

AGGRESSIEVE NH-LYMFOMEN: ziektebeeld en behandelstrategie

KRISTEL BUVE

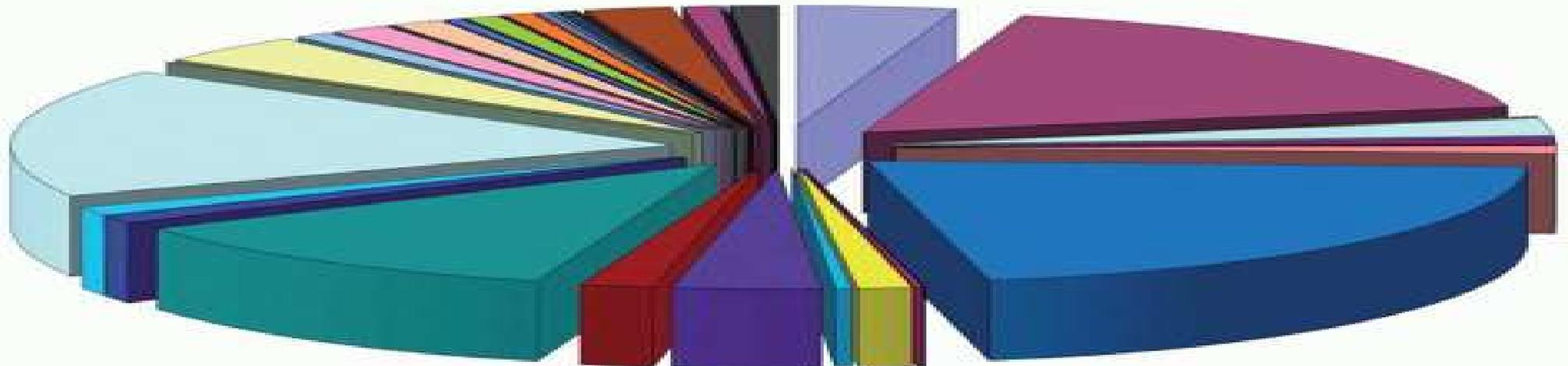
JESSA

04/10/2025



- Precursor Non-Hodgkin lymphoma, B-cell
- Chronic/Small lymphocytic leukemia/lymphoma
- Prolymphocytic leukemia, B-cell
- Mantle-cell lymphoma
- Lymphoplasmacytic lymphoma
- Waldenstrom macroglobulinemia
- DLBCL, NOS
- Intravascular large B-cell lymphoma
- Primary effusion lymphoma
- Mediastinal large B-cell lymphoma
- Burkitt lymphoma/leukemia
- Splenic MZL
- Extra nodal MZL, MALT
- Nodal MZL
- Follicular lymphoma
- Hairy-cell leukemia
- Plasmacytoma
- Multiple myeloma/plasma-cell leukemia
- Heavy chain disease
- NHL, B cell, NOS
- Precursor Non-Hodgkin lymphoma, T-cell
- Mycosis fungoides

- Sezary syndrome
- Peripheral T cell lymphoma, NOS
- Angioimmunoblastic T-cell lymphoma
- Subcutaneous panniculitis-like T-cell lymphoma
- Anaplastic large cell lymphoma, T-cell or null-cell type
- Hepatosplenic T-cell lymphoma
- Enteropathy-type T-cell lymphoma
- Cutaneous T cell lymphoma, NOS
- Primary cutaneous anaplastic large cell lymphoma
- Adult T-cell leukemia/lymphoma
- NK/T-cell lymphoma, nasal-type/aggressive NK-cell leukemia
- T-cell large granular lymphocytic leukemia
- Prolymphocytic leukemia, T-cell
- NHL T cell NOS
- NHL, unknown lineage
- Precursor lymphoblastic leukemia/lymphoma, unknown lineage
- Prolymphocytic leukemia, unknown lineage
- NHL, NOS, unknown lineage



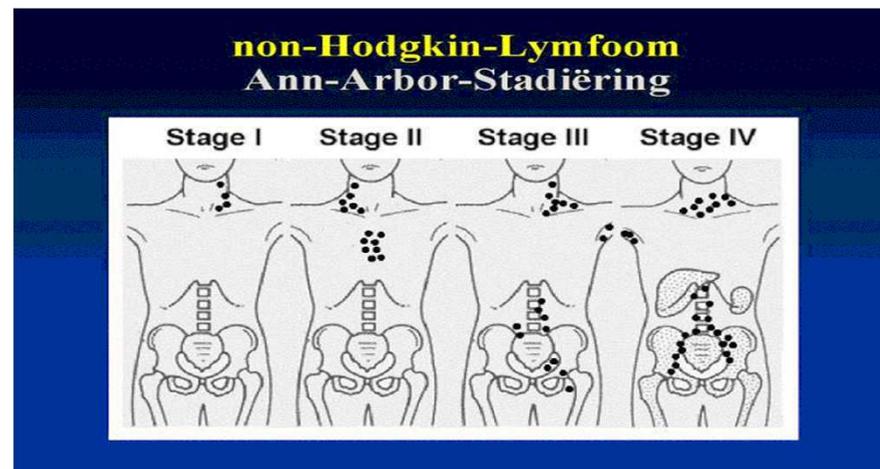
Aggressieve B-NHL

1. DLBC , Diffuus grootcellig lymfoom
2. MCL , Mantel Cel lymfoom (blastoide variant)
3. Burkitt Lymfoom
4. PCNS , Primair Central Zenuwstelsel Lymfoom
5. Primair Mediastinaal Lymfoom

1. Diffuus grootcellig B-cel NHL

DLBCL : ziektebeeld

- 25-30% van alle NHL
- Pijnloze harde klieren die snel groeien
- 1/3 B-symptomen : vermagering, koorts en nachtzweeten
- 40% extranodale aantasting met symptomen van orgaan van aantasting (longen, buik...)
- 10-20% beenmerginvasie
- 50% stage I-II, 50% stage III-IV



DLBCL : ziektebeeld en prognose

Tabel 2: prognostische scores

Prognostisch ongunstige factoren IPI:	Leeftijd > 60 jaar LDH > 1x normaal Performance status > 2 Stadium III of IV > 1 extranodale lokalisatie Nier- en/of bijnierbetrokkenheid (alleen CNS-IPI)
IPI:	
Laag risico	0 of 1 risicofactor
Laag intermediair risico	2 risicofactoren
Hoog intermediair risico	3 risicofactoren
Hoog risico	4 of 5 risicofactoren
'Age adjusted' IPI (aaIPI) NB Geen punten voor extranodale lokalisaties; leeftijd vervalt	
Laag risico	Geen risicofactor
Laat intermediair risico	1 risicofactor
Hoog intermediair risico	2 risicofactoren
Hoog risico	3 risicofactoren
CNS IPI	
Laag	0-1 risicofactor
Intermediair risico	2-3 risicofactoren
Hoog risico	4-6 risicofactoren

DLBCL : ziektebeeld

Het verschil is dat bij een "hit" lymfoom (**double/triple**) sprake is van specifieke genetische veranderingen (herschikkingen of translocaties) in de genen MYC en BCL (zoals BCL2 of BCL6) op de chromosomen, terwijl bij een "expressor" lymfoom (**double expressor**) de genen MYC en BCL zelf niet herschikt zijn, maar wel de eiwitten die ze produceren overmatig tot uiting komen (overexpressie) op de lymfoomcellen

DLBCL : behandelingen -> chemo-immunotherapie first line

- Gouden standaard first line : R-CHOP of R-mini-CHOP afh leeftijd en ECOG
 - Om 3 weken cyclus
 - Meestal 6 cycli , beperkt stadium : 4 cycli en IVNRT
 - Altijd echocardiografie vooraf en ev tussentijds of na behandeling ovw cardiotoxiciteit anthracycline
 - Cave neuropathie, obstipatie tgv vincristine
 - Tussentijdse PET controle
- CNS (Central nervous system) profylaxe : soms afhankelijk risico





DLBCL double/triple hit : behandeling first line

Intensievere chemoschema's

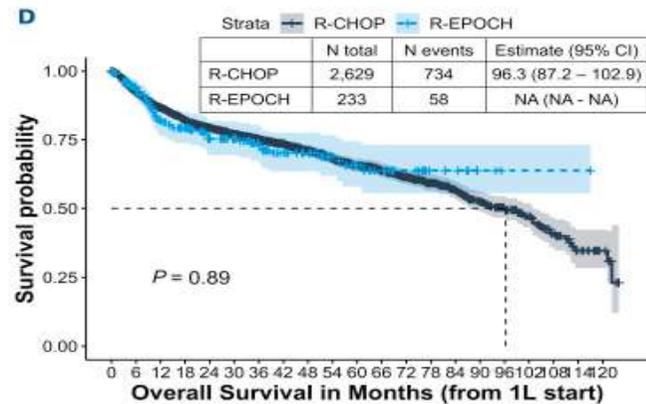
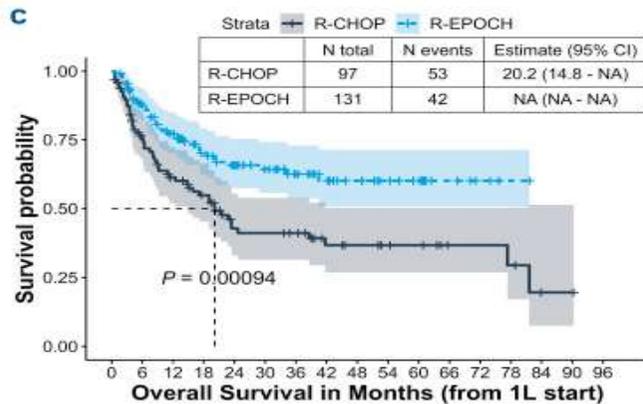
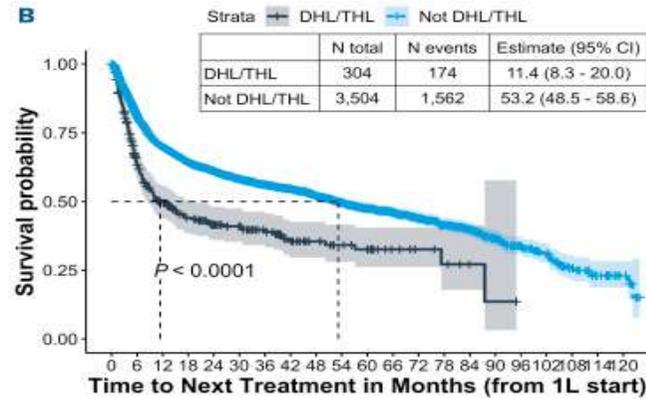
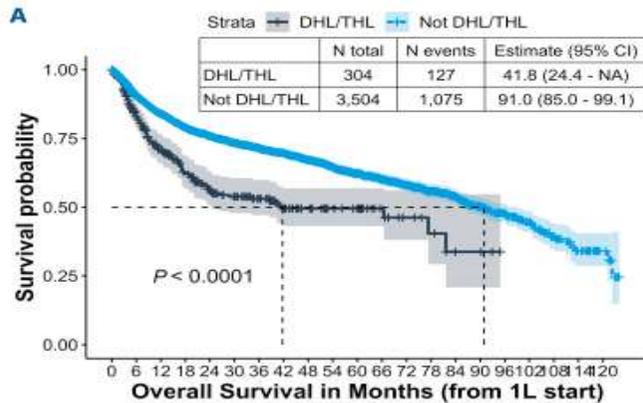
CNS profylaxe altijd

→R-DA-EPOCH met CNS profylaxe wordt geadviseerd.

Dit schema is ook prospectief geëvalueerd en resulteerde in een 4-jaars EFS van 71% en OS van 77%

Er is geen evidentie om in complete remissie te consolideren met een autologe stamceltransplantatie

DLBCL : ziektebeeld



Kaplan-Meier curves of overall survival.

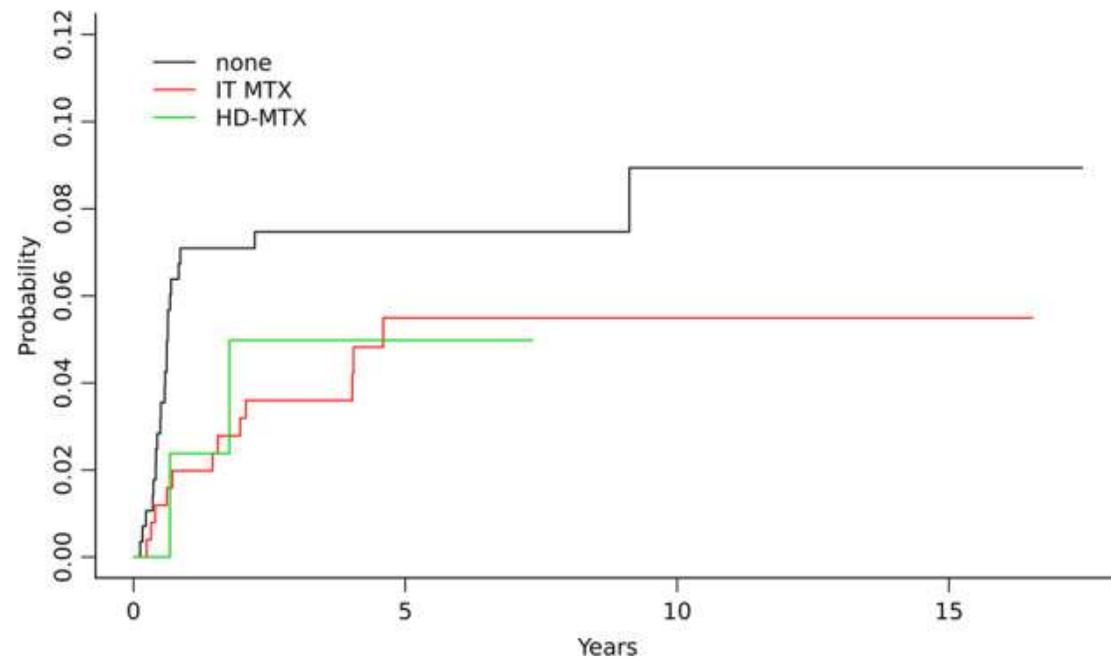
(A, B) Real-world overall survival (A) and time to next treatment (B) stratified by gene-rearrangement status among patients who had undergone cytogenetic testing.

(C, D) Real-world overall survival stratified by first-line treatment (R-CHOP vs. R-EPOCH) among patients with diffuse large B-cell lymphoma divided by cytogenetic group into those with double/triple hit lymphoma (C) and those without double/triple hit lymphoma (D).

CNS profylaxe

- Intraveneuze HD Methotrexaat met hydratatie, folinaat rescue bij R-CHOP/R-Polivy-CHP
- Intrathecale chemo MTX bij DA-EPOCH

Prophylaxis among High risk CNS category



Blood Cancer J 2021 Jun 16;11(6):113.

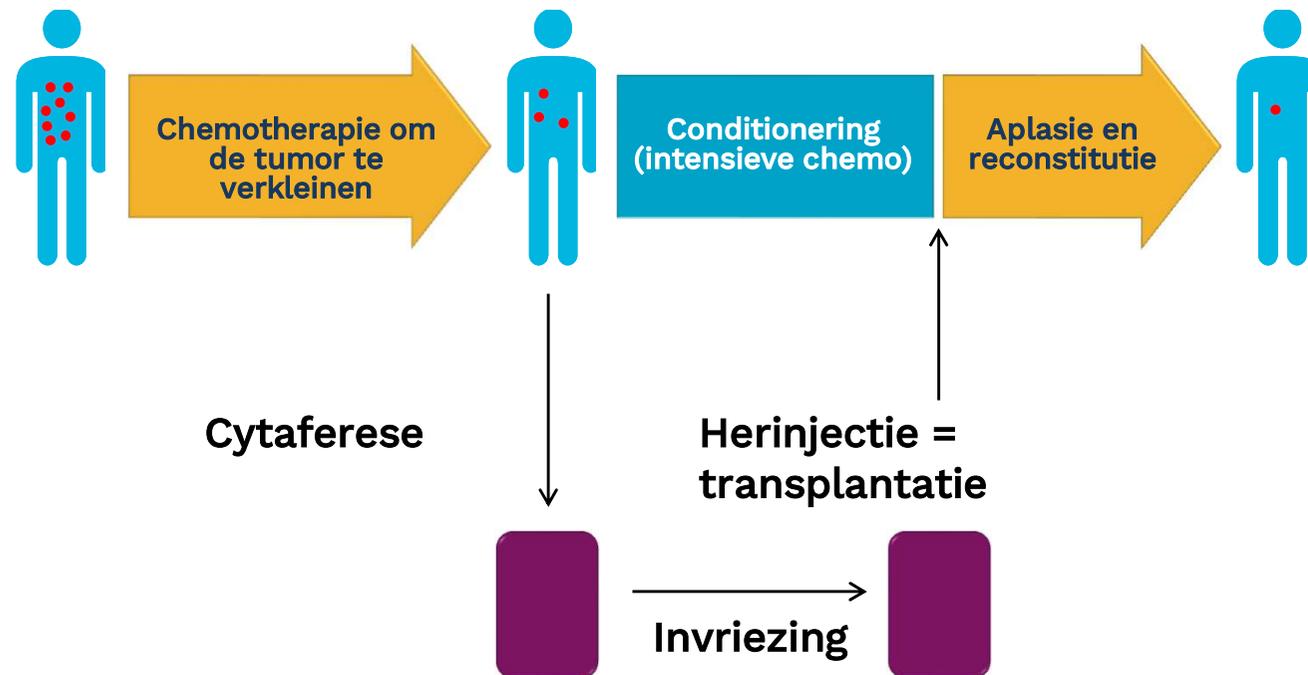
DLBCL herval, wat nu ?

CHEMO ? AUTOLOGE TX? BISPECIFICS ? CAR-T TRANSPLANTATIE?

Autologe stamtransplantatie

2^e lijn

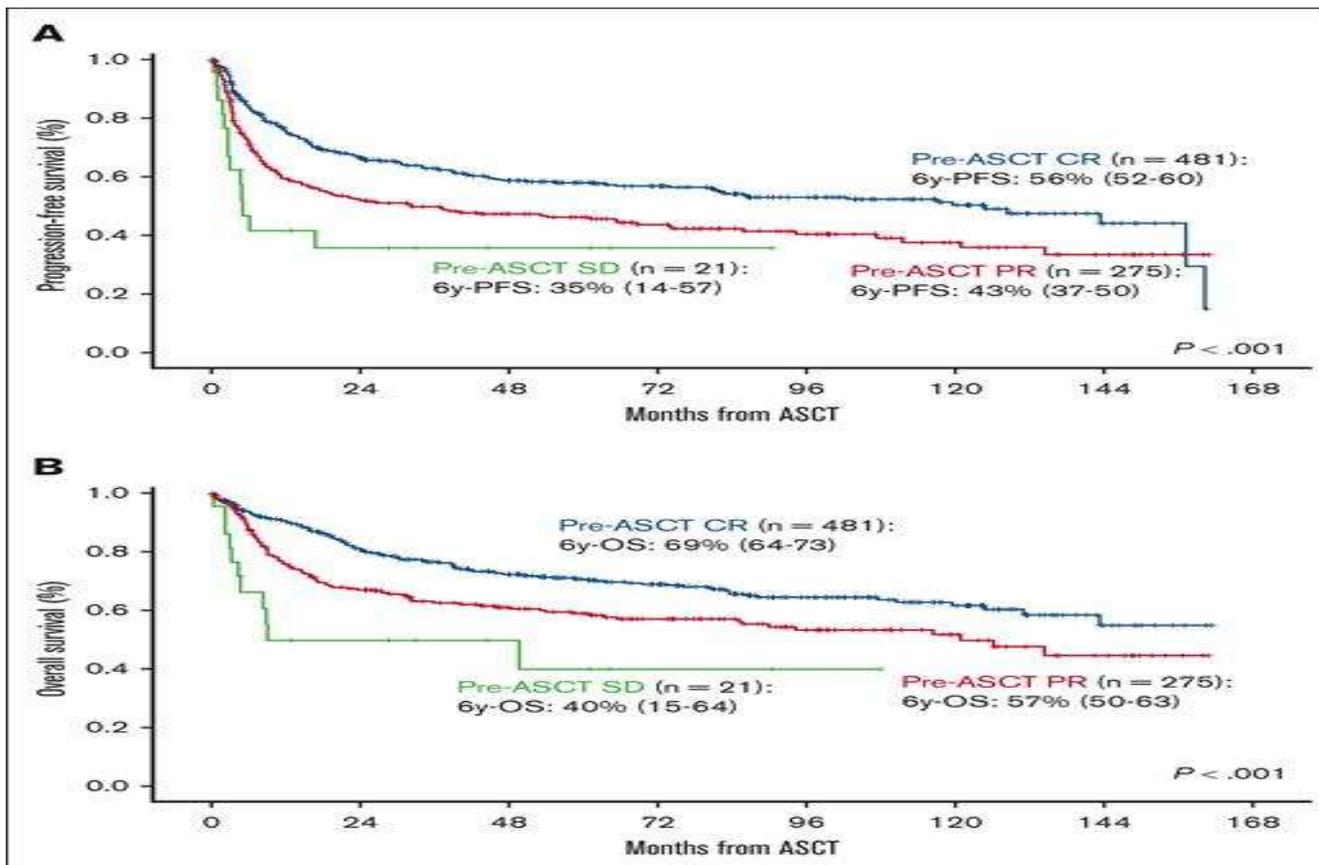
Autologe stamceltransplantatie: verloop



DLBCL : Autologe TX

- Patienten die niet in aanmerking komen voor CAR-T (>1 jaar na vorige behandeling recidief)
- Cave stamcelcollectie is niet altijd mogelijk
- Eerst chemo gevolgd door BEAM en autologe transplantatie
- Curatieve optie bij chemogevoelige lymfomen
- Leeftijdsgrens 70 jaar of obv comorbiditeiten

DLBCL : Autologe TX



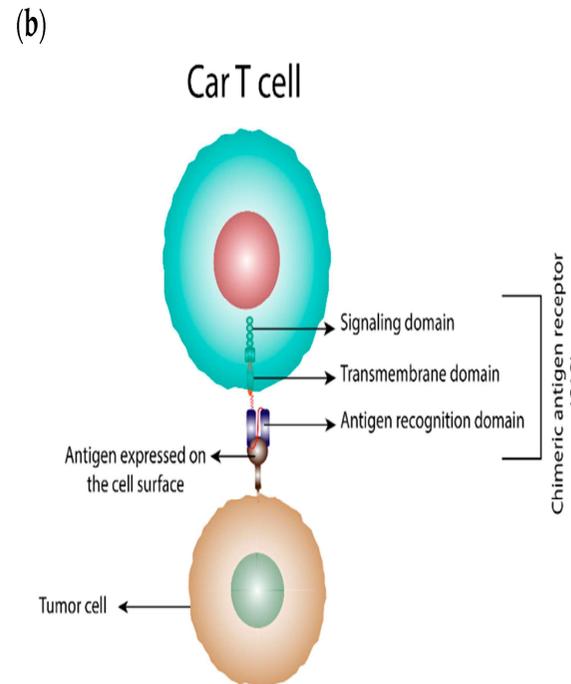
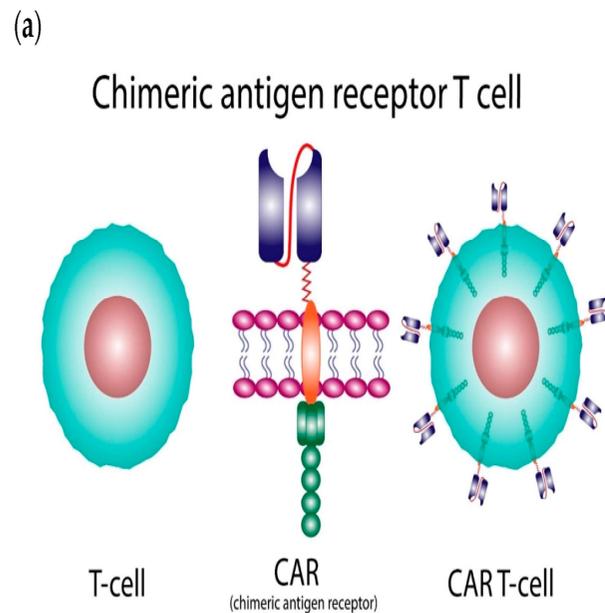
Complete remissiestatus pretransplant beïnvloedt PFS en OS!

