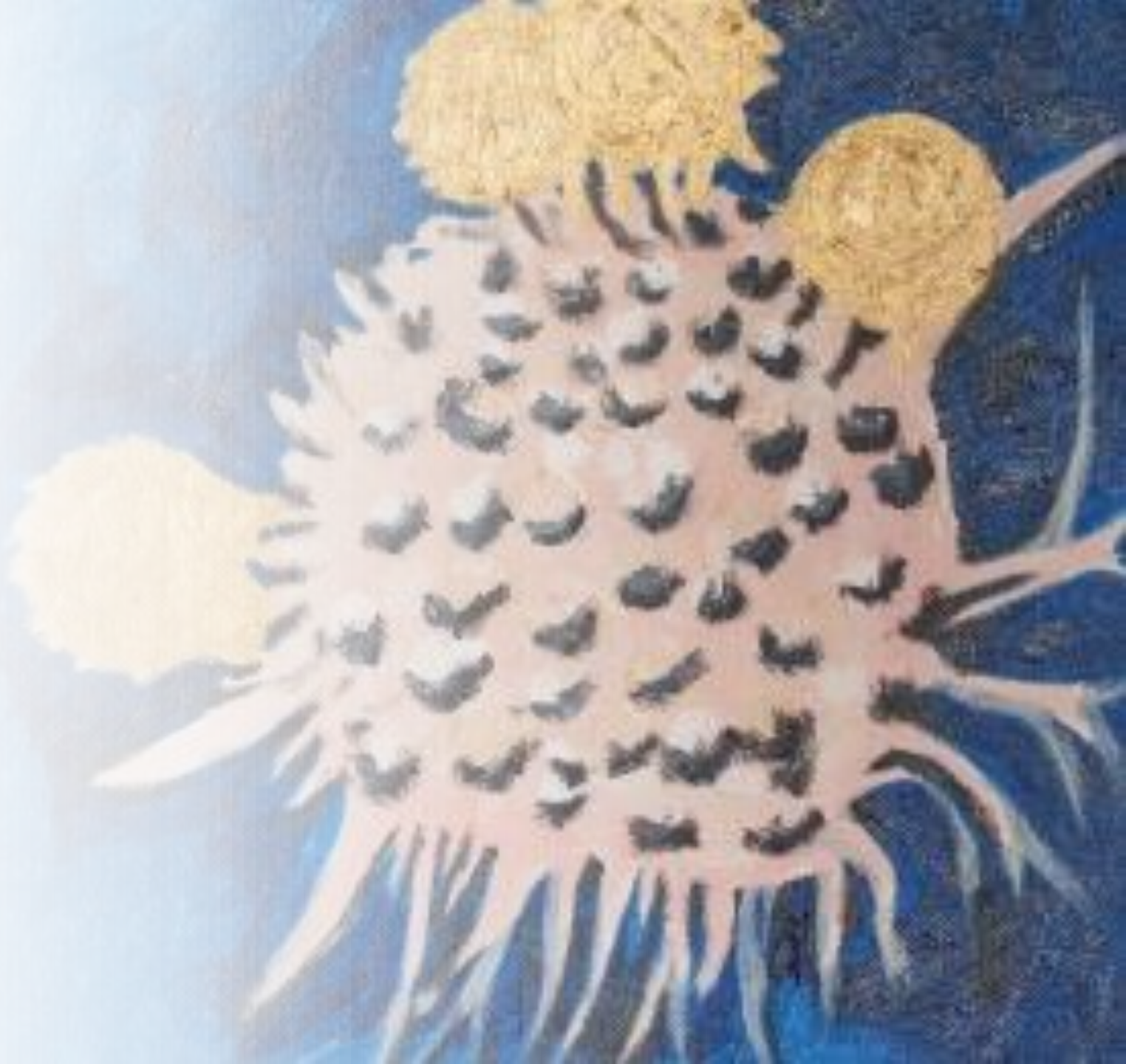
DLBCL 2021

Dr. Sylvia Snauwaert
MD, PhD



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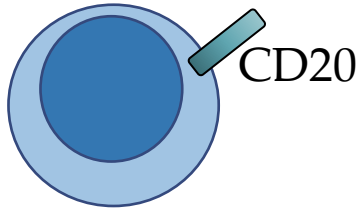
Wat is DLBCL?

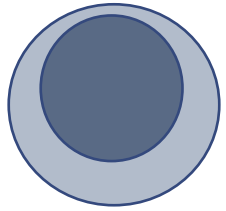
Welke subtypes non-Hodgkin lymfomen bestaan er?

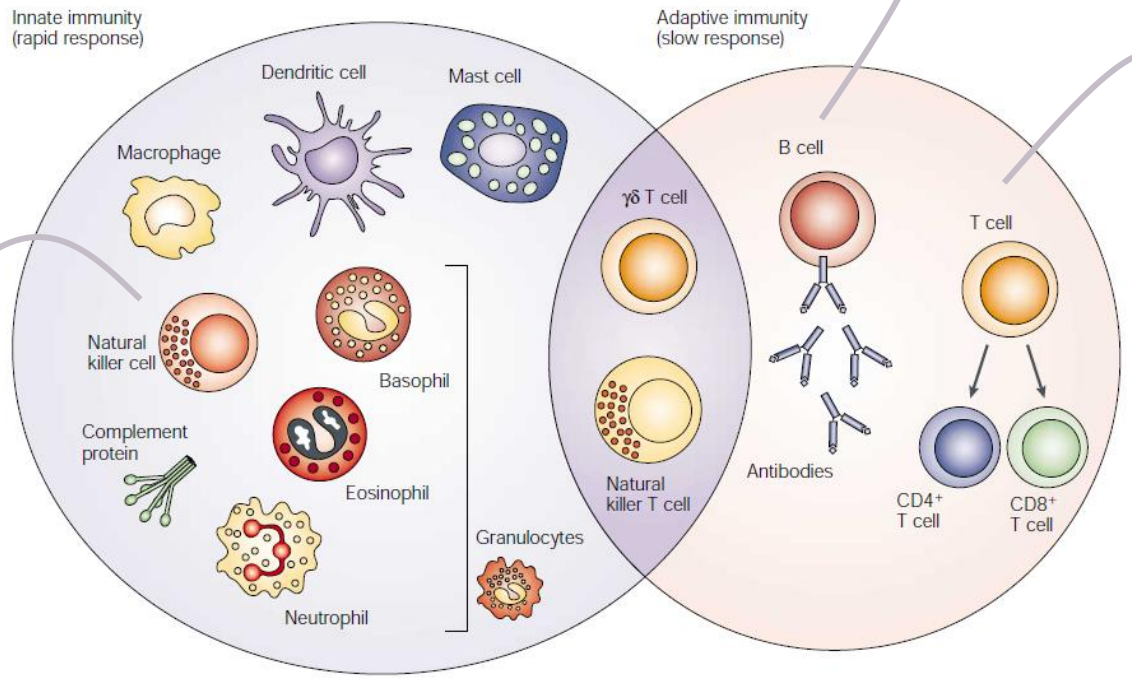
Non-Hodgkin lymfomen

B-cel lymfomen

T/NK- cel lymfomen







Dranoff, Nat.Rev. Cancer, 2004

Welke subtypes non-Hodgkin lymfomen bestaan er?

Swerdlow et al. Blood 2016BLOOD, 19 MAY 2016 • VOLUME 127, NUMBER 20

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

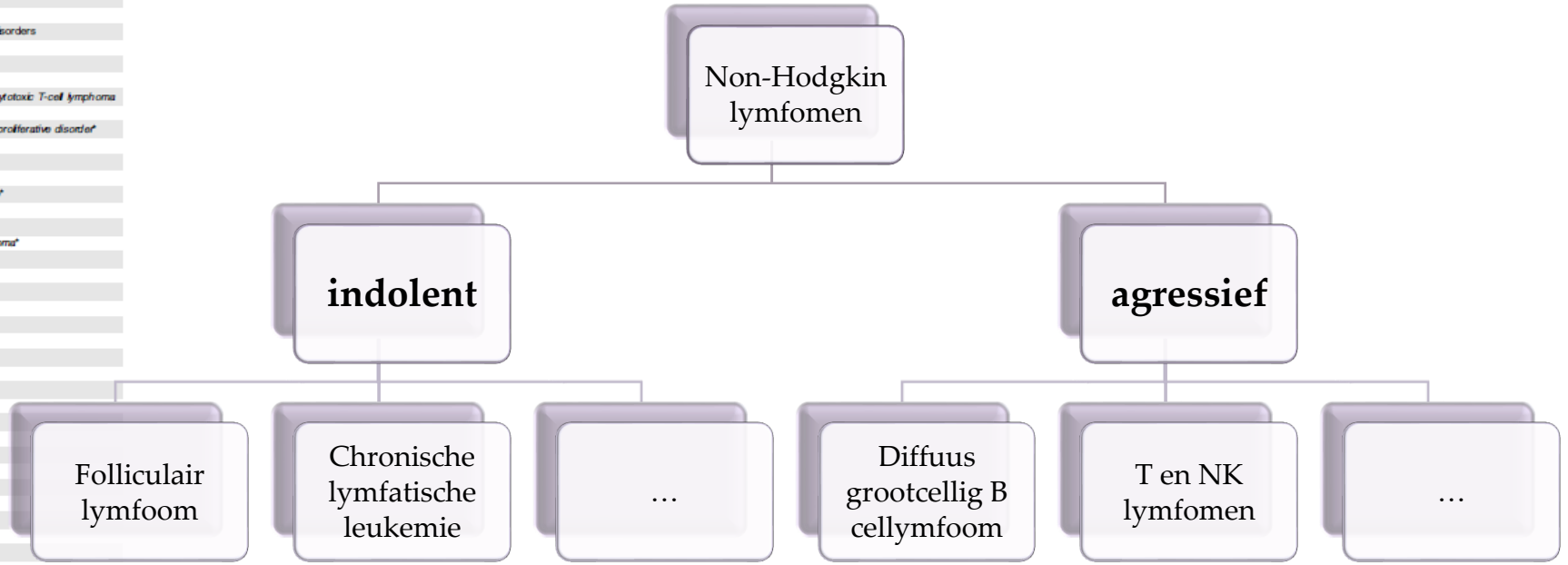
Mature B-cell neoplasms
Chronic lymphocytic leukemia/small lymphocytic lymphoma
Monoclonal B-cell lymphocytosis*
B-cell prolymphocytic leukemia
Splenic marginal zone lymphoma
Hairy cell leukemia
Splenic B-cell lymphoma/leukemia, unclassifiable
Splenic diffuse red pulp small B-cell lymphoma
Hairy cell 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



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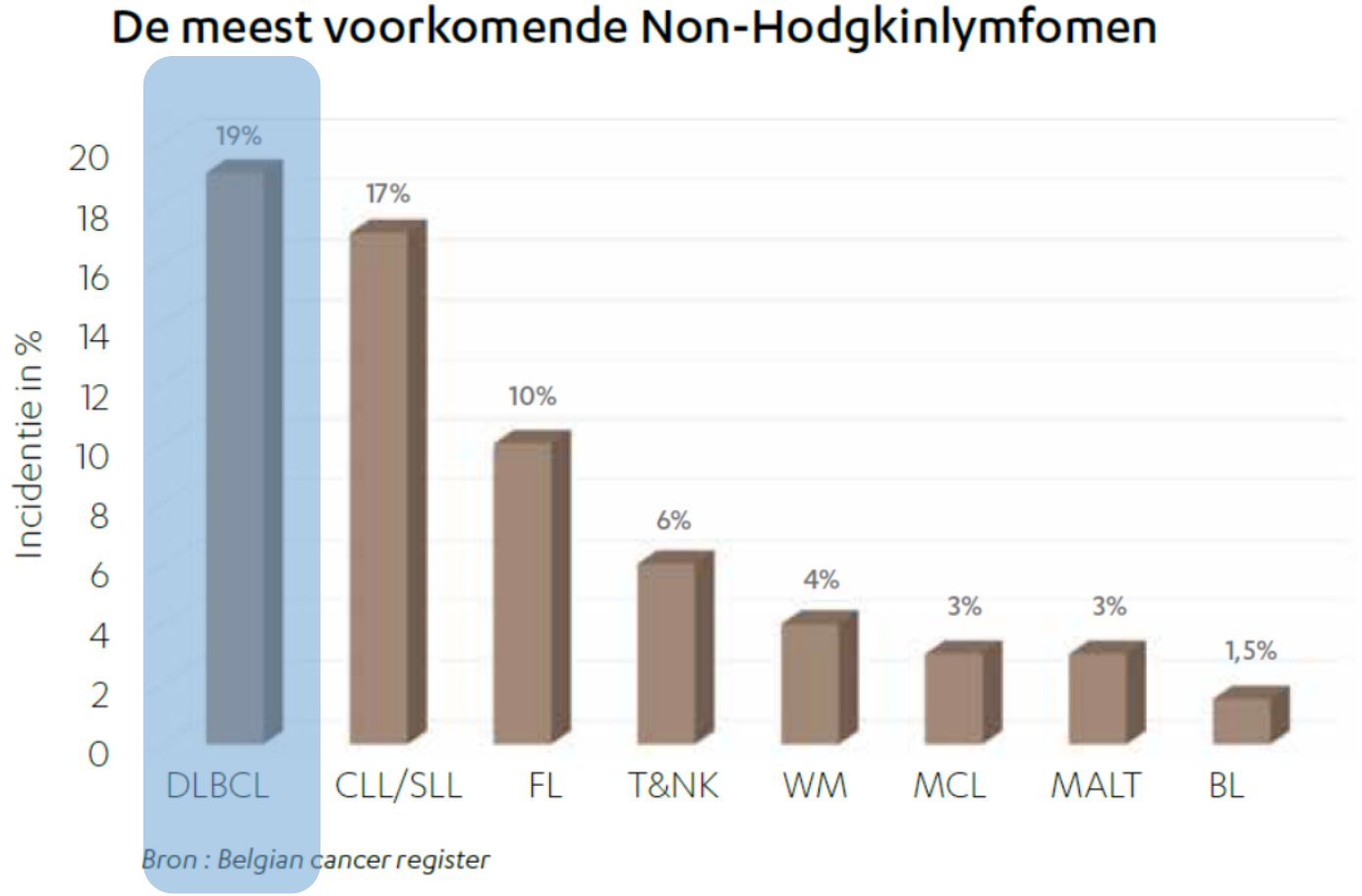
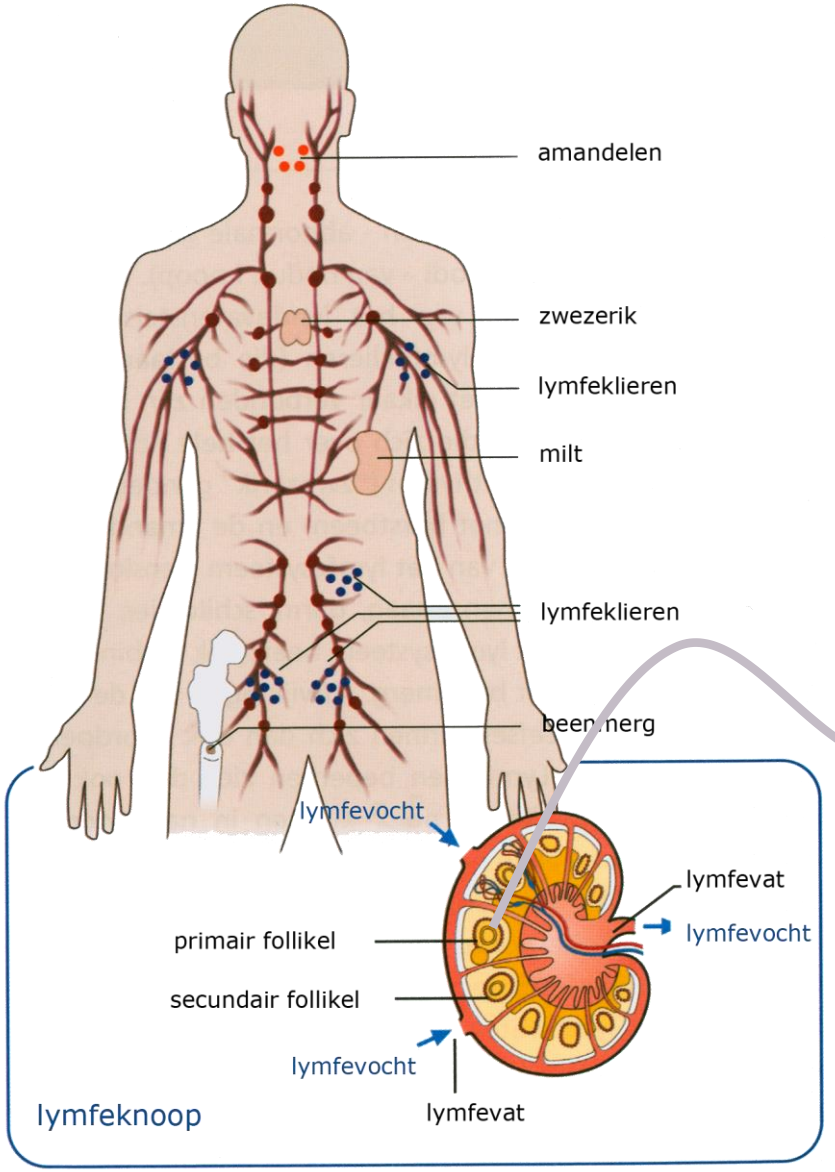
Welke Non-Hodgkin lymfomen komen het meest voor?

