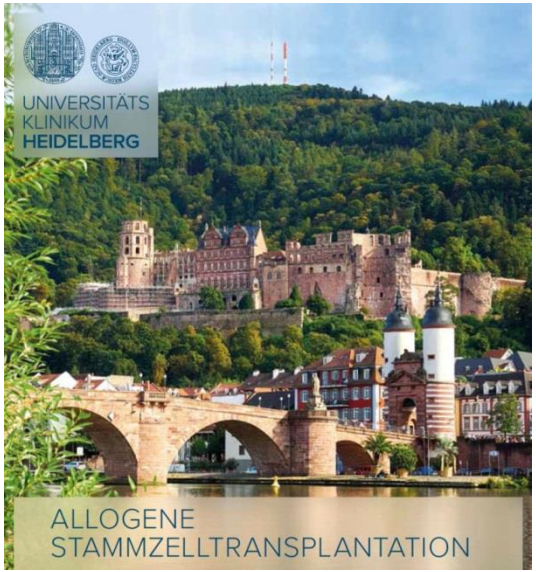
UNIVERSITÄTS
KLINIKUM
HEIDELBERG

Sektion Stammzelltransplantation:

Jahresbericht 2020



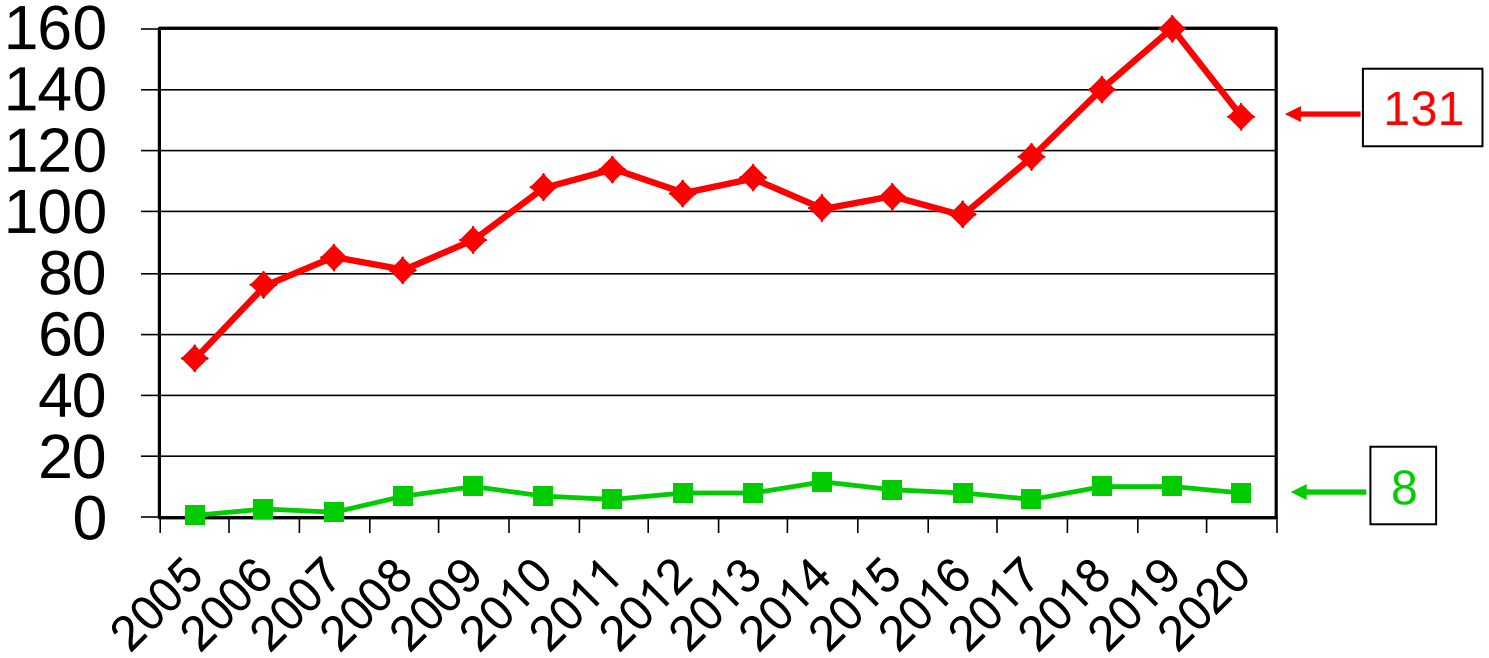
Prof. Dr. Peter Dreger

Klinik Innere Medizin V

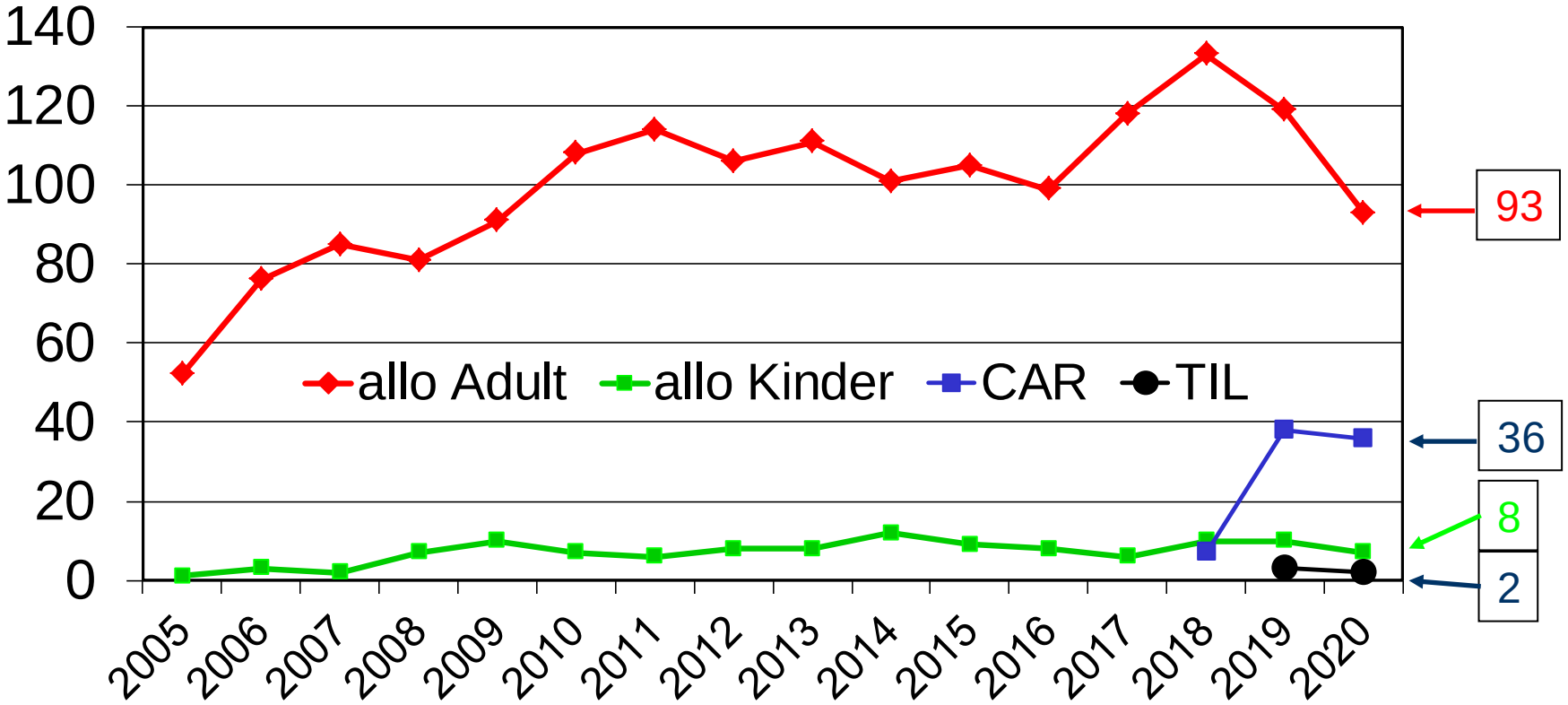
Universitätsklinikum Heidelberg

Zelluläre Immuntherapien HD 2019

(Erwachsene + Kinder, ohne DLI)