CAR-T transplantatie 2^e lijn

Chimeer Antigen Receptor T-cel



DLBCL : wat zijn CAR-T cellen?



The primary construct of a **CAR** consists of **three parts**:

1. antigen recognition domain
2. transmembrane domain
3. signaling domain

When the antigen recognition domain of CAR binds to the antigen on the tumor cell, the CAR-T cell will be activated and serve as a 'living drug' that attacks and eliminates the tumor cell.

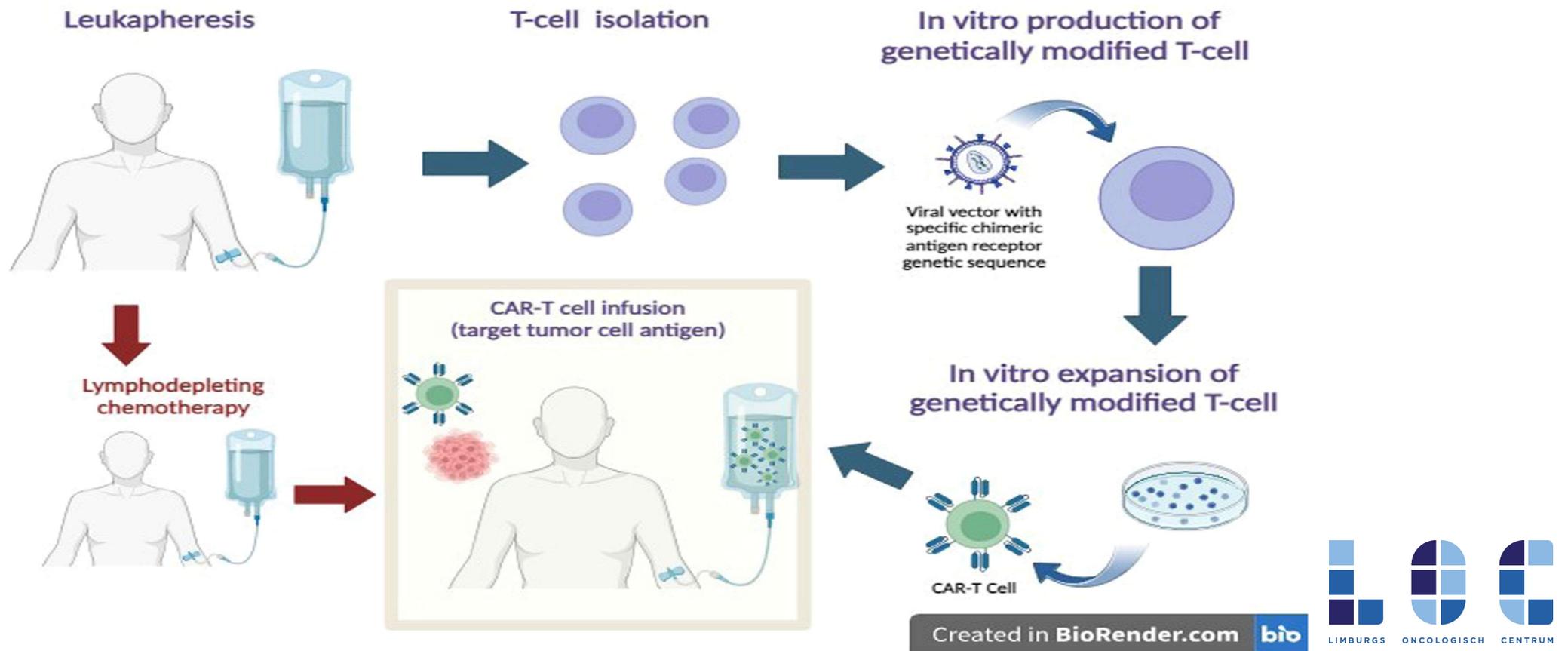
DLBCL : CAR-T

Axicabtagen ciloleucel (Yescarta)

2^e lijn R/R DLBCL sinds 01/12/2023, herval binnen het jaar na therapie

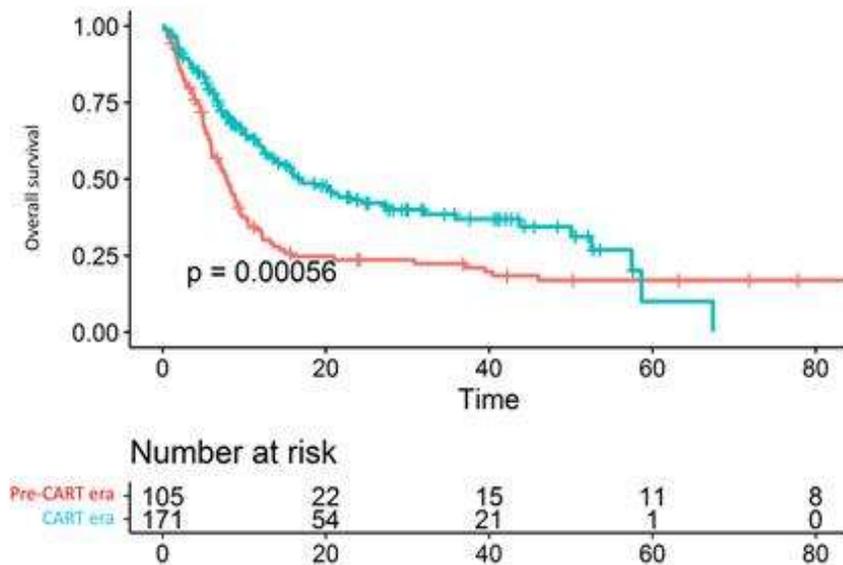
CAVE CRS (Cytokine Release Syndrome) en ICANS (Immune Effector Cell-Associated Neurotoxicity Syndrome) : maar behandelbaar !

DLBCL : CAR-T , patiëntentraject





DLBCL : behandelings CAR-T in R/R double-triple hit NHL

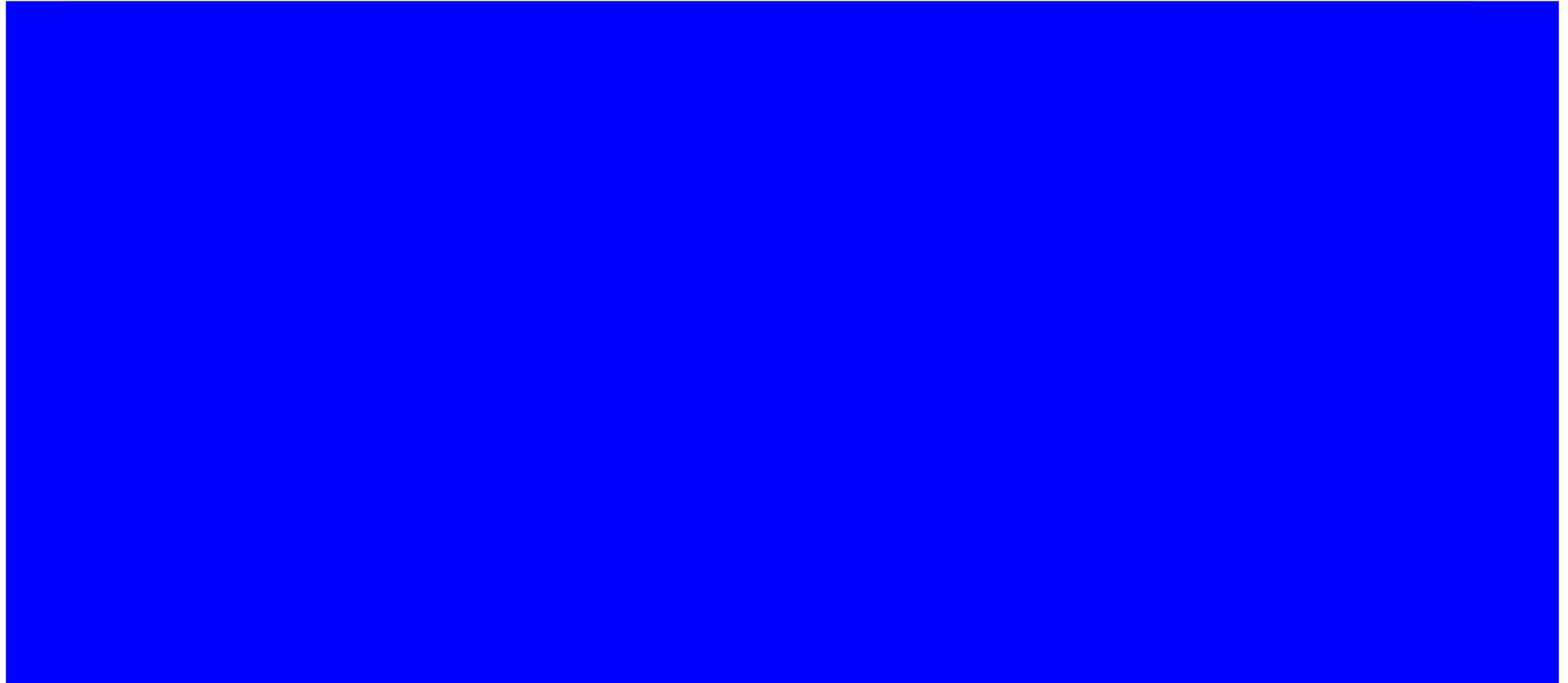


Patients treated in CAR-T cell era had significantly higher OS (2 yr OS: 43% [CI₉₅: 35-53]) compared to pts treated in pre-CAR-T cells era (2-year OS: 24% [CI₉₅: 16-34], $p=0.0006$)

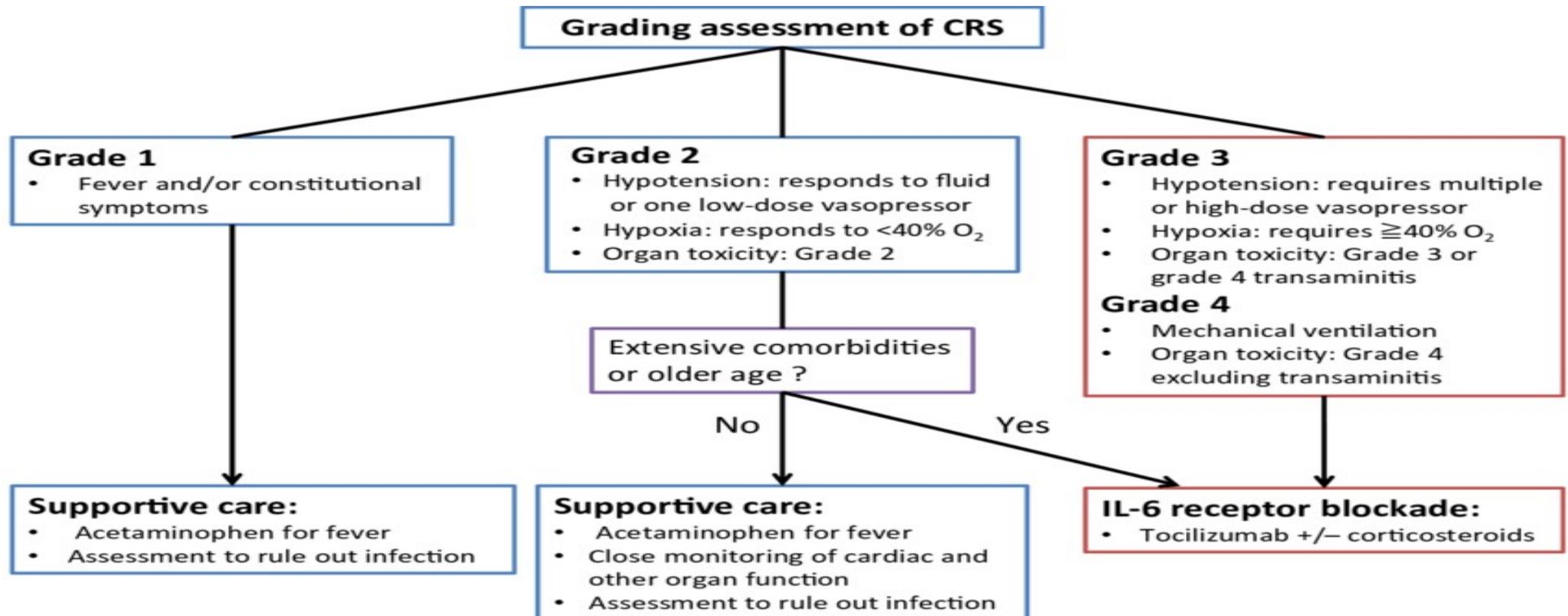
Blood (2023) 142 (Supplement 1): 308.

CAR-T en CRS en ICANS

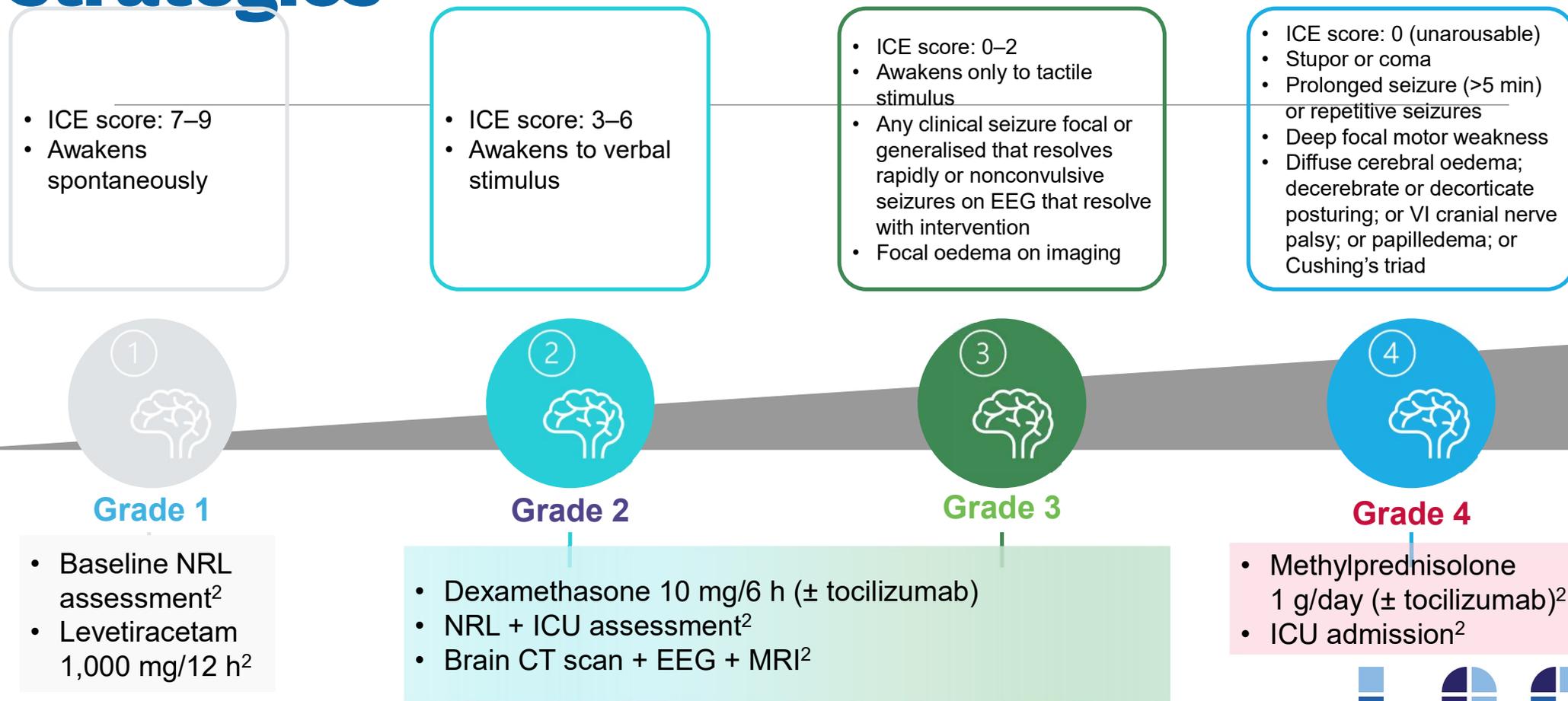
CAR-T: Cytokine Release Syndrome , CRS



CRS scoring



ICANS scoring and local management strategies¹



Please refer to your local guidelines and SmPCs for full licenced indications and further information

MRI: magnetic resonance imaging; NRL: neurological

1. Lee DW, et al. *Biol Blood Marrow Transplant* 2019; 25:625-638. 2. Speaker's own opinion.

ICANS : ICE score

Table 4. Immune Effector Cell Encephalopathy (ICE) Scoring

	Task	Points
Orientation	Orientation to year, month, city, hospital	4
Naming	Ability to name 3 objects (e.g., pen, mouse, keyboard)	3
Follow commands	Ability to follow simple commands (e.g., point to the computer)	1
Language/writing	Ability to write a simple sentence	1
Attention	Ability to count backwards from 100 by 10	1

Note. Adapted from Rees et al. (2022).

