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UniversitätsKlinikum Heidelberg

# Allogene Stammzelltransplantation: Jahresbericht 2016

Sektion Stammzelltransplantation

Klinik Innere Medizin V

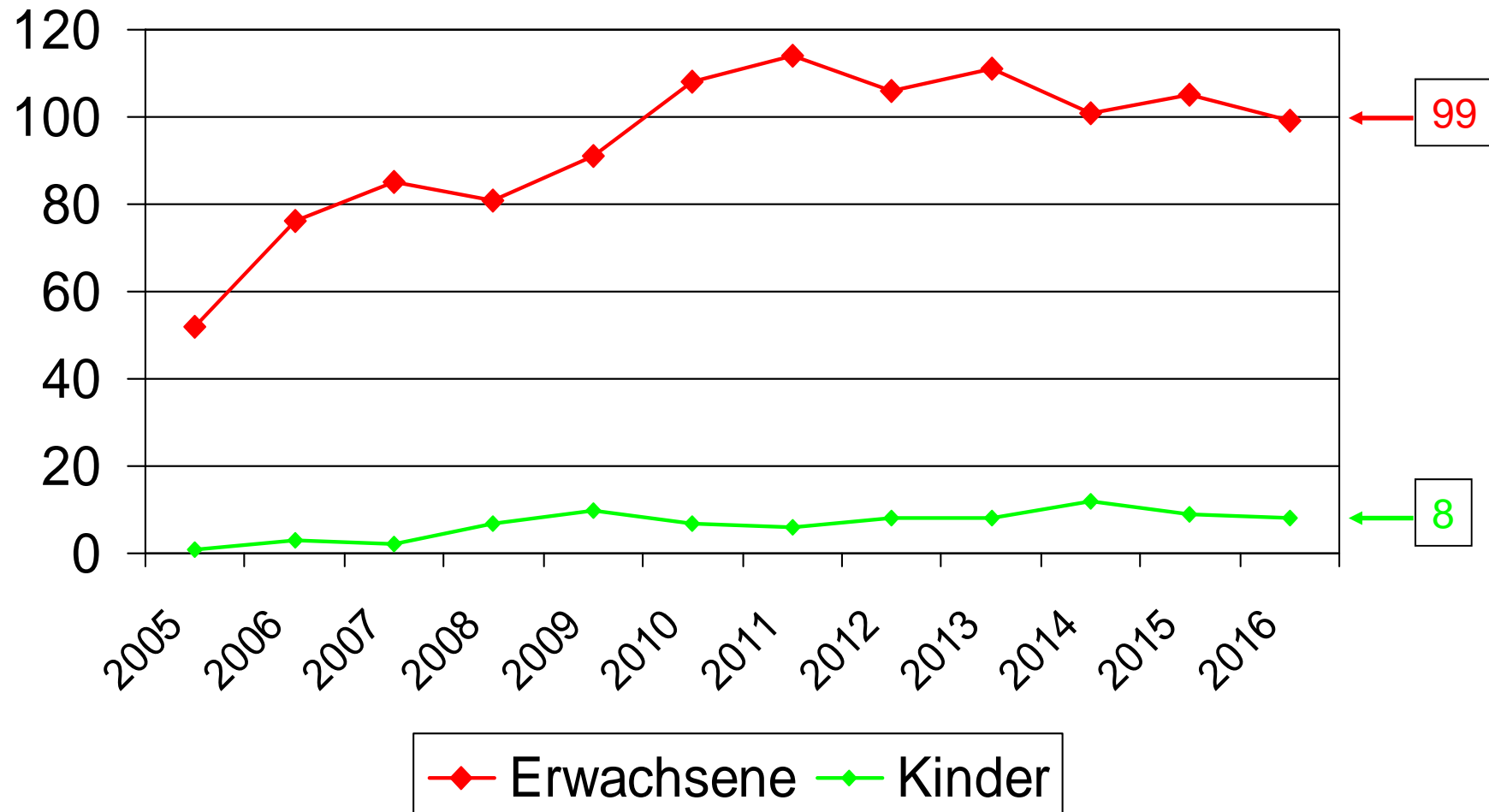
Universitätsklinikum Heidelberg

13.03.2017

Patienten

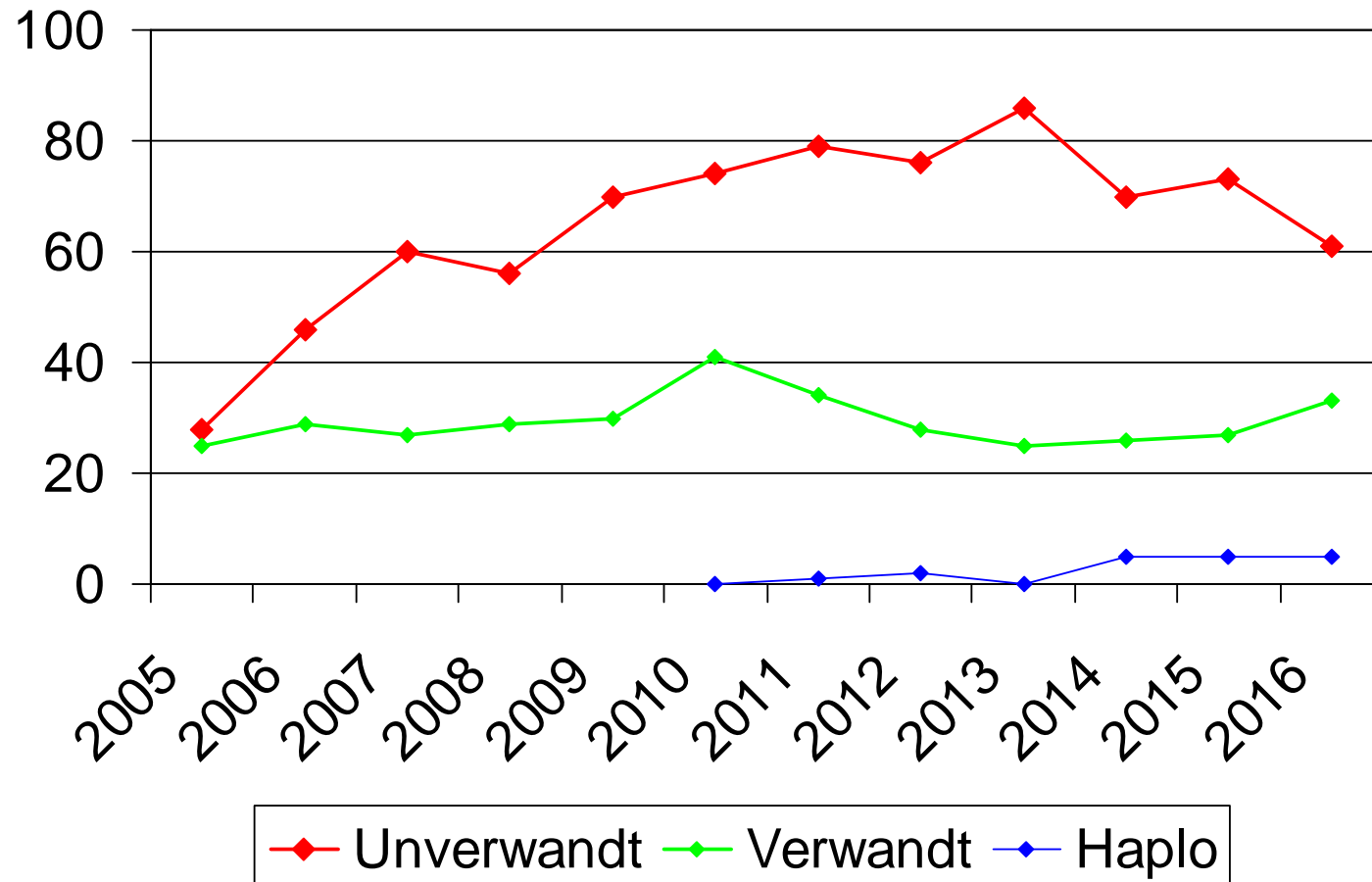