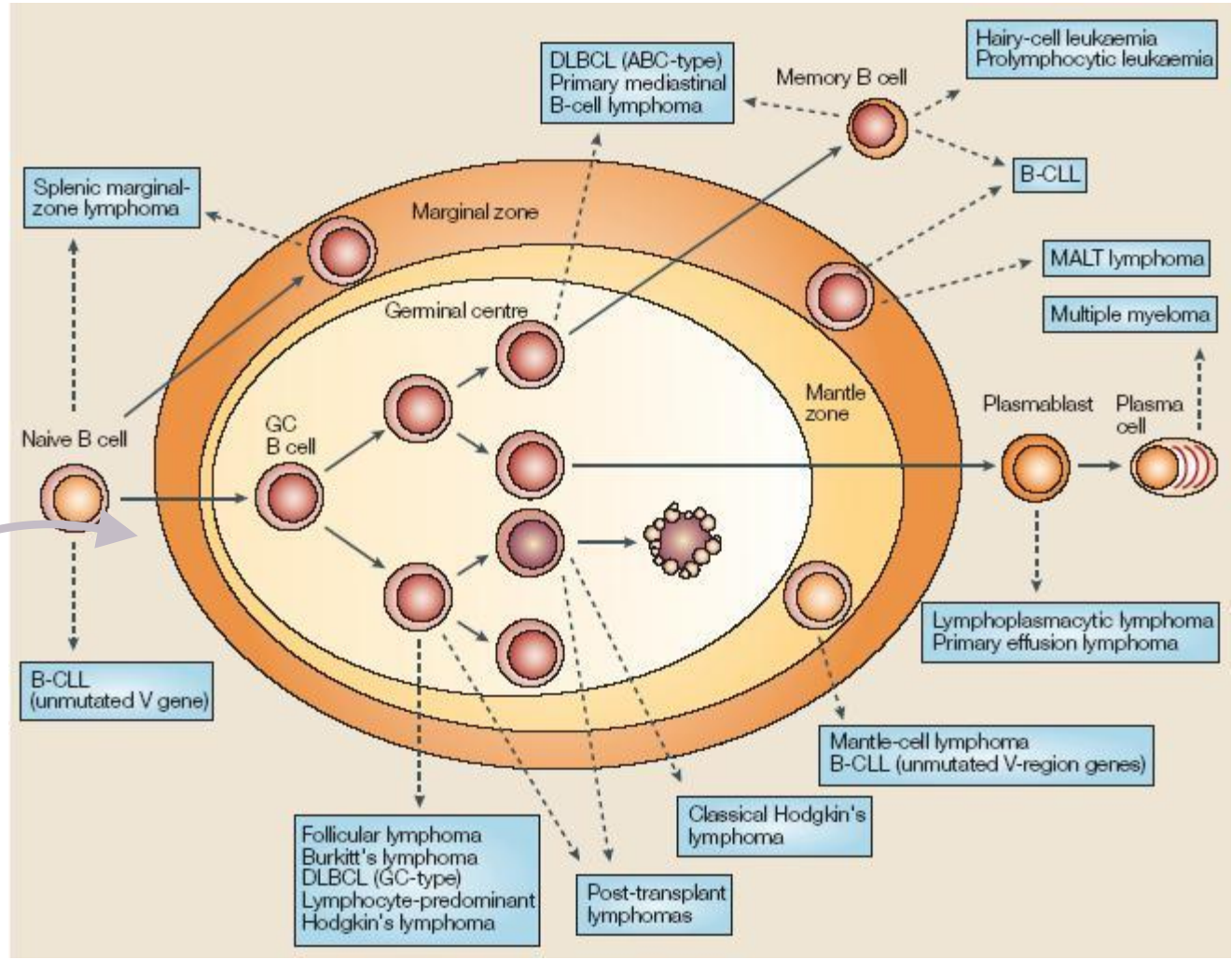


Bron: Patiëntenbrochure leven met lymfeklierkanker

Figuur: lymfevatensysteem: lymfevaten, klieren en klierregio's

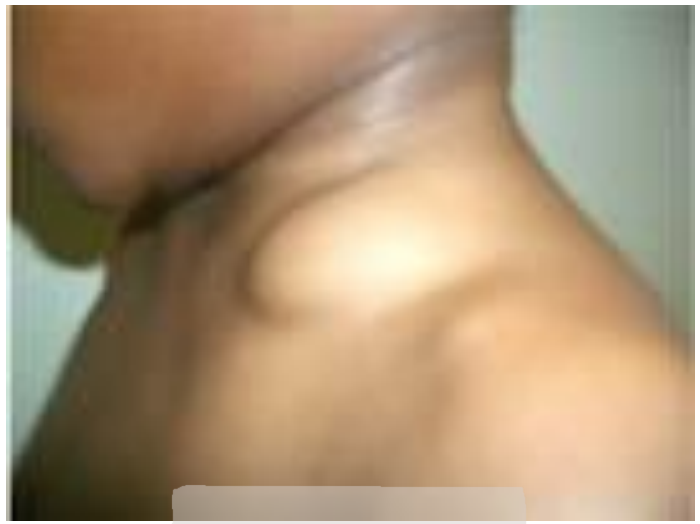
Hoe ontstaat een B cel non-Hodgkin lymfoom?





Kuppers, 2005, Nature Reviews Cancer

Wat zijn de klachten?



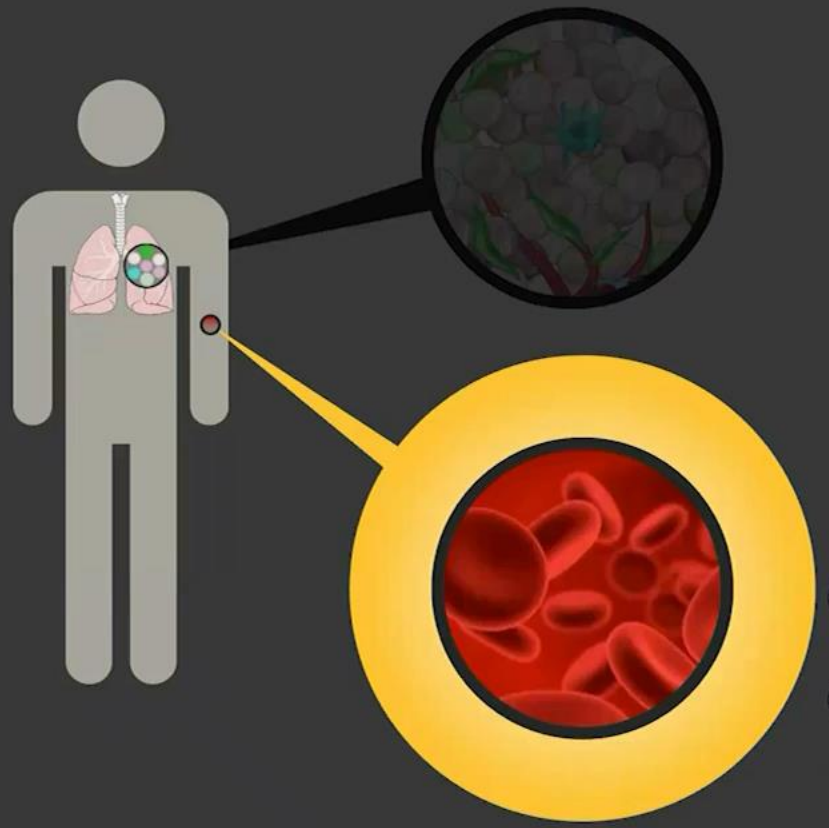
- vergrote lymfeklieren in de hals, in de oksels en/of in de liezen
- rugpijn (veroorzaakt door vergrote lymfeklieren)
- buikpijn (vanwege vergrote lever en/of milt en/of lymfeklieren)
- Andere ….

- **B-symptomen**
  - vermoeidheid
  - nachtzweten
  - gewichtsverlies
  - koorts van ongekende oorsprong
  - jeuk

Hoe wordt de diagnose gesteld? de biopsie

De toekomst??

“Liquid Biopsy”

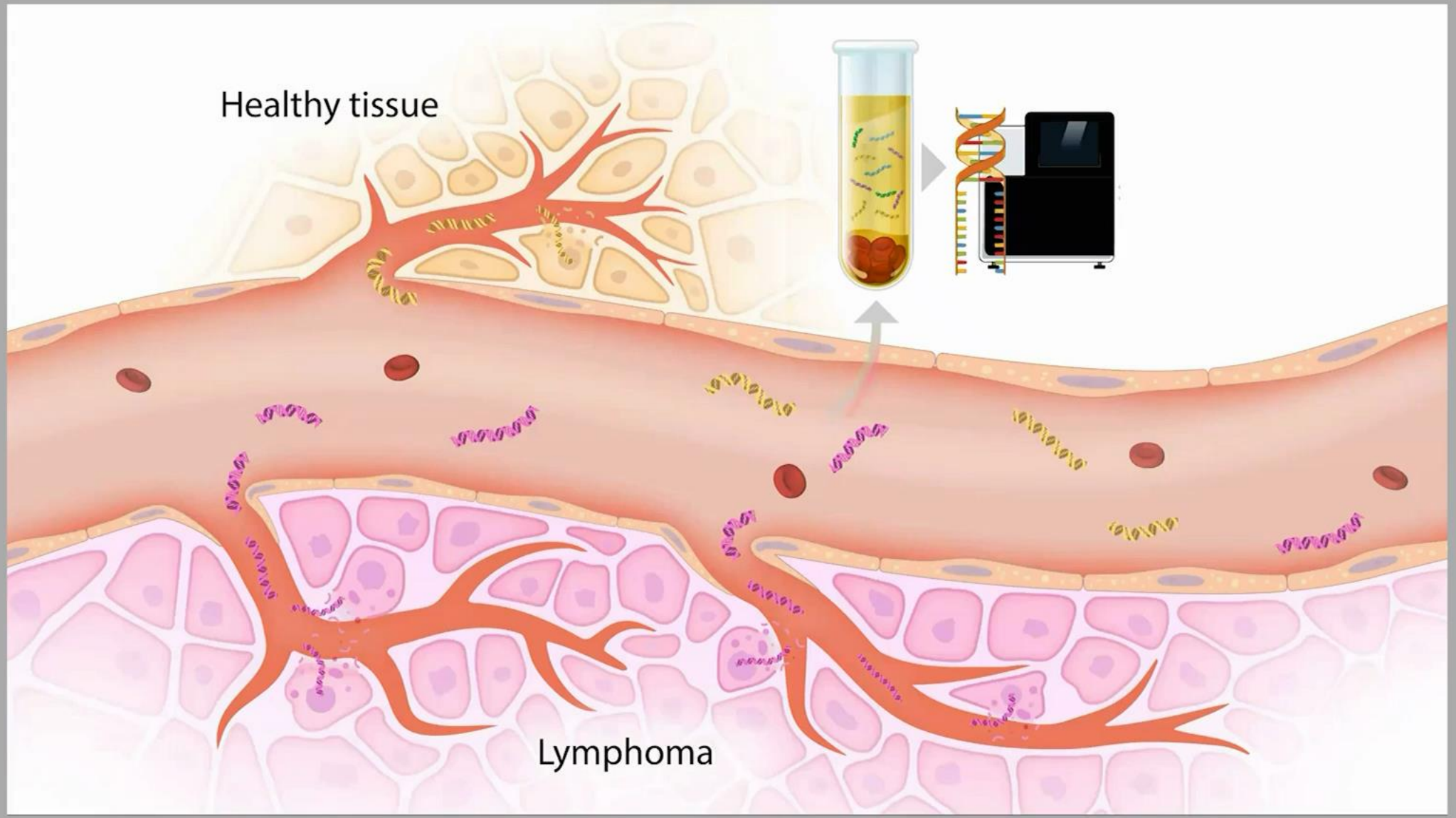


“*From a liquid window through which physicians could view the body's inner workings*” (Armstrong JA, 2007).

Circulating tumor cells (CTCs)
and
Circulating tumor DNA (ctDNA)

16th ICML

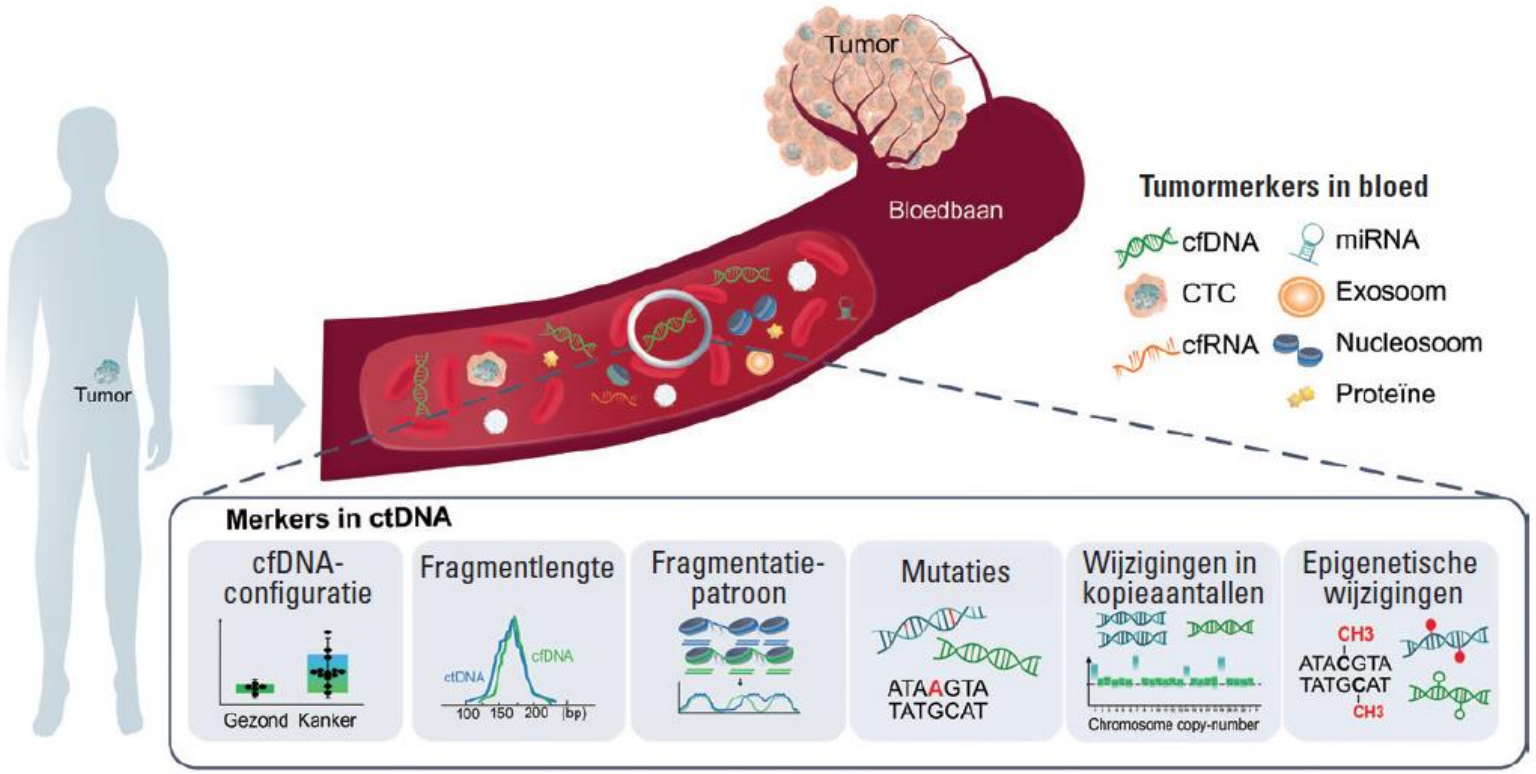
A. Alizadeh, Stanford, CA (USA)



16th ICML

A. Alizadeh, Stanford, CA (USA)

Figuur 1: Mogelijke toepassingen van celvrij tumor-DNA (ctDNA).



