USZ Universitäts Spital Zürich

Patientenveranstaltung «Lymphome»

Prof. Dr. med. Thorsten Zenz

Erik Aerts

PD Dr. med. Alexandre Theocharides

Medizinische Onkologie und Hämatologie

15. März 2022

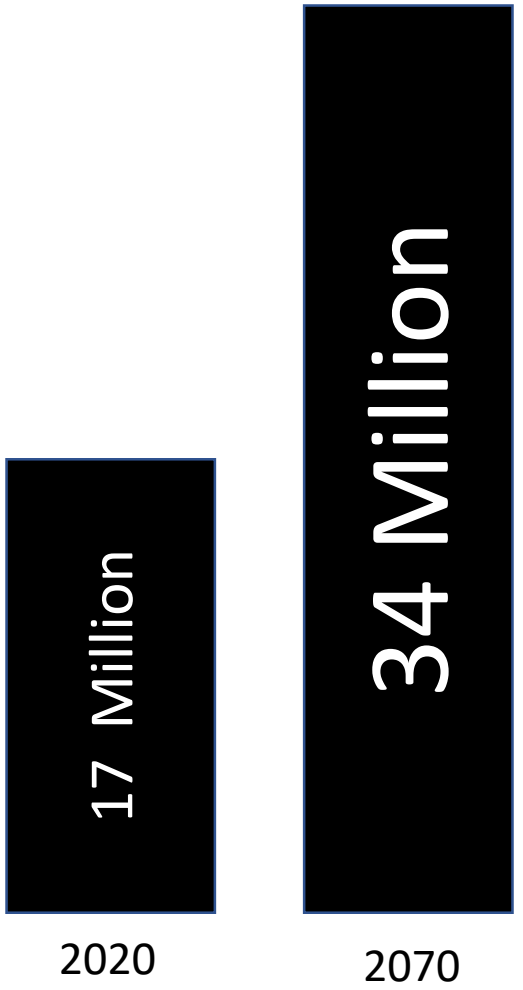
Programm

1.	Einleitung	PD Dr. med. Alexandre Theocharides
2.	Pflegeaspekte	Erik Aerts
3.	Hauptreferat	Prof. Dr. med. Thorsten Zenz
4.	Diskussion	Alle

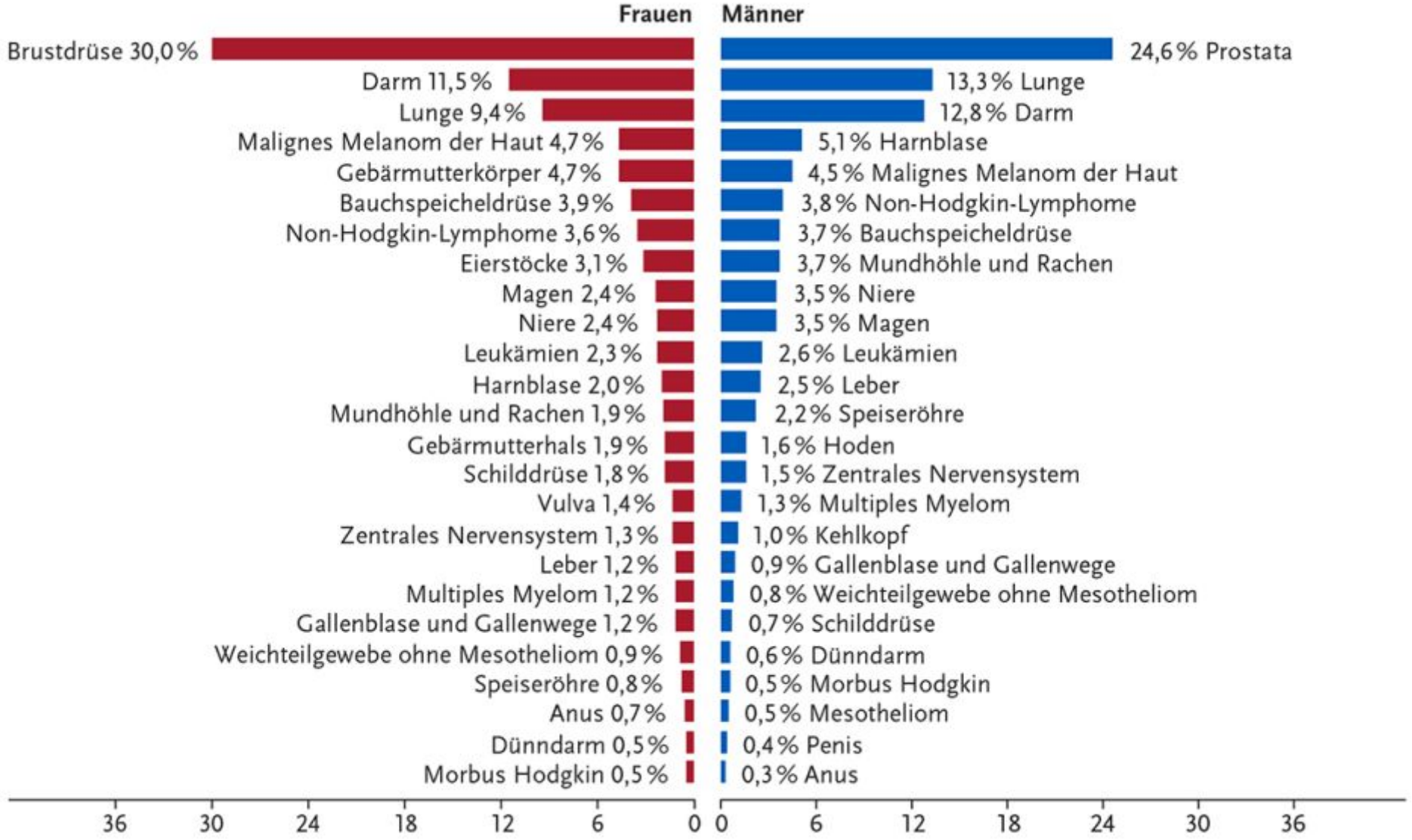
GLOBALE KREBS-INZIDENZ

Verdoppelung der Krebs-Inzidenz bis 2070 vorausgesagt

Entspricht 34 Millionen Krebs-Neudiagnosen in 2070



Nat Rev Clin Oncol . 2021 Oct;18



Lymphome machen ca. 4% aller Krebserkrankungen aus

www.krebsinformationsdienst.de

2. Pflegerische Aspekte

Pflegerische Aufgaben

- Stationäre und ambulante Betreuung und Begleitung
- Verabreichung und Überwachung von Therapien
- Durchführung / Mithilfe bei diagnostischen Massnahmen
- Psychosoziale Begleitung

Pflegerische Schwerpunkte

- Durchführung und Begleitung während der Therapie

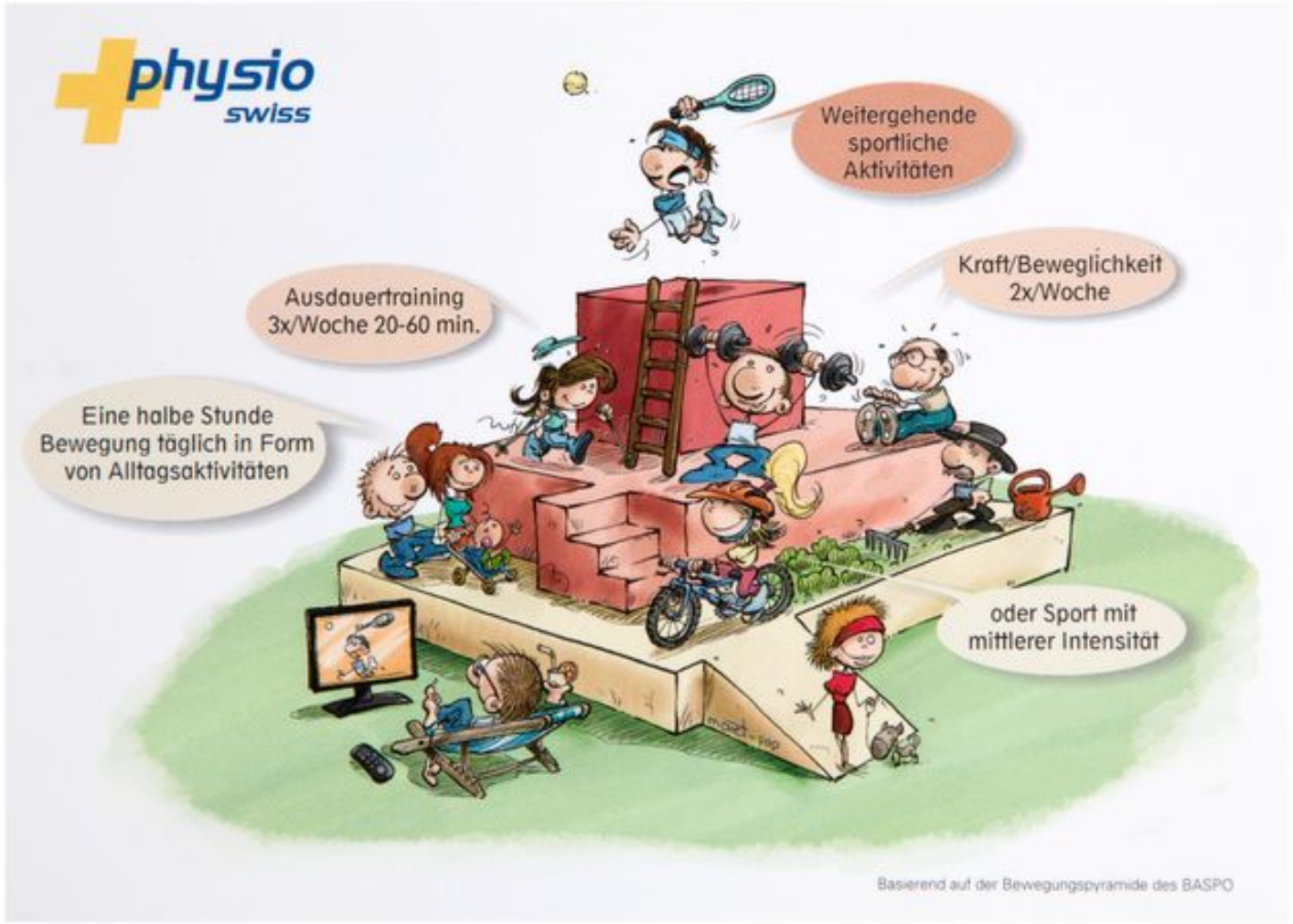
- Verabreichung und Überwachung der Chemotherapie, Medikamente und Blutprodukte gemäss ärztlicher Verordnung
- Sorgfältige Überwachung und Beobachtung der Patienten,
  Einsatz systematischer Assessmentinstrumente, z.B. **Belastungsthermometer**
- Überwachung von venösen Zugängen /
  Blutentnahmen
- Sicherstellung einer kontinuierlichen Betreuung