# Allogene Transplantationen



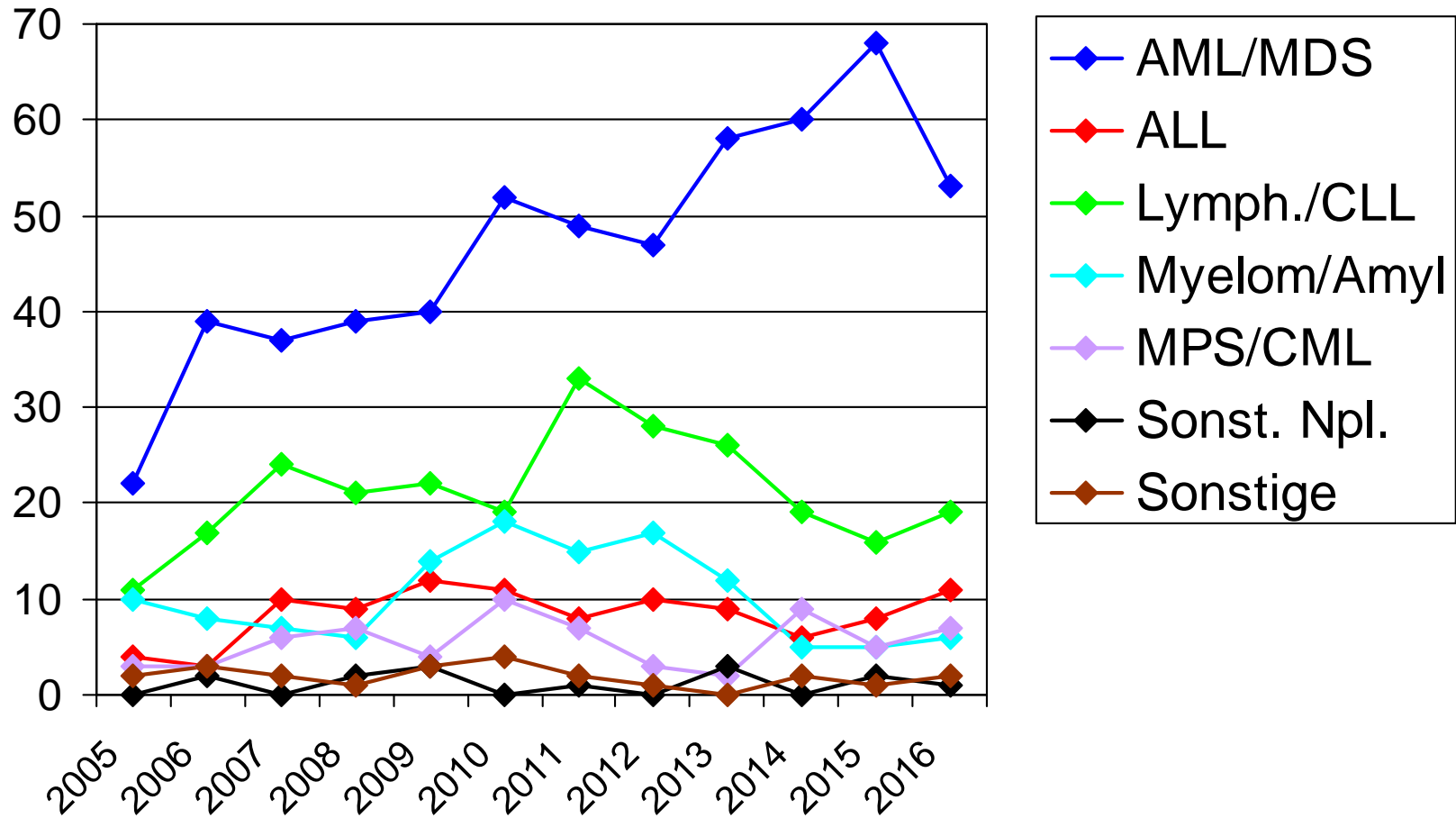


# Spender



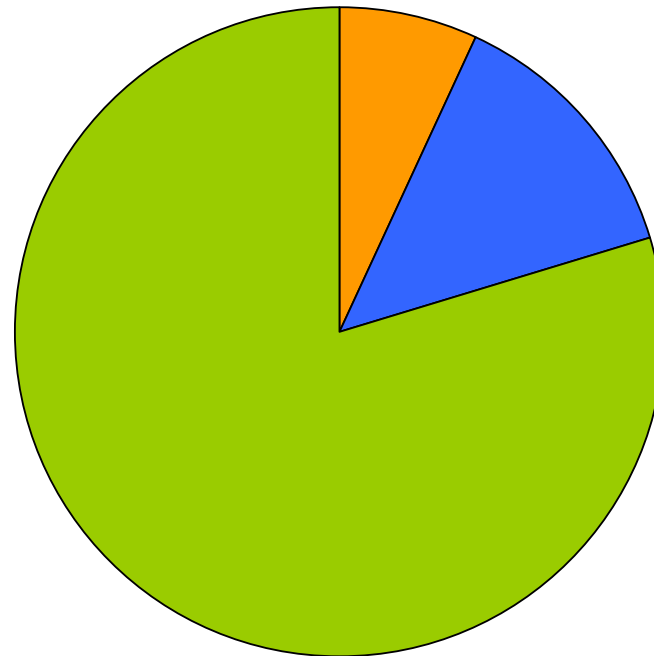


# Indikationen





# Patientenherkunft 2016

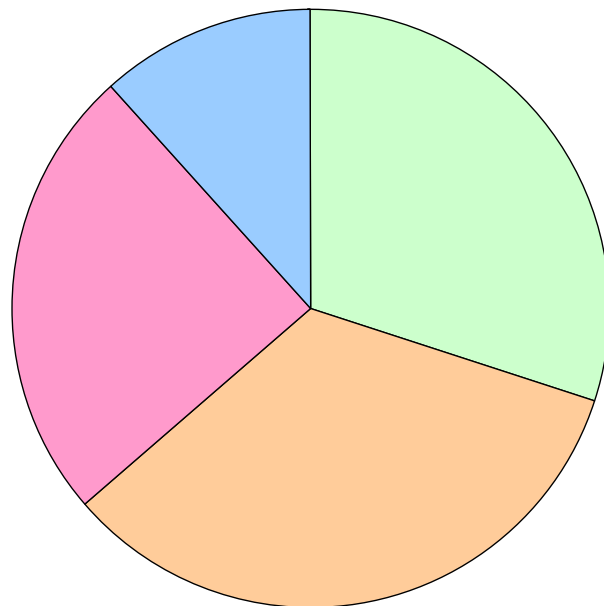


International National Regional

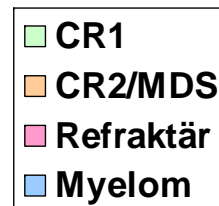
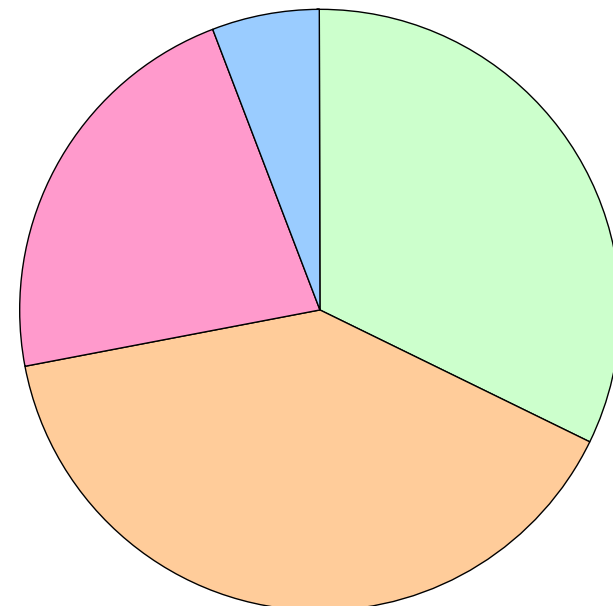