Toepassingen

Screening	Diagnose/prognose	Monitoring
Vroegtijdige kankerdetectie Bepalen van tumoroorsprong	Bepalen van prognose Selectie van behandeling Identificatie van nieuwe doelwitten	Opvolgen van kankerbehandeling Detectie van minimale residuele ziekterest en terugval

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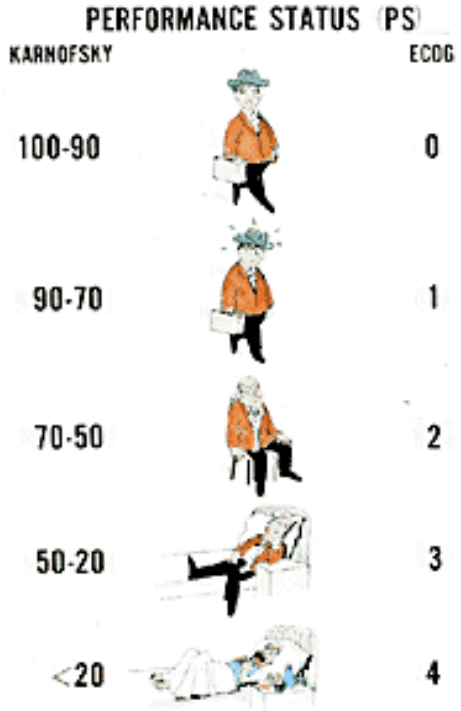
Oncohemato 2019 Lenaerts et al.

Hoe wordt de prognose bepaald?



Diffuse Large B-Cell Lymphoma Prognosis (R-IPI)

Determine prognosis in diffuse large B-cell lymphoma

Questions

1. Age?
2. Performance?
3. LDH?
4. Extranodal Sites?
5. Stage?

Klinisch onderzoek
(PET)-CT
Beenmergbiopsie

Bloedafname

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esmo.org

Hoe wordt het stadium bepaald?

Stadium I

De ziekte blijft beperkt tot één lymfeklierregio (hals, lies...) of één orgaan.

Stadium II

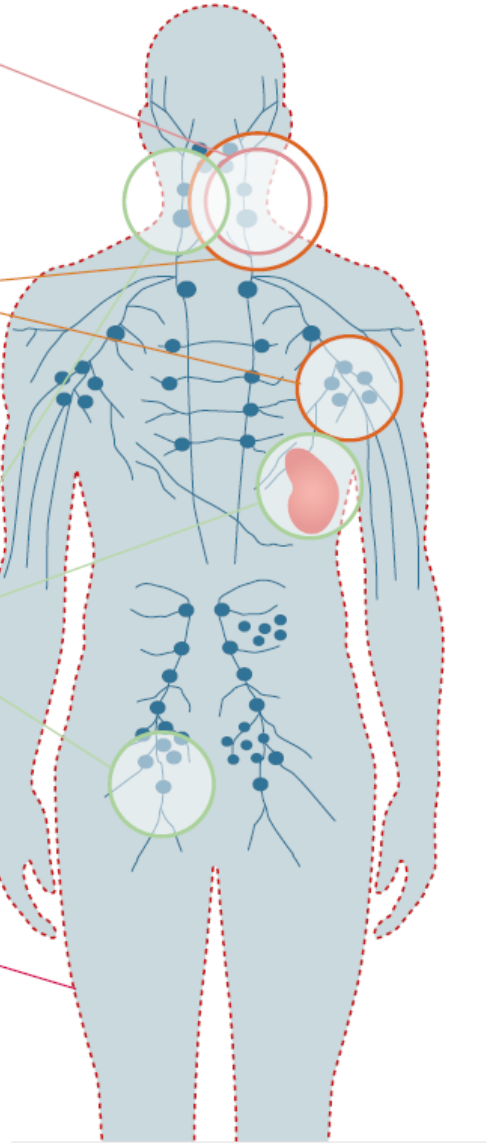
De ziekte beperkt zich tot twee of meer klierregio's, maar wel aan dezelfde kant van het middenrif.

Stadium III

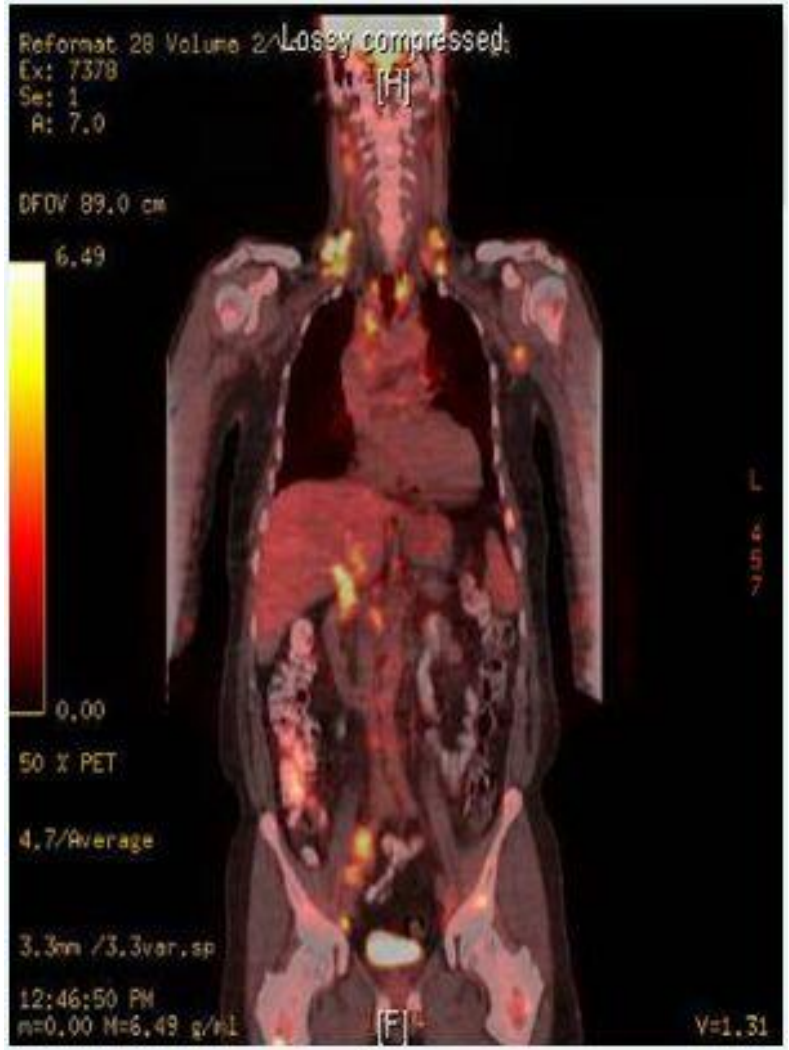
De ziekte heeft zich verspreid naar kliergebieden aan beide kanten van het middenrif, en soms ook naar de milt.

Stadium IV

De ziekte heeft zich verspreid naar andere organen (longen, lever, beenmerg, huid...).

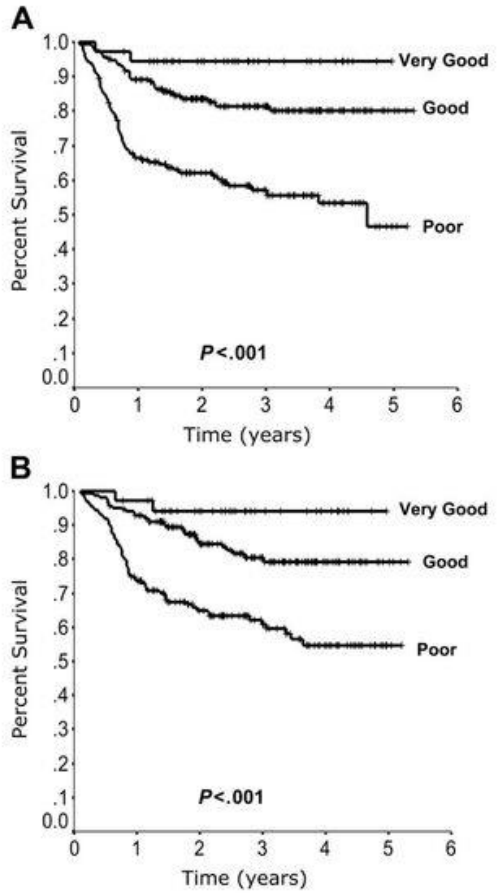


PET-CT



Bron: Patiëntenbrochure leven met lymfeklierkanker

Outcome according to the revised International Prognostic Index (R-IPI).



Laurie H. Sehn et al. Blood 2007;109:1857-1861

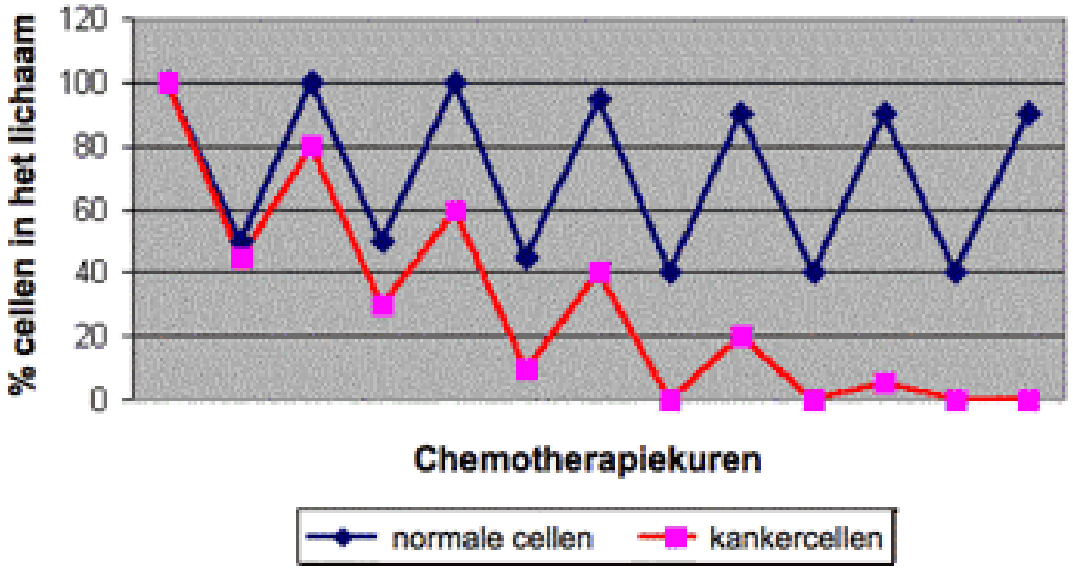
Behandeling

Klassieke behandelingsstrategieën : chemotherapie

Meest gebruikte kuur:

CHOP

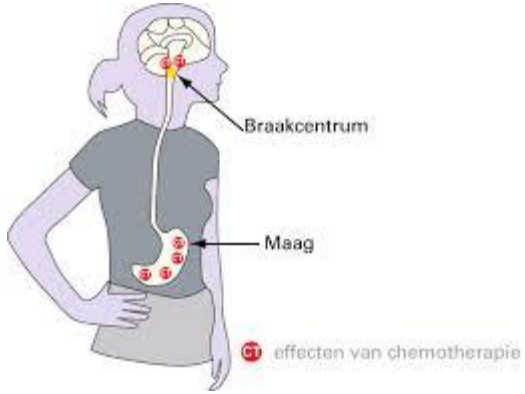
C yclofosfamide
H ydroxydaunorubicine = doxorubicine
O ncovin = vincristine
P rednisone = 'cortisone'



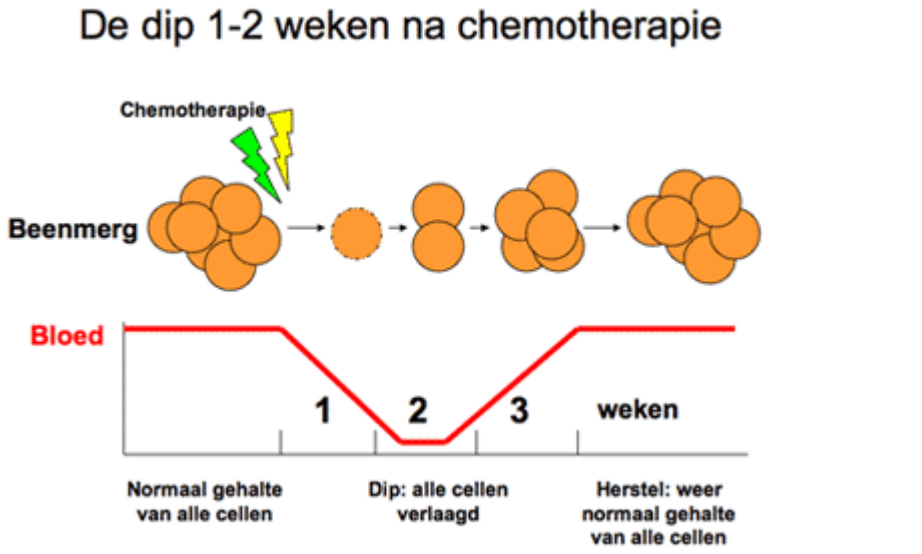
Klassieke behandelingsstrategieën: bijwerkingen