Immunomodulatoren 2^e lijn

DLBCL : Immuunmodulatoren

Lenalidomide (PO-Revlimid) + Tafasitamab
 (=anti-CD 19) (Minjuvi)

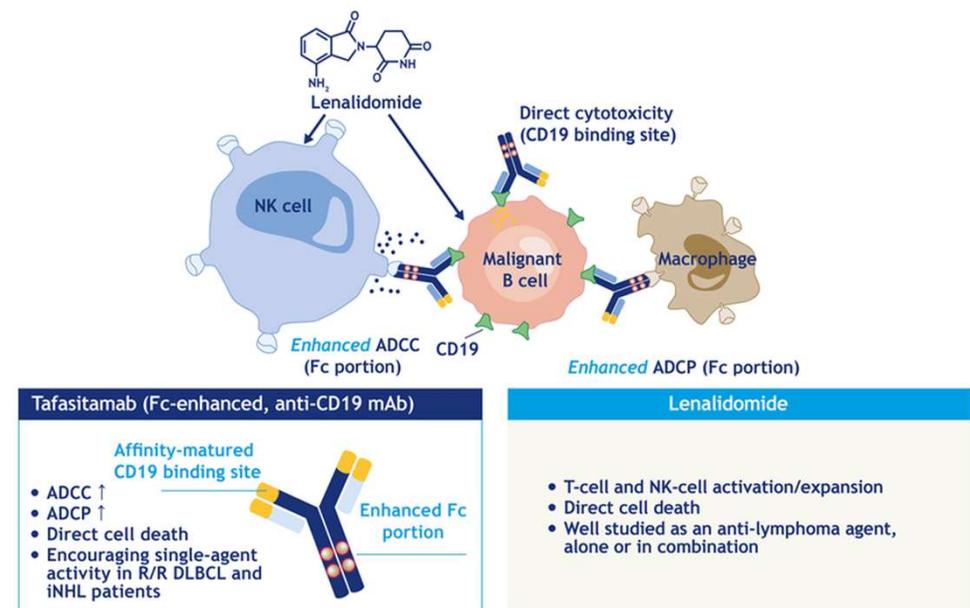
R/R DLBCL , vanaf 2^e lijn, bij patienten die niet in
 aanmerking komen voor een autologe
 transplantatie

Cyclus 1 : Dag 1+4+8+15+22

Cyclus 2+3 : Dag 1+8+15+22

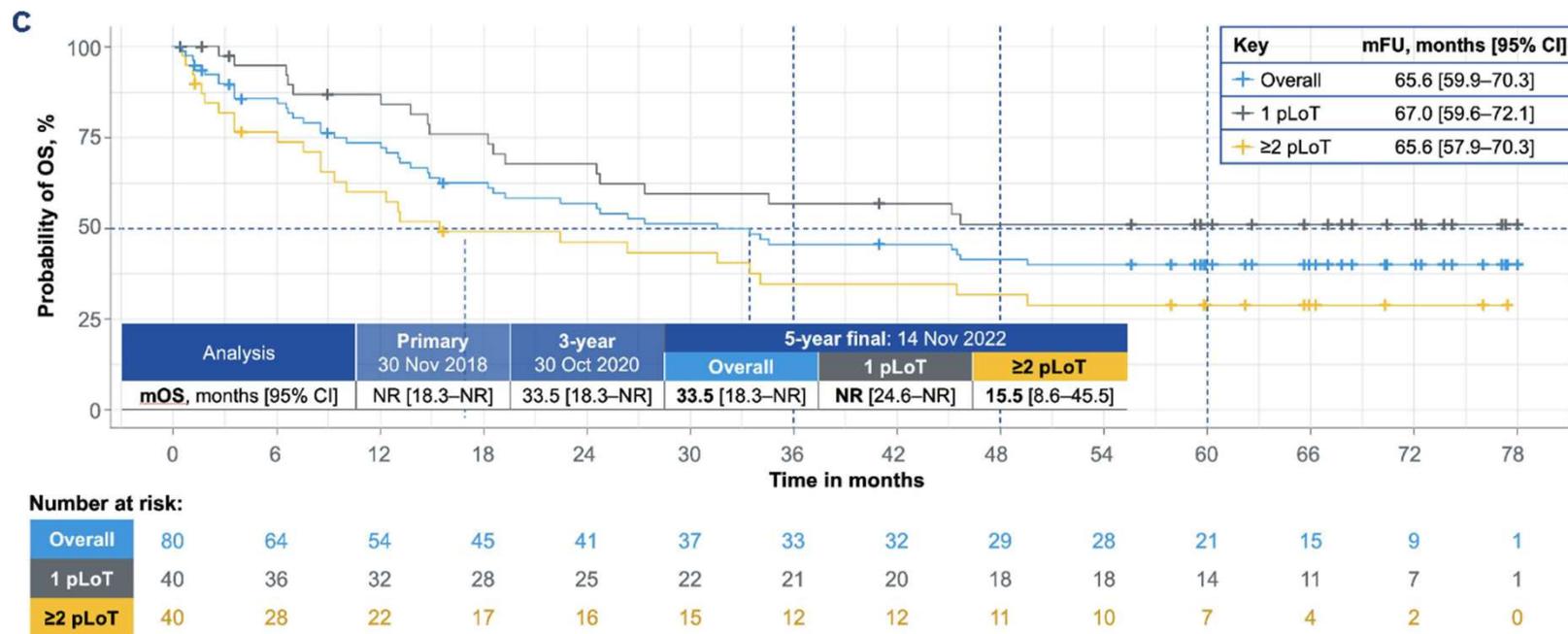
Cyclus 4- tot ziekteprogressie : Dag 1+15

na C12: Lenalidomide stop



ADCC, antibody-dependent cellular cytotoxicity; ADPC, antibody-dependent cellular phagocytosis; DLBCL, diffuse large B-cell lymphoma; iNHL, indolent non-Hodgkin's lymphoma; mAb, monoclonal antibody; NK, natural killer; R/R, relapsed/refractory.

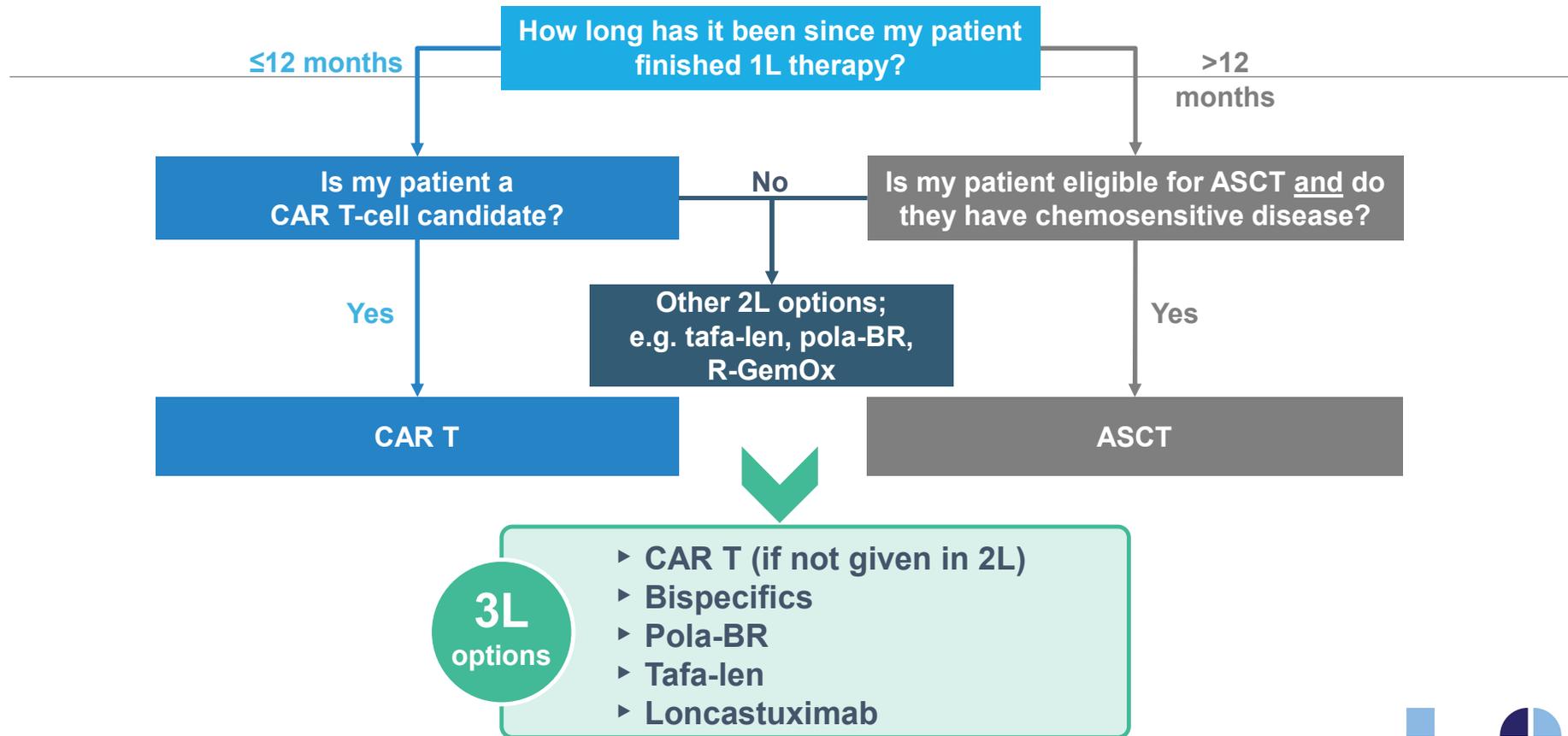
DLBCL : Tafa 5 jaar follow-up



Hematologica Vol. 109 No. 2 (2024): February, 2024

Bispecifics 3^e lijn

If a patient does not respond to 2L therapy, what treatment options are available in the 3L setting?^{1,2}



This proposed treatment algorithm should not replace local clinical guidelines and recommendations. Some drugs/indications may not be licensed for use in EU; please refer to local prescribing information for full details

1. Westin JR & Sehn L. *Blood* 2022; 139:2737–2746. 2. Ryan CE & Jacobson CA. *Semin Hematol* 2023; 60:322–328.

DLBCL : bispecifics

Soort “tweeledige” antibody (gekend bij ALL en MM)

DLBCL : Glofitamab ([Columvi](#)) en Epcoritamab ([Tepkinly](#))

[Tepkinly](#) , 1 cyclus = 4 weken

wekelijks C1-3 , 2-wekelijks C3-9

maandelijks vanaf C10 tot ziekteprogressie

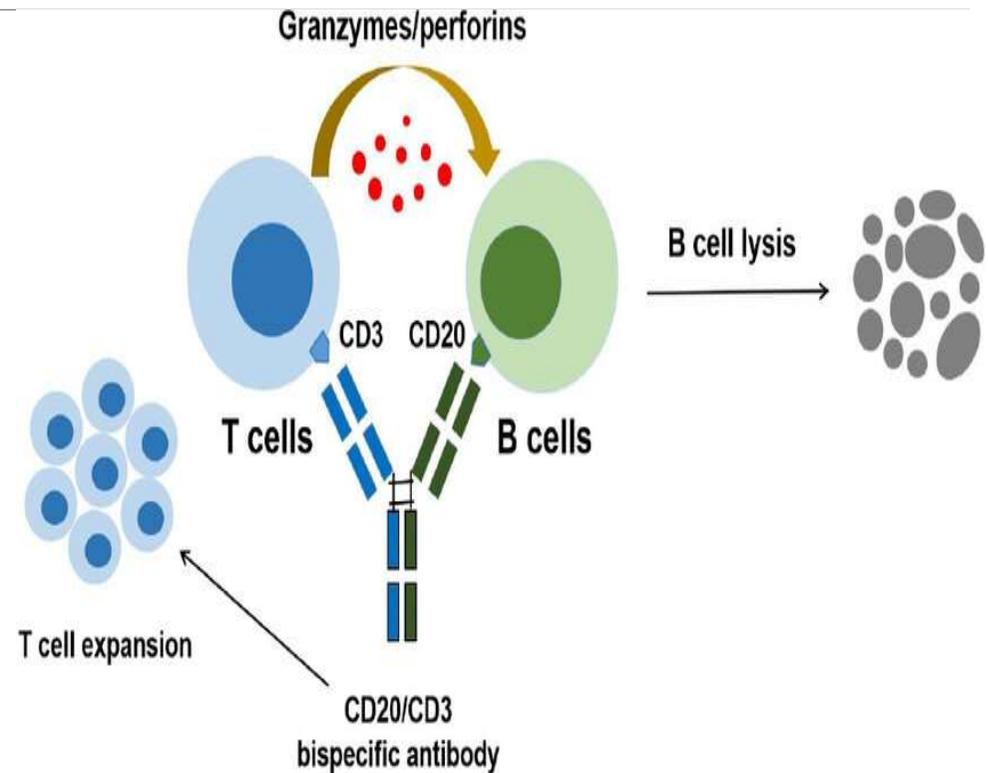
[Columvi](#) , 1 cyclus = 3 weken,

wekelijks C1 met op dag 1 voorbehandeling
Obinutuzumab

3-wekelijks C2-12

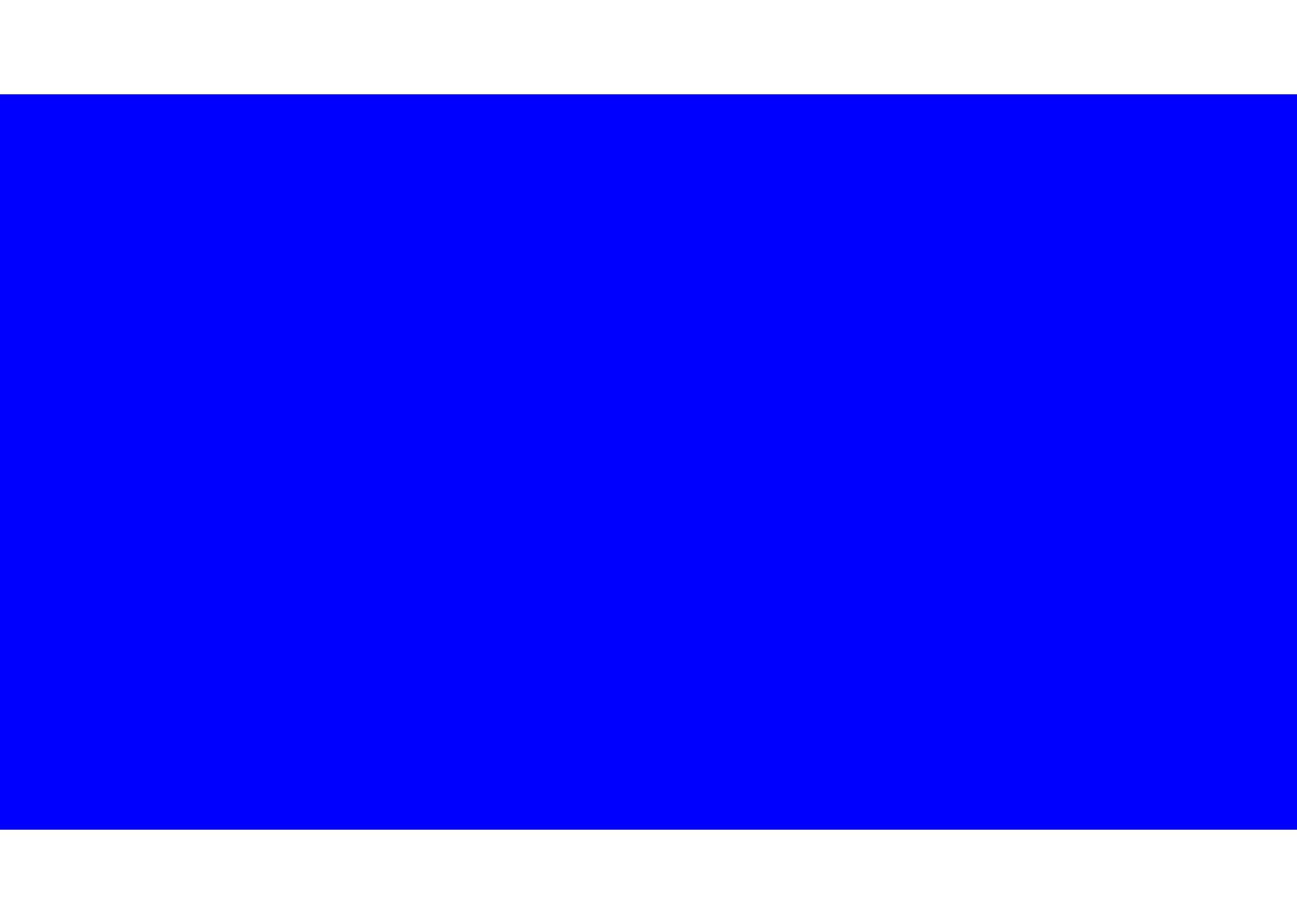
Terugbetaald R/R DLBCL die ten minste 2 eerdere
systemische behandelingen kregen

Cave CRS en ICANS , maar behandelbaar



Glofitamab/Columvi





Epcoritamab/Tepkinly



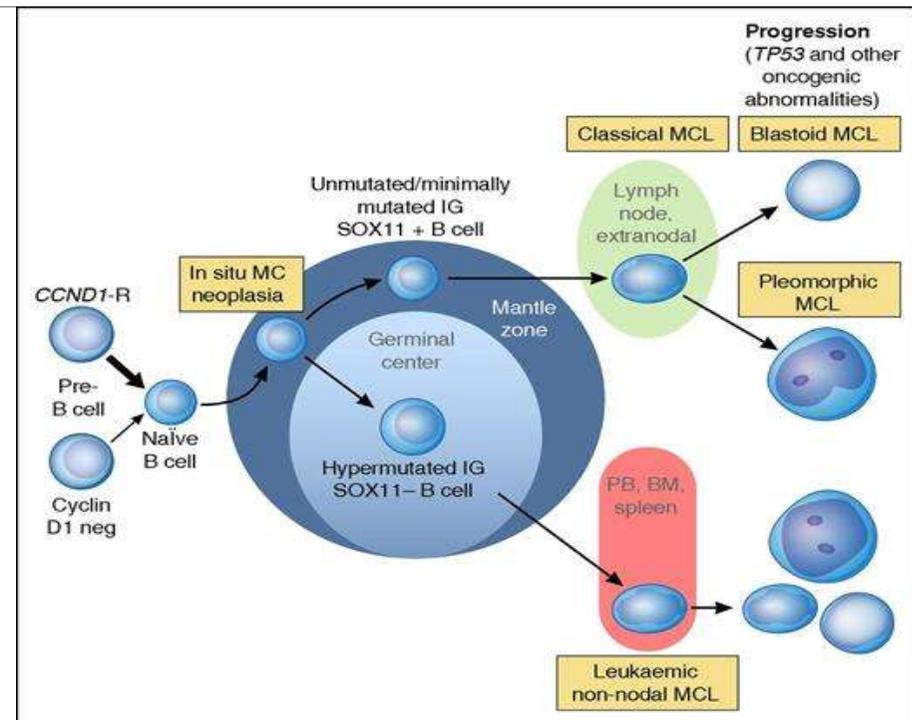


2. Mantelcelllymfoom

Mantelcelllymfoom, MCL : ziektebeeld

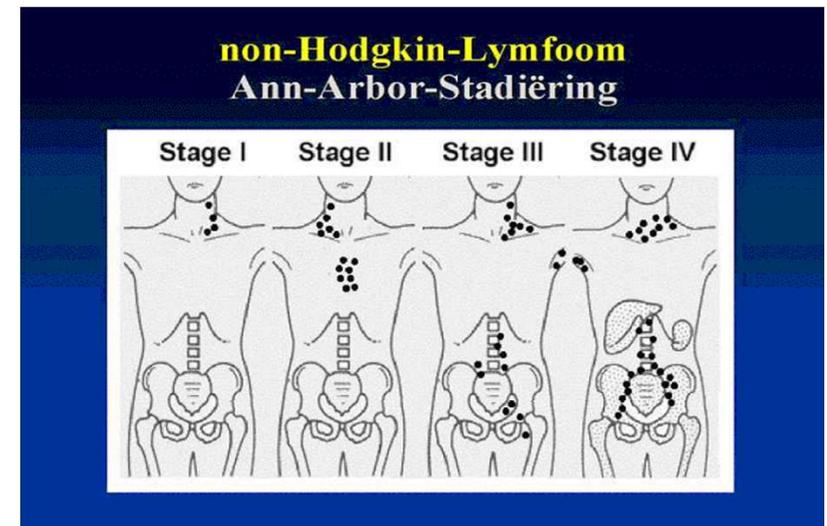
2 subtypes van ziektebeelden

- Blastoide en pleiomorfe meer aggressief
Ongunstig : blastoid , TP 53 , hoge KI-67%
- Indolente → aggressieve vorm



MCL : ziektebeeld

- Klierzwellingen , pijnloos
- Splenomegalie
- BM aantasting : verhoogde bloedingsneiging , verhoogd infectierisico, vermoeidheid
- B-symptomen
- Extranodale aantasting , vaak abdominaal



MCL : risicoscore , MIPI , MIPI-C

Points	Age (years)	ECOG Performance Status	LDH/ULN	Leukocytes (x10 ⁹ /L)
0	<50	0-1	<0.670	6700
1	50-59	-	0.670-0.999	6700-9999
2	60-69	2-4	1.000-1.499	10000-14999
3	>69	-	>1.499	>14999

For each prognostic factor, 0 to 3 points are given to each patient and points are summed up to define a category of risk

Risk stratification

0-3 points	low-risk
4-5 points	intermediate-risk
6-11 points	high-risk

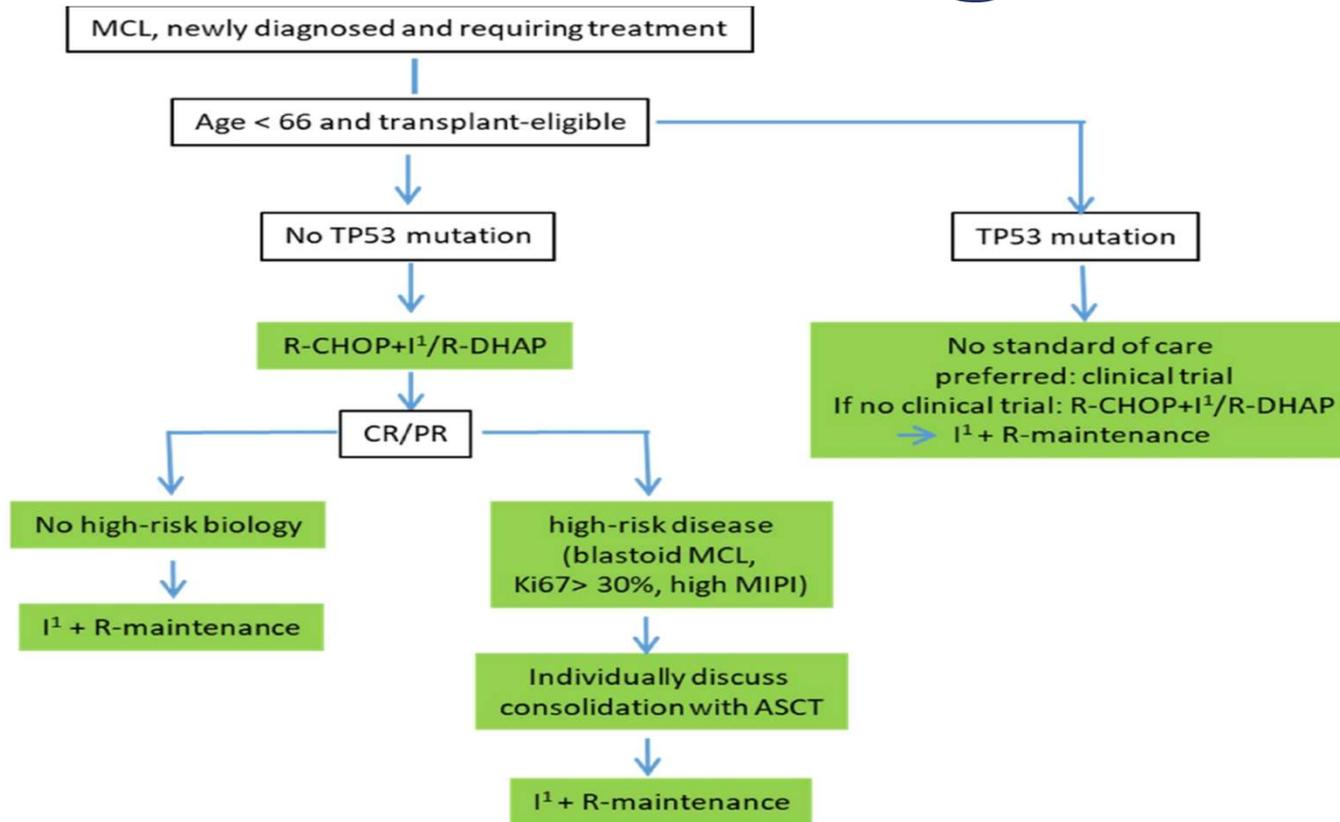
MIPI: Mantle cell lymphoma International Prognostic Index; ECOG: Eastern Cooperative Oncology Group; LDH: lactate dehydrogenase; ULN: upper limit of normal; L: liter.