Pflegerische Beratung

- Umgang mit Symptomen und Nebenwirkungen

– Fatigue (Müdigkeit)
  - Ruhepausen in Alltag einplanen
  - Gute Phasen nutzen
  - Körperliche Aktivität aufrechterhalten
– Appetitlosigkeit
  - regelmässig kleine Mahlzeiten über den Tag verteilt
  - (kalorienreiche) Zwischenmahlzeiten / Getränke
– Ansprechpersonen vermitteln (z.B. Ernährungsberatung, …)

(Elphee, 2008; Kelly, Dowling, & Meenaghan, 2011; Krebsliga Schweiz, 2014a, 2014b; Lynn et al., 2003; Wilkes, 2008)

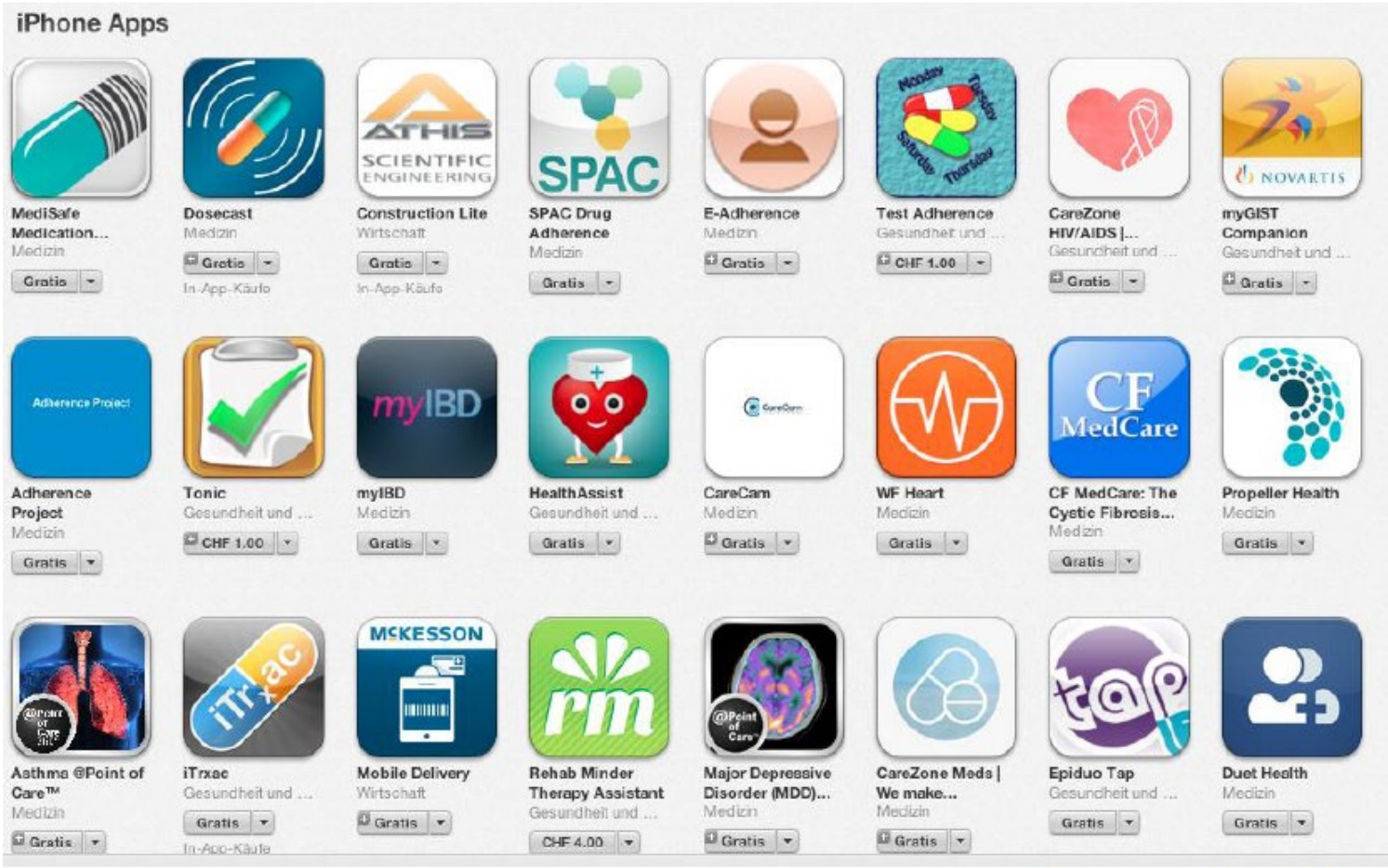

physio swiss
Weitergehende sportliche Aktivitäten
Kraft/Beweglichkeit 2x/Woche
Ausdauertraining 3x/Woche 20-60 min.
Eine halbe Stunde Bewegung täglich in Form von Alltagsaktivitäten
oder Sport mit mittlerer Intensität
Basierend auf der Bewegungspyramide des BASPO

Positive Auswirkungen des körperlichen Trainings

- Muskelkraft +
- Ausdauer +
- Fatigue +
- Angst, Selbstwahrnehmung
- Lebensqualität +