haarverlies

Misselijkheid



Verminderde weerstand tegen infecties



www.hematologiegroningen.nl

Andere

- ontstoken slijmvliezen
- Vermoeidheid
- Bloedingen
- …

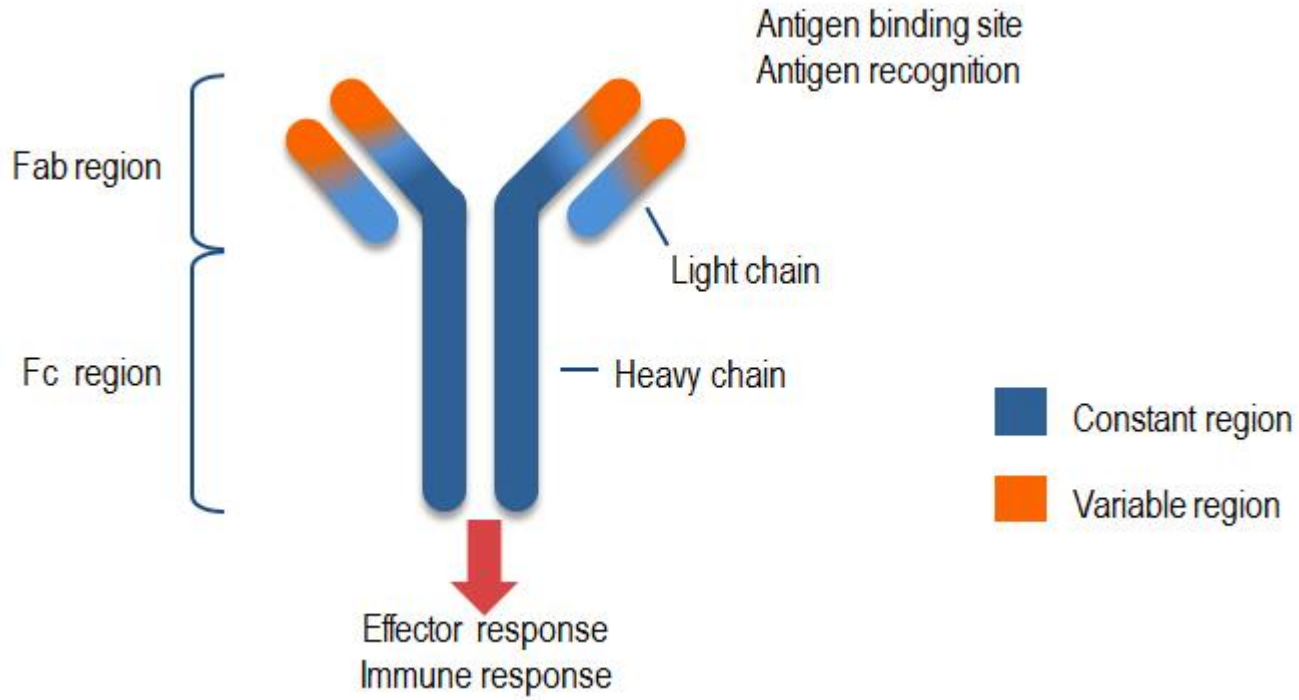
www.allesoverkanker.be/bijwerkingen-chemotherapie-en-hoe-ermee-omgaan

www.kanker.be/alles-over-kanker/bijwerkingen

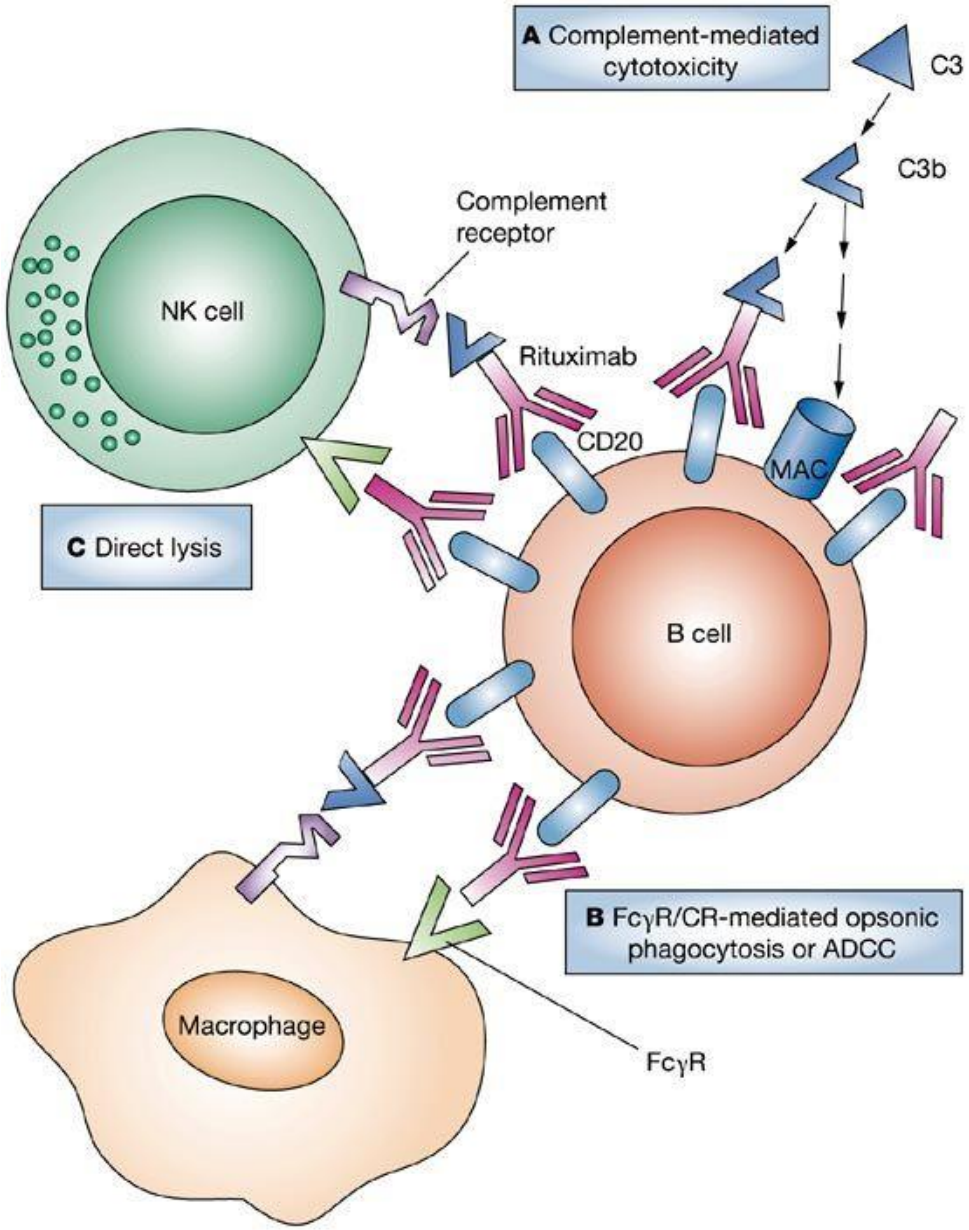
Patiëntenbrochure Leven met lymfeklierkanker

Klassieke behandelingsstrategieën : rituximab

‘monoclonale antistof’

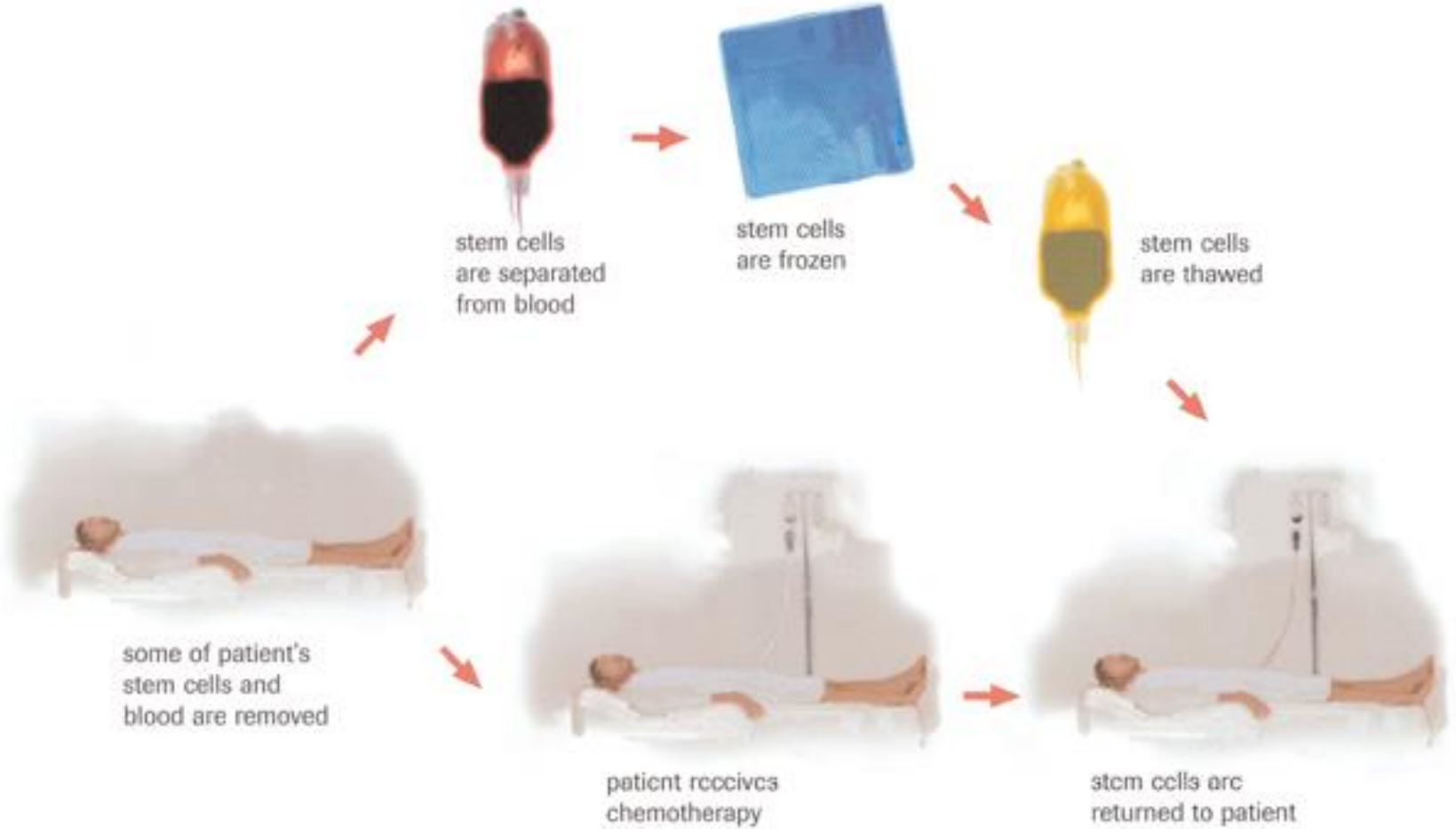


Klassieke behandelingsstrategieën : rituximab

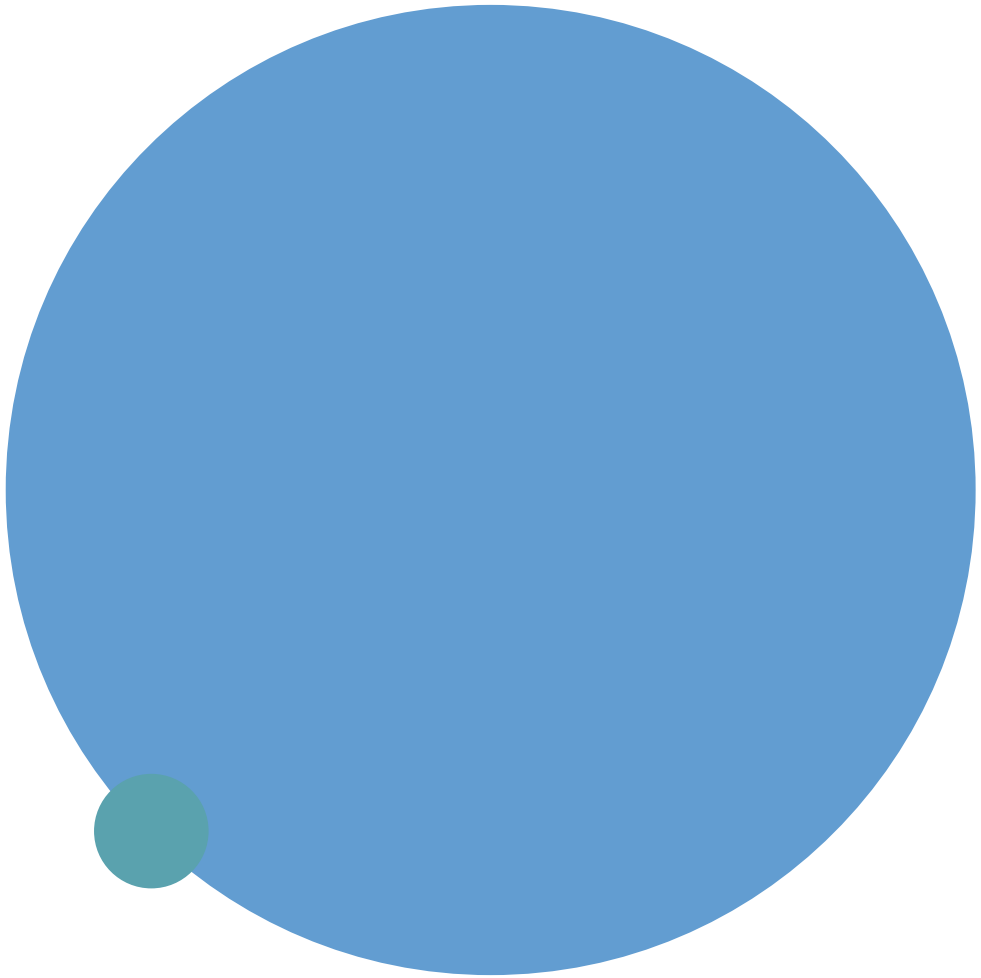


Taylor, Nature Reviews 2007

Autologe stamceltransplantatie



Nieuwe therapieën voor DLBCL

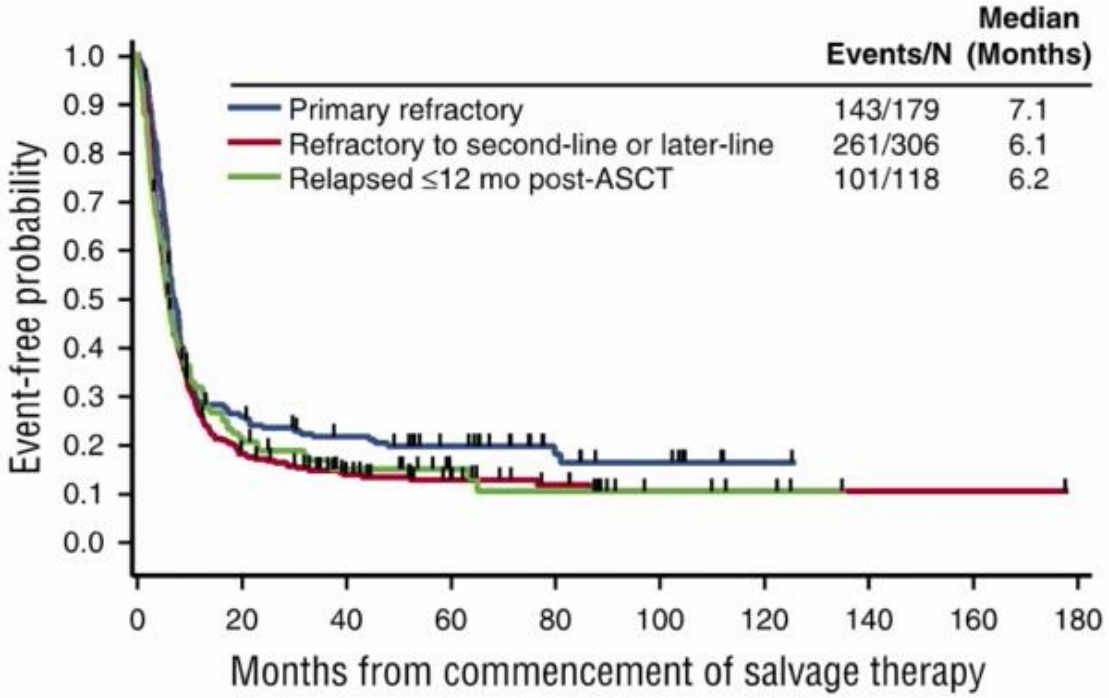


• 40 % van de patiënten zullen refractair zijn aan deze standaardbehandeling of hervallen …