TABLE 2. MIPI-c and MIPI Risk Categories and Associated Survival Outcomes³³

MIPI-c Risk Group	MIPI Risk Group	Ki-67, %	Median OS, years
Low	Low	<30	9.4
Low-intermediate	Low	≥30	4.9
	Intermediate	<30	
High-intermediate	Intermediate	≥30	3.2
	High	<30	
High	High	≥30	1.8

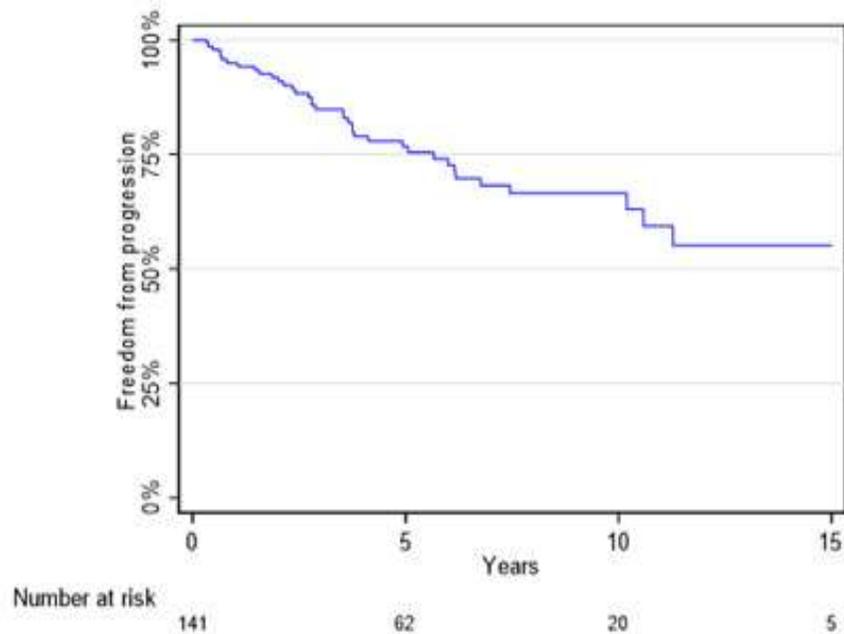
MIPI indicates Mantle Cell Lymphoma International Prognostic Index; MIPI-c, Mantle Cell Lymphoma International Prognostic Index combined with Ki-67 index; OS, overall survival.

MCL : behandelings first line <65



MCL behandeling : autologe Tx first line

Figure 1: Freedom from progression after first-line ASCT for mantle cell lymphoma



-lange termijn FU studie : inductiechemo, autologe TX en maintenance
-141 patienten , gemiddelde leeftijd 60j

Median PFS 11,3 jaar
Median OS 14 jaar

Afname RR van 4,4 % (jaar 0-5 na TX) naar 2,5%/jaar (jaar 6-12 na TX)

→ Triangle trial ?

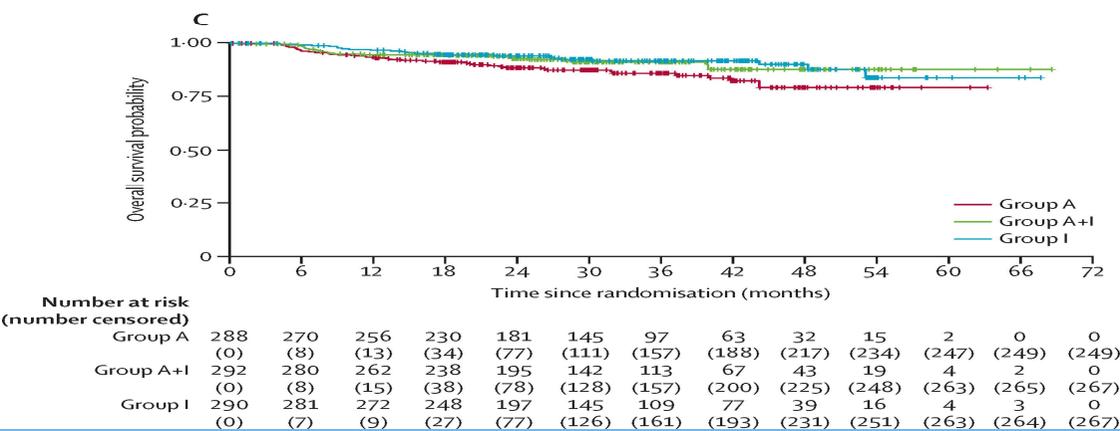
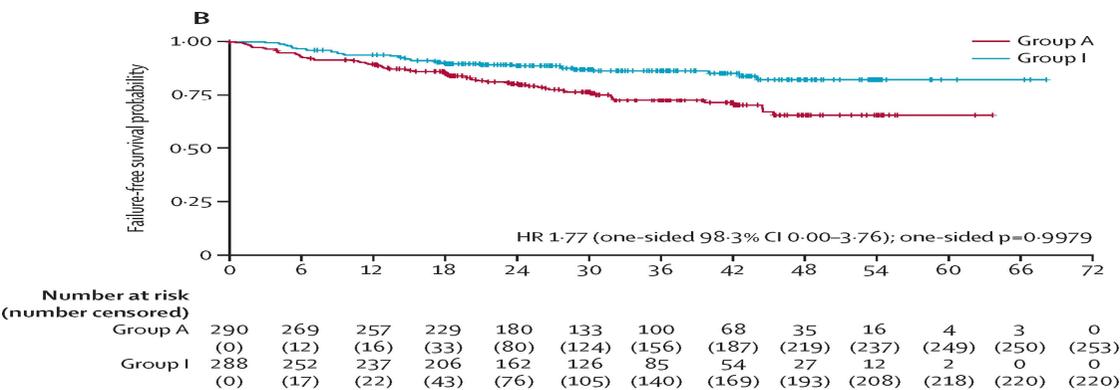
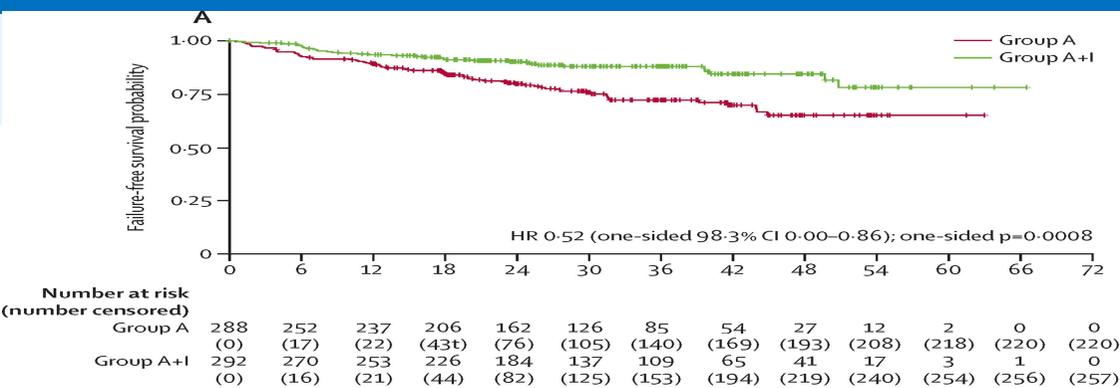
Blood (2023) 142 (Supplement 1): 3599.

MCL : behandelning first line autologe TX ?

Ibrutinib combined with immunochemotherapy with or without autologous stem-cell transplantation versus immunochemotherapy and autologous stem-cell transplantation in previously untreated patients with mantle cell lymphoma (TRIANGLE): a three-arm, randomised, open-label, phase 3 superiority trial of the European Mantle Cell Lymphoma Network

[The Lancet , Volume 403, Issue 10441P2293-2306May 25, 2024](#)

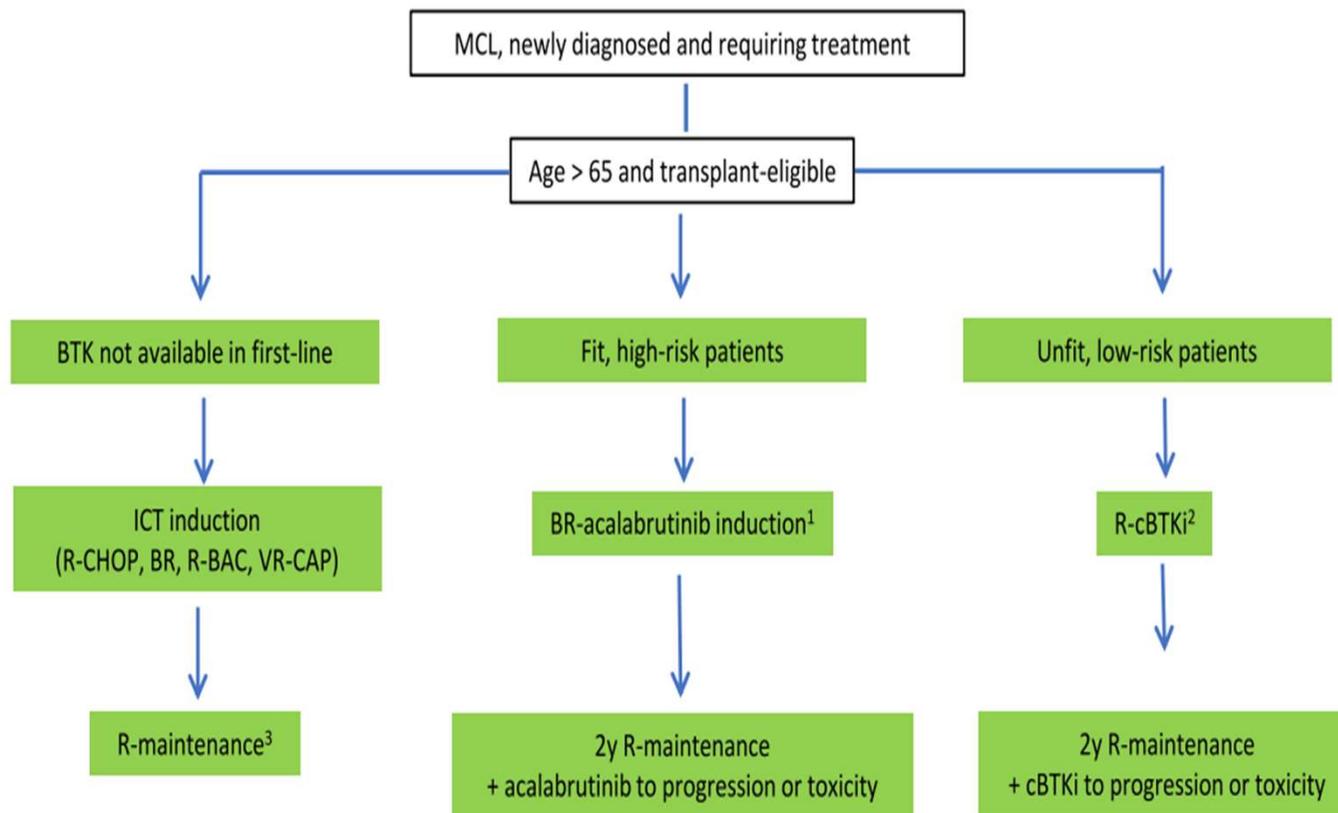
= TRIANGLE TRIAL

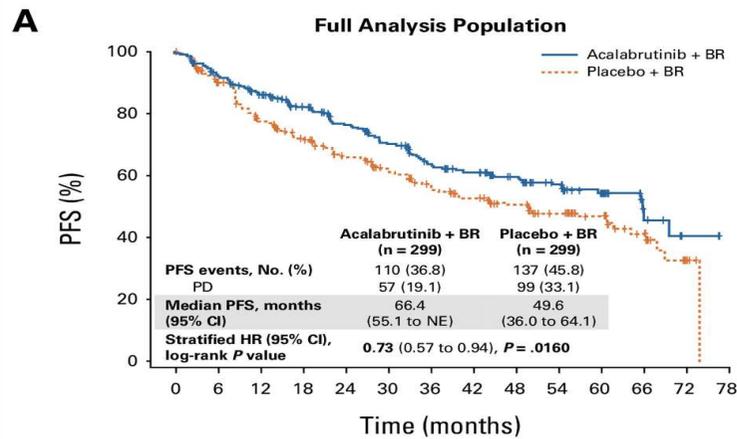


A= standaard immunochemo + autologe Tx
 I= Ibrutinib met immunochemo zonder autologe TX
 A+I = ibrutinib+ immunochemo+autologe TX

- Vooral bij high risk patient (TP53) heeft Ibrutinib een meerwaarde
- Geen duidelijke superioriteit van autologe TX boven Ibrutinib schema zonder TX
- Plaats autologe TX gezien toxiciteit? Langere FU nodig

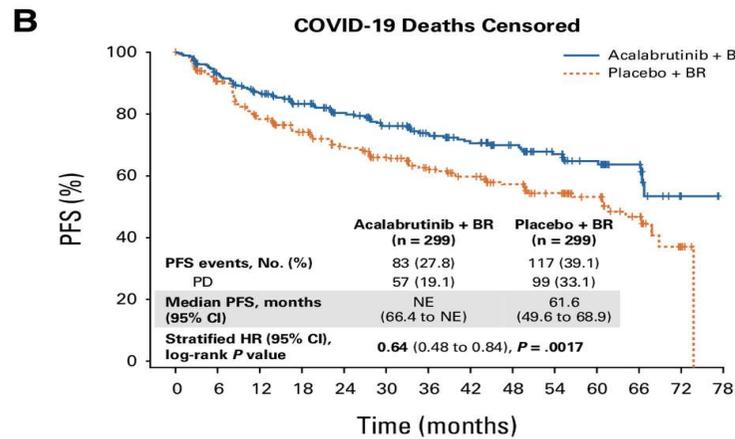
MCL : behandelings first line >65





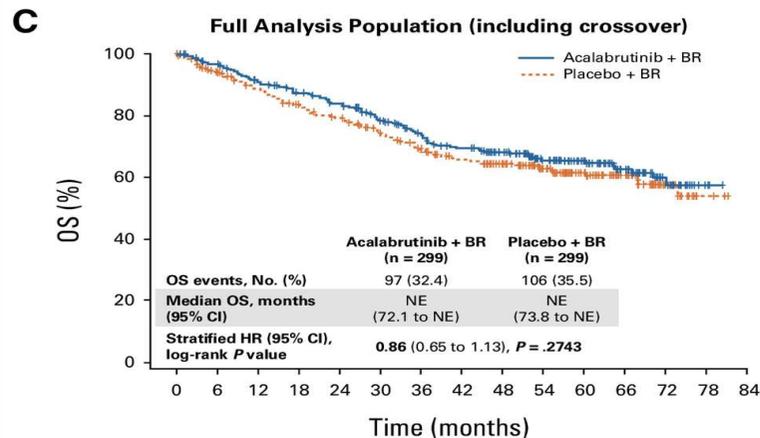
Number at risk

	0	6	12	18	24	30	36	42	48	54	60	66	72	78
Acalabrutinib + BR	299	258	232	205	182	156	136	122	98	73	53	34	2	0
Placebo + BR	299	243	204	181	159	142	118	102	84	63	44	25	4	0



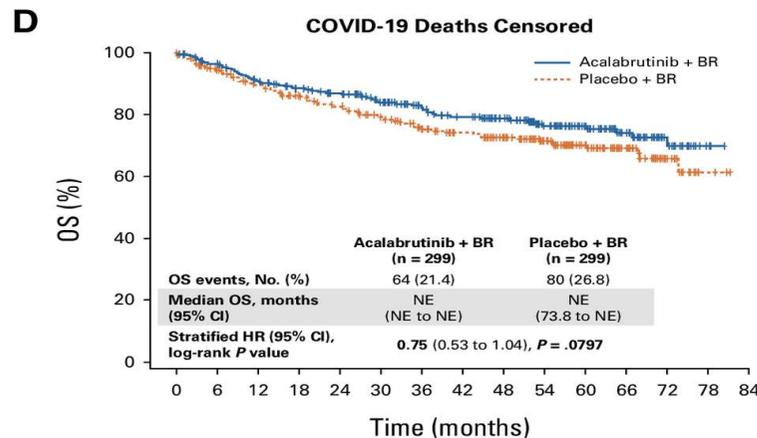
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Number at risk

	0	6	12	18	24	30	36	42	48	54	60	66	72	78	84
Acalabrutinib + BR	299	280	259	243	230	207	181	163	146	110	86	58	25	3	0
Placebo + BR	299	268	247	229	215	193	175	157	141	108	78	51	21	3	0



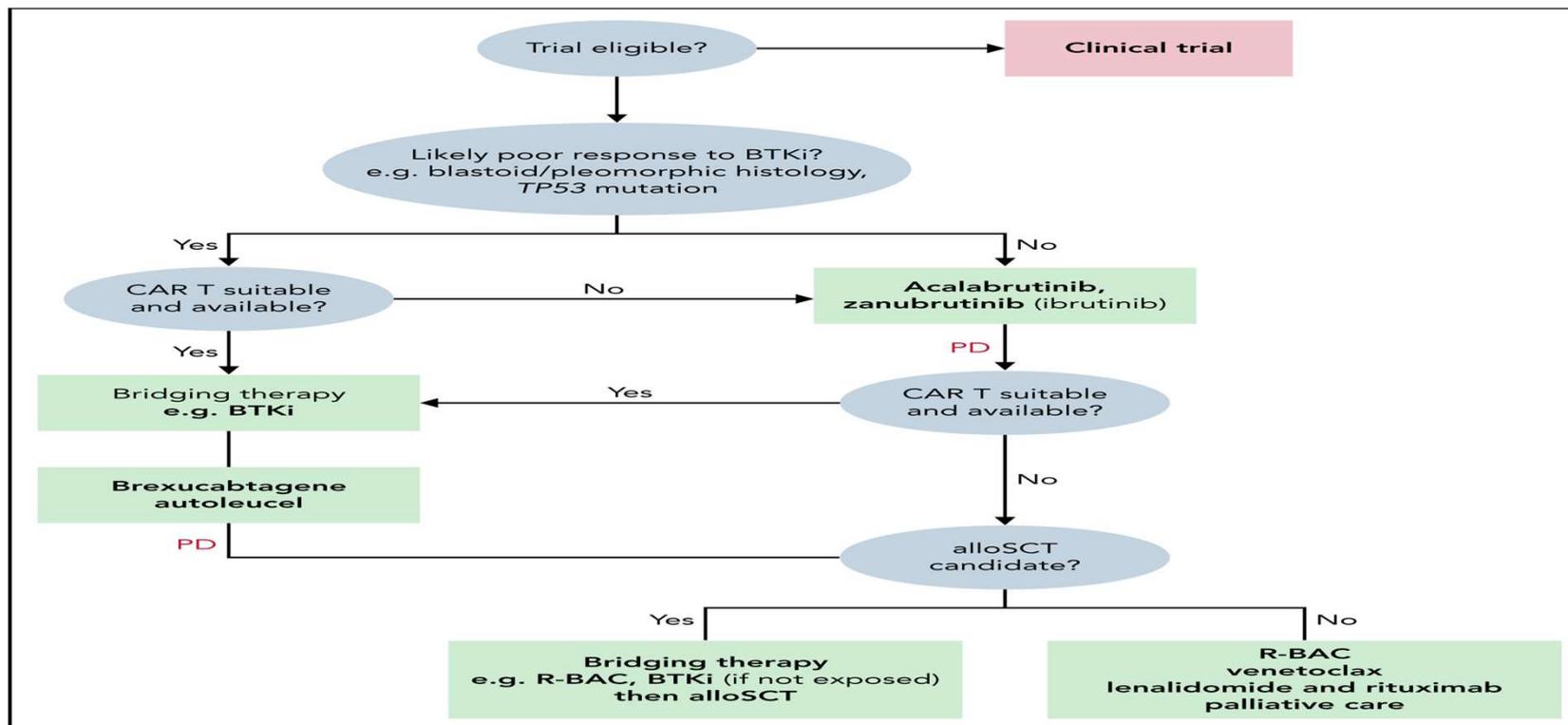
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Placebo + BR	299	268	247	229	215	193	175	157	141	108	78	51	21	3	0

