Lymphoma in Later Life – Prioritizing What Matters

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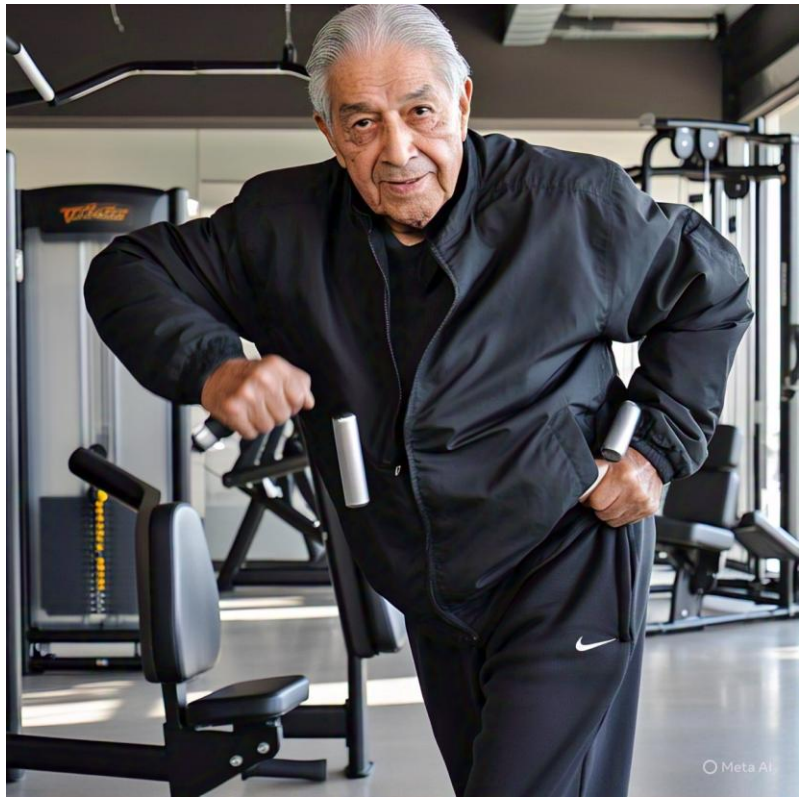
Outline

- Dilemma in managing older adults - curative vs palliative vs comfort
- Age related assessment and optimization
- Older adults with DLBCL
- Older adults with classical Hodgkin Lymphoma
- Older adults with indolent NHL

How old is old?



AI generated picture of 80 year old man

Geriatric Oncology - Hematological cancers

ASCO Special Articles

Check for upd

Practical Assessment and Management of Vulnerabilities in Older Patients Receiving Systemic Cancer Therapy: ASCO Guideline Update

William Dale, MD, PhD[1]; Heidi D. Klepin, MD, MS[2]; Grant R. Williams, MD, MSPH[3]; Shabbir M.H. Alibhai, MD[4]; Cristiane Bergerot, PhD[5]; Karlynn Brintzenhofeszoc, PhD, MSW[6]; Judith O. Hopkins, MD[7]; Minaxi P. Jhawer, MD[8]; Vani Katheria, MS[9]; Kah Poh Loh, MBBCh BAO, MS[10]; Lisa M. Lowenstein, PhD[11]; June M. McKoy, MD, MPH, JD, MBA[12]; Vanita Noronha, MD[13]; Tanyanika Phillips, MD[14]; Ashley E. Rosko, MD[15]; Tracy Ruegg, PhD, ANP[16]; Melody K. Schiaffino, PhD[17]; John F. Simmons Jr, MD[18]; Ishwaria Subbiah, MD[19]; William P. Tew, MD[20]; Tracy L. Webb, PA-C[21]; Mary Whitehead, BFA[22]; Mark R. Somerfield, PhD[23]; and Supriya G. Mohile, MD, MS[10]

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ESMO GOOD SCIENCE BETTER MEDICINE BEST PRACTICE

ESMO OPEN SCIENCE FOR OPTIMAL CANCER CARE

REVIEW

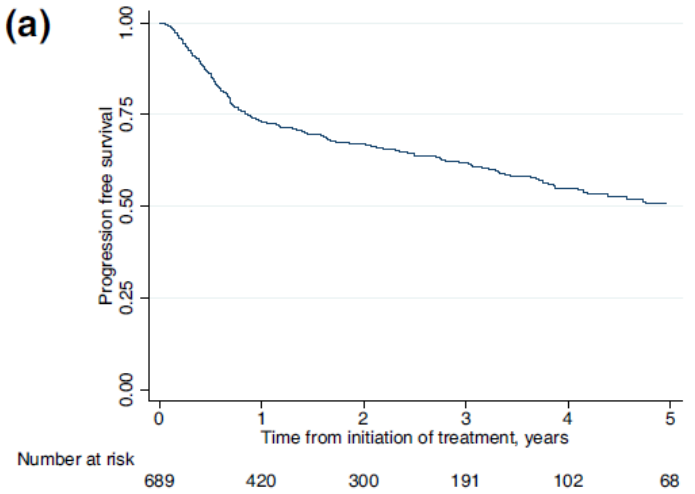
Adequate assessment yields appropriate care—the role of geriatric assessment and management in older adults with cancer: a position paper from the ESMO/SIOG Cancer in the Elderly Working Group

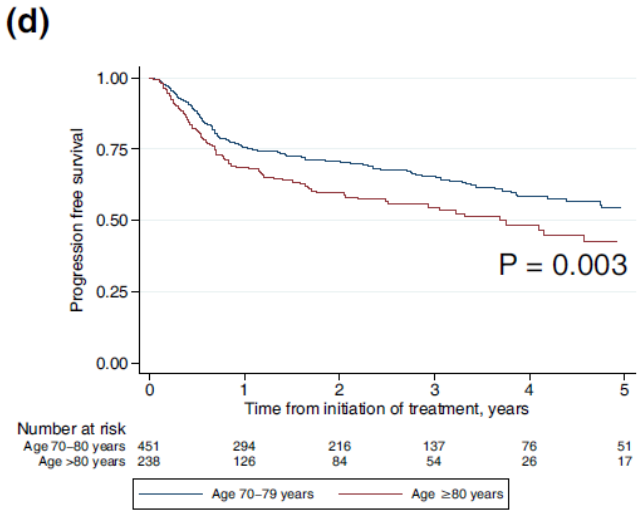
K. P. Loh[1*], G. Liposits[2], S. P. Arora[3], N. R. Neuendorff[4], F. Gomes[5,6], J. L. Krok-Schoen[7,8], T. Amaral[9], E. Mariamidze[10,11], L. Biganzoli[12], E. Brain[13], C. Baldini[14,15], N. M. L. Battisti[16], M. Frélaut[17], R. Kanesvaran[18], A. R. A. Mislang[19,20], D. Papamichael[21], C. Steer[22,23,24†] & S. Rostoft[25,26†]

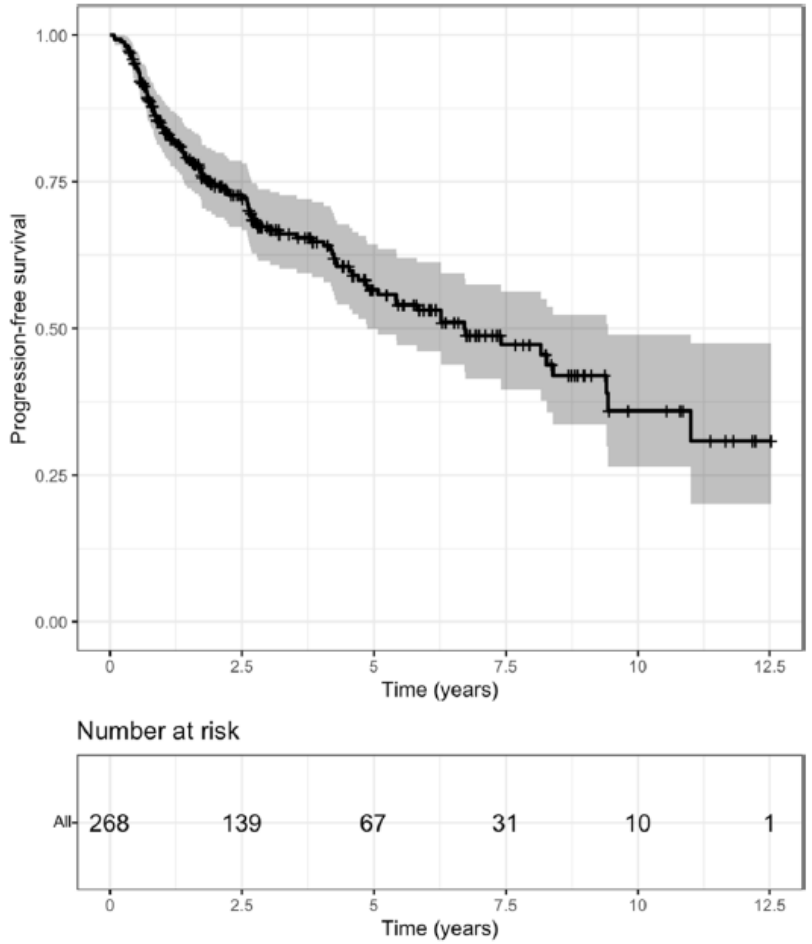
- ASCO and ESMO: recommend GA in ≥65 year-old cancer patient

Dale JCO 2021, Loh ESMO open 2024

Older patients still benefit from definitive treatment





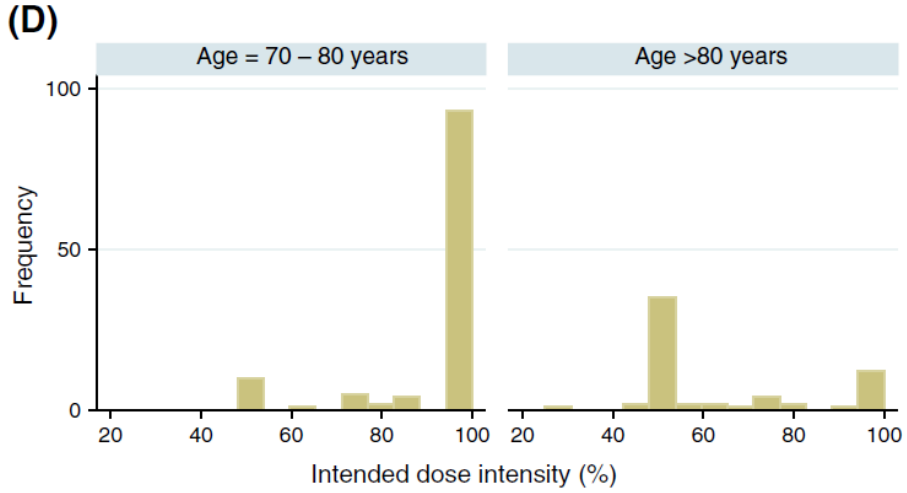


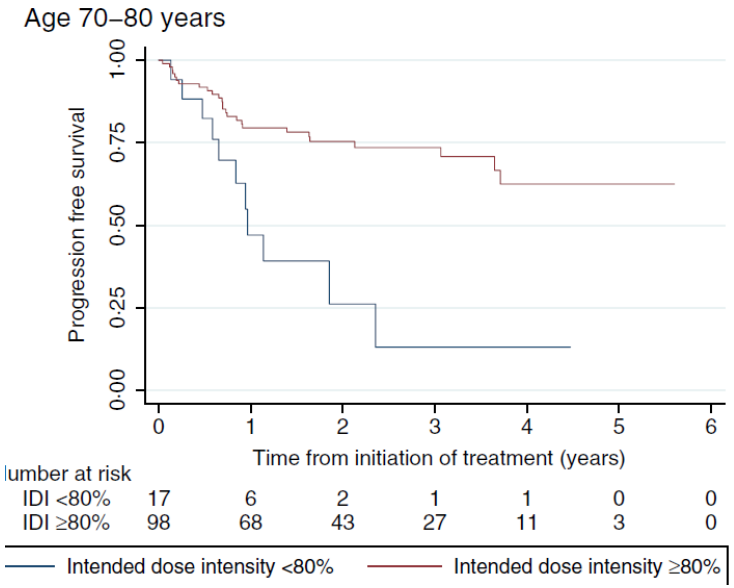
(B) 5-year overall progression-free survival was 56.63% (95% Confidence Interval 49.45 – 63.81).

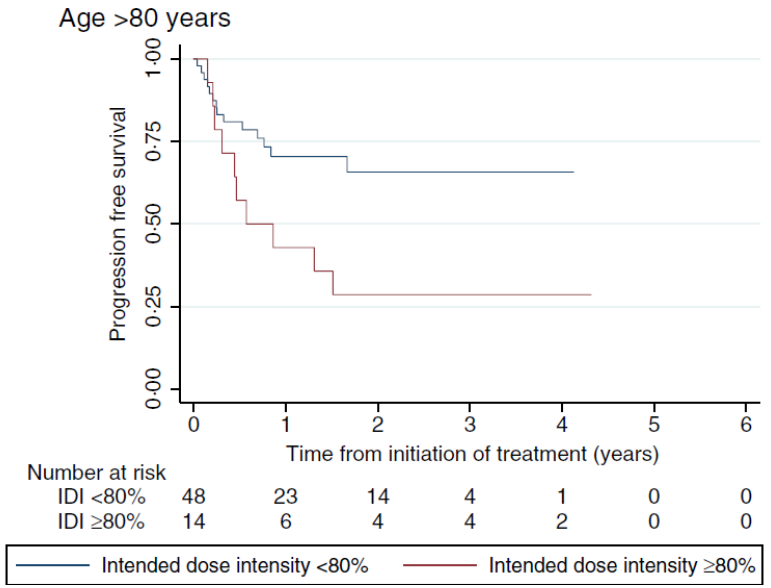
- Approx 50% of older adult with DLBCL cured by 1st line therapy
- Both UK and SG data (median age 76)

Eyre Journal IM 2019
Lim Ann Hematol 2024

Chemotherapy dose intensity matter?



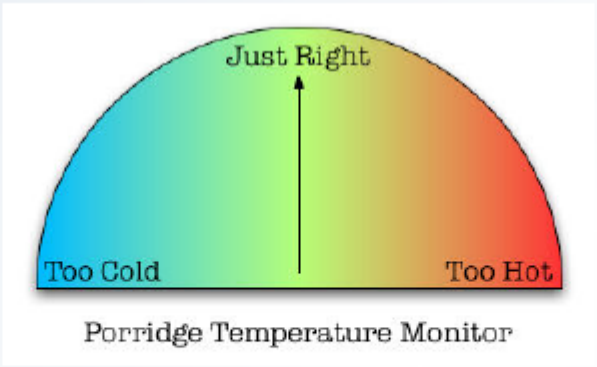




- 177 patients with DLBCL, age ≥70

Eyre Br J Haem 2015

Use of reduced intensity treatment regimens can minimize toxicity but might also lead to poorer outcomes due to reduced disease control.



Porridge Temperature Monitor

Toxicity is more common in older adults, and those who experience it derive less benefit from treatment.

Prospective identification of pts at greatest risk of toxic events may allow tailored dose reductions in those vulnerable individuals and mark them for closer monitoring during therapy

- Older adults are susceptible to complications that might affect their ability to receive subsequent cycles, which lead to inadequate disease control
- Resilience issue: inability to bounce back from complication (deconditioned)
- Quality of life issue: spending more time in hospital/ICU/rehab center/nursing home than at home with family

Picture courtesy of Torka 2025

FIL – simplified GA

- Geriatric Assessment: Comprehensive/Simplified

Table I. Definition of three geriatric risk categories according to age, comorbidities and functional abilities of daily living.

	CGA category		
	Fit	Unfit	Frail
ADL	6	5*	≤4*
IADL	8	6–7*	≤5*
CIRS-G	No comorbidity score 3–4 and <5 comorbidities score 2	No comorbidity score 3–4 and 5–8 comorbidities score 2	≥1 Comorbidity score 3–4 or >8 comorbidities score 2
Age		≥80 fit	≥80 unfit

ADL, activity of daily living; IADL, instrumental activity of daily living; CIRS-G, Cumulative Illness Rating Score for Geriatrics; CGA, comprehensive geriatric assessment.
*Number of residual functions.

