UNIVERSITÄTS
KLINIKUM
HEIDELBERG

2nd POSTGRADUATE
CLL
Conference

CLL: When and how to use allotransplantation

Prof. Dr. Peter Dreger

Department Medicine V

University of Heidelberg

UK HD

Conflicts of Interest Peter Dreger

- Advisory Board: AbbVie, AstraZeneca, Gilead, Janssen, Novartis, MSD, Riemser, Roche
- Speaker: Gilead, Novartis, Riemser, Roche
- Research support: Riemser

AlloHCT in CLL – why?

GVL !

BLOOD. VOL. 25, NO. 2 (FEBRUARY), 1965

Successful Allogenic Bone Marrow Transplantation in Man: Chimerism, Induced Specific Tolerance and Possible Anti-Leukemic Effects

By G. MATHÉ, J. L. AMIEL, L. SCHWARZENBERG, A. CATTAN, M. SCHNEIDER, M. J. DE VRIES, M. TUBIANA, C. LALANNE, J. L. BINET, M. PAPIERNIK, G. SEMAN, M. MATSUKURA, A. M. MERY, V. SCHWARZMANN AND A. FLAISLER

IT HAS BEEN demonstrated in various animal species that allogenic (homologous) bone marrow transplantation is possible after conditioning the recipient by a lethal dose of total-body irradiation.[19] A successful transplant is usually complicated by a secondary syndrome,[2] the mechanism of which probably involves the reaction of immunologically competent cells against host antigens.[4]

If the recipient is leukemic, the immune reaction of the graft against the leukemic cells[3,20,25,28,29] and perhaps against the leukemia virus[19b] may prove to be a powerful therapeutic weapon. Hence, the idea of using allogenic bone marrow grafts in the treatment of leukemia. The object in such cases would be to obtain prolonged acceptance of the graft, followed by the secondary syndrome which indicates the graft versus host reaction, and then to control the undesirable effects of the secondary syndrome.

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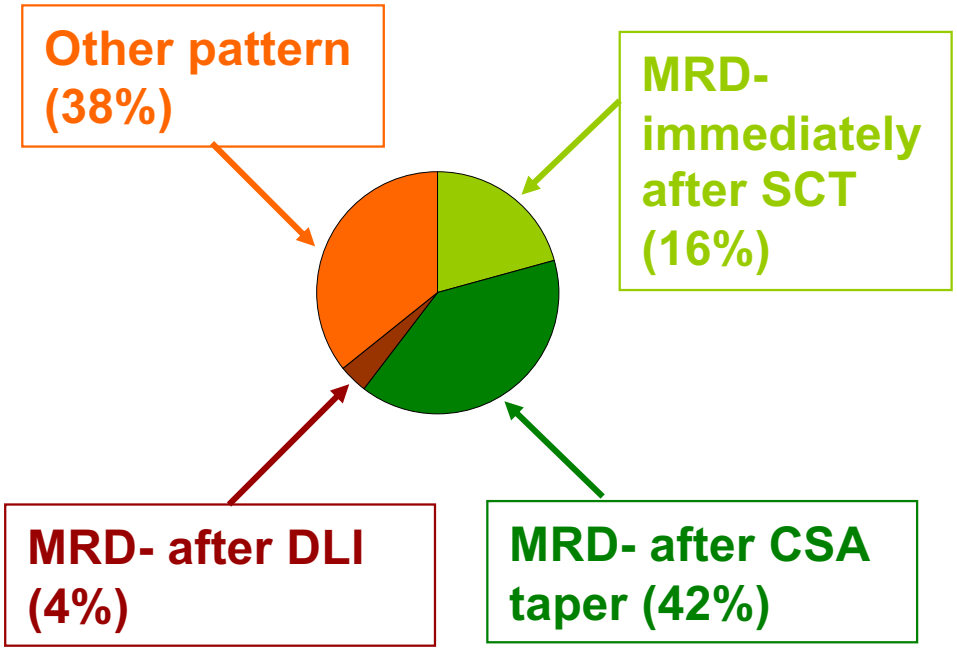
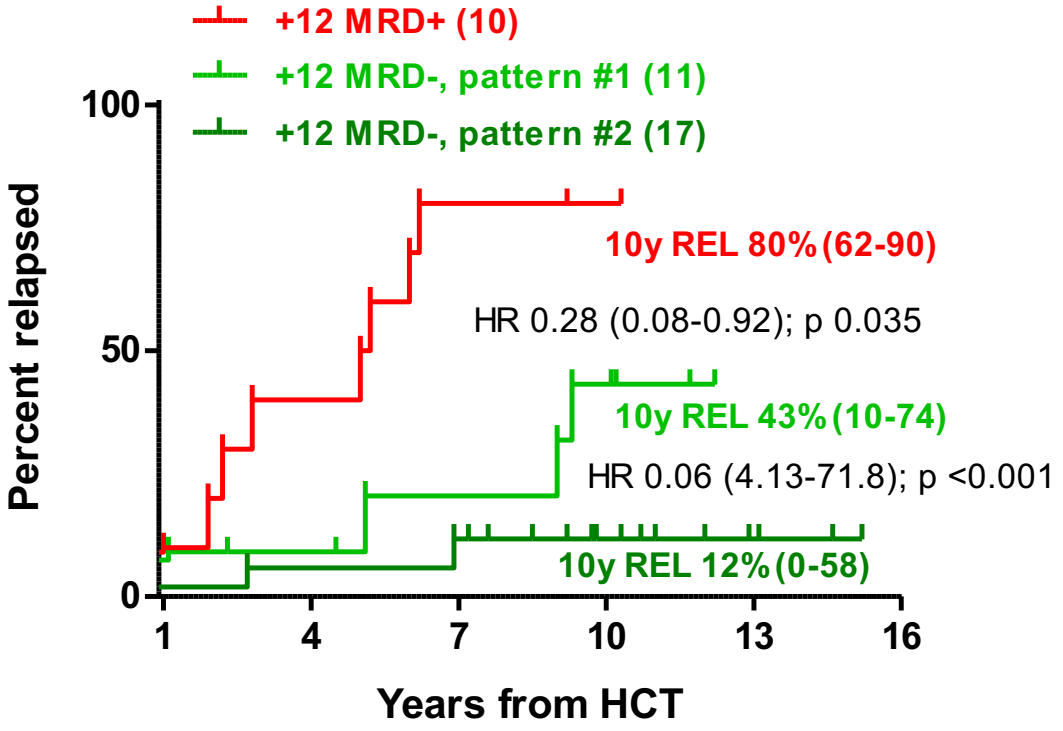
CLL3X: Relapse by MRD pattern