Benda+Mabthera+Acalabrutinib
-verbetering PFS
-aanvaardbare toxiciteit
-ook voordeel bij high risk



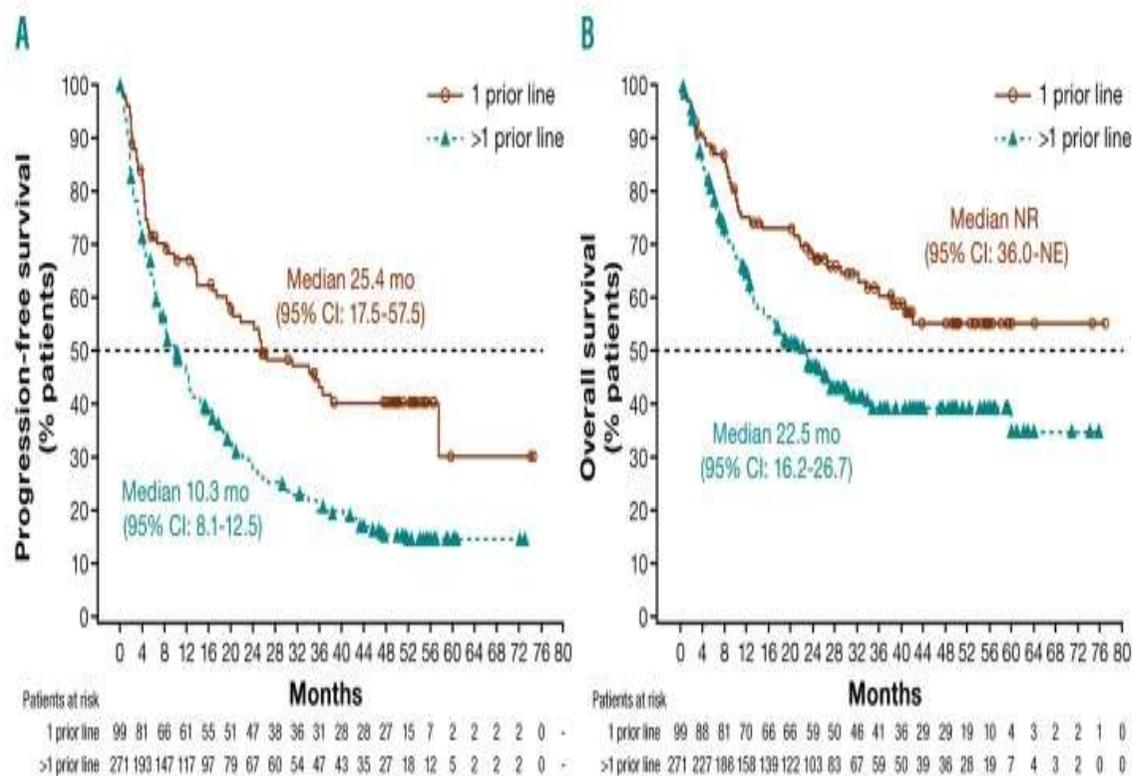
Herval MCL behandelning



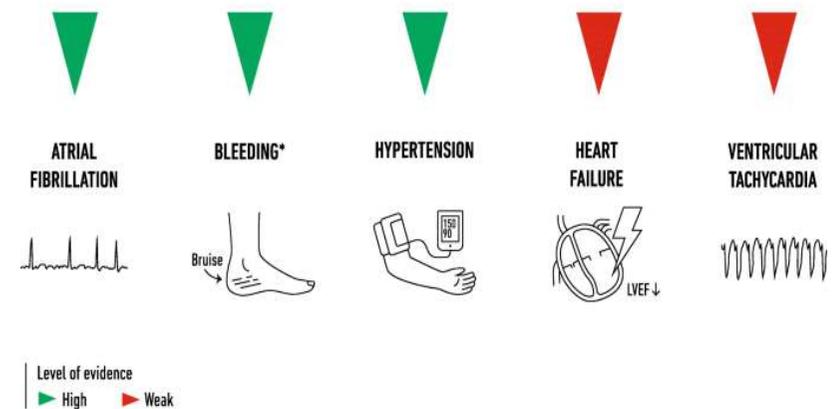
Blood (2022) 139 (5): 666-677.

Bruton Kinase Inhibitor : 2^e en 3^e lijn

Covalente BTK inhibitor : Ibrutinib(Imbruvica)



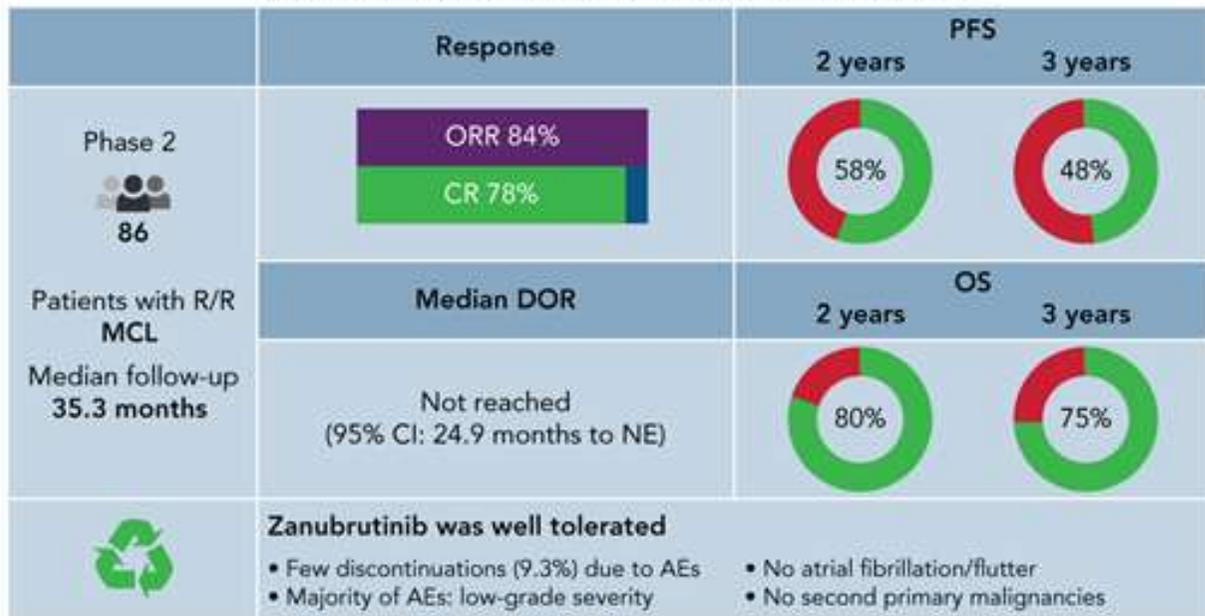
IBRUTINIB CARDIOVASCULAR ADVERSE EFFECTS



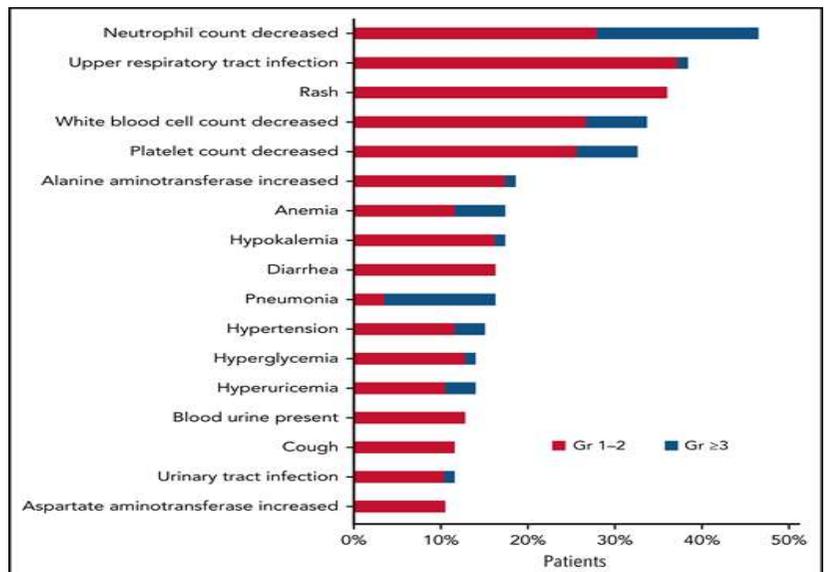
Covalente BTK inhibitor: Zanubrutinib (Brukinsa)



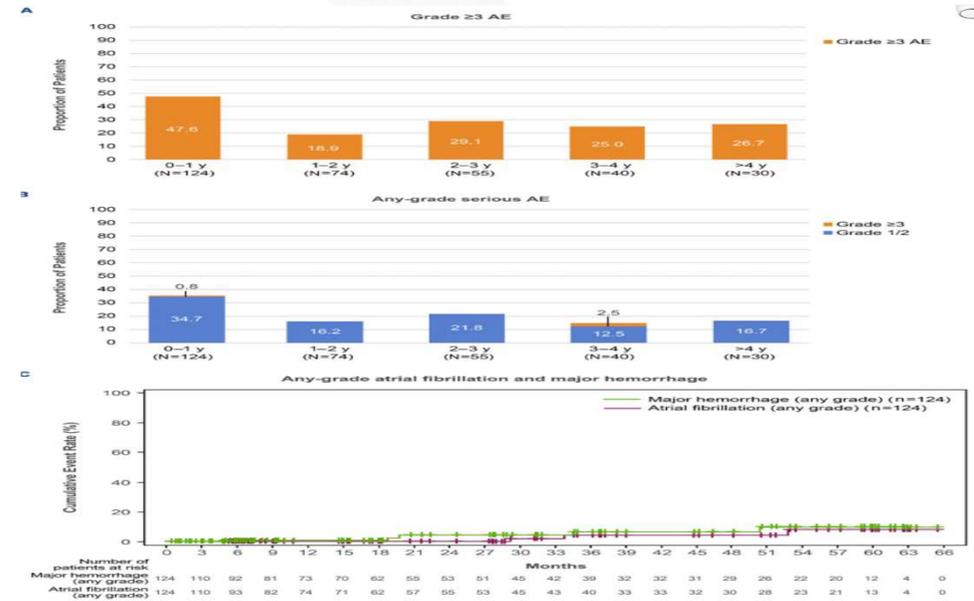
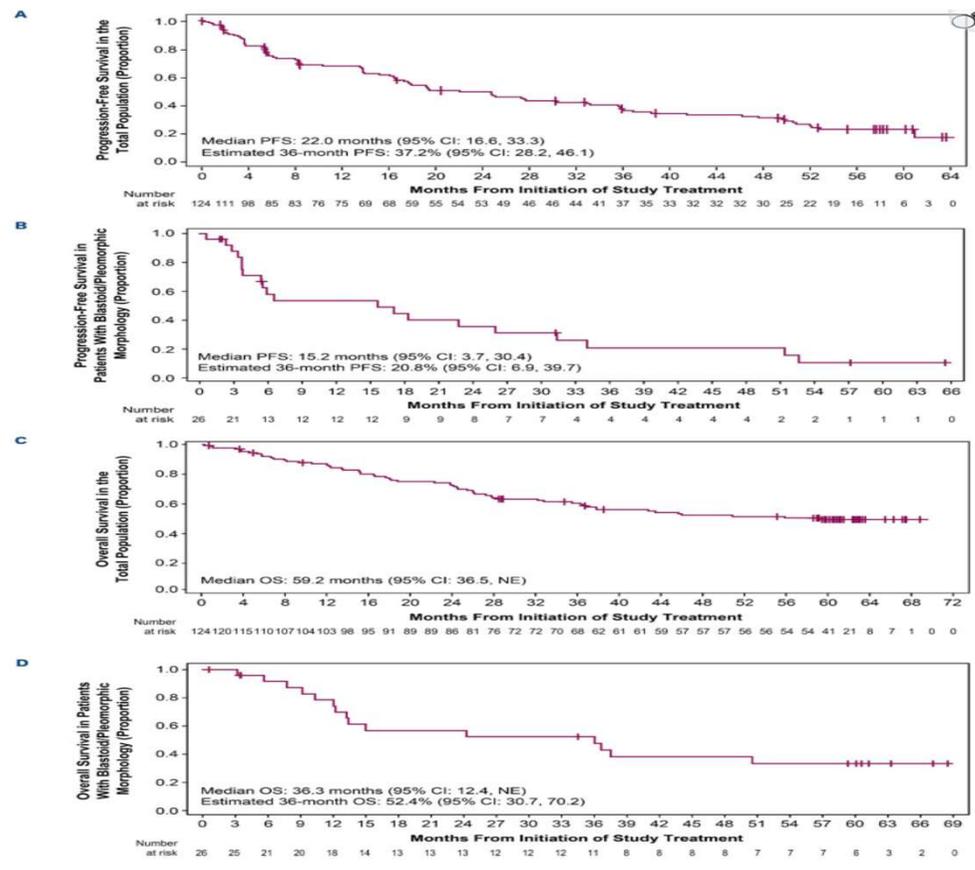
Zanubrutinib monotherapy demonstrates durable clinical benefit in the long-term follow-up of patients with relapsed/refractory MCL



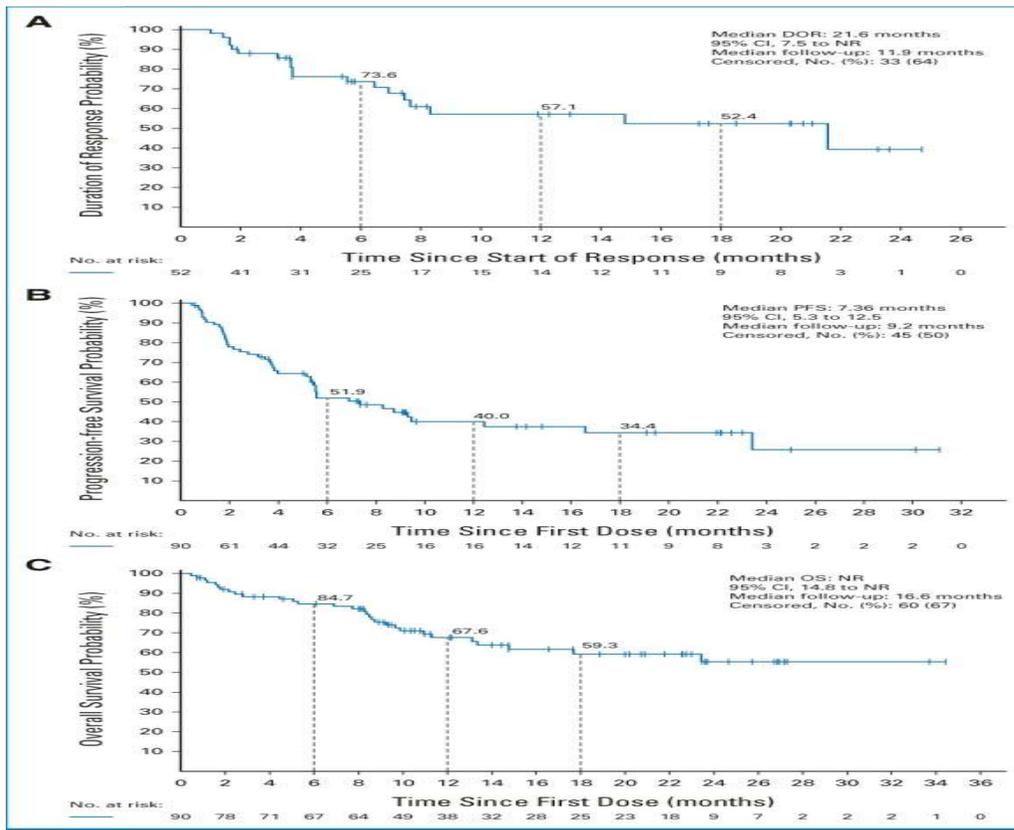
AEs adverse events; CR complete response; DOR duration of response; MCL mantle cell lymphoma; NE not estimable; ORR overall response rate; OS overall survival; PFS progression-free survival; R/R relapsed/refractory.



Covalente BTK inhibitor: Acalabrutinib (Calquence)



non-c BTKI inhibitor : Pirtobrutinib (Jaypirca)



BRUIN CLL-321: Safety

TEAE, n (%)	Pirtobrutinib (n = 116)			IdelaR or BR (n = 109)		
	Any Grade	Grade ≥3	EAIR	Any Grade	Grade ≥3	EAIR
Any	108 (93.1)	67 (57.7)	94.5	107 (98.2)	80 (73.4)	125.5
▪ TEAE leading to d/c	20 (17.2)			38 (34.9)		
▪ TRAE leading to d/c	6 (5.2)			23 (21.1)		
Infection	74 (63.8)	25 (21.6)		54 (49.5)	21 (19.3)	
▪ Pneumonia	26 (22.4)	18 (15.5)	20.4	13 (11.9)	9 (8.3)	19.5
▪ COVID-19	15 (12.9)	0	11.1	20 (18.3)	4 (3.7)	33.4
Anemia	23 (19.8)	13 (11.2)	18.5	19 (17.4)	8 (7.3)	30.3
Neutropenia	31 (26.7)	24 (20.7)	26.4	37 (33.9)	30 (27.5)	66.5
Cough	19 (16.4)	0	14.3	19 (17.4)	0	30.8
Diarrhea	19 (16.4)	0	15.3	34 (31.2)	6 (5.5)	63.7
Pyrexia	15 (12.9)	1 (0.9)	11.1	29 (26.6)	1 (0.9)	52.4
Fatigue	13 (11.2)	2 (1.7)	9.5	22 (20.2)	1 (0.9)	34.2
Nausea	13 (11.2)	1 (0.9)	9.8	22 (20.2)	0	38.3
Vomiting	8 (6.9)	1 (0.9)	5.8	19 (17.4)	0	29.6
Increase in ALT	4 (3.4)	1 (0.9)	2.8	19 (17.4)	10 (9.2)	33.6
Weight loss	4 (3.4)	0	2.8	18 (16.5)	0	28.5
Infusion-related reaction	0	0	NR	19 (17.4)	3 (2.8)	NR

▪ Patients developing Richter transformation: pirtobrutinib, n = 0; IdelaR/BR, n = 3

Sharman. JCO. 2025;43:2538. Sharman. ASH 2024. Abstr 886.

Slide credit: clinicaloptions.com



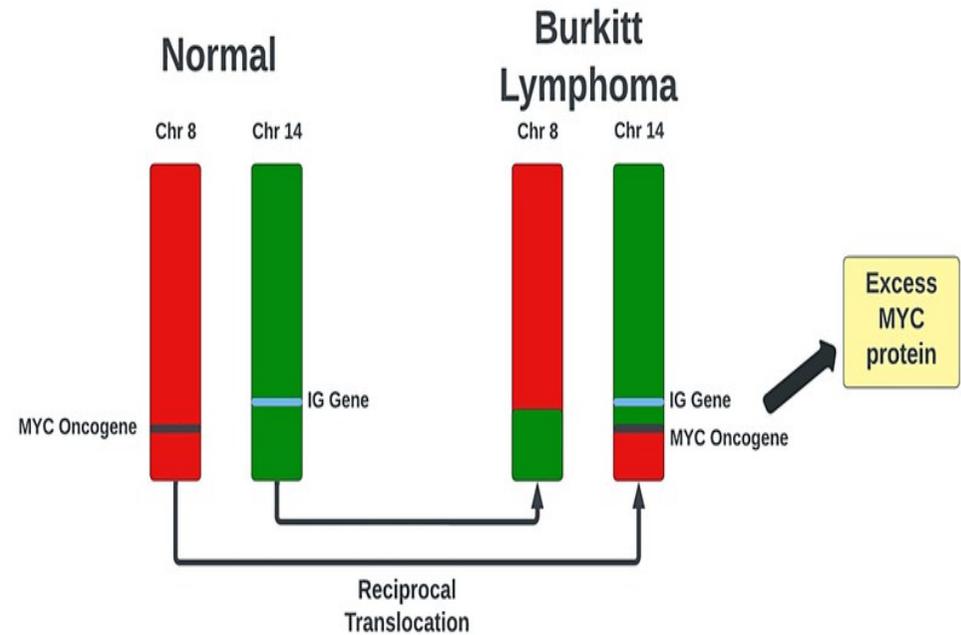
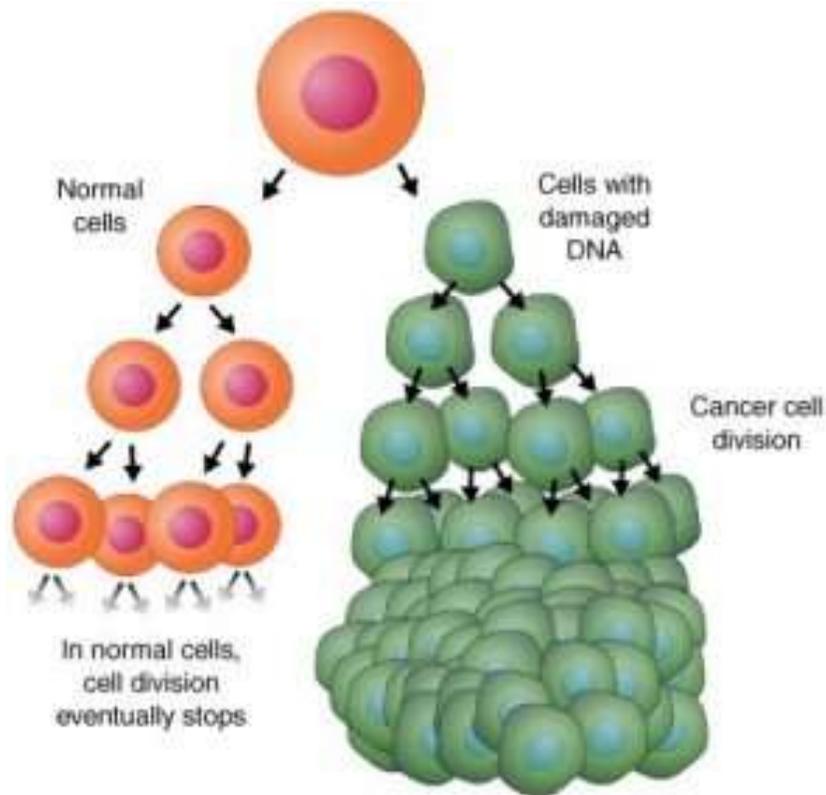
→Derdelijn na eerdere BTKI !