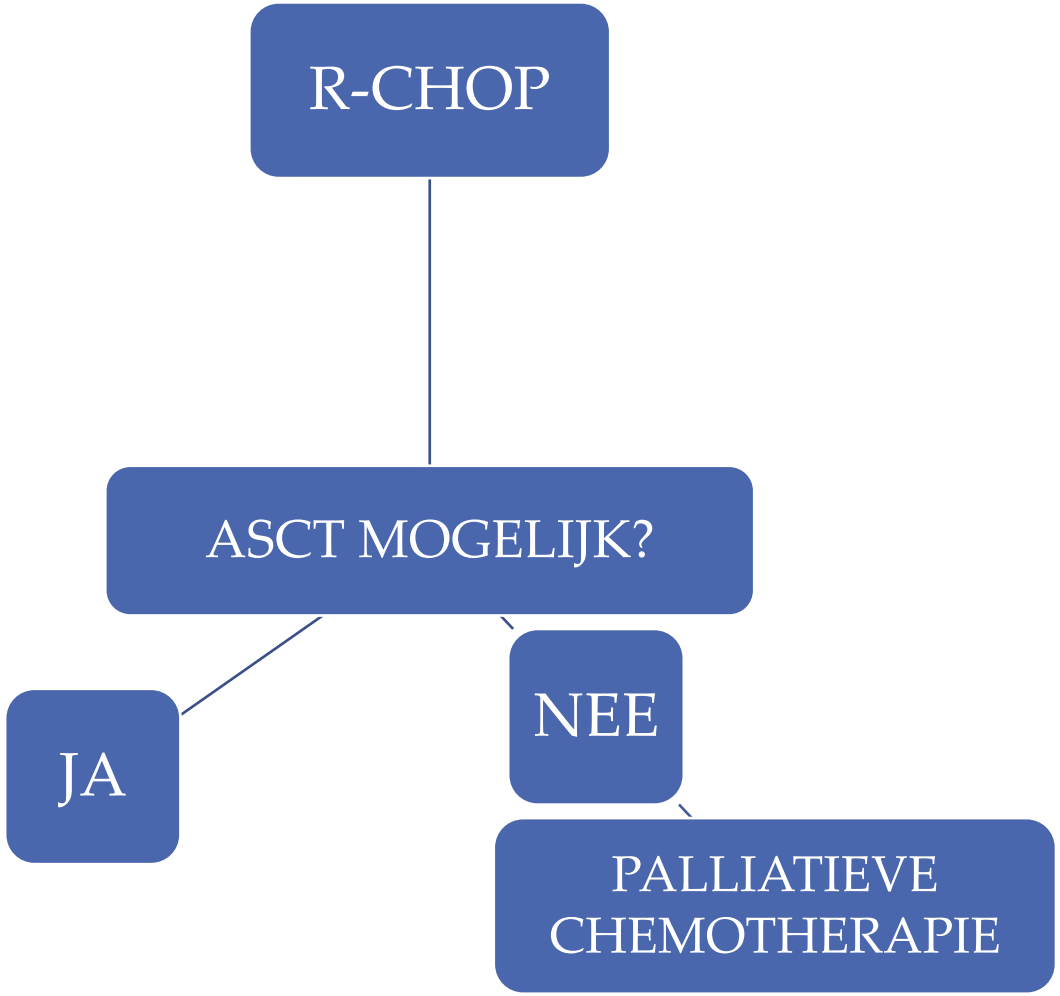
• De helft van deze patiënten komen niet in aanmerking voor een autologe stamceltransplantatie …

VOOR 2018

SCHOLAR-1

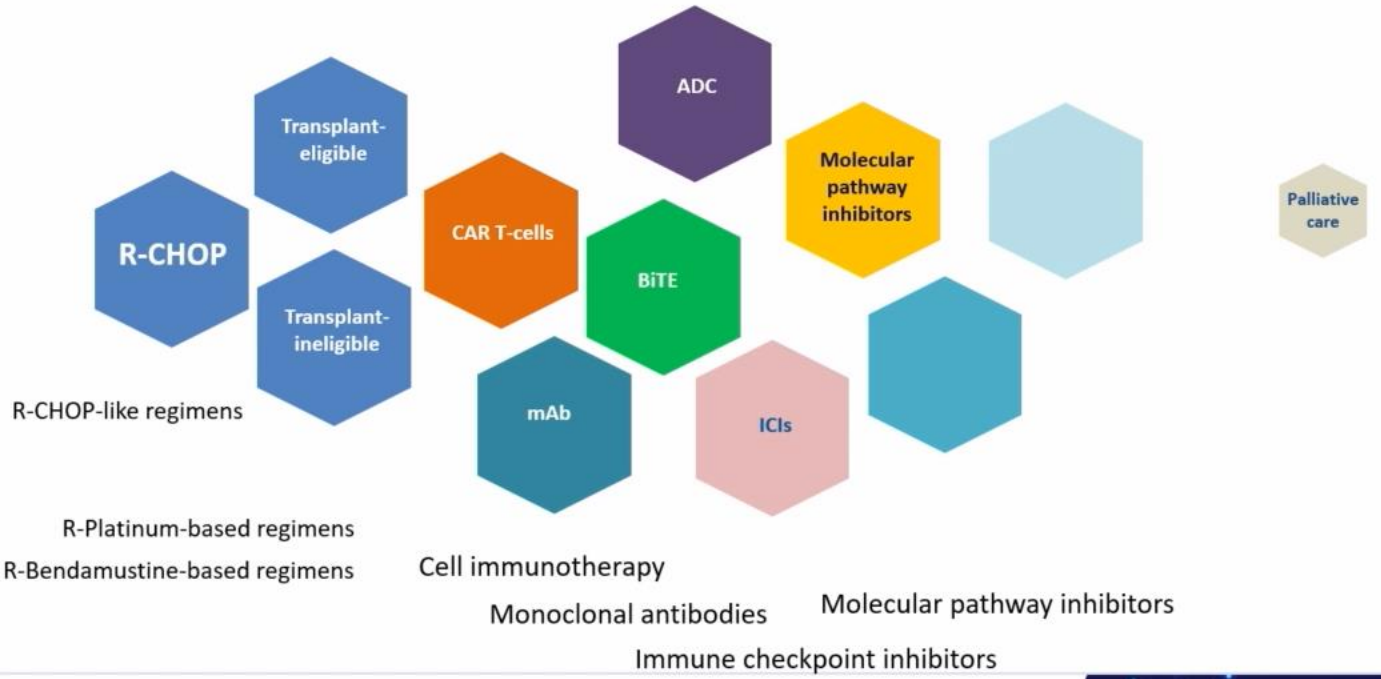


Mediane overleving: 6,3 maand



Crump et al. Blood 2017

Paving the treatment in 2021



Catherine Thieblemont

IMMUNOTHERAPIE

Immunotherapie afgeleid van antistoffen

Monoclonale antistoffen

Immunoconjugaten

BiTEs

Immunotherapie op basis van T cellen

CAR T cellen

Nieuwe monoclonale antistoffen

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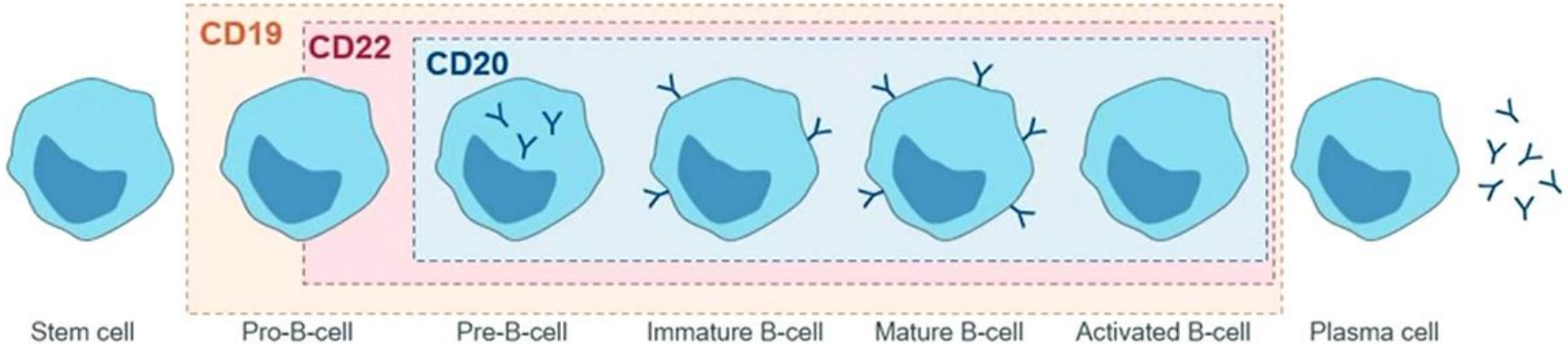
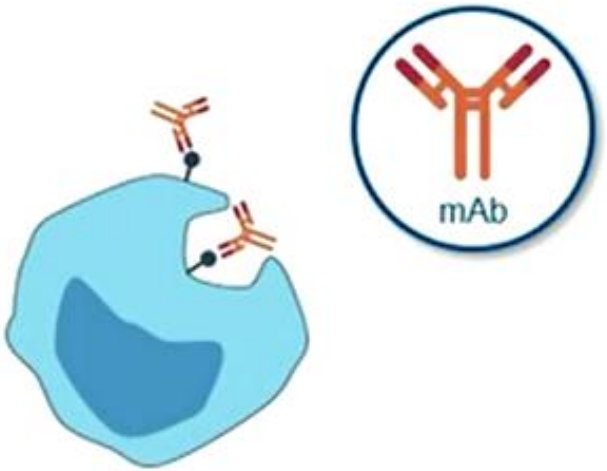

CD19
CD22
CD20
Stem cell
Pro-B-cell
Pre-B-cell
Immature B-cell
Mature B-cell
Activated B-cell
Plasma cell

FDA (2020) only*

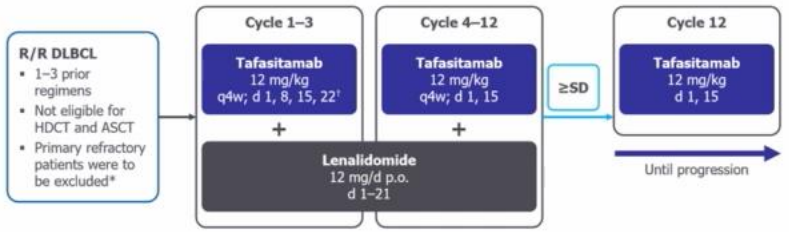
Tafasitamab-cxix[1]
(enhanced anti-CD19 mAb)

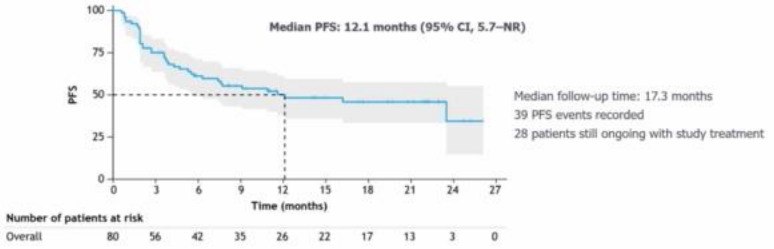


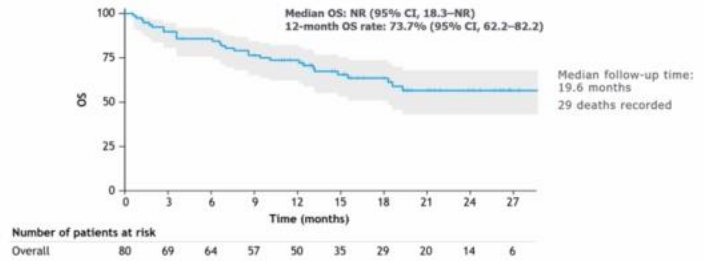
Monoclonal antibodies

L-MIND Tafasitamab (CD19 mAb) combined with Lenalidomine

Phase 2, single-arm, open-label, multicenter study (NCT02399085)







- ORR, 60.0% (95% CI, 48.4–70.8)
- CR rate, 42.5%
  - 82% of CRs PET-confirmed
  - 18% of CRs based on CT only

Salles G et al. Lancet Oncol 2020

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IMMUNOCONJUGATEN

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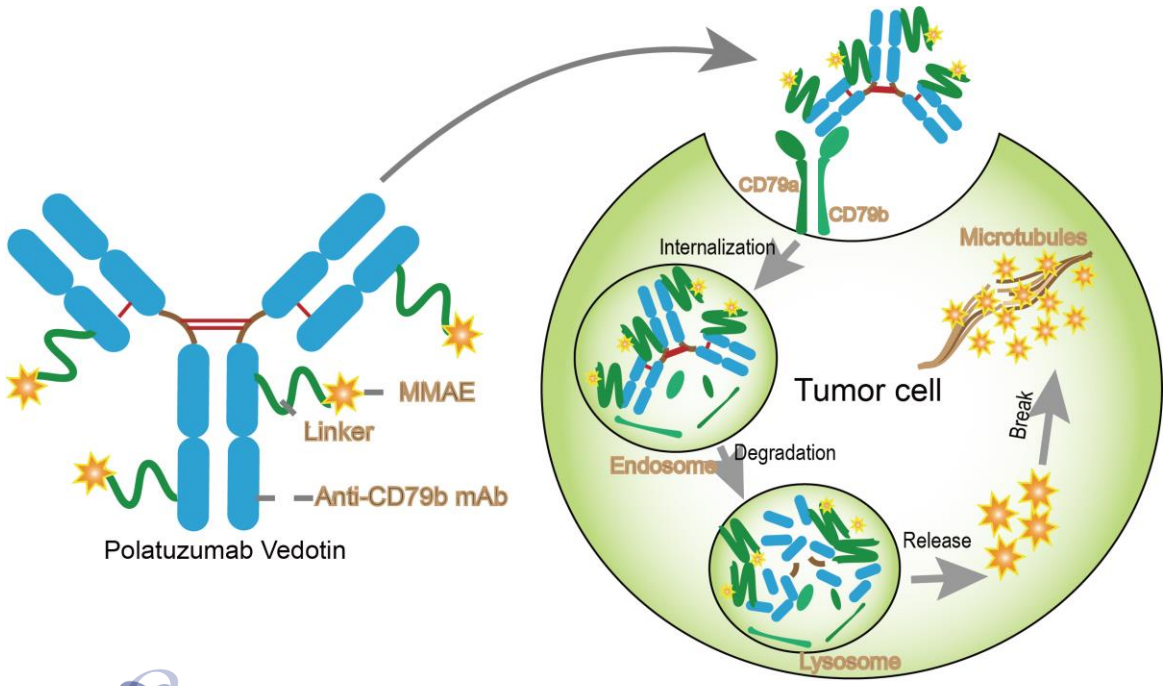
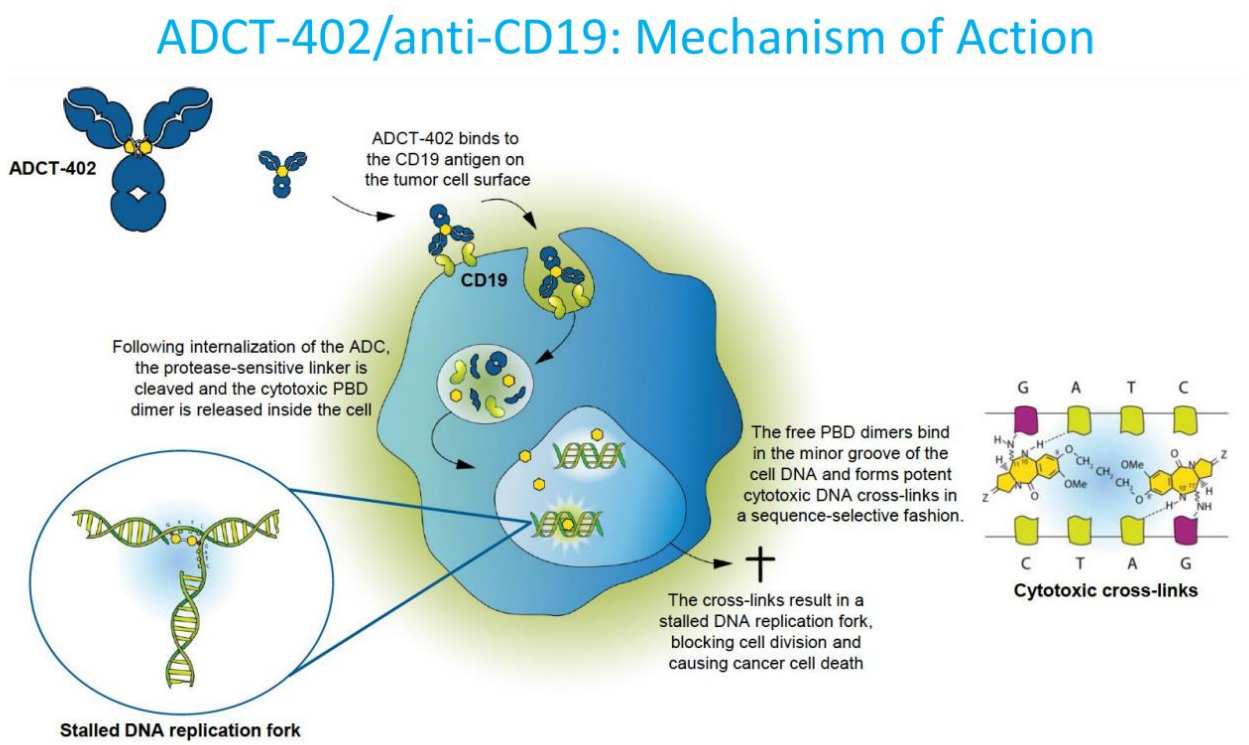
Doel-antigen	naam	toxine
CD19	Loncastuximab tesirine	SC3199
CD79b	Polatuzumab vedotin	MMAE
CD22	Inotuzumab ozogamicin	calicheamicin