All patients with MRD monitoring (n=52)



Patients event-free at mo +12 (n=38)



Krämer Blood 2017 September 21

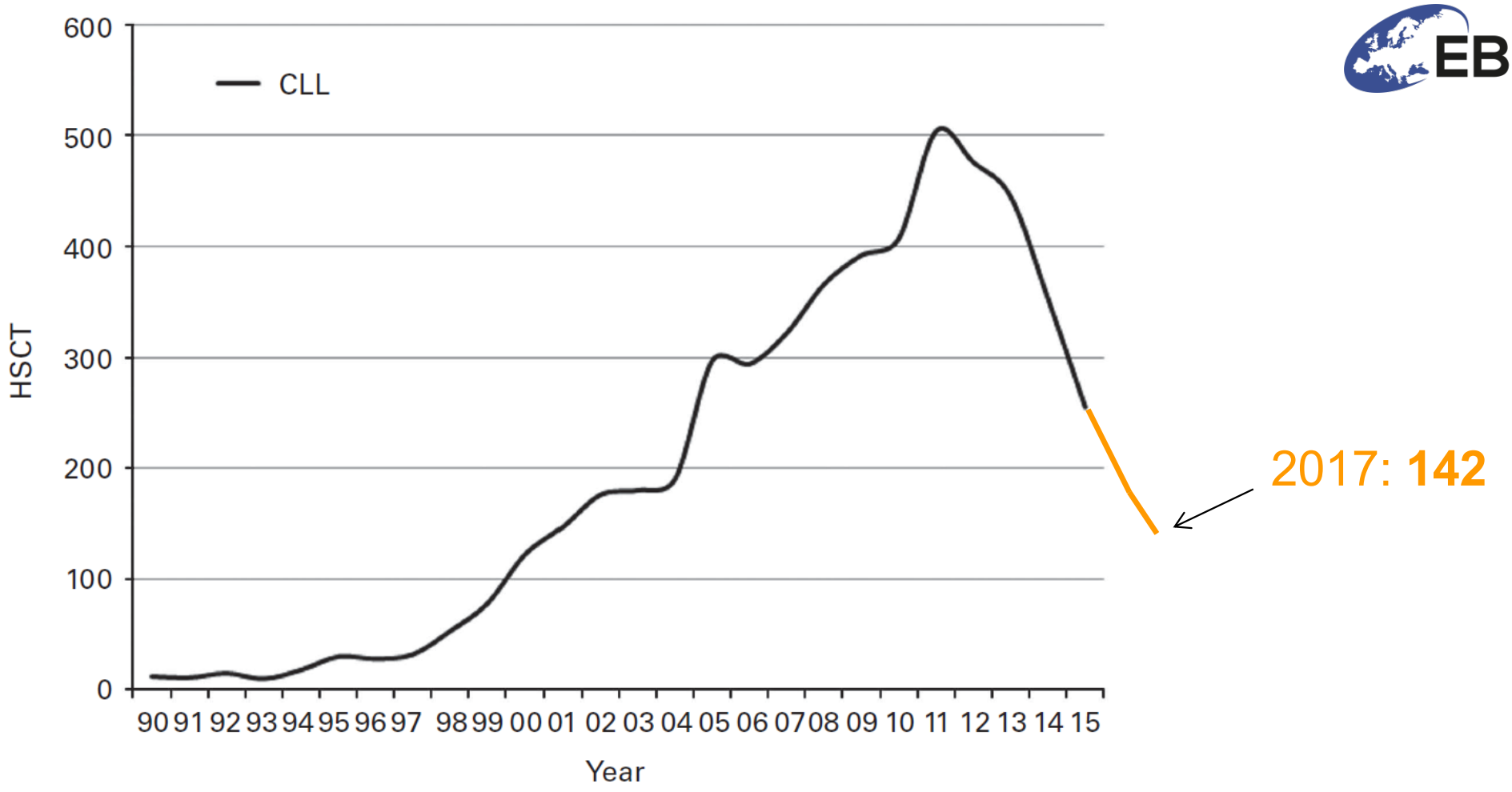


Figure 2. The rise and fall in absolute numbers of allogeneic HSCT for CLL in Europe 1990–2015.

