






Stammzelltransplantation  
und CAR-T Zelltherapie

## Patienten- und Angehörigentag im USB

Samstag, 4. Oktober 2025,  
9.30–16.30 Uhr

Zentrum für Lehre und Forschung (ZLF)  
Hebelstrasse 20  
4031 Basel



## Programm Patienten- und Angehörigentag

|                 |                                                                                                                                                                                                                                                                                                                                                                                                                      |                                                                                                                 |
|-----------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------|
| 9.30 Uhr        | Begrüssung durch Jakob Passweg, Hämatologie USB                                                                                                                                                                                                                                                                                                                                                                      |                                                                                                                 |
| 9.35–10.20 Uhr  | <b>Blutstammzelltransplantation</b><br>Vom Abenteuer gestern bis zur hochspezialisierten Medizin heute                                                                                                                                                                                                                                                                                                               | Jakob Passweg<br>Hämatologie USB                                                                                |
| 10.25–11.10 Uhr | <b>Wechselwirkung Microbiom-Immunsystem</b><br>Die Mikroben auf und in uns und was sie für unsere Gesundheit bedeuten                                                                                                                                                                                                                                                                                                | Pauline Göller<br>Institut für medizinische Mikrobiologie, Universität Zürich                                   |
| 11.10–11.30 Uhr | Pause                                                                                                                                                                                                                                                                                                                                                                                                                |                                                                                                                 |
| 11.30–12.00 Uhr | <b>Neue Impfungen</b>                                                                                                                                                                                                                                                                                                                                                                                                | Veronika Bättig<br>Marcel Stöckle<br>Infektiologie USB                                                          |
| 12.00–13.00 Uhr | Mittagessen                                                                                                                                                                                                                                                                                                                                                                                                          |                                                                                                                 |
| 13.00–14.00 Uhr | <b>Leben nach der Transplantation – Herausforderungen</b><br>– Neurokognitive Defizite<br>– Umgang mit GvHD/Rezidiv: Bedürfnisse von An- und Zugehörigen<br>– Round table mit Patient*innen, Angehörigen und Behandlungsteam                                                                                                                                                                                         | Birgit Maier<br>Malui Frei<br>Hämatologie/Psychosomatik USB im Gespräch mit:<br>Claude Cueni<br>Martina Schmidt |
| 14.15–15.00 Uhr | <b>Workshops: was ich immer schon wissen wollte – Fragen und Antworten</b><br>Parallelworkshops<br>– In den ersten 5 Jahren nach Transplantation<br>– Länger als 5 Jahre nach Transplantation<br>– CAR-T                                                                                                                                                                                                             | Jörg Halter<br>Anne Stelmes<br>Dominik Heim<br>Hämatologie USB                                                  |
| 15.00–16.30     | <b>«Marktplatz»</b><br>Sie flanieren zwischen verschiedenen Infoständen und lassen sich von Expert*innen aus den entsprechenden Fachgebieten beraten und in Gespräche ein zu Ernährung, Blutdruck und Cholesterin, Haut- und Augenpflege, Frauenmedizin, Reisen, Sport, Fatigue, Finanzen, beruflicher Wiedereinstieg, Pflege von Angehörigen, Spendernachsorge, Bedürfnisse von Patienten sowie An- und Zugehörigen |                                                                                                                 |

# IMMUNOLOGICAL RECONSTITUTION OF SEX-LINKED LYMPHOPENIC IMMUNOLOGICAL DEFICIENCY



RICHARD A. GATTI  
M.D. St. Louis  
RESEARCH FELLOW

HUGH D. ALLEN  
M.D. Cincinnati  
PEDIATRIC RESIDENT

HILAIRE J. MEUWISSEN  
M.D. Nymegen  
RESEARCH FELLOW

RICHARD HONG  
M.D. Illinois  
ASSOCIATE PROFESSOR

ROBERT A. GOOD

The infant who received the 1968 transplant grew up to healthy adulthood. He is reported to be alive and himself a father.

*Laboratories, University of Minnesota, Minneapolis, Minnesota  
55455*

Histocompatibility matching of peripheral leucocytes was performed between the patient and all members of his immediate family by lymphocytotoxic assay (Terasaki et al. 1967) and by the one-way mixed leucocyte-culture technique (Bach and Voynow 1966). An 8-year-old sister was indicated as the donor of choice. Although in the lymphocytotoxic assay her lymphocytes lacked one antigen present on the lymphocytes of the patient, when tested by mixed leucocyte culture her cells showed complete absence of response to the patient's cells (Meuwissen, Gatti, Terasaki, Hong, and Good 1968).

# GvHD - GvL

TRUCK

MORTIMER M. BORTIN

FIGURE 1. Reported human bone marrow transplants from 1958 to

TABLE 1. Results of 203 reported human bone marrow transplants

| Disease           | No. of patients | No. with no engraftment | No. with secondary disease | No. of allogeneic chimeras |
|-------------------|-----------------|-------------------------|----------------------------|----------------------------|
| Aplastic anemia   | 73              | 66                      | 5                          | 0                          |
| Leukemia          | 84              | 33                      | 32                         | 3                          |
| Malignant disease | 31              | 23                      | 1                          | 1                          |
| Immune deficiency | 15              | 3                       | 11                         | 7                          |
| Total             | 203             | 125                     | 49                         | 11 <sup>a</sup>            |

<sup>a</sup> Three alive at the time of this report.

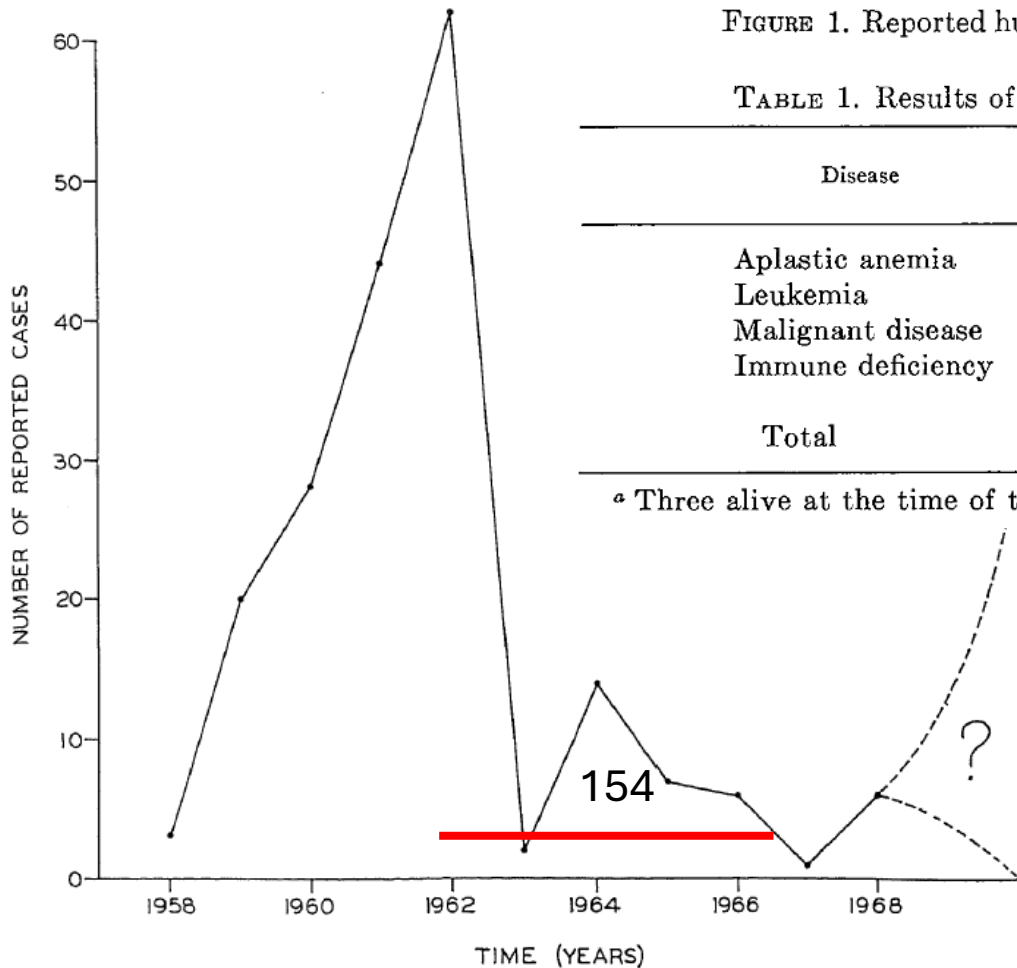
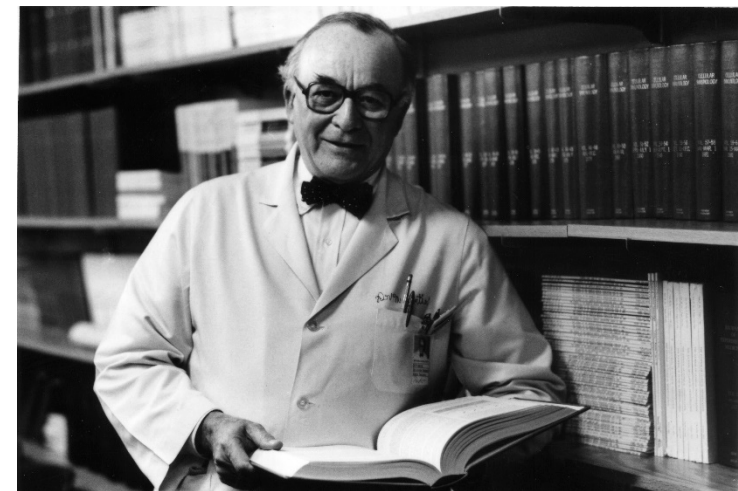


FIGURE 1. Reported human bone marrow transplants from 1958 to 1968.



# Where it all started

1174

THE NEW ENGLAND JOURNAL OF MEDICINE

Oct. 26, 1989

## MEDICAL INTELLIGENCE



### HEMATOPOIETIC RECONSTITUTION IN A PATIENT WITH FANCONI'S ANEMIA BY MEANS OF UMBILICAL-CORD BLOOD FROM AN HLA-IDENTICAL SIBLING

ELIANE GLUCKMAN, M.D.,  
HAL E. BROXMEYER, PH.D.,  
ARLEEN D. AUERBACH, PH.D.,  
HENRY S. FRIEDMAN, M.D.,  
GORDON W. DOUGLAS, M.D.,

AGNÈS DEVERGIE, M.D., HÉLÈNE ESPEROU, M.D.,  
DOMINIQUE THIERRY, PH.D., GÉRARD SOCIE, M.D.,  
PIERRE LEHN, M.D., SCOTT COOPER, B.S.,  
DENIS ENGLISH, PH.D., JOANNE KURTZBERG, M.D.

the patient. We used a pretransplantation conditioning procedure developed specifically for the treatment of such patients<sup>8</sup>; this technique makes use of the hypersensitivity of the abnormal cells to alkylating agents that cross-link DNA<sup>9,10</sup> and to irradiation.<sup>11</sup> In this case, the availability of cord blood obviated the need for obtaining bone marrow from the infant sibling.

This use of cord blood followed the suggestion of one of us that blood retrieved from umbilical cord at delivery, usually discarded, might restore hematopoiesis — a proposal supported by preparatory studies by some of us<sup>12</sup> and consistent with reports on the presence of hematopoietic stem and multipotential (CFU-GEMM), erythroid (CFU-E), and myelomonocyte-macrophage (CFU-GM) colonies in human umbilical-cord blood (see Broxmeyer et al.<sup>12</sup>).

#### CASE REPORT

The patient, a five-year-old boy, was born with Fanconi's anemia at 24 months of age. An evaluation (Cleveland Clinic Foundation Hematology Center) showed the following hematologic findings: hemoglobin concentration, 9.5 g per deciliter; white-cell count,  $4.3 \times 10^9$  per liter,

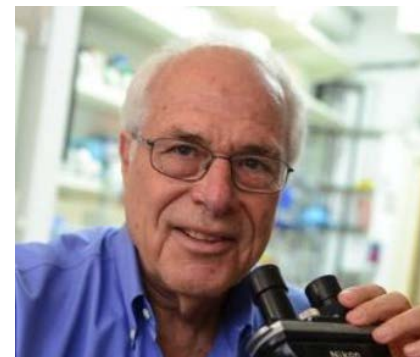


Review article

## Functional expression of chimeric receptor genes in human T cells

Zelig Eshhar\*, Tova Waks, Alain Bendavid, Daniel G. Schindler

*Department of Immunology, The Weizmann Institute of Science, Rehovot 76100, Israel*



The NEW ENGLAND JOURNAL of MEDICINE

### BRIEF REPORT

## Chimeric Antigen Receptor–Modified T Cells for Acute Lymphoid Leukemia

Stephan A. Grupp, M.D., Ph.D., Michael Kalos, Ph.D., David Barrett, M.D., Ph.D., Richard Aplenc, M.D., Ph.D., David L. Porter, M.D., Susan R. Rheingold, M.D., David T. Teachey, M.D., Anne Chew, Ph.D., Bernd Hauck, Ph.D., J. Fr

), Ph.D.,  
1.D.



2001



2013



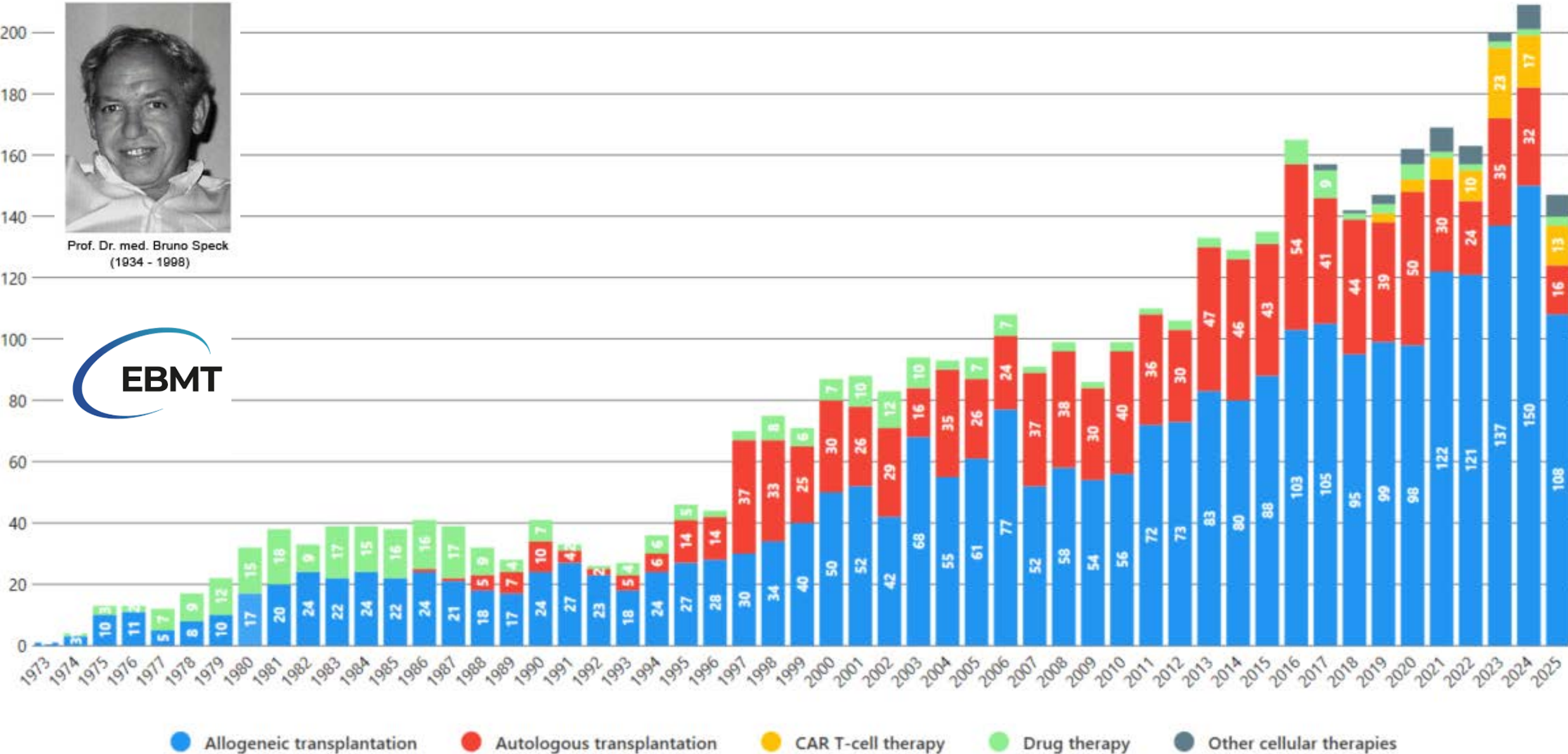
2018



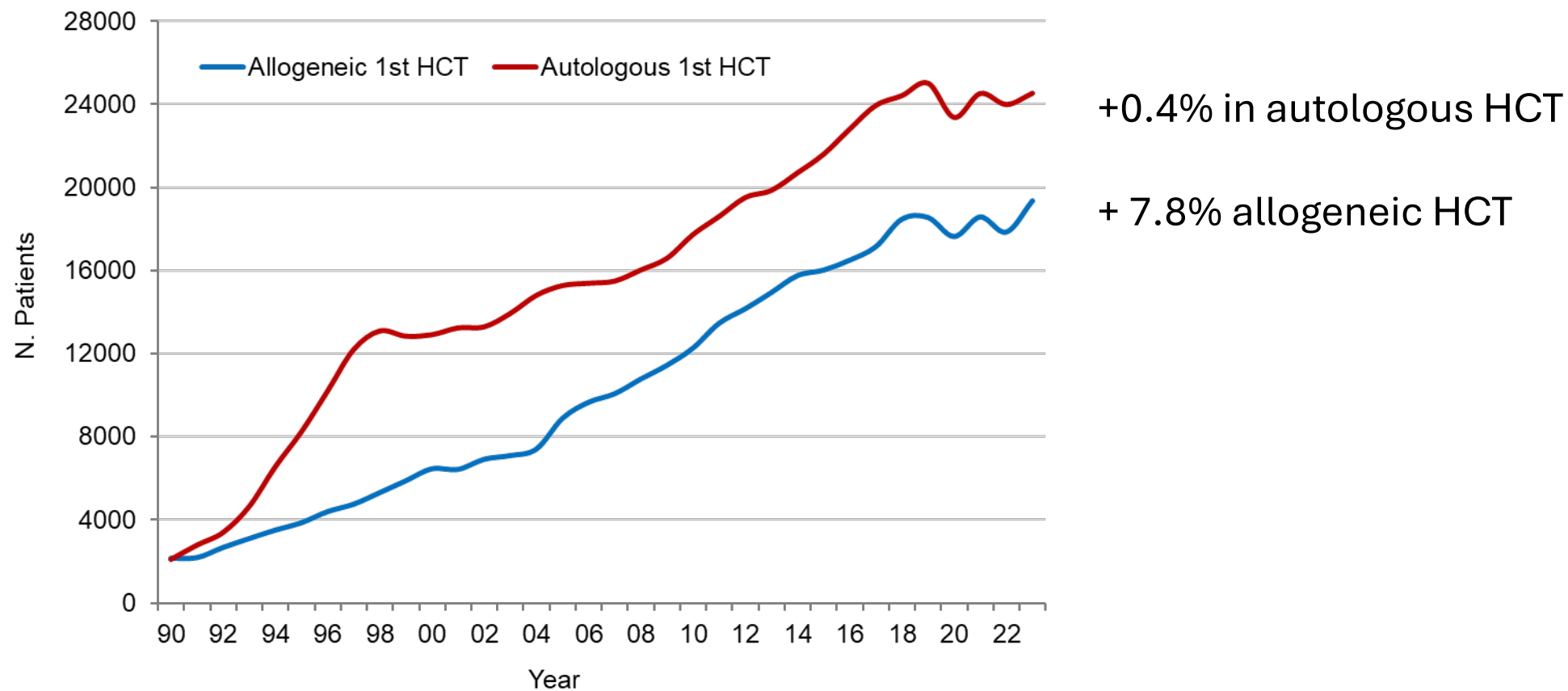
Treatments per year



Prof. Dr. med. Bruno Speck  
(1934 - 1998)