Zelluläre Immuntherapien (Arten)



JACIE

JACIE
Joint Accreditation Committee
ISCT | EBMT

The Joint Accreditation Committee ISCT-EBMT (JACIE)

hereby declares that

Department of Internal Medicine V,
Universitätsklinikum Heidelberg
Heidelberg, Germany

has been found to meet the standards as set out in the FACT-JACIE International Standards for Cellular Therapy, edition 6.01 in the following area(s):

Autologous & Allogeneic Transplantation in Adult Patients
Allogeneic Transplantation in Paediatric Patients
Collection of HPC, Marrow
Collection of HPC, Apheresis
Cell Processing - minimally manipulated
Immune Effector Cells administration

Programme Director: Prof. Dr. Med. Peter Dreger

Riccardo Saccardi
JACIE Medical Director

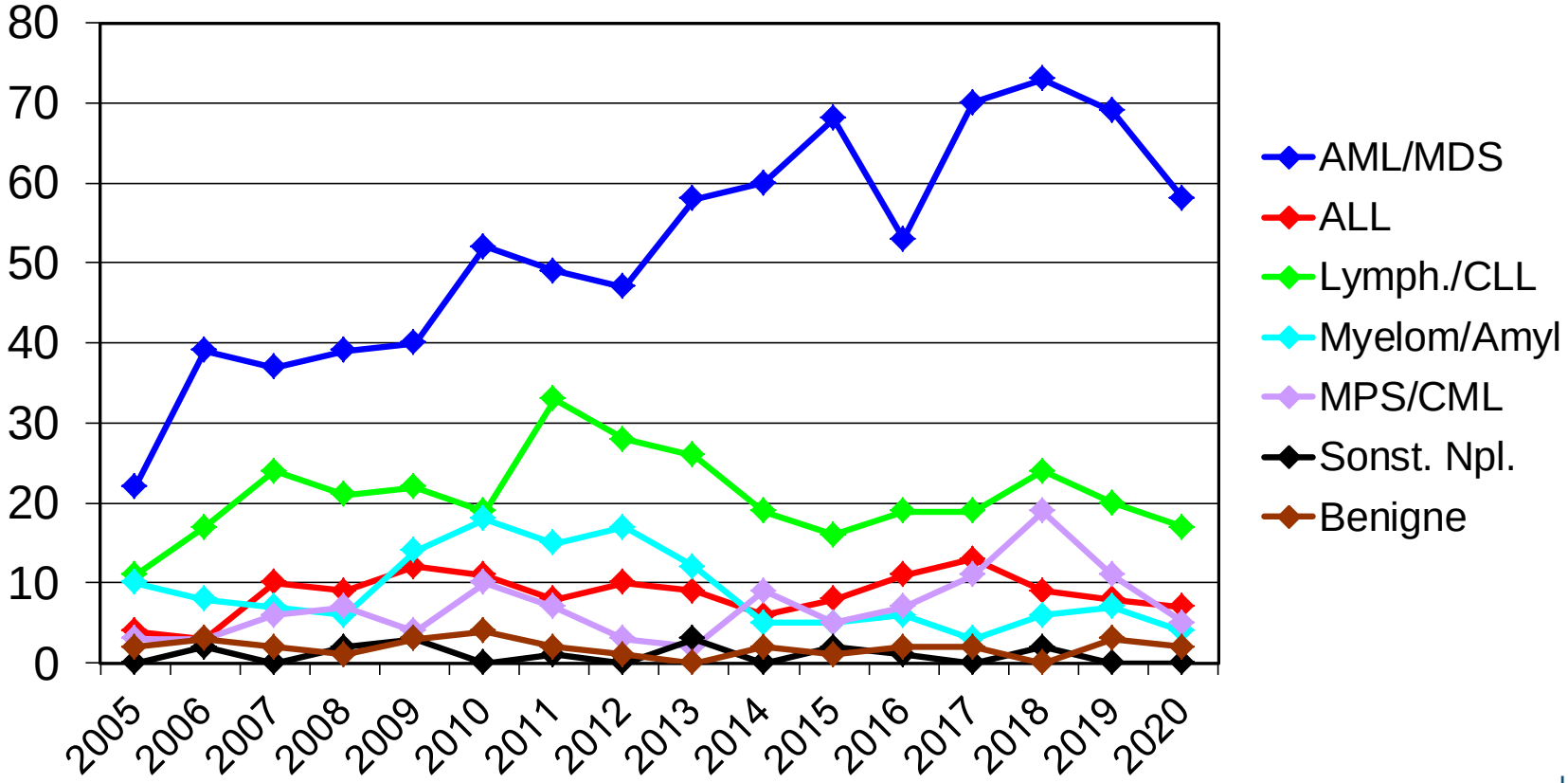
Kim Orchard
Chair, JACIE Accreditation Committee