Passweg et al, BMT 2017;52:811
and EBMT, data on file

BMT

2017;52:552

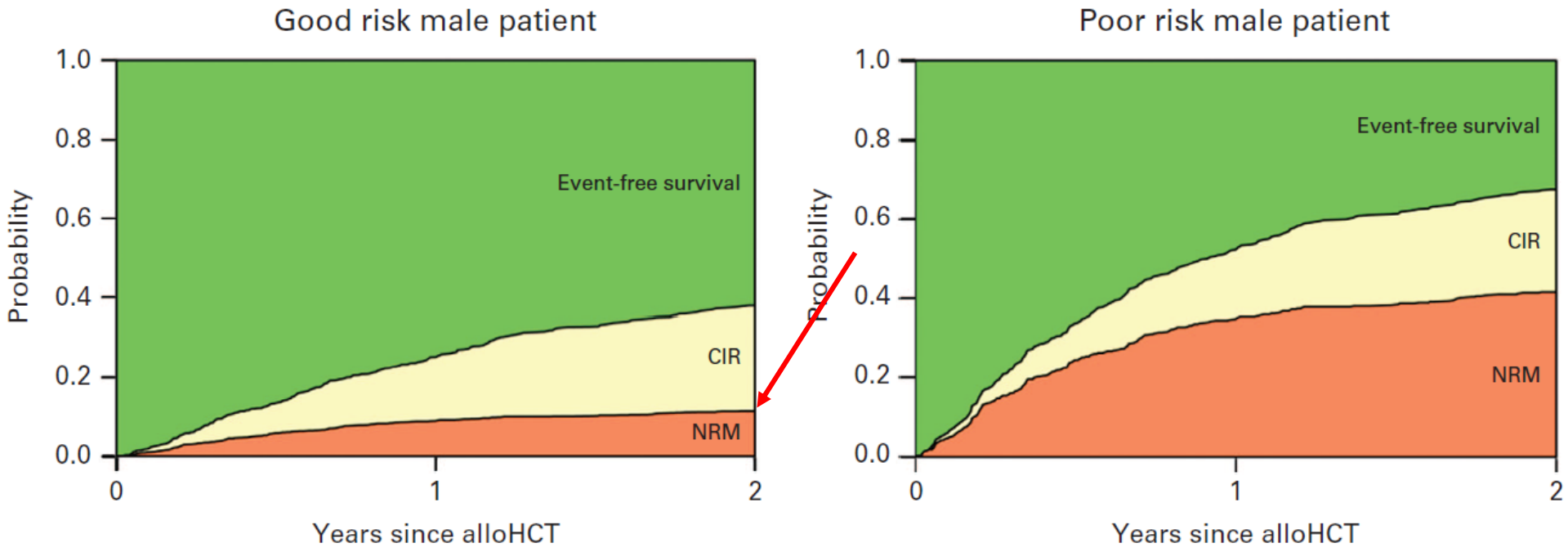
ORIGINAL ARTICLE

Risk factors for treatment failure after allogeneic transplantation of patients with CLL: a report from the European Society for Blood and Marrow Transplantation

J Schetelig[1,2,19], LC de Wreede[2,3,19], M van Gelder[4], NS Andersen[5], C Moreno[6], A Vitek[7], M Karas[8], M Michallet[9], M Machaczka[10], M Gramatzki[11], D Beelen[12], J Finke[13], J Delgado[14], L Volin[15], J Passweg[16], P Dreger[17], A Henseler[3], A van Biezen[3], M Bornhäuser[1], SO Schönland[17] and N Kröger[18] on behalf of the CLL subcommittee, Chronic Malignancies Working Party

EBMT

N=694, HCT 2000-2011



45y, PS 100%, sensitive disease, matched related **male** donor

55y, **PS 80%, resistant disease**, unrelated **female** donor

BMT

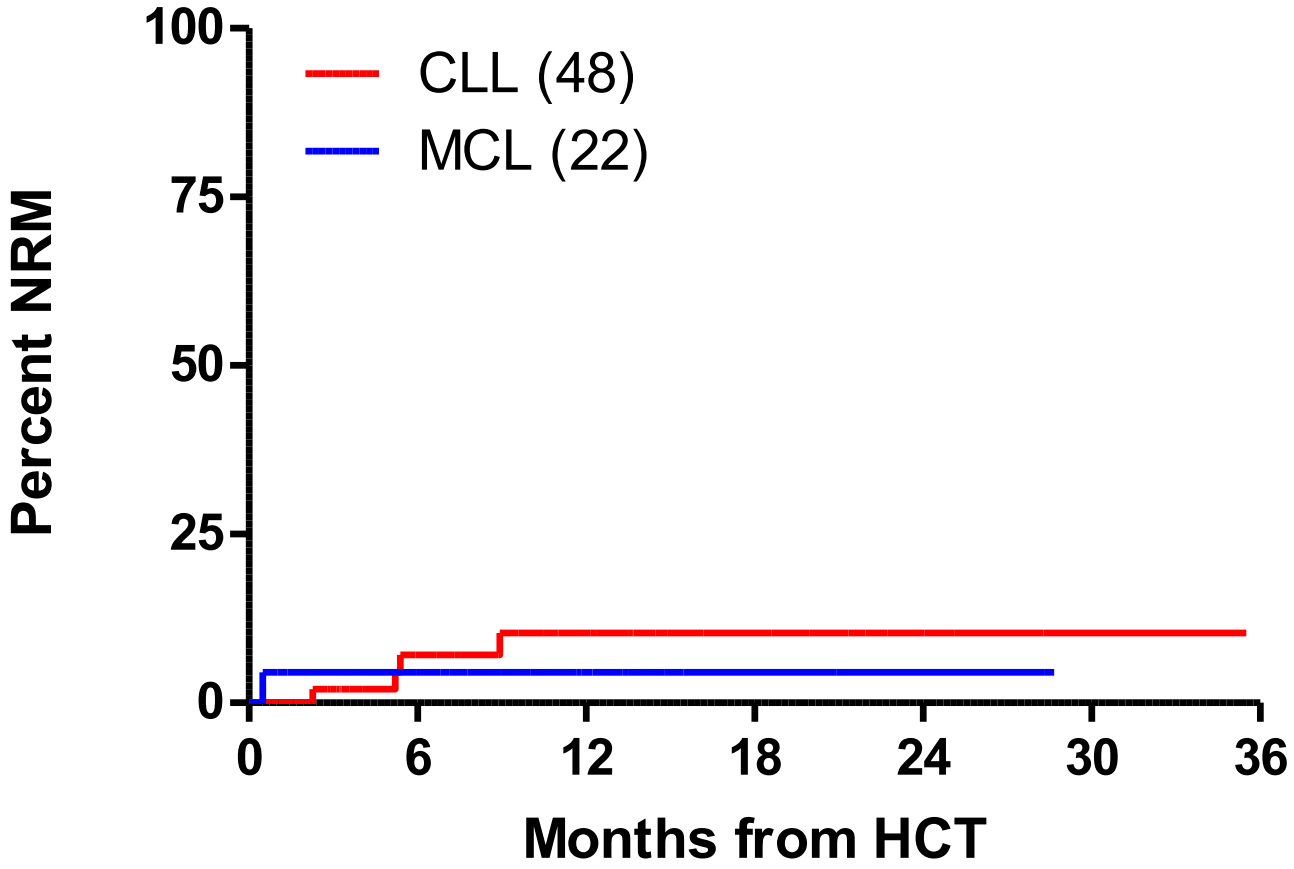
2019;54:44

Ibrutinib for bridging to allogeneic hematopoietic cell transplantation in patients with chronic lymphocytic leukemia or mantle cell lymphoma: a study by the EBMT Chronic Malignancies and Lymphoma Working Parties