CAR-T : 3^e lijn , Tecartus (Brexu-cel)



3. Burkitt Lymfoom

Burkitt lymfoom : ziektebeeld



Reciprocal translocation $t(8;14)(q24;q32)$ leading to the activation of the c-myc protooncogene. MYC: Myc Protooncogene. IG: immunoglobulin

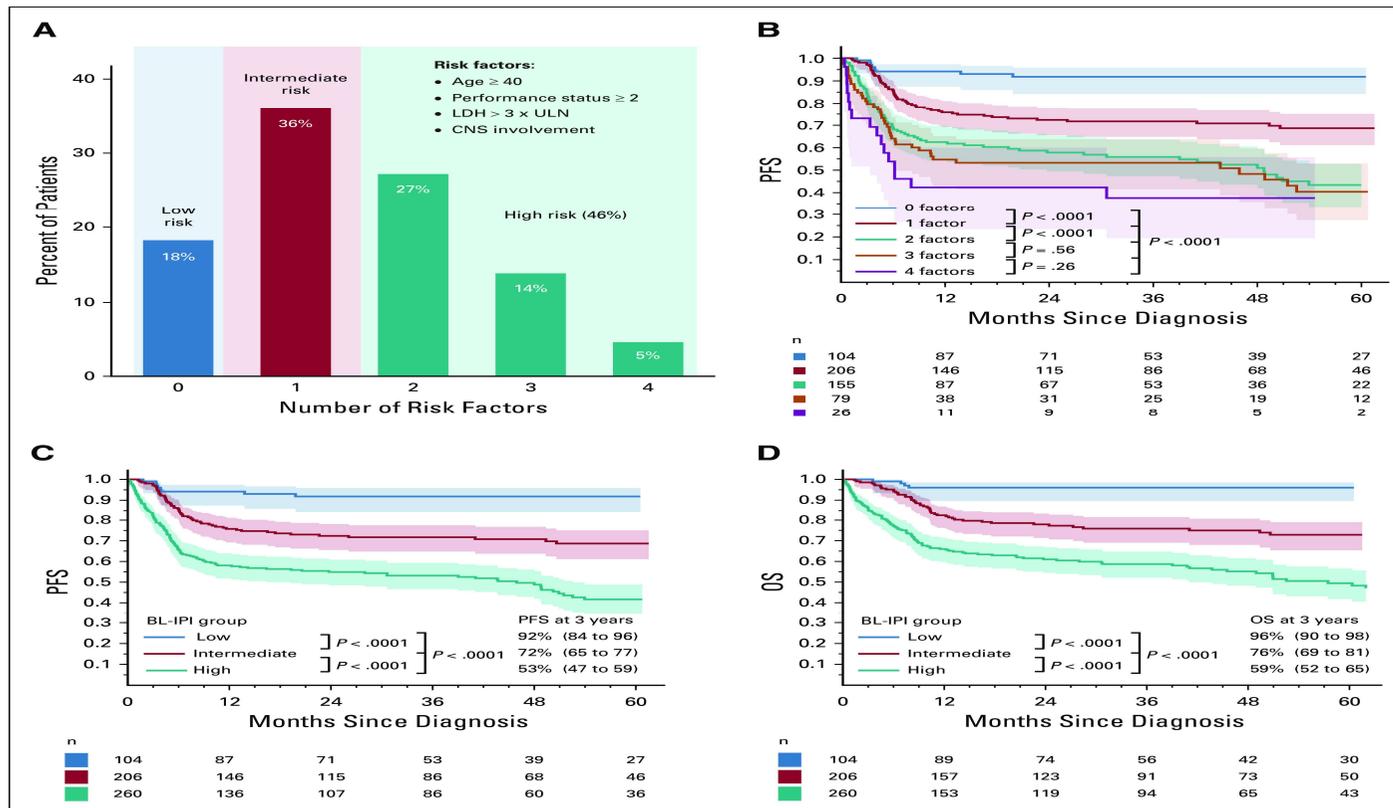
Burkitt Lymfoom : ziektebeeld

Table 1. Comparison of Endemic, Sporadic, and HIV-Associated Burkitt's Lymphoma

Variable	Endemic	Sporadic	HIV Associated
Epidemiology	Equatorial Africa and Papua, New Guinea. Regions of South America.	Worldwide	Worldwide
Incidence	Five to 10 cases per 100,000 people	Two to three cases per 1 million people	Six per 1,000 AIDS cases
Age and sex	Peak incidence: 4-7 years. Male/female ratio of 2:1.	Median age: 30 years. Male/female ratio of 2-3:1.	Median age: 44 years. Associated with CD4 counts > 100/mm ³ .
Epstein-Barr virus positivity	100%	25% to 40%	25% to 40%
Genomics	<i>MYC</i> mutation, 100%; <i>ID3</i> and/or <i>TCF3</i> mutations, 40%; <i>CCND</i> mutations, 1.8%.	<i>MYC</i> mutation, 100%; <i>ID3</i> and/or <i>TCF3</i> mutations, 70%; <i>CCND</i> mutations, 38%.	<i>MYC</i> mutation, 100%; <i>ID3</i> and/or <i>TCF3</i> mutations, 67%; <i>CCND</i> mutations, 67%.
Clinical presentation	Jaw and facial bones in approximately 50% of cases. Also involves mesentery and gonads. Increased risk of CNS dissemination.	Ileocecal region is most common area of involvement. Other extranodal sites include bone marrow, ovaries, kidneys, and breasts. Increased risk of CNS dissemination.	Nodal presentation most common, with occasional bone marrow. Increased risk of CNS dissemination.

Dunleavy K, et al. *J Clin Oncol* 2018;14:665-72

Burkitt Lymfoom : ziektebeeld



BL International Prognostic Index (BL-IPI)

groups with low (zero risk factors), intermediate (one factor) high risk (≥ 2 factors)

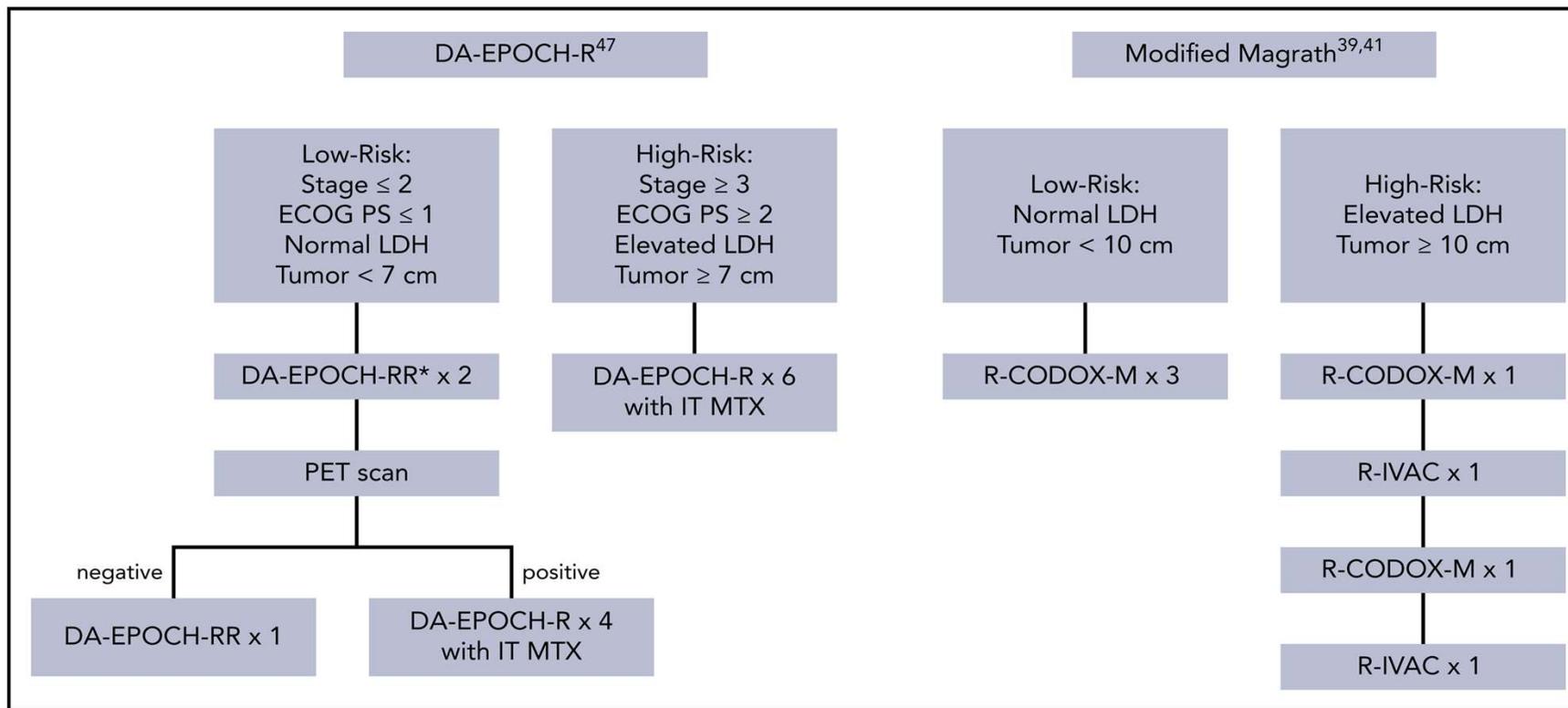


Burkitt Lymfoom: behandelingsopties

Table 2. Selected Regimens for High-Risk Burkitt's Lymphoma

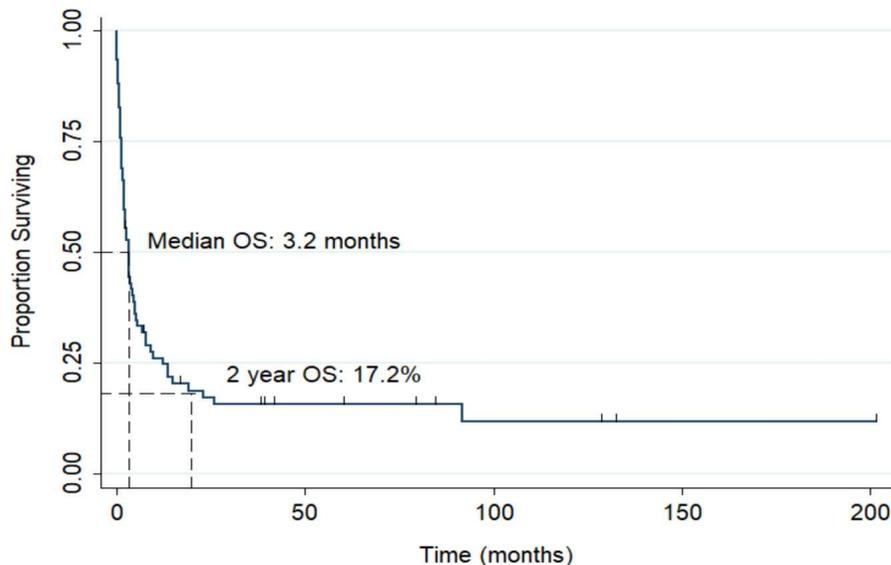
Regimen	No. of Patients	Histology	Median Age, Years (range)	Stage (%)	EFS
LMB 89 ¹⁹	561	Burkitt's/B-ALL	8 (0.17-18)	III-IV (79)	92% at 5 years
Modified LMB ²⁰	72	Burkitt's/B-ALL	33 (18-76)	III-IV (67)	65% at 2 years
BFM 90 ²¹	413	Burkitt's/B-ALL	9 (1.2-17.9)	III-IV (60)	89% at 6 years
CODOX-M/IVAC ²²	21 children 20 adult	Burkitt's B-ALL	12 (3-17) 25 (18-59)	III-IV (78)	85% (children) and 100% (adults) at 2 years
CODOX-M/IVAC ¹⁵	52	Burkitt's	35 (15-60)	III-IV (61)	65% at 2 years
Hyper-CVAD ²³	26	Burkitt's/B-ALL	58 (17-79)	NA	61% at 3 years for DFS
R-Hyper-CVAD ²⁴	31	Burkitt's/B-ALL	46 (17-77)	NA	80% at 3 years
GMALL-B-ALL/NHL 2002 ²⁸	363	Burkitt's/B-ALL	42 (16-85)	III-IV (71)	PFS 75% at 5 years
DA-EPOCH-R ²⁶	19	Burkitt's	25 (15-88)	III-IV (58)	FFP 95% at 7 years
SC-EPOCH-RR ²⁶	11	Burkitt's HIV positive	44 (24-60)	III-IV (82)	FFP 100% at 6 years
LMB +/- R ²⁵	260	Burkitt's	NA	III-IV (62)	EFS 75% v 62% (+R/-R) at 3 years
AMC 048 ²⁷	34	Burkitt's HIV positive	42 (19-55)	III-IV (74)	PFS 69% at 1 year
Modified R-CODOX-M/IVAC					
Modified R-CODOX-M/IVAC ¹⁵	128	Burkitt's HIV negative	47 (IQR, 31-59)	III-IV (62)	EFS 75% at 3 years
RA-DA-EPOCH-R ¹⁸	113	Burkitt's HIV negative and HIV positive	49 (18-86)	III-IV (64)	PFS 86% at 3 years

Burkitt Lymfoom : behandelning first line



Crombie J, LaCasce A. Blood 2021;137:743-50

Burkitt lymfoom : herhaal behandeling



Oudere patienten en patienten met CNS aantasting hebben meer risico op relapse

Zo relapse binnen 6 maand na behandeling: slechtere prognose

Figure 1: Overall survival (OS) for patients with relapsed Burkitt's lymphoma

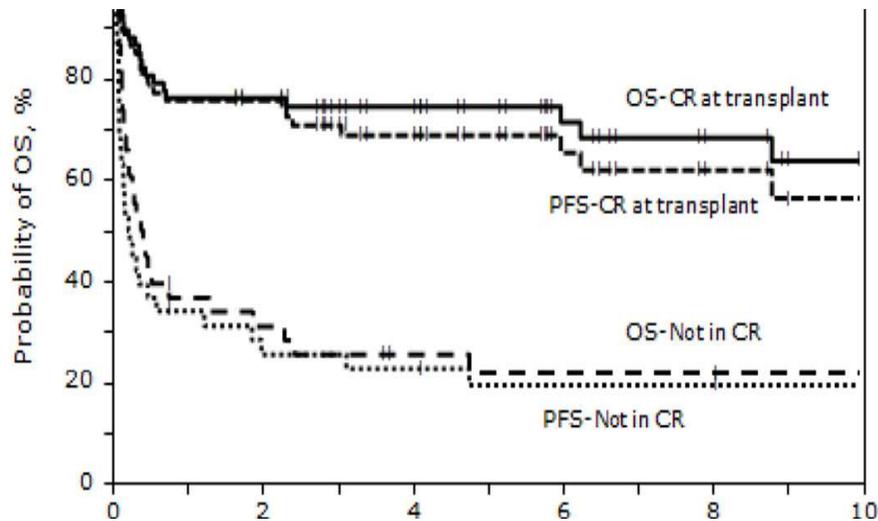
Blood (2021) 138 (Supplement 1): 2525.

Burkitt Lymfoom : hervat behandeling

- Indien primair R-CODOX/M/R-IVAC, valt een behandeling met R-GDP of HD-araC te overwegen.
- Indien primair DA-EPOCH-R, heeft R-DHAP afgewisseld met HD-MTX of R-ICE de voorkeur.

- Consolidatie na salvage chemotherapie met autologe stamceltransplantatie.
- Allogene stamceltransplantatie.

Burkitt Lymfoom : herval behandelning - Transplantatie

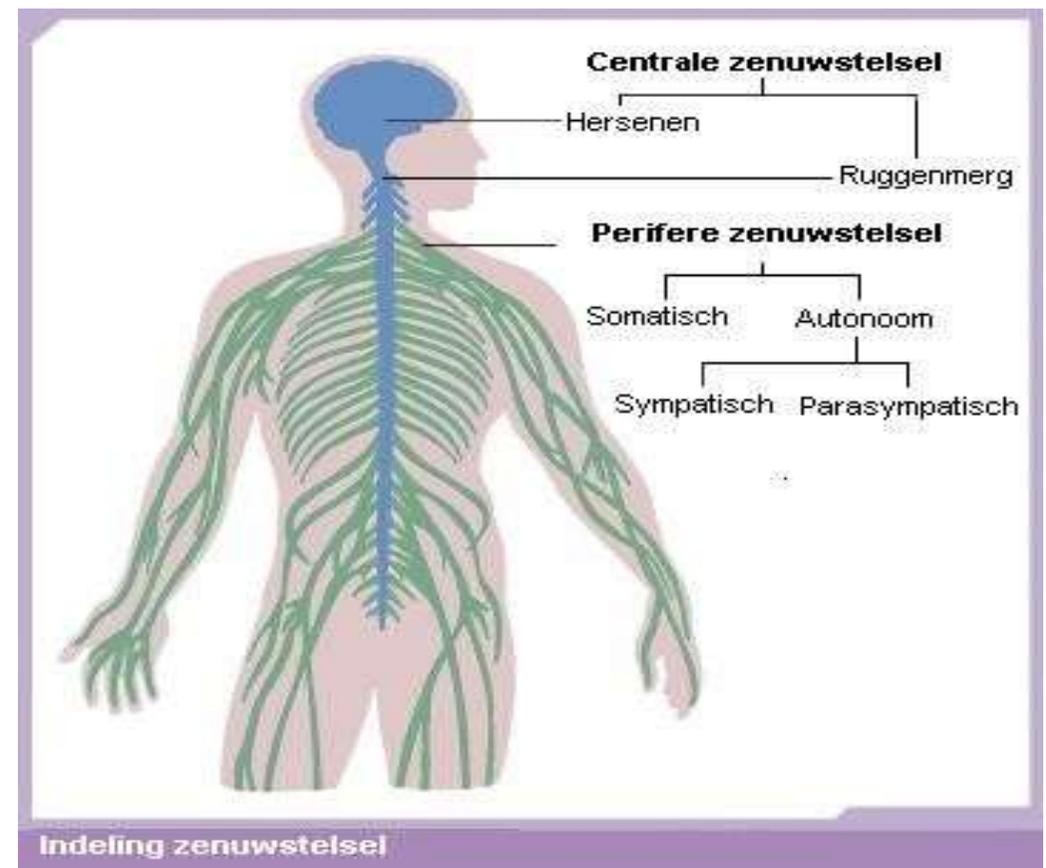
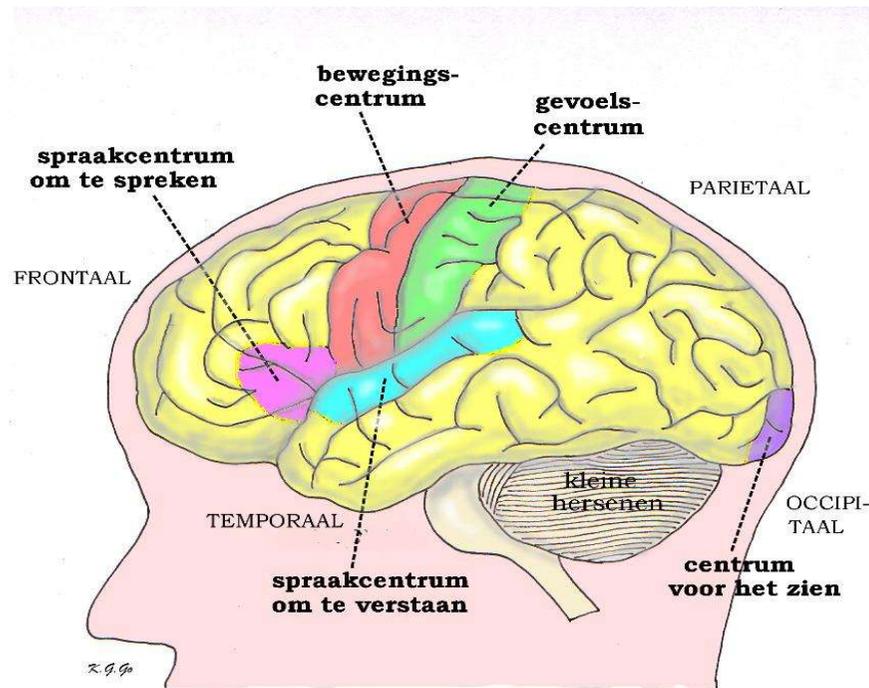


Probability of OS and PFS after allogeneic transplantation for BL by disease status

Probability of OS and PFS after autologous transplantation for BL by disease status

