[3] Clara D. Bloomfield,[4] James W. Vardiman,[5] Paul Gaynon,[6] Richard A. Larson,[1] and James Nachman[7]





	CR	EFS	OS
CALGB	90%	34%	46%
CCG	90%	63%	67%

What are the Differences Between Paediatric and Adult Protocols?

- Up to 3x vinca alkaloids
- Up to 5x prednisolone
- Up to 20x asparaginase
- Less use of myelosuppressive drugs
  - eg, anthracyclines, cyclophosphamide, cytarabine
- Less use of BMT
  - BMT still recommended by pediatricians for very high-risk ALL (eg, Ph+/t[4;11])

GRAALL

- GRAALL 2003 / 2005 studies
- CR1 Allo if <55, with at least 1 conventional HR feature
- Candidates for SCT in CR1 N=522
  - Number of SCT patients: 282
  - No SCT: 240

Regular Article

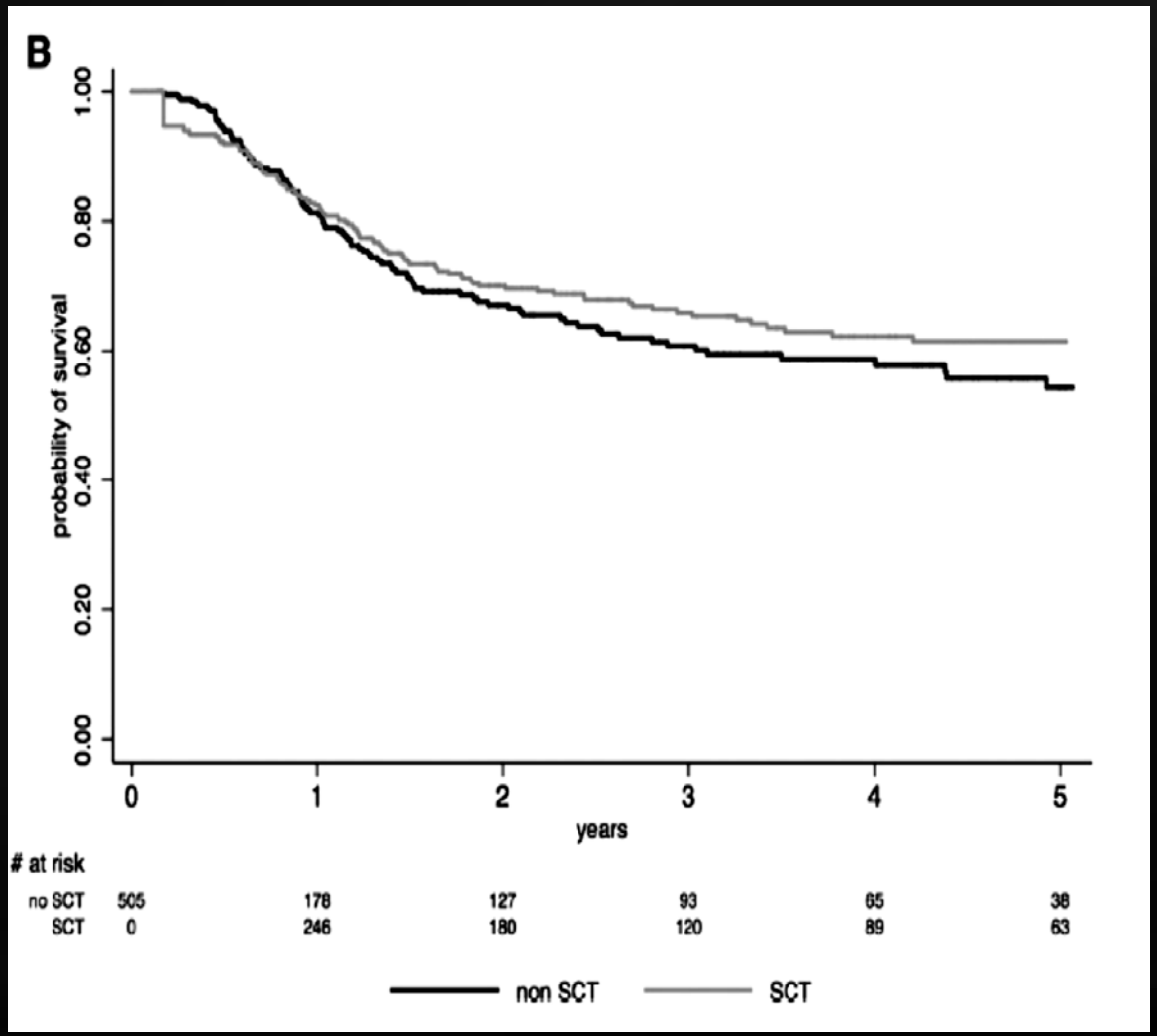
CLINICAL TRIALS AND OBSERVATIONS

CME Article

Role of allogeneic stem cell transplantation in adult patients with Ph-negative acute lymphoblastic leukemia

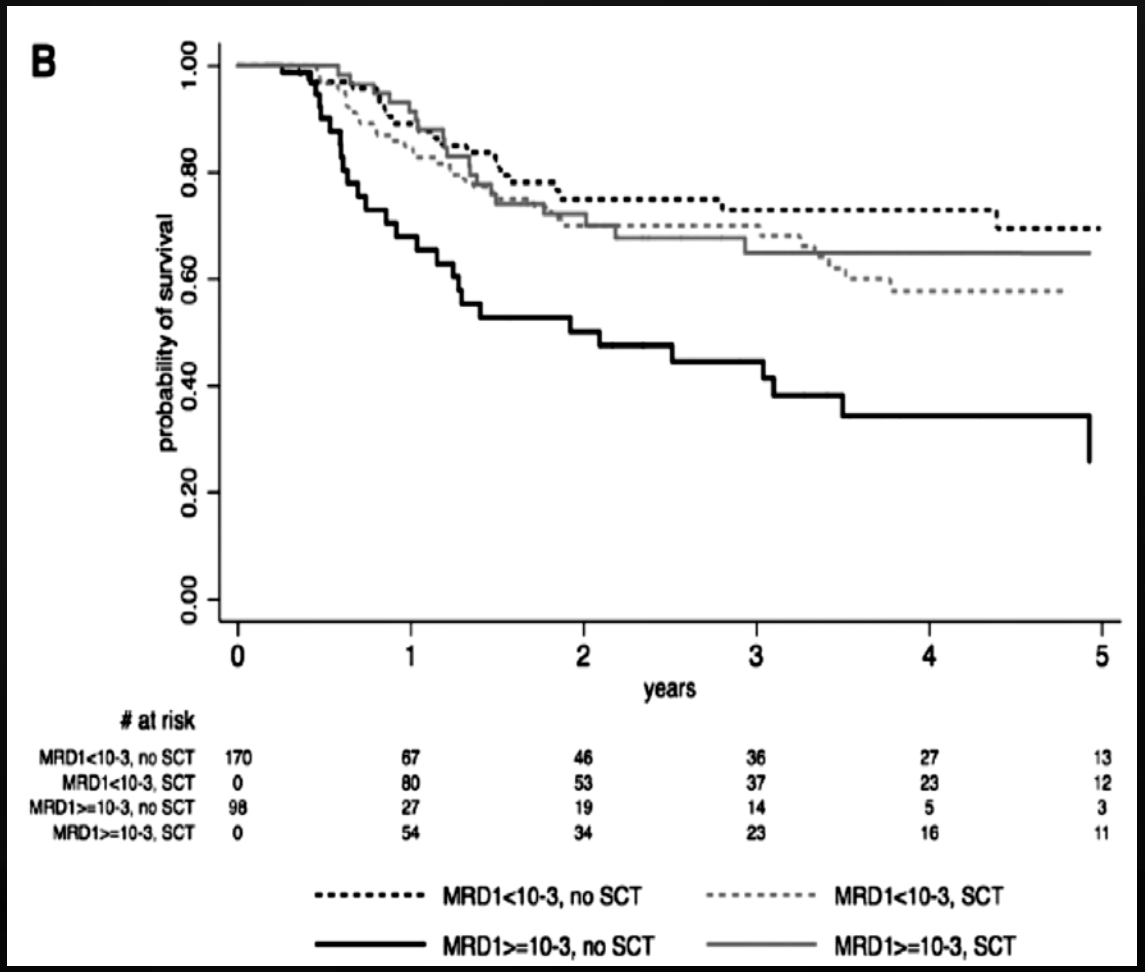
Nathalie Dhédin,[1] Anne Huynh,[2] Sébastien Maury,[3] Reza Tabrizi,[4] Kheira Beldjord,[1] Vahid Asnafi,[5] Xavier Thomas,[6] Patrice Chevallier,[7] Stéphanie Nguyen,[8] Valérie Coiteux,[9] Jean-Henri Bourhis,[10] Yosr Hichri,[11] Martine Escoffre-Barbe,[12] Oumedaly Reman,[13] Carlos Graux,[14] Yves Chalandon,[15] Didier Blaise,[16] Urs Schanz,[17] Véronique Lhéritier,[18] Jean-Yves Cahn,[19] Hervé Dombret,[1] and Norbert Ifrah,[20] on behalf of the GRAALL group