# Patientenstruktur

2005-2007

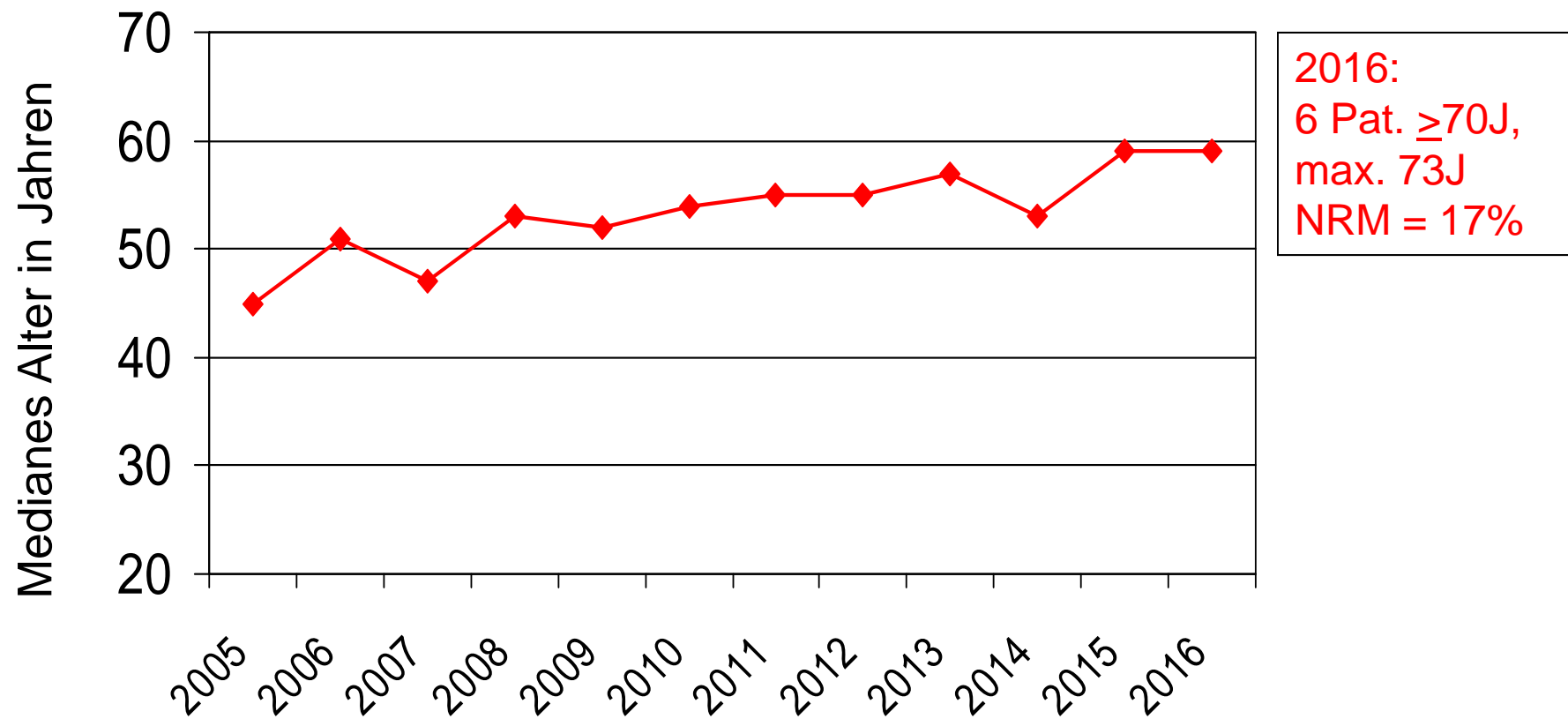


2015-2016





# Entwicklung des medianen Patientenalters

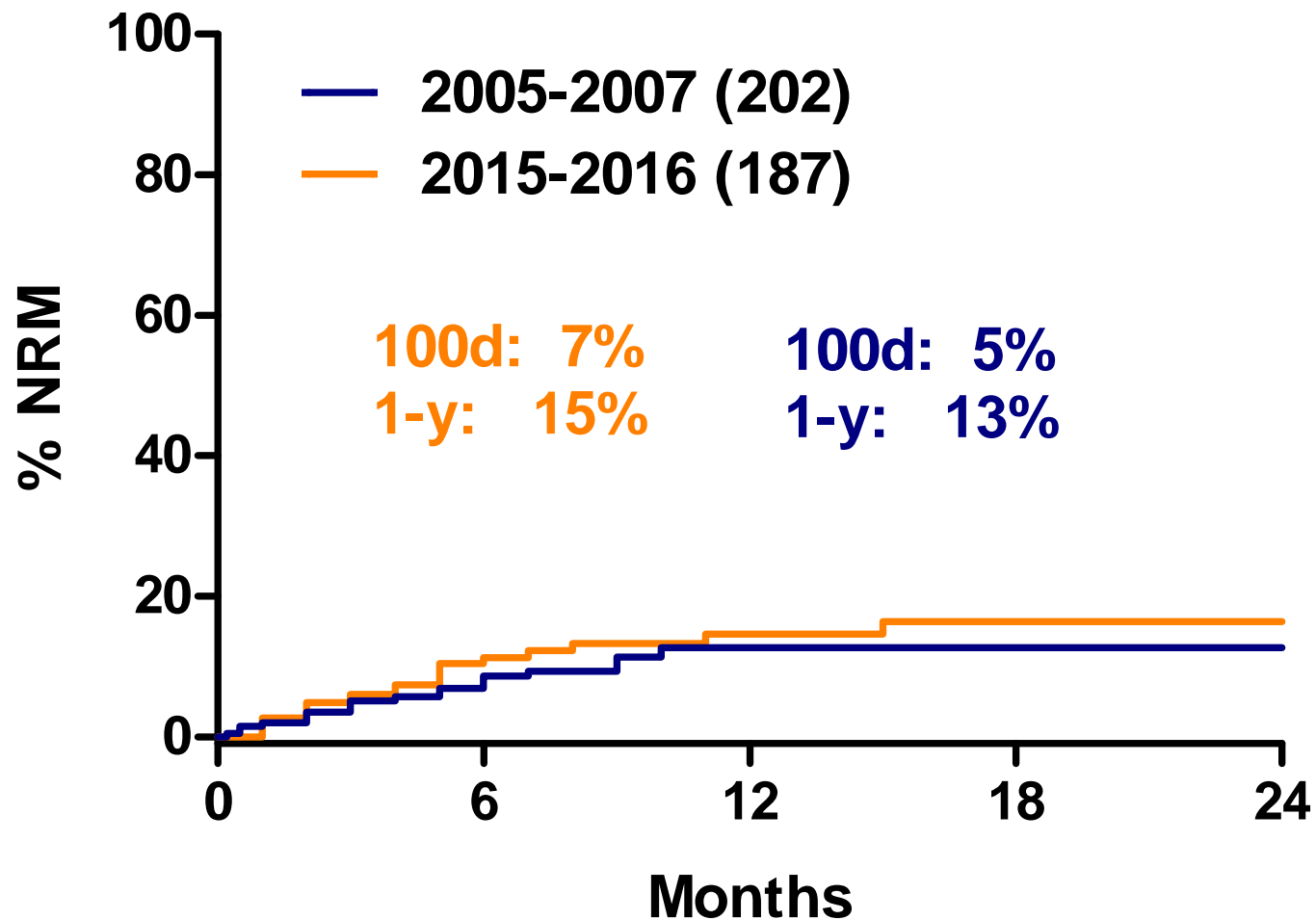




Qualität



# Non-relapse mortality by period



# Klinische Studien



# Allogene Stammzelltransplantation: Studien

Studie	Studienart	Thema	PI HD	Sponsor	n
MC Flud T14	Phase-3 AMG	BuFlu vs TreoFlu	Luft	medac	52
<b>Letermovir</b>	<b>Phase-3 AMG</b>	<b>CMV-Prophylaxe</b>	<b>Schmitt</b>	<b>MSD</b>	<b>19</b>
LFG	Phase-2/3 AMG	TMA	Luft	Novartis	3
STUD RIG	Phase-2 AMG	Ref aGVHD	Dreger	UK FR	-
CLL TX1	Phase-2 AMG	CLL	Dreger	UK Köln	-
TFT2	Phase-2 AMG	Zweit-allo AML	Dreger	UK FR	8
CHARLY	Phase-2 AMG	NHL haplo	Dietrich	UK HD	0
CART19	Phase-1/2 AMG	ALL, CLL, NHL	Schmitt	UK HD	-
PETRA cont.	Non-AMG	Sport-Intervention	Wiskem.	NCT	125+
ECP-Register	Register	ECP	A Schmitt	Therakos	
Restmaterial	Biobank	GVHD, TMA etc	Luft	selbst	