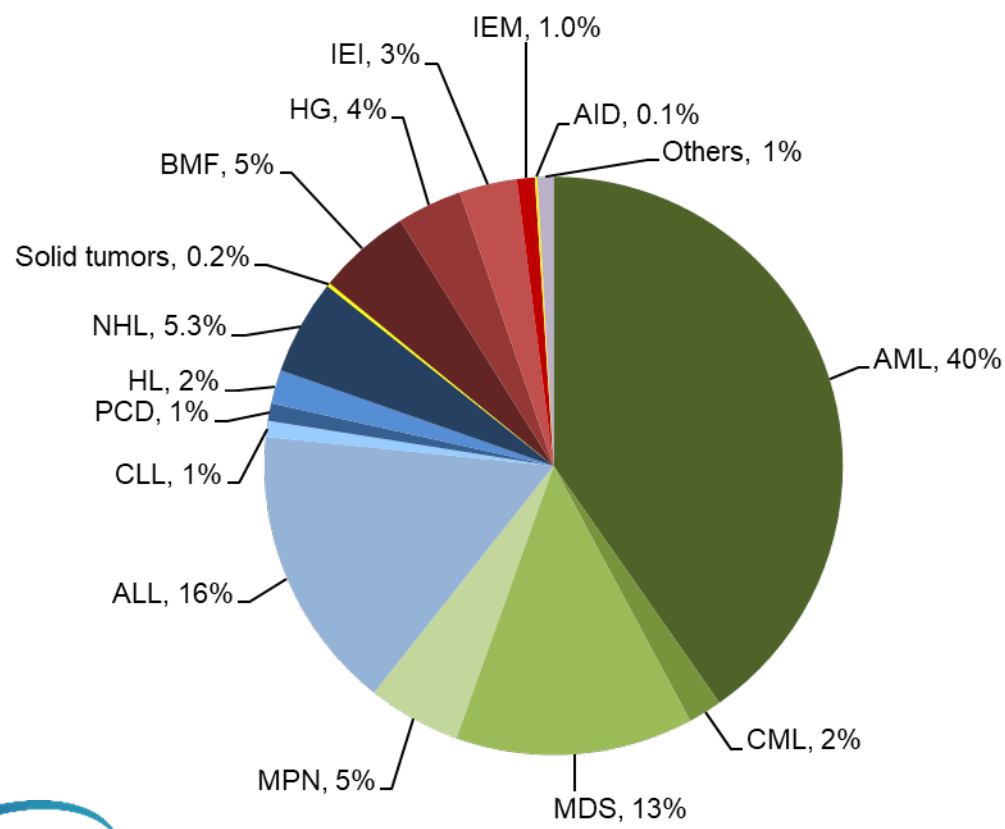
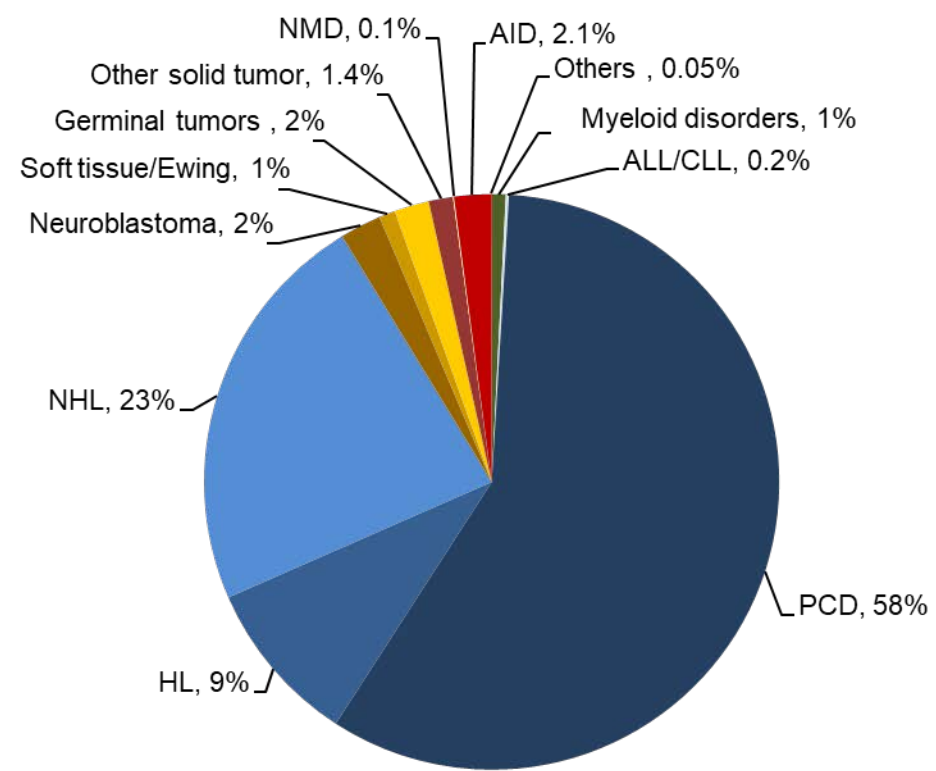
# Zahl Patienten in Europa autologe / allogene Transplantation 1990-2023



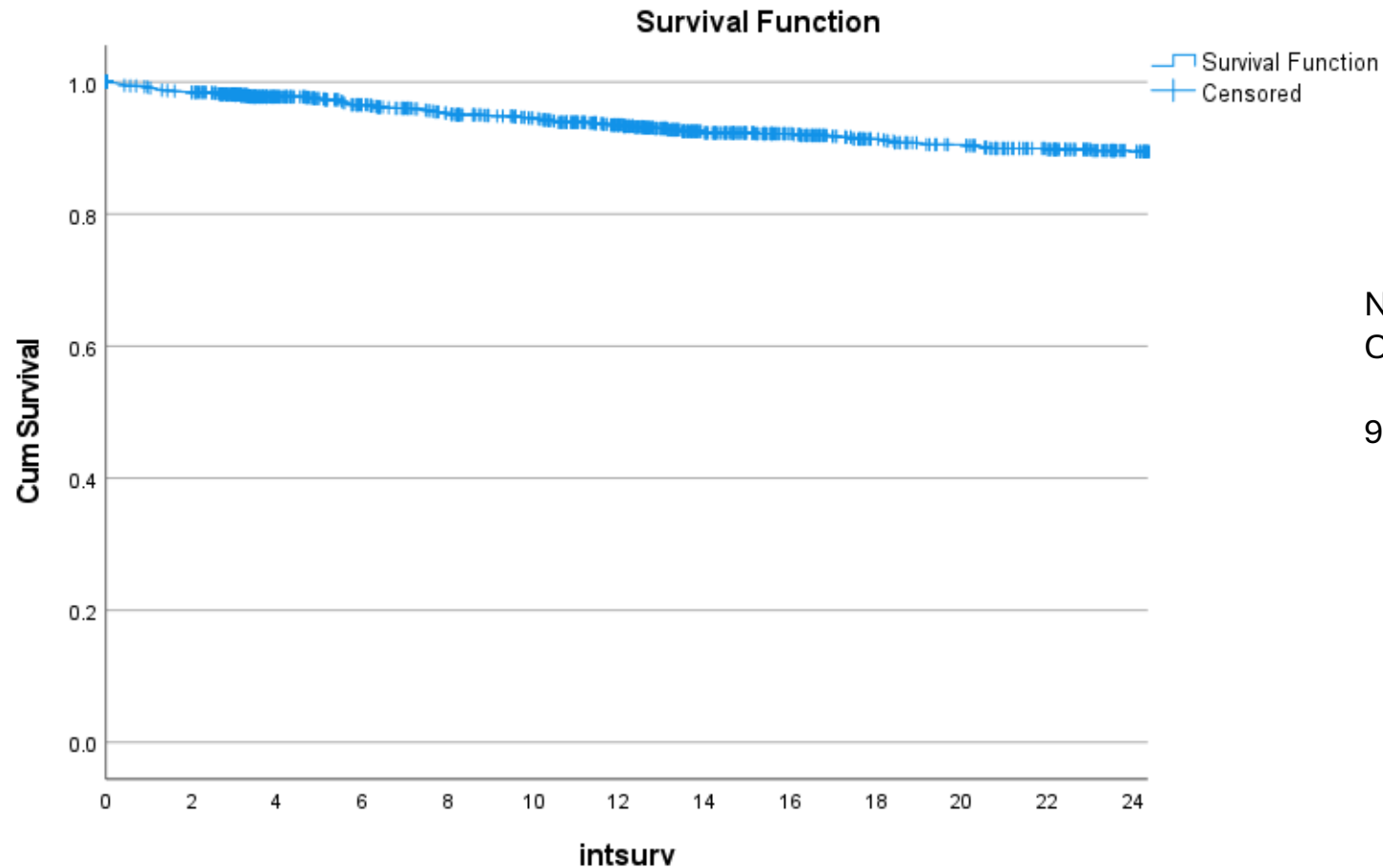
# Verteilung der Krankheiten für allogene und autologe HCT 2023

Allogeneic 1st HCT

Autologous 1st HCT



# Autologe HCT: Ueberleben 2020-2023

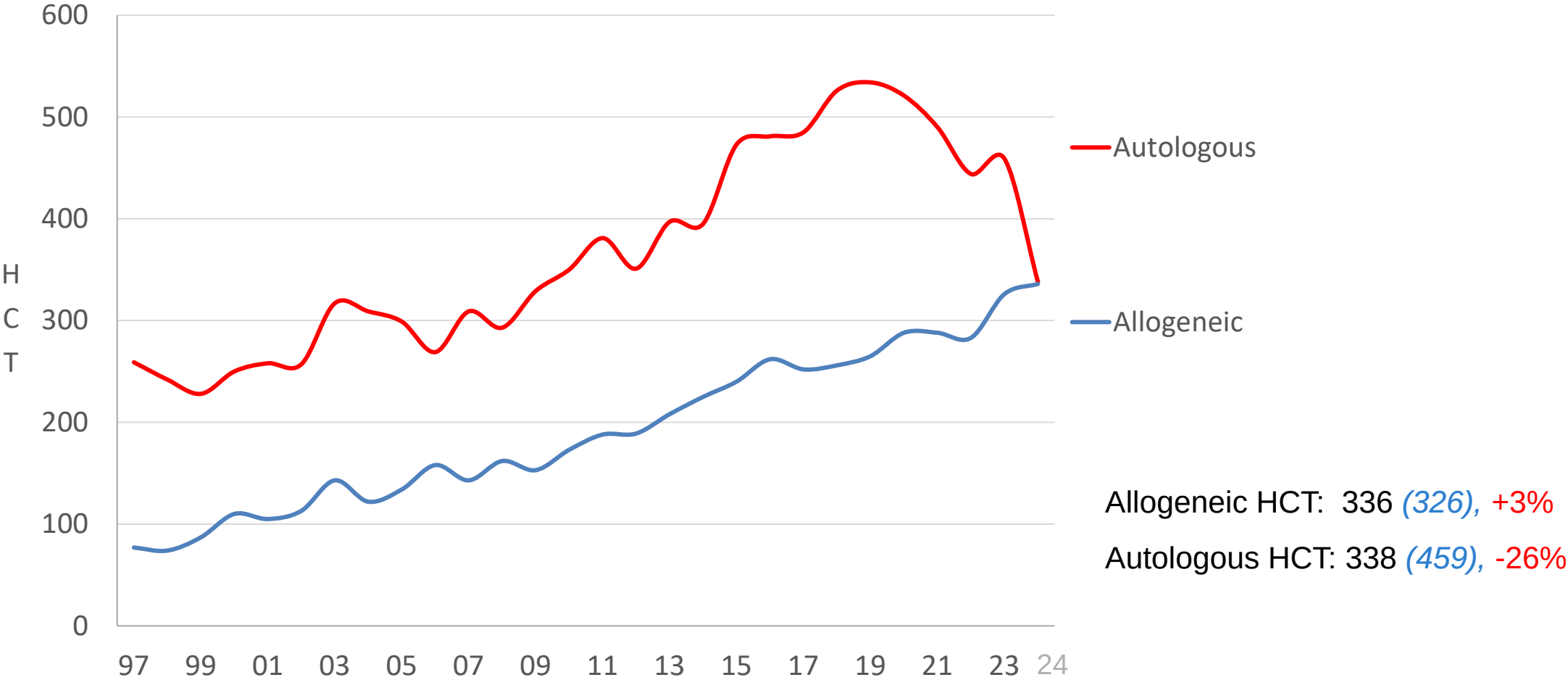


N = 1585

Overall survival at 2 years post therapy: 90%

95% confidence interval: 88-92%

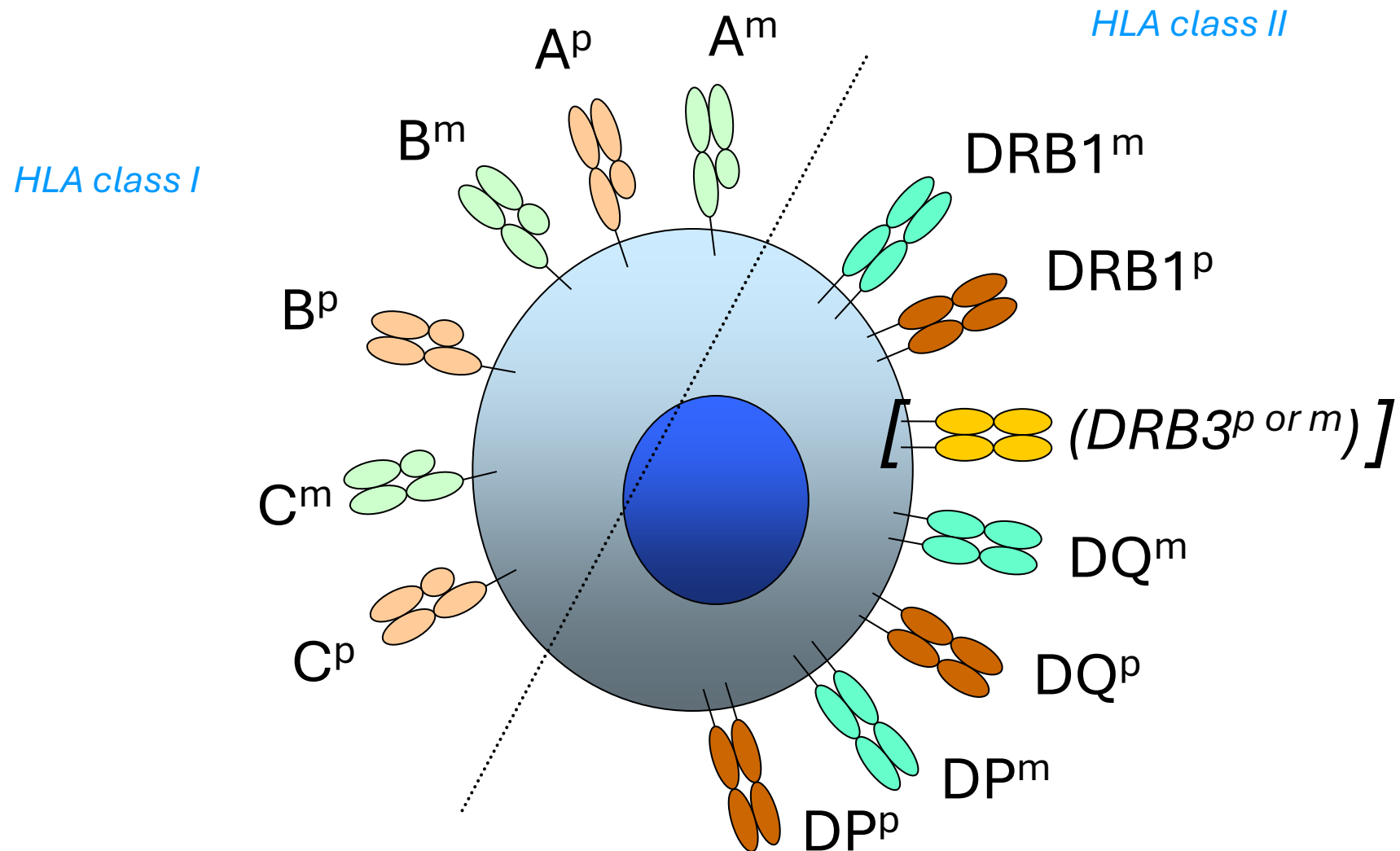
# Schweizer Statistik: 1997-2024: Trends autologe allogene HCT



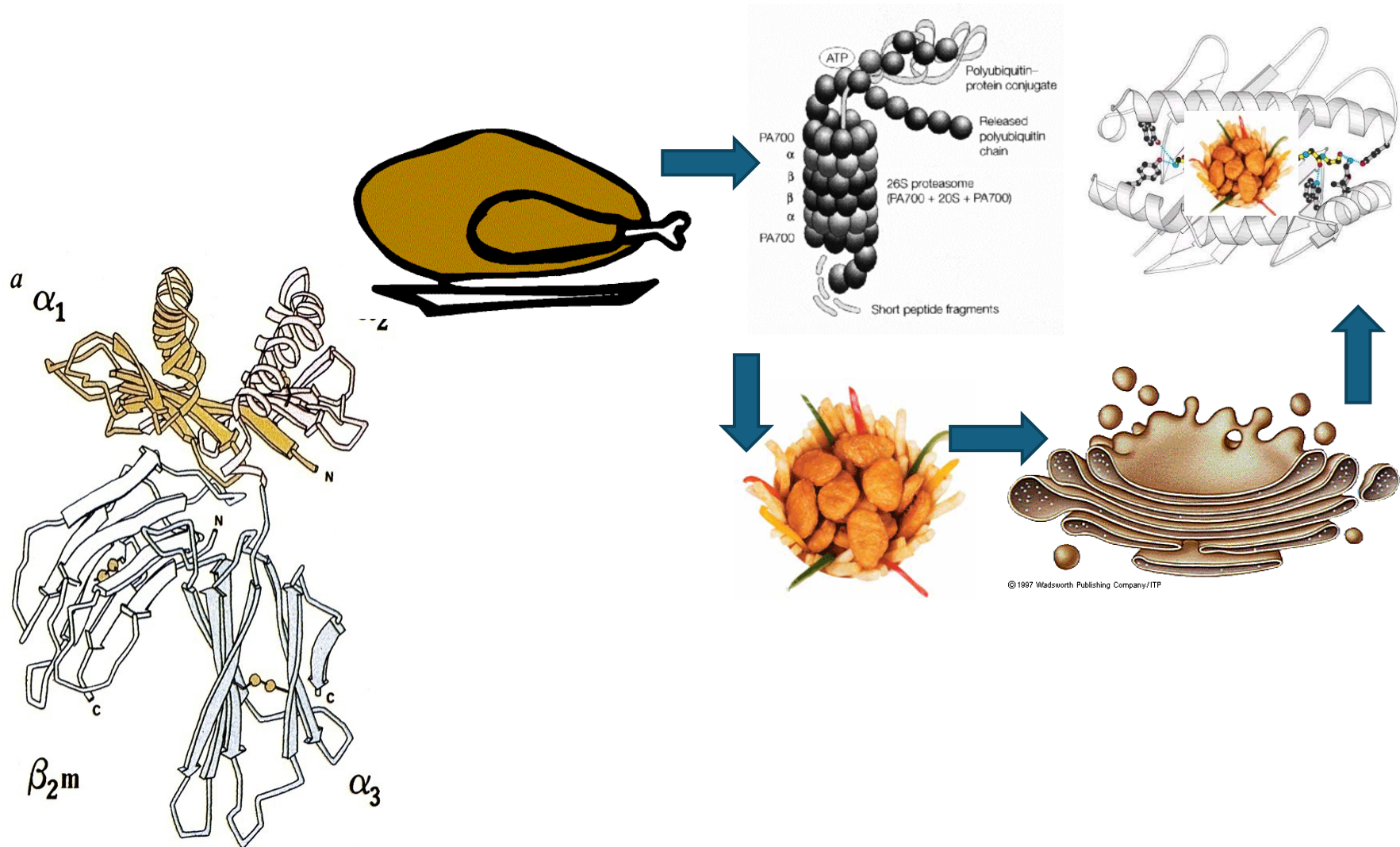


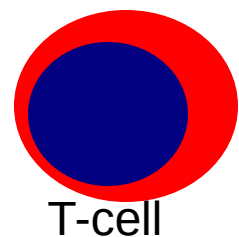
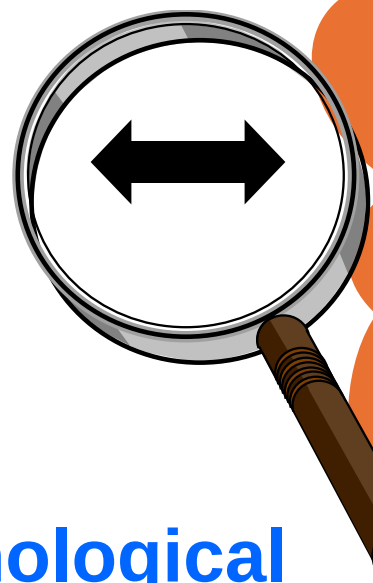
Welchen Spender?

# Expression of 12-14 HLA Antigens



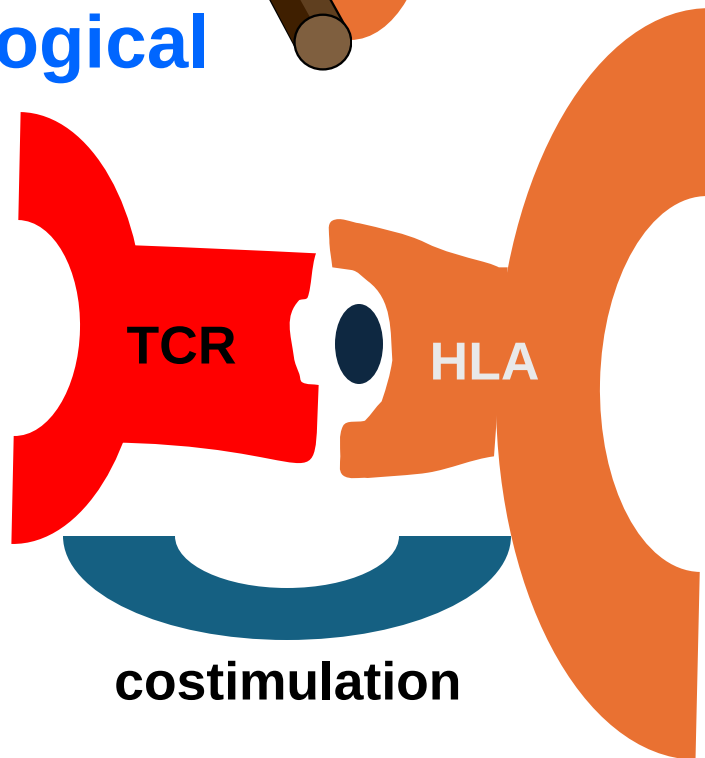
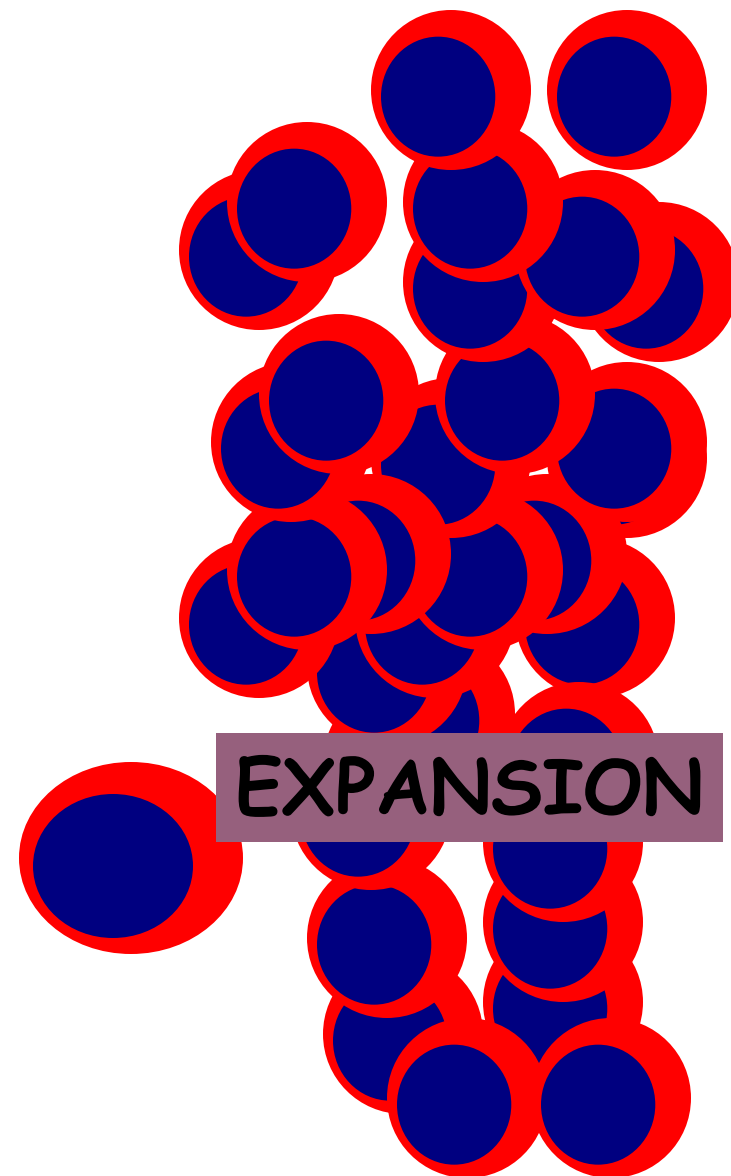
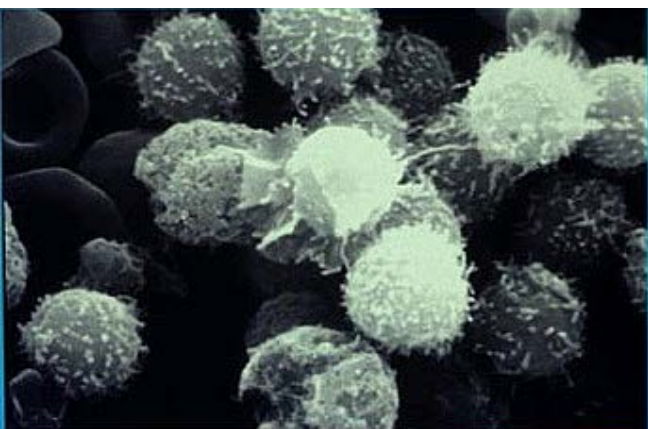
# HLA