Speck; J Cancer Surviv, 2010

Medikamenteneinnahme

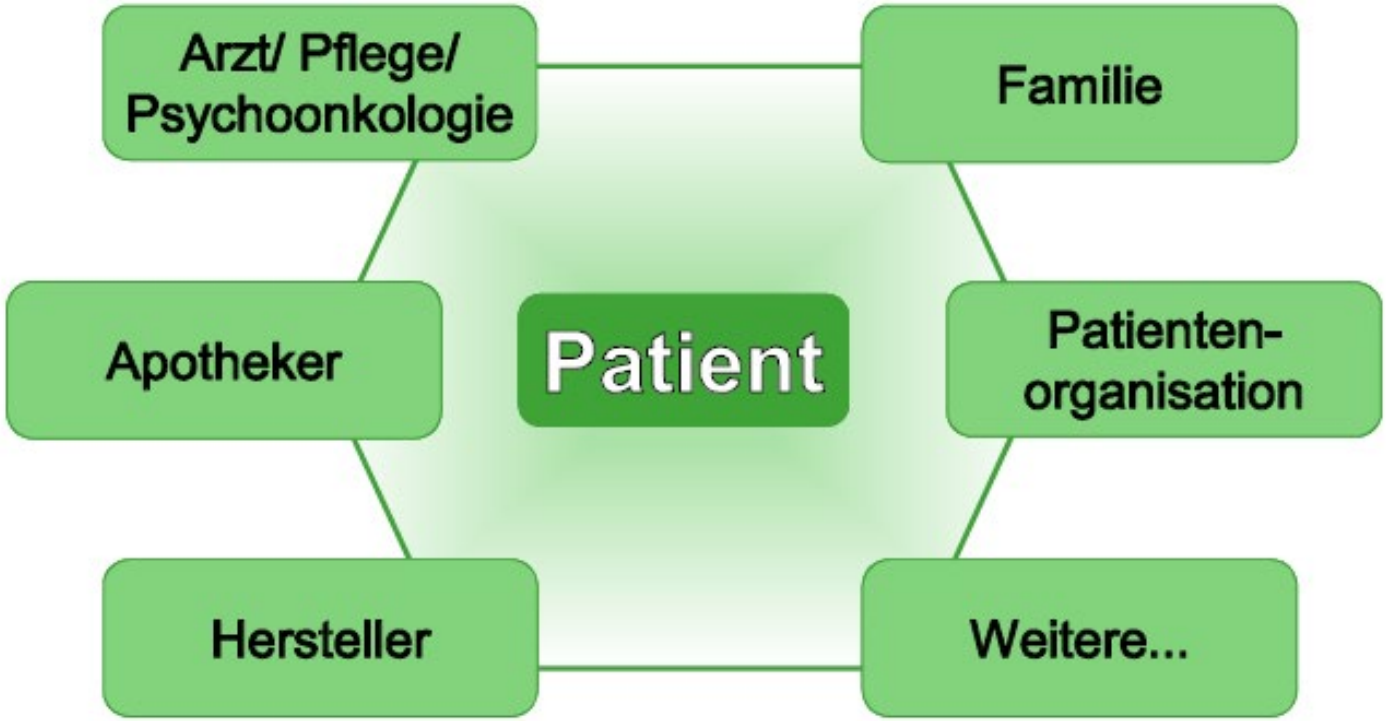


iTunes Auszug vom 11.05.2014

www.lymphome.ch

lymphome.ch
patientennetz
schweiz

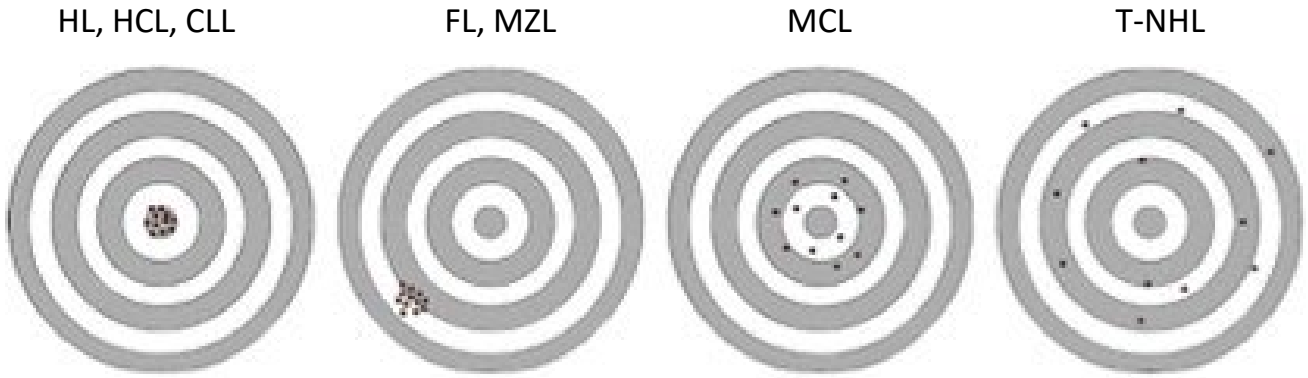
Zusammenarbeit zwischen…



- **(Arnet & Hersberger, 2010)**

3. Lymphome

Patientenveranstaltung Lymphome



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Thorsten Zenz

THE UPDATED WHO CLASSIFICATION OF HEMATOLOGICAL MALIGNANCIES

The 2016 revision of the World Health Organization classification of lymphoid neoplasms

Table 1. 2016 WHO classification of mature lymphoid, histiocytic, and dendritic neoplasms

Mature B-cell neoplasms
Chronic lymphocytic leukemia/small lymphocytic lymphoma
Monoclonal B-cell lymphocytosis*
B-cell prolymphocytic leukemia
Splenic marginal zone lymphoma
Hairy cell leukemia
Splenic B-cell lymphoma/leukemia, unclassifiable
Splenic diffuse red pulp small B-cell lymphoma
Hairy cell leukemia-variant
Lymphoplasmacytic lymphoma
Waldenström macroglobulinemia
Monoclonal gammopathy of undetermined significance (MGUS), IgM*
μ heavy-chain disease
γ heavy-chain disease
α heavy-chain disease
Monoclonal gammopathy of undetermined significance (MGUS), IgG/A*
Plasma cell myeloma
Solitary plasmacytoma of bone
Extraosseous plasmacytoma
Monoclonal immunoglobulin deposition diseases*
Extranodal marginal zone lymphoma of mucosa-associated lymphoid tissue (MALT lymphoma)
Nodal marginal zone lymphoma
Pediatric nodal marginal zone lymphoma
Follicular lymphoma
In situ follicular neoplasia*
Duodenal-type follicular lymphoma*
Pediatric-type follicular lymphoma*
*Large B-cell lymphoma with IRF4 rearrangement**
Primary cutaneous follicle center lymphoma
Mantle cell lymphoma
In situ mantle cell neoplasia*
Diffuse large B-cell lymphoma (DLBCL), NOS
Germinal center B-cell type*
Activated B-cell type*
T-cell/histiocyte-rich large B-cell lymphoma
Primary DLBCL of the central nervous system (CNS)
Primary cutaneous DLBCL, leg type
EBV$^+$ DLBCL, NOS*
*EBV$^+$ mucocutaneous ulcer**
DLBCL associated with chronic inflammation
Lymphomatoid granulomatosis
Primary mediastinal (thymic) large B-cell lymphoma
Intravascular large B-cell lymphoma
ALK$^+$ large B-cell lymphoma
Plasmablastic lymphoma
Primary effusion lymphoma
*HHV8$^+$ DLBCL, NOS**
Burkitt lymphoma
*Burkitt-like lymphoma with 11q aberration**
High-grade B-cell lymphoma, with *MYC* and *BCL2* and/or *BCL6* rearrangements*
High-grade B-cell lymphoma, NOS*
B-cell lymphoma, unclassifiable, with features intermediate between DLBCL and classical Hodgkin lymphoma
Mature T and NK neoplasms
T-cell prolymphocytic leukemia
T-cell large granular lymphocytic leukemia
Chronic lymphoproliferative disorder of NK cells
Aggressive NK-cell leukemia
Systemic EBV$^+$ T-cell lymphoma of childhood*
Hydroa vacciniforme-like lymphoproliferative disorder*
Adult T-cell leukemia/lymphoma
Extranodal NK-/T-cell lymphoma, nasal type
Enteropathy-associated T-cell lymphoma

Table 1. (continued)

Monomorphic epitheliotropic intestinal T-cell lymphoma*
*Indolent T-cell lymphoproliferative disorder of the GI tract**
Hepatosplenic T-cell lymphoma
Subcutaneous panniculitis-like T-cell lymphoma
Mycosis fungoides
Sézary syndrome
Primary cutaneous CD30$^+$ T-cell lymphoproliferative disorders
Lymphomatoid papulosis
Primary cutaneous anaplastic large cell lymphoma
Primary cutaneous γδ T-cell lymphoma
*Primary cutaneous CD8$^+$ aggressive epidermotropic cytotoxic T-cell lymphoma**
*Primary cutaneous acral CD8$^+$ T-cell lymphoma**
*Primary cutaneous CD4$^+$ small/medium T-cell lymphoproliferative disorder**
Peripheral T-cell lymphoma, NOS
Angioimmunoblastic T-cell lymphoma
*Follicular T-cell lymphoma**
*Nodal peripheral T-cell lymphoma with TFH phenotype**
Anaplastic large-cell lymphoma, ALK$^+$
Anaplastic large-cell lymphoma, ALK$^-$*
*Breast implant-associated anaplastic large-cell lymphoma**
Hodgkin lymphoma
Nodular lymphocyte predominant Hodgkin lymphoma
Classical Hodgkin lymphoma
Nodular sclerosis classical Hodgkin lymphoma
Lymphocyte-rich classical Hodgkin lymphoma
Mixed cellularity classical Hodgkin lymphoma
Lymphocyte-depleted classical Hodgkin lymphoma
Posttransplant lymphoproliferative disorders (PTLD)
Plasmacytic hyperplasia PTLD
Infectious mononucleosis PTLD
Florid follicular hyperplasia PTLD*
Polymorphic PTLD
Monomorphic PTLD (B- and T-/NK-cell types)
Classical Hodgkin lymphoma PTLD
Histiocytic and dendritic cell neoplasms
Histiocytic sarcoma
Langerhans cell histiocytosis
Langerhans cell sarcoma
Indeterminate dendritic cell tumor
Interdigitating dendritic cell sarcoma
Follicular dendritic cell sarcoma
Fibroblastic reticular cell tumor
Disseminated juvenile xanthogranuloma
Erdheim-Chester disease*