# Letermovir Ph3 MSD

(FM Marty et al; Late-breaking abstract Tandem 2017)

## Frage:

- Letermovir-Prophylaxe (d +28 – d +100):  
Reduktion von CMV-Virämie + -Disease?

## Design:

- Randomisierter Vergleich LET (n=325) vs  
PBO (n=170) vs R-Idela + Placebo (n=209)

→ **Primärer Endpunkt erreicht!**



# Allogene Stammzelltransplantation: Studien

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<b>TFT-TX2</b>	<b>Phase-2 AMG</b>	<b>Zweit-allo AML</b>	<b>Dreger</b>	<b>UK FR</b>	<b>8</b>
CHARLY	Phase-2 AMG	NHL haplo	Dietrich	UK HD	0
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PETRA cont.	Non-AMG	Sport-Intervention	Wiskem.	NCT	125+
ECP-Register	Register	ECP	A Schmitt	Therakos	
Restmaterial	Biobank	GVHD, TMA etc	Luft	selbst	



## AML TFT-TX2 Ph2

(Abstract geplant zu EBMT Tandem 2018)

### Frage:

- Verträglichkeit und Wirksamkeit einer 2. allogenen MUD-HCT bei AML-Spätrezidiv nach 1. HCT (Konditionierung TT/Flu/Treo/ATG)?