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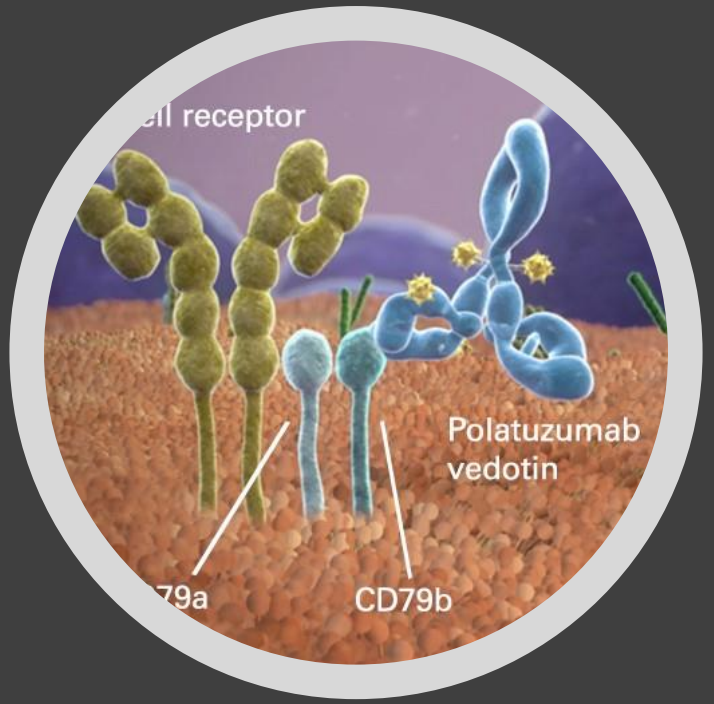


POLARIX: A PHASE 3 STUDY OF POLATUZUMAB VEDOTIN (POLA) PLUS RCHP VERSUS R-CHOP IN PATIENTS (PTS) WITH UNTREATED DLBCL

LOTIS 5: A Phase 3, randomized, open-label study of Lonca combined with rituximab in R/R DLBCL[1]

OBJECTIVE: To evaluate the efficacy and safety of Lonca plus rituximab in patients with R/R DLBCL or high-grade B-cell lymphoma

Screening Period | **Treatment Period** | **Follow-Up Period**

Patient population

- Age ≥18 years
- ECOG PS 0–2
- R/R DLBCL or high-grade B-cell lymphoma,* with *MYC-BCL2* and/or *BCL6* rearrangements after ≥1 prior multi-agent systemic treatment regimen
- Lymphoma with active central nervous system involvement not permitted†
- No prior R-GemOx or Lonca
- Prior CD19-directed therapy permitted if biopsy confirms CD19 expression
- AHCT or alloHCT permitted if received ≥30 or ≥60 days prior to start of study drug, respectively

N~350

30-minute IV infusions

Non-randomized safety run-in (N=20)

Lonca
Cycles 1–2: 150 µg/kg IV Q3W
Cycles 3–8: 75 µg/kg IV Q3W
+ rituximab
375 mg/m² IV Q3W

R

Lonca
Cycles 1–2: 150 µg/kg IV Q3W
Cycles 3–8: 75 µg/kg IV Q3W
+ rituximab
375 mg/m² IV Q3W

R-GemOx
Cycles 1–8: IV Q2W
Gemcitabine 1000 mg/m²
Oxaliplatin 100 mg/m²
Rituximab 375 mg/m²

EOT

Patients will be followed for up to 4 years after EOT

PRIMARY ENDPOINT
- PFS

SECONDARY ENDPOINTS
- OS, ORR, CRR, DOR, safety, PK, HRQoL

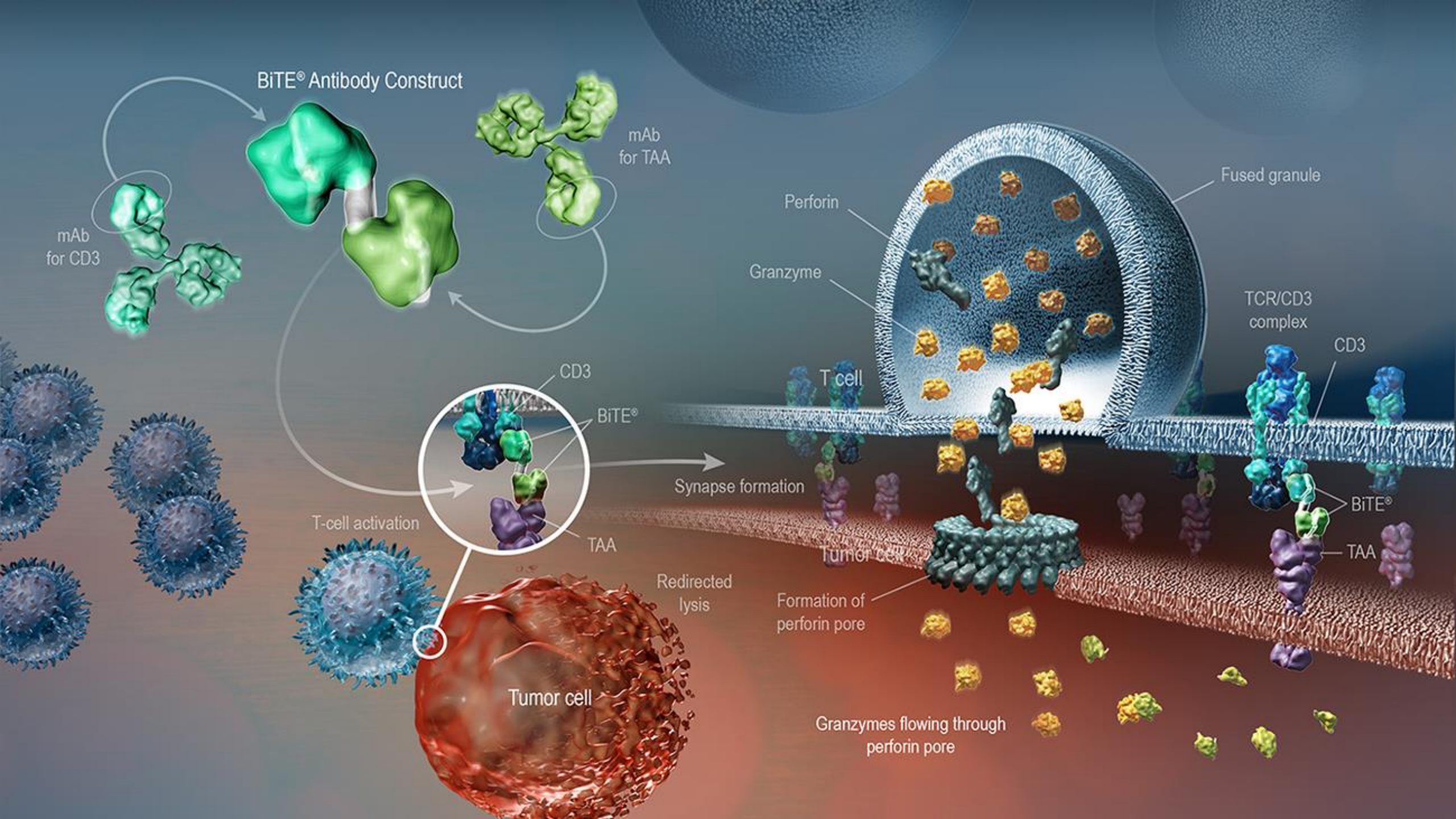
*As defined by the World Health Organization classification of lymphoid neoplasms[2]; †Including leptomeningeal disease.
AHCT, autologous hematopoietic cell transplantation; alloHCT, allogenic hematopoietic cell transplantation; CD, cluster of differentiation; CRR, complete response rate; DLBCL: relapsed/refractory diffuse large B-cell lymphoma; DOR, duration of response; ECOG PS, Eastern Cooperative Oncology Group performance status; EOT, end of treatment; HRQoL, health-related quality of life; IV, intravenous; Lonca, loncastuximab tesirine-lpyl; ORR, overall response rate; OS, overall survival; PFS, progression-free survival; PK, pharmacokinetics; Q2W, every 2 weeks; Q3W, every 3 weeks; R-GemOx, rituximab, gemcitabine, oxaliplatin; R/R, relapsed or refractory.

1. ClinicalTrials.gov. NCT04384484. Available at: https://clinicaltrials.gov/ct2/show/NCT04384484. Accessed April 01, 2021; 2. Swerdlow SH, et al. *Blood*. 2016;127:2375–90.

Prof. Carmelo Carlo-Stella, MD
Humanitas University
Humanitas Clinical and Research Center
Milan, Italy

“BITES”

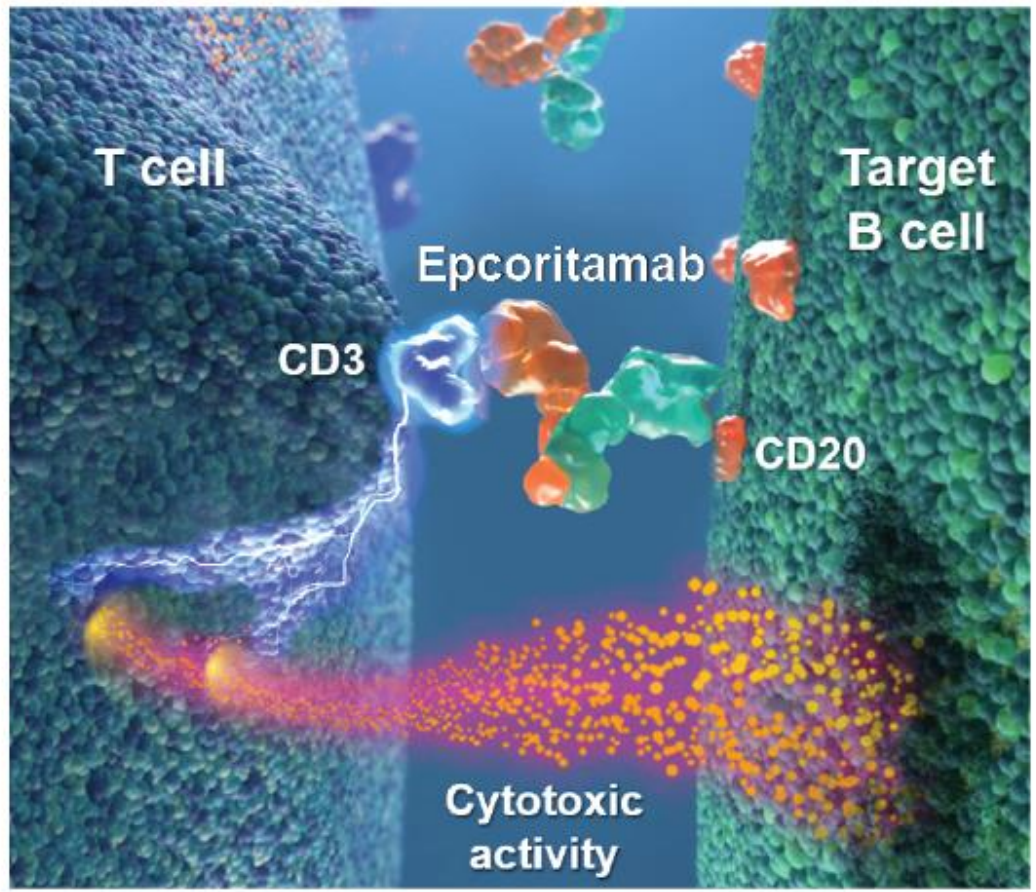
az sint-jan
brugge - oostende av


BiTE® Antibody Construct
mAb for TAA
mAb for CD3
CD3
BiTE®
TAA
T-cell activation
Redirected lysis
Tumor cell
Synapse formation
Perforin
Granzyme
Fused granule
T cell
TCR/CD3 complex
CD3
BiTE®
TAA
Tumor cell
Formation of perforin pore
Granzymes flowing through perforin pore

Epcoritamab

- Epcoritamab is a novel bispecific (CD3xCD20) T-cell–engaging antibody that promotes activation of a patient´s own immune system (CD3+ T-cells) to attack and kill CD20+ malignant B-cells[9,10] (**Figure 1**)
- The Fc domain of epcoritamab has been modified to silence Fc-mediated effector functions (eg, antibody-dependent cellular cytotoxicity, antibody-dependent cellular phagocytosis, or complement-dependent cytotoxicity) ensuring that epcoritamab does not activate T-cells through IgG Fc receptor–mediated CD3 crosslinking[9]
- Preserved binding to the neonatal Fc receptor induces a long plasma half-life[9]
- Subcutaneous administration provides more convenient dosing and may improve safety[9]

Figure 1. Epcoritamab Mechanism of Action



DOEL ANTIGEN	NAAM
CD19/CD3	BLINATUMOMAB
CD20/CD3	RG6026 GLOFITAMAB
CD20/CD3	MOSUNETUZUMAB
CD20/CD3	REGN1979 ODRONEXTAMAB
CD20/CD3	EPCORITAMAB