[1]Department of Hematology and University Paris Diderot, Institut Universitaire d'Hématologie, EA-3518, University Hospital Saint-Louis, Assistance Publique Hôpitaux de Paris, Paris, France; [2]Department of Hematology, University Institute of Cancer, Toulouse, France; [3]Department of Hematology, University Hospital Henri Mondor, AP-HP, Créteil, France; [4]Department of Hematology, University Hospital, Bordeaux, France; [5]Department of Hematology, University Paris Descartes Sorbonne Cité, Institut Necker-Enfants Malades, INSERM U1151, and Onco-Hematology Laboratory, Assistance Publique Hôpitaux de Paris, Hôpital Necker-Enfants Malades, Paris, France; [6]Department of Hematology, Hospital Lyon Sud, Pierre Bénite, France; [7]Department of Hematology, University Hospital, Nantes, France; [8]Department of Hematology, University Hospital Pitié-Salpêtrière, Assistance Publique Hôpitaux de Paris, Paris, France; [9]Department of Hematology, University Hospital, Lille, France; [10]Department of Hematology, Institut Gustave Roussy, Villejuif, France; [11]Department of Hematology, University Hospital, Montpellier, France; [12]Department of Hematology, University Hospital, Rennes, France; [13]Department of Hematology, University Hospital, Caen, France; [14]Department of Hematology, University Hospital, Yvoir, Belgium; [15]Division of Hematology, Department of Medical Specialties, University Hospital, Geneva, and Faculty of Medicine, University of Geneva Switzerland and Swiss Group for Clinical Cancer Research, Bern, Switzerland; [16]Department of Hematology, Institut Paoli Calmettes, Marseille, France; [17]Division of Hematology, University Hospital of Zurich, Zurich, Switzerland; [18]Group for Research on Adult Acute Lymphoblastic Leukemia, Coordination Office, Pierre Bénite, France; [19]Department of Hematology,



No Benefit of SCT based on conventional high risk factors

Dhedin et al 2015



MRD+ : SCT

MRD+ : No SCT

Regular Article

CLINICAL TRIALS AND OBSERVATIONS

Oncogenetics and minimal residual disease are independent outcome predictors in adult patients with acute lymphoblastic leukemia