CERTIFICATE NUMBER:	DATE OF ISSUE:	DATE OF EXPIRY:
891	23/06/2020	22/06/20204

Issued by the JACIE Accreditation Office, Barcelona, Spain

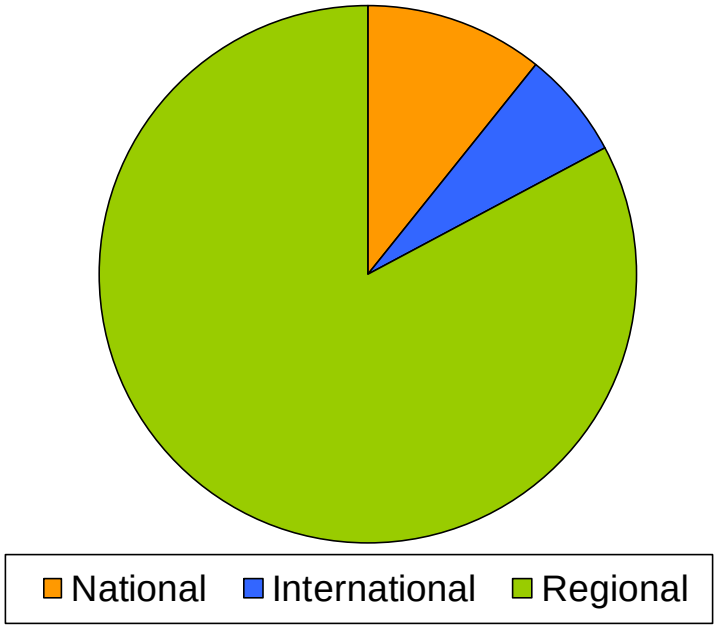
Kennzahlen alloHCT

Indikationen

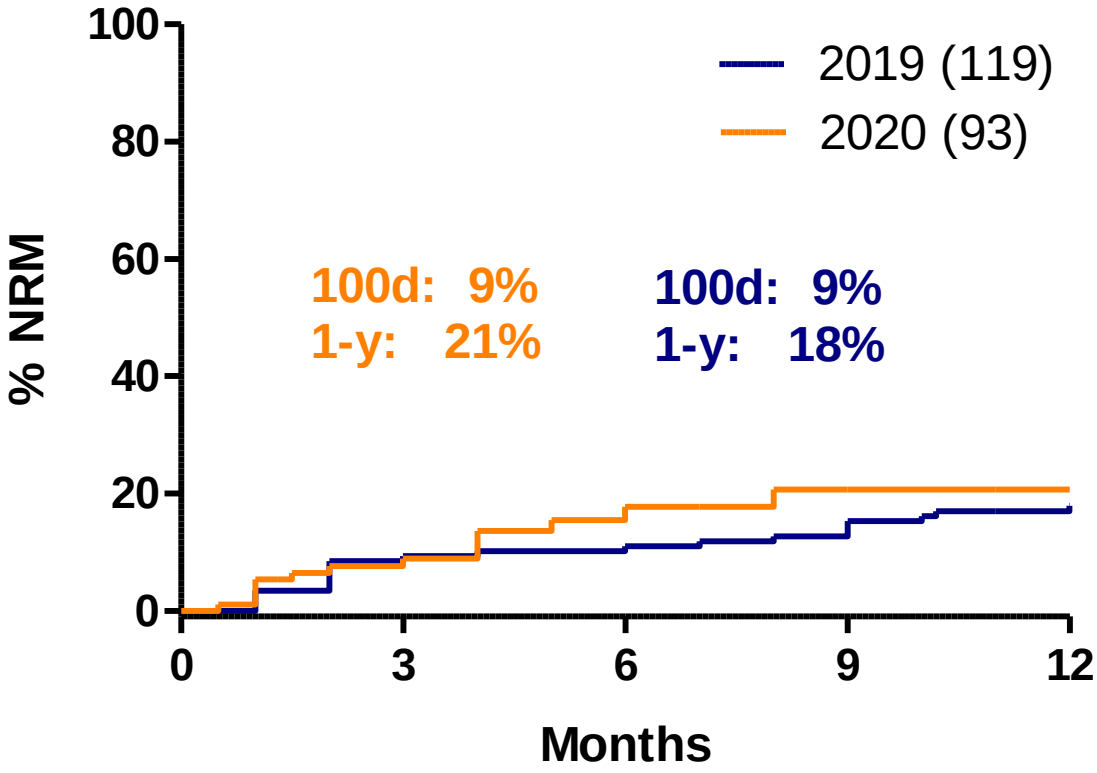


Zuweiser 2020 (alloHCT)

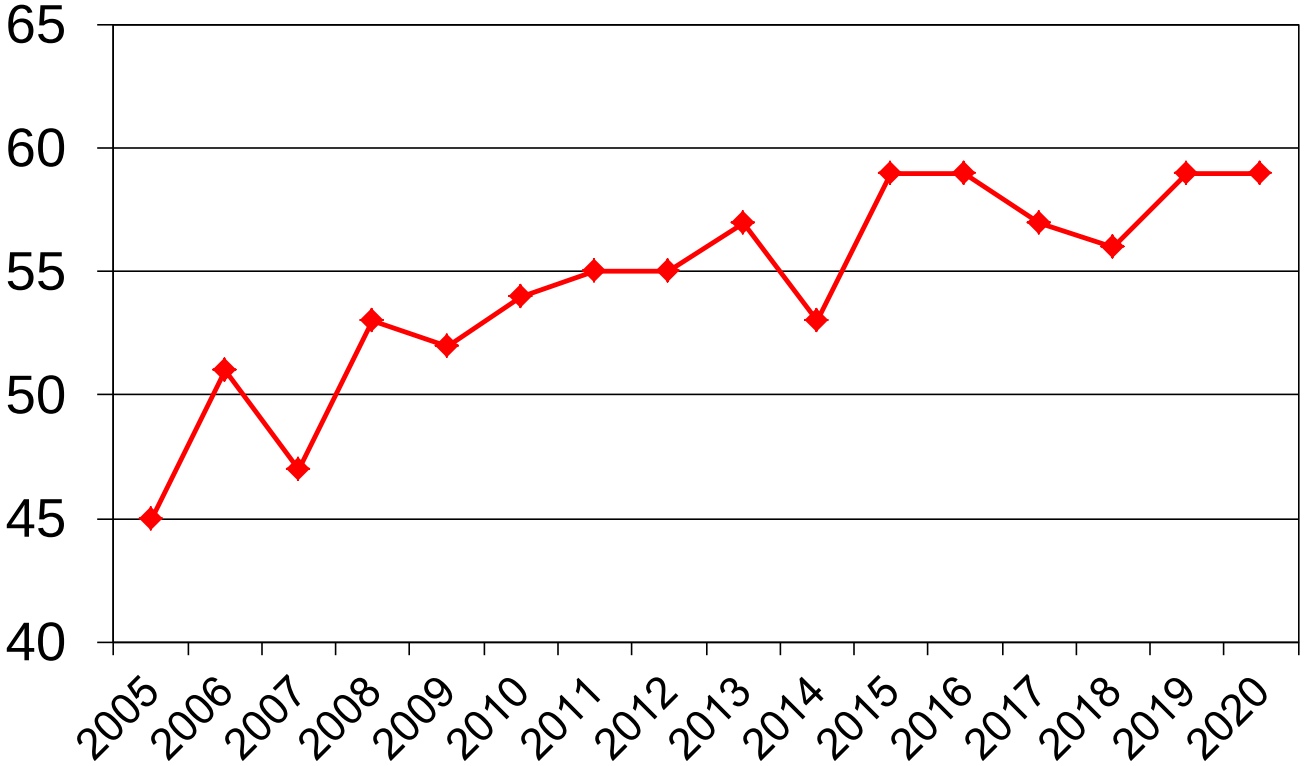
Insgesamt (Transplantierte)



Non-relapse mortality by period



Medianes Patientenalter



2020:

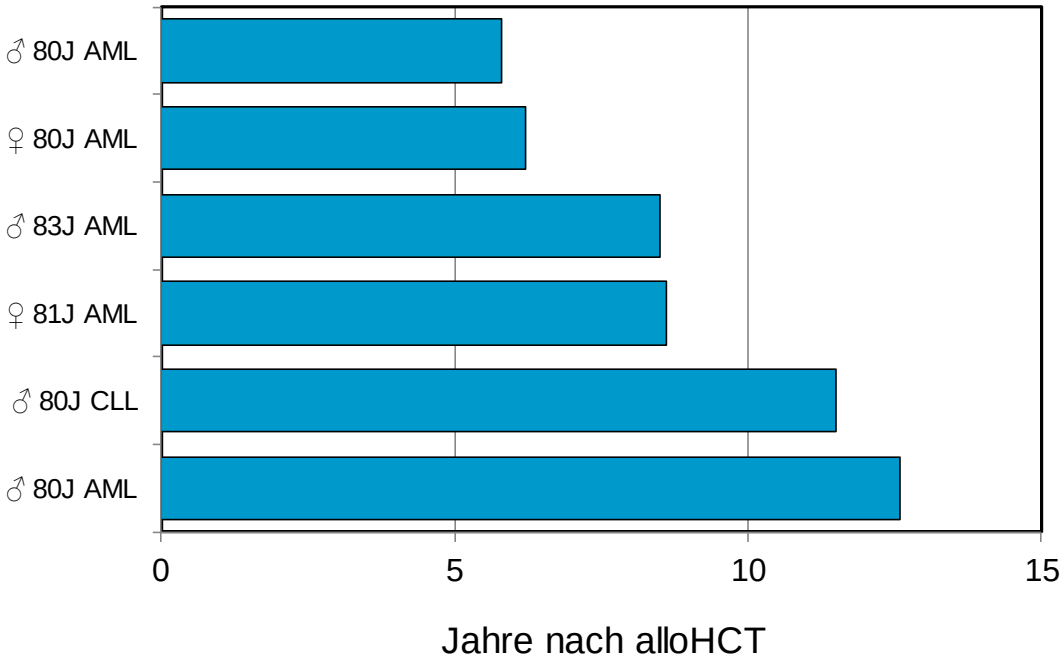
Median: 59J

Range: 7-76

IQR: 47-64

≥70J: 10 Pt. (11%)