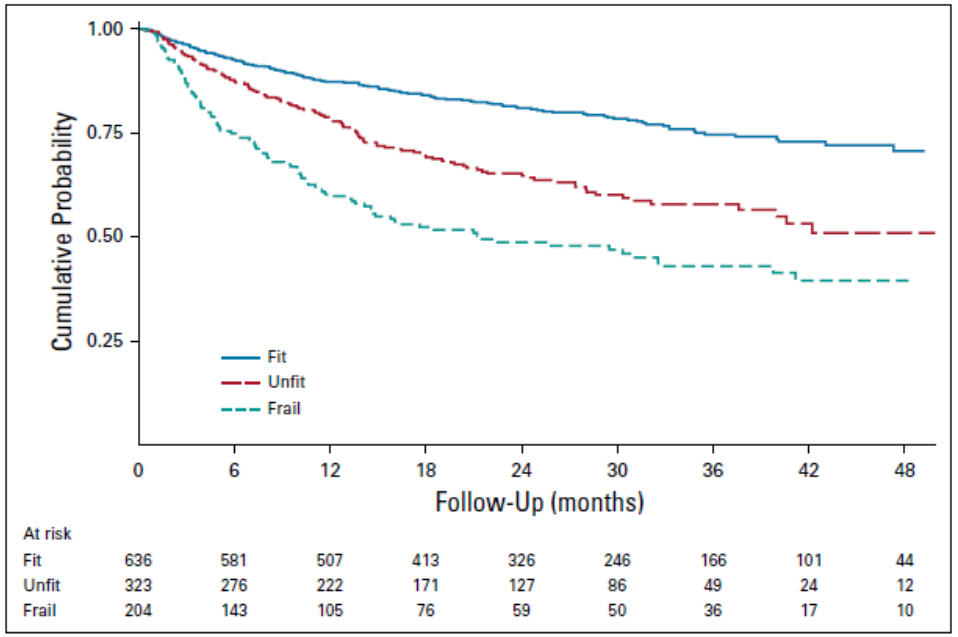


FIG 1. Overall survival by sGA in all patients with treatment details (N = 1,163). sGA, simplified geriatric assessment.

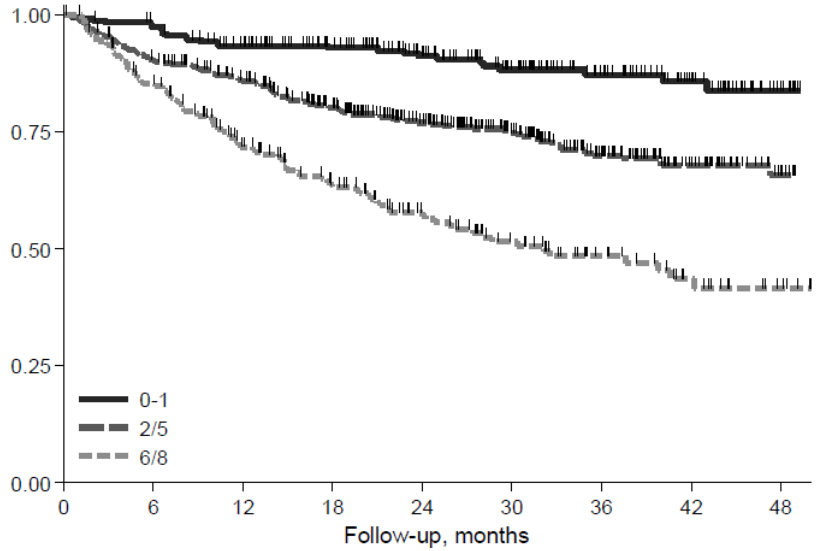
Merli Leukemia Lymphoma 2014
Merli JCO 2021

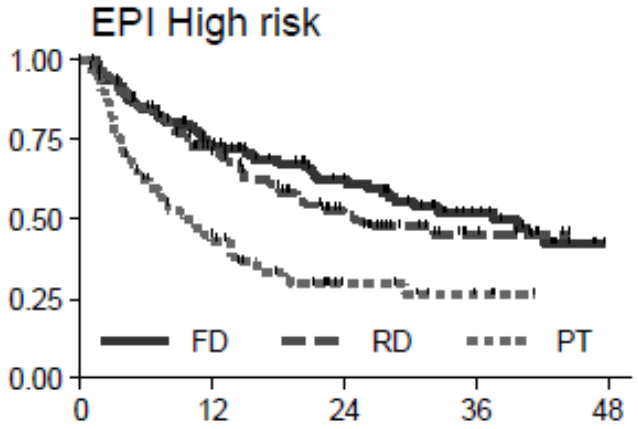
Elderly Prognostic Index (EPI)

Table 1B Elderly Prognostic Index (EPI)[37]

Criteria		Score
sGA	Fit	0
	Unfit	3
	Frail	4
IPI	IPI 1	0
	IPI 2	1
	IPI 3-5	3
Hemoglobin <12 g/dL		1
Risk Groups (score)		**3-year OS (95% CI)**
Low (0-1)		87% (81-91)
Intermediate (3-5)		69% (63-73)
High (6-8)		42% (36-49)

Abbreviations: CI = confidence interval; HR = hazard ratio; IPI = international prognostic index; sGA = simplified geriatric assessment; OS = overall survival.





Merli Leukemia Lymphoma 2014
Merli JCO 2021

Timed Up-to-Go

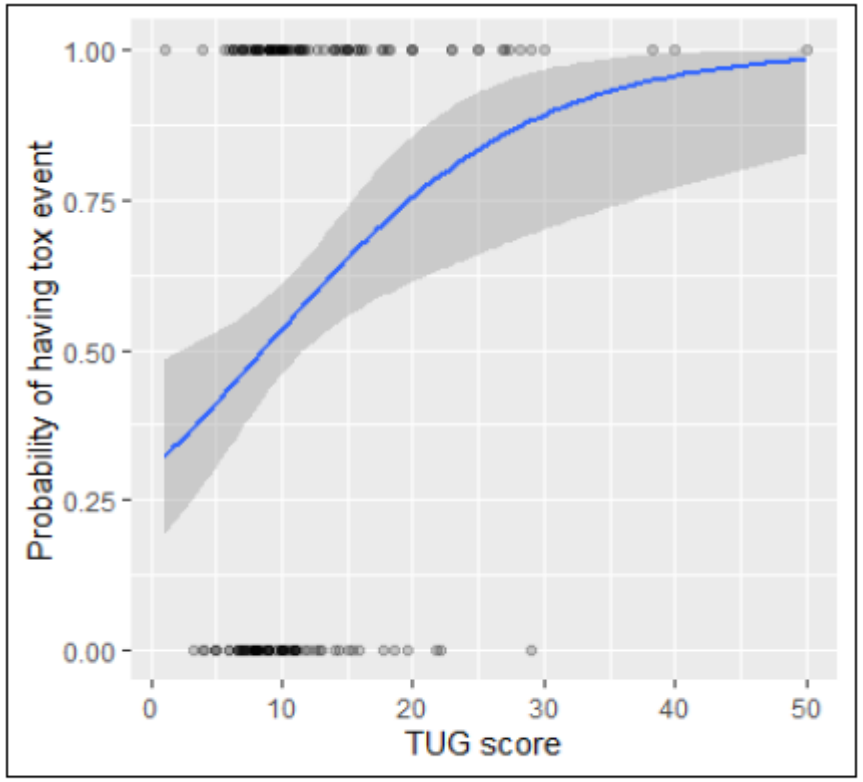


Figure 4. Effect of TUG on toxicity risk as modeled by logistic regression

Table 2. Patient Outcomes

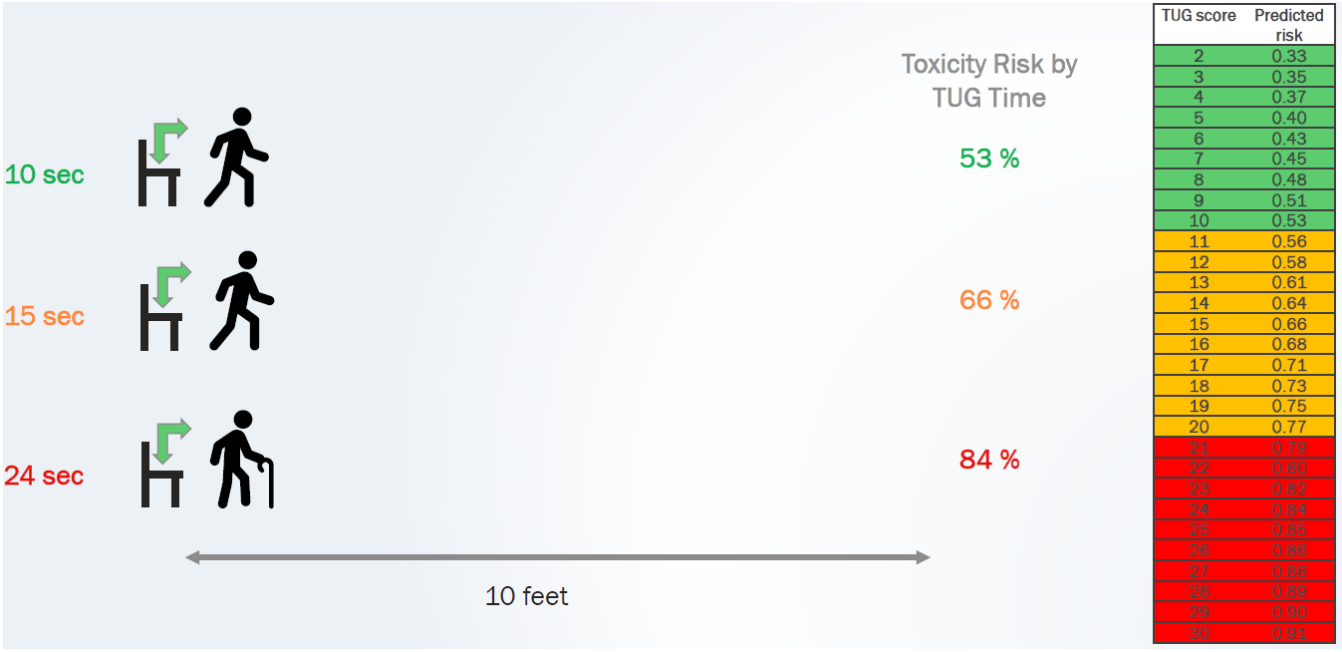
Category of events	N = 194
Toxicity events	110 (57%)
Early induction deaths	4 (2.1%)
Grade 4+ hematologic toxicities	74 (38%)
Grade 3+ non-hematologic toxicities	49 (25%)
Grade 3+ non-hematologic toxicities plus grade 4+ hematologic toxicities	88 (46%)

- Among 152 survivors out of 194, median follow-up time was 4.3 (IRQ 2.4-5.3) years.
- Median overall survival was not reached.
- **5-year PFS and OS were 63% (CI 56%, 72%) and 77% (CI 71%, 84%) respectively.**

- Baseline TUG time was independently associated with toxicity in multivariate analysis.
- For each 1-sec increase in TUG score, the odds of an event increased by a factor of 1.1 (11%) (p=0.008).
- A 5-second increase would increase odds by a factor of 1.6, and a 10-second increase would increase odds by a factor of 2.6.
- A logistic longitudinal mixed effects model showed that change in TUG time between cycles was not significant in predicting STox, but rather it was the TUG score itself which had the effect at any given cycle, and the effect was similar to that of the TUG baseline score analysis.

Torka ASH 2023 2024

Example of geriatric assessment



TUG score	Predicted risk
2	0.33
3	0.35
4	0.37
5	0.40
6	0.43
7	0.45
8	0.48
9	0.51
10	0.53
11	0.56
12	0.58
13	0.61
14	0.64
15	0.66
16	0.68
17	0.71
18	0.73
19	0.75
20	0.77
21	0.79
22	0.80
23	0.82
24	0.84
25	0.85
26	0.86
27	0.88
28	0.89
29	0.90
30	0.91

Primary endpoint

- **Serious Toxicity event (STox) defined as any of the following:**
  - Hospitalization during or within 30 days following chemotherapy
  - Dose delay or reduction to a dose intensity ≤80% of planned
  - Discontinuation of chemo due to tox
  - Death

- Timed Up-and-Go. Predicting rate of toxicity events during chemo

ASH 2024 Torka et al

Screening tool-VES-13 VS FIL sGA

c. walking across the room? USE OF CANE OR WALKER IS OK.

☐ YES → Do you get help with walking? ☐ YES * ☐ NO
☐ NO
☐ DON'T DO → Is that because of your health? ☐ YES * ☐ NO

d. doing light housework (like washing dishes, straightening up, or light cleaning)?

☐ YES → Do you get help with light housework? ☐ YES * ☐ NO
☐ NO
☐ DON'T DO → Is that because of your health? ☐ YES * ☐ NO

e. bathing or showering?

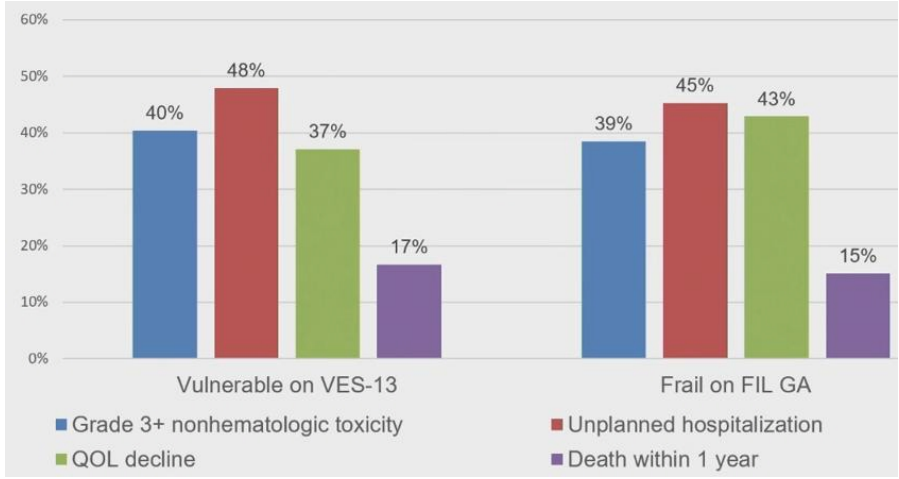
☐ YES → Do you get help with bathing or showering? ☐ YES * ☐ NO
☐ NO
☐ DON'T DO → Is that because of your health? ☐ YES * ☐ NO

- 13 items self-reported survey, score 0-10, +3 considered vulnerable
- Median age 73
- 90% DLBCL, 10% MCL
- Comparable outcome between both methods

Outcome	Not Vulnerable (N=57)	Vulnerable (N=48)
Grade 3+ non-hematologic toxicity	23% (13/57)	40% (19/47)
Dose reduction	16% (9/57)	31% (15/48)
Early therapy cessation	7% (4/57)	13% (6/46)
Unplanned hospitalization	30% (17/57)	48% (23/48)
Intensive care unit admission	7% (4/57)	8% (4/48)
Quality of life decline	16% (8/49)	37% (13/35)
PFS, median, months (95% CI)	Not reached	33.9 (29.6-not reached)
Death within 1 year	0% (0/57)	17% (8/48)

PFS: progression-free survival

Vulnerable on VES-13 highly associated with death within 1 year: p=0.001



Johnson ASH 2024

Supportive Measures

- Prephase steroid
- Growth Factor Prophylaxis
- Role of antiviral and antiPCP
- Role of supplementary Vitamin D
- IVIG replacement

Prephase Steroid

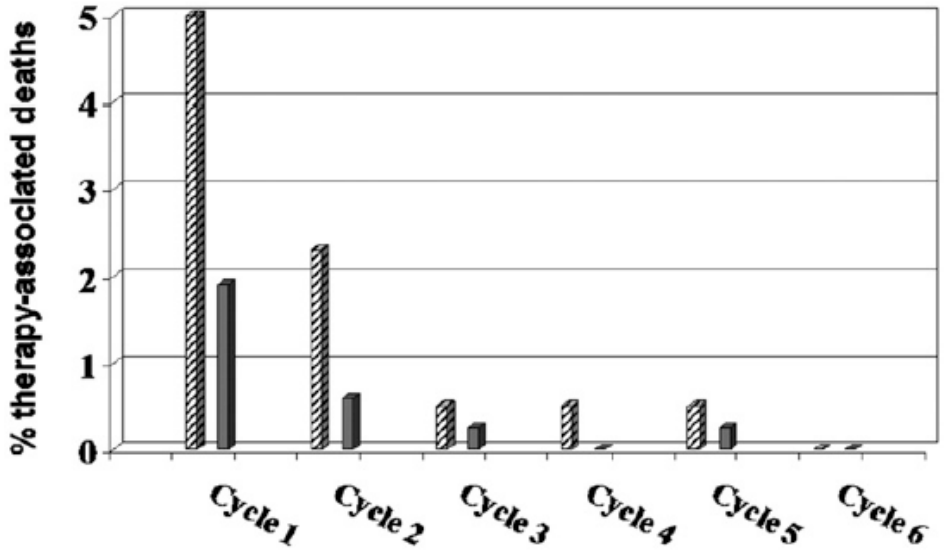


Figure 1. Therapy-associated deaths in the NHL-B2 trial of CHOP in DLBCL before and after the introduction of prephase treatment. Before (▨) and after (▤) the introduction of prephase treatment. Reprinted with permission. Reprinted from Pfreundschuh[14] with permission of the American Society of Hematology.