### Design:

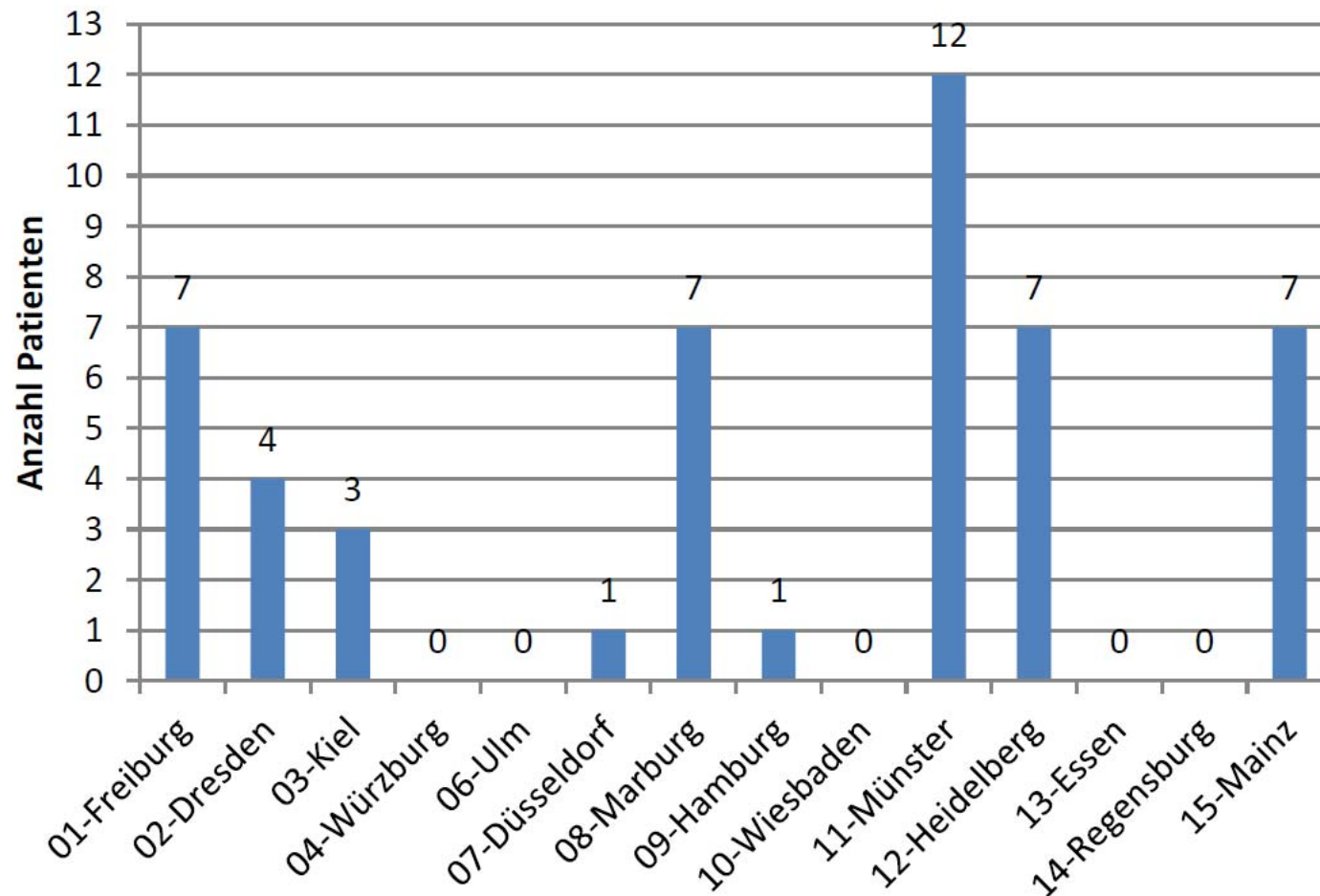
- Phase-2 prospektiv (n=50)



# AML TFT-TX2 Ph2

(Finale Rekrutierung 2/2017)

## TFT-2Tx - Rekrutierung/Zentrum







## TFT-TX2: Heidelberger Patienten

Patient	Status at Tx1	Tx1 - REL	Status at Tx2	Status aktuell	COD
1	Refraktär	17 mo	Refraktär	a&w 26+	-
2	CR nach PIF	27 mo	CRi	a&w 22+	-
3	CR nach PIF	17 mo	CR	a&w 21+	-
4	CR1	58 mo	Mol Rez	Dead +7	Infection
5	CR1	15 mo	Refraktär	Dead +7	Relapse
6	CR1	35 mo	Refraktär	Dead +6	GVHD
7	CR nach PI	30 mo	Refraktär	a&w 5+	-
8	CR1	9 mo	Refraktär	a&w 3+	-



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<b>CHARLY</b>	<b>Phase-2 AMG</b>	<b>NHL haplo</b>	<b>Dietrich</b>	<b>UK HD</b>	<b>0</b>
CART19	Phase-1/2 AMG	ALL, CLL, NHL	Schmitt	UK HD	-
PETRA cont.	Non-AMG	Sport-Intervention	Wiskem.	NCT	125+
ECP-Register	Register	ECP	A Schmitt	Therakos	
Restmaterial	Biobank	GVHD, TMA etc	Luft	selbst	



PHASE-II STUDY ON THE VALUE OF POST-  
TRANSPLANT **C**YCLOPHOSPHAMIDE AFTER  
**H**APLO-IDENTICAL STEM CELL TRANSPLANTATION  
FOR **R**ELAPSED/ REFRACTORY NON-HODGKIN  
**L**YMPHOMA  
(**CHARLY** trial)

# CHARLY: Status March 13, 2017

- Budget secured
- Protocol finalized
- Contracting finalized
- 22.01.2016 1st Investigator Meeting (FM)
- 20.04.2016 BfArM submission
- 20.05.2016 BfArM Änderungswünsche
- 27.05.2016 KKS HD Pflichtberatungs-OK
- 17.08.2016 BfArM Genehmigung
- 25.10.2016 Positives Ethikvotum
- 28.10.2016 Initiierung (FM)
- 12.12.2016 Studienstart HD



# TBF conditioning for lymphoma haploSCT

Heidelberg experience (March 13, 2017)