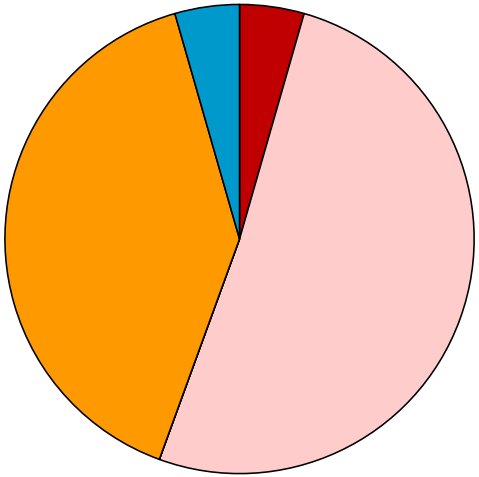
80 ist möglich…

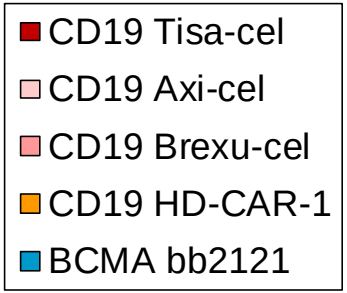


Kennzahlen CARTs

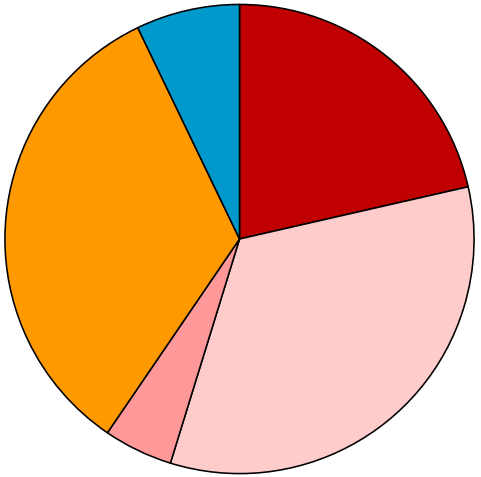
Verwendete CARTs (2018-2020)

2018-2019 (n=45)

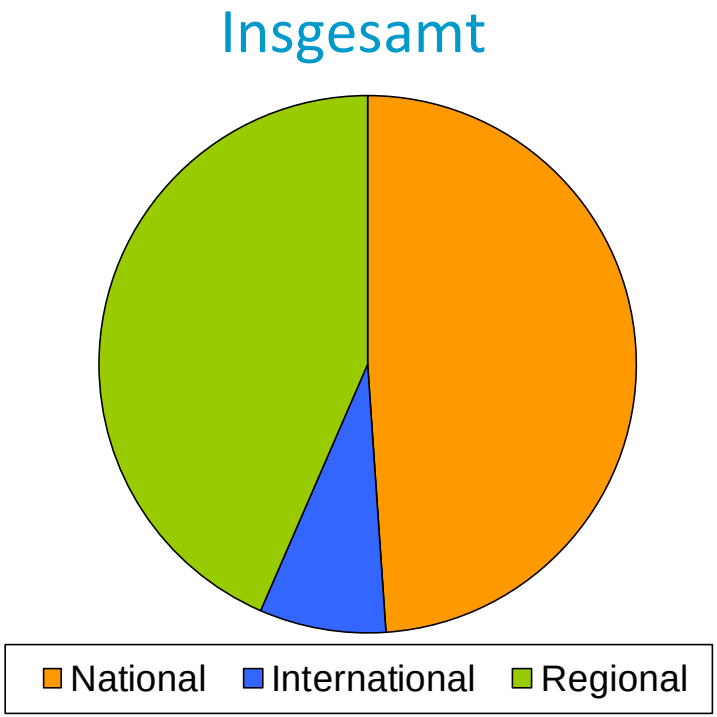




2020-2021 (n=41)



Zuweiser CARTs (2018-2020)



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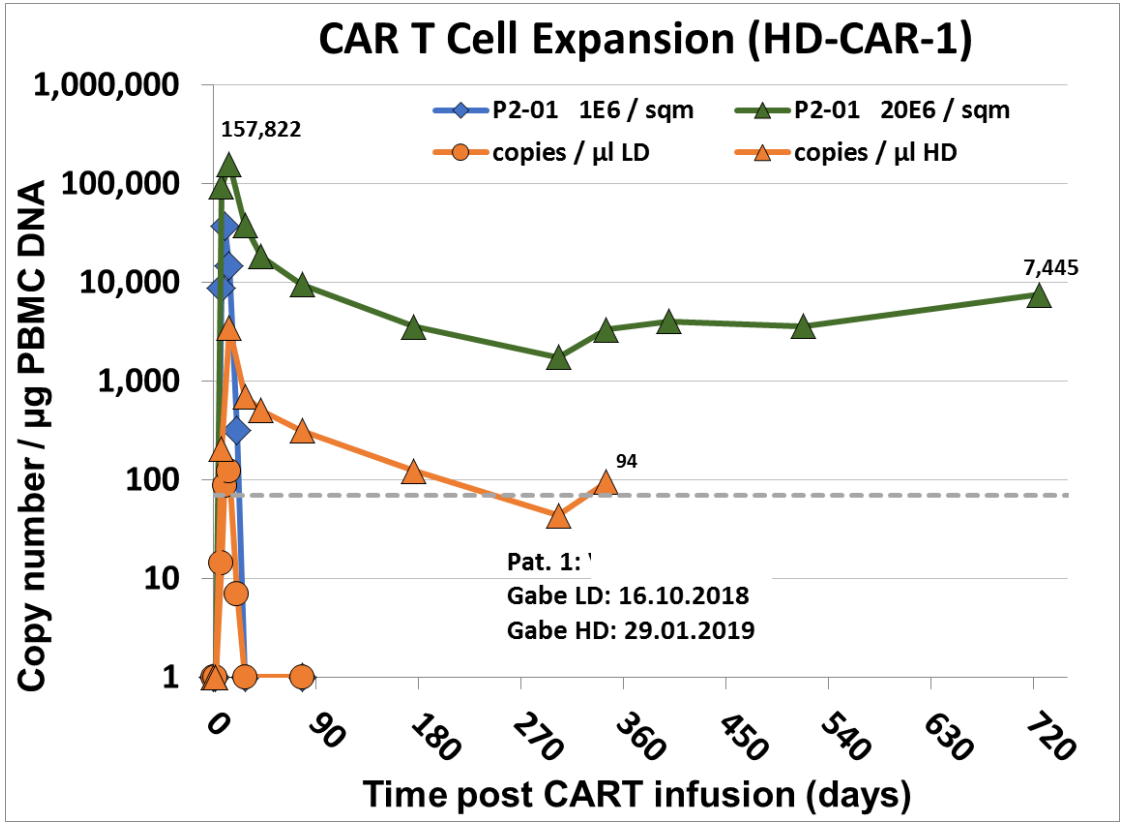
CLINICAL TRIAL PROTOCOL

[3G-CART therapy for CD19+ lymphoid disease]

EudraCT No. 2016-004808-60

[V02 D01 /Date 2018-02-16]