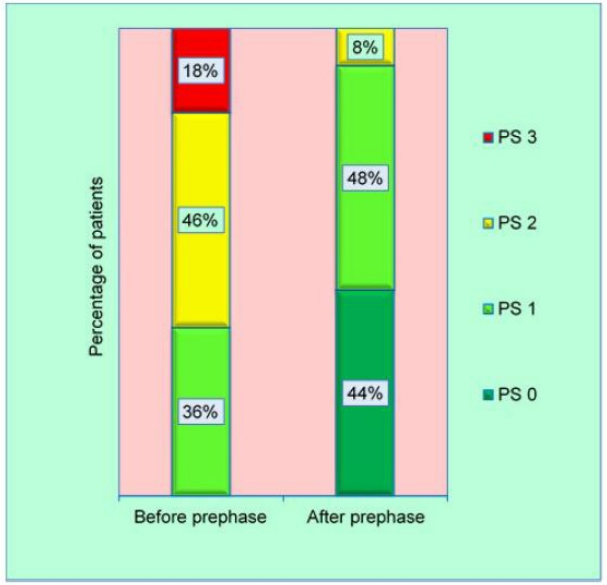
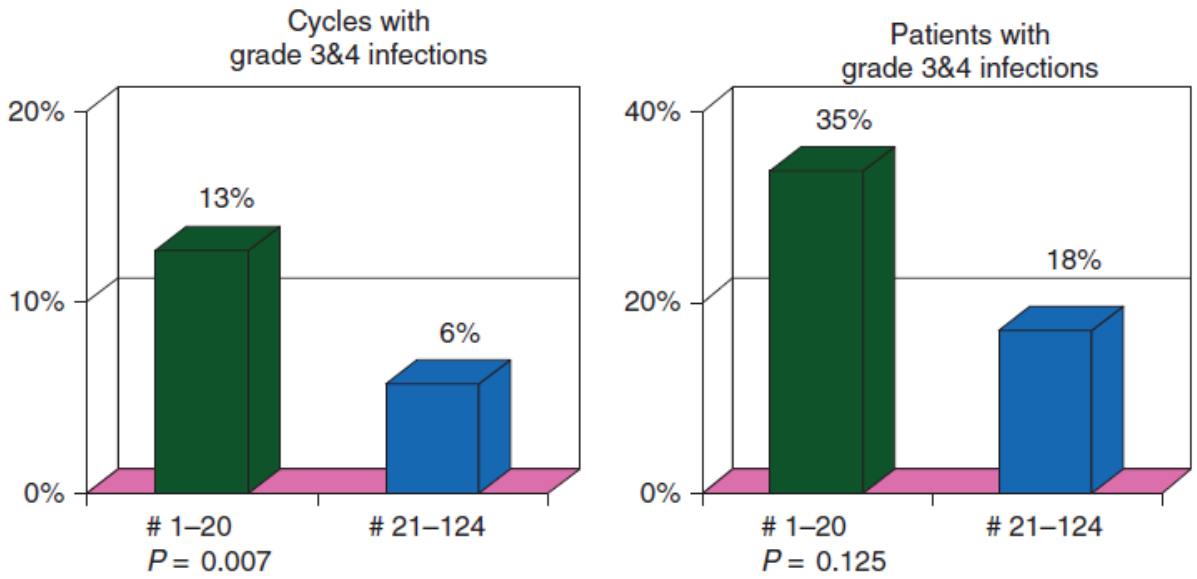


FIGURE 1 Eastern Cooperative Oncology Group performance status (PS) before and after prephase treatment. Percentage of patients in each PS category is shown [Colour figure can be viewed at wileyonlinelibrary.com]

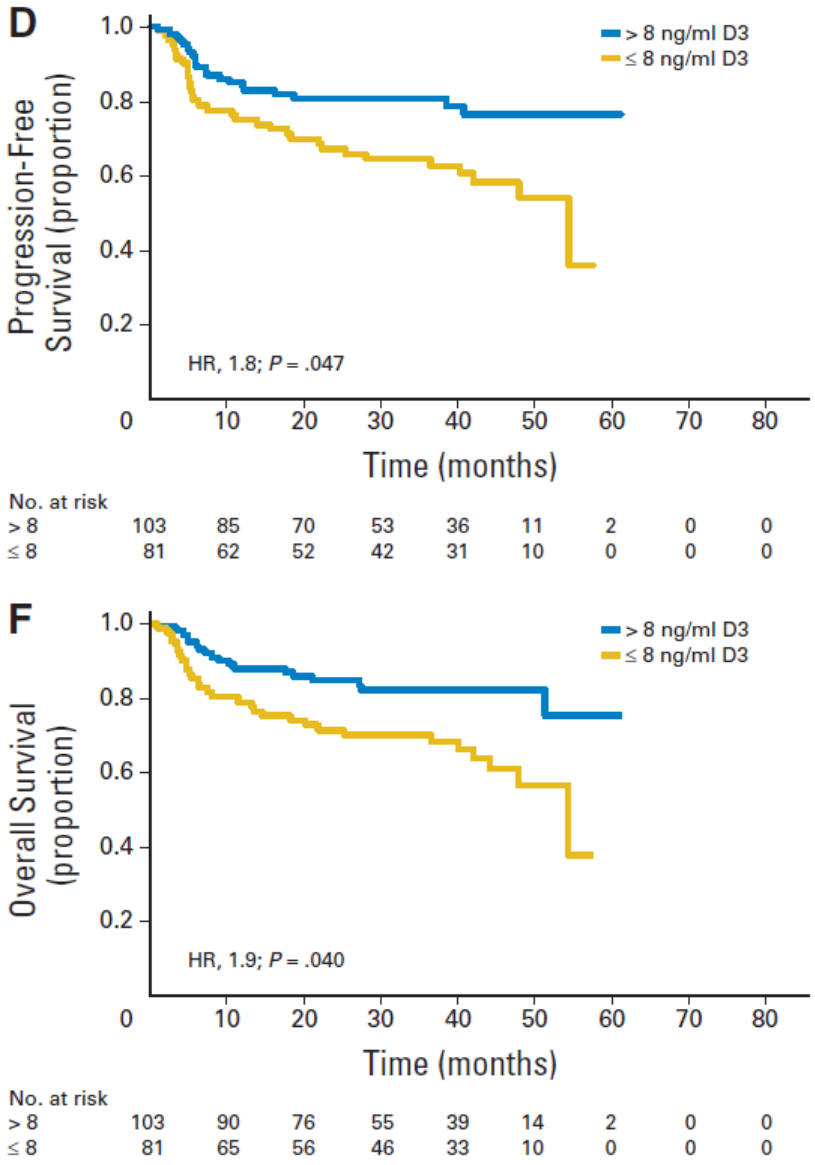
- Reduced senescence-related proinflammatory cytokine mileu that affecting well-being
- Improve performance status
- Reduced treatment related mortality in the first 2 cycles

Barlett Blood 2020, Lin Hematologica 2022, Lashmaiah Eur J Haem 2018

Acyclovir&AntiPCP, Vitamin D

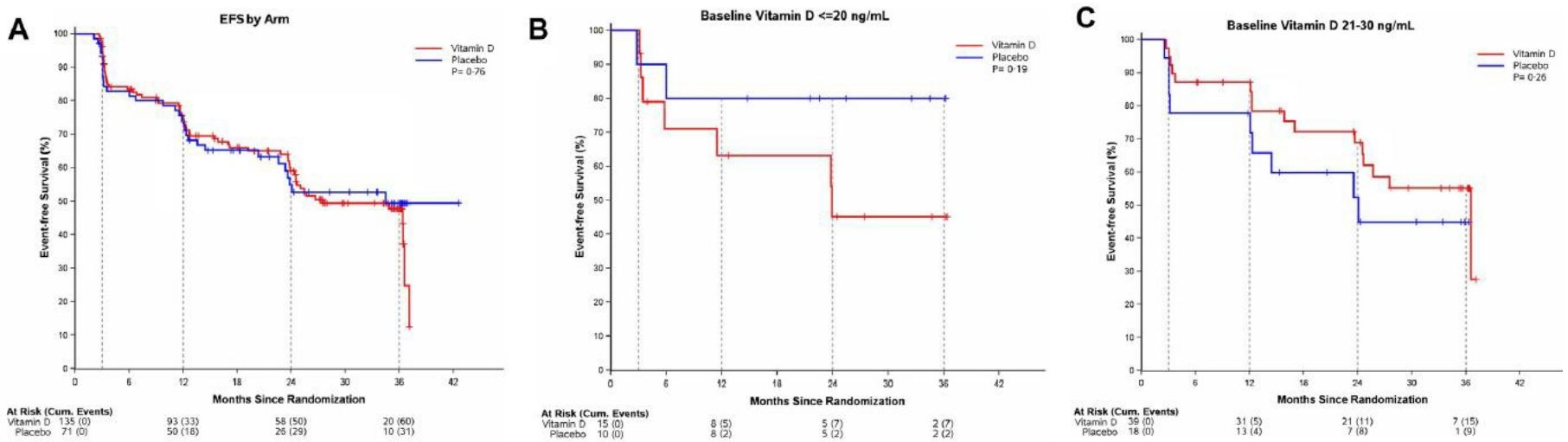


- Less G3/4 infection after addition of acyclovir/Bactrim
- In rituximab arm, lower vitamin D level confers inferior survival outcome



Murawski Ann Oncol 2014, Bittenbring JCO 2014

Replacing Vitamin-D in FL



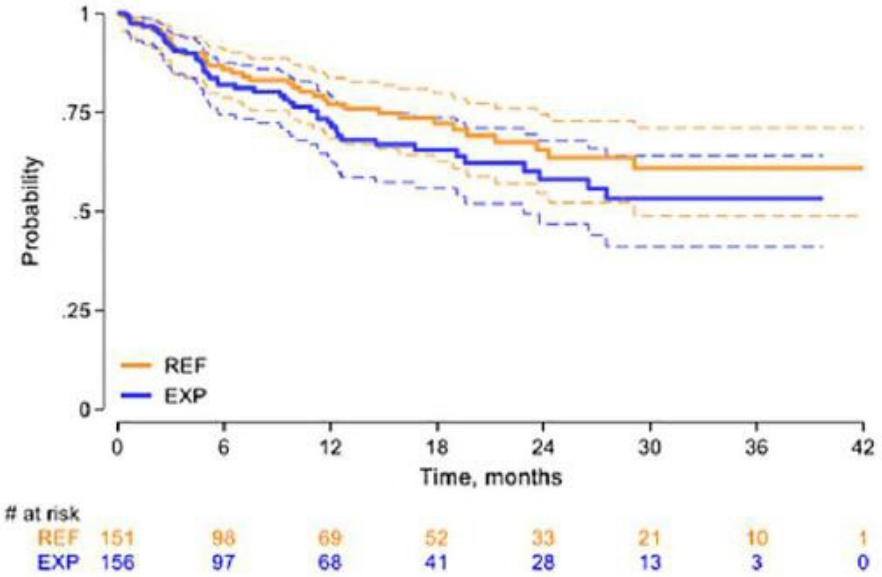
- Low tumor burden Follicular Lymphoma on rituximab monotherapy – randomized vit-D vs placebo
- No EFS benefit in overall but trends of benefit seen in low baseline Vit-D patients

Friedberg eClinicalMedicine 2024

Pre-phase vitamin D replacement in DLBCL

Figure 1a

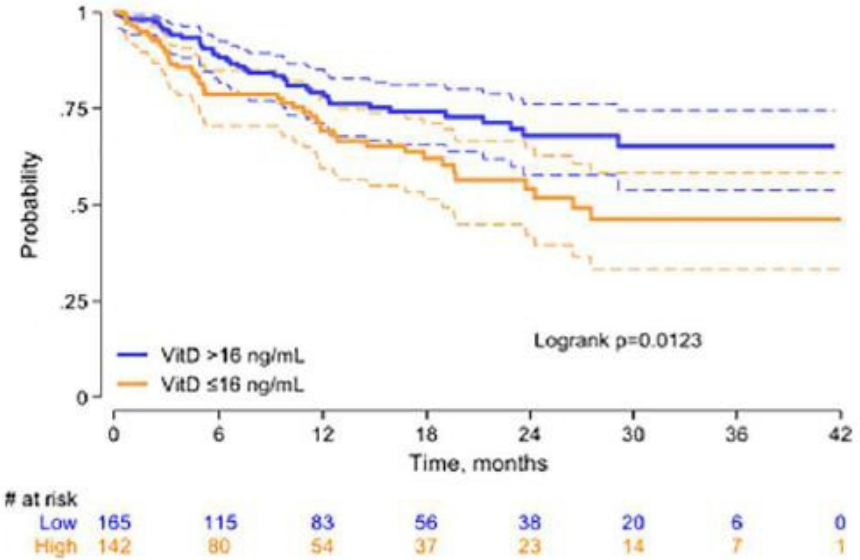
Progression Free Survival by treatment arm



# at risk								
REF	151	98	69	52	33	21	10	1
EXP	156	97	68	41	28	13	3	0

Figure 1b

Progression Free Survival by baseline VitD



# at risk								
Low	165	115	83	56	38	20	6	0
High	142	80	54	37	23	14	7	1

ICML 2025 Merli

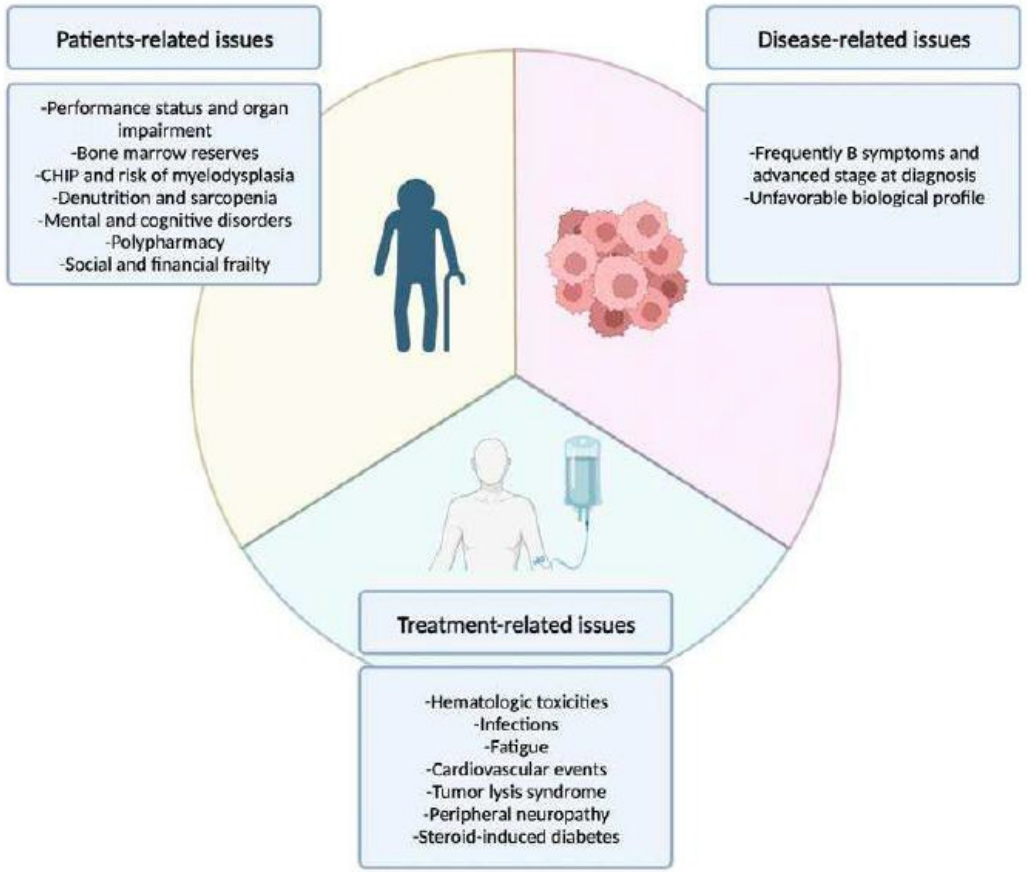


Table 1. Prevention of major side effects in older patients with non-Hodgkin lymphoma.