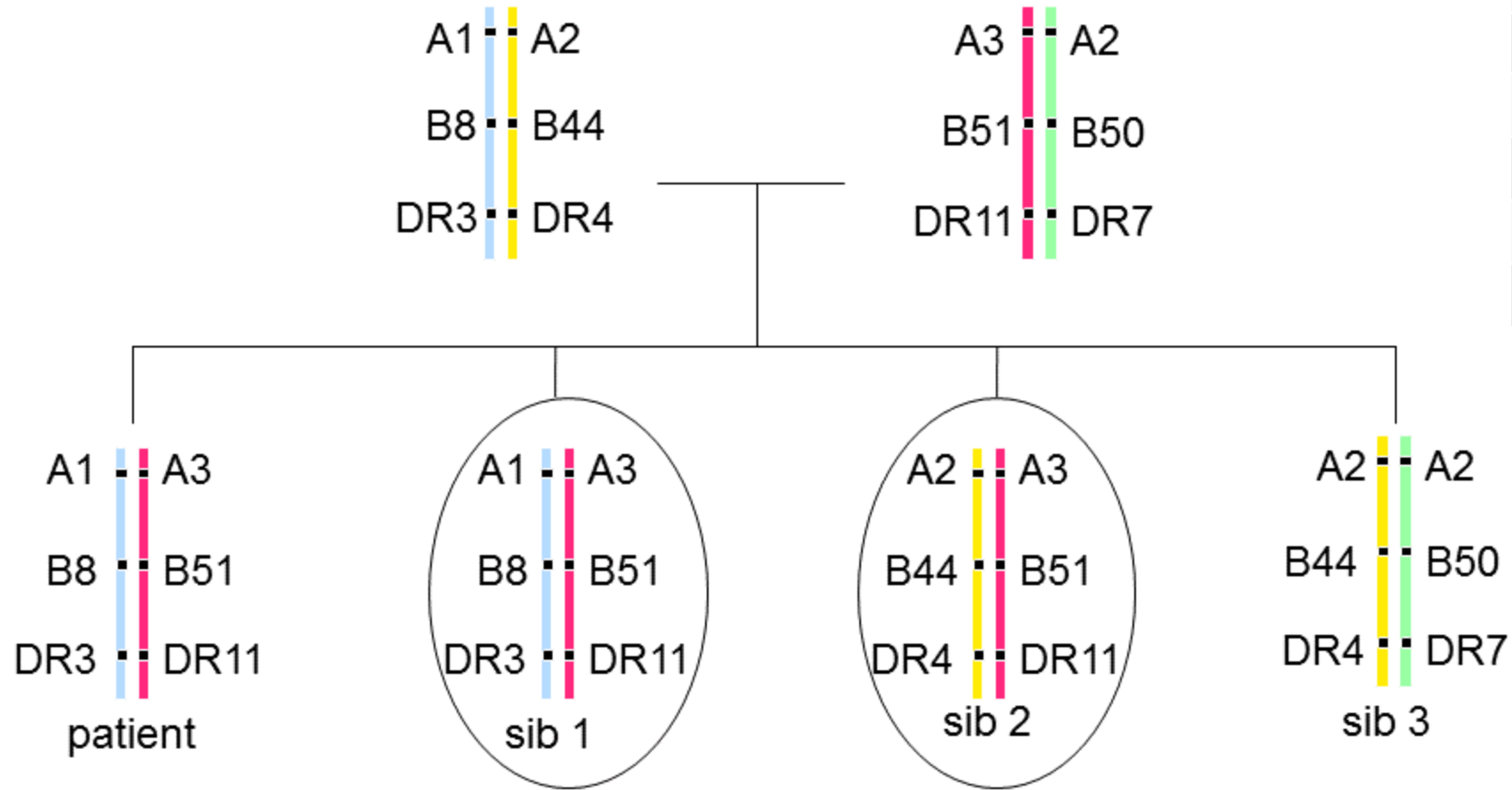


APC

## The immunological Synapse



# Segregation of HLA haplotypes



Patient and sibling 1 are HLA **genotypically identical**  
 Patient and sibling 2 are HLA haplo-identical  
 Patient and sibling 3 are HLA non-identical

| Sibs | Chance (%) |
|------|------------|
| 0    | 0          |
| 1    | 25         |
| 2    | 43         |
| 3    | 58         |
| 4    | 68         |
| 5    | 76         |
| 6    | 82         |

$$\text{prob} = 1 - (0.75^{\# \text{ sibs} - 1})$$

Photo: courtesy J Steiger pictures on the German Autobahn

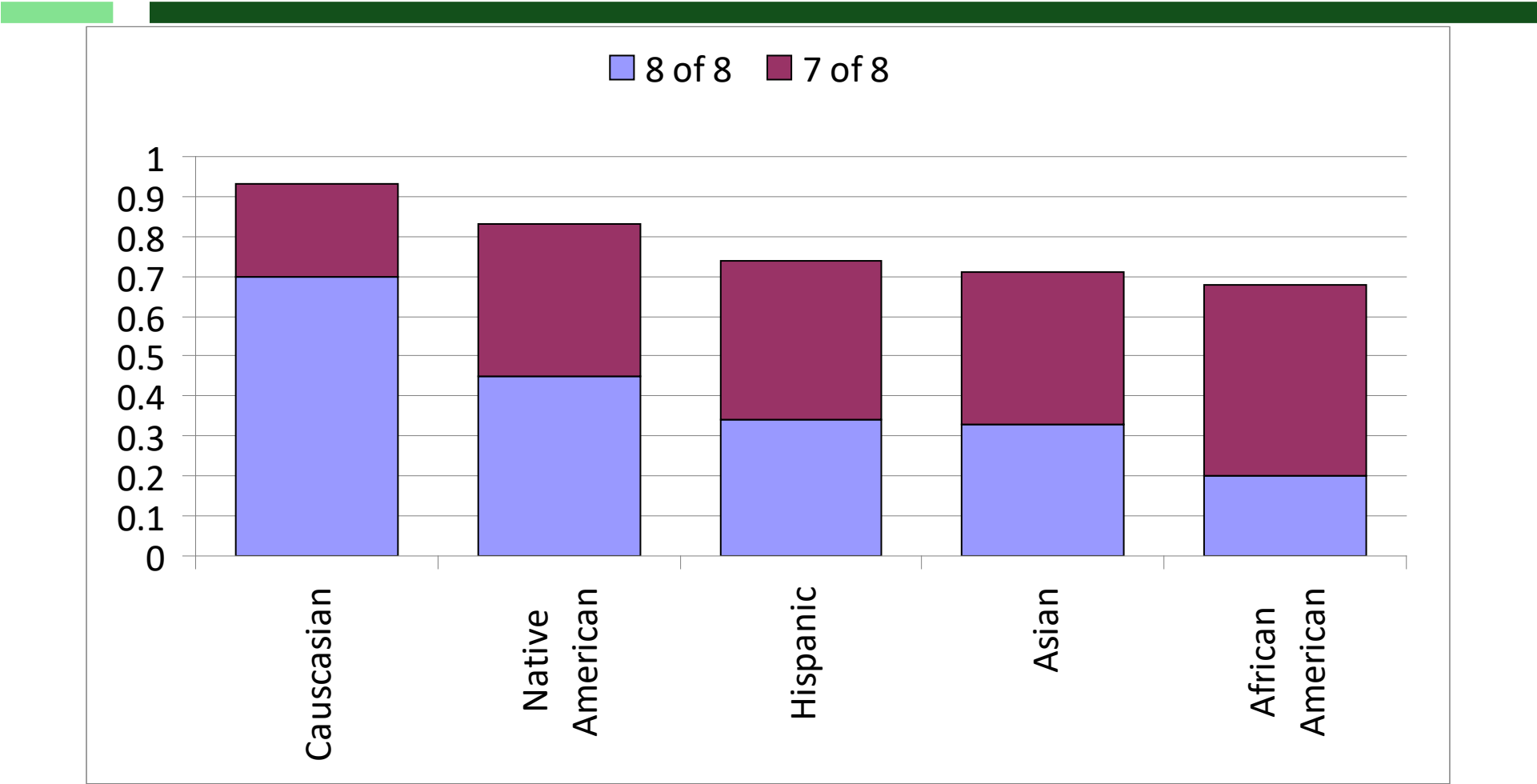


# Advertising Stem Cell Donation

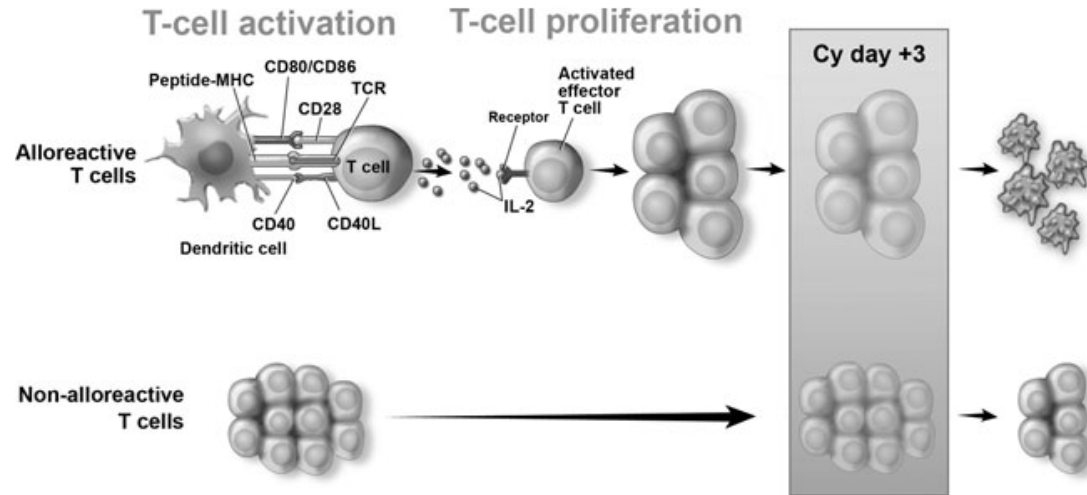
43 million  
Donors

the largest  
charitable  
volunteer  
Organization  
In the  
World

# NMDP Daten: nicht alle Patienten haben einen unverwandten Spender

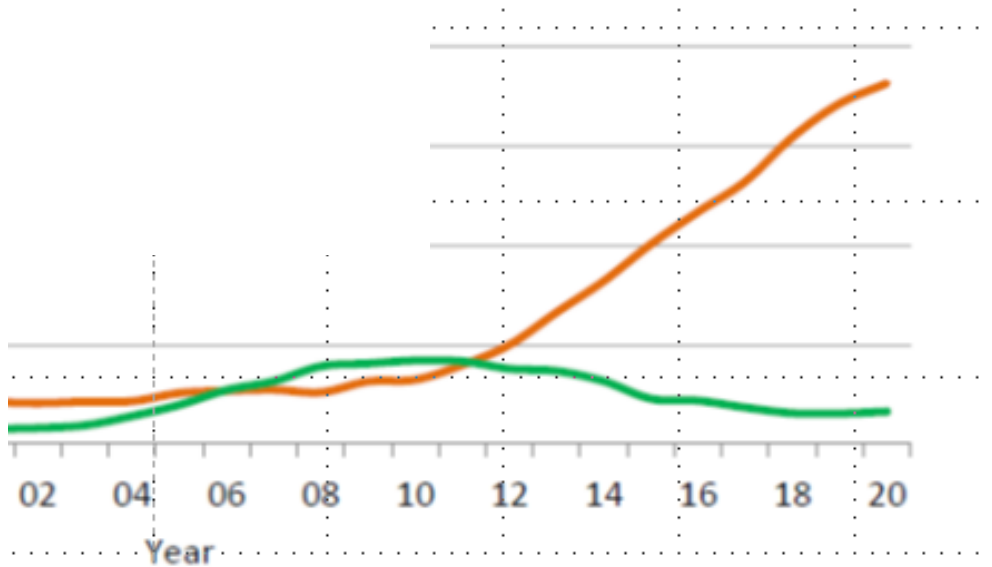
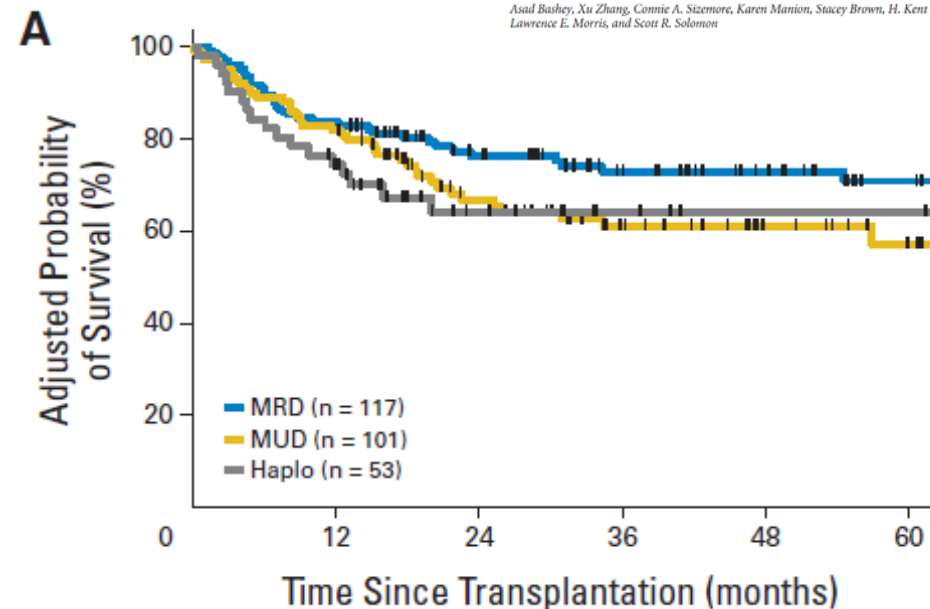


# Rationale für haploidente (halbpassende) Spender

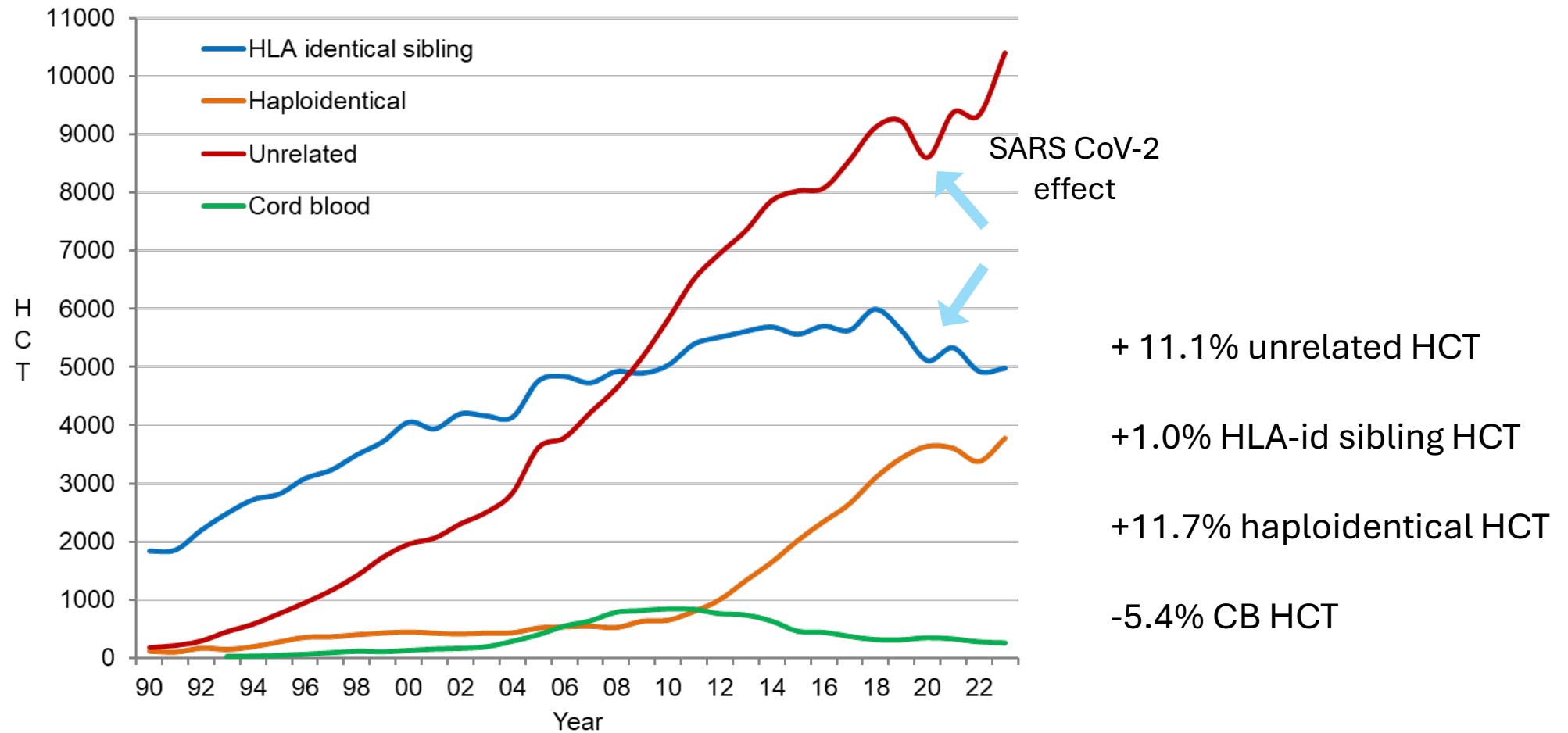


T-Cell-Replete HLA-Haploidentical Hematopoietic Transplantation for Hematologic Malignancies Using Post-Transplantation Cyclophosphamide Results in Outcomes Equivalent to Those of Contemporaneous HLA-Matched Related and Unrelated Donor Transplantation

Asad Bashey, Xu Zhang, Connie A. Sizemore, Karen Manion, Stacey Brown, H. Kent Holland, Lawrence E. Morris, and Scott R. Solomon



# Allogene HCT Spenderwahl Europa 1990-2023





Woher die  
Stammzellen?