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


CAR T Cell Expansion (HD-CAR-1)
1,000,000
100,000
10,000
1,000
100
10
1
Copy number / µg PBMC DNA
P2-01 1E6 / sqm
P2-01 20E6 / sqm
copies / µl LD
copies / µl HD
157,822
7,445
94
Pat. 1:
Gabe LD: 16.10.2018
Gabe HD: 29.01.2019
0
90
180
270
360
450
540
630
720
Time post CART infusion (days)

HD-CAR-1: Safety & response

#	Age	Diagnosis	treatment prior CARTs	Dose level	°3-4 CRS	°3-4 ICANS	Best response
1	72	MCL	2xalloSCT, autoSCT, R-CHOP, R-DHAP, Ibr, R	I	-	-	PR
10	59	MCL	R-DHAP, R, Ibr, R.BEAM, alloSCT, RT	III	-	-	CR
16	63	MCL	R-CHOP, R-DHAP, autoSCT, Ibr, R^2	III	-	-	CR
15	48	FL	CHOP, Inf, DHAP, R-Benda, R-ICE, Ide	III	-	-	PR
2	56	CLL	FC, R-Benda, DHAP, R, Ibr, Ide, Rev, Ofa, Vclx	I	-	-	SD
8	61	CLL	FCR, BR, R, Alemtuz, alloSCT, Ibr, Vclx	II	+	-	SD
3	73	tFL/DLBCL	RT, R, R-Benda, R-DAEPOCH, Ibr, Ide, Obi, Rev	I	-	-	PR
5	53	tFL/DLBCL	Obi-Ibr, R-CHOP, R-DHAP, autoSCT, R-ICE	II	-	-	PD
6	44	DLBCL	R-CHOP, Rev, Vclx	II	-	-	PD
11	59	tFL/DLBCL	R-Benda, R, ABVD, RT, DHAP, autoSCT, Ide	III	-	-	SD
4	32	ALL	2x alloSCT, Blina, Tki^{I,D,N}	I	-	-	CR§
7	21	ALL	alloSCT, Blina, Ino	I	-	-	CR
9	67	ALL	Ino	I	-	-	PD
12	32	ALL	alloSCT	II	-	-	CR§
13	63	ALL	alloSCT, Blina	II	-	-	CR§
14	28	ALL	alloSCT, Tki ^{I,D,P}	II	-	-	CR§
17	67	ALL	Tki ^{I,P}, alloSCT	III	-	-	CR§
18	36	ALL	Ino, Blina; high tumor burden	III	+	-	PD
19	45	ALL	Tki ^{I,D,P}, alloSCT	III	-	-	CR§
20	47	ALL	alloSCT, Ino	III	-	-	CR

Responses

Overall (n = 20)	
ORR	65 %
CR	50%

ALL (n = 10)	
ORR	80%
CR	80%
MRD-	60%

NHL (n = 10)	
MCL/FL	100%
CLL	0%
DLBCL	25%

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2 Jahre zugelassene CARTs in Heidelberg – Ergebnisse 05.02.2021

4th CELL THERAPY SYMPOSIUM

November 6 & 7, 2020

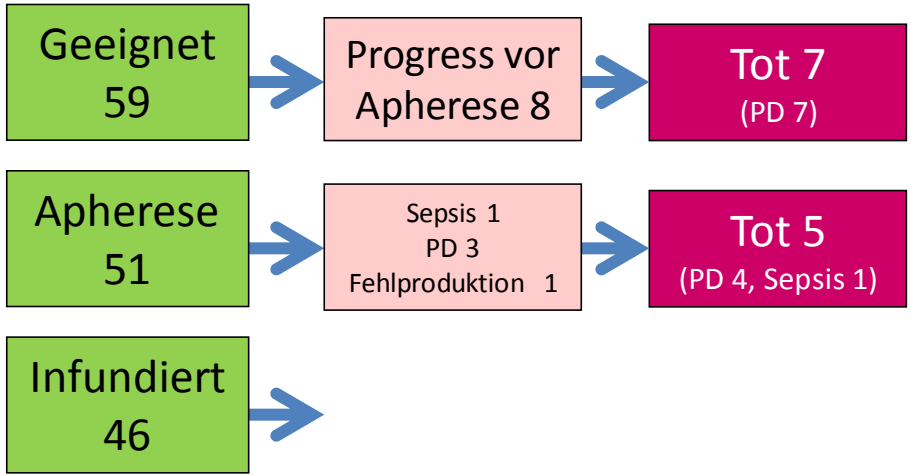
Prof. Dr. Peter Dreger

Innere Medizin V

Universitätsklinikum Heidelberg

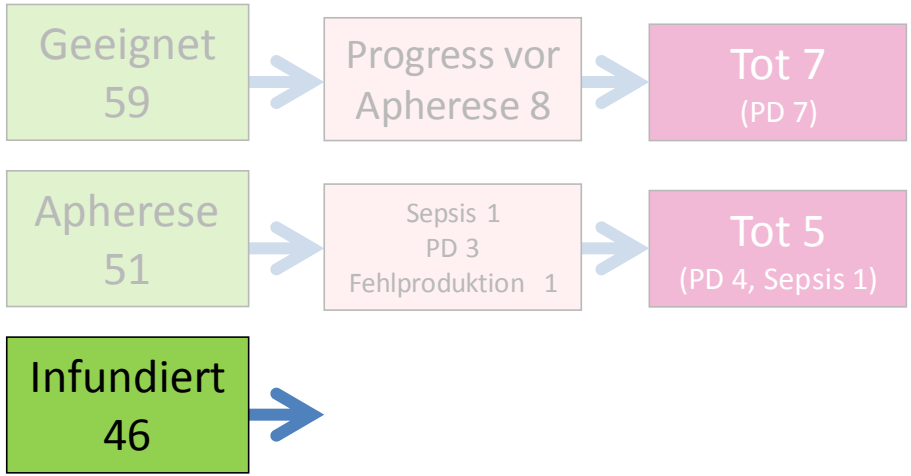
UK HD

Infundierte Patienten: Charakteristika



Feb 5, 2021	HD SOC CARTs
N dosed	46
Axi-cel / Tisa-cel	34 / 12
Age, years	57 (20-76)
ECOG >1 at LD	3 (7%)
Prior lines	3 (2-9)
Prior HSCT	27%
Bulk >10cm	17%
Bridging	70%
ZUMA-1 ineligible	59%
Refractory at LD	83%
LDH >N at lympodepletion	43%