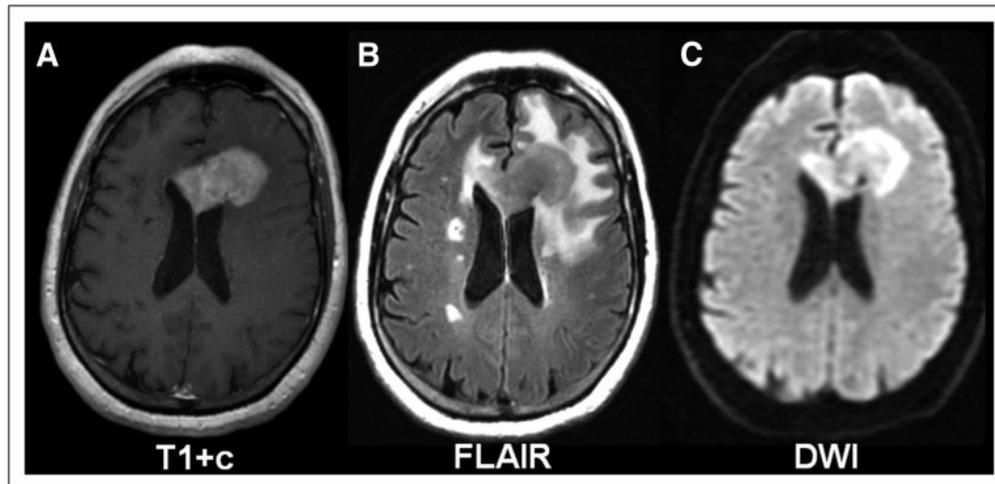
4. Primair CZS (centraal zenuwstelsel) lymfoom

Primair CNS lymfoom : symptomen



Primair CNS lymfoom : symptomen

SYMPTOMEN	FREQUENTIE
Focale neurologische uitval	56-70%
Veranderingen mentaal of gedrag	32-43%
Verhoogde intracraniële druk	32-33%
Epilepsie	11-14%



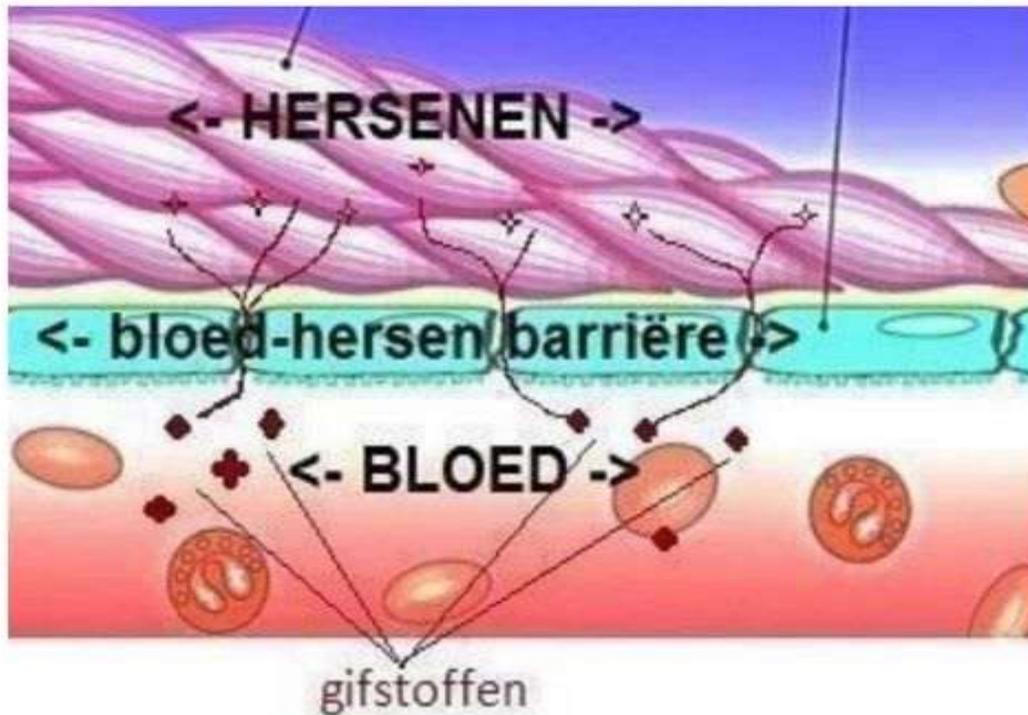
Eén letsel hersenen > meerdere letsels

Ogen (15-25%)

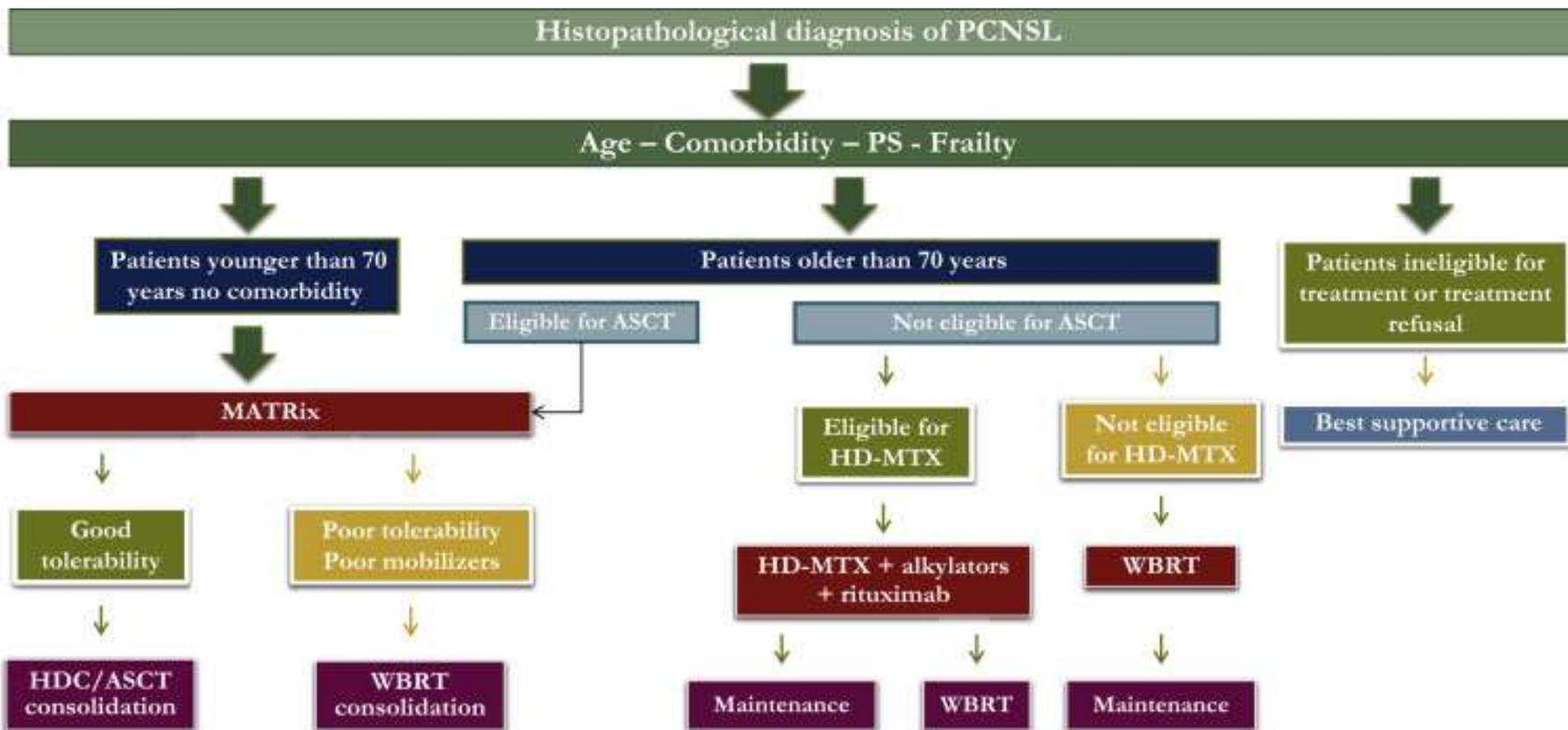
Cerebrospinaal vocht (7-42%)

Grommes C, deAngelis LM. *J Clin Oncol* 2017

Primair CNS lymfoom : behandeling , blood-brain-barrier

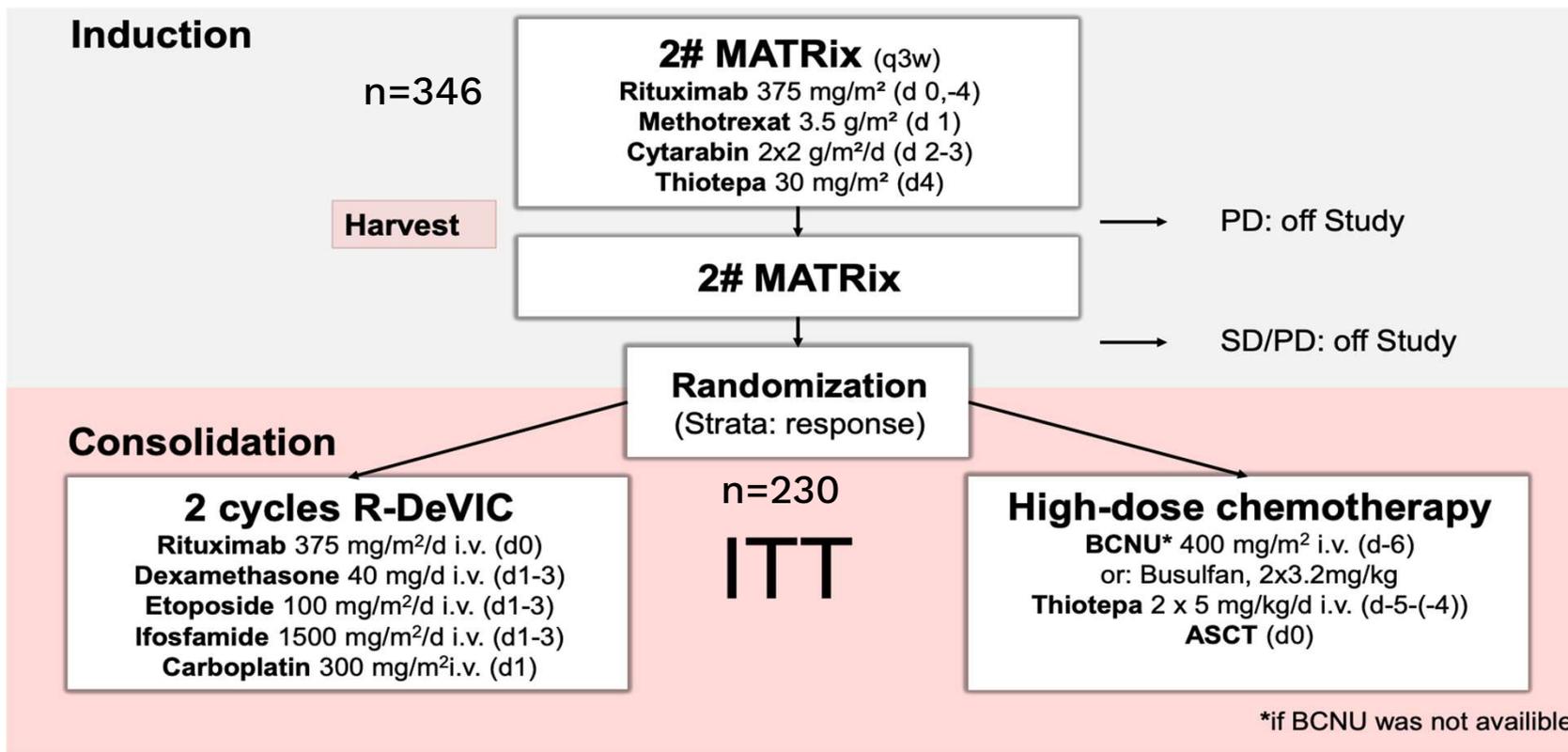


Primair CNS lymfoom : first line behandelning



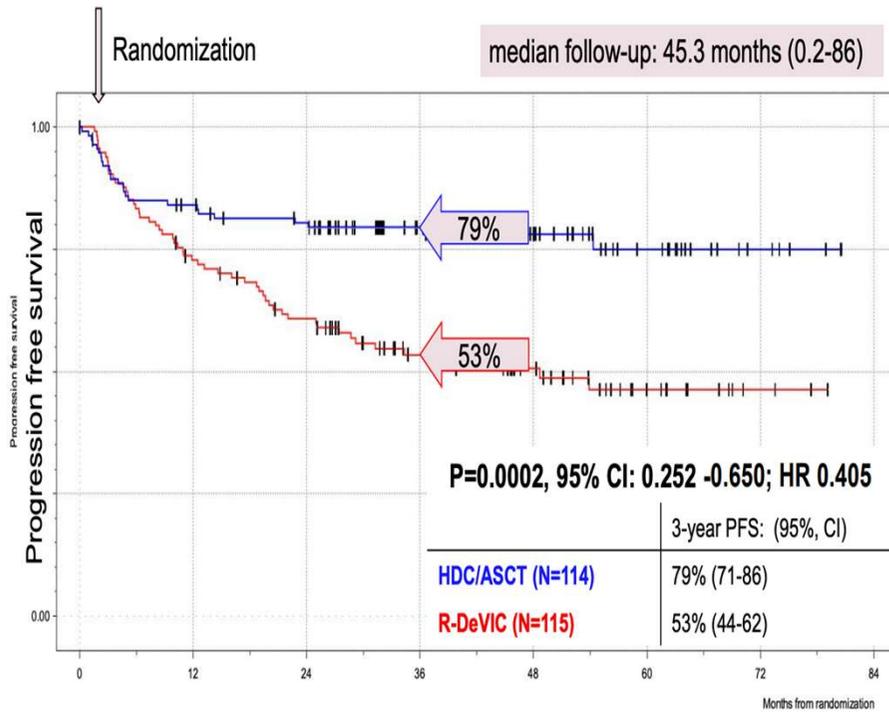
Primair CNS lymfoom: first line <70

MATRix/IELSG43



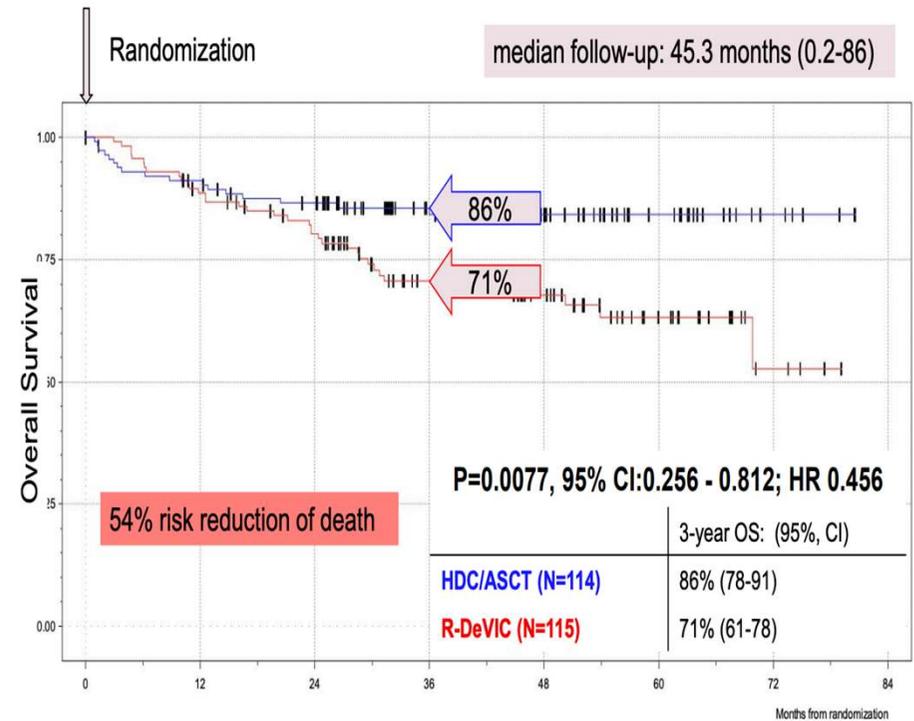
Primair CNS lymfoom: first line <70

MATRix/IELSG43 Trial – PFS (ITT)



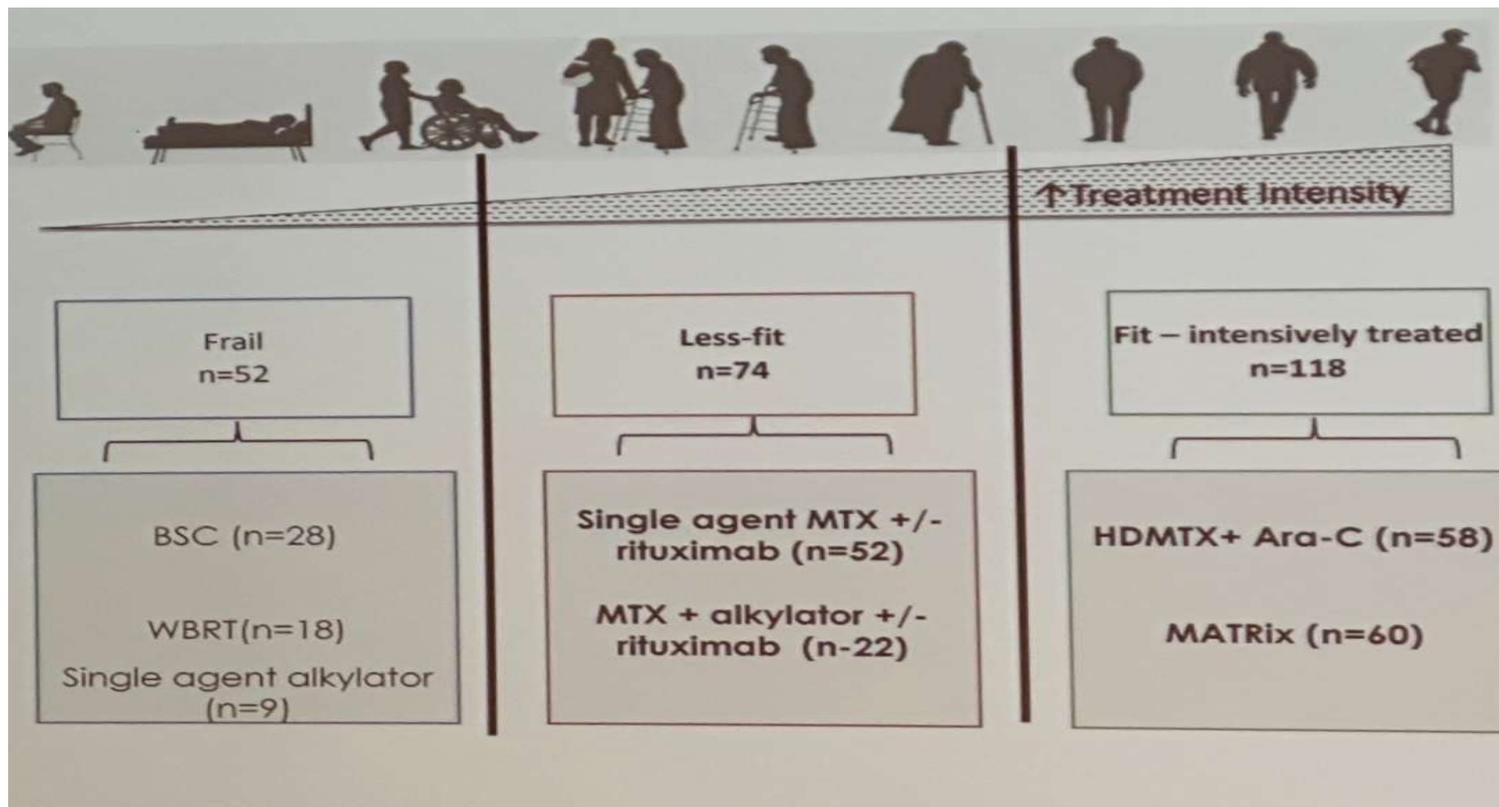
Gerald Illerhaus | ASH 2022

MATRix/IELSG43 Trial – OS (ITT)