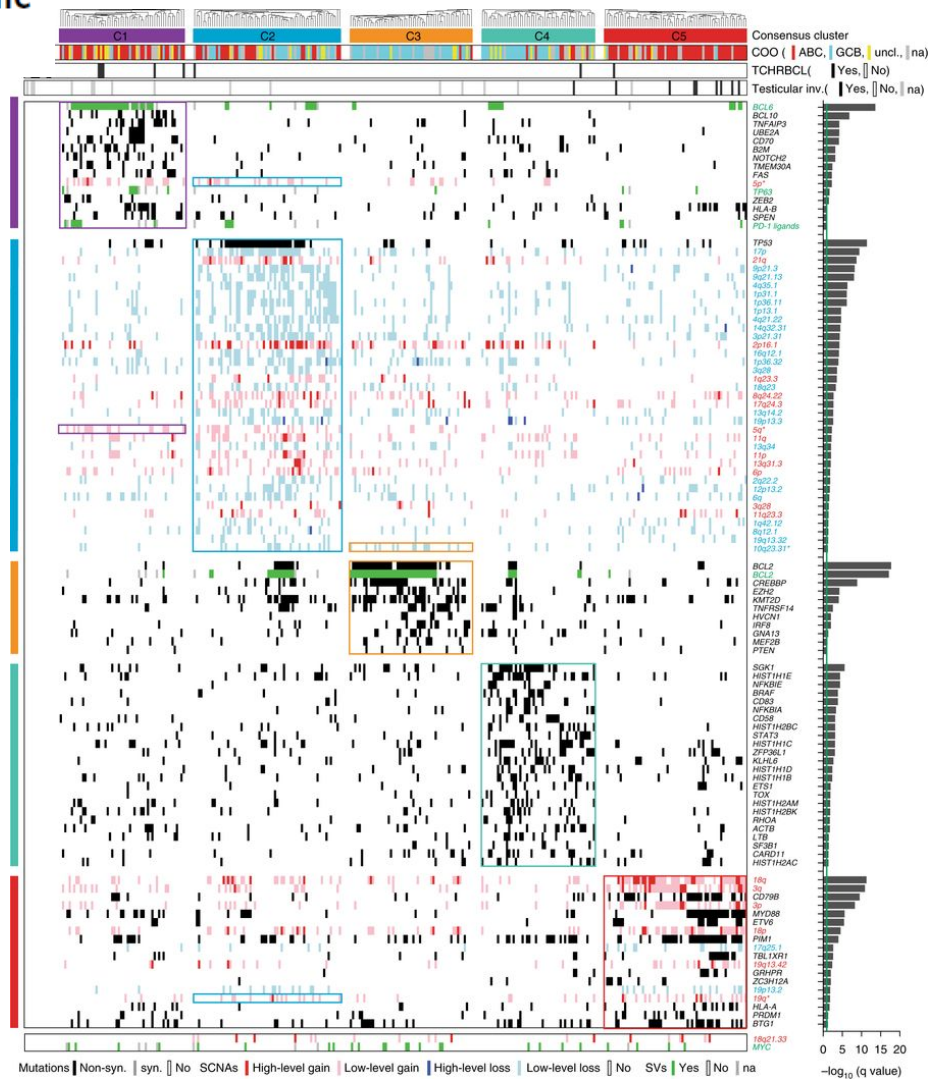
Provisional entities are listed in italics.
*Changes from the 2008 classification.

small population, but in others associated with a lymphocytosis.[4] Whereas in 2008 it was unknown whether MBL was a precursor of CLL, we now know that MBL precedes virtually all cases of **CLL/small lymphocytic lymphoma** (SLL).[5] The updated WHO will retain the current criteria for MBL, but will emphasize that "low-count" MBL, defined as a PB CLL count of $<0.5 \times 10^9$/L, must be distinguished from "high-count" MBL because low count MBL has significant differences from CLL, an extremely limited, if any, chance of progression, and, until new evidence is provided, does not require routine follow-up outside of standard medical care.[6,7] In contrast, high-count MBL requires routine/yearly follow-up, and has very similar phenotypic and genetic/molecular features as Rai stage 0 CLL, although immunoglobulin heavy chain variable region (IGHV)-mutated cases are more frequent in MBL.[8] Also impacting our diagnostic criteria, the revision will eliminate the option to diagnose CLL with $<5 \times 10^9$/L PB CLL cells in the absence of extramedullary

Diagnose muss stimmen

nature medicine
RESOURCE
https://doi.org/10.1038/s41591-018-0016-8

Molecular subtypes of diffuse large B cell lymphoma are associated with distinct pathogenic mechanisms and outcomes



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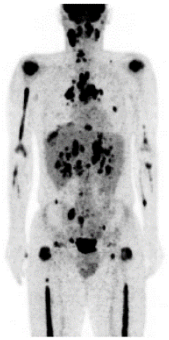
Es wird immer komplizierter

Clonal evolution by circulating tumour DANN

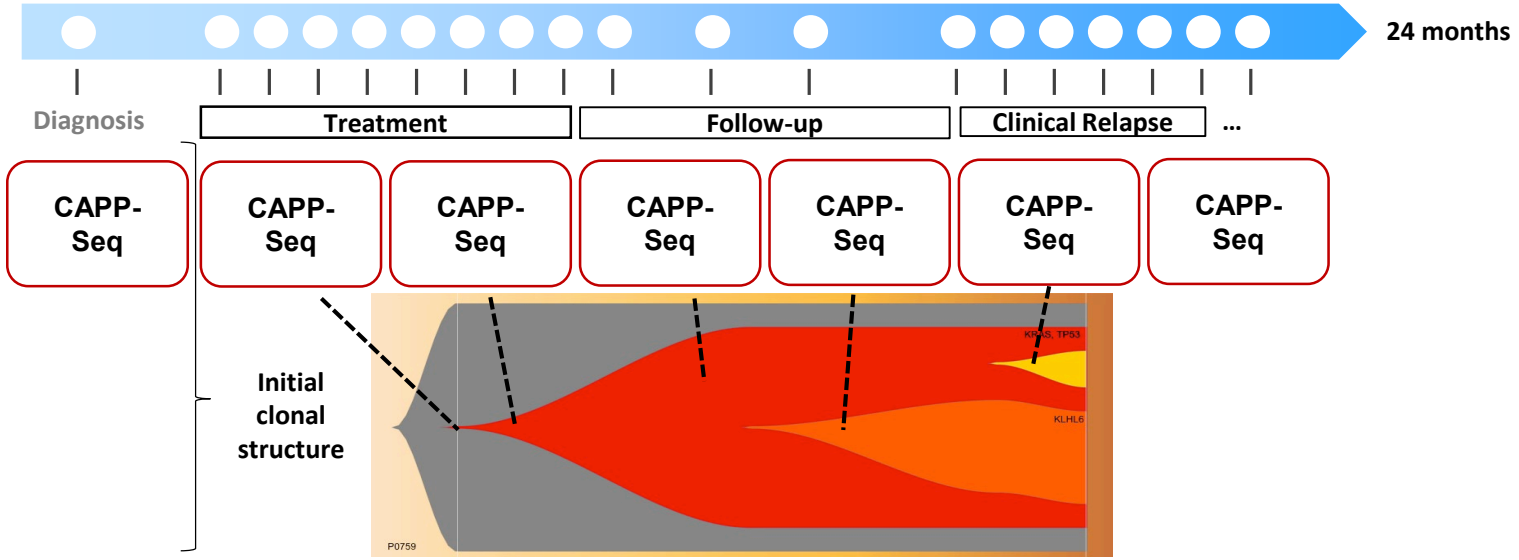
Spuren des Lymphoms im Blut nachweisen



Imaging

Clinical data

- Study of **liquid biopsy** after every therapy and planned follow-up –



5-15ml zusätzliches Blut

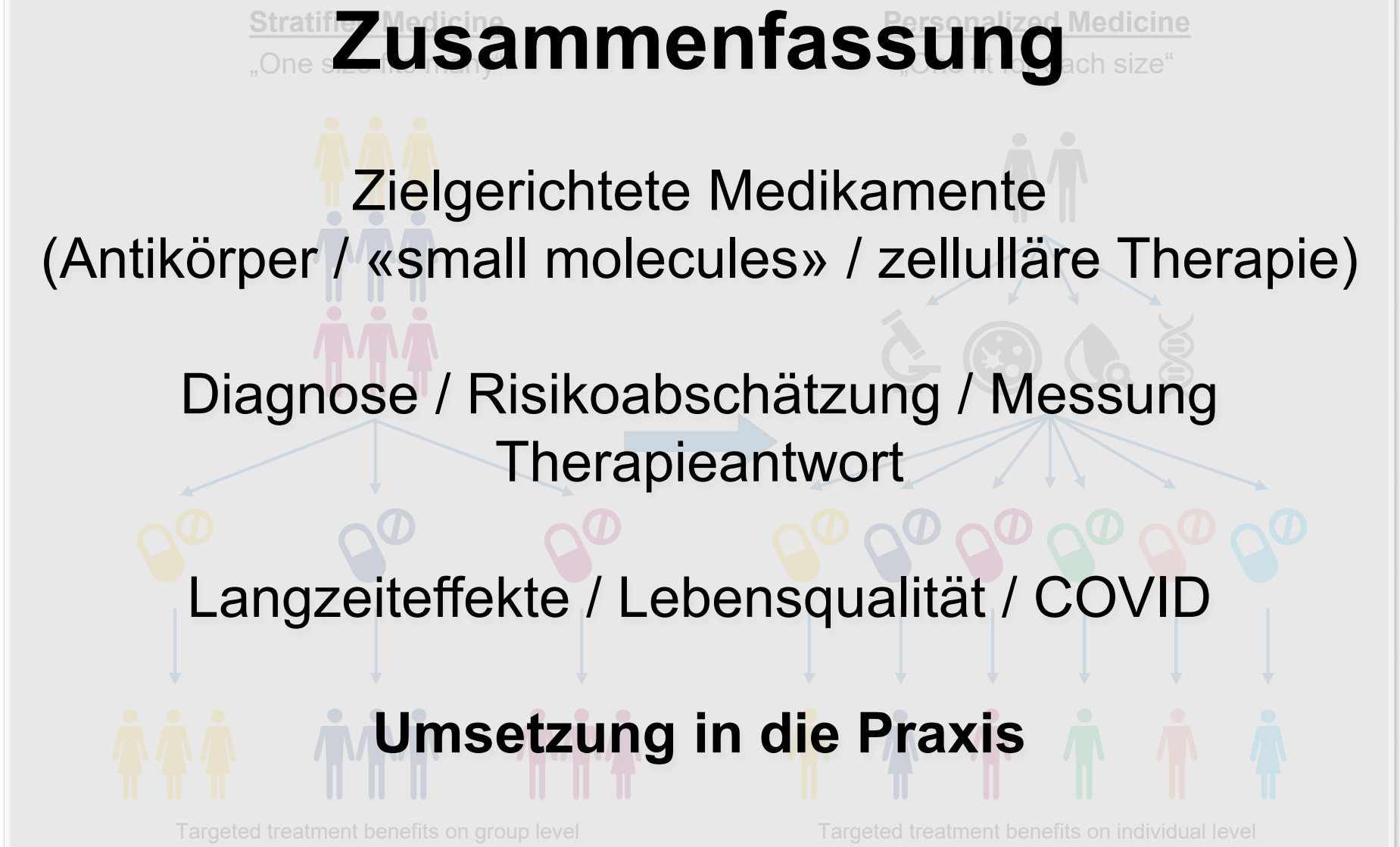
Zusammenfassung

Zielgerichtete Medikamente
(Antikörper / «small molecules» / zellulläre Therapie)