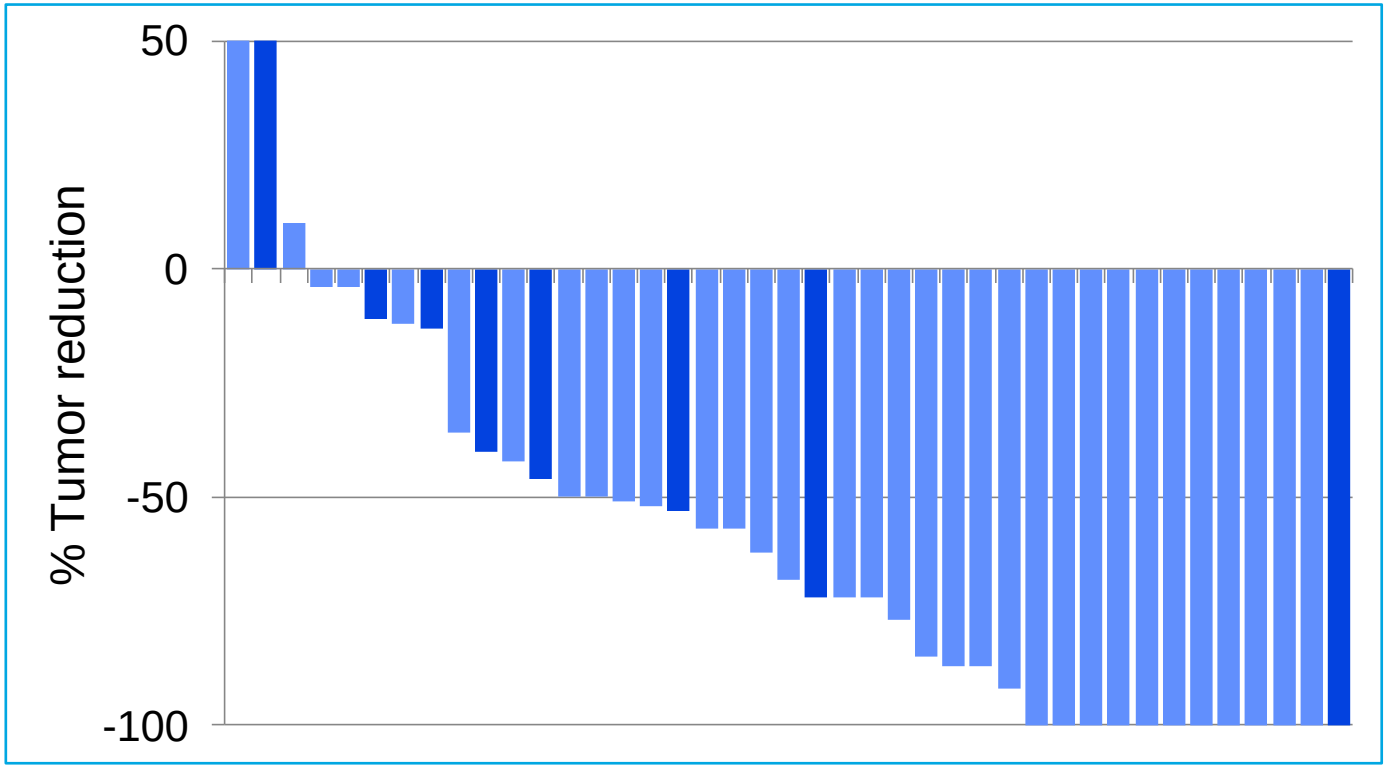
Infundierte Patienten: Frühtoxizität

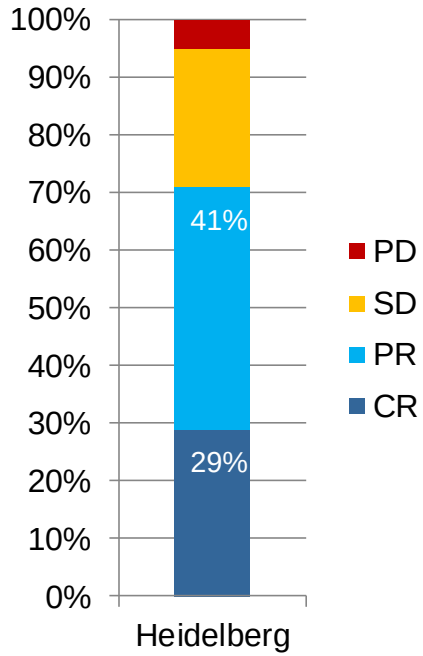


Feb 5, 2021	HD SOC CARTs
n	46
CRS (grade ≥ 3)	68% (3%)
Neurotox (grade ≥ 3)	44% (19%)
Days WBC >1.0/nl	10 (0-48)
Infections grade ≥ 3	12%
Grade 5 AEs	2
Hospitalization (d)	14 (9-69)

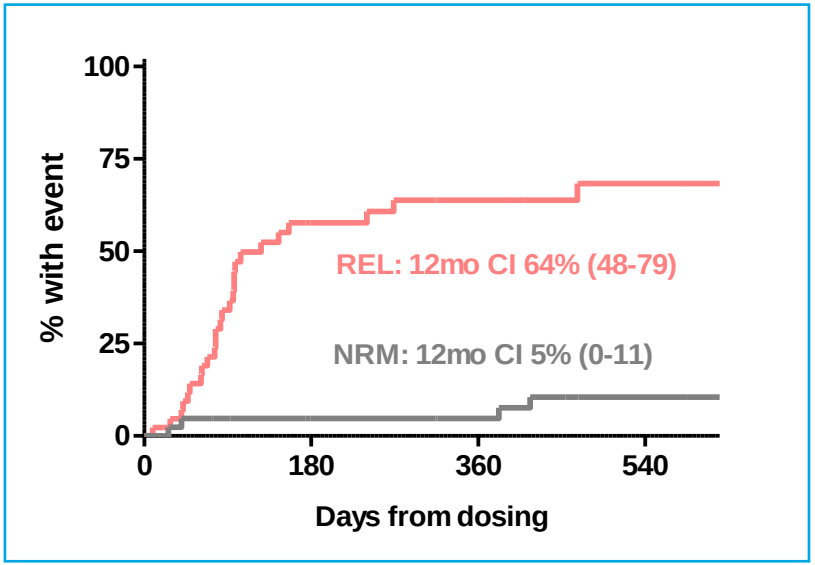
- **G3 Sepsis**
- **G3 Pneumonia**
- **G4 Peritonitis**
- **G5 Aspergillosis**
- **G5 Sepsis**

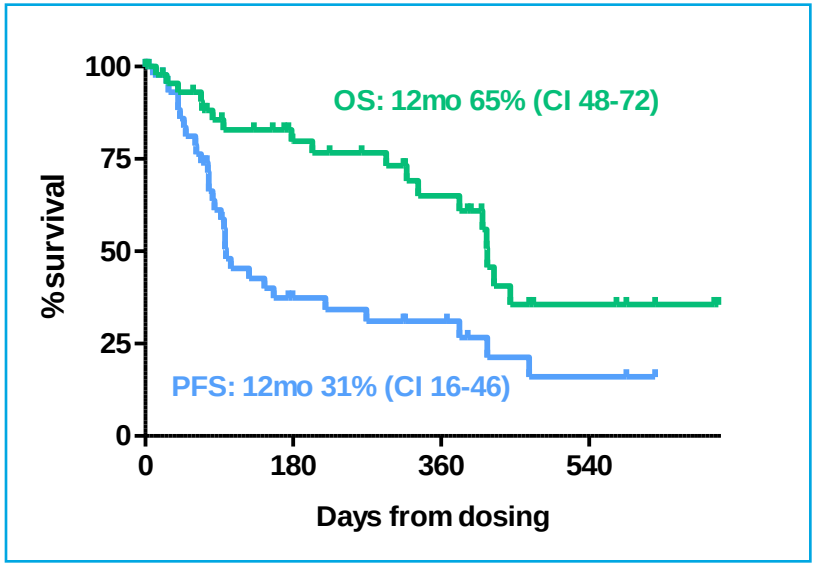
Heidelberg CAR T SOC: Best Response





Heidelberg CAR T SOC: Outcome





Output Wissenschaft

Biol Blood Marrow Transplant 26 (2020) e77–e85

Biology of Blood and Marrow Transplantation

journal homepage: www.bbmt.org

Review

Cellular Immunotherapy for Refractory Diffuse Large B Cell Lymphoma in the Chimeric Antigen Receptor-Engineered T Cell Era: Still a Role for Allogeneic Transplantation?