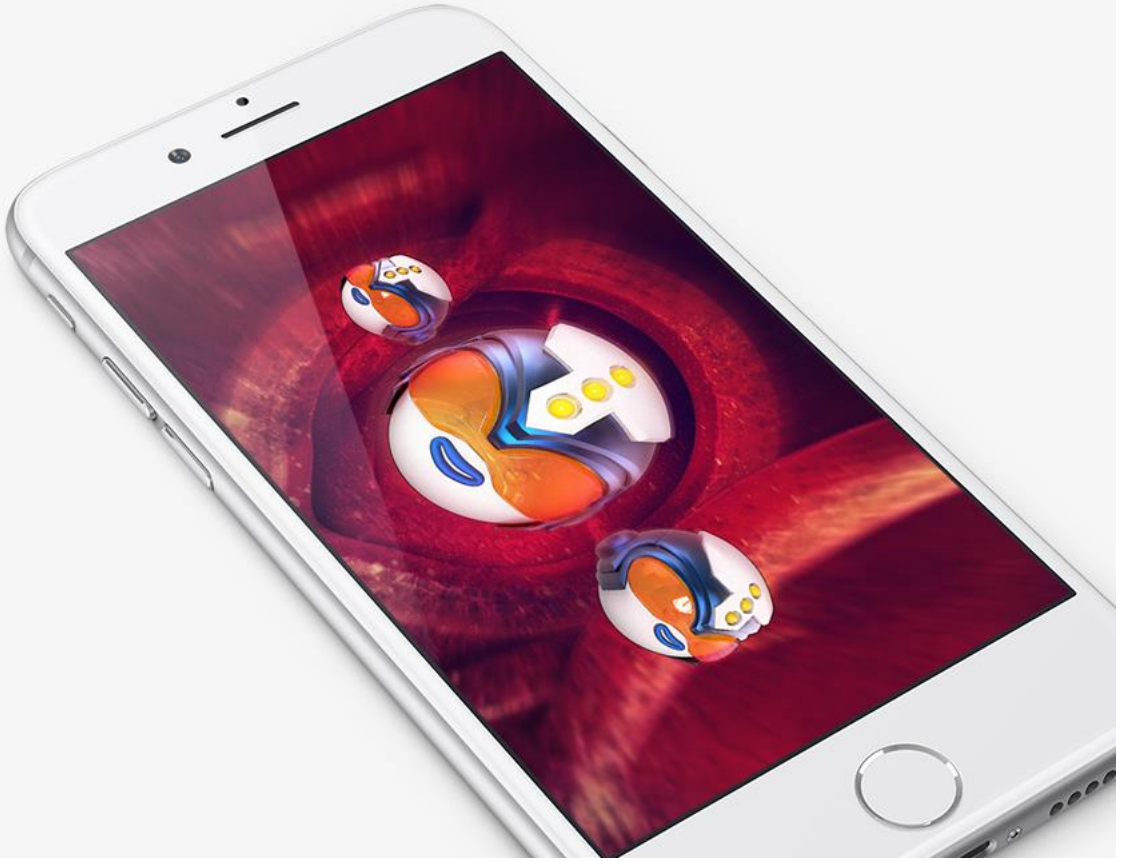
CAR T CELLEN

az sint-jan
brugge - oostende av

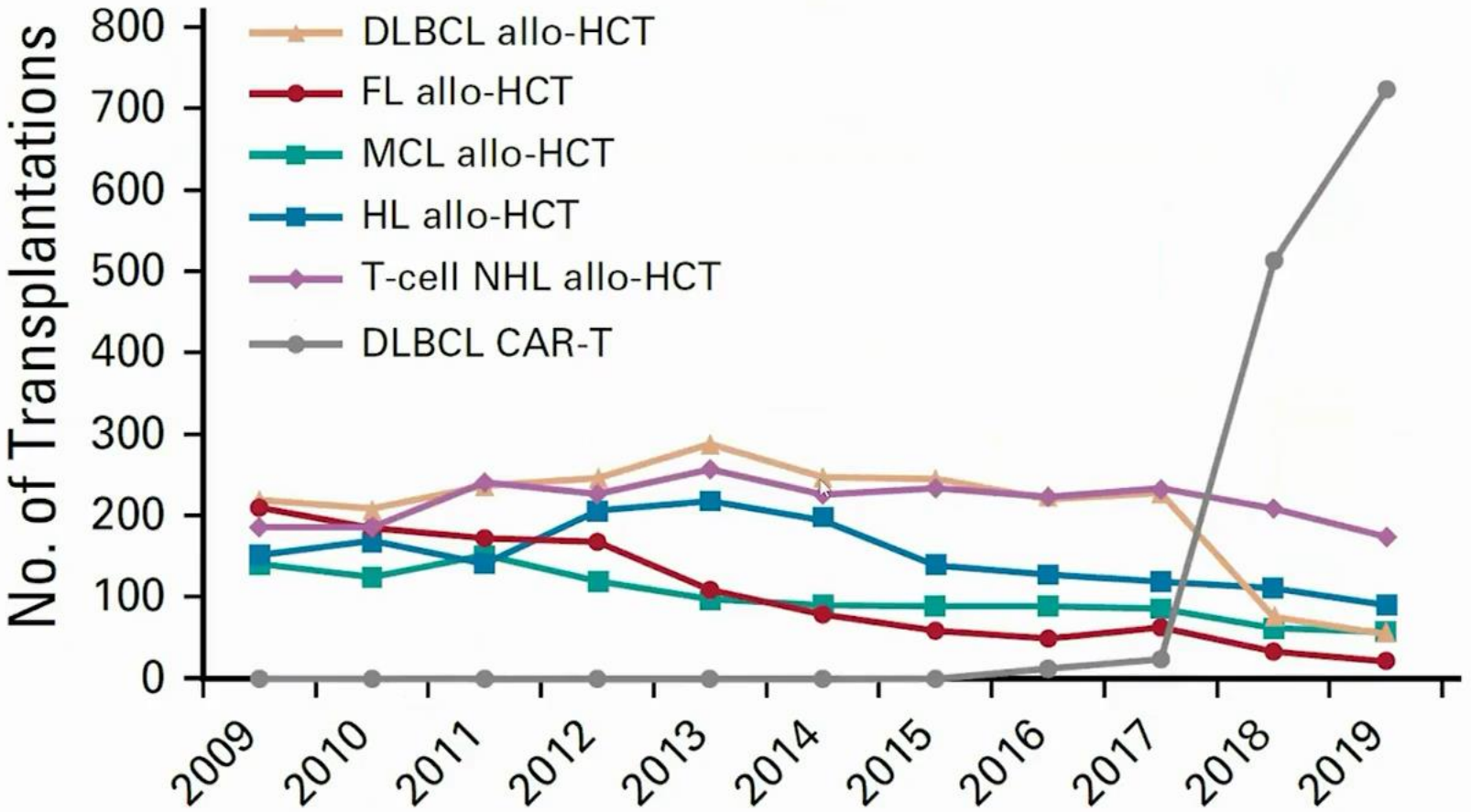
IMMUNO-T IN MOTION

Deze tool legt immunotherapie op een eenvoudige manier uit.

Welkom op de website van Immuno-T, de eerste motion comic om aan patiënten, en hun familie en vrienden, uit te leggen hoe verschillende vormen van immunotherapie werken. Immuno-T werd ontwikkeld door het UZ Gent en UGent, in de schoot van het Cancer Research Institute Gent (CRIG) en het Immuno-Oncologisch Network Gent (ION). Immunotherapie is een recent ontwikkelde, totaal nieuwe, vorm van behandeling voor kanker. Het betekent een doorbraak in de behandeling van vele kankers, en verdere ontwikkelingen stemmen onderzoekers en artsen hoopvol. Immunotherapie werkt totaal anders dan de klassieke behandelingen van kanker, zoals chemotherapie of radiotherapie (bestraling). Immunotherapie gebruikt het immuunsysteem van de patiënt om de kankercellen aan te vallen en te doden. Er bestaan verschillende vormen van immunotherapie, die allemaal complex zijn, en niet gemakkelijk uit te leggen. Daarom hebben we deze tool ontwikkeld.
Gebruik Immuno-T webversie (PC/Mac) / voor iPhone (via de App Store) / voor Android (via de Google Play Store).



CIBMTR: Lymphoma alloHCT activity over time



Shah & Hamadani, JCO 2021;39:487 CIBMTR

P. Dreger, Heidelberg (DE)

Revolutionaire therapie herprogrammeert afweersysteem

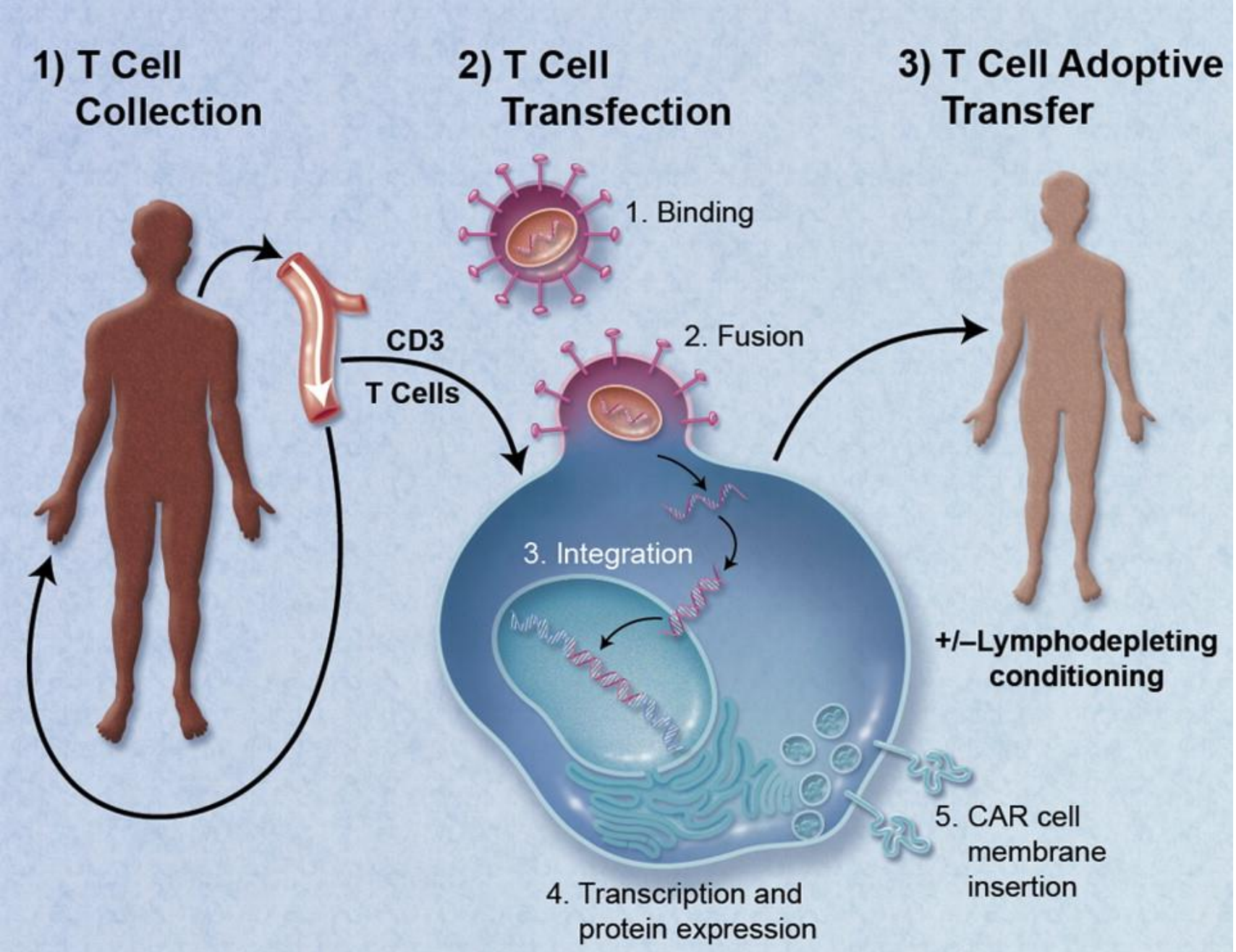
Genetisch gemanipuleerde cellen verslaan leukemie

De zevenjarige Emma Whitehead dankt haar leven aan een experimentele bloedkankertherapie. Door een variant van het hivvirus toe te voegen, konden haar eigen cellen leukemie verslaan. Met succes.