Peter Dreger[1,2,3] · Mauricette Michallet[4] · Paul Bosman[1] · Sascha Dietrich[2,3] · Mohamad Sobh[4] · Ariane Boumendil[2] · Arnon Nagler[5] · Christof Scheid[6] · Jan Cornelissen[7] · Dietger Niederwieser[8] · Lutz Müller[9] ·

EBMT

N=70, HCT 2013-2016



alloHCT in CLL: Prejudices

- NRM is high and comes early
- Relapse after HCT is immediately fatal

alloHCT in CLL: Prejudices

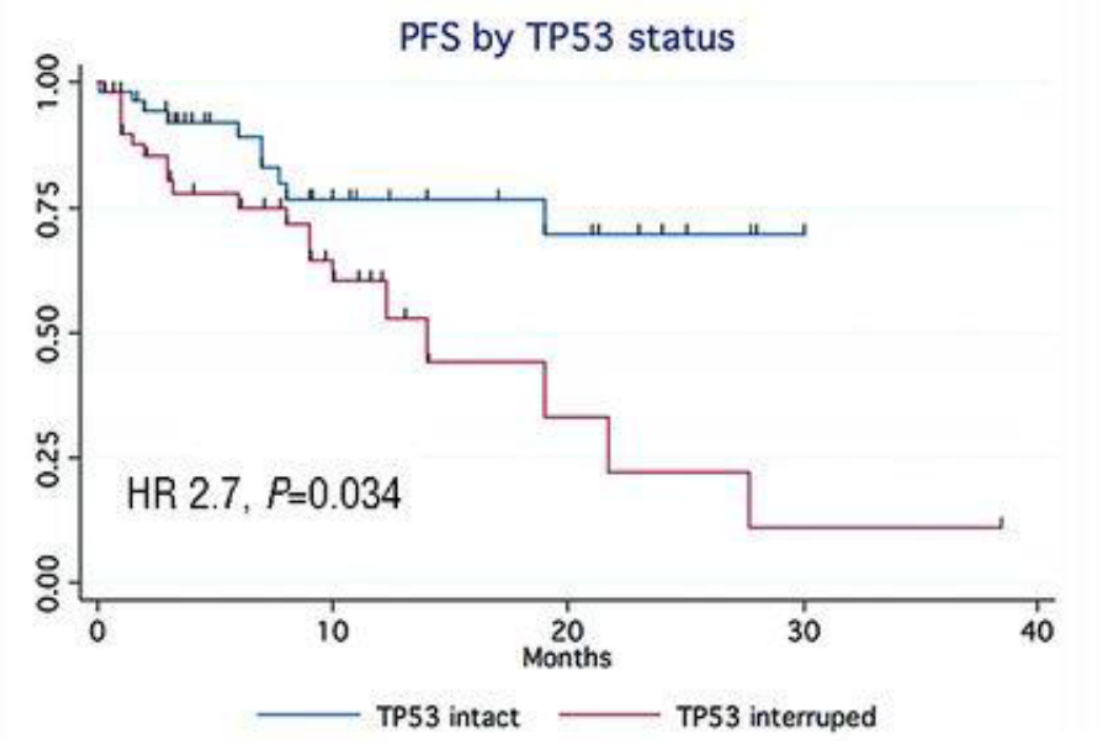
- NRM is high and comes early
- Relapse after HCT is immediately fatal
- It is unclear if HCT is feasible after PI (failure)

Haematologica 2018
Volume 103(9):1511-1517

Real-world outcomes and management strategies for venetoclax-treated chronic lymphocytic leukemia patients in the United States

Anthony R. Mato,[1] Meghan Thompson,[2] John N. Allan,[3] Danielle M. Brander,[4] John M. Pagel,[5] Chaitra S. Ujjani,[6] Brian T. Hill,[7] Nicole Lamanna,[8] Frederick Lansigan,[9] Ryan Jacobs,[10] Mazyar Shadman,[11] Alan P. Skarbnik,[12]

Variable	
n	141
Age (y)	67 (37-91)
Prior lines	3 (0-11)
Prior ibrutinib	82%
TP53 aberation	53%
Follow-up (mo)	7 (0.1-38)



PI in R/R CLL: Prejudices

- Progress under BCRi: can be safely and durably rescued by BCL2i
- Progress under BCL2i: we will find something else

JOURNAL OF CLINICAL ONCOLOGY

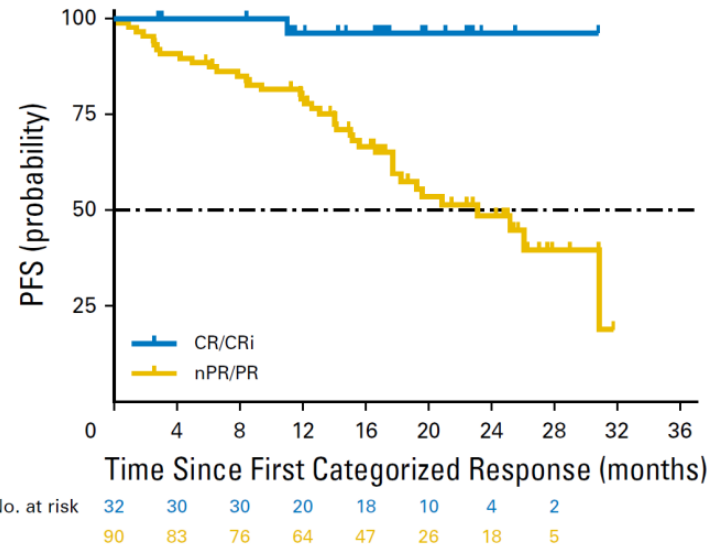
ORIGINAL REPORT

jco.org on May 1, 2018.