Peter Dreger[1,*], Timothy S. Fenske[2], Silvia Montoto[3], Marcelo C. Pasquini[4], Anna Sureda[5], Mehdi Hamadani[4], on behalf of the European Society for Blood and Marrow Transplantation (EBMT) and the Center for International Blood and Marrow Transplant Research (CIBMTR)

Biology of Blood and Marrow Transplantation

journal homepage: www.bbmt.org

Feasibility and Safety of CD19 Chimeric Antigen Receptor T Cell Treatment for B Cell Lymphoma Relapse after Allogeneic Hematopoietic Stem Cell Transplantation

Maria-Luisa Schubert[1,*], Sascha Dietrich[1,5], Stephan Stilgenbauer[2,3], Anita Schmitt[1], Petra Pavel[6], Alexander Kunz[1], Andrea Bondong[1], Mandy Wegner[1], Peter Stadtherr[1], Susanne Jung[4], Anthony D. Ho[1,5], Carsten Müller-Tidow[1,5], Michael Schmitt[1,5], Peter Dreger[1,5]

cancers

MDPI

Brief Report

Assessment of CAR T Cell Frequencies in Axicabtagene Ciloleucel and Tisagenlecleucel Patients Using Duplex Quantitative PCR

Maria-Luisa Schubert [1,†], Alexander Kunz [1,†], Anita Schmitt [1], Brigitte Neuber [1], Lei Wang [1], Angela Hückelhoven-Krauss [1], Sascha Langner [1], Birgit Michels [1], Antje Wick [2], Volker Daniel [3], Carsten Müller-Tidow [1,4], Peter Dreger [1,4] and Michael Schmitt [1,4,*]

REGULAR ARTICLE

blood advances

CAR T cells or allogeneic transplantation as standard of care for advanced large B-cell lymphoma: an intent-to-treat comparison

Peter Dreger,[1] Sascha Dietrich,[1] Maria-Luisa Schubert,[1] Lorenz Selberg,[1] Andrea Bondong,[1] Mandy Wegner,[1] Peter Stadtherr,[1] Christoph Kimmich,[1] Florentina Kosely,[1] Anita Schmitt,[1] Petra Pavel,[2] Nora Liebers,[1] Thomas Luft,[1] Ute Hegenbart,[1] Aleksandar Radujkovic,[1] Anthony Dick Ho,[1] Carsten Müller-Tidow,[1] and Michael Schmitt[1]

[1]Department of Medicine V, University of Heidelberg, Heidelberg, Germany; and [2]Institute for Clinical Transfusion Medicine and Cell Therapy, Heidelberg, Germany

ESMO GOOD SCIENCE BETTER MEDICINE BEST PRACTICE

ANNALS OF ONCOLOGY driving innovation in oncology

REVIEW

Side-effect management of chimeric antigen receptor (CAR) T-cell therapy

M.-L. Schubert[1*], M. Schmitt[1,2], L. Wang[1], C. A. Ramos[3], K. Jordan[1], C. Müller-Tidow[1,2] & P. Dreger[1,2]

[1]Department of Medicine V, University Hospital Heidelberg, Heidelberg; [2]National Centre for Tumor Diseases (NCT), Heidelberg, Germany; [3]Center for Cell Gene Therapy, Baylor College of Medicine, Texas Children's Hospital and Houston Methodist Hospital, Houston, Texas, USA

CHECK FOR UPDATES

Available online 21 October 2020

Chimeric antigen receptor (CAR) T cells directed against the B-cell marker CD19 are currently changing the landscape for treatment of patients with refractory and/or relapsed B-cell malignancies. Due to the nature of CAR T cells as living drugs, they display a unique toxicity profile. As CAR T-cell therapy is extending towards other diseases and being more broadly employed in hematology and oncology, optimal management strategies of side-effects associated with CAR T-cell therapy are of high relevance. Cytokine release syndrome (CRS), immune effector cell-associated neurotoxicity syndrome (ICANS), and cytopenias constitute challenges in the treatment of patients with CAR T cells. This review summarizes the current understanding of CAR T-cell toxicity and its management.

EBMT virtual 47th Annual Meeting of the EBMT 14-17 March 2021 #EBMT21

AA2-2
Mar 16
17:30

Jian-Jian Luan Award for best Lymphoma Research abstract

Standard-of-care CAR-T cell therapy for large B-cell lymphoma: Real World Data Germany

Bethge WA, Ayuk F, Holtick U, Wagner E, Wulf G, Penack O, Bonin M, von Tresckow B, Stelljes M, Baldus C, Vucinic V, Mougiakakos D, Topp M, Schroers R, Beelen DW & Dreger P. on behalf of the German Lymphoma Alliance (GLA) and the German Stem Cell Transplantation Registry (DRST)

Jian-Jian Luan † 2011

Ferrata Storti Foundation

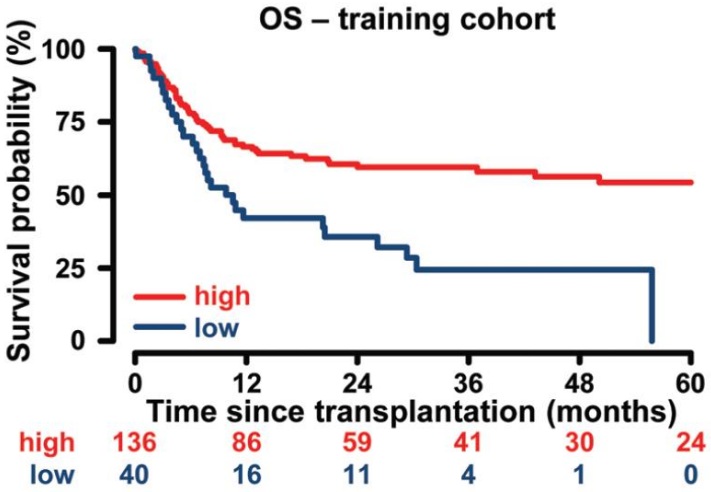
Pre-transplant testosterone and outcome of men after allogeneic stem cell transplantation

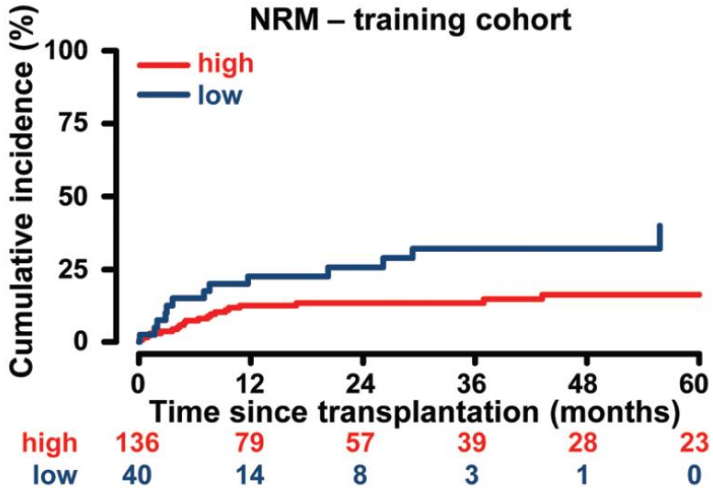
Aleksandar Radujkovic,[1] Lambros Kordelas,[2] Julia Krzykalla,[3] Axel Benner,[3] David Schult,[1] Joshua Majer-Lauterbach,[1] Dietrich W. Beelen,[2] Carsten Müller-Tidow,[1] Christian Kasperk,[4] Peter Dreger[1] and Thomas Luft[1]

[1]Department of Internal Medicine V, University of Heidelberg, Heidelberg; [2]Department of Bone Marrow Transplantation, University Hospital, Essen; [3]Division of Biostatistics, German Cancer Research Center, Heidelberg and [4]Department of Internal Medicine I, University of Heidelberg, Heidelberg, Germany

Haematologica 2020

N=136/141; nur Männer; nur AML





Publikationen alloHCT 2020 (n=24)

Med V - interne Forschungsförderung: Sektion Stammzelltransplantation (ohne AG Schmitt)