Sources of hematopoietic stem cells  
Bone marrow  
Mobilization into peripheral blood  
Cord blood

Bone marrow harvest in the OR

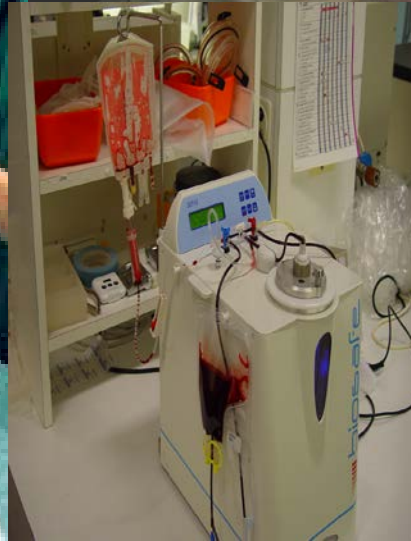


Peripheral stem cell collection by apheresis





Collection and processing of cord blood



# The banker's view

Evolution of cord blood units per CBB

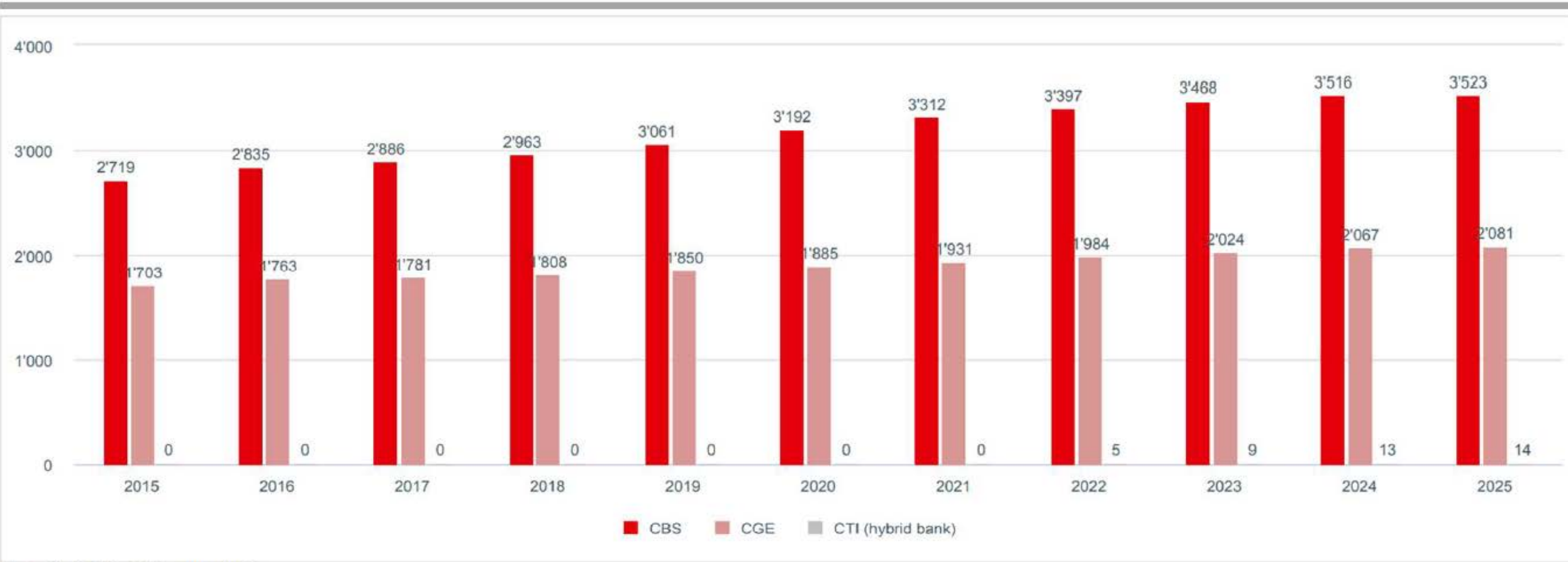
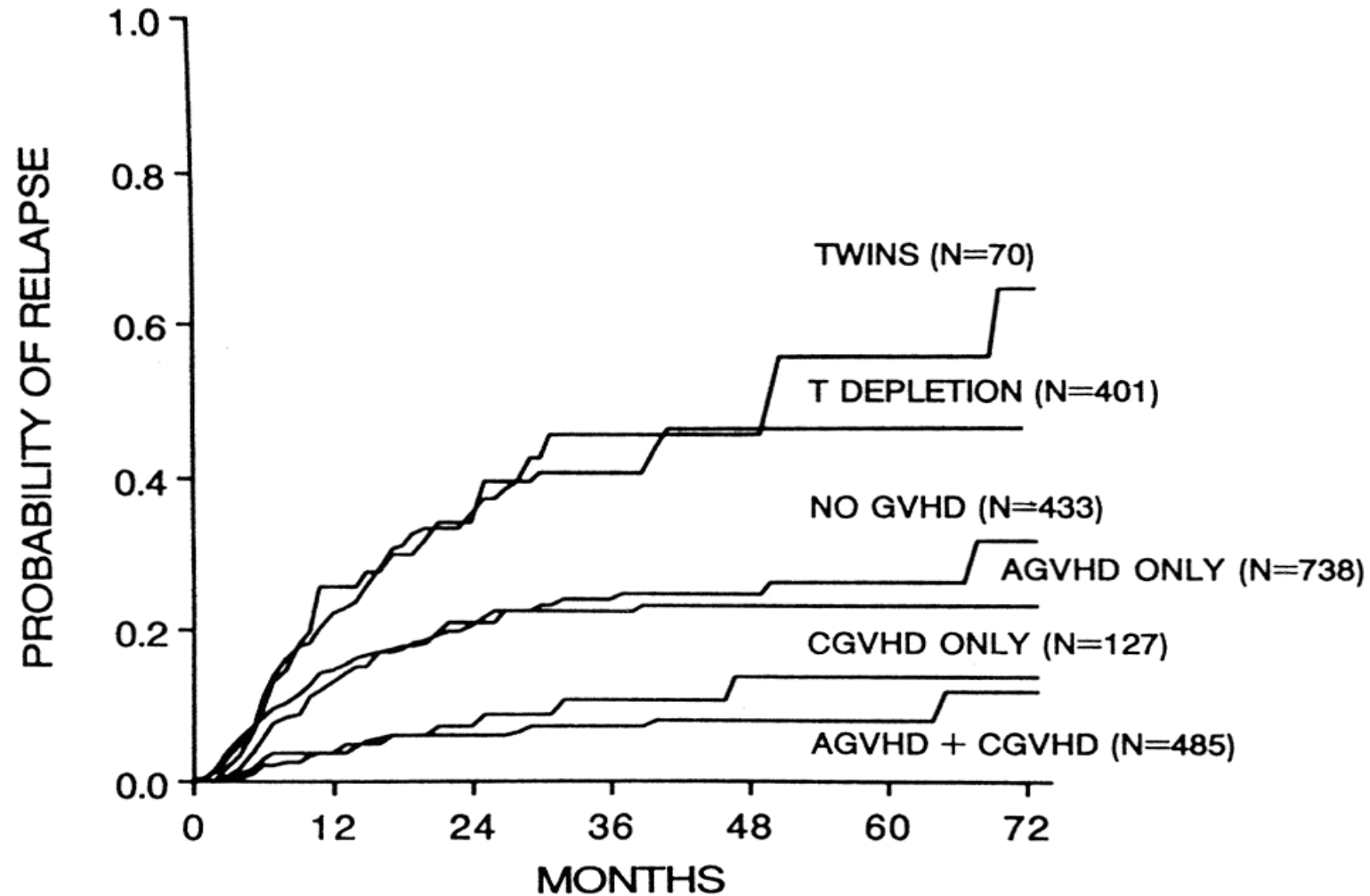


chart with data for 2025 per month 03

Was ist  
GvL GvHD?

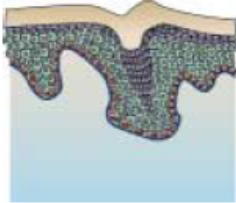
# Stärke Graft versus Leukemia Effect



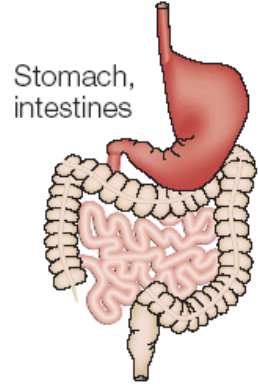
# Minor Histocompatibility Antigens

## Epithelial tissues

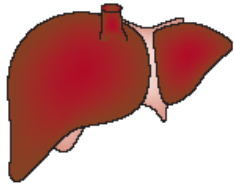
Skin



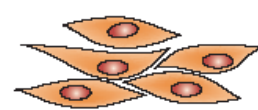
Stomach, intestines



Liver

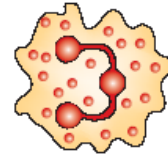


Fibroblasts



## Haematopoietic system

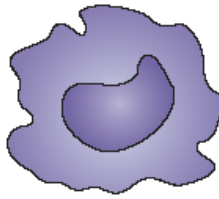
Neutrophil



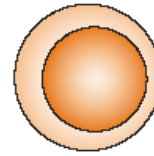
Antigen-presenting cell



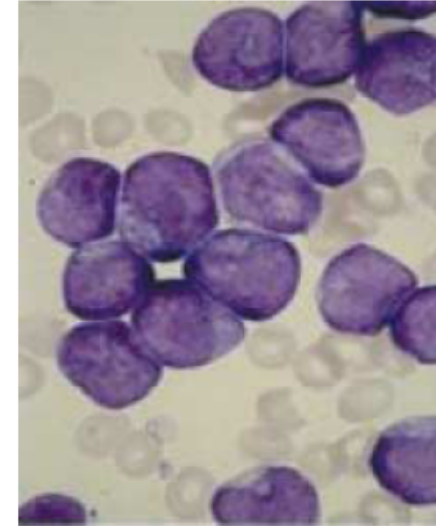
Macrophage



T cell

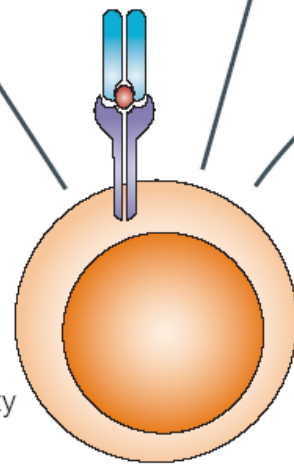


## Leukaemia



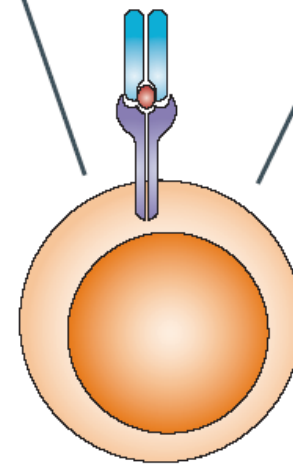
### GVHD

T cell responding to broadly expressed minor histocompatibility antigen

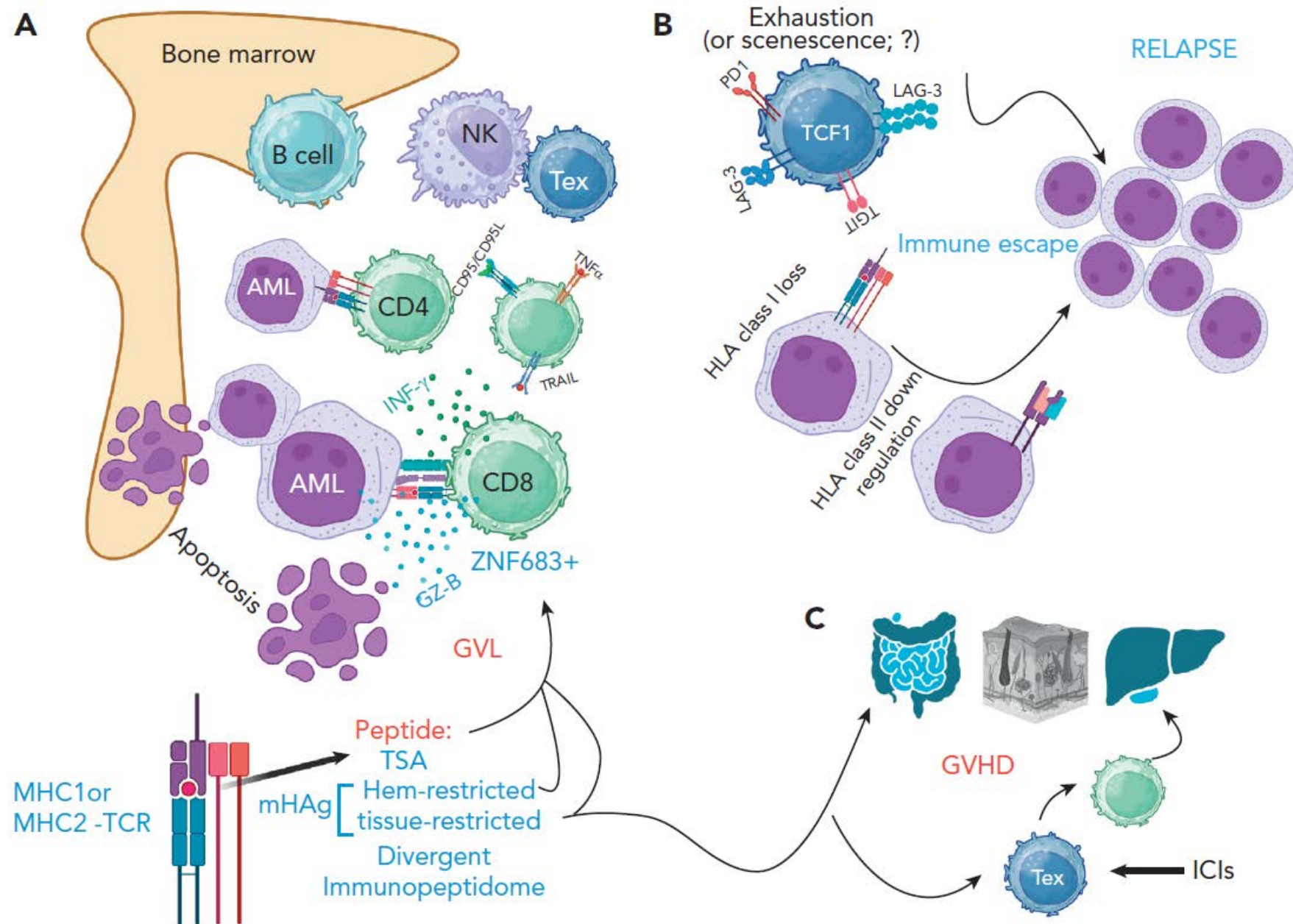


### GVL

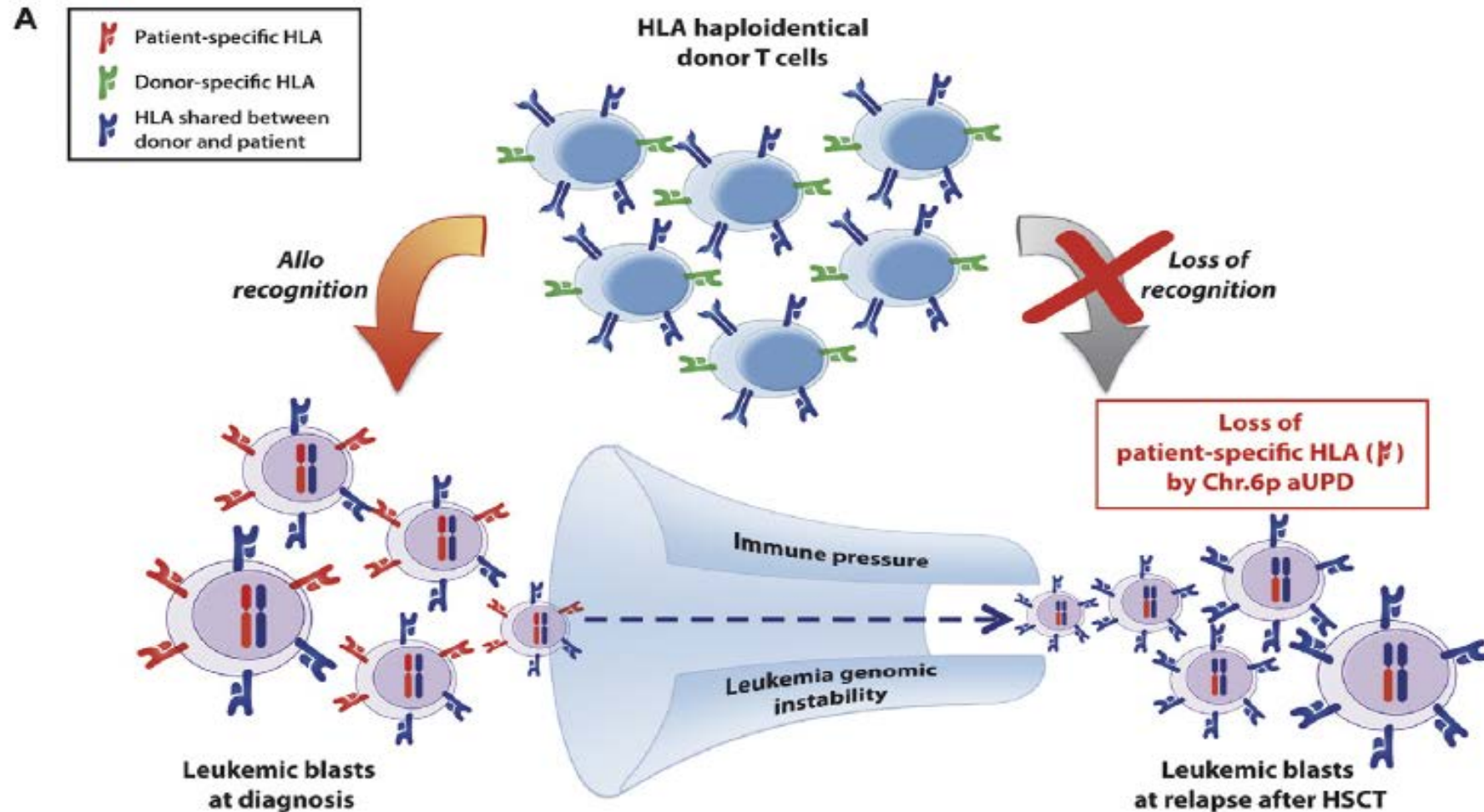
T cell responding to haematopoietic-restricted minor histocompatibility antigen



# GvL



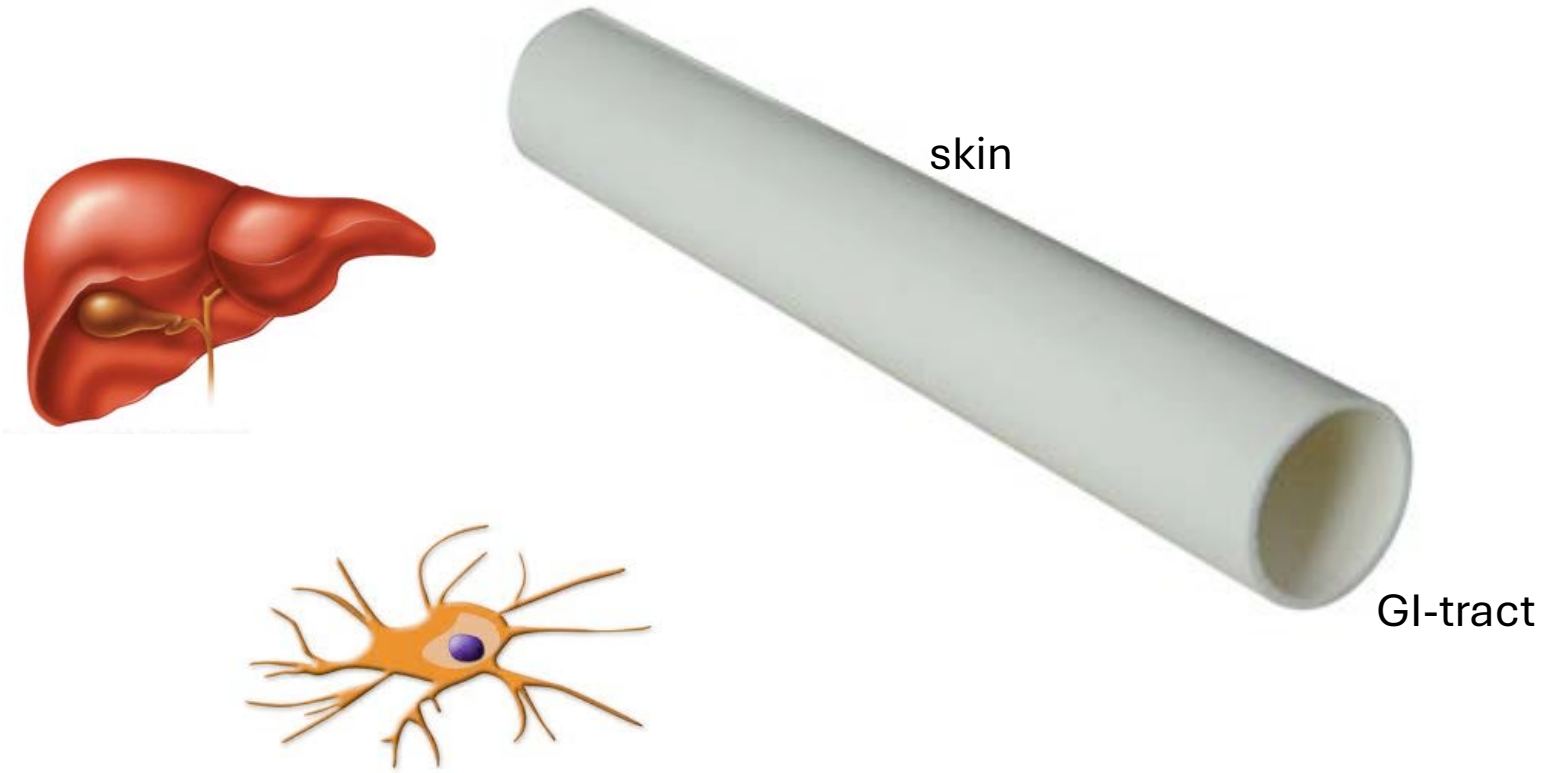
# GvL in haploidentical HSCT



# The reductionist model of the human body

## Interactions with the exterior

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Interface organs are tightly controlled immune networks with abundant APCs that are easily activated. Barrier function lost due to conditioning and/or infection in the peri-transplant period.