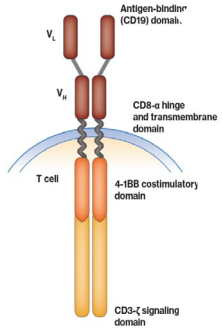
Diagnose / Risikoabschätzung / Messung Therapieantwort

Langzeiteffekte / Lebensqualität / COVID

Umsetzung in die Praxis



Präzisionsmedizin in der Therapie der Lymphome



Gentherapie (CAR-T)

Messbare Resterkrankung/funktionelle Bildgebung

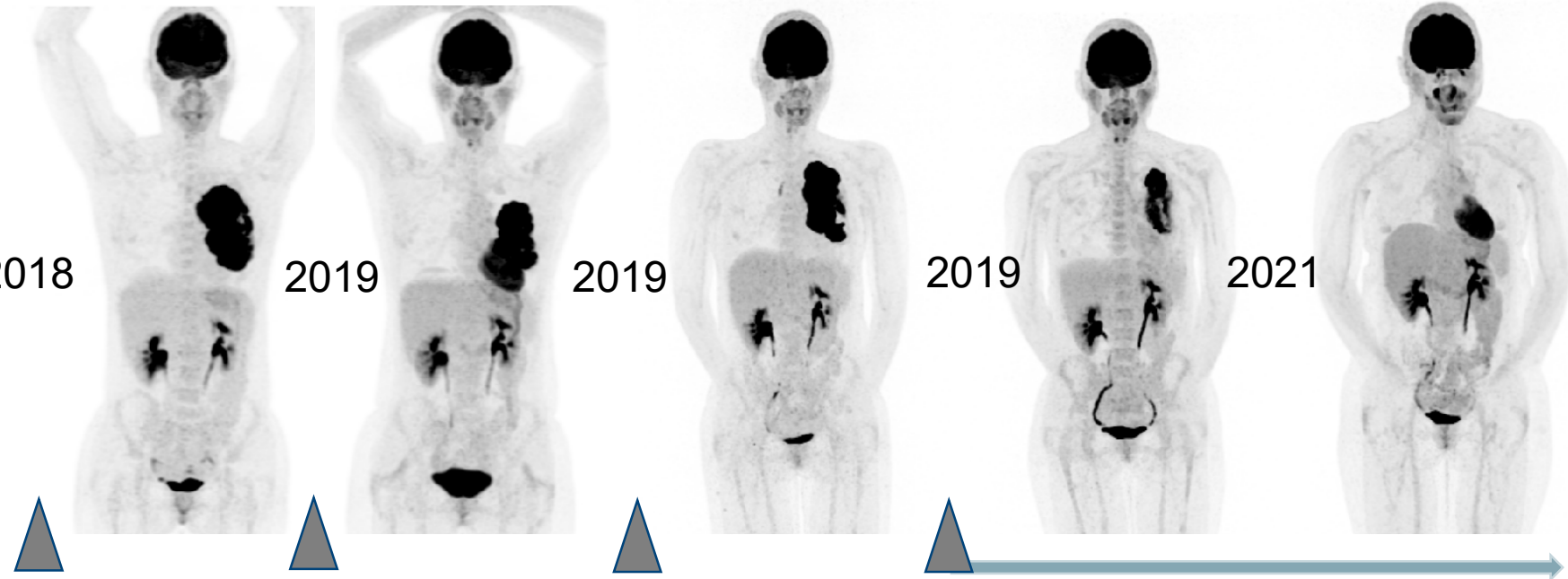
Immuntherapie

Präzise Strahlentherapie

Zielgerichtete Inhibitoren
(essentieller Signalwege des Tumors)

Fallbeispiel: 32-jährige Patientin

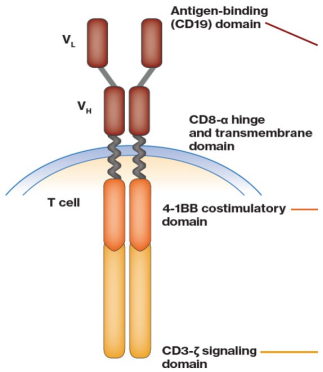
Chemoimmuntherapie und CAR-T refraktäres DLBCL



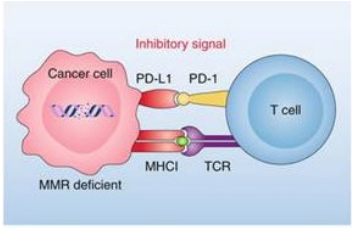
R-CHOP

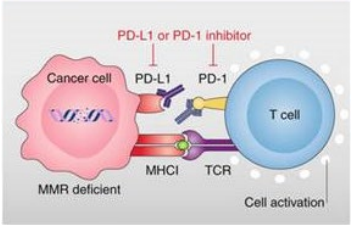
3 Zyklen R-ICE + Brentuximab

CAR-T



Checkpoint Inhibitor





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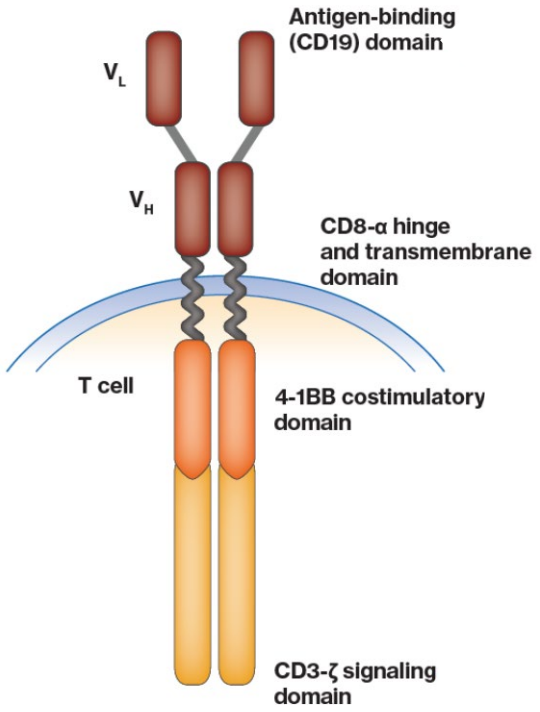
Chimeric Antigen Receptor T Cell Therapy- Tisagenlecleucel (CTL019)1-3

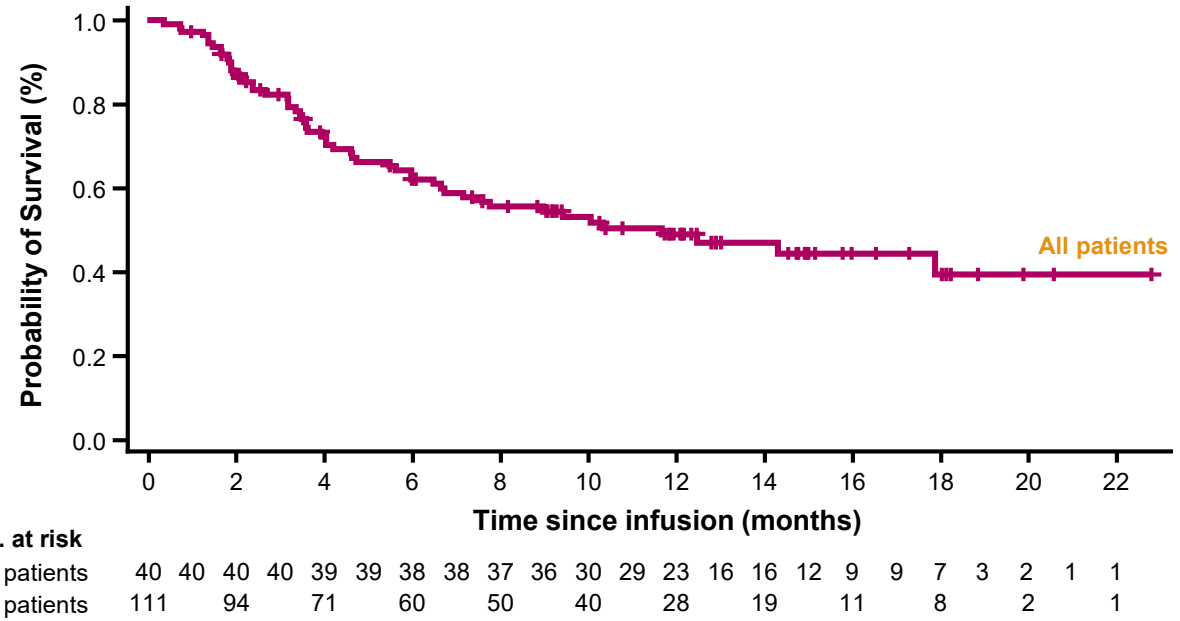
First approved CAR-T cell therapy in the United States

- August 2017: for patients up to 25 years of age with B-cell precursor ALL refractory or in second or later relapse
- May 2018: for adult patients with r/r DLBCL after 2 or more lines of systemic therapy, based on the phase 2 JULIET study



1. Milone MC, et al. *Mol Ther*. 2009;17:1453-1464. 2. Zhang H, et al. *J Immunol*. 2007;179:4910-4918.
3. Kalos M, et al. *Sci Transl Med*. 2011;3:95ra73.