Kheira Beldjord,[1] Sylvie Chevret,[2] Vahid Asnafi,[3] Françoise Huguet,[4] Marie-Laure Boulland,[5] Thibaut Leguay,[6] Xavier Thomas,[7] Jean-Michel Cayuela,[1] Nathalie Grardel,[8] Yves Chalandon,[9] Nicolas Boissel,[1] Beat Schaefer,[10] Eric Delabesse,[4] Hélène Cavé,[11] Patrice Chevallier,[12] Agnès Buzyn,[3] Thierry Fest,[5] Oumedaly Reman,[13] Jean-Paul Vernant,[14] Véronique Lhéritier,[15] Marie C. Béné,[12] Marina Lafage,[16] Elizabeth Macintyre,[3] Norbert Ifrah,[17] and Hervé Dombret,[1] on behalf of the Group for Research on Adult Acute Lymphoblastic Leukemia (GRAALL)

[1]Department of Hematology and [2]Department of Biostatistics, University Paris Diderot, Institut Universitaire d'Hématologie, EA-3518 and UMR-S-717, University Hospital Saint-Louis, Assistance Publique – Hôpitaux de Paris, Paris, France; [3]Laboratory of Oncohematology, AP-HP, Hôpital Necker Enfants-Malades, University Paris Descartes Sorbonne Cité, Institut Necker-Enfants Malades, Institut National de Recherche Médicale U1151, Paris, France; [4]Department of Hematology, University Hospital Purpan, Toulouse, France; [5]Department of Hematology, University Hospital, Rennes, France; [6]Department of Hematology, University Hospital Haut-Lévèque, Bordeaux, France; [7]Department of Hematology, University Hospital Lyon Sud, Lyon, France; [8]Department of Hematology, University Hospital Claude Huriez, Lille, France; [9]Department of Hematology, University Hospital, Geneva, Switzerland; [10]Department of Hematology, University Hospital, Zürich, Switzerland; [11]Department of Hematology, University Hospital Robert Debré, Assistance Publique – Hôpitaux de Paris, Paris, France; [12]Department of Hematology, University Hospital, Nantes, France; [13]Department of Hematology, University Hospital, Caen, France; [14]University Hospital Pitié-Salpêtrière, Assistance Publique – Hôpitaux de Paris, Paris, France; [15]GRAALL Coordination Office, University Hospital Lyon Sud, Lyon, France; [16]Department of Genetics, Aix-Marseille University, Marseille, France; and [17]Department of Hematology, University Hospital, INSERM U892/CNRS 6299, Angers, France

Modern high risk features

Beldjord et al. blood 2014

1. MRD

- MRD level >10^{-4} post Induction

2. *B-CELL* :

- t(4;11) or other MLL rearrangement
- Focal IKZF1 gene deletion

3. *T-CELL* :

- Absence of NOTCH1/FBXW7 mutation and/or
- N/K-RAS mutation and/or
- PTEN gene alteration

High CIR and shorter relapse-free and overall survival

RESEARCH ARTICLE

AJH

Pediatric-inspired therapy compared to allografting for Philadelphia chromosome-negative adult ALL in first complete remission

Matthew D. Seftel,[1*] Donna Neuberg,[2] Mei-Jie Zhang,[3,4] Hai-Lin Wang,[3] Karen Kuhn Ballen,[5] Julie Bergeron,[6] Stephen Couban,[7] César O. Freytes,[8] Mehdi Hamadani,[3] Mohamed A. Kharfan-Dabaja,[9] Hillard M. Lazarus,[10] Taiga Nishihori,[9] Kristjan Paulson,[1] Wael Saber,[3] Stephen E. Sallan,[11] Robert Soiffer,[12] Martin S. Tallman,[13] Ann E. Woolfrey,[14] Daniel J. DeAngelo,[12] and Daniel J. Weisdorf,[15]
for the Acute Leukemia Committee of the CIBMTR and the Dana Farber ALL Consortium[16]