Photos: courtesy H Greinix



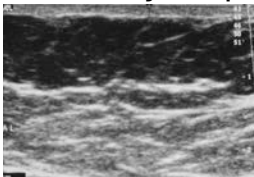
Dry eyes



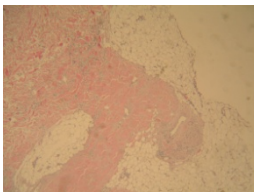
Oral lesions



Nail dystrophy



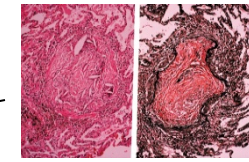
Skin sclerosis



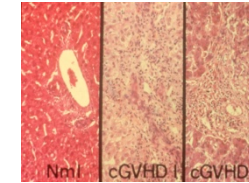
Deep sclerosis

# Mr chronic GvHD

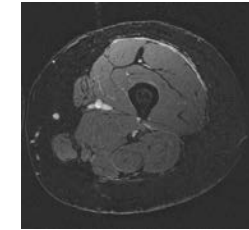
Infections  
Endocrine  
Metabolism  
Nutrition  
Pain  
Quality of life  
Disability



Bronchiolitis obliterans



Loss of bile ducts



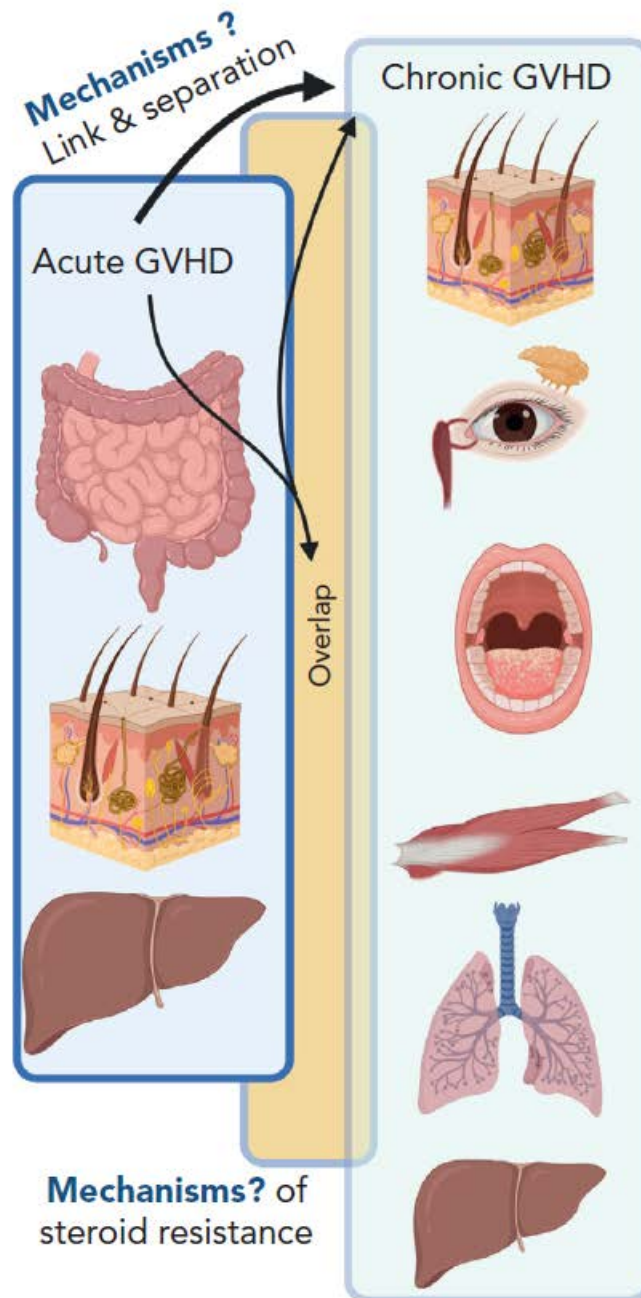
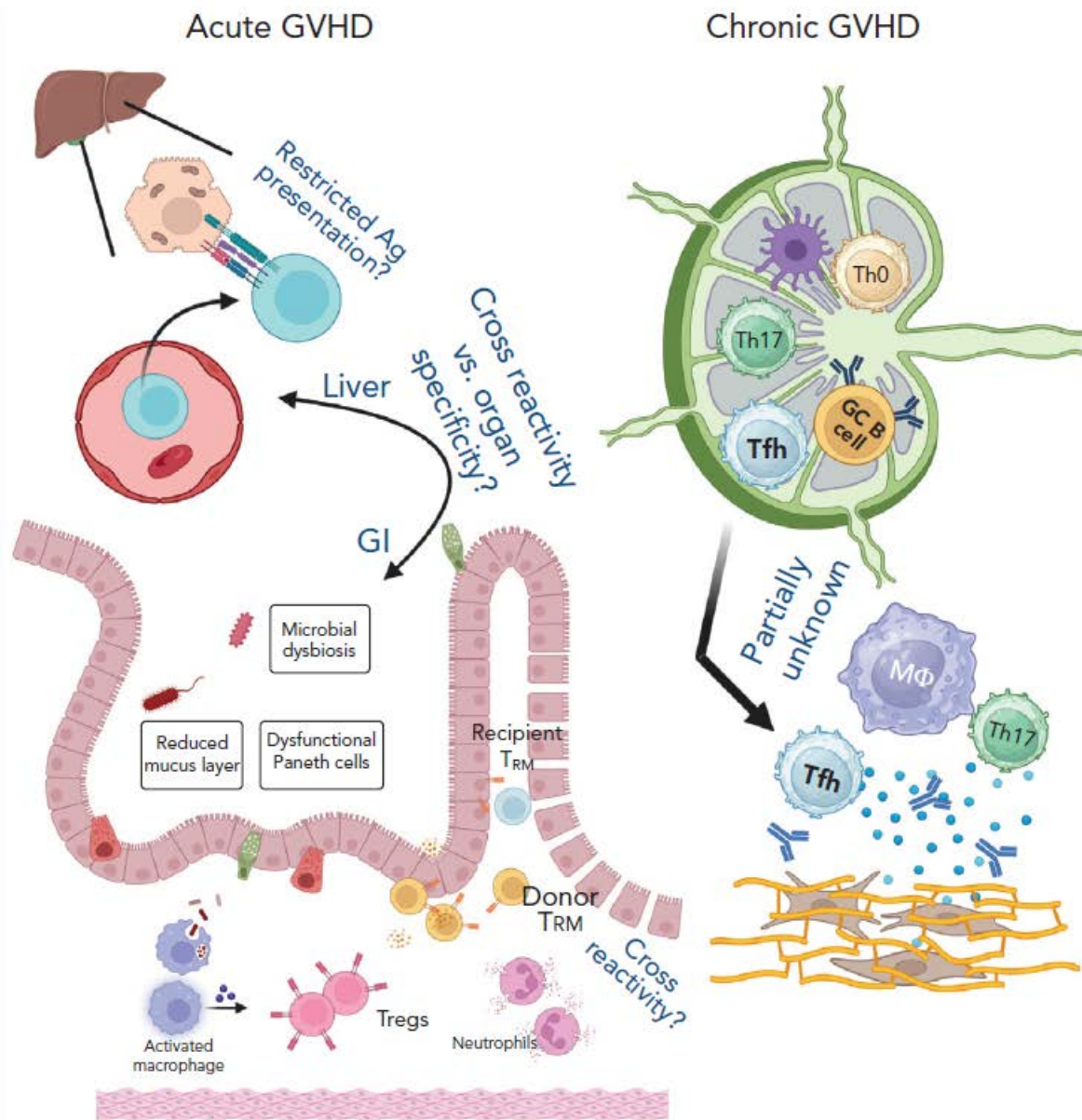
Fasciitis



Skin ulcers

**manifestations  
of cGVHD**

# GvHD



# Recent FDA Approvals in the Treatment of Graft-Versus-Host Disease

aGvHD

**Ruxolitinib**, oral selective JAK1/2 inhibitor,  
steroid-refractory aGVHD

cGvHD

**Ibrutinib**, oral BTK inhibitor 2nd line

**Belumosudil** oral selective inhibitor  
3rd line

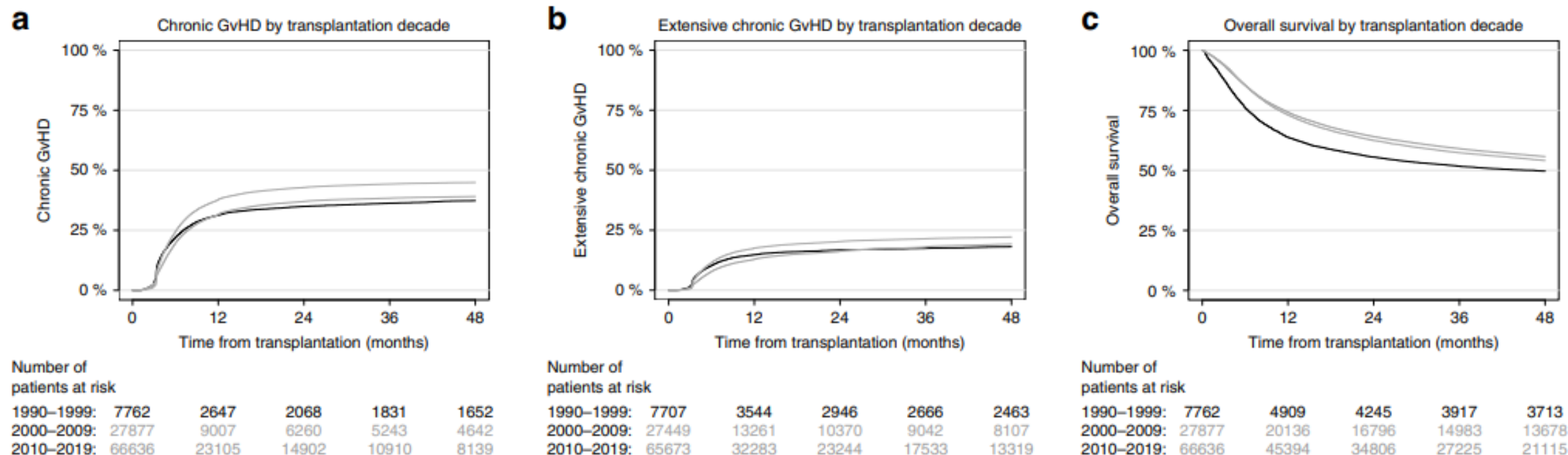
**Axatilimab** iv, CSF-1R 3rd line



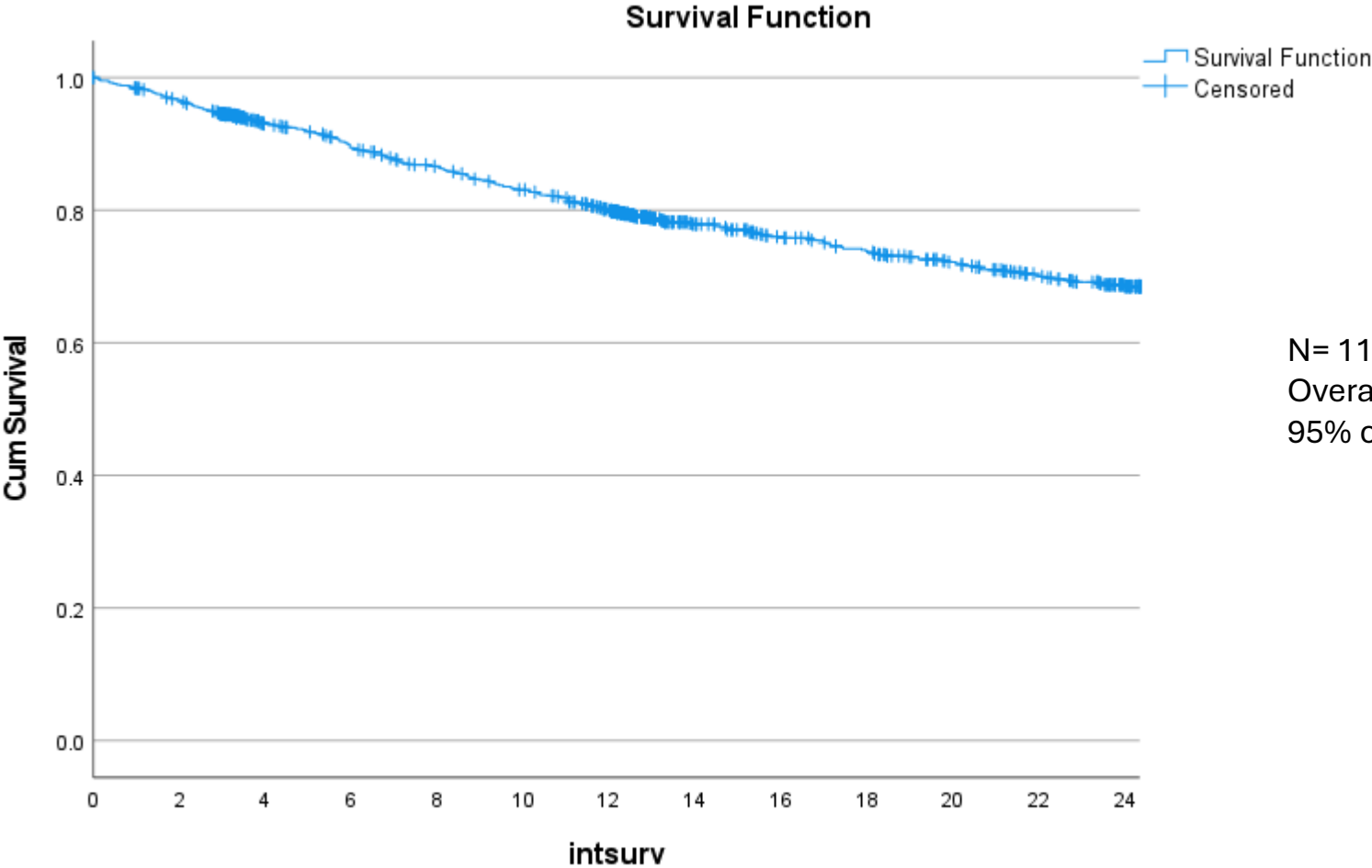
# Chronic Graft-versus-Host disease trends over 30 years - a study by the EBMT transplant complications working party

Drazen Pulanic<sup>1,2</sup>✉, Christophe Peczynski<sup>3</sup>, William Boreland<sup>3</sup>, Christina Rautenberg<sup>4</sup>, Nicolaus Kröger<sup>5</sup>, David Michonneau<sup>6</sup>, Urpu Salmenniemi<sup>7</sup>, Robert Zeiser<sup>8</sup>, Katharina Egger-Heidrich<sup>9</sup>, Edouard Forcade<sup>10</sup>, Didier Blaise<sup>11</sup>, Thomas Luft<sup>12</sup>, Hélène Labussière-Wallet<sup>13</sup>, Ivan Moiseev<sup>14</sup>, Christian Koenecke<sup>15</sup>, Helene Schoemans<sup>16,17</sup>, Grzegorz Basak<sup>18</sup>, Olaf Penack<sup>19</sup> and Zinaida Peric<sup>20,21</sup>

Bone Marrow Transplantation; <https://doi.org/10.1038/s41409-025-02697-w>



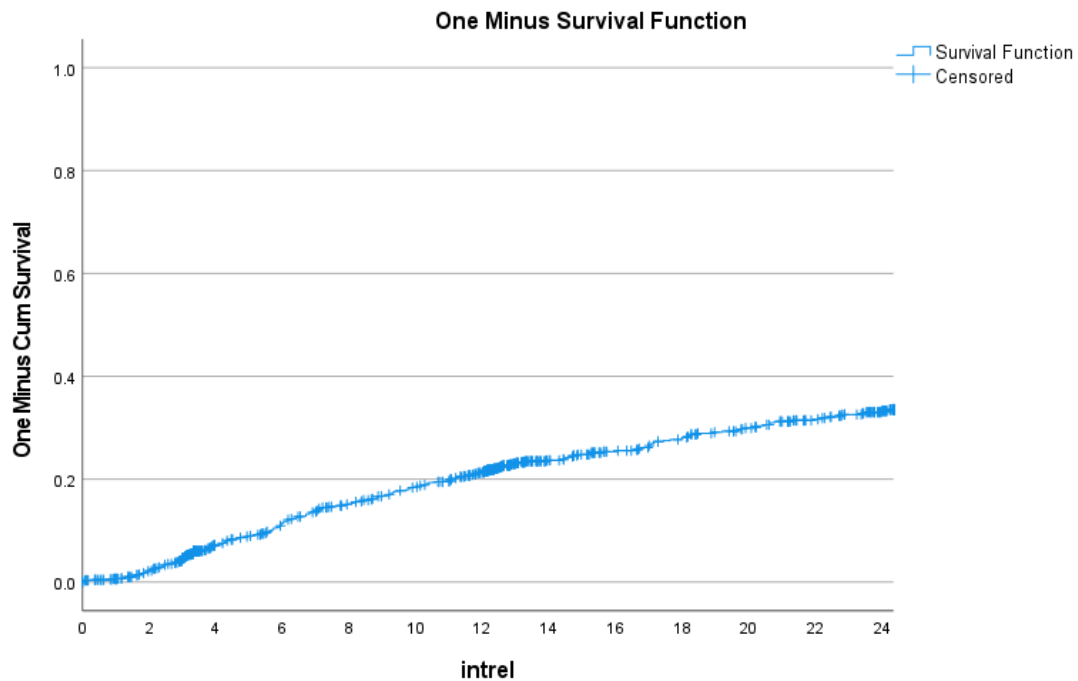
# Schweiz Allogene HCT: Ueberleben: 2020-2023



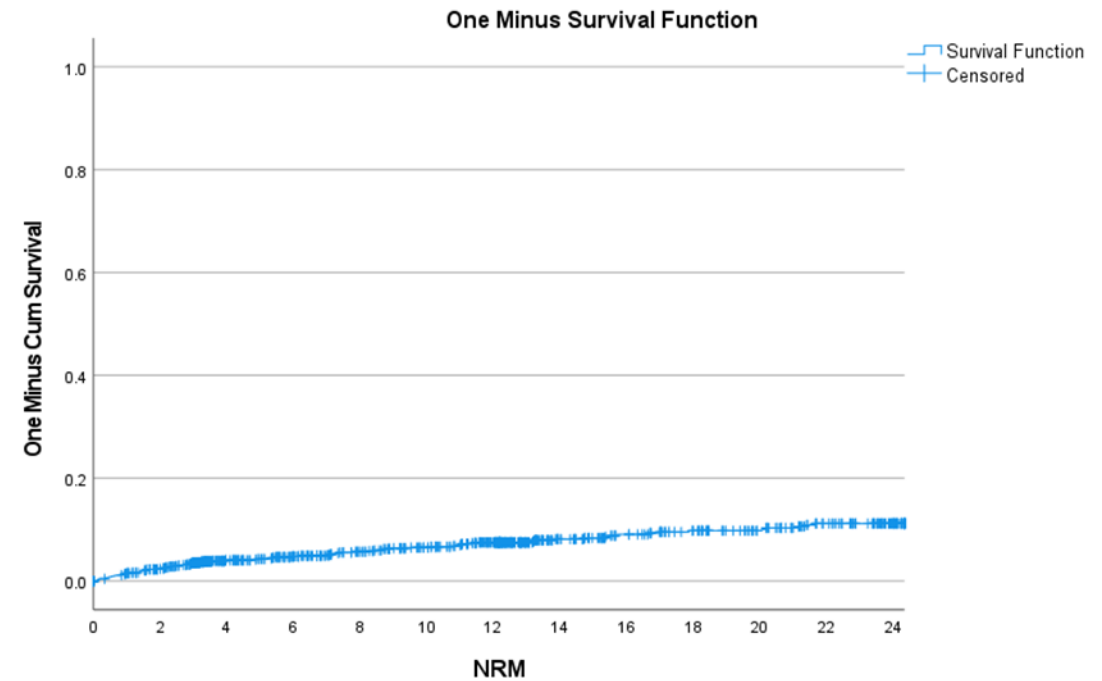
N= 1102  
Overall survival at 2 years post therapy: 69%;  
95% confidence interval: 65-73%

# Allogeneic HCT: Outcome: 2020-2023

Cumulative Incidence of relapse at 2 years post therapy: 34%;  
95% confidence interval: 42-52%



Cumulative Incidence of non-relapse mortality at 2 years post therapy: 11%, 95% confidence interval: 8-14%

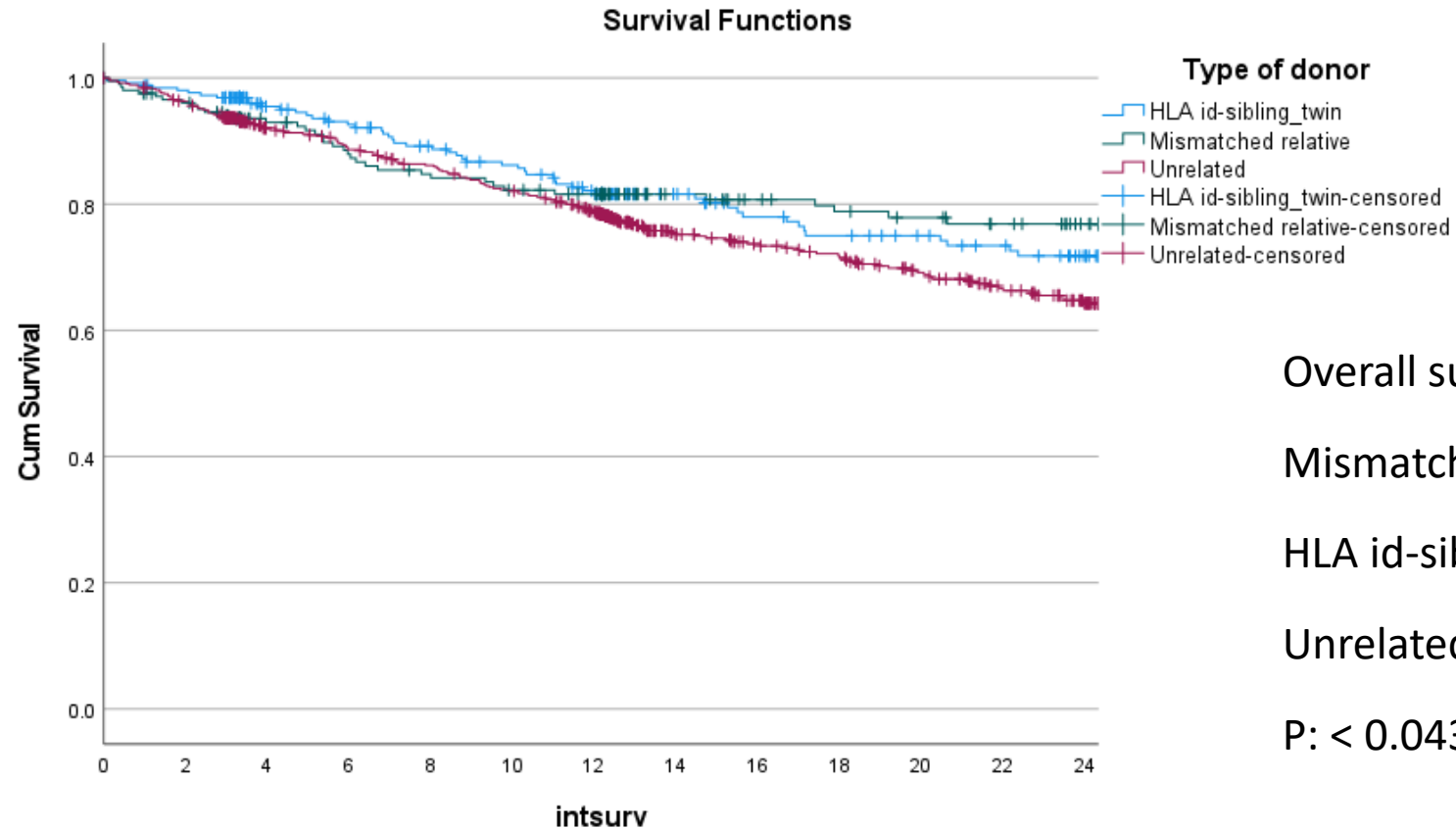


## RELAPSE

Donor lymphocyte infusion

Mother of all cellular therapies

# Allogeneic HCT: Outcome by donor: 2020-2023



Overall survival at 2 years post therapy by donor:

Mismatched relative: 77%, C.I.: 70-77%

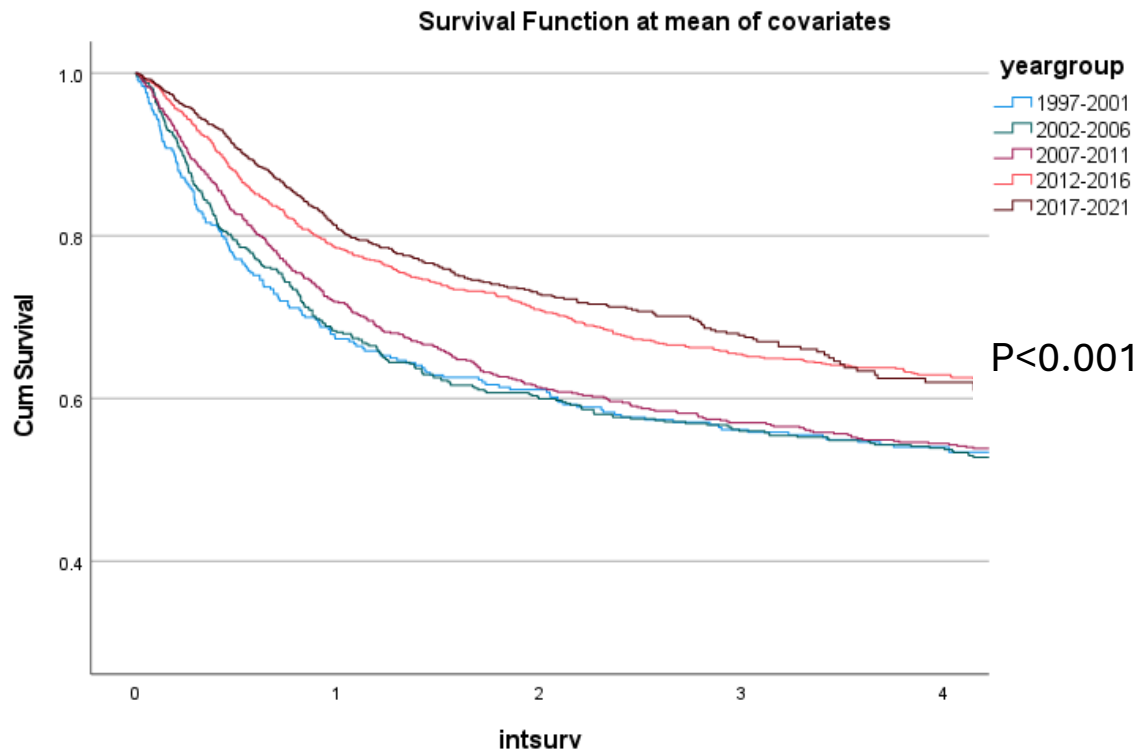
HLA id-sibling\_twin: 72%, C.I.: 65-79%

Unrelated: 64%, C.I.: 59-69%

P: < 0.043

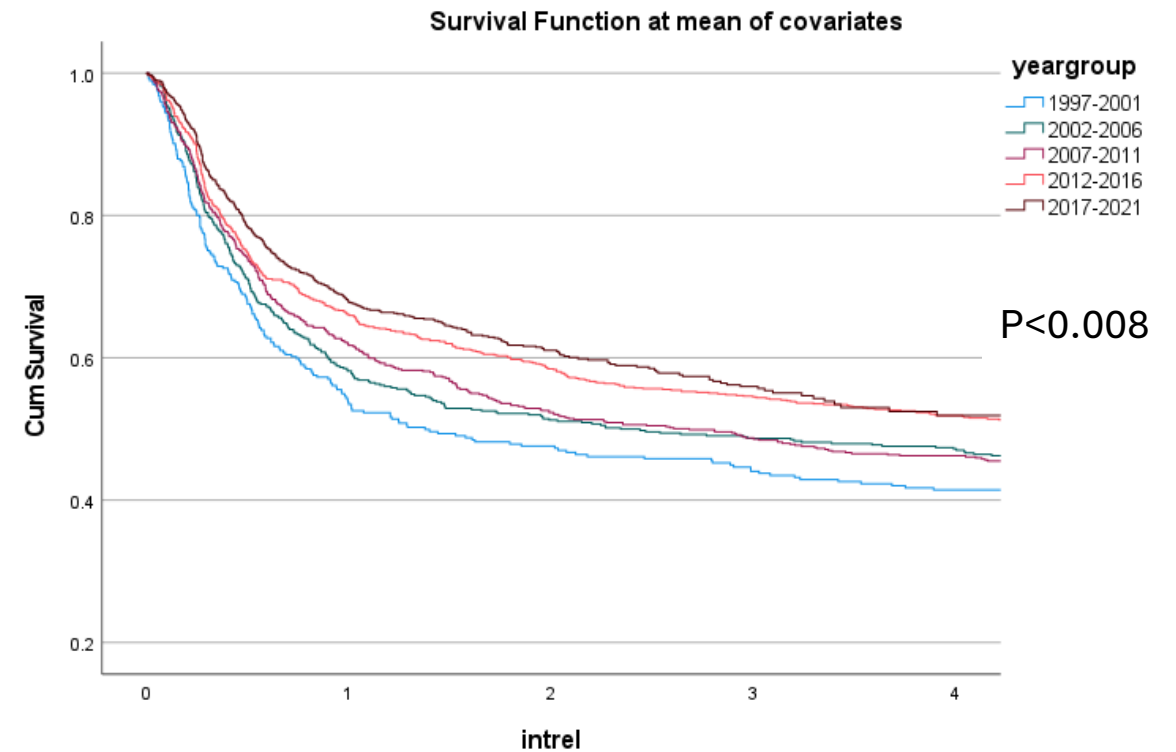
# Outcome by quinquennia 1997-2021: 1st allo HCT N= 4031

OS



Adjusted for  
Age  
Donor  
Disease stage  
Myeloablative conditioning  
CMV DR

PFS



Adjusted for  
Age  
Donor  
Disease  
Disease stage  
Myeloablative conditioning  
Interval dx tx

# Wie wird entschieden?

## Disease Risk Index

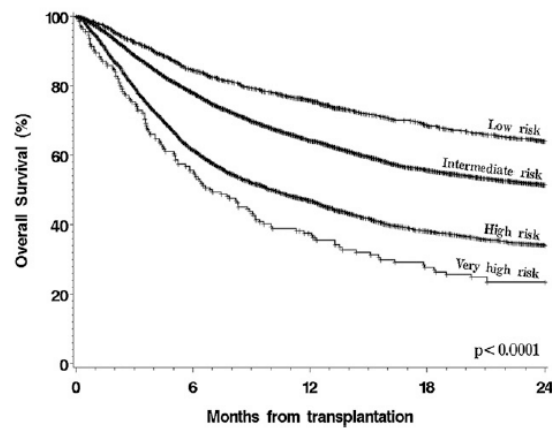
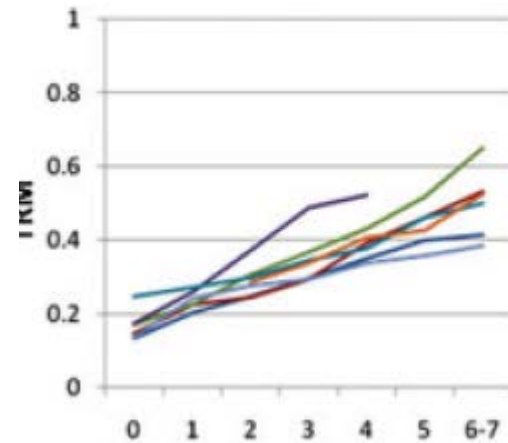
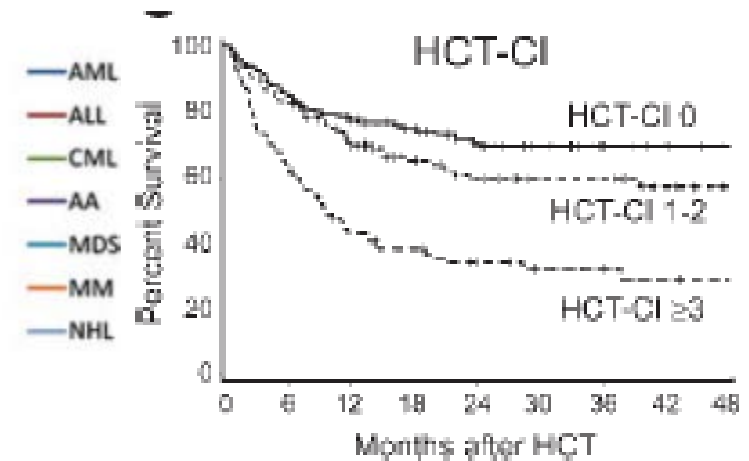


Figure 1. OS in entire cohort, stratified by the original DRI.

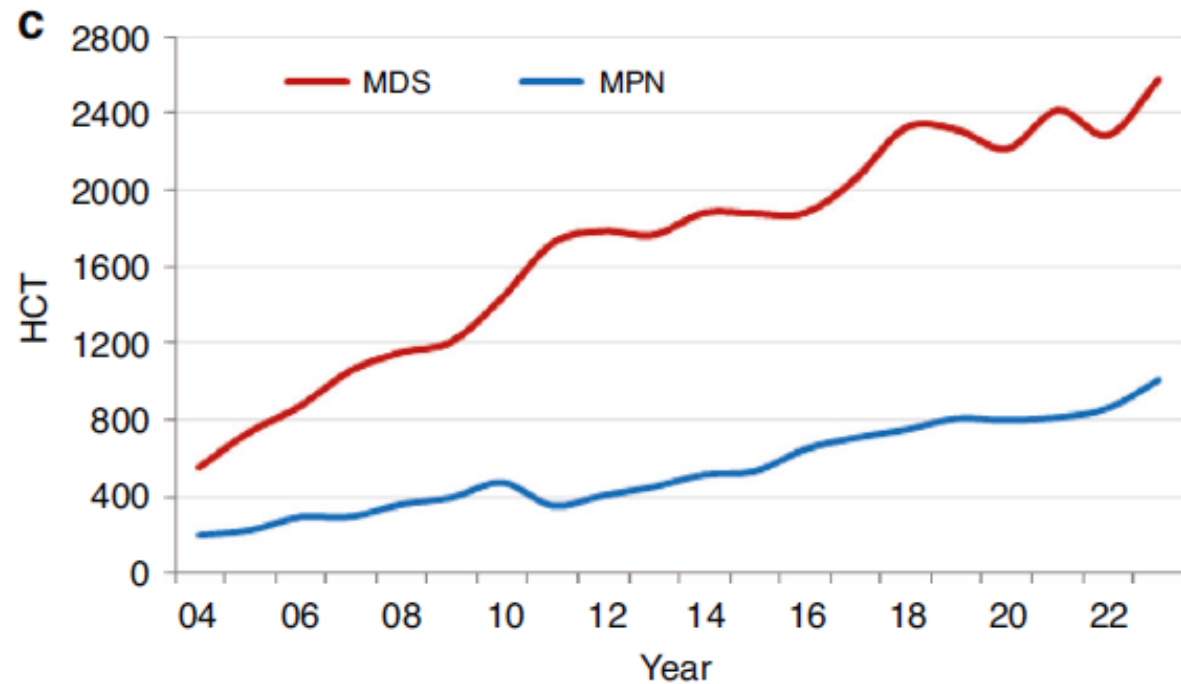
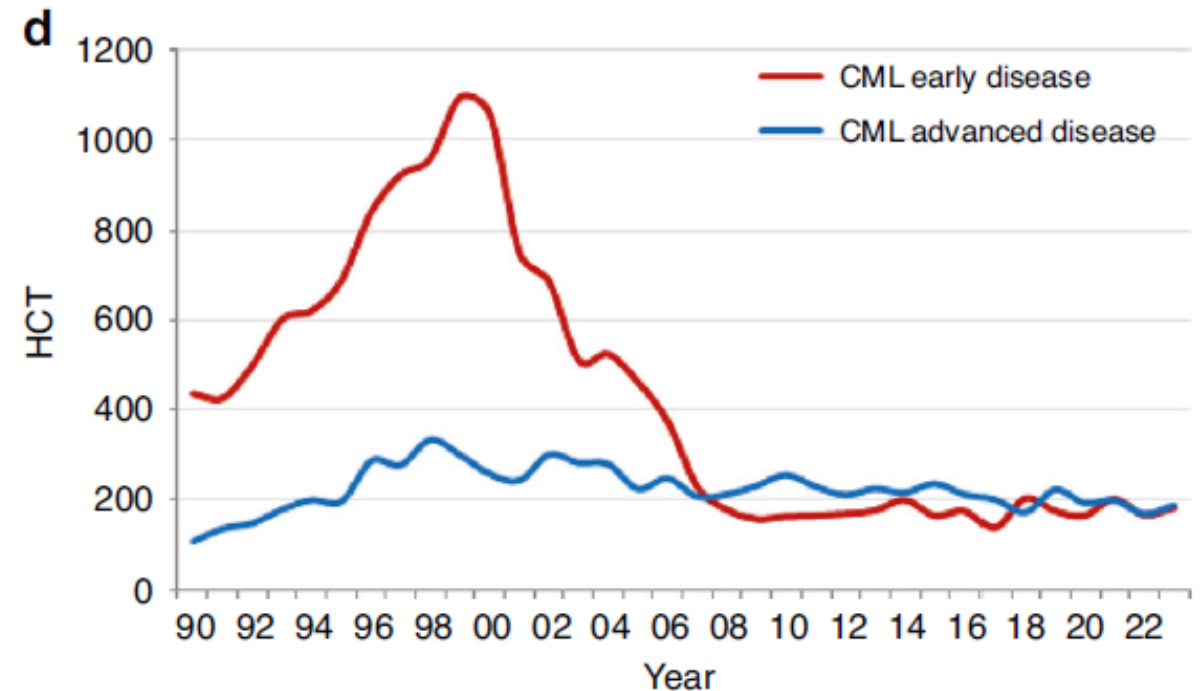
## Transplant Score



## Comorbidity Index



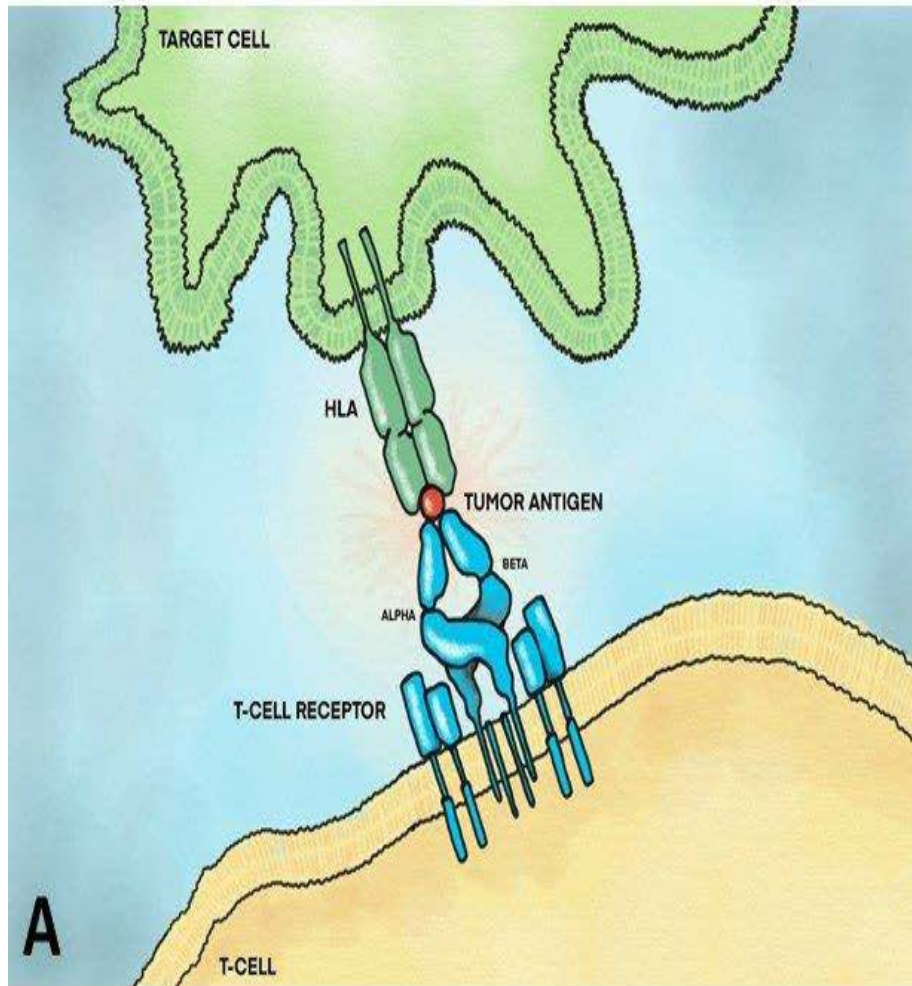
# Stammzelltransplantation in Konkurrenz mit anderen Therapien