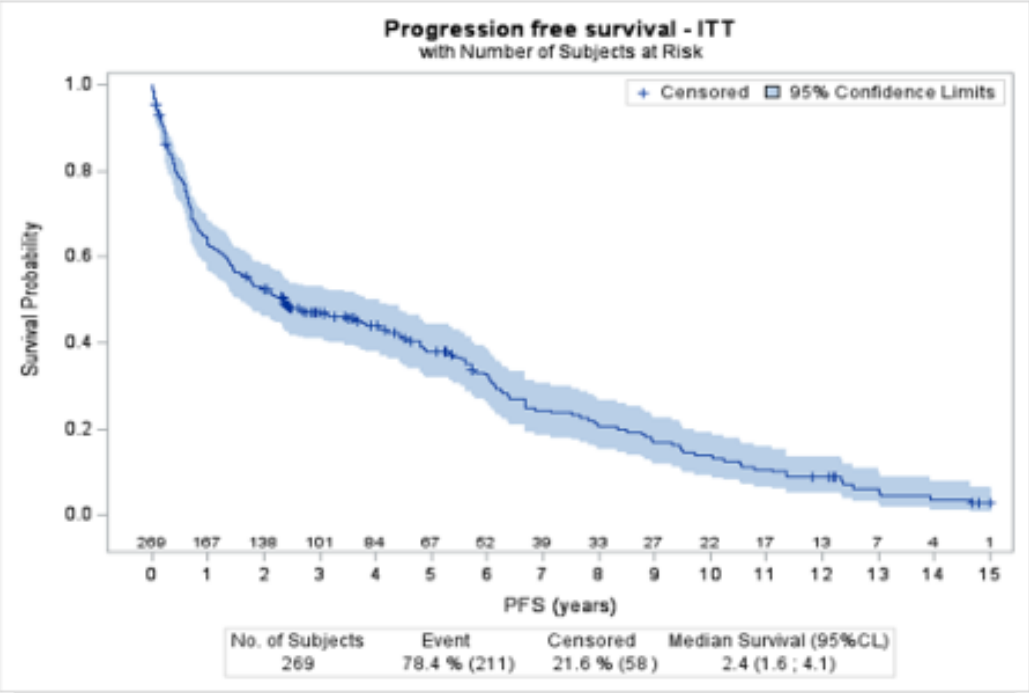
Neutropenia (>60% above 80y, 40% grade III) and febrile neutropenia (mortality rate: 9–23%)	➢ **G-CSF/Peg G-CSF** **IVIG, TMP/SMX** . . .if required
Anemia (with low EPO response)	➢ Erythropoiesis stimulating agents
Cardiovascular problems (arterial hypertension, atrial fibrillation, late heart failure)	➢ **Cardiovascular** monitoring
Tumor lysis syndrome (most important toxicity and toxic death during first cycle)	➢ **Rasburicase** or allopurinol administration **Prephase** with Steroids
Diabetes	➢ Cautious administration of **steroids and vincristine**
Drugs Interactions	➢ Be attentive of **polypharmacy**
Neuropathies	➢ Reduced doses of **vincristine**
Secondary tumor (late event: lung, MDS)	➢ **Long-term follow-up** for second tumors

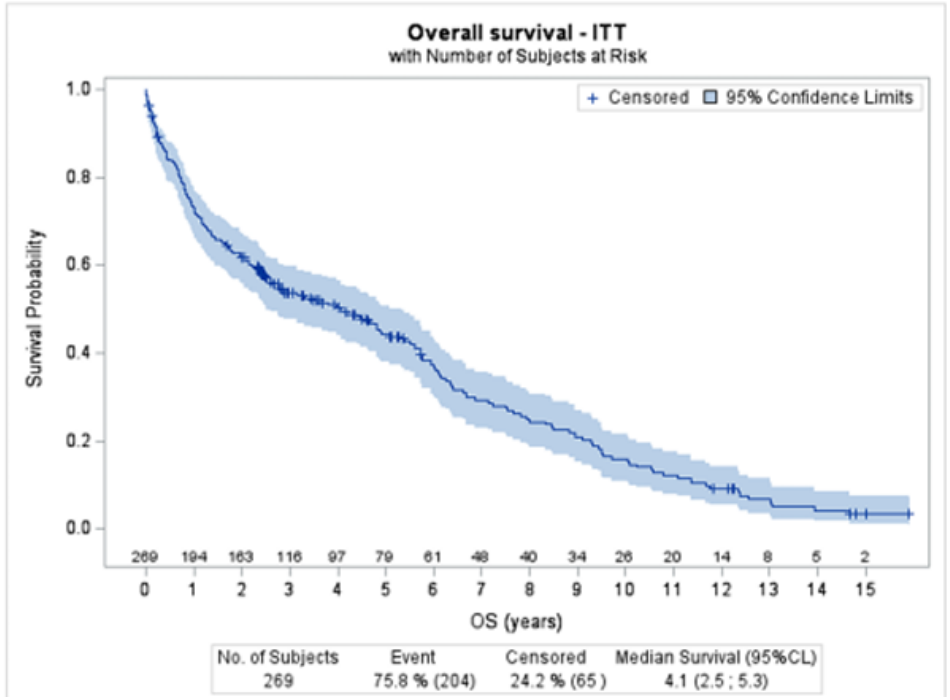
EPO = erythropoietin, G-CSF = growth-colony stimulating factor, IVIG = intravenous immunoglobulins, TMP/SMX = trimethoprim/sulfamethoxazole, MDS = myelodysplastic syndrome.

Massaro Cancers 2023

Older Adult of DLBCL – First Line

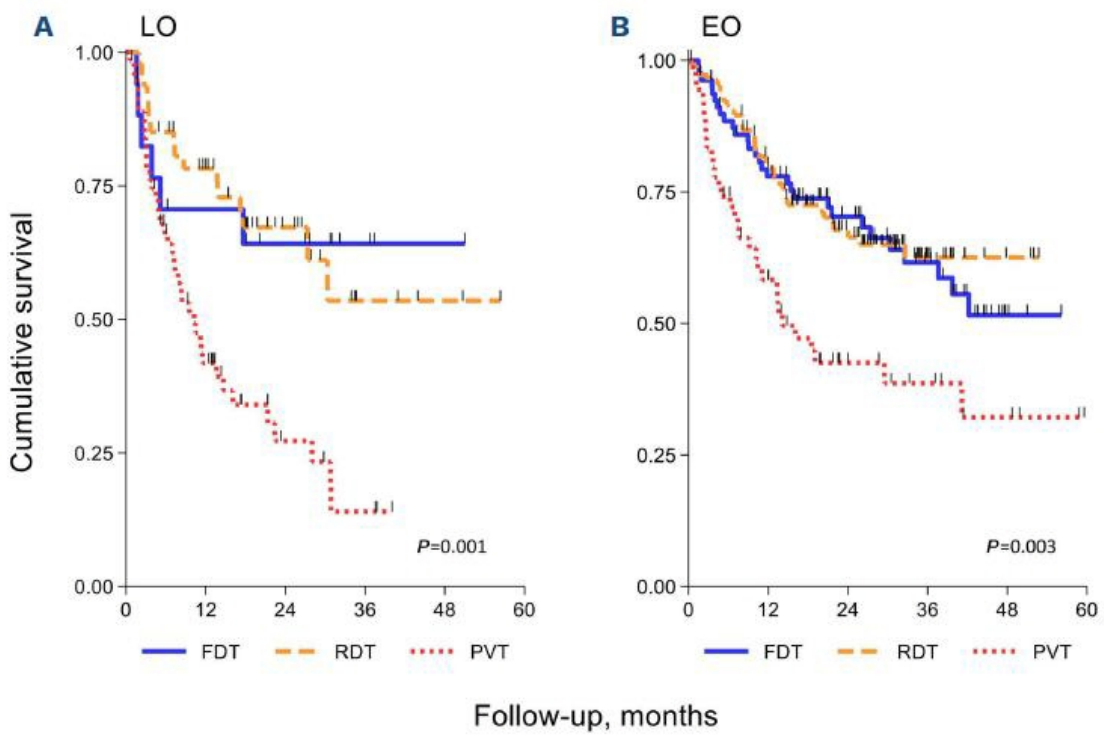
- Anthracycline eligible
- Anthracycline ineligible but fit for some chemo
- Frail – non-chemotherapy eligible

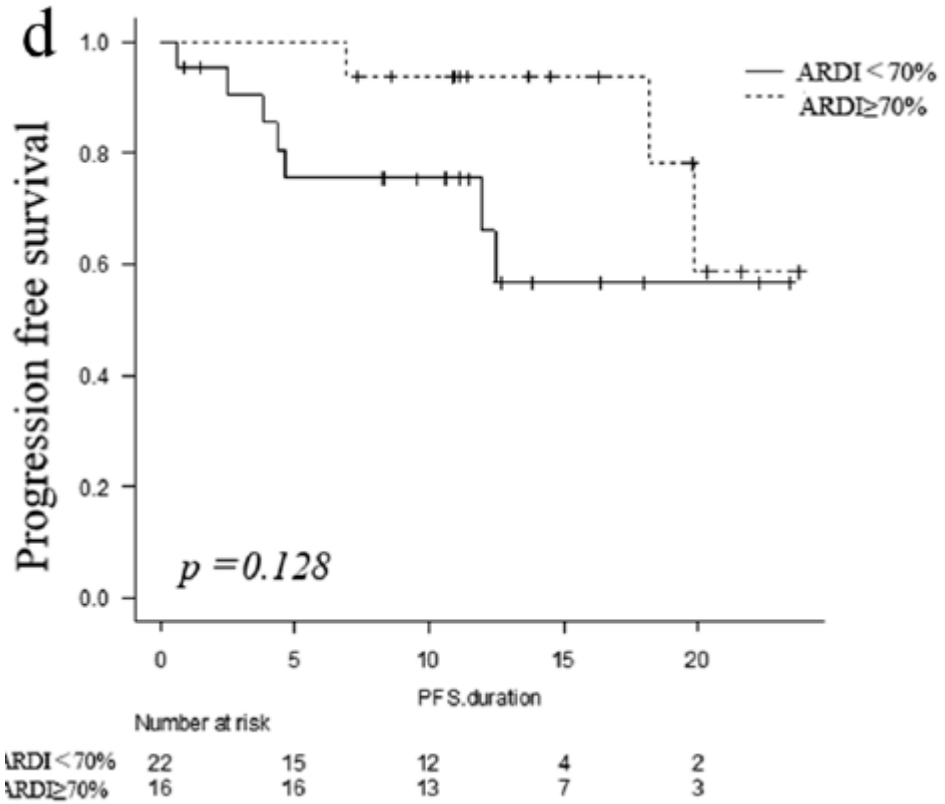




- RminiCHOP set the standard for older adult – median age 83 years.
- Median PFS 2.4 years, OS 4.1 years

Michot ASH 2024

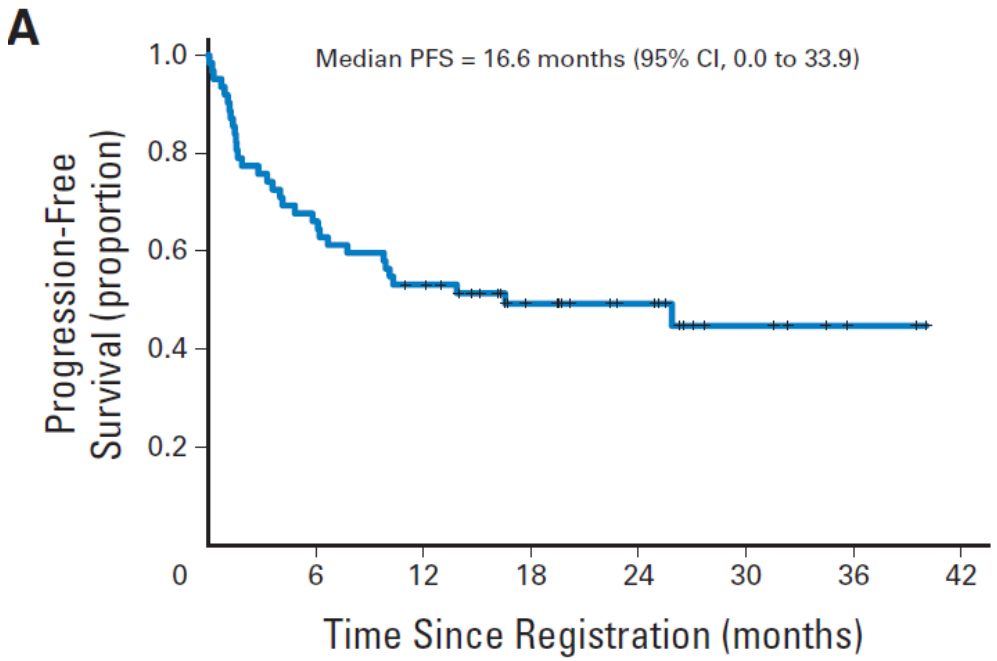


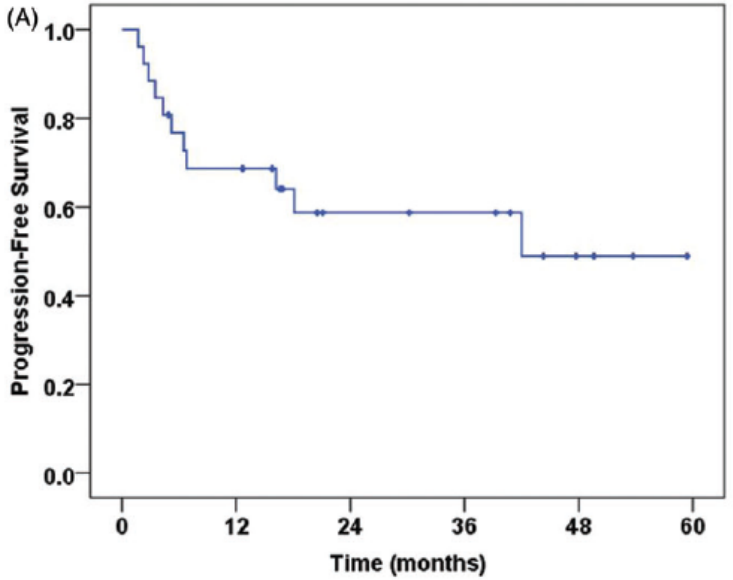


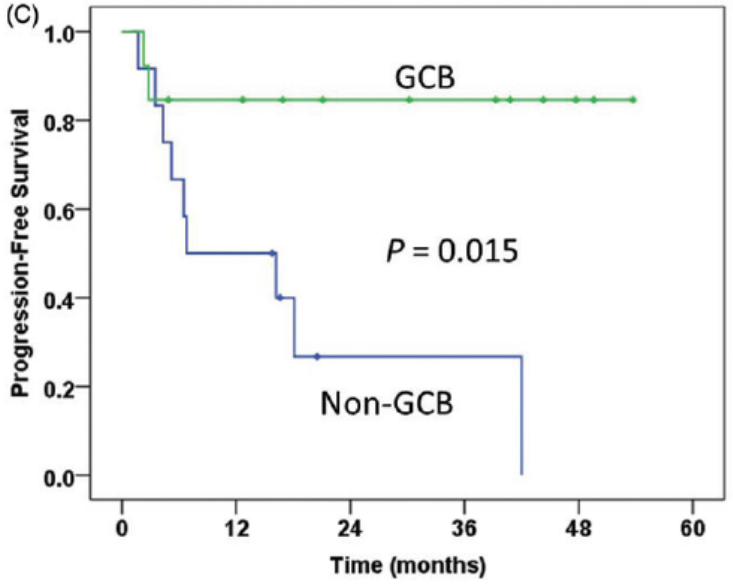
- Reduced dose RCHOP similar outcome to full dose RCHOP in those age 80s
- Reduced dose Pola-RCHP appear feasible in older adult (median age 84 years)