Jahr	Titel	Veröffentlicht in	Gruppe	Journal Impact Faktor 2019	ultiplika	Publikationspunkte	Autor Med V
2020	Clinical Response to the CD95-Ligand Inhibitor Asunercept Is Defined by a Pr	Cancers	Erst-/Letztautorenschaft	**6,13**	10	61,26	**Radujkovic, Luft**
2020	CAR T cells or allogeneic transplantation as standard of care for advanced la	Blood Adv	Erst-/Letztautorenschaft	**4,91**	10	49,10	**Dreger, Schmitt**
2020	Letermovir prophylaxis is effective in preventing cytomegalovirus reactivatio	Annal of Hematology	Erst-/Letztautorenschaft	**2,90**	10	29,04	**Derigs, Schmitt**
2020	Haematopoietic stem cell transplantation in adult soft-tissue sarcoma: an ar	ESMO Open	Erstautorenschaft	**5,33**	8	42,63	**Heilig**
2020	Side-effect management of chimeric antigen receptor (CAR) T-cell therapy	Annals of Oncology	Erst-/Letztautorenschaft (Review)	**18,27**	0	0,00	**Schubert, Dreger**
2020	Interleukin-18 and Hematopoietic Recovery after Allogeneic Stem Cell Transp	Cancers	Erst-/Letztautorenschaft	**6,13**	10	61,26	**Radujkovic, Luft**
2020	Idelalisib treatment prior to allogeneic stem cell transplantation for patients	Bone Marrow Transplant	Letztautorenschaft	**4,73**	8	37,80	**Dreger**
2020	Evaluation of six different types of sequential conditioning regimens for allo	Leuk Lymphoma	Koautorenschaft	**2,76**	1	2,76	**Dreger**
2020	Allogeneic stem cell transplantation for chronic lymphocytic leukemia in the	Blood Adv	Zweitautorenschaft	**4,91**	3	14,73	**Dreger**
2020	Association of Country-Specific Socioeconomic Factors With Survival of Patie	Front Immunol	Koautorenschaft	**4,53**	1	4,53	**Dreger**
2020	Allogeneic hematopoietic cell transplantation for patients with TP53 mutant	Bone Marrow Transplant	Letztautorenschaft	**4,73**	8	37,80	**Dreger**
2020	The impact of allogeneic hematopoietic cell transplantation on the mortality	Bone Marrow Transplant	Erst-/Letztautorenschaft	**4,73**	10	47,25	**Selberg, Dreger**
2020	Idelalisib exposure before allogeneic stem cell transplantation in patients wi	Bone Marrow Transplant	Erst-/Letztautorenschaft	**4,73**	10	47,25	**Sellner, Dreger**
2020	Feasibility and safety of CD19 CAR T cell treatment for B-cell lymphoma relap	Biol Blood Marrow Transplant	Erst-/Letztautorenschaft	**3,85**	10	38,53	**Schubert, Dreger**
2020	Influence of donor type, stem cell source and conditioning on outcomes afte	Brit J Haematol	Koautorenschaft	**5,52**	1	5,52	**Dreger**
2020	Pre-transplant testosterone and outcome of men after allogeneic stem cell t	Haematologica	Erst-/Letztautorenschaft	**7,12**	10	75,70	**Radujkovic, Luft**
2020	Determinants of survival in myelofibrosis patients undergoing allogeneic her	Leukemia	Koautorenschaft	**8,67**	1	8,67	**Dreger**
2020	A randomized phase 3 trial of auto vs allo transplantation as part of first-line	Blood	Koautorenschaft	**17,54**	1	17,54	**Dreger**
2020	Long-term survival benefit after allogeneic hematopoietic cell transplantatio	Biol Blood Marrow Transplant	Koautorenschaft	**3,85**	1	3,85	**Radujkovic, Luft**
2020	Outcome of allogeneic haematopoietic stem cell transplantation in myeloprc	Brit J Haematol	Koautorenschaft	**5,52**	1	5,52	**Radujkovic**
2020	High leukemia-free survival after TBI-based conditioning and mycophenolate	Annal of Hematology	Erst-/Letztautorenschaft	**2,90**	10	29,04	**Radujkovic, Luft**
2020	Predicting sinusoidal obstruction syndrome after allogeneic stem cell transpl	Haematologica	Letztautorenschaft	**7,57**	8	60,56	**Luft**
2020	CXCL9 predicts Severity at Onset of Chronic Graft-Versus-Host Disease.	Transplantation	Erst-/Letztautorenschaft	**4,74**	10	47,40	**Giesen/Luft**
2020	Cellular immunotherapy for refractory DLBCL in the CART era: still a role for	Biol Blood Marrow Transplant	Erstautorenschaft (Konsensus)	**3,60**	0	0,00	**Dreger**
				145,64		727,74	

Zusätzliche Publikationen der AG Schmitt 2020

(n=7)

Med V - interne Forschungsförderung: weitere Papers der AG Schmitt

Jahr	Titel	Veröffentlicht in	Gruppe	Journal Impact Faktor 2019	ultiplikat	Publikationspunkte	Autor Med V
2020	Mortality Analysis of Letermovir Prophylaxis for Cytomegalovirus (CMV) in CM	Clin Inf Dis	Zweitautorenschaft	**8,31**	3	24,94	**Schmitt M**
2020	Phase-I trial of donor-derived modified immune cell infusion in kidney transpla	J Clin Invest	Erstautorenschaft	**11,86**	8	94,91	**Schmitt A & M**
2020	Optimized Assessment of qPCR-Based Vector Copy Numbers as a Safety Param	Mol Ther Meth Clin Dev	Erst-/Letztautorenschaft	**4,53**	10	45,33	**Kunz, Schubert**
2020	Comments on "Cost of decentralized CAR T cell production in an academic nor	Int J Cancer	Erst-/Letztautorenschaft (Komment	**5,15**	0	0,00	**Schmitt M, Müller-Tidow**
2020	Pre-sensitization of Malignant B Cells Through Venetoclax Significantly Improv	Front Immunol	Erst-/Letztautorenschaft	**4,53**	10	45,30	**Yang, Schmitt A**
2020	Assessment of CAR T Cell Frequencies in Axicabtagene Ciloleucel and Tisagenle	Cancers	Erst-/Letztautorenschaft	**6,13**	10	61,26	**Schubert, Schmitt M**
2020	B-cell maturation antigen-specific chimeric antigen receptor T cells for multipl	Int J Cancer	Erst-/Letztautorenschaft (Review)	**5,15**	0	0,00	**Sellner, Schmitt M**
				45,66		271,74	

Danke!

„von Dusch“
M Lommatzsch
A Dugimont
...und das Team!

Station
T Liebregts
E Mai
K Ristoski
K Braunauer
H Hennemann
N Hohmann
F Korell
T Roider
J Schnorbach
M Singh
A Martin

JACIE
B Beck
& Team

Koordination
P Stadtherr
I Opitz

Ambulanz
U Hegenbart
S Schönland
A Radujkovic
C Pabst
ML Schubert
L Simons
B Beck
T Feisthammel

CART
M Schmitt
A Schmitt
ML Schubert

ECP
A Schmitt
R Alexi
& Team

Case Manager & CART
A Bondong
M Wegner

Labor
T Luft
M Hess
A Radujkovic

EBMT-Reporting
M Fischer

Psychologie
D Tönnessen

Sucheinheit
H Tran
K Nerbel
& Team

Sozialdienst
A Bergner
G Daiß
S Sontowski

Studienzentrale
J Klemmer
& Team

I.O. und andere Affairs
M Geiss
N Giesen

Anleitung
T Luft
P Dreger

Klinikleitung
K Jordan
C Müller-Tidow