Patient #	1	2	3	4	5	6
Diagnosis	GZL	DLBCL	MM	DLBCL	PTCL	PTCL
Age at HCT (y)	26M	37M	36M	24M	54M	63M
Previous autoSCT	+	-	+	-	-	-
Status at HCT	PR	PR	PR	CR	PR	PR
Donor source	<b>Father</b>	<b>SIB</b>	<b>SIB</b>	<b>Father</b>	<b>Daughter</b>	<b>Son</b>
Conditioning	TB3F	TB3F	TB2F	TB3F	TB2F	TB1F
GVHD (A/C, grade)	mC	-	-	-	-	-
COD	-	<b>Sepsis</b>	-	-	-	-
PFS	<b>16</b>	<b>1</b>	18+	<b>8</b>	11+	5+
OS	23+	<b>1</b>	18+	12+	11+	5+



# Allogene Stammzelltransplantation: Studien

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TFT2	Phase-2 AMG	Zweit-allo AML	Dreger	UK FR	7
CHARLY	Phase-2 AMG	NHL haplo	Dietrich	UK HD	0
<b>CART19</b>	<b>Phase-1/2 AMG</b>	<b>ALL, CLL, NHL</b>	<b>Schmitt</b>	<b>UK HD</b>	<b>-</b>
PETRA cont.	Non-AMG	Sport-Intervention	Wiskem.	NCT	125+
ECP-Register	Register	ECP	A Schmitt	Therakos	
Restmaterial	Biobank	GVHD, TMA etc	Luft	selbst	

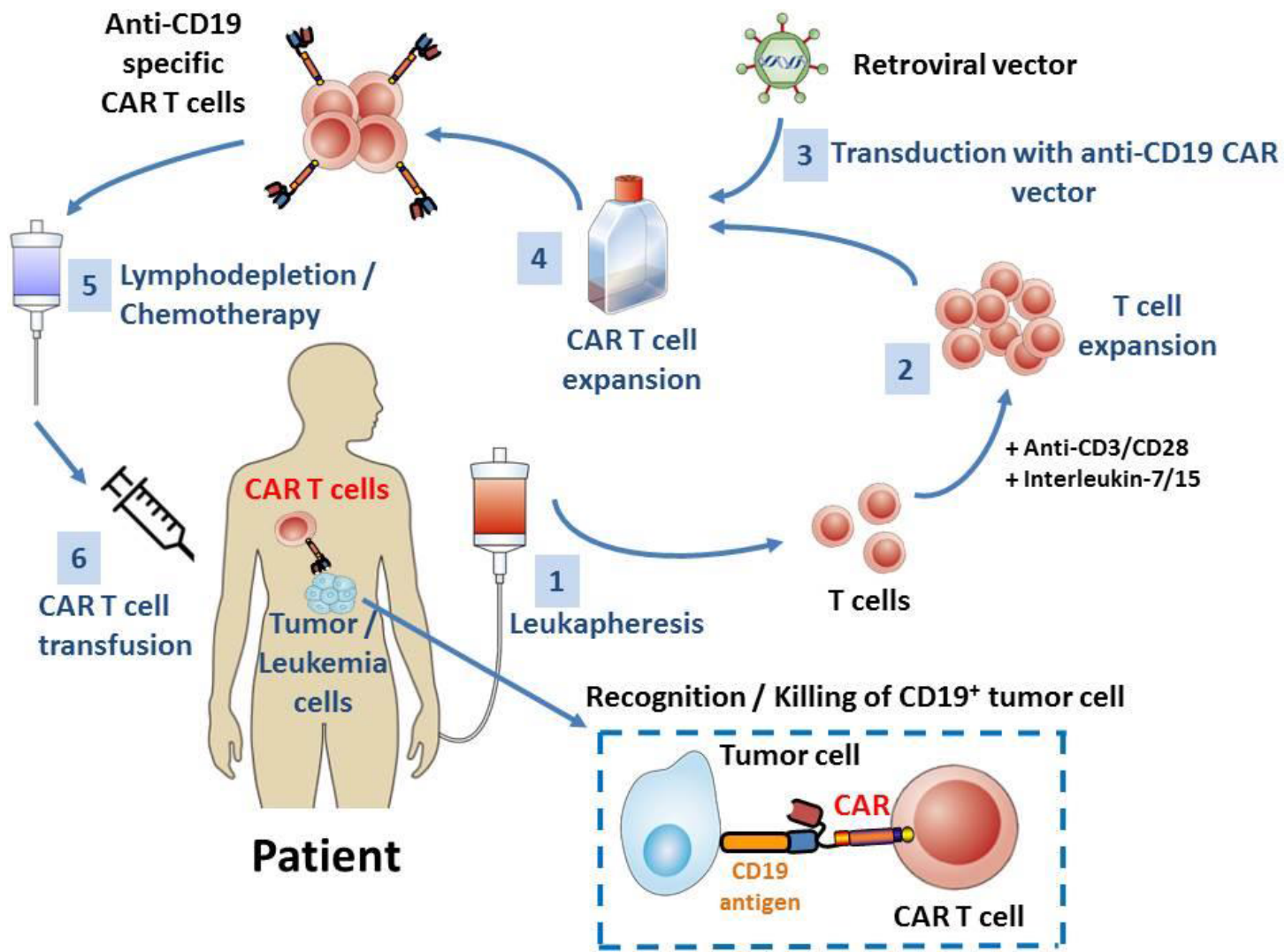


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UniversitätsKlinikum Heidelberg

**Treatment of patients with relapsed or refractory CD19+ lymphoid disease with T lymphocytes transduced by RV-SFG.CD19.CD28.4-1BB $\zeta$  retroviral vector - A unicenter Phase I/II clinical trial**

**LKP: Michael Schmitt**





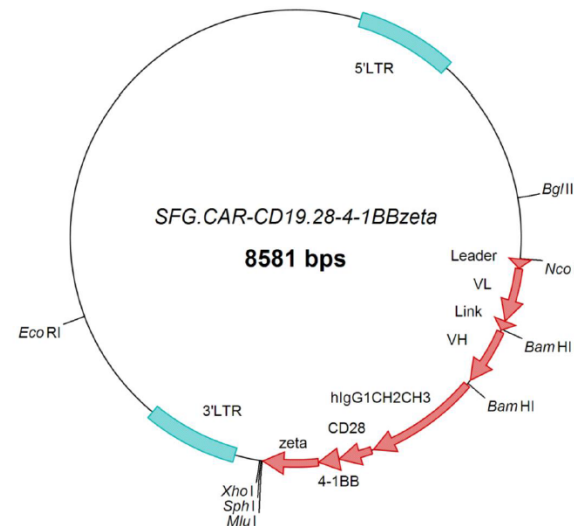
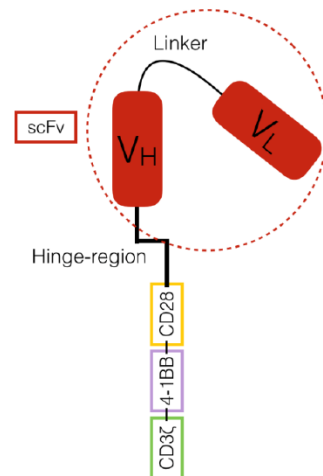
## Indications