Tucci Hematologica 2022, Sato Blood Res 2025

Non-anthracycline chemo



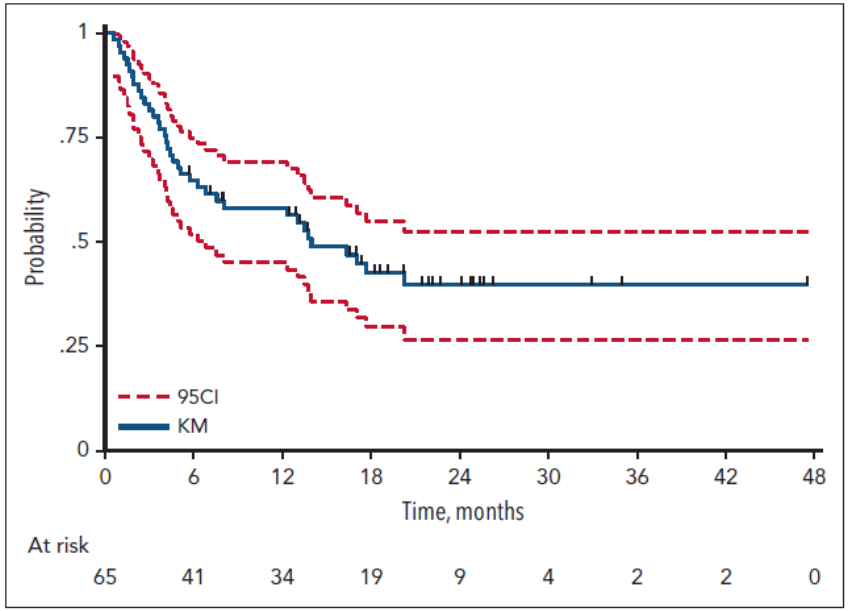




- R-gemcitabine-CVP: 2year PFS 50%
- R-C-etoposide-VP: 2year PFS 49%

Fields JCO 2014, Rashidi Leuk Lymphoma 2015

Frail, chemo unfit



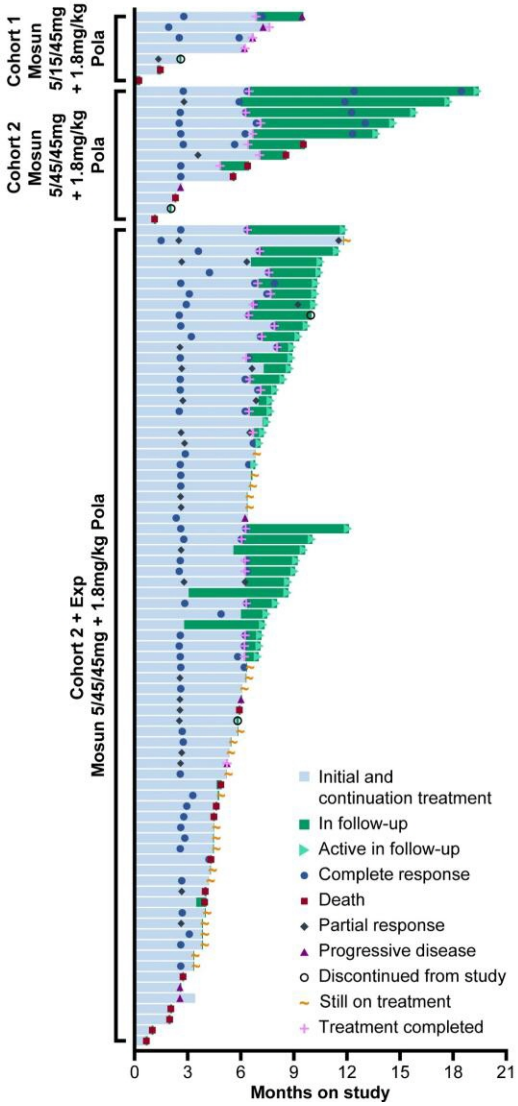
- R2 in frail patient
- Mosunetuzumab n=54, age 83 years, 12m PFS 39%
- Mosu-Pola n=108, age 81 years. ORR 80%, CRR 61%
- Palliative Radiotherapy

Table: Baseline and disease characteristics

Characteristics, n (%)	M-Pola Cohort (N=108)
Median age (range), years	81.0 (66–94)
Age ≥80	66 (61.1)
sGA*	
Fit	1 (0.9)
Unfit	64 (59.3)
<80 years	41 (38.0)
≥80 years	23 (21.3)
Frail	43 (39.8)
Gender	
Female	56 (51.9)
ECOG PS	
0–1	87 (80.6)
2	21 (19.4)
Ann Arbor stage	
III–IV	71 (65.7)
aa-IPI	
0	21 (19.4)
1	32 (29.6)
2	41 (38.0)
3	14 (13.0)
Extranodal involvement	77 (71.3)
Elevated LDH	59 (54.6)
Bulky disease (≥7.5cm)	30 (27.8)
HGBCL†‡	
Double hit	8 (7.4)
Triple hit	2 (1.9)
Cell of origin‡	
GCB	49 (45.4)
Non-GCB	56 (51.9)
Unknown	3 (2.8)

*Eligible patients were ≥80 years or per sGA (Merli et al. J Clin Oncol 2021): 65–79 years and ineligible for chemoimmunotherapy with at least: ≥2 ADL and/or IADL impairments, and/or a CIRS-G score of ≥1 comorbidity with a severity score of 3–4, or score of 2 in ≥8 comorbidities (unfit) or ≥80 years with ≥1 ADL and/or ≥1 IADL impairments and/or a CIRS-G score of ≥1 comorbidity with a severity score of 3–4, or score of 2 in ≥5 comorbidities (frail). Fit patients were any patients who did not meet the criteria for unfit or frail per sGA. Due to protocol violation, one fit patient was included in the M-Pola Cohort. †Double hit/triple hit: MYC, BCL2, and/or BCL6. ‡Local testing. aa-IPI, age-adjusted International Prognostic Index; ADL, activity of daily living; CIRS-G, Cumulative Illness Rating Scale-Geriatric; ECOG PS, Eastern Cooperative Oncology Group performance status; GCB, germinal center B-cell-like; HGBCL, high-grade B-cell lymphoma; IADL, instrumental activity of daily living; LDH, lactate dehydrogenase; Mosun, Mosunetuzumab; M-Pola, mosunetuzumab plus polatuzumab vedotin; Pola, polatuzumab vedotin; sGA, simplified geriatric assessment.

Figure: Response and time on M-Pola treatment



Gini Blood 2023 , Olszewski ASH 2022, 2023

Zanubrutinib with Rituximab and Lenalidomide in *de novo* Diffuse Large B Cell Lymphoma

Context of Research

Older patients with diffuse large B cell lymphoma (DLBCL) may have more unfavorable tumor microenvironmental features, which could lead to worse clinical outcomes

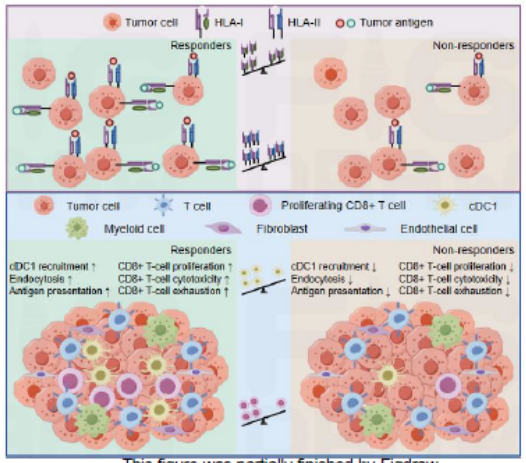
Aim of This Study

To assess the efficacy and safety of zanubrutinib in combination with rituximab and lenalidomide (ZR2) in patients with *de novo* DLBCL aged ≥75 years (NCT04460248)

Findings

The CR rate with ZR2 was 65%

Microenvironmental features related to ZR2 efficacy



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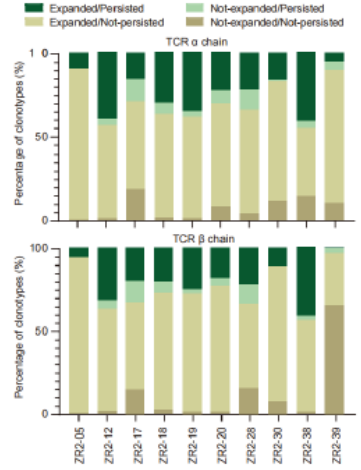
TCR sequencing of PBMCs from patients with durable remission



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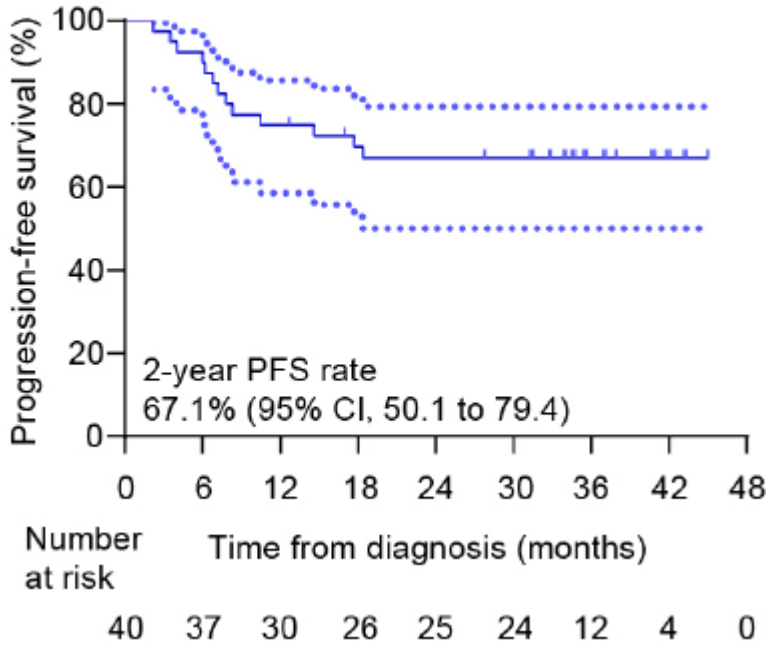


- Median age 78
- Median dose intensity 95-98%

Xu et al Blood 2025

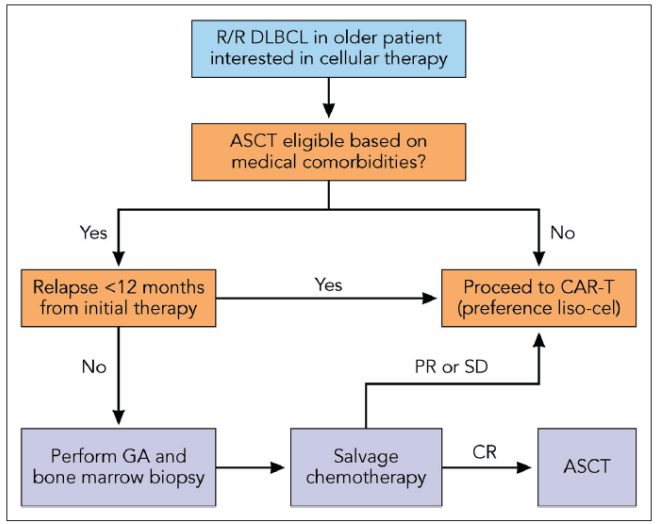
Older Adult of DLBCL – Relapse Refractory

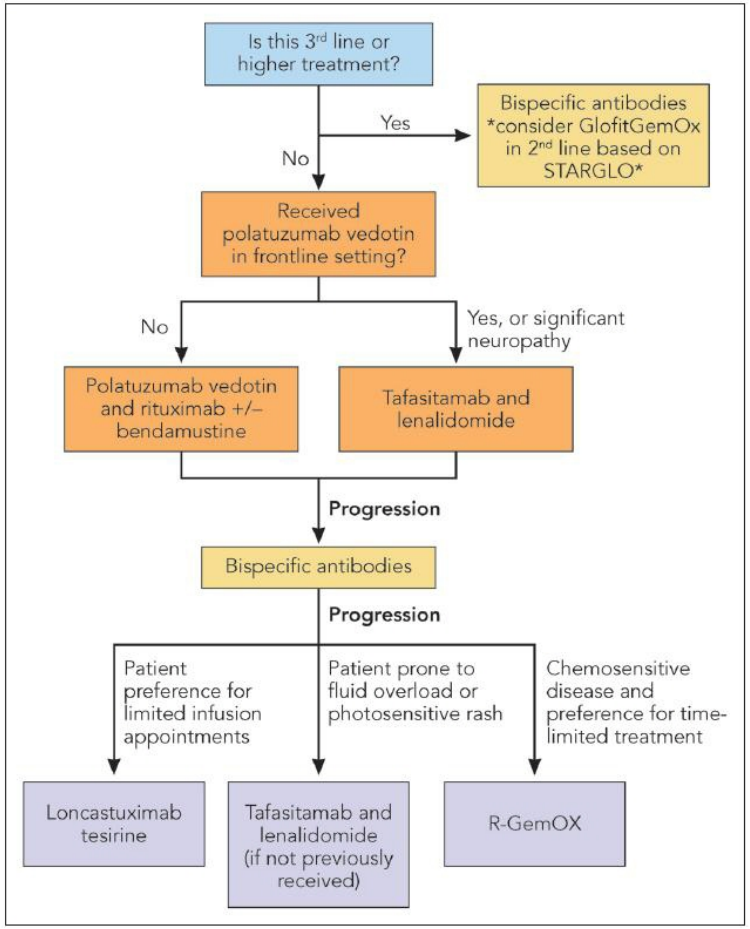
blood® How I Treat

How I treat older patients with relapsed/refractory diffuse large B-cell lymphoma

Danielle S. Wallace, Kah Poh Loh, and Carla Casulo

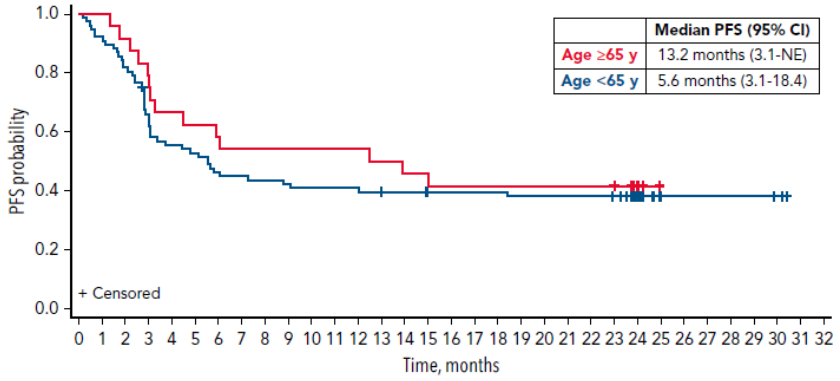
Division of Hematology/Oncology, Department of Medicine, Wilmot Cancer Institute, University of Rochester Medical Center, Rochester, NY

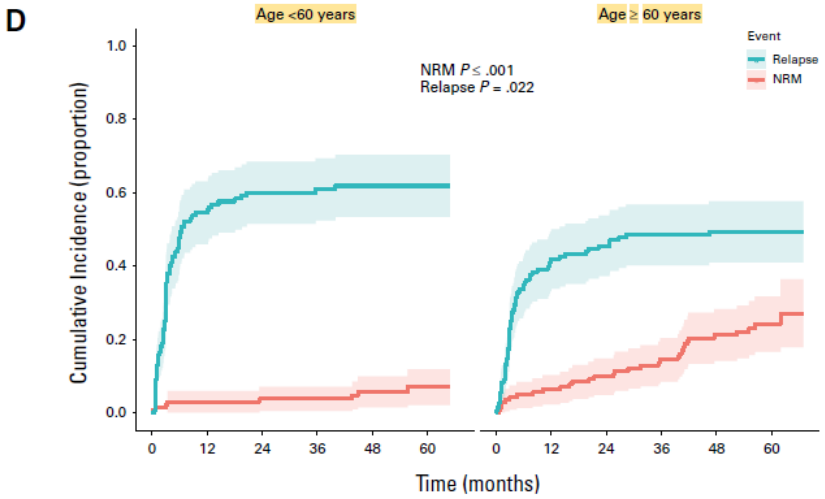




Wallace Blood 2024

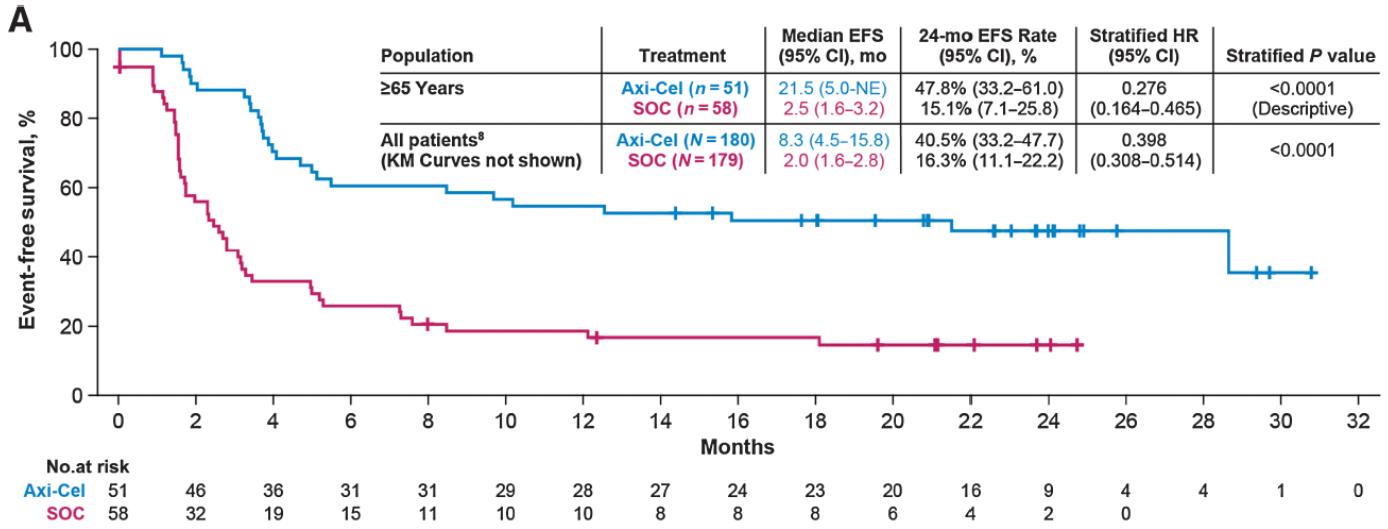
CAR-T outcome in elderly similar to younger