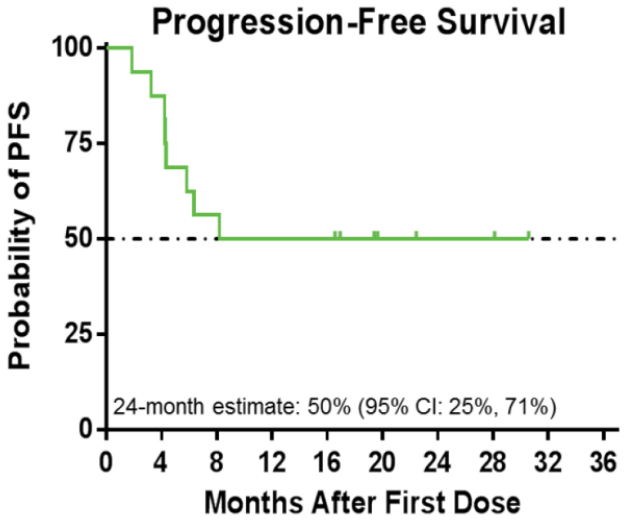
Venetoclax for Patients With Chronic Lymphocytic Leukemia With 17p Deletion: Results From the Full Population of a Phase II Pivotal Trial

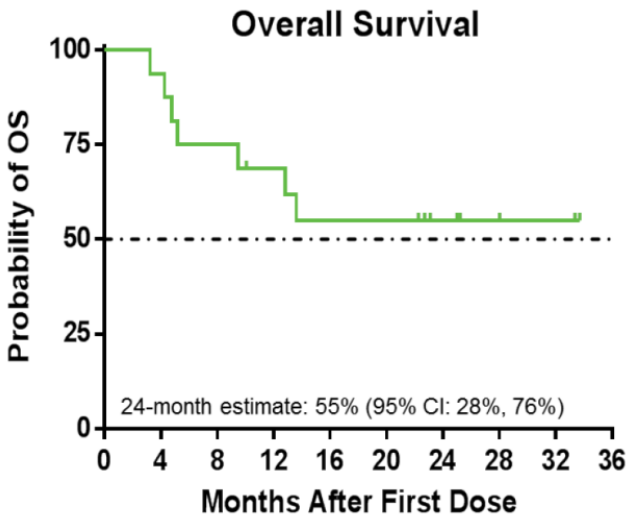
Stephan Stilgenbauer, Barbara Eichhorst, Johannes Schetelig, Peter Hillmen, John F. Seymour, Steven Coutre, Wojciech Jurczak, Stephen P. Mulligan, Anna Schuh, Sarit Assouline, Clemens-Martin Wendtner, Andrew W. Roberts, Matthew S. Davids, Johannes Bloehdorn, Talha Munir, Sebastian Böttcher, Lang Zhou, Ahmed Hamed Salem, Monali Desai, Brenda Chyla, Jennifer Arzt, Su Young Kim, Maria Verdugo, Gary Gordon, Michael Hallek, and William G. Wierda

All patients



Patients after BCRi failure





Who should be offered cellular immunotherapy ?

Who should be offered cellular immunotherapy ?

blood®

2018 132: 892-902
doi:10.1182/blood-2018-01-826008 originally published online July 11, 2018

High-risk chronic lymphocytic leukemia in the era of pathway inhibitors: integrating molecular and cellular therapies

Peter Dreger, Paolo Ghia, Johannes Schetelig, Michel van Gelder, Eva Kimby, Mauricette Michallet, Carol Moreno, Tadeusz Robak, Stephan Stilgenbauer and Emili Montserrat

ERIC european research initiative on CLL

EBMT

Relapse after CIT or refractory to CIT, *now on BTKi or BCL2i*

Response?

Yes

No

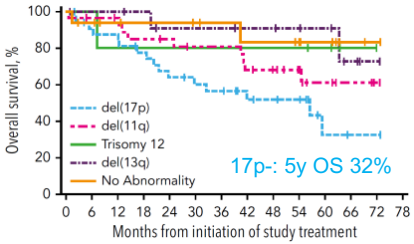
TP53^{abn} ?

Yes

HR I

CR, MRD-

Complex karyotype, multiple lines*



O'Brien et al;
Blood 2018;131:1910

5y OS <50%

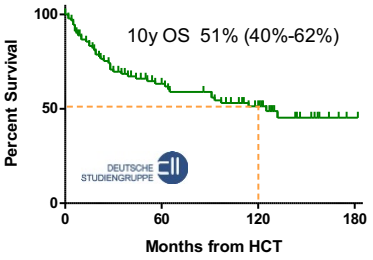
High CI risk
- Age >65y *and/or*
- Comorbidity *and/or*
- No well-matched donor available *and*
- No access to approved CART product

Low CI risk
- Access to approved CART product *or*
- Age ≤ 65y *plus* no comorbidity *plus* well-matched donor available