JULIET Studie: CAR-T Zelltherapie



Median, mo (95% CI)
CR patients, NE (17.9-NE)
All patients, 11.7 (6.6-NE)

Overall survival at 12 mo

- **49% among all infused patients**
- **95% among CR patients**

CR, complete response; NE, not evaluable.

NZZ 7.1.22

«Dann hast du keine Chance»:
Eine Krankenkasse lässt ihren Kunden sterben, weil das rettende Medikament zu teuer ist

In der Grundversicherung gelten theoretisch für alle die gleichen Regeln.

Kritiker sprechen von einer «Lotterie».

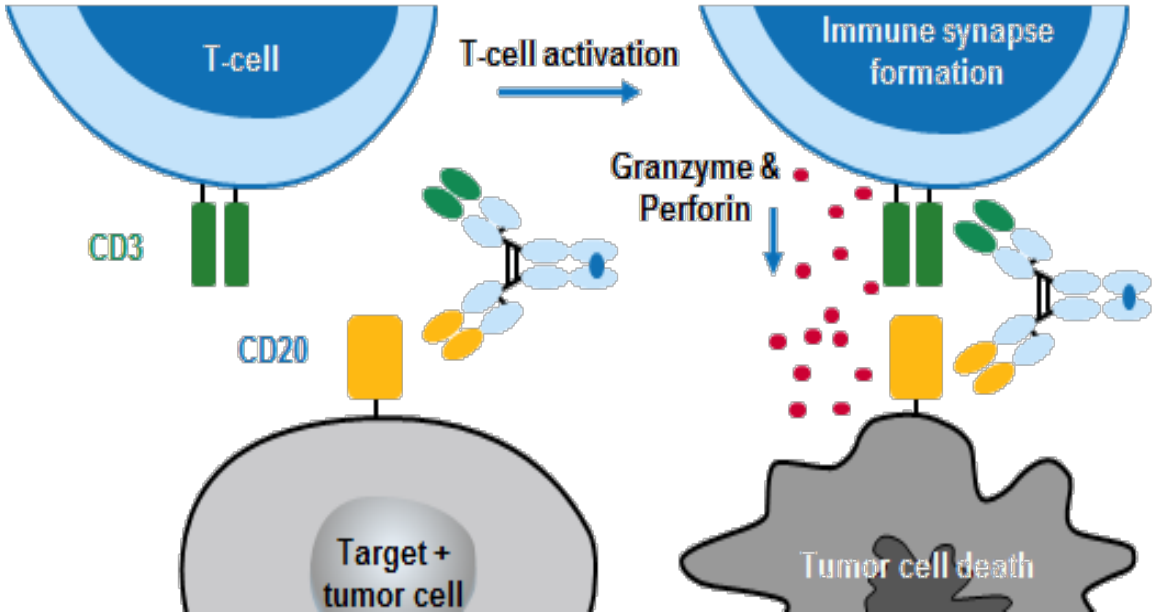
CAR-T vs. Bispezifische Antikörper

Mosunetuzumab Induces Complete Remissions In Poor Prognosis Non-Hodgkin Lymphoma Patients, Including Those Who Are Resistant To Or Relapsing After Chimeric Antigen Receptor T-cell (CAR-T) Therapies, And Is Active In Treatment Through Multiple Lines

Stephen J Schuster et al

Hintergrund bispezifische AK

- Mosunetuzumab (RG7828; BTCT4465A)

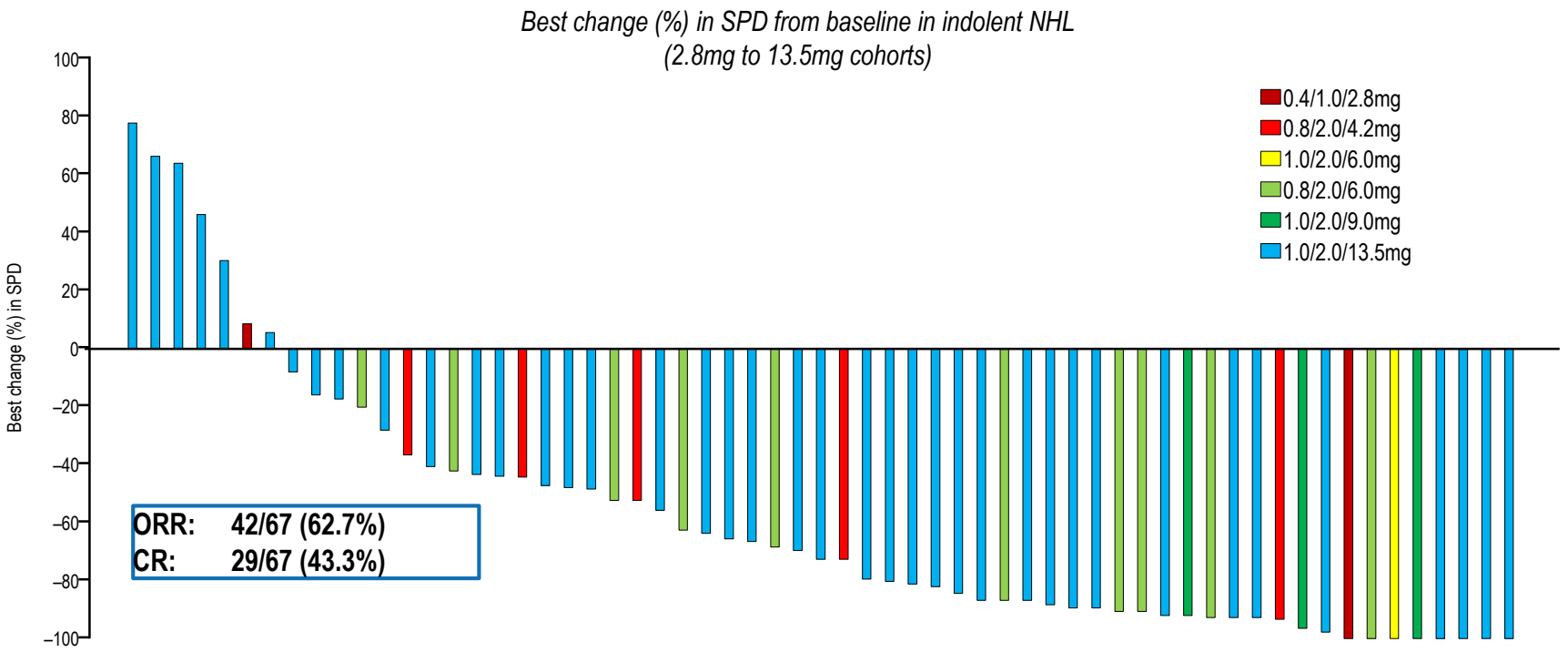


Registry number: NCT02500407

CRS, cytokine release syndrome; NHL, non-Hodgkin lymphoma; pts, patients; R/R, relapsed or refractory; TILs, tumor-infiltrating lymphocytes

1. Sun et al. Sci Transl Med 2015
2. Budde et al. ASH 2018; 3 Bartlett et al. ASCO 2019

Objective response rate in indolent NHL



Indolent NHL: FL (Grade 1–3A), marginal zone lymphoma and small lymphocytic lymphoma
CCOD: Aug 9, 2019

Verfügbar in klinischen Studien und compassionate use

Zusammenfassung

Zielgerichtete Medikamente
(Antikörper / «small molecules» / zellulläre Therapie)

Diagnose / Risikoabschätzung / Messung Therapieantwort

Langzeiteffekte / Host-Faktoren

Umsetzung in die Praxis (Klinische Studien)

Studien am USZ (Lymhome - Auswahl)

A multi-center, open label, uncontrolled, phase II clinical trial evaluating the safety and efficacy of Venetoclax in combination with Atezolizumab and Obinutuzumab in Richter Transformation of CLL

A Phase III, Open-Label, Multicenter, Randomized Study Evaluating the Efficacy and Safety of **Glofitamab in Combination with Gemcitabine plus Oxaliplatin versus Rituximab** in Combination with Gemcitabine and Oxaliplatin in Patients with Relapse/Refractory Diffuse Large B Cell Lymphoma

A Randomized, Double-blind, Placebo-Controlled, Active-Comparator, Multicenter, Phase 3 Study of **Brentuximab Vedotin** or Placebo in Combination With **Lenalidomide and Rituximab** in Subjects with Relapsed or Refractory Diffuse Large B-cell Lymphoma (DLBCL)