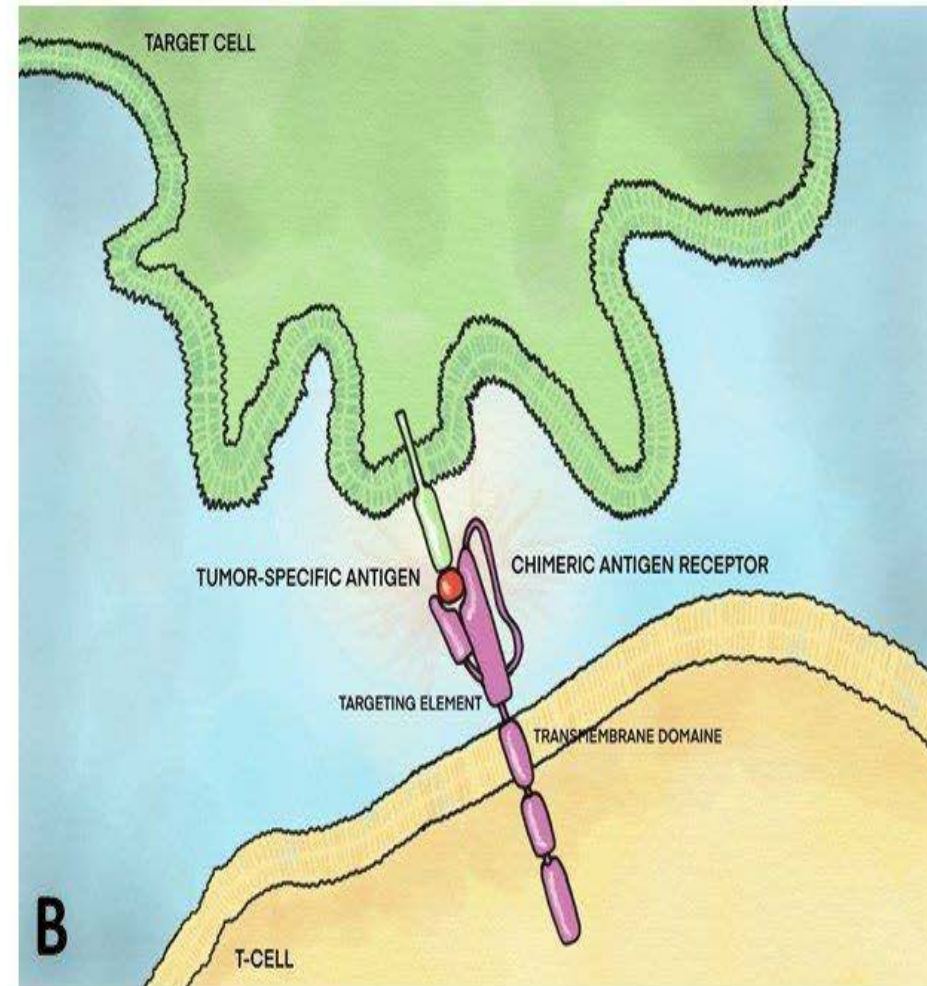


Zelluläre Therapien  
Reinraum Technik

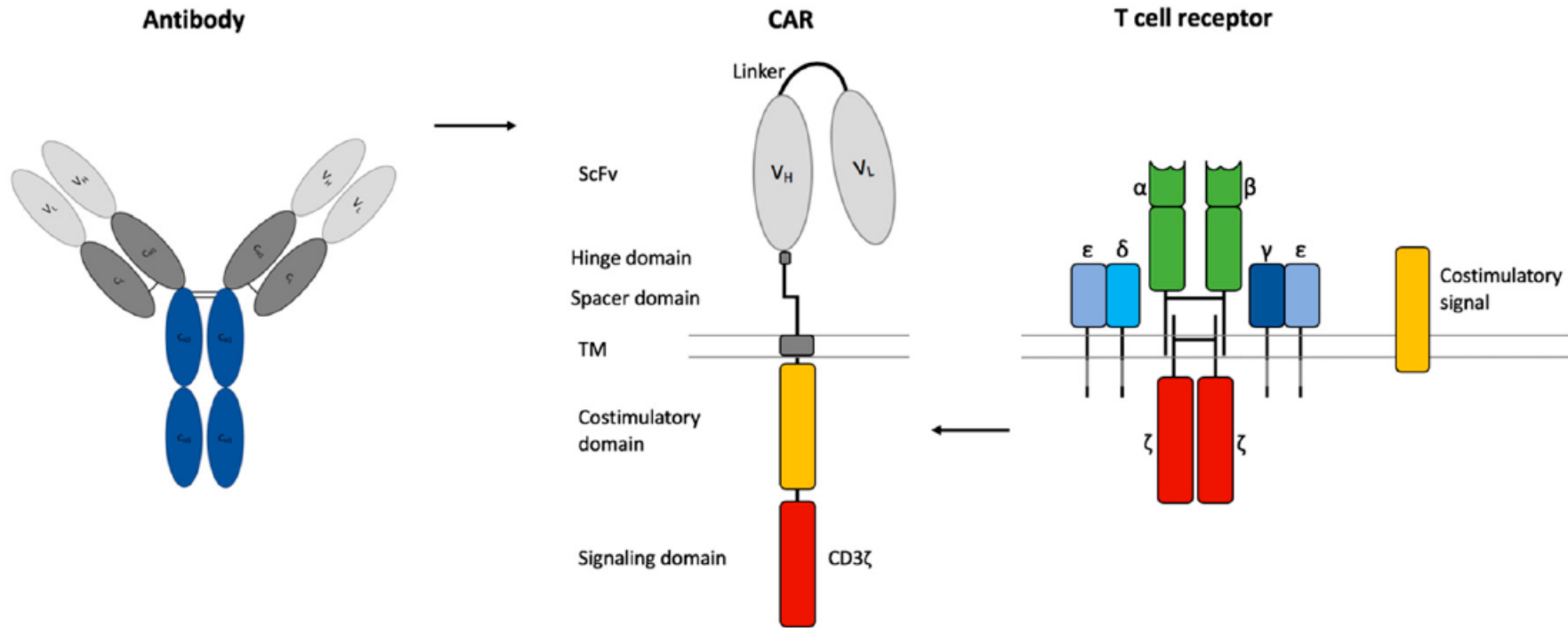
# T – Lymphozyt



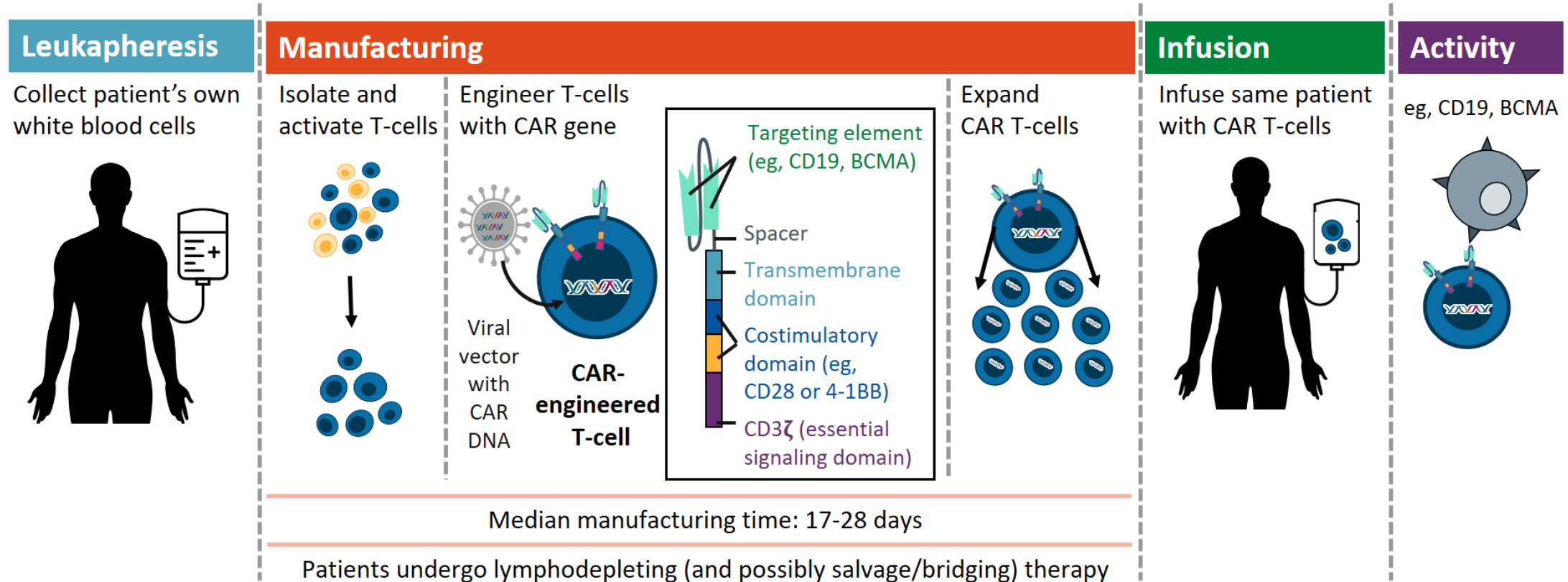
# CAR-T



# Chimärer Antigen Rezeptor? This is?

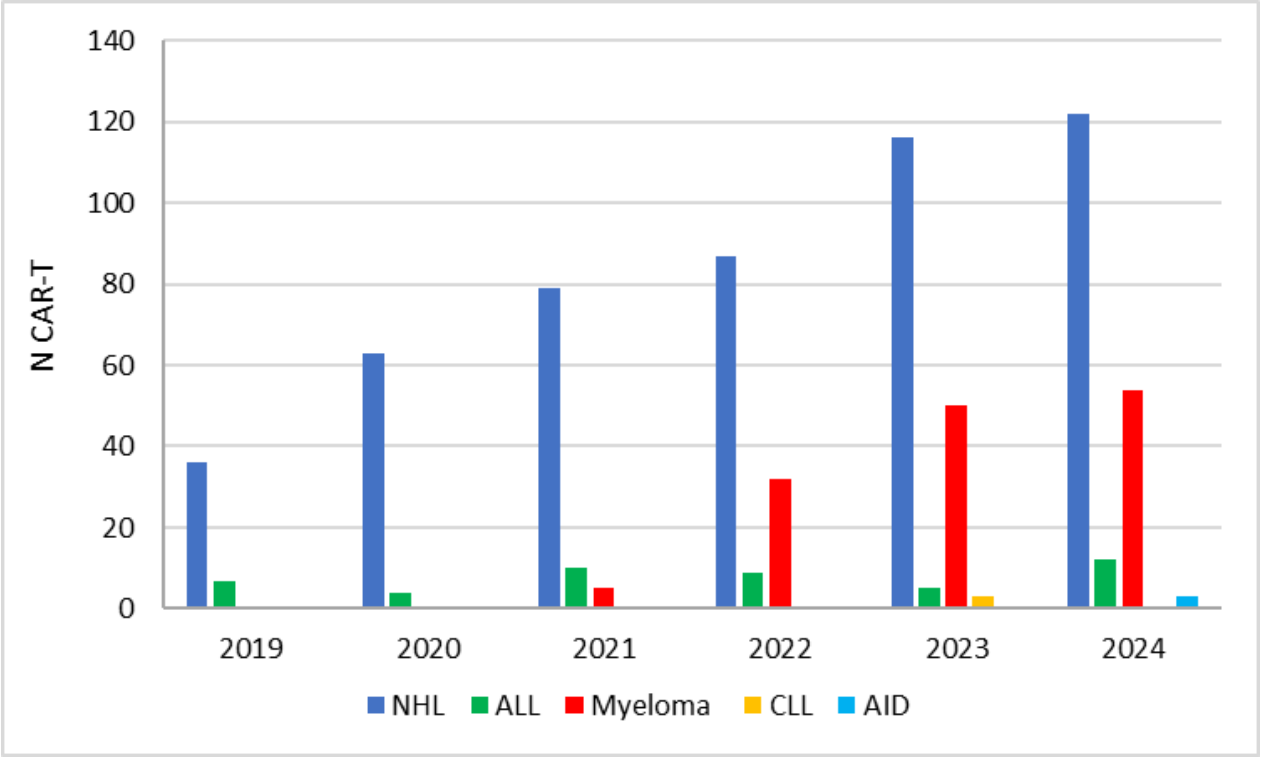


# Process CAR-T Production

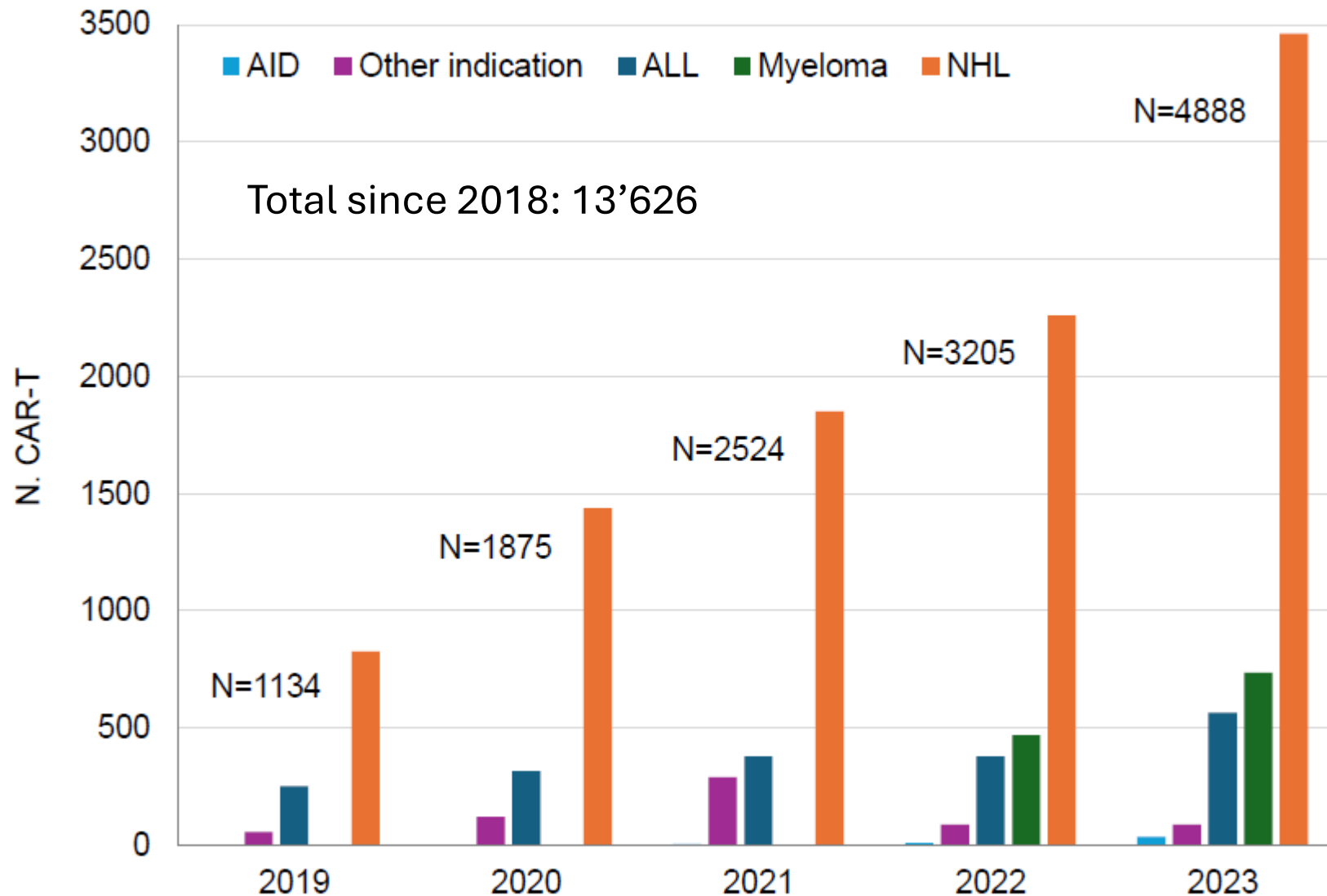


# CAR-T therapies: overview by diagnosis and year: 2019-2024

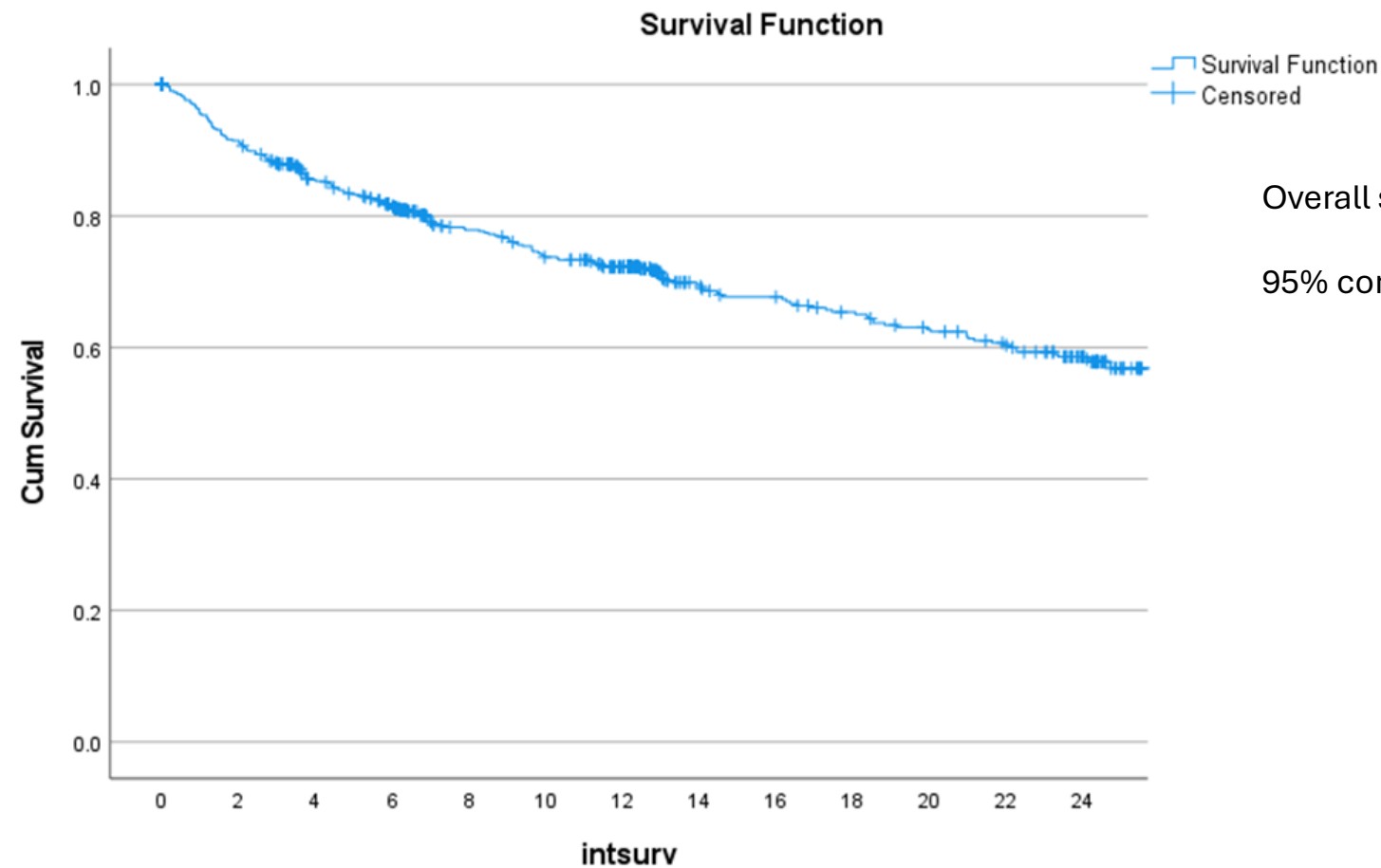
| CAR-T   | 2019 | 2020 | 2021 | 2022 | 2023 | 2024 | Total |
|---------|------|------|------|------|------|------|-------|
| NHL     | 36   | 63   | 79   | 87   | 116  | 122  | 503   |
| ALL     | 7    | 4    | 10   | 9    | 5    | 12   | 47    |
| Myeloma | 0    | 0    | 5    | 32   | 50   | 54   | 141   |
| CLL     | 0    | 0    | 0    | 0    | 3    | 0    | 3     |
| AID     | 0    | 0    | 0    | 0    | 0    | 3    | 3     |
| Total   | 43   | 67   | 94   | 128  | 174  | 191  | 697   |



# Number of CAR-T patients Europe 2018 - 2023



# CAR-T therapy: Outcome: 2019-2024

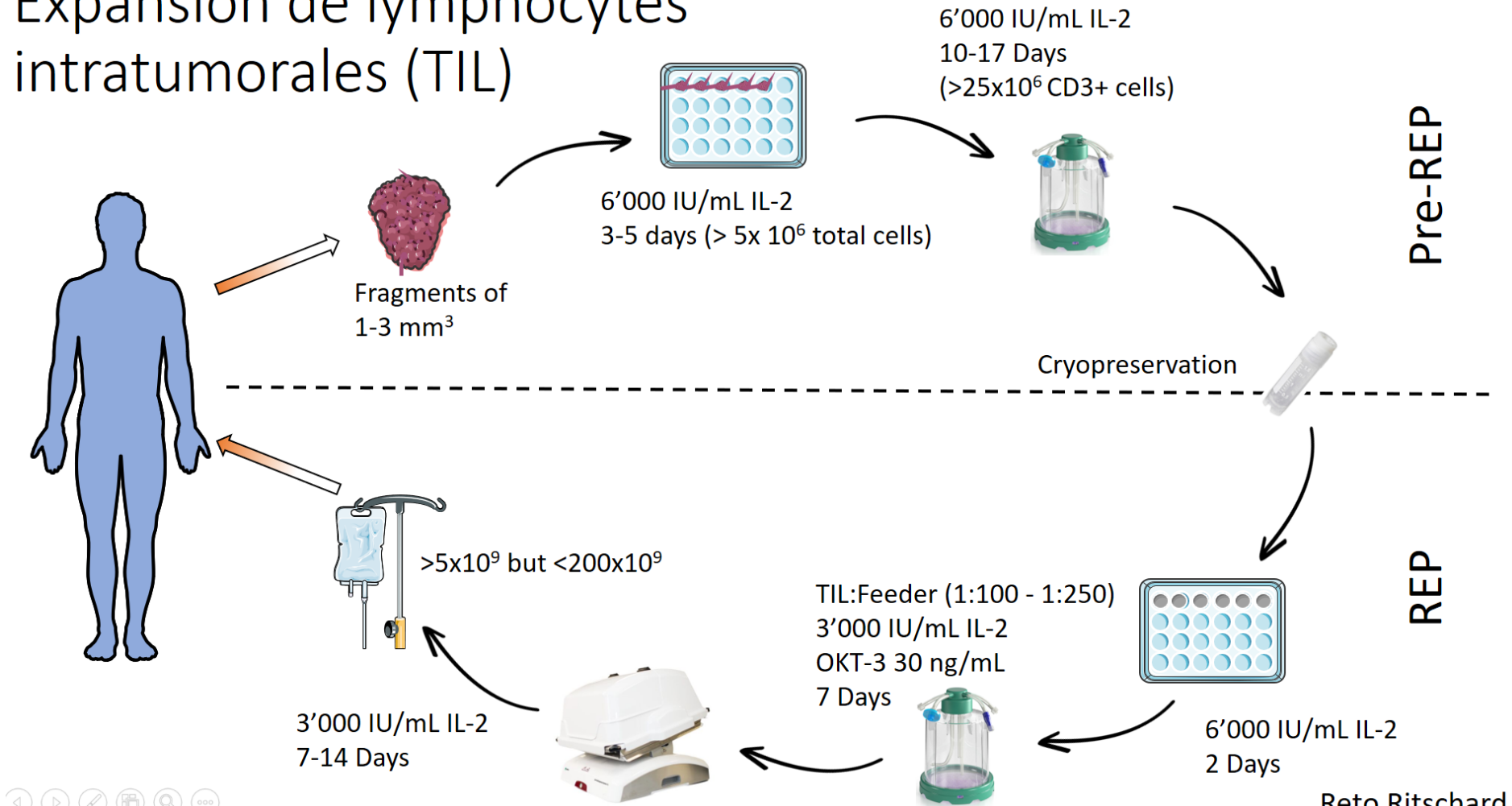


Overall survival at 2 years post therapy: 58%

95% confidence interval: 53-63%

# Tumor Infiltrierende Lymphozyten Expansion

Expansion de lymphocytes  
intratumorales (TIL)



Reto Ritschard

# How far will this go?

## How to avoid fratricide?

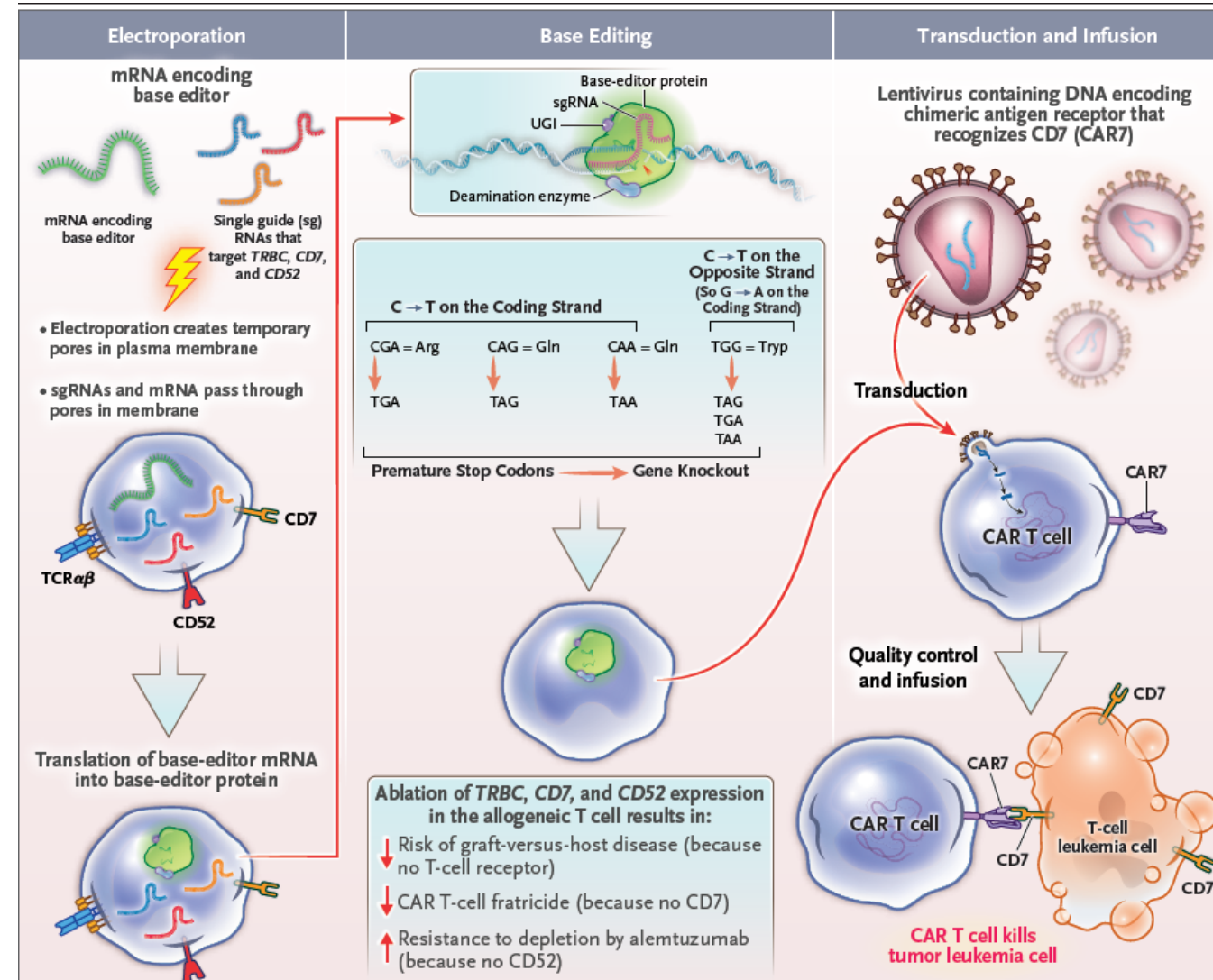
The NEW ENGLAND JOURNAL of MEDICINE

### ORIGINAL ARTICLE

## Base-Edited CAR7 T Cells for Relapsed and Refractory T-Cell Acute Lymphoblastic Leukemia

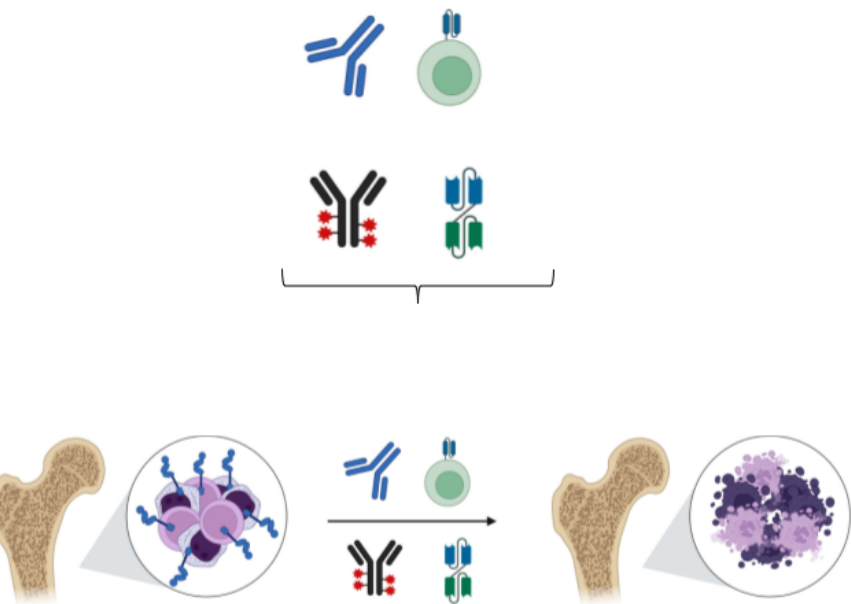
Robert Chiesa, M.D., Christos Georgiadis, Ph.D., Farhatullah Syed, Ph.D., Hong Zhan, Ph.D., Annie Etuk, Ph.D., Soragia Athina Gkazi, Ph.D., Roland Preece, Ph.D., Giorgio Ottaviano, M.D., Toni Braybrook, M.Bio., Jan Chu, M.Sc., Agnieszka Kubat, B.Sc., Stuart Adams, Ph.D., Rebecca Thomas, Ph.D., Kimberly Gilmour, Ph.D., David O'Connor, M.B., Ch.B., Ajay Vora, M.B., B.S., and Waseem Qasim, M.B., B.S., Ph.D., for the Base-Edited CAR T Group\*