5y OS >50%

Continue PI

Consider CI



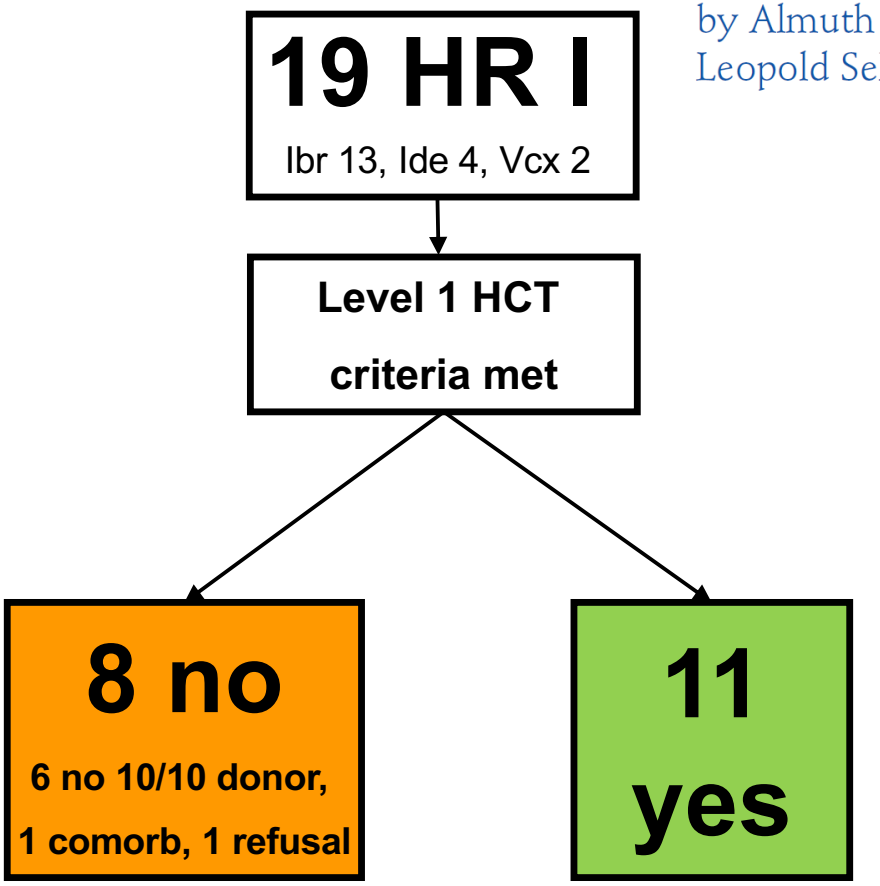
Krämer et al;
Blood 2017;130:1477

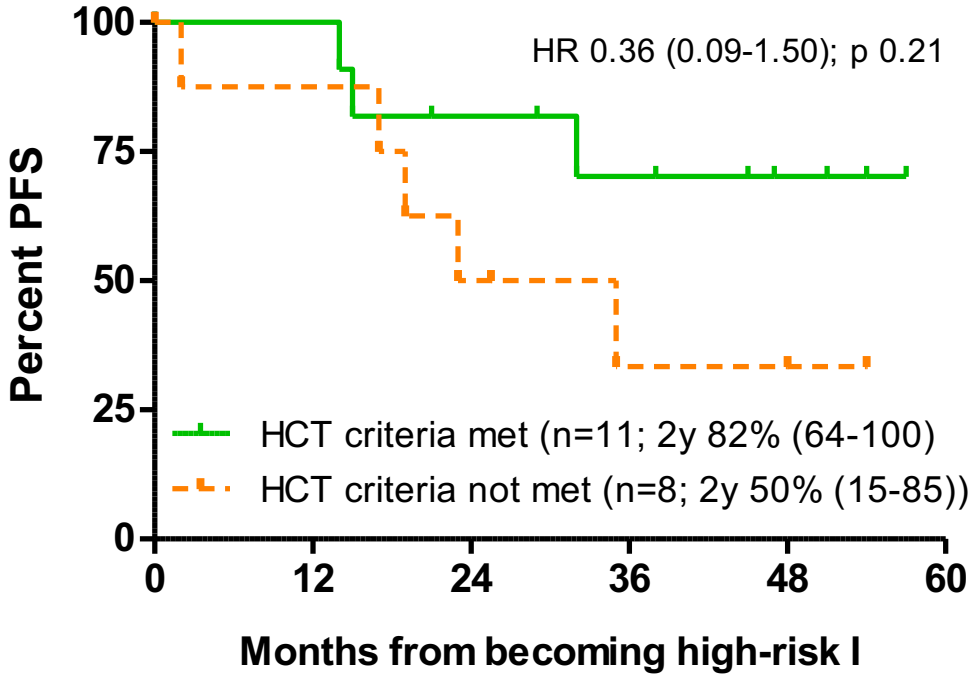
Haematologica 2019

January 10, 2019

Allogeneic transplantation in high-risk chronic lymphocytic leukemia: a single-center intent-to-treat analysis

by Almuth Hoffmann, Sascha Dietrich, Susanne Hain, Michael Rieger, Ute Hegenbart, Leopold Sellner, Anthony Ho, Carsten Müller-Tidow, and Peter Dreger





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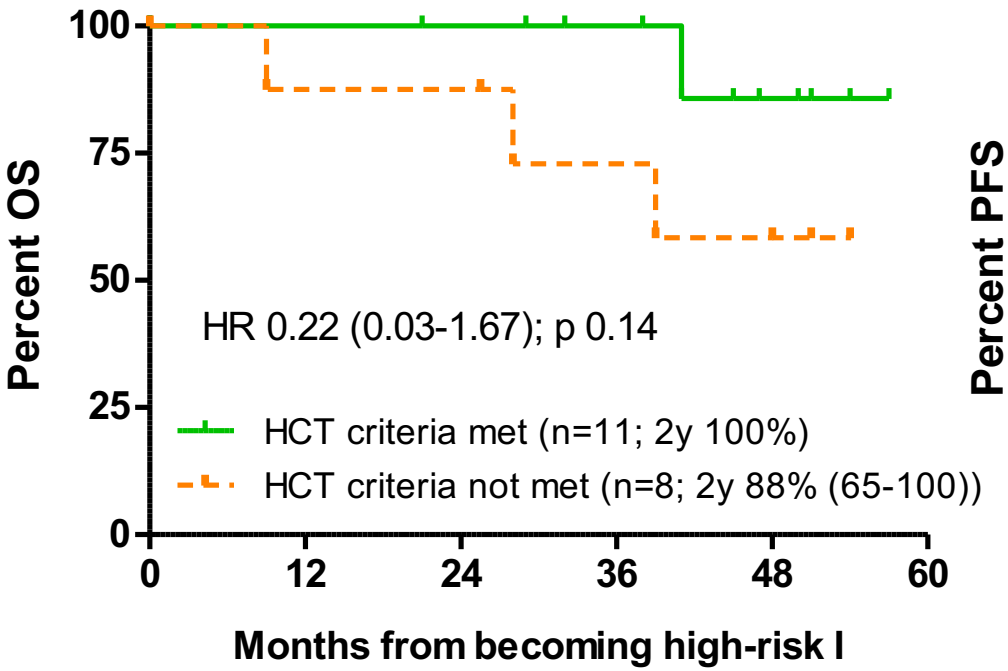
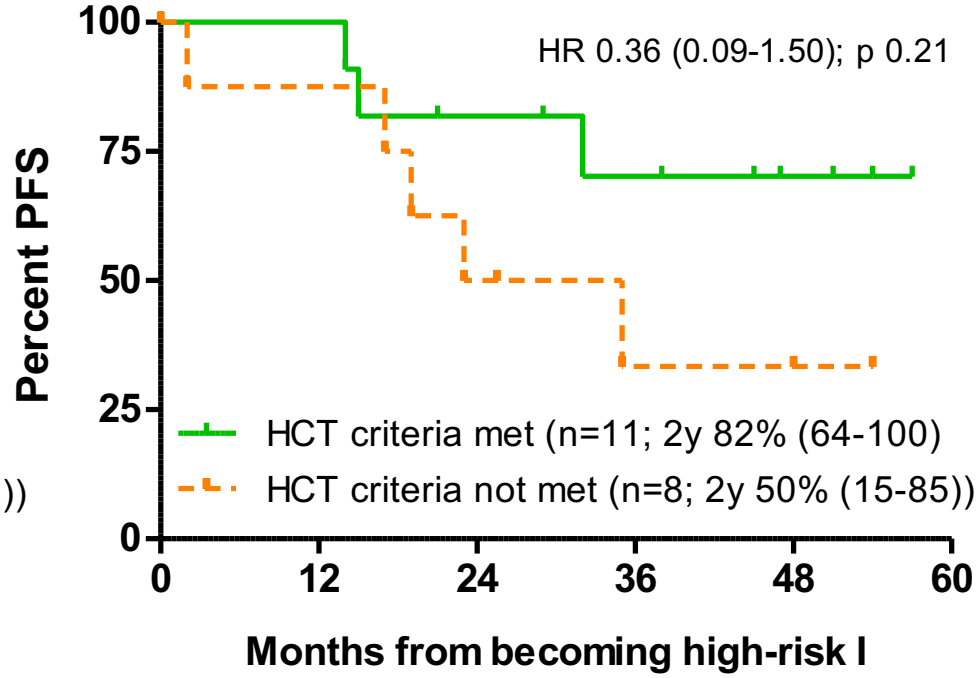
CLL HR-I: OS by HCT criteria