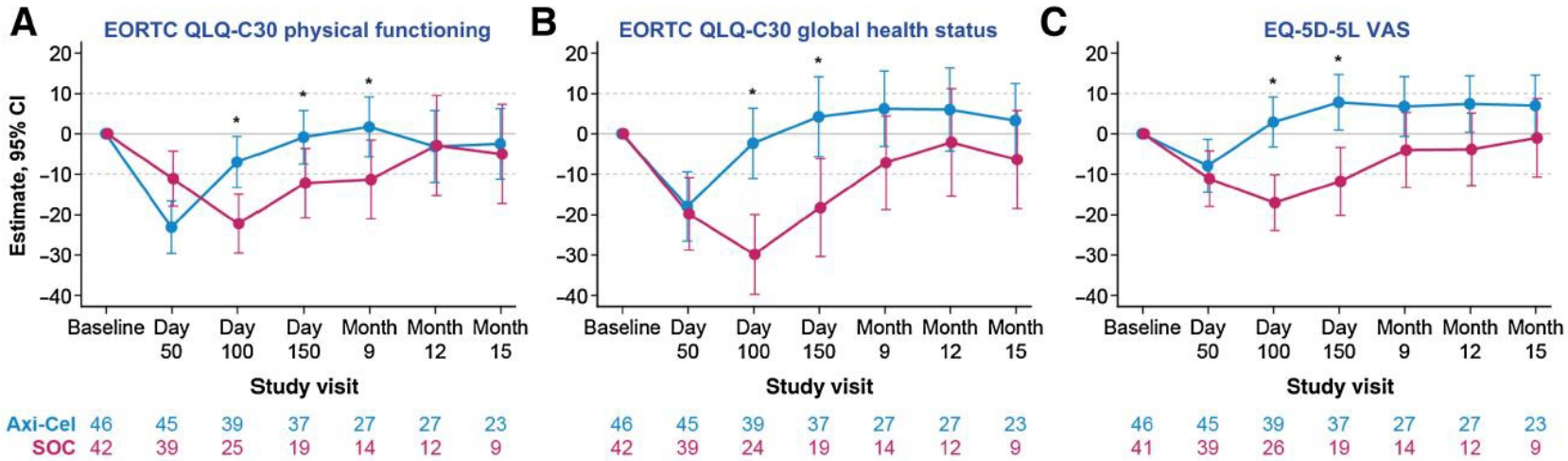


- Zuma-1, age more than 65 similar PFS and OS
- Axi-cel realworld data: similar PFS/OS. NRM 16%, higher in age >60 due to infection and SPM

Blood 2020 Neelapu et al
JCO 2024 Jain et al

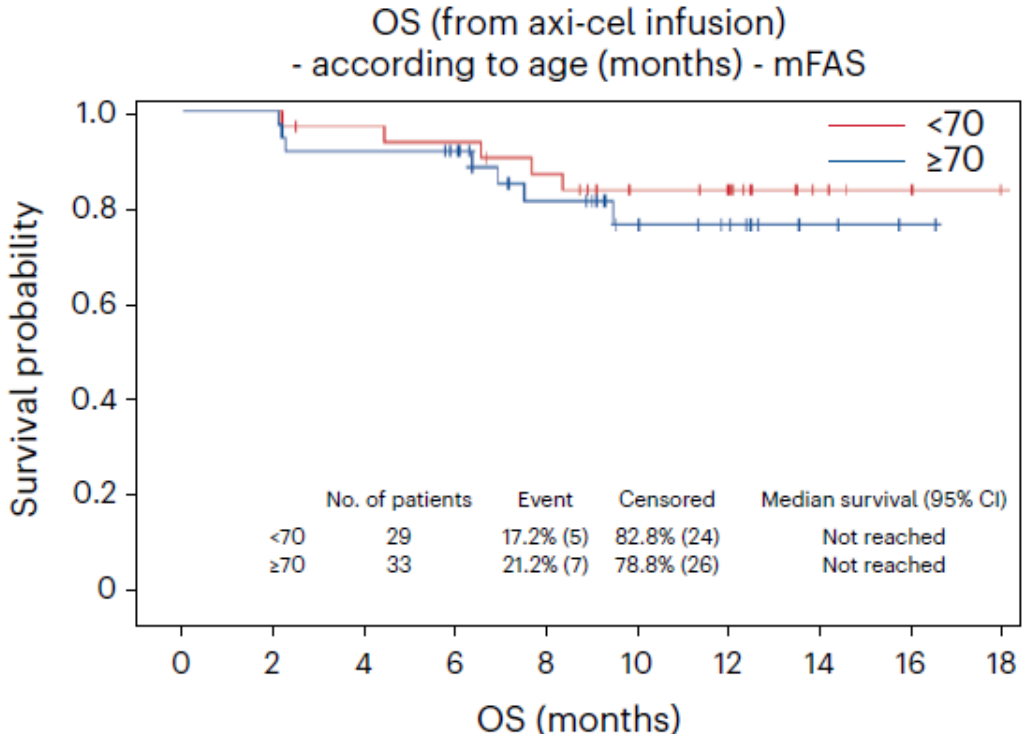


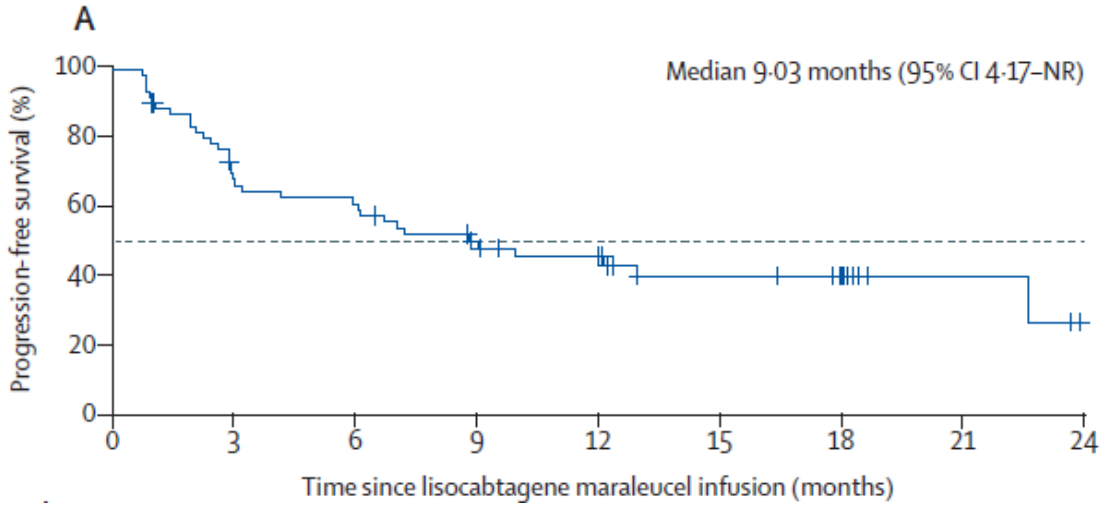
Population	Treatment	Median EFS (95% CI), mo	24-mo EFS Rate (95% CI), %	Stratified HR (95% CI)	Stratified *P* value
≥65 Years	Axi-Cel (*n* = 51)	21.5 (5.0-NE)	47.8% (33.2–61.0)	0.276 (0.164–0.465)	<0.0001 (Descriptive)
	SOC (*n* = 58)	2.5 (1.6–3.2)	15.1% (7.1–25.8)		
All patients[8] (KM Curves not shown)	Axi-Cel (*N* = 180)	8.3 (4.5–15.8)	40.5% (33.2–47.7)	0.398 (0.308–0.514)	<0.0001
	SOC (*N* = 179)	2.0 (1.6–2.8)	16.3% (11.1–22.2)		



- Zuma-7 preplanned subanalysis. Age ≥ 65 year old

Clin Cancer Res 2023 Westin et al

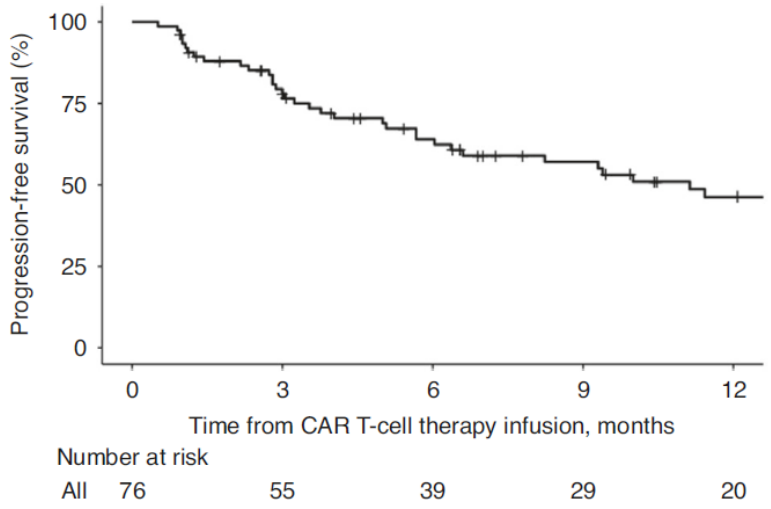


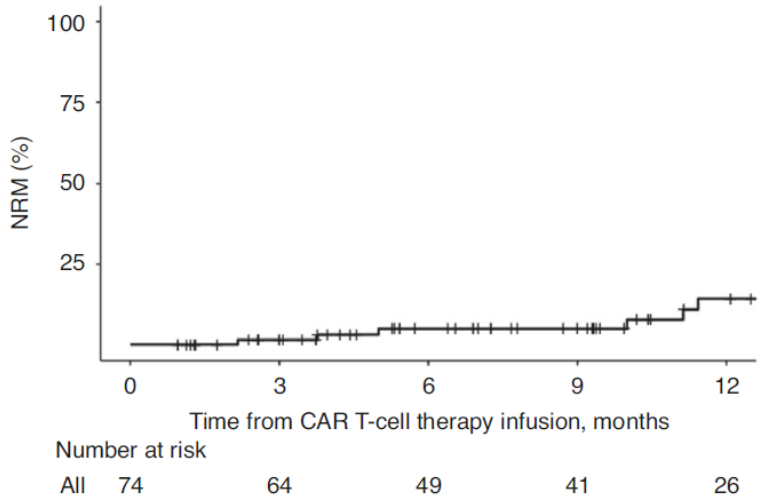


- ALYCANTE median age 70, CR 71%, mPFS 11.8, NRM 10%
- PILOT median age 74, ORR 80%, mPFS 9m, NRM 7%

Houot Nature Med 2023, Sehgal Lancet Onco 2022

CAR-T in Octogenarian





- Real world US data – median age 82
- 57% Axi-cel/Brexu-cel
- 1-yr NRM 12%, 1-yr PFS 48%

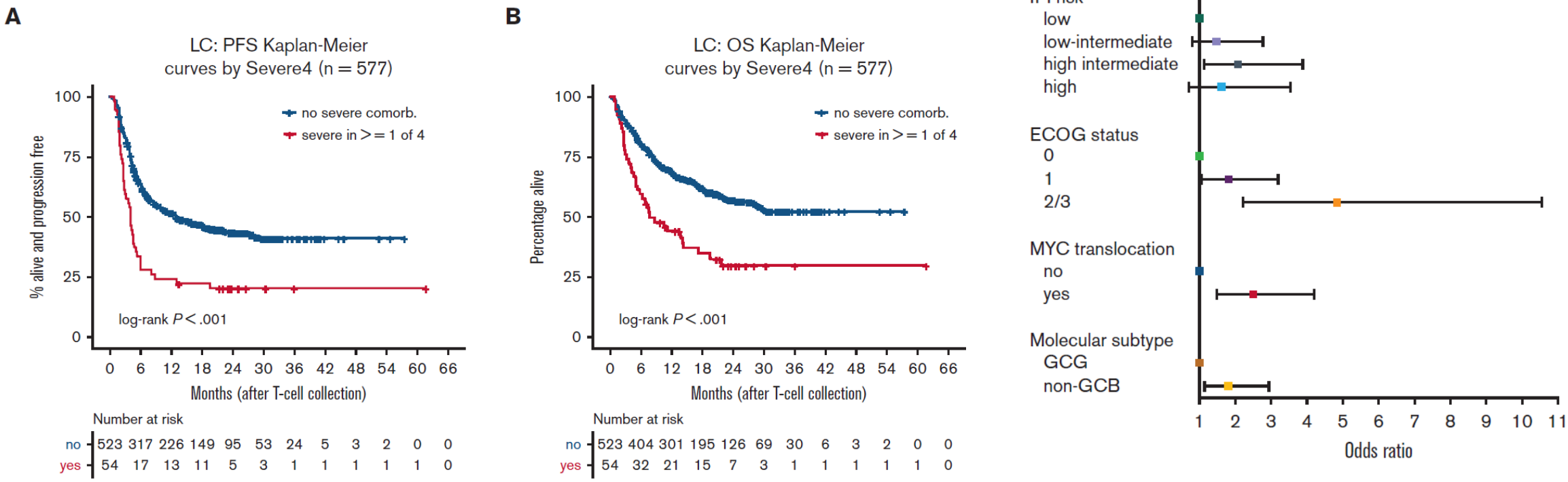
Kharfan-Dabaja BMT 2025

CAR-T and geriatric assessment

1. Real-world DLBCL, multicentric, n=577, CIRS-G above 7 confers poorer PFS (HR 1.26) and OS (HR1.35)
2. Cachexia and Sarcopenia both are associated with frailty, associated with poorer OS (3m vs 17m)
3. Weight loss within 3m of CAR-T confers poorer outcome (↓CR↓OS)

ASH 2022 Shouse, AACR 2023 Rejeski, Br J Haem 2022 Roy, Blood Adv 2024 Valtis

Severe4 score



- Severe4 identify comorbidities associated with inferior CAR-T outcome
- respiratory, upper gastrointestinal, renal, or hepatic
- CIRS ≥7 associated ICANS G3+

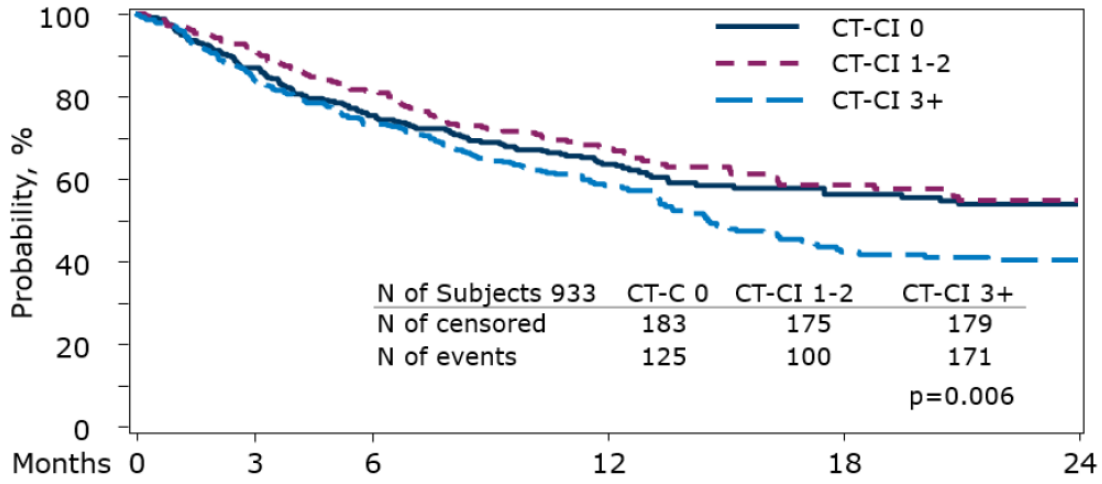
Shouse Blood Adv 2023

Cellular Therapy-comorbidity index (CT-CI)