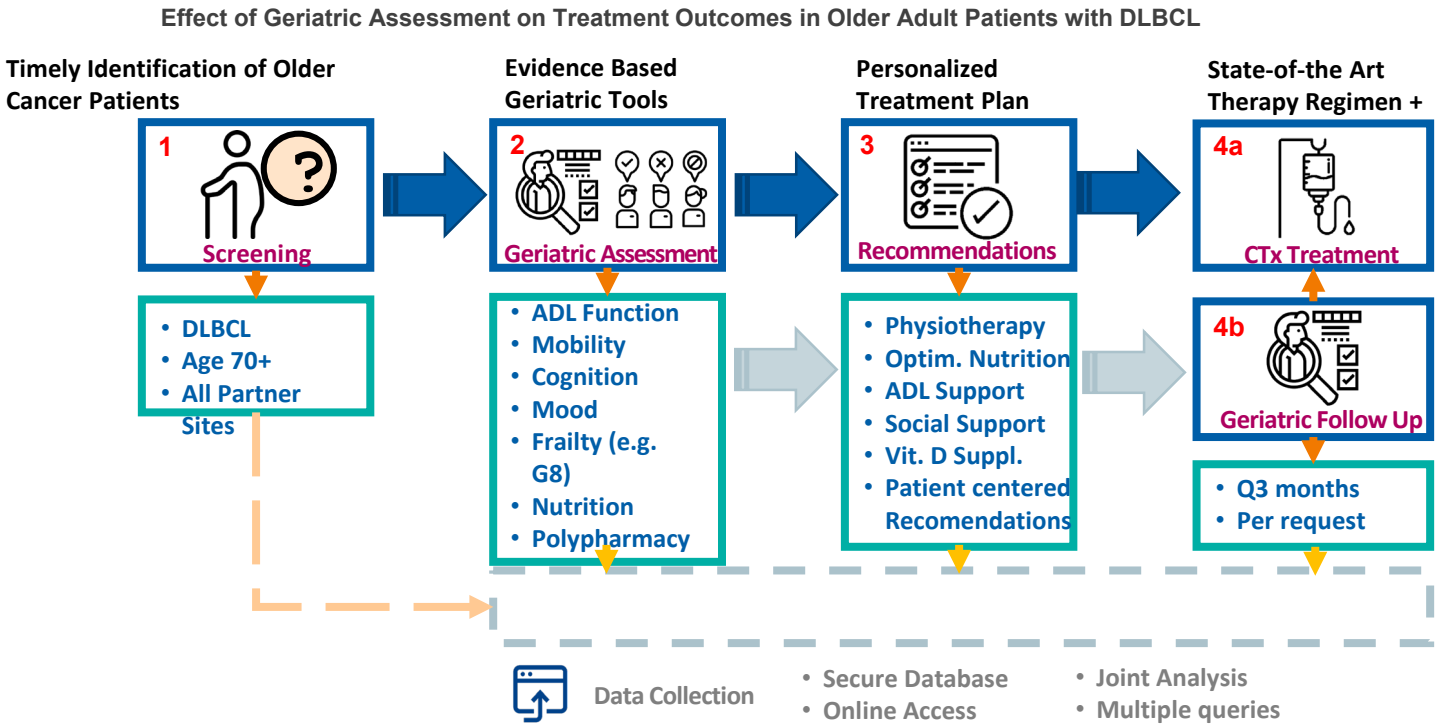
Assessing **a ctDNA and PET-oriented therapy** in patients with DLBCL, a multicenter, open-label, phase II trial

CLL17


H. Bischoff-Ferrari/ M. Gagesch

Zusammenarbeit Altersmedizin Lymphome

W. Rösler



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Flow chart Randomization SNF

INCLUSION CRITERIA

- Aggressive Lymphoma (B and T-cell lymphoma)
- Age > 70 yrs
- Fit for (R)-CHOP/(R)-mini-CHOP/Standard of care (incl. future new therapy options as polatuzumab, brentuximab)

DIAGNOSIS

PET-CT-scan/ ctDNA

2:1 RANDOMIZATION
est. pts. numbers:
320 pts over 4 yrs*.

* Statistical Background:
- Endpoint: mEFS
- Statistical test: Log-rank test
- Power: 80%
- Control: 40% at 2 years
- Treatment: 50% at 2 years -> Hazard ratio 0.75647
- Accrual: 320 patients in 4 years -> 80 patients per year
- Calculated with 4 years accrual and 2 years FU

COMPREHENSIVE GERIATRIC ASSESSMENT & CARE
(est. pts: 214)

STANDARD OF CARE
(est. pts: 106)

CHEMOTHERAPY
6 CYCLES (R)-CHOP/ (R)-MINI-CHOP /
NEW STANDARD AT INVESTIGATORS CHOICE

PET-CT-scan/ctDNA

16.09.2021

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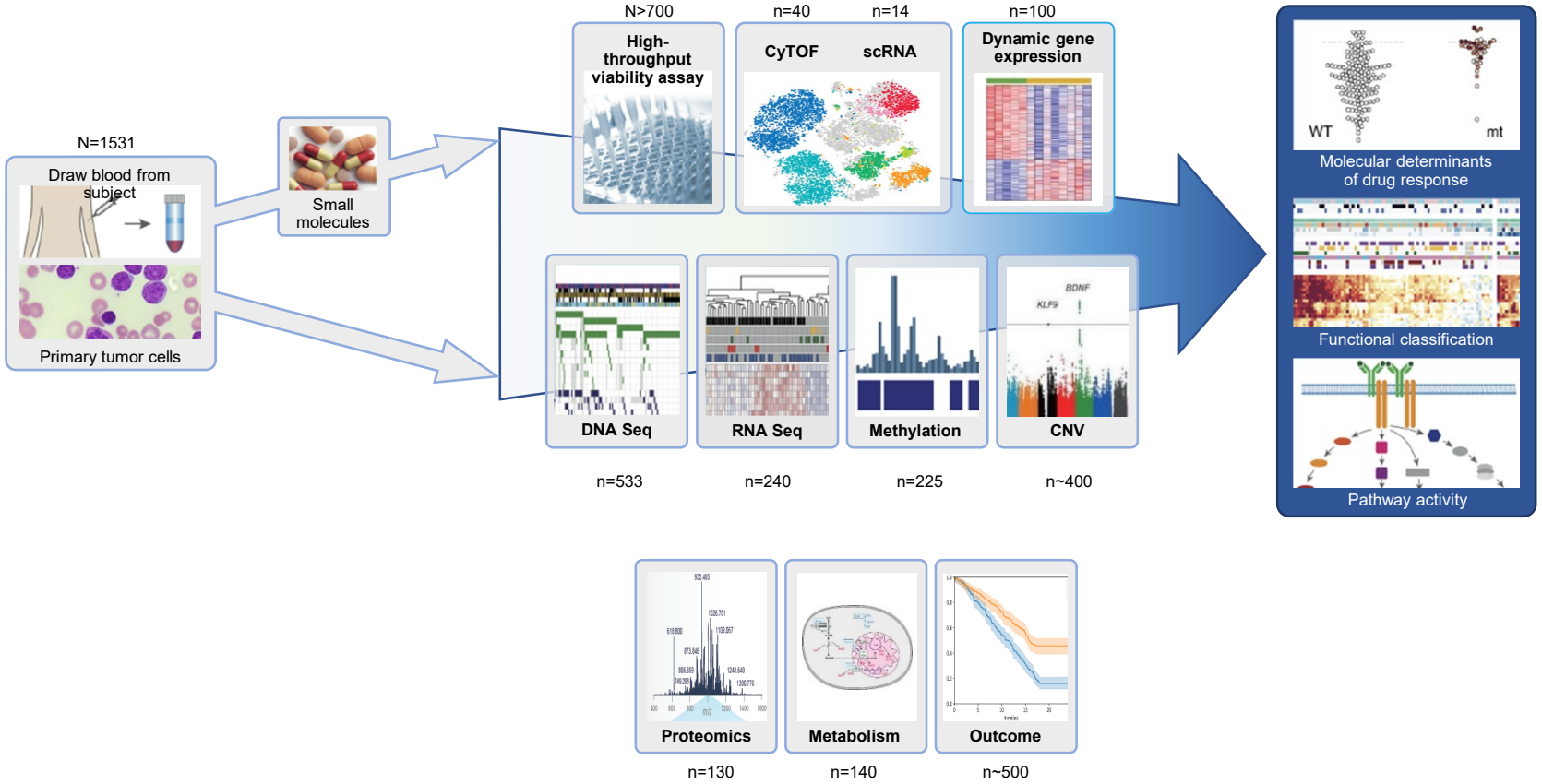
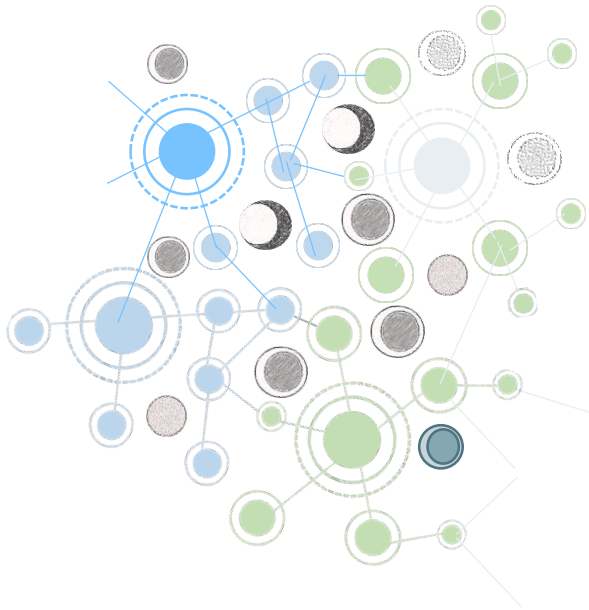
“Multiomics Profiling”
Leukämia & Lymphome