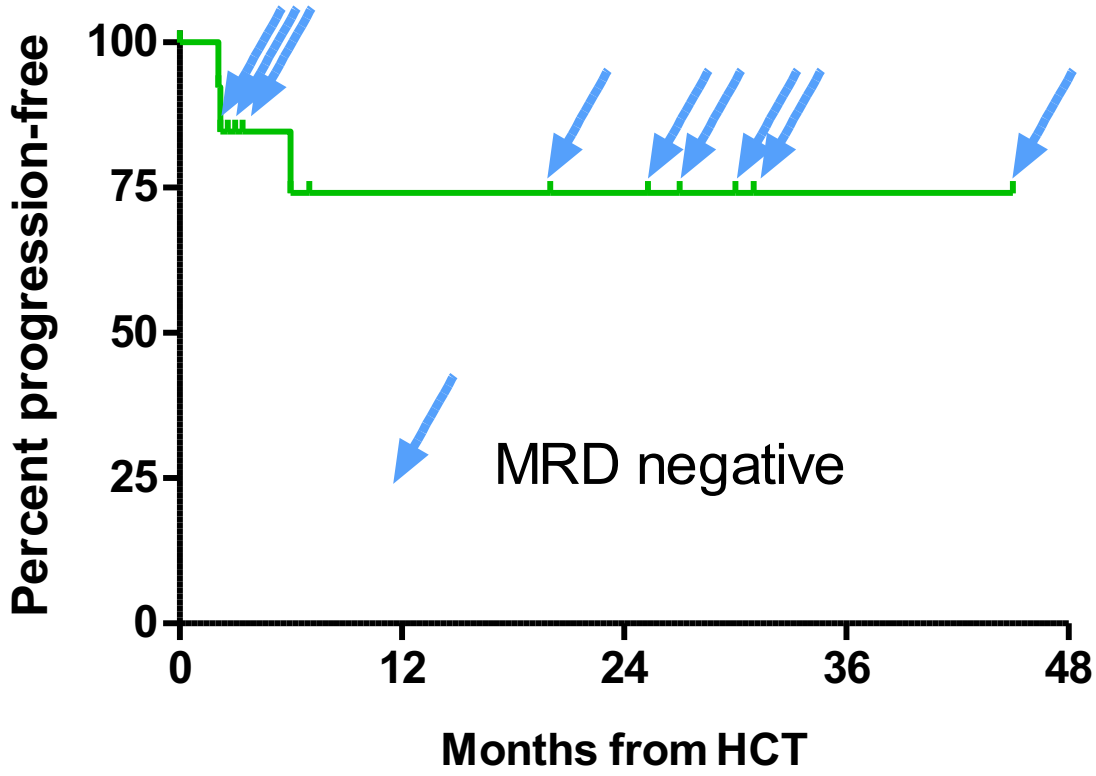


CLL HR-I: PFS by HCT criteria



HCT for CLL HR-II: PFS

(Heidelberg; n=13; f-u 23 mo (3-45))



BJH
2017;178:521

Centre characteristics and procedure-related factors have an impact on outcomes of allogeneic transplantation for patients with CLL: a retrospective analysis from the European Society for Blood and Marrow Transplantation (EBMT)

Johannes Schetelig,[1,2] Liesbeth C. de Wreede,[2,3] Niels S. Andersen,[4] Carol Moreno,[5] Michel van Gelder,[6] Antonin Vitek,[7] Michal Karas,[8] Mauricette Michallet,[9] Maciej Machaczka,[10] Martin Gramatzki,[11] Dietrich Beelen,[12] Jürgen Finke,[13] Julio Delgado,[14] Liisa Volin,[15]

EBMT

N=684, HCT 2000-2011

Table III. Risk factors for event-free survival

Favorable	HR	Unfavorable	HR	Not significant
# CLL transplants	0.96	Status SD/PD	1.7	# overall transplants
JACIE	0.7	F → M	1.4	Donor MUD/MMUD
		CD52 TCD	1.5	RIC vs MAC
		Karnofsky <90	1.4	Del 17p