Relapsed or refractory CD19<sup>+</sup> lymphoid disease

- Acute lymphoblastic leukemia (ALL)
- Chronic lymphocytic leukemia (CLL)
- Diffuse large B-cell lymphoma (DLBCL)
- Follicular lymphoma (FL)
- Mantle cell lymphoma (MCL)

## Sample size

- Phase I/II dose-escalation trial is designed to evaluate the safety of escalating doses of CAR T cells expressing antigen receptors targeting the CD19 molecule (CD19.CAR)
- 2-16 patients are planned to be treated within this study
- Three dose levels are being evaluated:
  - $1 \times 10^6$  transduced cells/m<sup>2</sup>
  - $5 \times 10^6$  transduced cells/m<sup>2</sup>
  - $20 \times 10^6$  transduced cells/m<sup>2</sup>



Q1  
2016

7) QC: Transduktionseffizienz  
Immunphänotyp, Zytotox-Assay

Q2+3  
2016

8) Briefing Documents & SOPs

Q3+Q4  
2016

9) Vorbesprechungen/Scientific Advices mit RP und PEI

10) Erwerb des Vektors!

RP

PEI

AKTUELL

11a) Antrag auf HE

11b) Antrag auf Erlaubnis der  
Klinischen Prüfstudie

12) Inspektion vor Ort

13a) Erteilung der HE durch RP

13a) Erlaubnis der Klin. Studie  
durch PEI

2017

14) First-Patient-In (FPI) 2017



# Allogene Stammzelltransplantation: Studien

Studie	Studienart	Thema	PI HD	Sponsor	n
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ECP-Register	Register	ECP	A Schmitt	Therakos	
<b>Restmaterial</b>	<b>Biobank</b>	<b>GVHD, TMA etc</b>	<b>Luft</b>	<b>selbst</b>	<b>&gt;800</b>

# Publikationen

# Publikationen 2015/2016 (Auswahl)

Thema	Artikel	IF 2015
GVHD	Zeisbrich M, Becker N, Benner A, Radujkovic A, Schmidt K, Beimler J, Ho AD, Zeier M, Dreger P, Luft T. Transplant -associated thrombotic microangiopathy is an endothelial complication associated with refractoriness of acute GVHD. <i>Bone Marrow Transplant</i> in press	3.636

- TMA ist bei Patienten mit ref. aGVHD überrepräsentiert (45% vs 2.3%)
- TMA-Risiko lässt sich vor der TPL durch Serummarker (ST2) und TM-SNPs präzisieren
- Endothelprotektion durch Statine & UDCA reduziert TMA und ref aGVHD

# Publikationen 2015/2016 (Auswahl)

Thema	Artikel	IF 2015
<b>GVHD</b>	Zeisbrich M, Becker N, Benner A, <b>Radujkovic A, Schmidt K</b> , Beimler J, <b>Ho AD</b> , Zeier M, <b>Dreger P, Luft T</b> . Transplant -associated thrombotic microangiopathy is an endothelial complication associated with refractoriness of acute GVHD. <i>Bone Marrow Transplant</i> in press	3.636
<b>Metabolic stress / aging</b>	<b>Radujkovic A</b> , Schnitzler P, <b>Ho AD, Dreger P, Luft T</b> . Low serum vitamin D levels are associated with shorter survival after first-line azacitidine treatment in patients with myelodysplastic syndrome and secondary oligoblastic acute myeloid leukemia. <i>Clin Nutr</i> 2016 Feb 10.	4.487
<b>Metabolic stress / aging</b>	<b>Radujkovic A</b> , Becker N, Benner A, Penack O, Platzbecker U, Stölzel F, ... <b>Dreger P, Luft T</b> . Pre-transplant weight loss predicts inferior outcome after allogeneic stem cell transplantation in patients with myelodysplastic syndrome. <i>Oncotarget</i> 2015 Aug 17;6(33):35095-106.	5.008
<b>CLL SCT</b>	<b>Sellner L</b> , Brüggemann M, Schlitt M, Knecht H, Herrmann D, Reigl T, ... <b>Dreger P</b> . GvL effects in T-prolymphocytic leukemia: evidence from MRD kinetics and TCR repertoire analyses. <i>Bone Marrow Transplant</i> 2016 Dec 12	3.636
<b>CLL SCT</b>	<b>Hahn M</b> , Böttcher S, <b>Dietrich S, Hegenbart U, Rieger M, Stadtherr P, .Dreger P</b> . Allogeneic hematopoietic stem cell transplantation for poor-risk chronic lymphocytic leukemia: Dissecting immune-modulating strategies for disease eradication and treatment of relapse. <i>Bone Marrow Transplant</i> 2015 Jul 6;50(10):1279-85	3.636

# Publikationen 2015/2016 (Auswahl)

Thema	Artikel	IF 2015
<b>EBMT-Studie</b>	<b>Meissner J</b> , Finel H, <b>Dietrich S</b> , Boumendil A, Kanfer E, Laboure G, ... <b>Dreger P</b> . Autologous hematopoietic stem cell transplantation for intravascular large B-cell lymphoma: the European Society for Blood and Marrow Transplantation experience. <i>Bone Marrow Transplant</i> 2016 Dec 19	3.636
<b>EBMT-Studie</b>	<b>Dietrich S</b> , Finel H, Martinez C, Tischer J, Blaise D, Chevallier P, ... <b>Dreger P</b> . Post-transplant cyclophosphamide-based haplo-identical transplantation as alternative to matched sibling or unrelated donor transplantation for non-Hodgkin lymphoma: A registry study by the European society for blood and marrow transplantation. <i>Leukemia</i> 2016 May 5;30(10):2086-9	12.104
<b>EBMT-Studie</b>	<b>Sellner L</b> , Boumendil A, Finel H, Choquet S, De RG, Falzetti F, ... <b>Dreger P</b> . Thiotepa-based high-dose therapy for autologous stem cell transplantation in lymphoma: a retrospective study from the EBMT. <i>Bone Marrow Transplant</i> 2016 Nov 16;51(2):212-8.	3.636
<b>EBMT-Studie</b>	Tanase A, Schmitz N, Stein H, Boumendil A, Finel H, Castagna L, ... <b>Dreger P</b> . Allogeneic and Autologous Stem Cell Transplantation for hepatosplenic T cell lymphoma. <i>Leukemia</i> 2015 Sep 19;29(3):686-8	12.104
<b>EBMT-Studie</b>	<b>Horstmann K</b> , Boumendil A, Finke J, Finel H, Kanfer E, Milone G, ... <b>Dreger P</b> . Second Allogeneic Stem Cell Transplantation in Patients with Lymphoma Relapse after a First Allogeneic Transplantation. <i>Bone Marrow Transplant</i> 2015 Mar 9;50(6):790-4	3.636