For adults with Philadelphia chromosome-negative (Ph−) acute lymphoblastic leukemia (ALL) in first complete remission (CR1), allogeneic hematopoietic cell transplantation (HCT) is an established curative strategy. However, pediatric-inspired chemotherapy may also offer durable leukemia-free survival in the absence of HCT. We compared 422 HCT recipients aged 18–50 years with Ph-ALL in CR1 reported to the CIBMTR with an age-matched concurrent cohort of 108 Ph− ALL CR1 patients who received a Dana-Farber Consortium pediatric-inspired non-HCT regimen. At 4 years of follow-up, incidence of relapse after HCT was 24% (95% CI 19–28) versus 23% (95% CI 15–32) for the non-HCT (chemo) cohort (P=0.97). Treatment-related mortality (TRM) was higher in the HCT cohort [HCT 37% (95% CI 31–42) versus chemo 6% (95% CI 3–12), P<0.0001]. DFS in the HCT cohort was 40% (95% CI 35–45) versus 71% (95% CI 60–79) for chemo, P<0.0001.

422 HCT vs 108 DFCI

RR: 24 VS 23

TRM: 37 VS 6

DFS: 40 VS 71

OS: 40 VS 73

Additional Supporting Information may be found in the online version of this article.

[1]Department of Medical Oncology and Haematology, CancerCare Manitoba, Winnipeg, Manitoba, Canada; [2]Department of Biostatistics and Computational Biology, Dana-Farber Cancer Institute, Boston, Massachutsetts; [3]Center for International Blood and Marrow Transplant Research (CIBMTR®), Department of Medicine, Medical College of Wisconsin, Milwaukee, Wisconsin; [4]Medical College of Wisconsin, Division of Biostatistics, Institute for Health and Society, Milwaukee, Wisconsin; [5]Department of Hematology/Oncology, Massachusetts General Hospital, Boston, Massachusetts; [6]Department of Hematology, Hôpital Maisonneuve-Rosemont, Montréal, Quebec, Canada; [7]Division of Haematology, Queen Elizabeth II Health Sciences Centre, Dalhousie University, Halifax, Nova Scotia, Canada; [8]South Texas Veterans Health Care System and University of Texas Health Science Center San Antonio, San Antonio, Texas; [9]Department of Blood and Marrow Transplantation, H. Lee Moffitt Cancer Center and Research Institute, Tampa, Florida; [10]Department of Medicine, Seidman Cancer Center, University Hospitals Case Medical Center, Cleveland, Ohio; [11]Department of Pediatric Oncology, Dana-Farber Cancer Institute, Boston, Massachusetts; [12]Department of Medical Oncology/Hematologic Malignancies, Dana-Farber Cancer Institute, Boston, Massachusetts; [13]Department of Medicine, Leukemia Service, Memorial Sloan Kettering Cancer Center, New York, New York; [14]Department of Pediatric Hematopoietic Cell Transplant, Fred Hutchinson Cancer Research Center, Seattle, Washington; [15]Division of Hematology, Oncology and Transplantation, Department of Medicine, University of Minnesota Medical Center, Minneapolis, Minnesota; [16]Gorgun Akpek: Stem Cell Transplantation and Cellular

EUROPEAN HEMATOLOGY ASSOCIATION

haematologica
Journal of the European Hematology Association

Improving results of allogeneic hematopoietic cell transplantation for adults with acute lymphoblastic leukemia in first complete remission: an analysis from Acute Leukemia Working Party of the European Society for Blood and Marrow Transplantation

by Sebastian Giebel, Myriam Labopin, Gerard Socie', Dietrich Beelen, Paul Browne, Liisa Volin, Slawomira Kyrcz-Krzemien, Ibrahim Yakoub-Agha, Mahmoud Aljurf, Depei Wu, Mauricette Michallet, Renate Arnold, Mohamad Mohty, and Arnon Nagler

Haematologica 2016 [Epub ahead of print]

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doi:10.3324/haematol.2016.145631