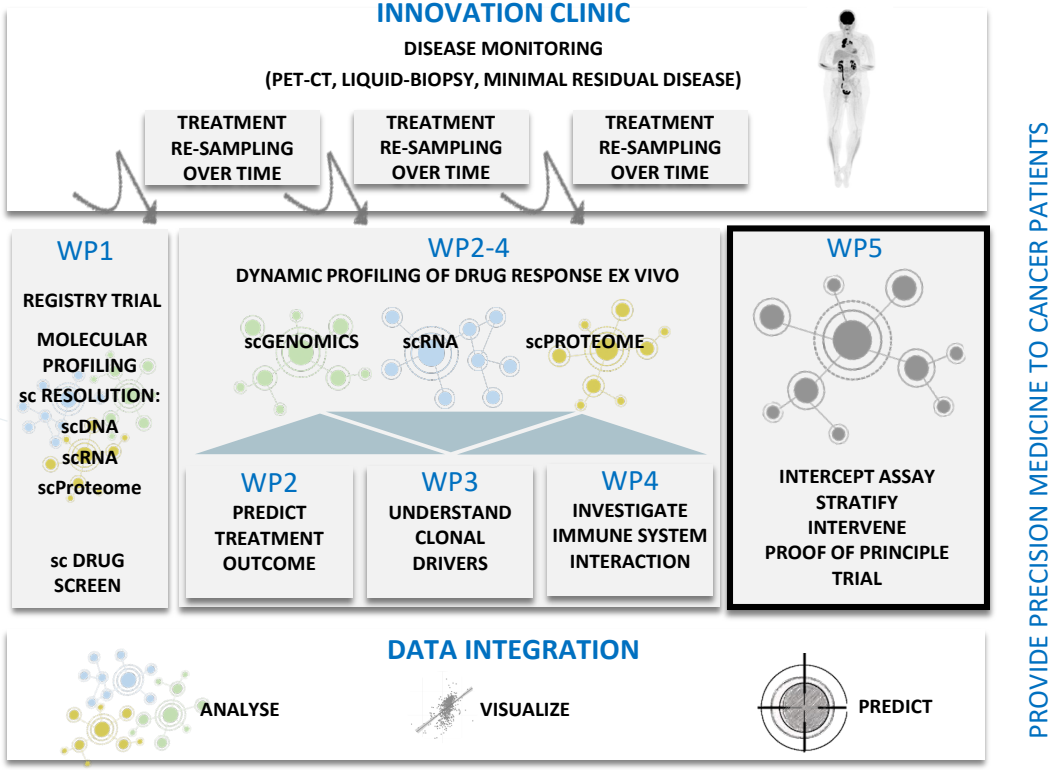


„INTeRCePT“
Einzelzellperspektive ausnutzen – Behandlungsversagen überwinden:
Blutkrebs bei Kindern und Erwachsenen.

„INTeRCePT“ Einzelzellperspektive ausnutzen – **Behandlungsversagen überwinden**: Blutkrebs bei Kindern / Erwachsenen

Zenz, Becher, Beerenwinkel, Bourquin, Moor, Huber, Snijder





PROVIDE PRECISION MEDICINE TO CANCER PATIENTS

Neue zelluläre Therapie
PTLD/
Immundefekt assoziierte NHL
Virus-assoziierte NHL (EBV, HHV)

THE LOOP ZURICH
MEDICAL RESEARCH CENTER

EMBL

Universität Zürich[UZH]

UniversitätsSpital Zürich

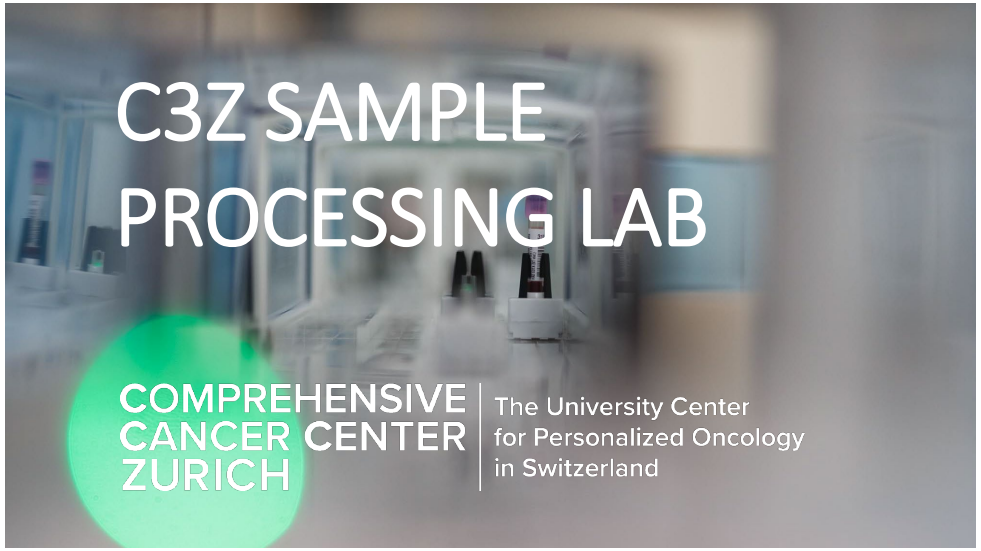
UNIVERSITÄTS-KINDERSPITAL ZÜRICH

ETH zürich

USZ Universitäts Spital Zürich

Insgesamt 6 Mio CHF (ETH/UZH; Horten Foundation)

Effiziente klinische Abläufe,
Leitlinien & strukturierte Datenerfassung
Klinische Studien & Forschung



Zusammenfassung

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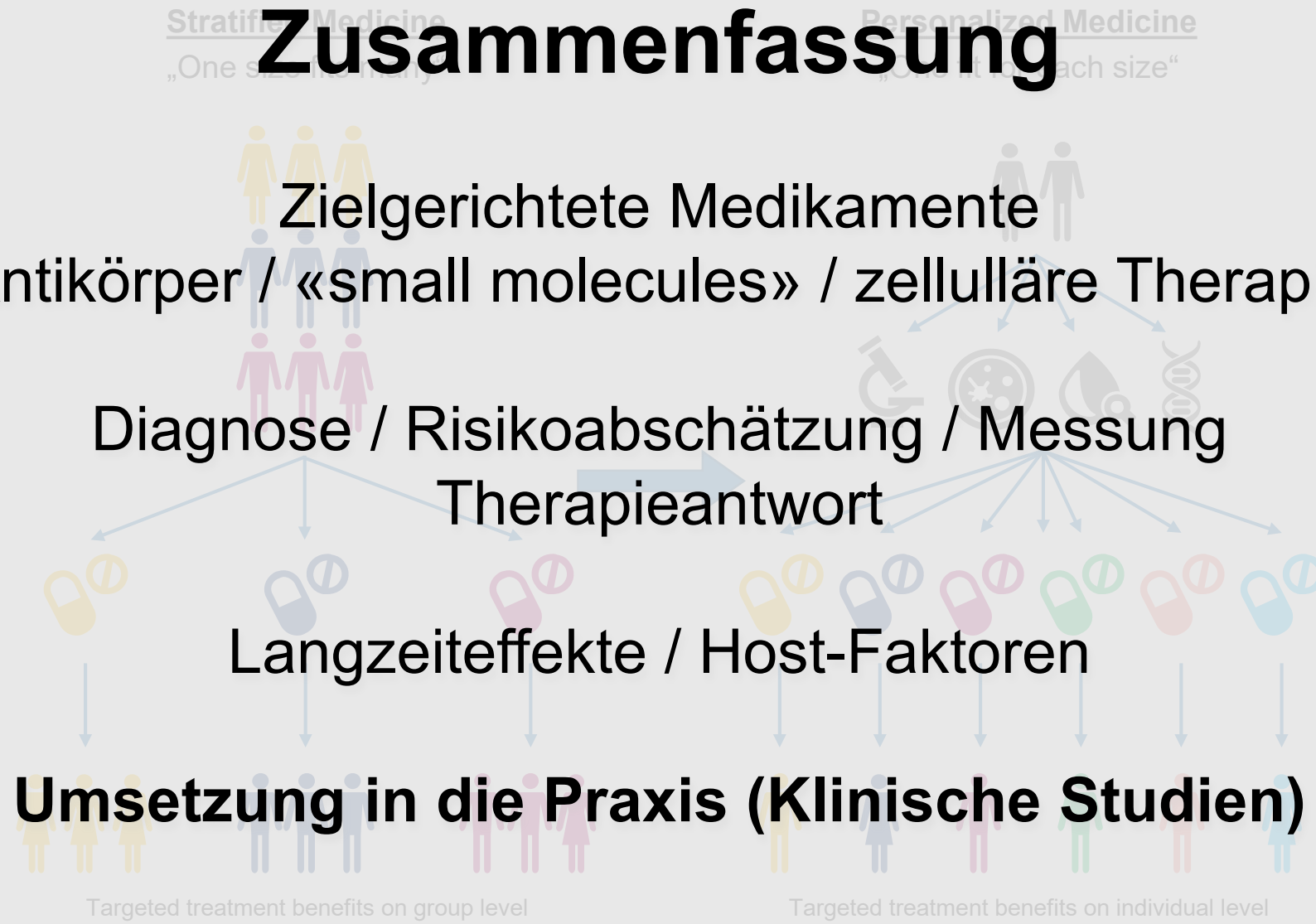

4. Diskussion