Table 2 Comorbidities with Significant Impact on Overall Mortality, Training Cohort, and Assigned CT-CI Weighted Score

Comorbidity prior to lymphodepletion	N = 951	HR	Score
Diabetes requiring non-diet treatment, in the last 4 weeks	139	1.199	1
Cerebrovascular disease, any history	25	1.167	1
Body Mass Index < 20	70	1.387	1
Pulmonary disease, severe, at the time of infusion	116	1.277	1
Renal disease, moderate to severe, at the time of infusion; or prior renal transplant	18	1.273	1
Hepatic disease, mild, any history or at the time of infusion	80	1.48	1
Infection requiring antimicrobial treatment, continuation after day 0	32	1.945	2
Hepatic disease, moderate to severe, any history or at the time of infusion	19	3.839	3

Figure 1a. Adjusted Curves for Overall Survival by CT-CI, Training Cohort



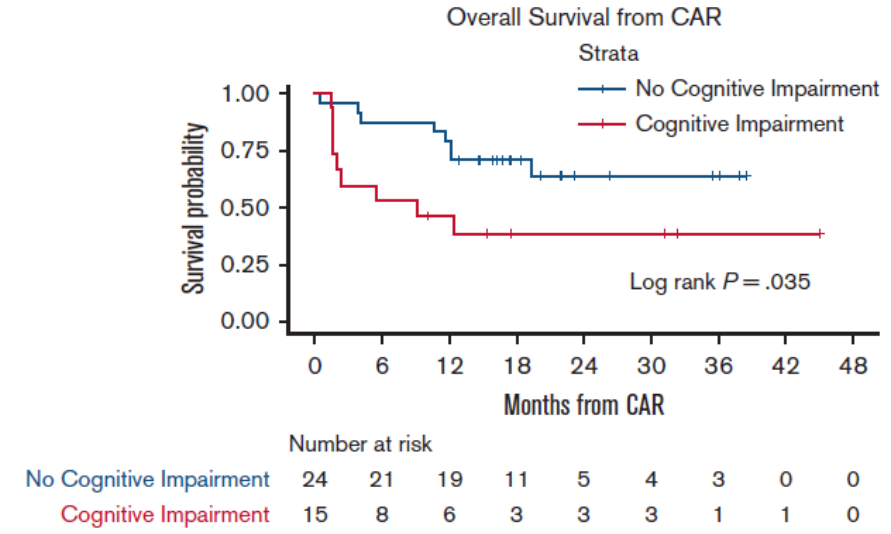
Greenbaum Blood Adv 2025

Prospective geriatric assessment and geriatric consultation in CAR T-cell therapy for older patients with lymphoma

Richard J. Lin,[1-3] Soo Jung Kim,[4] Samantha Brown,[5] Theresa A. Elko,[1,2] Josel D. Ruiz,[1] Danielle M. Hanley,[1] M. Lia Palomba,[2,3,6] Miguel-Angel Perales,[1-3] Gunjan L. Shah,[1-3] Parastoo B. Dahi,[1-3] Michael Scordo,[1-3] Craig S. Sauter,[1-3] Connie L. Batlevi,[2,3,6] Ana Alarcon Tomas,[1] Roni Shouval,[1-3] Nicole Lee,[1] Emma A. Pavkovic,[1] Danielle E. Engstler,[1] Jae H. Park,[2,3] Gilles A. Salles,[2,3,6] Sean M. Devlin,[3,5] Beatriz Korc-Grodzicki,[3,4] Paul A. Hamlin,[3,6] and Sergio A. Giralt[1-3]

- MSKCC, prospective, n=75, median age 72. GA group (64%) usual group (36%)
- LDH, Polypharmacy >5, impaired mobility affect ICANS
- Cognition impairment affect CRS and OS
- CRS and ICANS lower in GA group (OR 2.75)
- Hospital stay, re-adm, PFS and OS similar in both groups

B



Lin Blood Adv 2023

REGULAR ARTICLE

blood advances

Optimization of older adults by a geriatric assessment–guided multidisciplinary clinic before CAR T-cell therapy

Samuel J. Yates,[1] John F. Cursio,[2] Andrew Artz,[3] Keriann Kordas,[1] Michael R. Bishop,[1,4] Benjamin A. Derman,[1] Satyajit Kosuri,[1] Peter A. Riedell,[1] Justin Kline,[1] Andrzej Jakubowiak,[1] Mylove Mortel,[1] Shalitha Johnson,[1] and Mariam T. Nawas[1]

- Prospective, single center, n=61, GA-MDC, median age 73
- MDC recommends patient and treatment optimization
- Non-binding suitability provided: Proceed/Defer/Decline
- DLBCL n=35, MM n=14
- MM patients had higher geri-vulnerabilities index (with more prior line)

Yates Blood Adv 2024

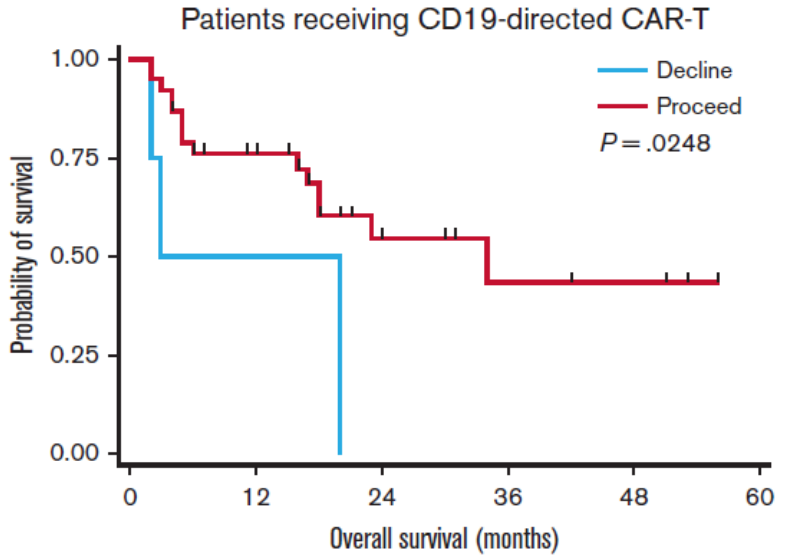
- NRM – 1-yr 8%, 2-yr 11%
- GA factors: 6min walk (more re-admission) and iADL (higher ICANS)
- MVA adjusted with LDH, CRP, KPS: GA-MDC remained prognostic for OS (HR3.26)

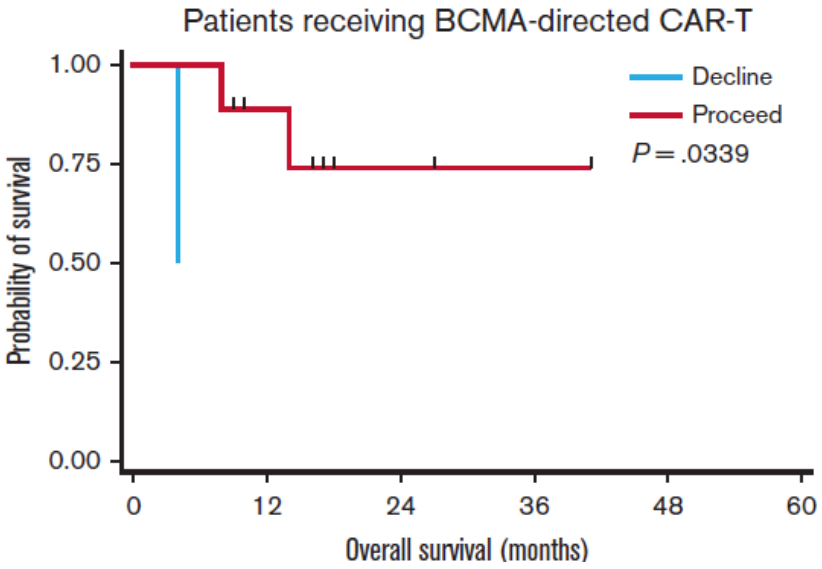
- 6 patient who received CAR-T against GA-MDC

- 5 had NRM, mOS 296 days

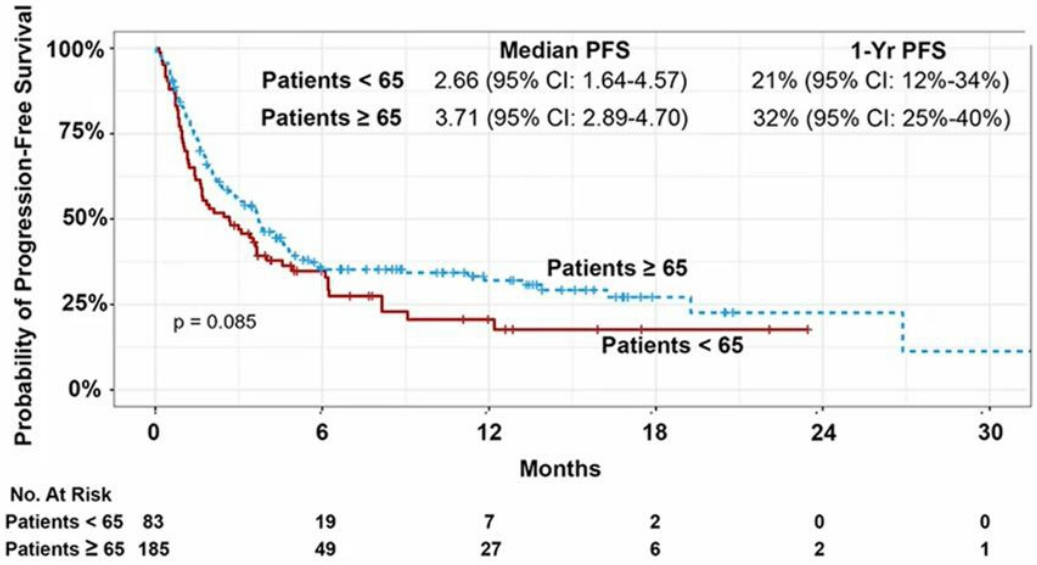
- 4 patients who did not received Car-T after follow GA-MDC

- All died with mOS 93 days (?consider bispecific Ab)

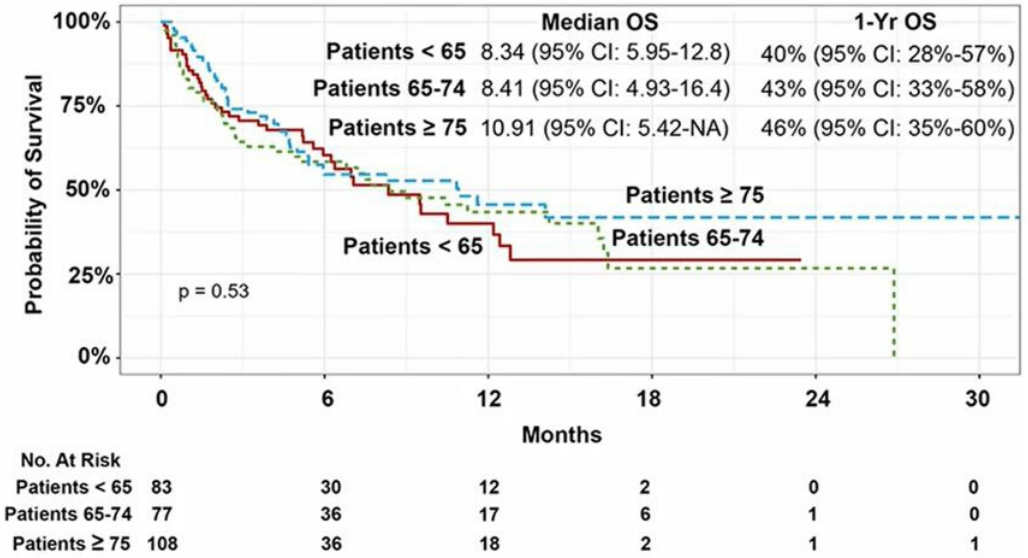




Progression Free Survival



Overall Survival



- Age does not limit the PFS and OS in CD3xCD20 bispecific antibodies

ICML 2025 Thiruvengadam

Older Adult of Classical Hodgkin Lymphoma

- Anthracycline eligible
- Anthracycline ineligible
- Frail – non-chemotherapy eligible

Geriatric Assessment Remained Important

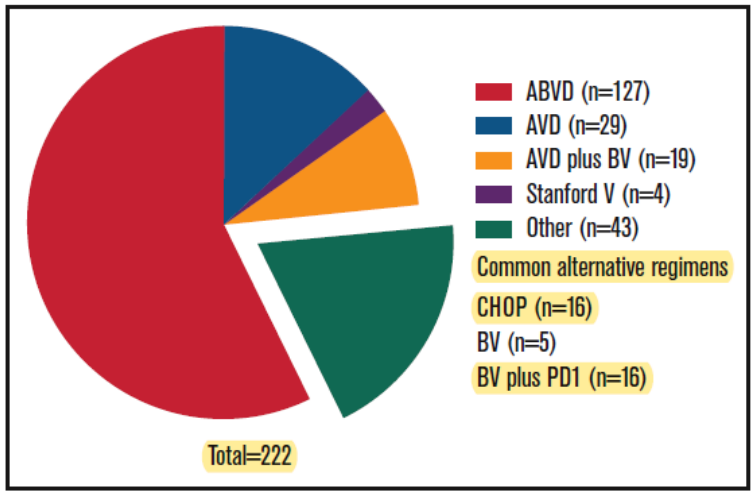
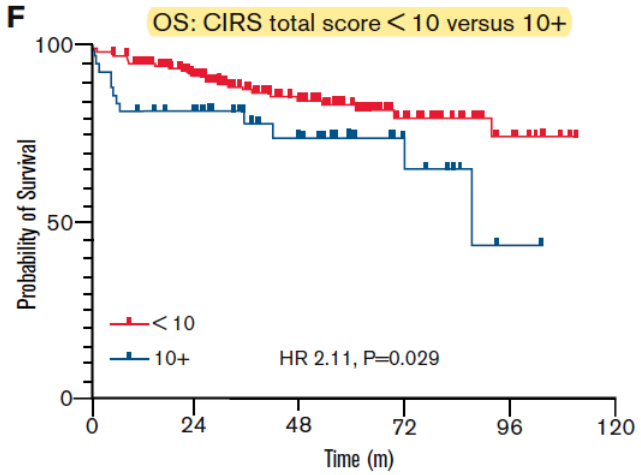
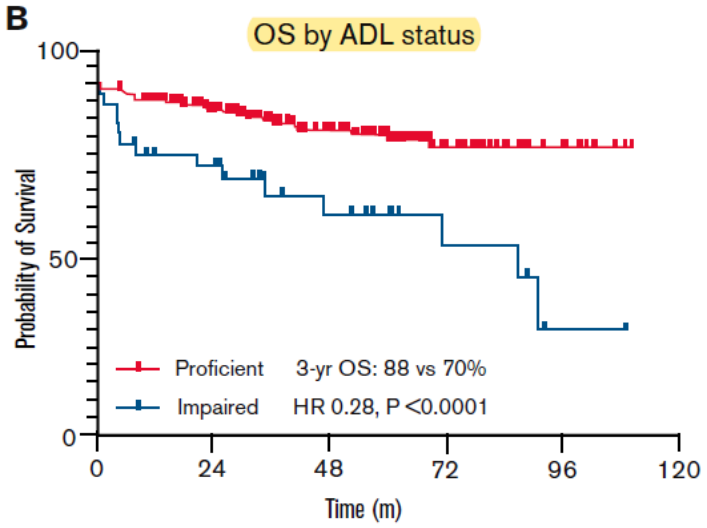
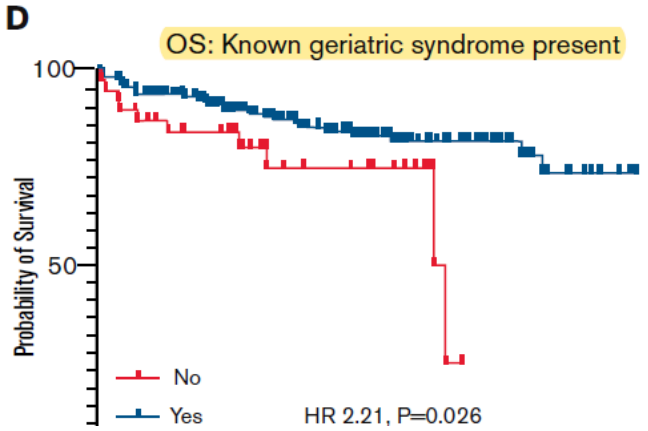


Figure 1. Frontline treatment regimens for stage II to IV disease. Common alternative regimens enumerated in figure; regimens used for less than 5 patients are not listed.