CIBMTR/DFCI **NRM 37%** **RI 24%** **LFS 40%** **OS 40%**

MSD-HCT

Age	Period	N	NRM (%, 95%CI)	RI (%, 95%CI)	LFS (%, 95%CI)	OS (%, 95%CI)
18-25 years	1993-2002	126	18.5 (13.7-24)	28 (20.3-36.2)	53.5 (44.6-62.4)	60.5 (51.8-69.2)
	2003-2007	278	10.9 (7.3-15.3)	22.9 (18-28.3)	66.2 (60.4-72)	73 (67.5-78.5)
	2008-2012	298	11.7 (8-16.3)	22.9 (17.5-28.7)	65.4 (58.9-71.8)	76.3 (70.5-82.2)
	P		0.47	0.34	0.05	0.04
26-35 years	1993-2002	167	14 (10-18.7)	25.8 (19.3-32.7)	60.2 (52.7-67.7)	68.1 (60.9-75.2)
	2003-2007	279	17.3 (12.8-22.4)	24 (19-29.5)	58.7 (52.6-64.7)	68.2 (62.4-74)
	2008-2012	318	11.2 (7.7-15.5)	32.4 (26.7-38.3)	56.1 (49.9-62.4)	69.3 (63.1-75.5)
	P		0.06	0.08	0.68	0.63
36-45 years	1993-2002	139	21 (15.8-26.7)	31.4 (23.8-39.3)	47.7 (39.3-56)	58.2 (49.8-66.5)
	2003-2007	303	23.3 (17.9-29.1)	27 (21.9-32.2)	49.4 (43.5-55.2)	58.6 (52.8-64.4)
	2008-2012	283	14.7 (10.4-19.8)	22.2 (16.9-28)	62.7 (56.2-69.2)	68.6 (62.2-75)
	P		0.02	0.19	0.002	0.002
46-55 years	1993-2002	74	26.1 (19.7-32.9)	40.9 (29.3-52.2)	33 (22-44)	41.2 (29.6-52.7)
	2003-2007	207	31.1 (24.4-38)	23.4 (17.7-29.6)	45.5 (38.5-52.5)	53.3 (46.3-60.3)
	2008-2012	209	23.5 (17.4-30.1)	23.7 (17.6-30.4)	52.8 (45.1-60.6)	59.7 (52-67.4)
	P		0.20	0.09	0.03	0.02
18-55 years	1993-2002	506	18.8 (16.2-21.5)	30 (26-34.1)	51.2 (46.7-55.6)	59.6 (55.2-63.9)
	2003-2007	1067	20 (17.4-22.8)	24.5 (21.9-27.2)	55.4 (52.3-58.5)	63.8 (60.7-66.8)
	2008-2012	1108	14.7 (12.4-17.1)	25.7 (22.8-28.7)	59.5 (56.2-62.9)	69.1 (65.8-72.3)
	P		0.003	0.07	0.009	0.00006

URD-HCT

18-55 y	1993-2002	183	28.2 (22-35.2)	28.5 (25.4-31)	43.4 (36.1-50.6)	51.2 (43.8-58.5)
	2003-2007	802	24.4 (21.7-27.1)	22 (19.1-25)	53.6 (50-57.1)	61 (57.5-64.5)
	2008-2012	1193	22.4 (19.8-25)	18.5 (16.1-21)	59.1 (56-62.2)	64.8 (61.7-67.8)
	P		0.27	0.006	0.0001	0.003