Denise Grady

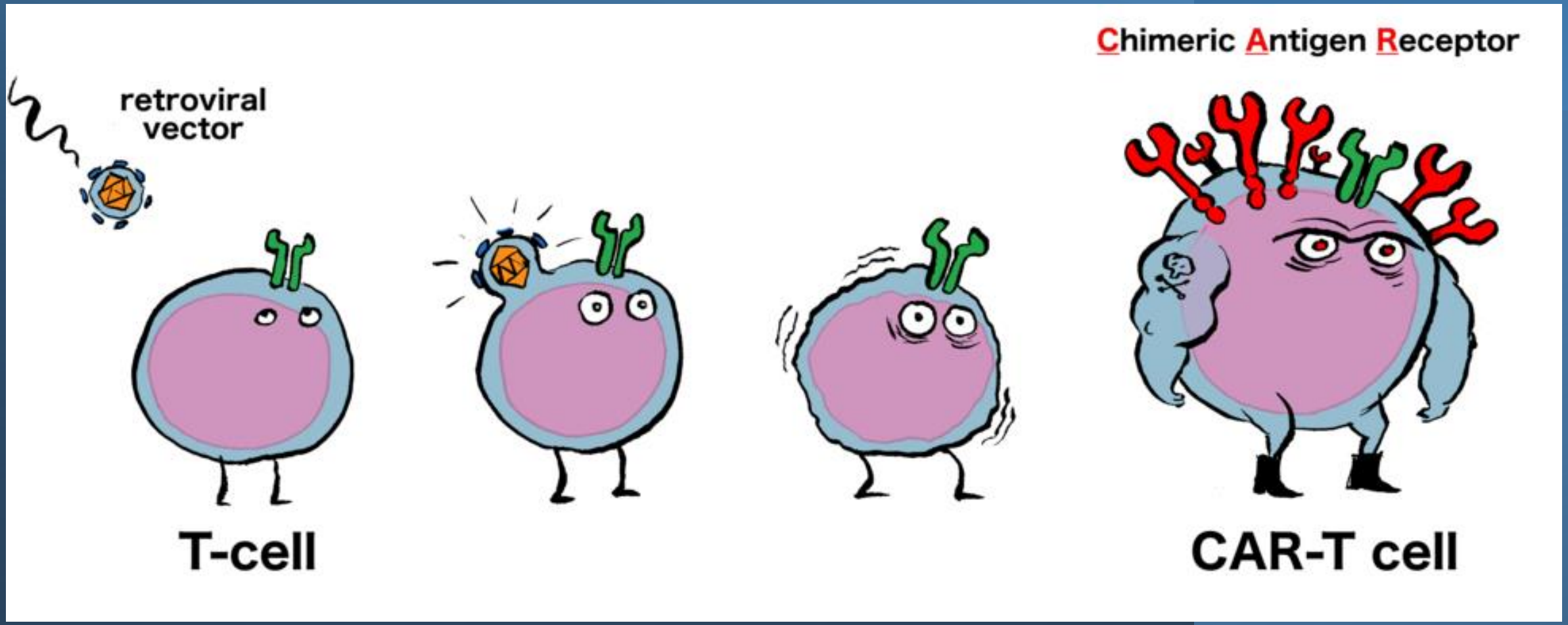
az sint-jan
brugge - oostende av

Bron: De Morgen, 29 december 2012



az sint-jan
brugge - oostende av

Lymphomation.org



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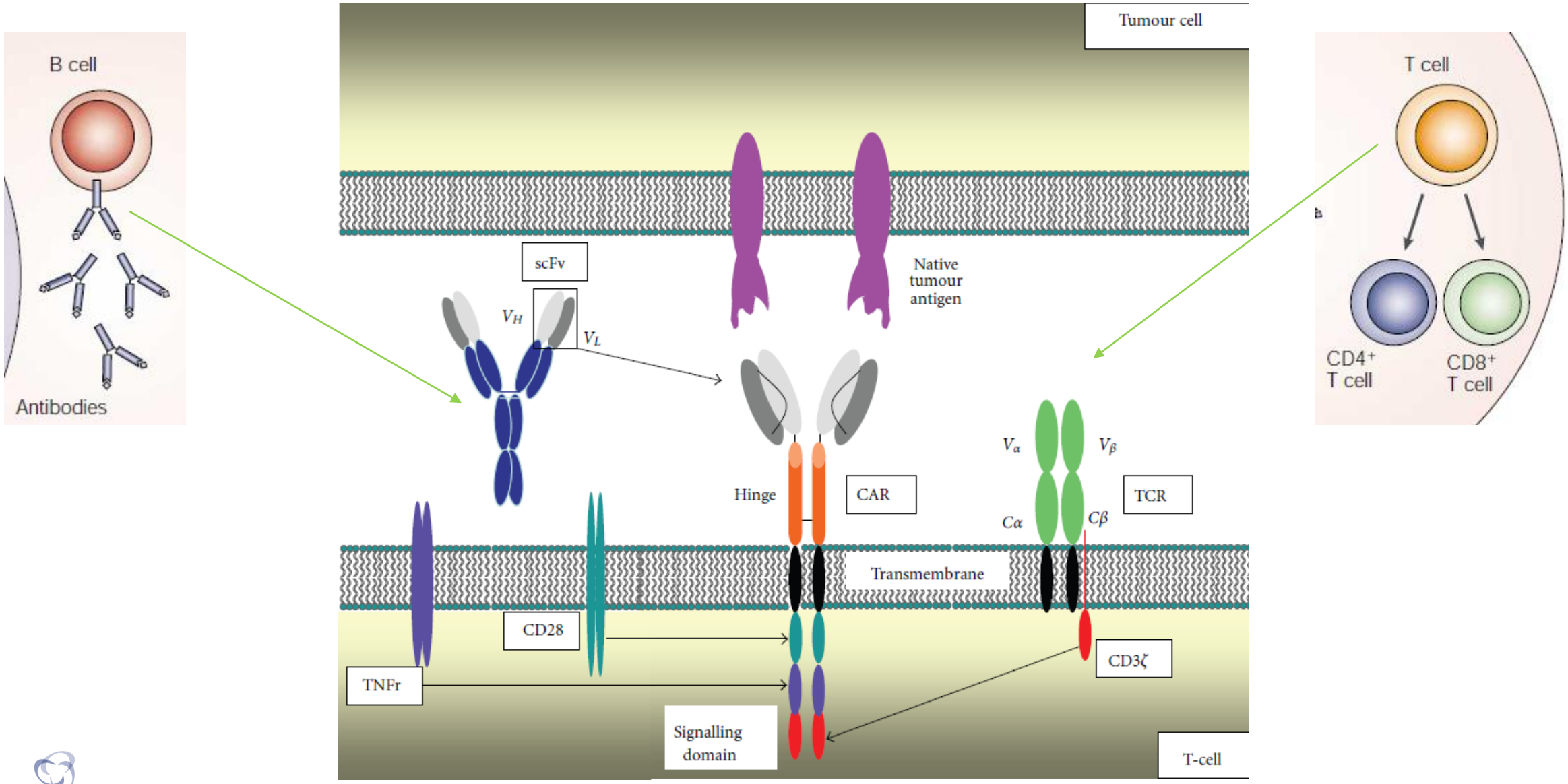
brugge - oostende av

CAR-T = chimeric antigen receptor T cellen

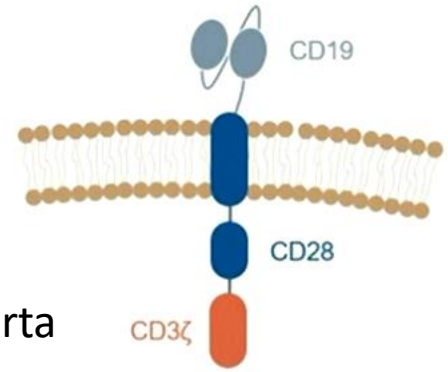


Maher, ISRN Oncology, 2012

CD19-directed CAR-T for R/R DLBCL

FDA (2017)[1] and **EMA** (2018)[2]

Axicabtagene ciloleucel[6] (Axi-cel)

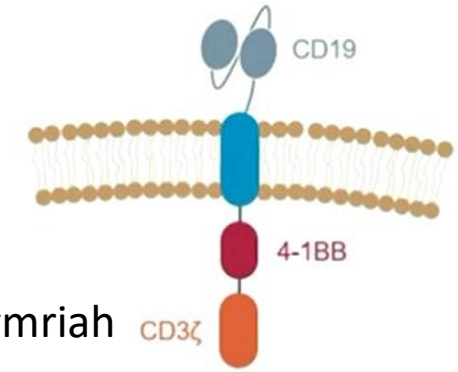


Yescarta

Gene transfer: Retroviral

FDA (2017)[3] and **EMA** (2018)[4]

Tisagenlecleucel[6] (Tisa-cel)

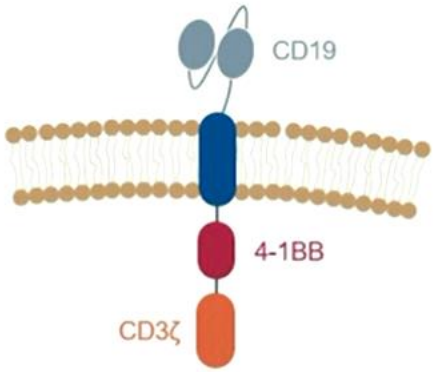


Kymriah

Gene transfer: Lentiviral

FDA (2021) only[5,*]

Lisocabtagene maraleucel[6] (Liso-cel)



Gene transfer: Lentiviral

*The Marketing Authorisation Application for lisocabtagene maraleucel was validated by the EMA on July 17, 2020. The submission is currently under centralized review.
CAR-T, chimeric antigen receptor T-cell therapy; CD, cluster of differentiation; CD3ζ, T-cell receptor zeta chain; DLBCL, diffuse large B-cell lymphoma; EMA, European Medicines Agency; FDA, Food and Drug Administration; R/R, relapsed or refractory.

1. Yescarta® (axicabtagene ciloleucel) [Prescribing Information]. Santa Monica, CA; Kite Pharma, Inc. Revised May 2020. Accessed April 22, 2021; 2. Yescarta® (axicabtagene ciloleucel) [Summary of Product Characteristics]. The Netherlands; Kite Pharma EU B.V. Revised July 26, 2020. Accessed April 22, 2021; 3. Kymriah™ (tisagenlecleucel) [Prescribing Information]. East Hanover, NJ; Novartis Pharmaceuticals Corporation. Revised December 2020. Accessed April 22, 2021; 4. Kymriah™ (tisagenlecleucel) [Summary of Product Characteristics]. Ireland; Novartis Europharm Ltd. Revised March 07, 2021. Accessed April 22, 2021; 5. Breyanzi® (lisocabtagene maraleucel) [Prescribing Information]. Bothwell, WA; Bristol-Myers Squibb. Revised February 2021. Accessed April 22, 2021; 6. Roex G, et al. *Pharmaceutics*. 2020;12:194.

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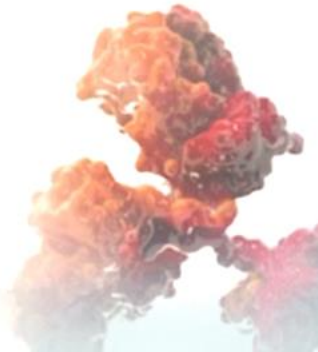
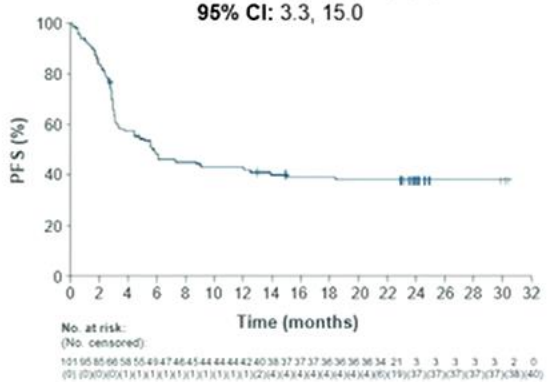


Approved CD19-directed CAR-T for R/R DLBCL: PFS

Weiyun Z. Ai, MD, PhD
University of California San Francisco,
San Francisco, CA, USA

Axi-cel[1]

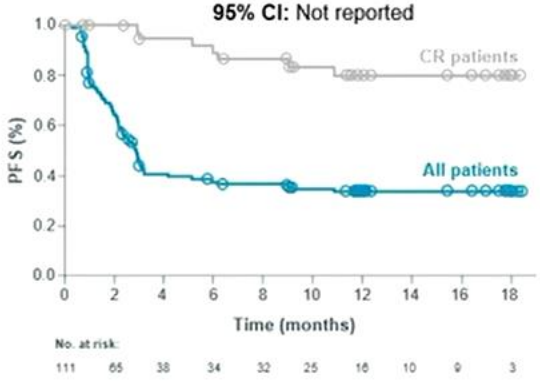
Median PFS: 5.9 months
95% CI: 3.3, 15.0



Median follow-up: 15.4 months†

Tisa-cel[2,*]

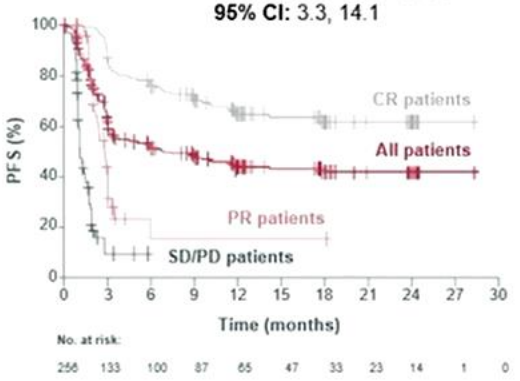
Median PFS: NR
95% CI: Not reported



Median follow-up: 28.6 months

Liso-cel[3]

Median PFS: 6.8 months
95% CI: 3.3, 14.1



Median follow-up: 18.8 months

DIRECT COMPARISONS CANNOT BE MADE IN THE ABSENCE OF HEAD-TO-HEAD TRIALS.

*Efficacy reported for the infused patient population (n=111); †All efficacy endpoints, except for median OS are reported with a median follow-up of 15.4 months. The median follow-up for median OS was 51.1 months.
Axi-cel, axicabtagene ciloleucel; CAR-T, chimeric antigen receptor T-cell therapy; CD, cluster of differentiation; CI, confidence interval; CR, complete response; DLBCL, diffuse large B-cell lymphoma; liso-cel, lisocabtagene maraleucel; NR, not reached; PD, progressive disease; PFS, progression-free survival; PR, partial response; R/R, relapsed or refractory; SD, stable disease; tisa-cel, tisagenlecleucel.
Figures reprinted with permission.

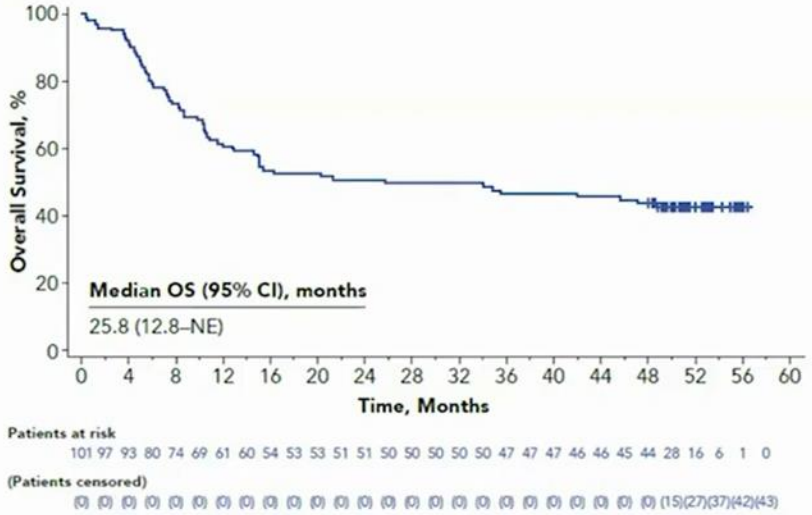
1. Locke FL, et al. *Lancet Oncol.* 2019;20:31–42; 2. Schuster SJ, et al. *N Engl J Med.* 2019;380:45–56; 3. Abramson JS, et al. *Lancet.* 2020;396:839–52.

UCSF

Long term follow up of CAR-T pivotal studies

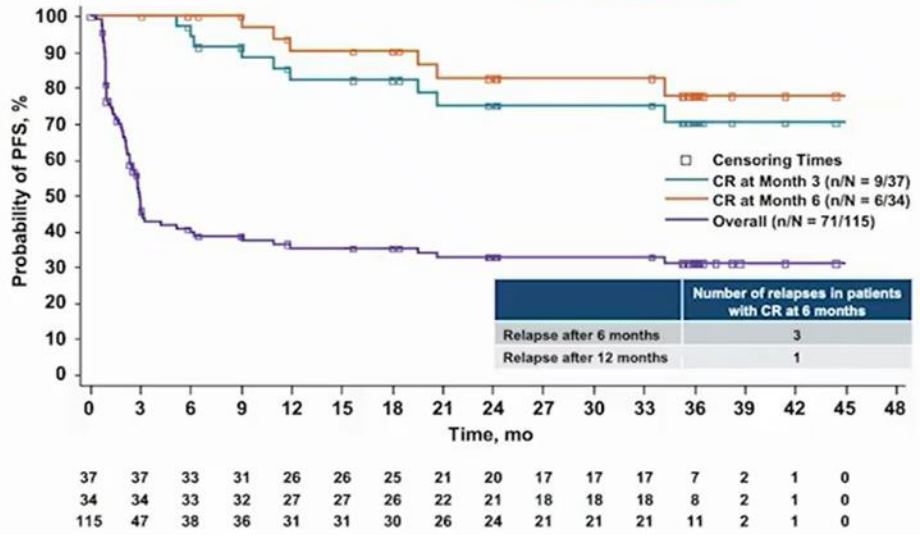
ZUMA-1: Overall Survival at 4 Years (mITT, n = 101)

The KM estimate of the 4-year OS rate was 44%
Median OS was 25.8 months



Juliet: DOR at 40 months (mITT, n = 115)

36-month PFS = 31%; 36 months OS = 36%



Jacobson CA et al. 2021 Transplantation & Cellular Therapy Meetings of ASTCT and CIBMTR. Abstract 494.

Jaeger U et al, ASH 2020, poster 1194

16th ICML

G. Salles, New York, NY (USA)

Limitations of CAR-T

Access

Can only be administered at certified CAR-T centers[1,2]

Not all patients have access to CAR-T due to logistical complexity[3]

Time

The time period between apheresis and CAR-T infusion ranges from 2 to 5 weeks[1]

Not all patients are eligible for effective bridging therapies, increasing the risk of relapse[2,4]

Data

Limited data in patients >65 years (many of whom are not suitable candidates for CAR-T)[5,6]

Only non-randomized study data available;[1] randomized comparisons vs. other therapies are ongoing[7]

Cost

High cost of individualized CAR-T products and adverse event management[1]

Resistance

Not all patients respond and many progress;[1] resistance mechanisms are not clearly elucidated

CAR-T, chimeric antigen receptor T-cell therapy.

1. Chavez JC, et al. *Ther Adv Hematol*. 2019;10:1–20. 2. Cahill KE, et al. *Leuk Lymphoma*. 2020;61:799–807; 3. Nastoupil LJ, et al. *J Clin Oncol*. 2020;38:3119–28; 4. Yakoub-Agha I, et al. *Haematologica*. 2020;105:297–316; 5. Kersten MJ, et al. *Curr Opin Oncol*. 2020;32:408–17; 6. Neelapu SS, et al. *Blood*. 2020;135:2106–9; 7. Vitale C, Strati P. *Front Oncol*. 2020;10:849.

UCSF

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