Allogeneic CD7 spec CAR-T  
Ablate CD7  
Ablate CD52  
Ablate TCR



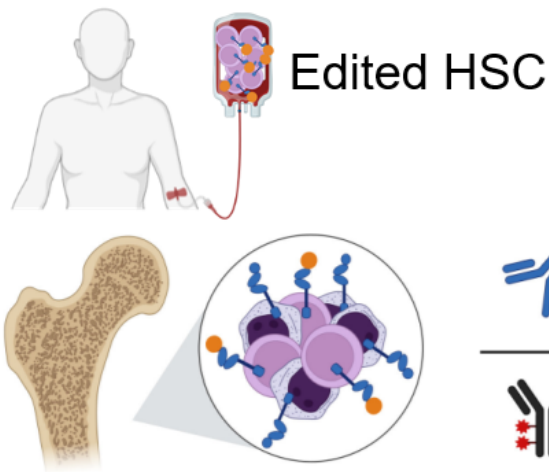
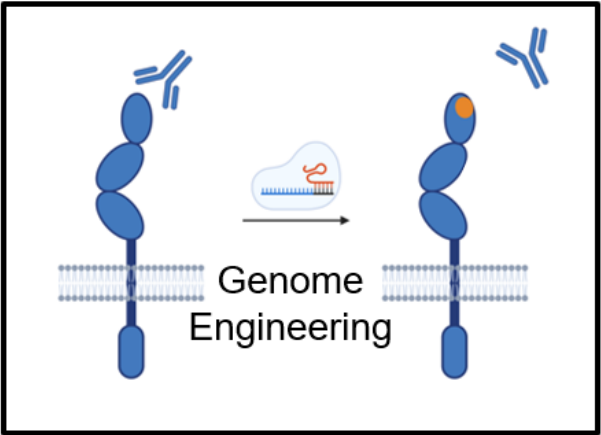
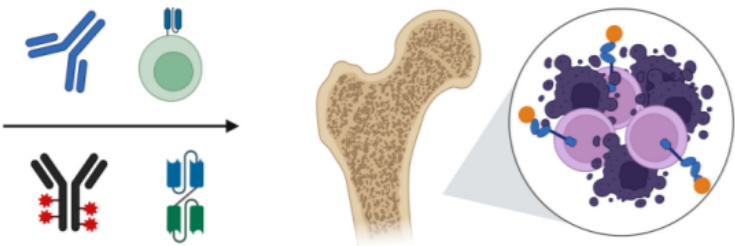
# HSCT with Epitope engineered HSC

## Antigen-specific approaches



**Cannot** discriminate diseased from healthy

## Solution:



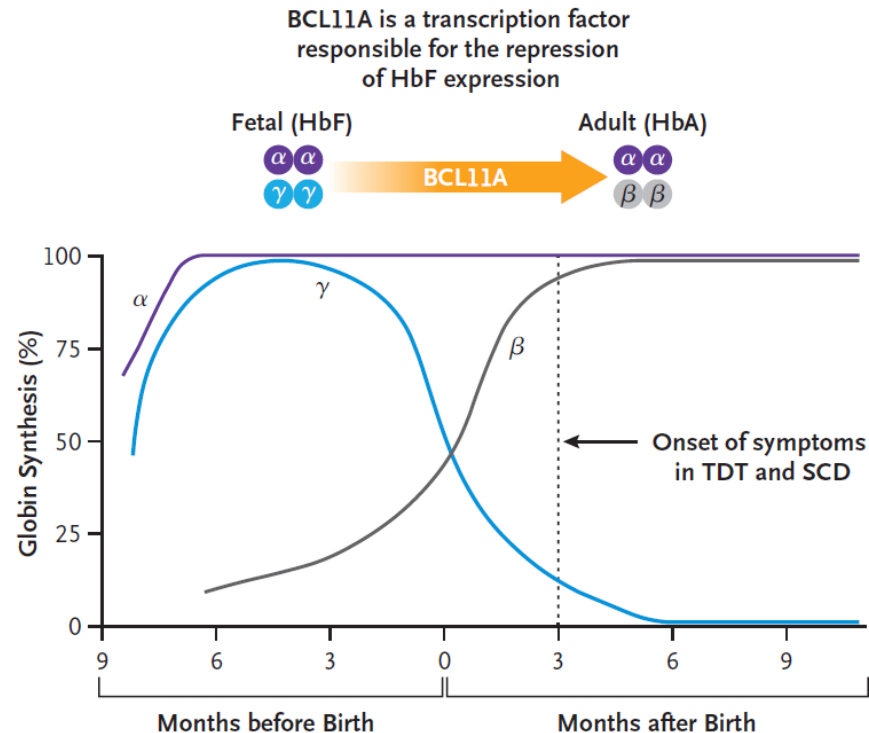
**Enables** antigen-specific post-transplant therapy

# CRISPR-Cas9 Gene Editing for Sickle Cell Disease and $\beta$ -Thalassemia

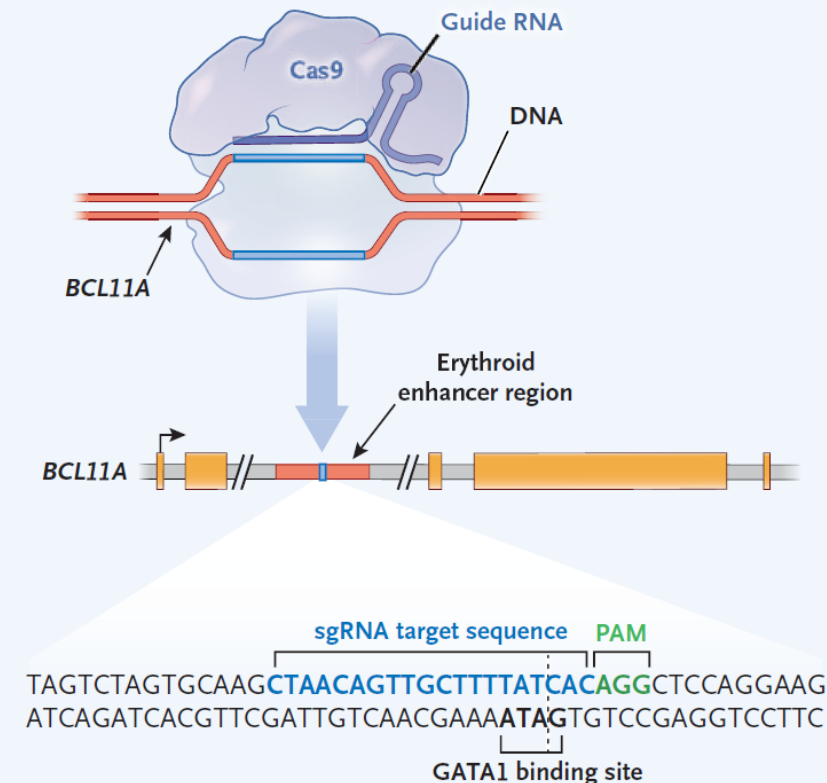
H. Frangoul, D. Altshuler, M.D. Cappellini, Y.-S. Chen, J. Domm, B.K. Eustace, J. Foell, J. de la Fuente, S. Grupp, R. Handgretinger, T.W. Ho, A. Kattamis, A. Kernytsky, J. Lekstrom-Himes, A.M. Li, F. Locatelli, M.Y. Mapara, M. de Montalembert, D. Rondelli, A. Sharma, S. Sheth, S. Soni, M.H. Steinberg, D. Wall, A. Yen, and S. Corbacioglu

*N Engl J Med* 2021;384:252-60.

## A Transition from Fetal to Adult Hemoglobin



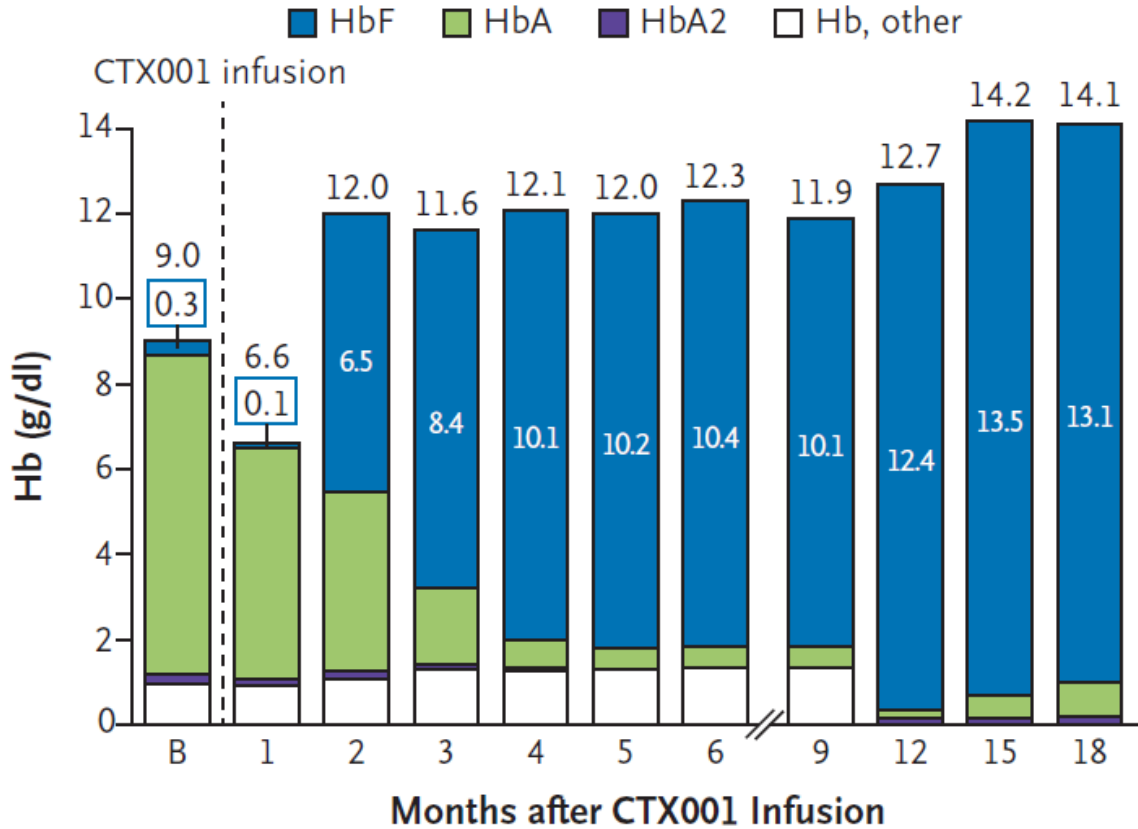
## B Targeting of Editing Site



# Autologous HCT; Bu conditioning

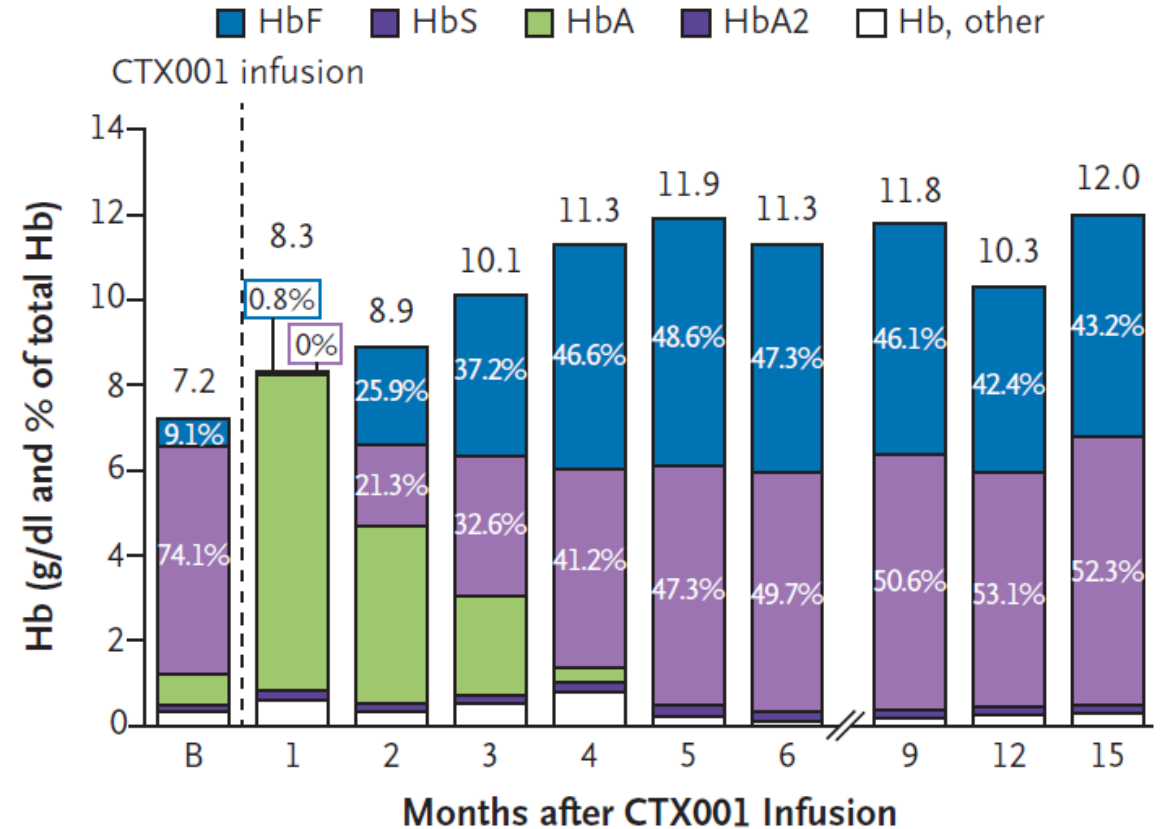
Patient 1

## A Hemoglobin Fractionation



Patient 2

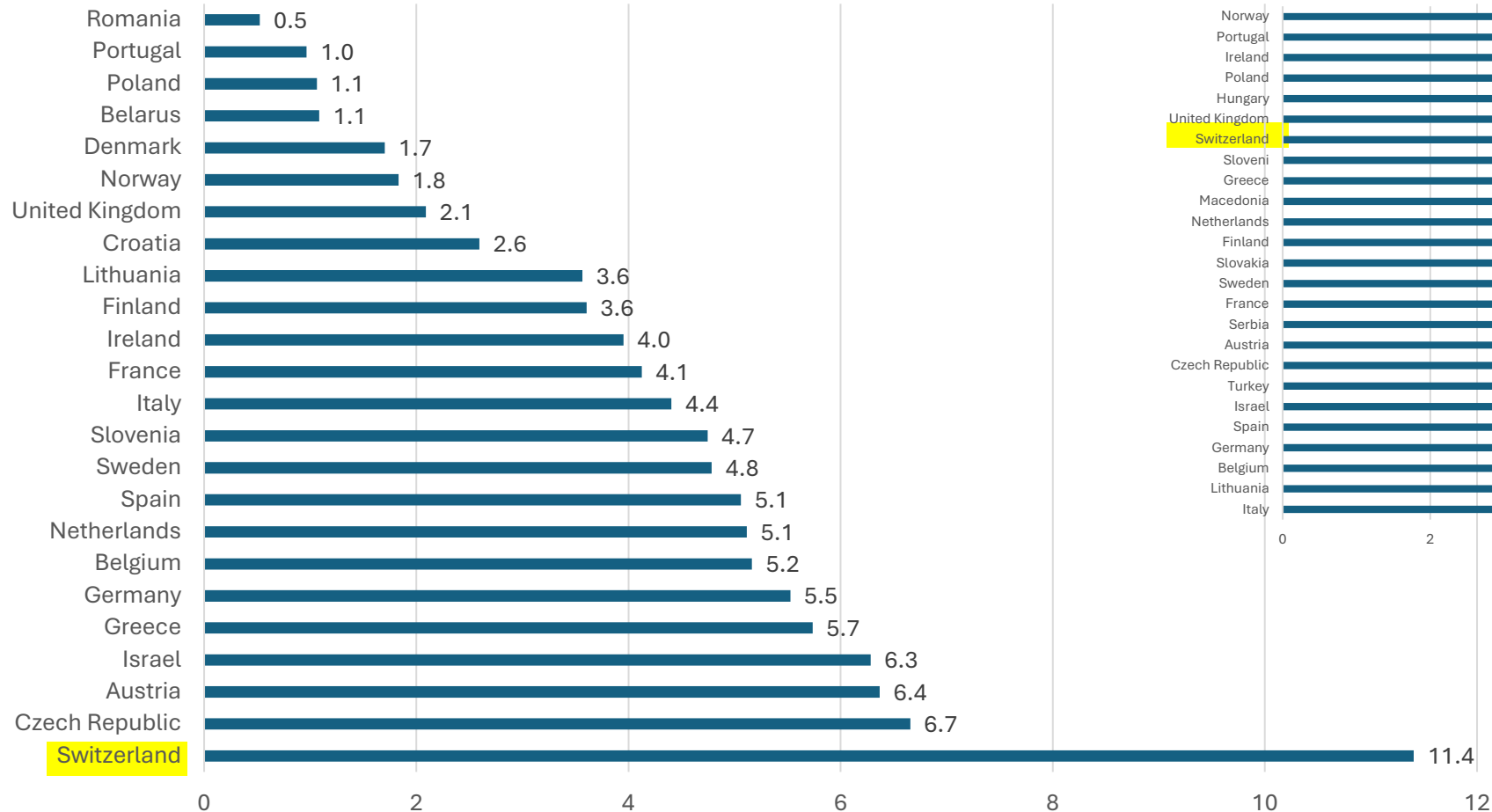
## D Hemoglobin Fractionation



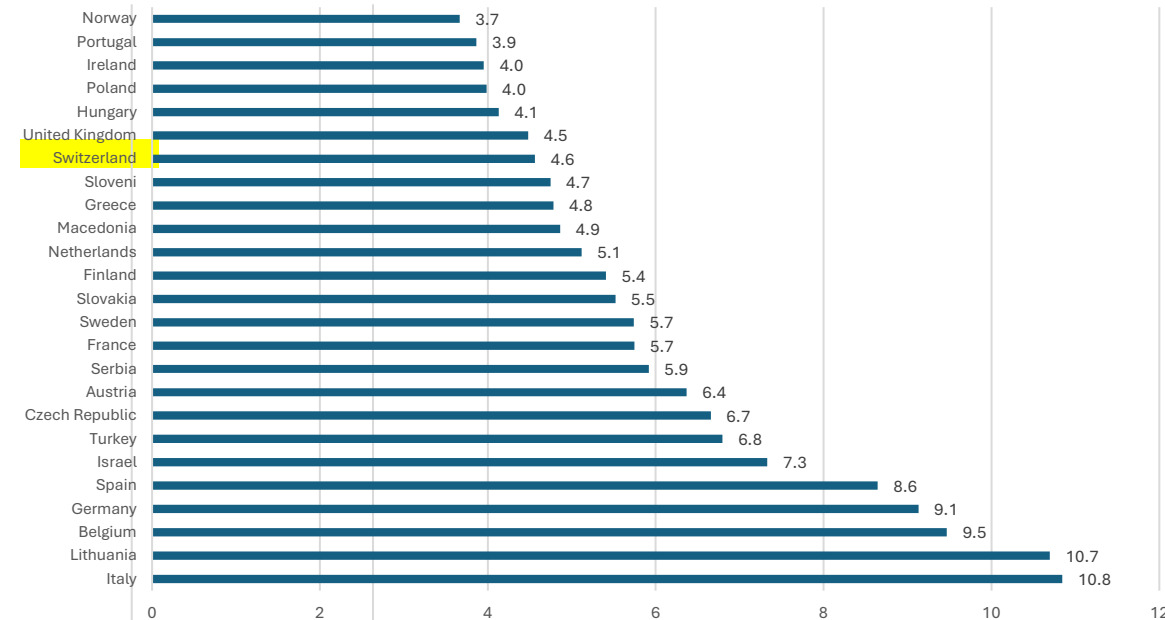
# Health policy HSM regulation in CH in 2022 # centers / 10Mio CAR-T / allogeneic



Density CART centers per 10 mil pop



Density allogeneic centers per 10 mil population





Long term  
consequences of  
intense treatment



Teamwork

**Danke für die Aufmerksamkeit**  
**Wir leben in aufregenden Zeiten**

**Zell Therapien haben die Medizin Praxis geändert**  
**Gentherapien werden die Medizin.....**