↓ NRM

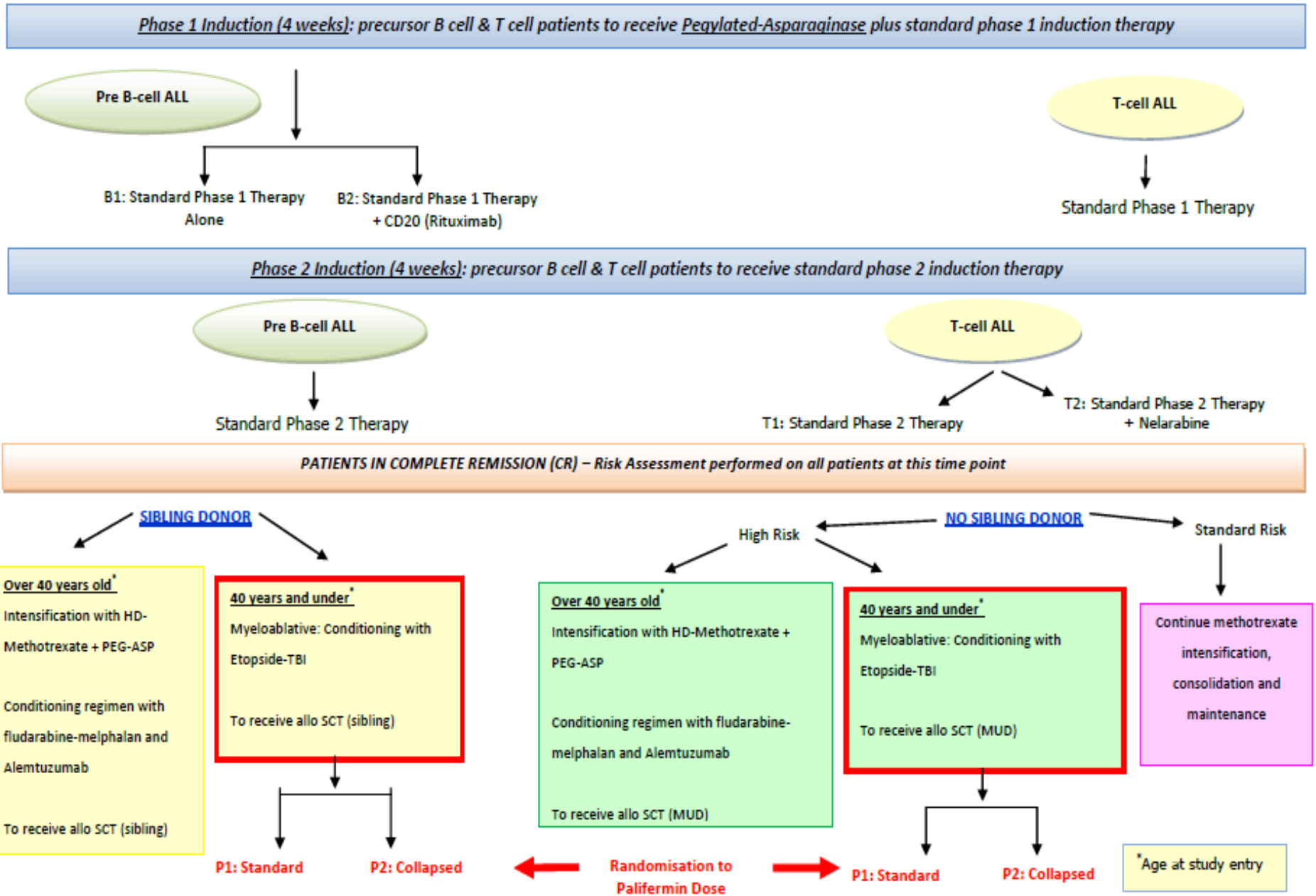
- Cooley et al. TRM decreased from 41 to 26% in SCT 2003-2007 as compared to 1993-1997
- Wood et al. TRM decreased from 43 to 31 % in SCT 2002-2007 as compared to 1990-1995
- Giebel et al.

Conclusion

- Adult ALL is not Pediatric ALL
  - age, comorbidities, organ dysfunction, difference in the genomic profile of adult and pediatric ALL, compliance…
- HCT should be offered for any patient with persistent MRD or modern poor prognostic factors
  - HCT for all risk groups if patient on adult type therapy is not wrong
- Pediatric protocols seem to be more effective
  - RCT needed
  - Role of HCT need to be clarified and defined
  - better understanding of the value of the conventional and new risk factors in the context of pediatric protocols
  - Auto for negative MRD??
- The dilemma of how to consolidate adult ALL patients in CR1 will not be solved easily as long as new therapies emerge and the risk/benefit ratio of allo-HCT continue to change

UKALL14 TRIAL SCHEMA

1.2 Trial schema:



THANK YOU