# Publikationen 2015/2016 (Auswahl)

Thema	Artikel	IF 2015
Guideline	Wendtner CM, <b>Dreger P</b> , Gregor M, Greil R, Knauf WU, Pritzkeleit R, et al. Leitlinie Chronische lymphatische Leukämie. Onkopedia Jan 2017	-
Guideline	Zeiser R, Wolff D, Scheid C, <b>Luft T</b> , Greinix H, <b>Dreger P</b> , et al. Leitlinie akute Graft-versus-Host-Erkrankung. Onkopedia Jan 2017	-
Guideline	Wolff D, Zeiser R, Scheid C, <b>Luft T</b> , Mielke S, <b>Dreger P</b> , et al. Leitlinie chronische Graft-versus-Host-Erkrankung. Onkopedia Jan 2017.	-
Guideline	<b>Dreger P</b> , Beelen DW, Bornhäuser M, Einsele H, Kröger N, Passweg J, Zeiser R. Allogene Stammzelltransplantation: Indikationen. Onkopedia Mai 2016	-
Guideline	Sureda A, Bader P, Cesaro S, <b>Dreger P</b> , Duarte RF, Dufour C, et al. Indications for Allogeneic and Autologous Stem Cell Transplantation for Haematological Diseases, Solid Tumours and Immune Disorders: Current Practice in Europe 2015. <i>Bone Marrow Transplant</i> 2015 Mar 23	3.636
Review	Montserrat E, <b>Dreger P</b> . Hope for High-Risk Chronic Lymphocytic Leukemia Relapsing After Allogeneic Stem-Cell Transplantation. <i>J Clin Oncol</i> 2015 Apr 13;33(14):1527-9	20.982



Veranstaltungen

## Speakers and Chairpersons

**Sebastian Böttcher**, University Hospital, Rostock (DE)  
**Jan Burger**, MD Anderson Cancer Center, Houston (USA)  
**Claire Dearden**, London (UK)  
**Sascha Dietrich**, University Hospital, Heidelberg (DE)  
**Peter Dreger**, University Hospital, Heidelberg (DE)  
**Jan Dürig**, University Hospital, Essen (DE)  
**Paolo Ghia**, Milan (IT)  
**Manfred Hensel**, Oncology Practice, Mannheim (DE)  
**Anthony Ho**, University Hospital, Heidelberg (DE)  
**Eva Kimby**, Karolinska Institute, Stockholm (SE)  
**Fabienne Lucas**, Ohio State University, Columbus (USA)  
**Uwe Martens**, SLK-Kliniken, Heilbronn (DE)  
**Emili Montserrat**, Hospital Clinic, Barcelona (SP)  
**Carsten Müller-Tidow**, University Hospital, Heidelberg (DE)  
**Kai Neben**, Stadtklinikum, Baden-Baden (DE)  
**Jae Park**, Memorial Sloan-Kettering Cancer Center, New York (USA)  
**Michael Schmitt**, University Hospital, Heidelberg (DE)  
**Victor Schneidt**, German Cancer Research Institute, Heidelberg (DE)  
**Martina Seiffert**, German Cancer Research Institute, Heidelberg (DE)  
**Stephan Stilgenbauer**, University Hospital, Ulm (DE)  
**Clemens-Martin Wendtner**, Städtisches Klinikum, Munich (DE)  
**Mathias Witzens-Harig**, University Hospital, Heidelberg (DE)  
**Thorsten Zenz**, National Centre for Tumor diseases, Heidelberg (DE)

## Local Organizing Committee

Sascha Dietrich, Peter Dreger, Anthony Ho, Carsten Müller-Tidow

## Venue

Hörsaal der Medizinischen Klinik

## Contact and Registration

CLL2017 Secretariat  
Petra Müller  
Tel.: 06221 56-39711, Fax: 06221 56-6824  
Email: [petra.mueller@med.uni-heidelberg.de](mailto:petra.mueller@med.uni-heidelberg.de)  
Department Medicine V, University of Heidelberg  
Im Neuenheimer Feld 410, 69120 Heidelberg

Registration by email to  
[petra.mueller@med.uni-heidelberg.de](mailto:petra.mueller@med.uni-heidelberg.de)

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Bronze Sponsor (1.000 EUR)



Weiterbildungspunkte der LÄK BW sind beantragt.



UniversitätsKlinikum Heidelberg

## Program

**Chronic lymphocytic leukemia:  
Where are we after  
the iwCLL 2017?**

**An International Symposium**



**May 19-20, 2017**  
**Medical Clinic, Lecture Hall**



## “Allo” sind...

### „von Dusch“

**M Lommatzsch**

R Gruß

...und das Team!

### Station

**M Schiller**

F Kosely

L Claßen

F Darche

E Mai

M Hahn

A Hoffmann

J Kunz

E Lasitschka

M Porsche

S Raffel

A Martin

G Rüger

### Sport

R Kühl

**J Wiskemann**

& Team

### Koordination

**P Stadtherr**

I Opitz

A Herrmann

### Ambulanz

T Luft

S Schönland

A Radujkovic

J Brandt

K Lisenko

J da Silva

J Tate

S Zink

### CART

**M Schmitt**

A Schmitt

& Team

### ECP

**A Schmitt**

R Alexi

& Team

### Case Manager

**A Bondong**

M Wegner

### Labor

**T Luft**

S Dietrich

M Hess

A Radujkovic

A Hoffmann

K Schmidt

A Hof

R Schulz

S Kräker

### Psychologie

**D Tönnessen**

### Sucheinheit

**H Tran**

K Nerbel

& Team

### Sozialdienst

A Bergner

G Daiß

S Sontowski

### Studienzentrale

**J Klemmer**

AM Geueke

A Gawlik

F Michel

& Team

### Anleitung

U Hegenbart

P Dreger

### (No more) Early Bird Team

J Meissner

JW Schmier

**AD Ho**

**C Müller-Tidow**

...alle Mitarbeiter der MedV !