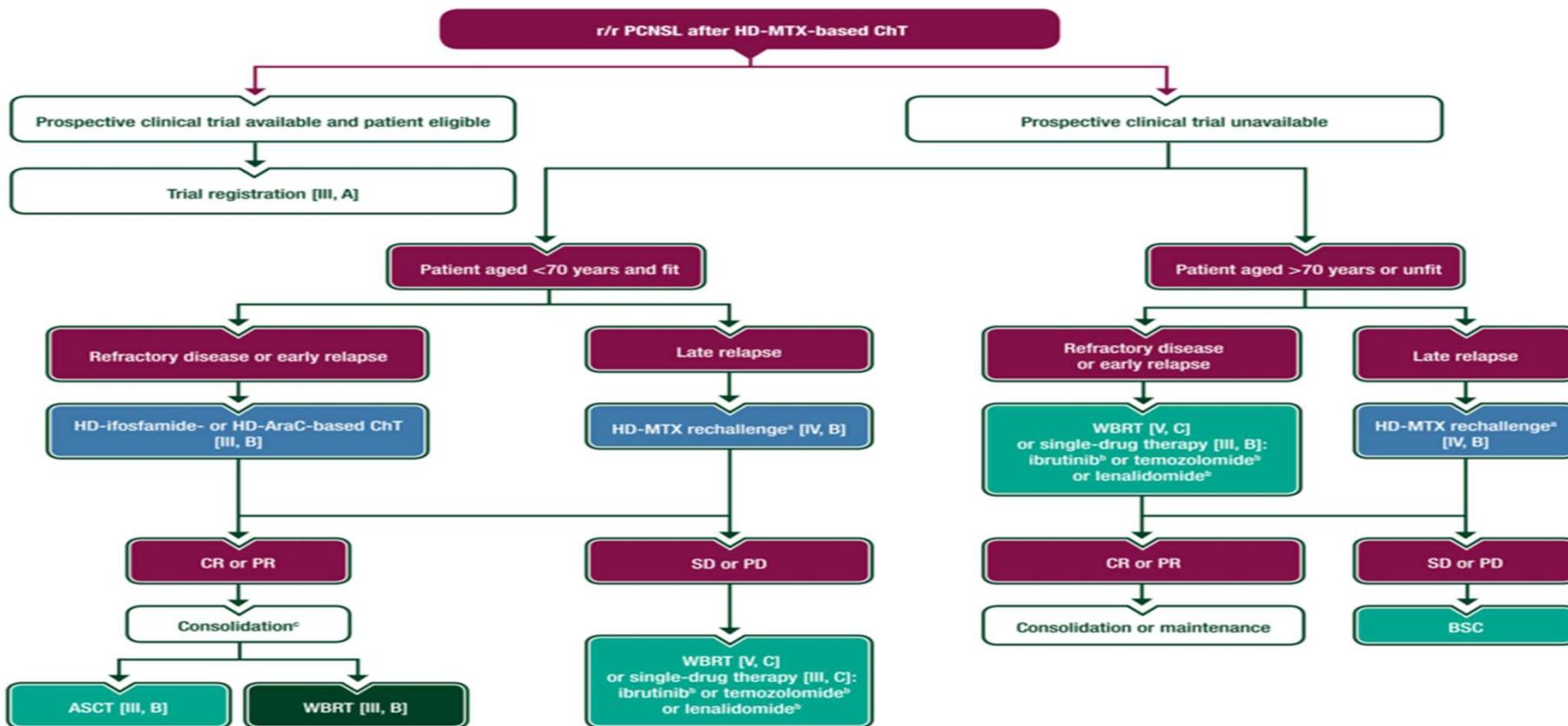
Gerald Illerhaus | ASH 2022

Primair CNS lymfoom : first line >70



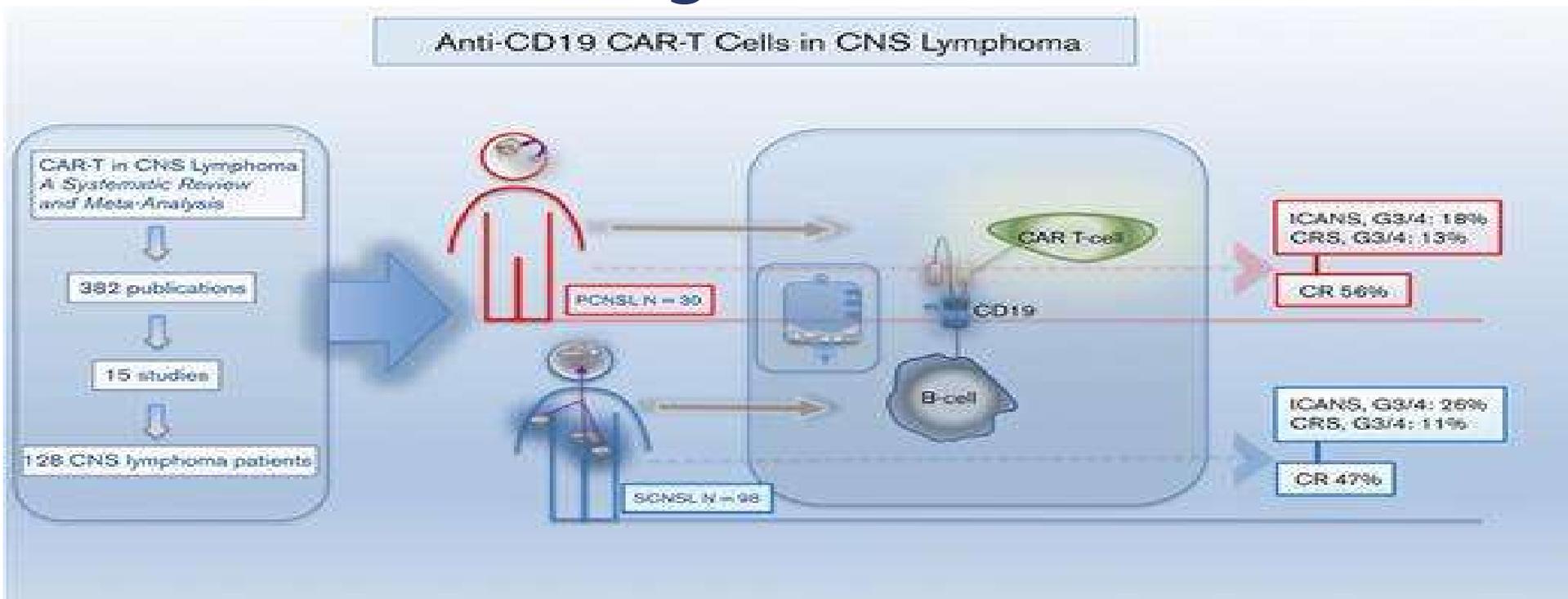
David KA et al , Am J Haem 2023 , multicentre retrospective UK study >65 y (n=244)
Nexly diagnosed 2012-2017

Primair CNS lymfoom : herhaalbehandeling



Ferreri et al, EHA/ESMO 2023

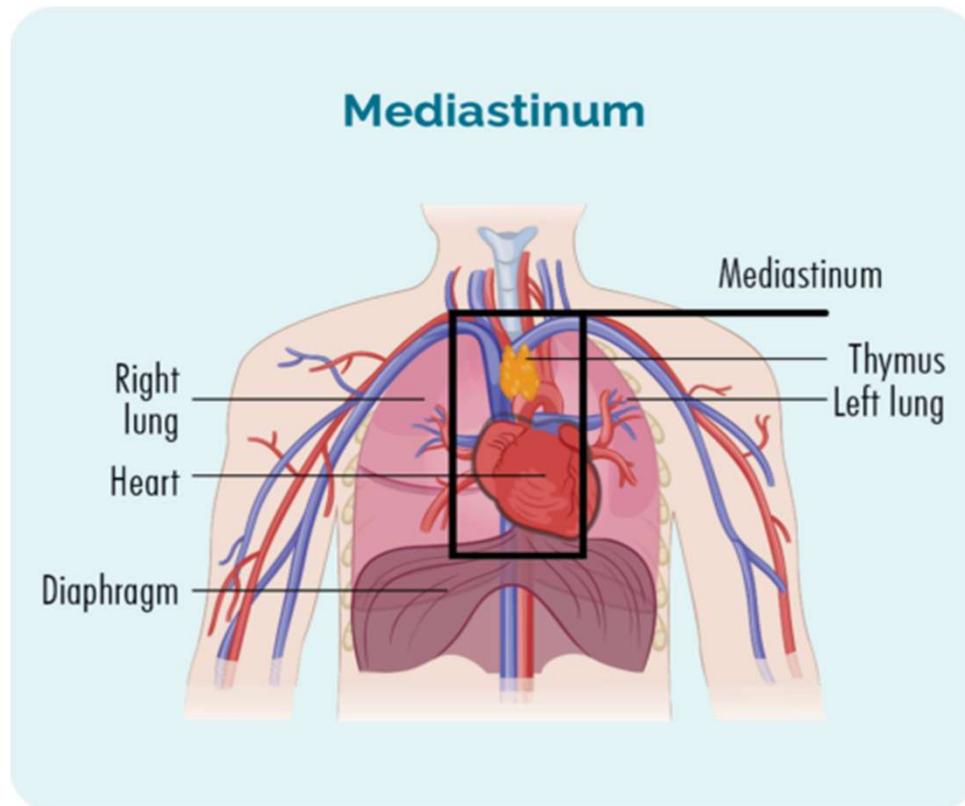
Primair CNS lymfoom : CAR-T ?



Blood Adv (2023) 7 (1): 32–39.

5. Primair mediastinaal lymfoom

PMBCL: ziektebeeld

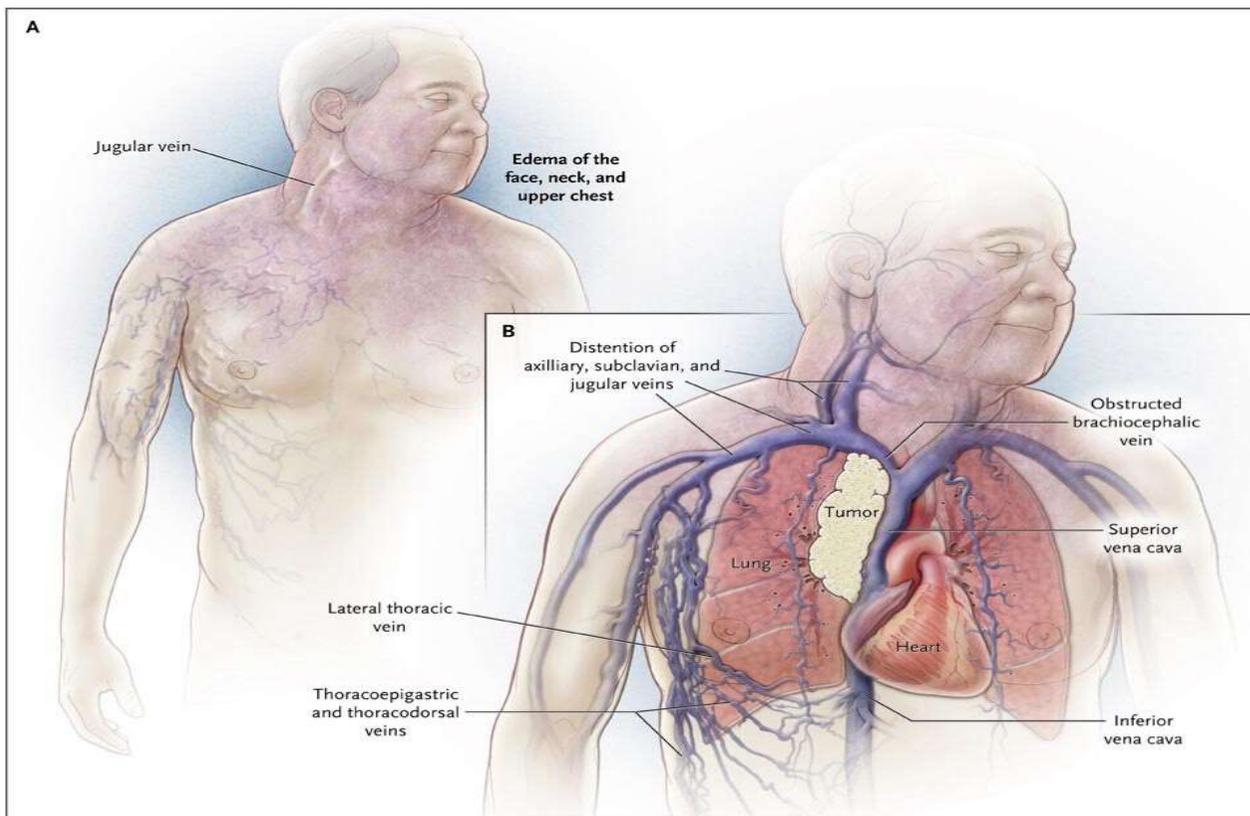


- 50-70% bulky mass >10cm
- 30-40% pleura/pericardeffusies
- 20-40% **vena cava superior syndroom**

S/ B-symptomen, hoesten ,
dyspnee , thoracale pijn ,
heesheid, dysfagie

Meer bij vrouwen , 20-35 jaar

PMBCL : vena cava superior syndroom = urgentie



Steroiden

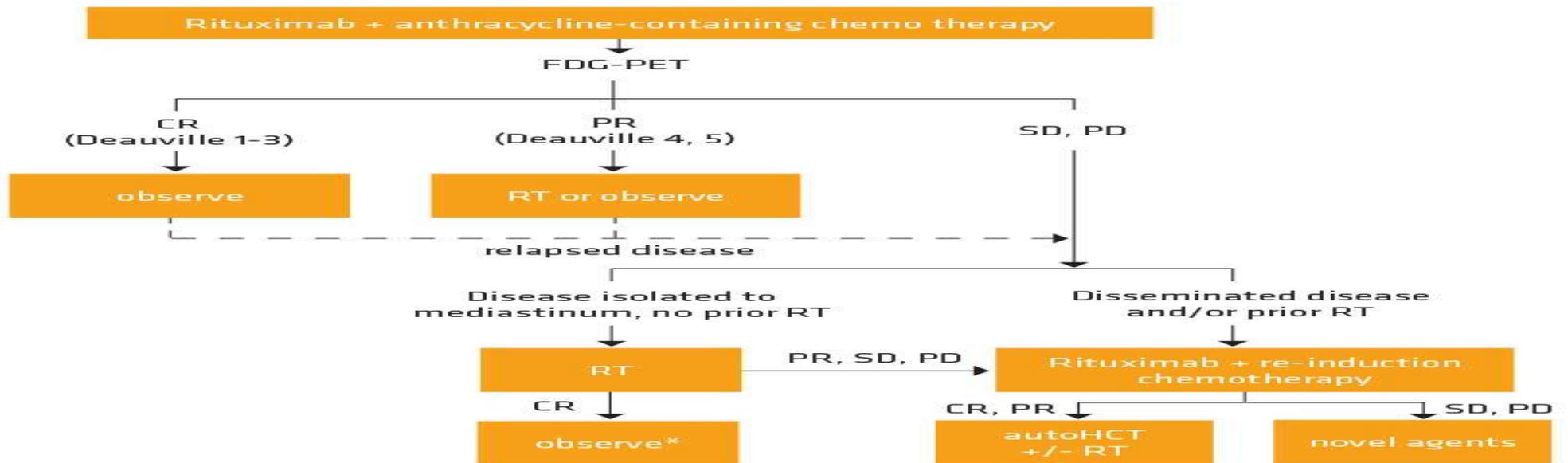
LMWH

Radiotherapie

Stenting

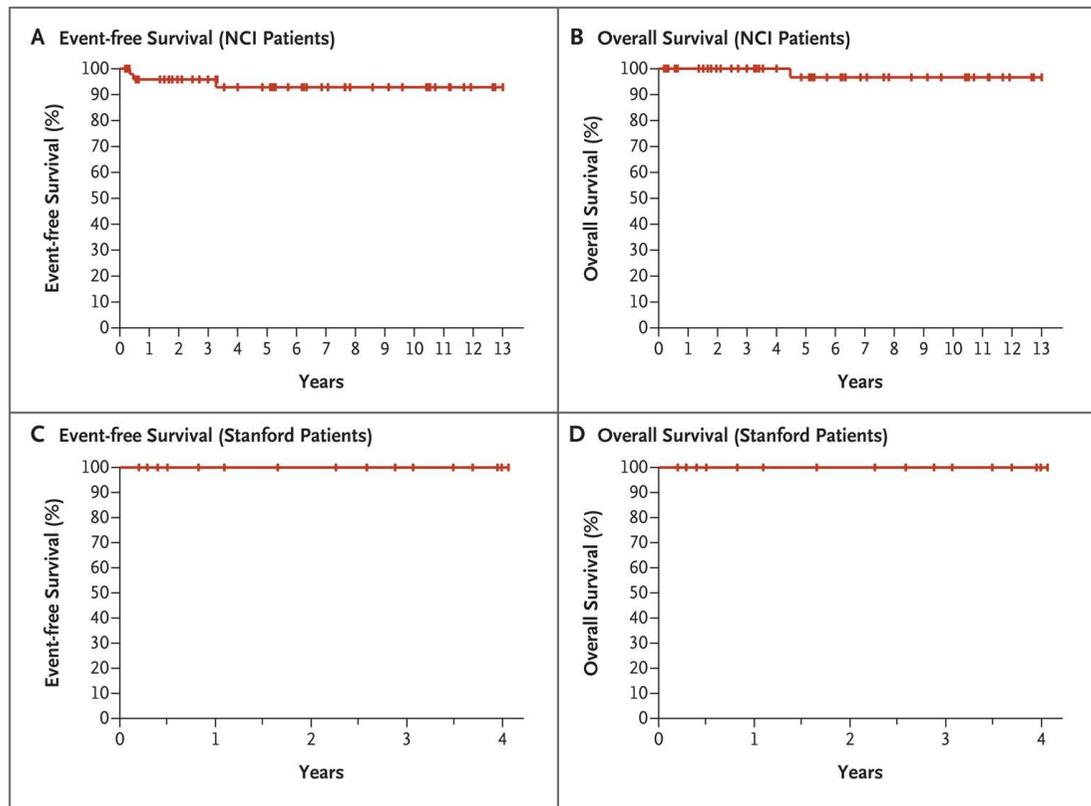
PMBCL : behandelning first line

FIGURE. Treatment Paradigm for the Management of PMBCL



*RT alone or combined modality with autoHCT are both reasonable approaches in this scenario and have not been compared in clinical trials. CR = complete response; PR = partial response; SD = stable disease; PD = progressive disease; RT = radiation therapy

PMBCL : behandelend first line

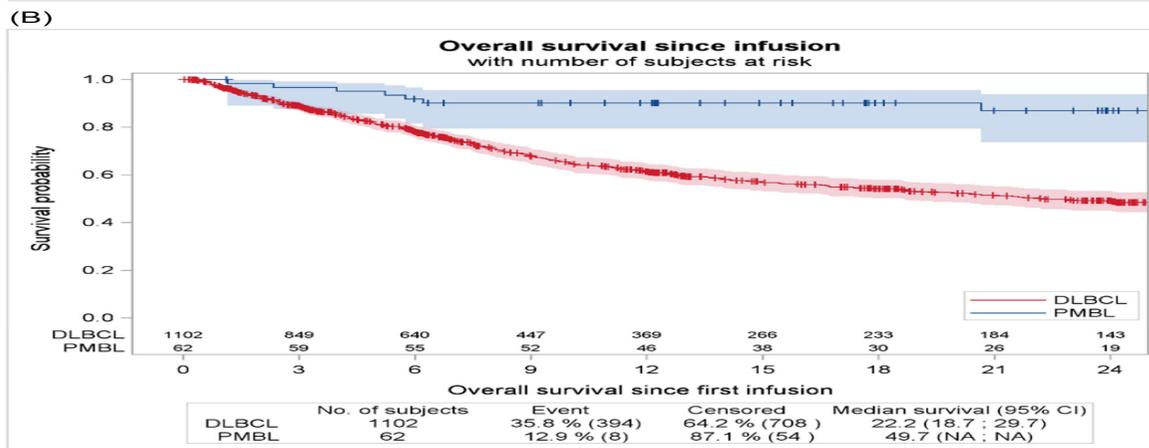
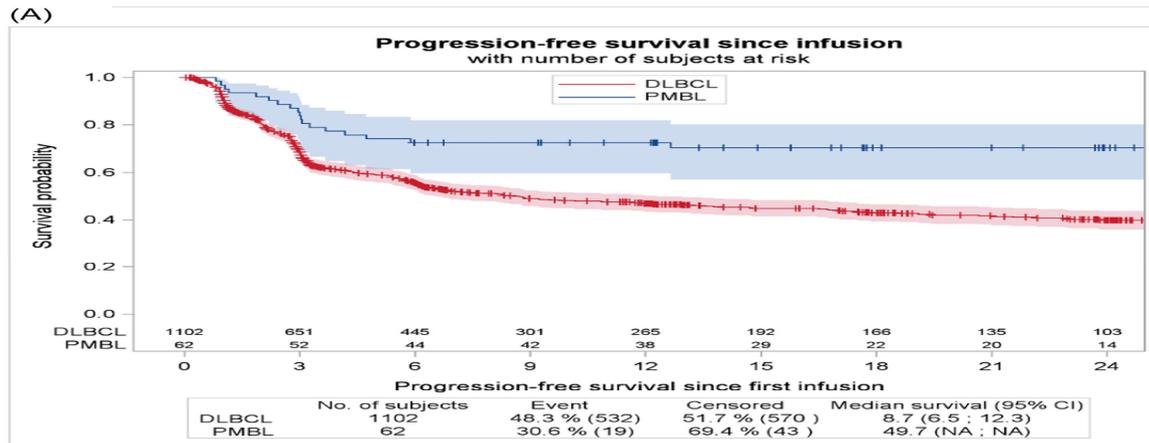


DA-EPOCH-R was administered to 51 patients in a prospective trial at the National Cancer Institute (NCI), and to 16 patients in a retrospective trial at Stanford University.

In the **prospective** NCI cohort, the event-free survival rate was 93% (Panel A) and the overall survival rate was 97% (Panel B) at a median follow-up of 63 months.

In the **retrospective** Stanford cohort, the event-free and overall survival rates were both 100% (Panel C and Panel D, respectively) at a median follow-up of 37 months.

Herval PMBCL : behandelning CAR-T



Outcomes of patients with relapsed or refractory primary mediastinal B-cell lymphoma treated with anti-CD19 CAR-T cells: CARTHYM, a study from the French national DESCAR-T registry

Outcomes of patients with relapsed or refractory primary mediastinal B-cell lymphoma treated with anti-CD19 CAR-T cells: CARTHYM, a study from the French national DESCAR-T registry

Population



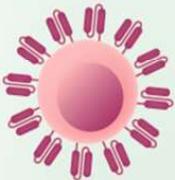
DESCAR-T registry
1534 LBCL patients infused with anti-CD19 CAR-T cells
↓
82 patients with R/R PMBL
Study population

Analysis

- Outcomes (PFS, OS, response rate)
- Survivals according to centrally reviewed PET at M1
- Baseline factors associated with outcomes



Findings



- Axi-cel is associated with CR rate 74.5%, 2y-PFS 70.4% and 2y-OS 86.9%
- DS 1-4 at M1 evaluation correlated with excellent outcome
- TMTV is the main baseline factor associated with treatment failure

Conclusion

Anti-CD19 CAR-T cells produce high cure rate in R/R PMBL, with PET imaging being a strong predictor of outcomes