BJH
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EBMT

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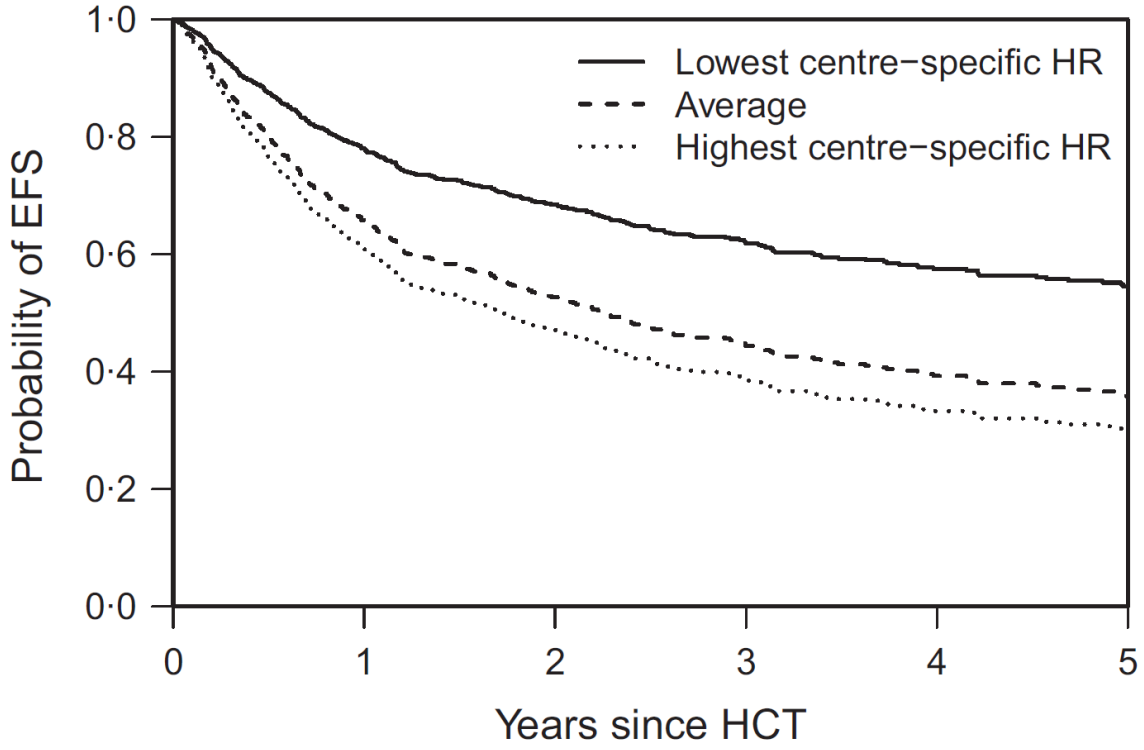
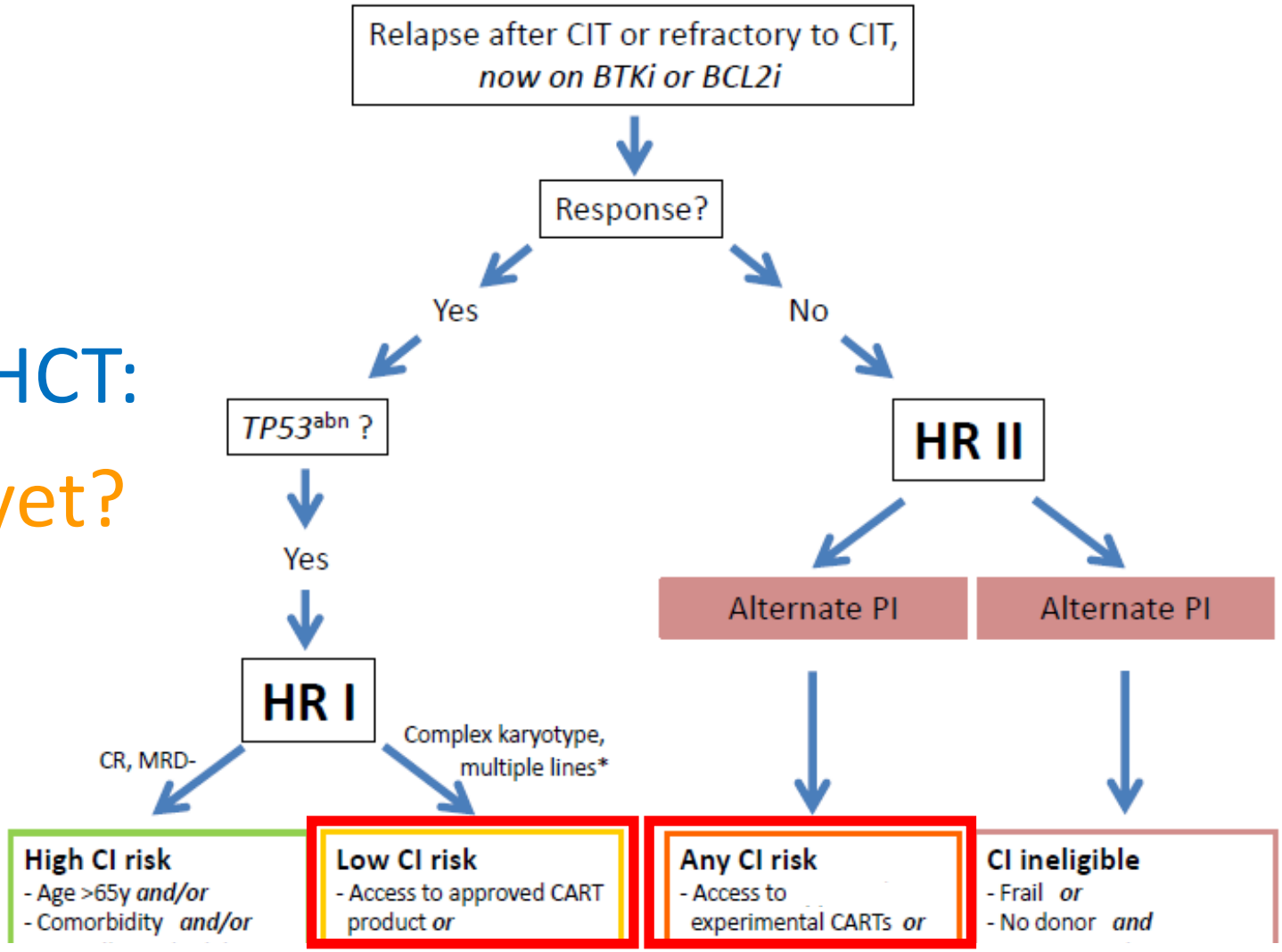
Fig 2. Impact of centre-effects on event-free survival



CARTs for replacing AlloHCT:

Are we there yet?



Blood 2018;132:892-902