- Geriatric syndrome defined as: Depression, Delirium, Dementia, Osteoporosis, Incontinence, Falls, Failure to thrive, Neglect abuse
- 18% had bleomycin pulmonary toxicity
- TRM 3.3%

Orellana-Noia Blood Adv 2021

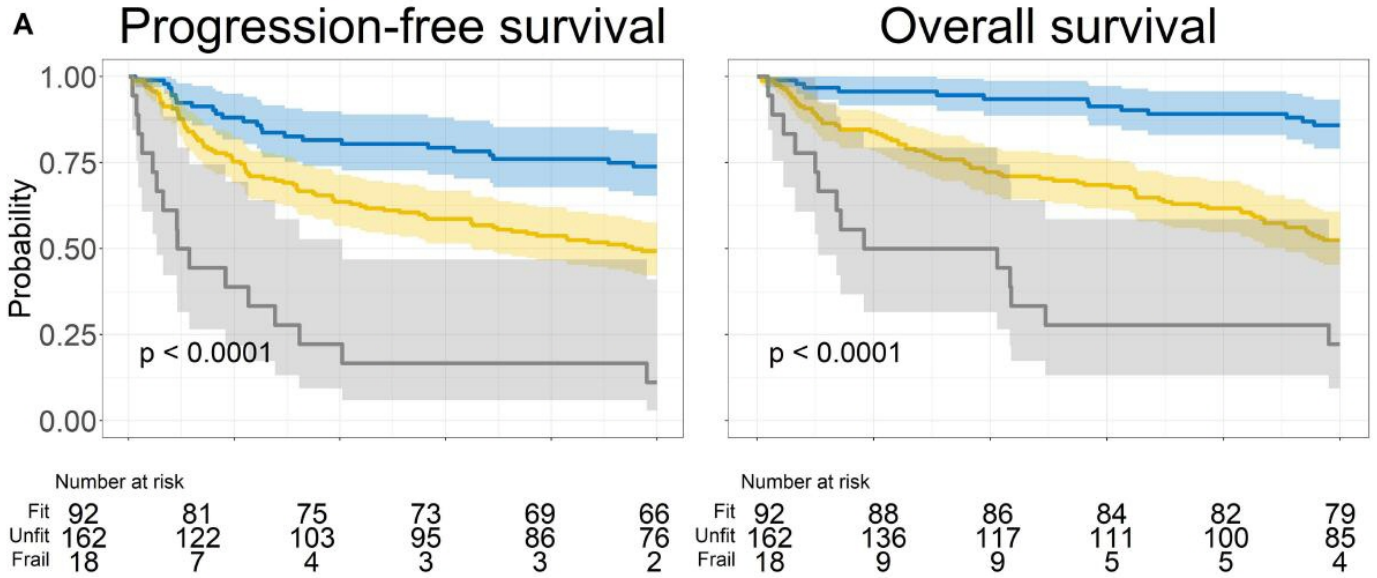
Simplified Frailty Score

Frailty score	Frailty group (n)	5-year progression-free survival		5-year overall survival	
		univariate analysis		univariate analysis	
		HR (95% CI)	*p*	HR (95% CI)	*p*
0	Fit (92)	ref		ref	
1-2	Unfit (162)	2.3 (1.5-3.6)	**<0.001**	4.2 (2.3-7.6)	**<0.001**
3	Frail (18)	7.9 (4.2-14.9)	**<0.001**	10.8 (5.0-23.0)	**<0.001**

Supplementary Table S6: Construction of a geriatric frailty index in the Norwegian training cohort

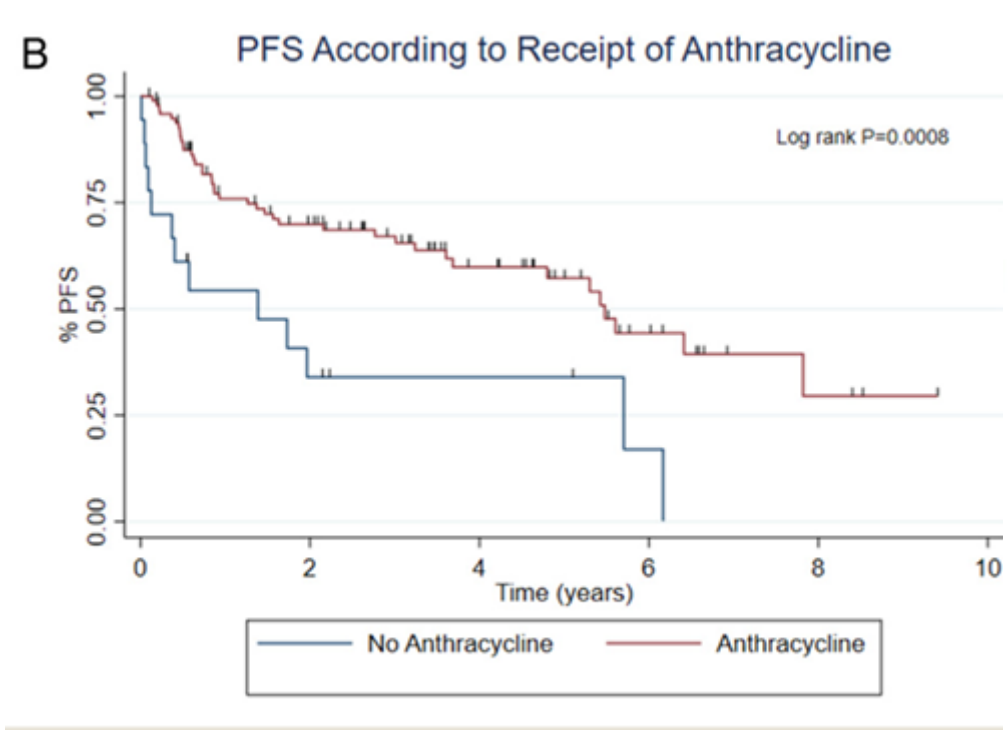
Independent variables predicting PFS	HR from multivariable analysis (95% CI)	*p*	Score in frailty index
Age at diagnosis/years			
< 70	ref		0
≥ 70	1.7 (1.1-2.5)	**0.012**	1
ECOG PS			
0-1	ref		0
≥ 2	1.6 (1.0-2.5)	**0.037**	1
CIRS-G			
< 8	ref		0
≥ 8	1.7 (1.2-2.5)	**0.007**	1

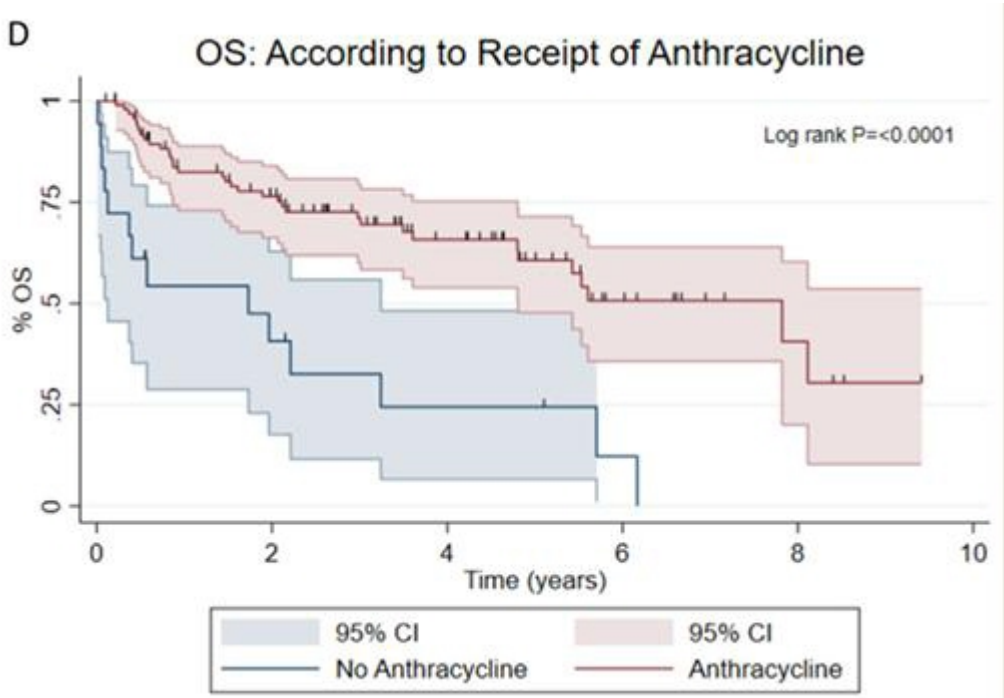
- Norwegian population based registry cohort. (n=279)
- All anthracycline (at least 50%) containing regimen
- Fit and Unfit group benefited from anthracycline intensity (≥80%) but not Frail group



Hematologica 2025 Lia et al

Role of anthracycline

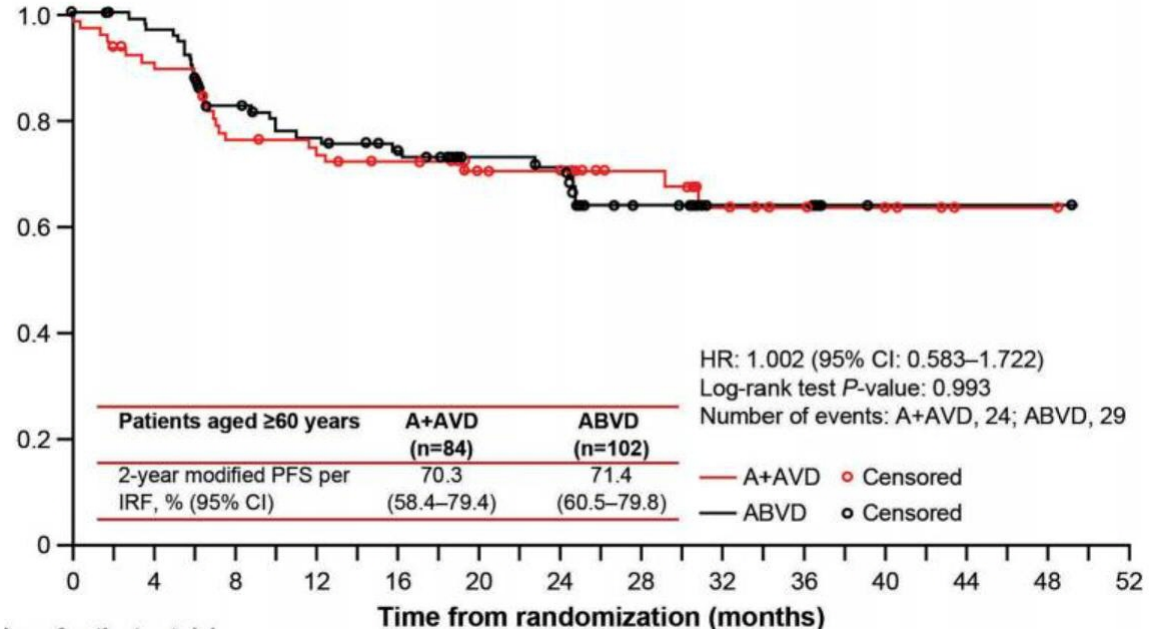




- cHL registry, 2011-2020, n=196, median age 72 years
- Improve survival with anthracycline

Goh Clin Lymph Myeloma Leuk 2023

ECHELON-1



Patients aged ≥60 years	A+AVD (n=84)	ABVD (n=102)
2-year modified PFS per IRF, % (95% CI)	70.3 (58.4–79.4)	71.4 (60.5–79.8)

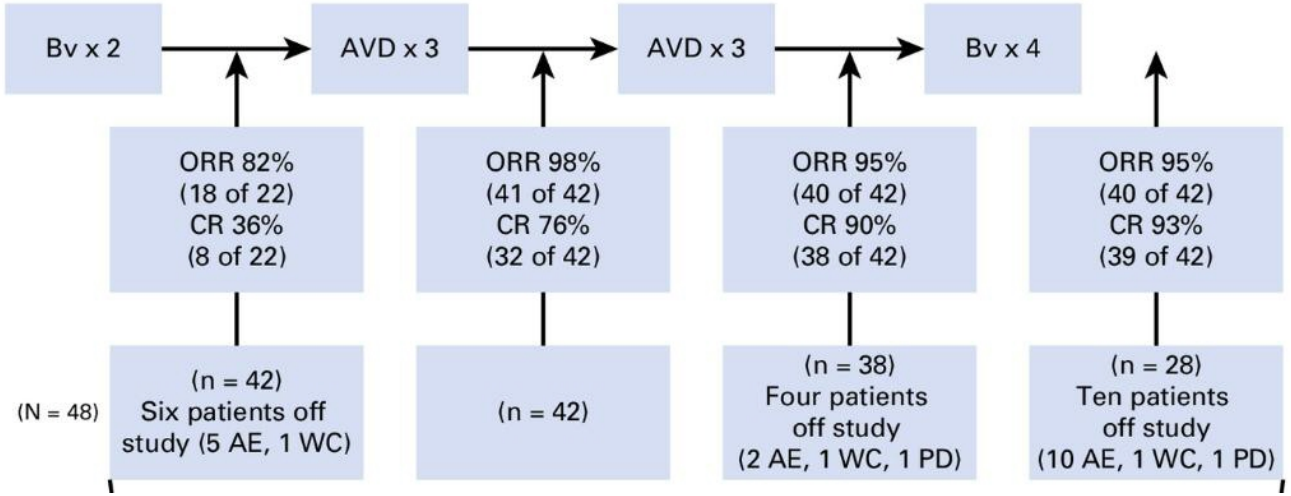
- Patients ≥ 60 years was not superior on BV-AVD
- 80% of older patients required one or more dose modification of brentuximab vedotin

Table 3. Safety summary.

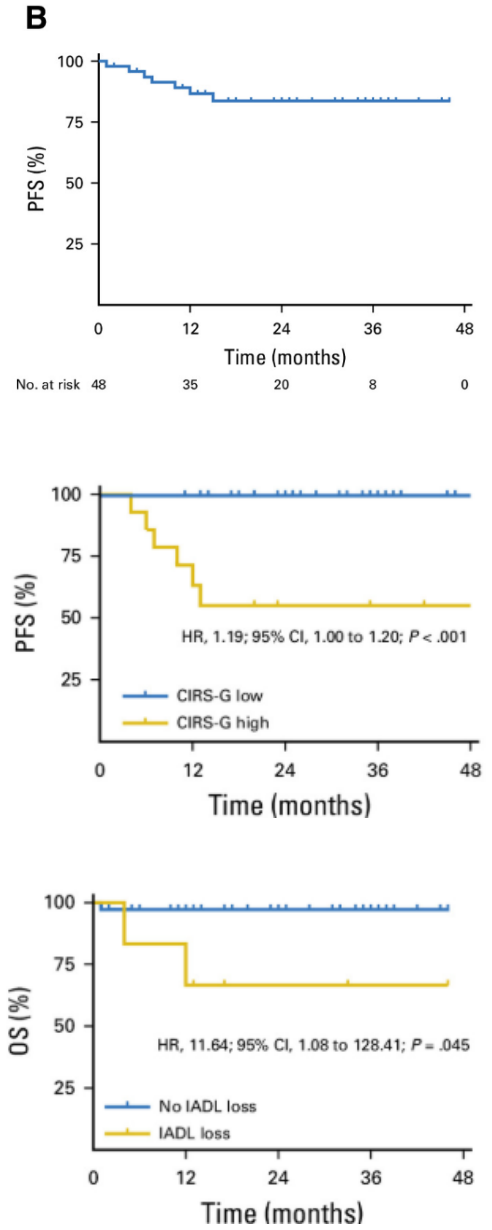
	Patients aged ≥60 years evaluable for safety* (n=181)		Patients aged <60 years evaluable for safety* (n=1,140)		Safety population*,38 (n=1,321)	
	A+AVD (n=83)	ABVD (n=98)	A+AVD (n=579)	ABVD (n=561)	A+AVD (n=662)	ABVD (n=659)
Grade ≥3 AE, n (%)	73 (88)	78 (80)	476 (82)	356 (63)	549 (83)	434 (66)
On-study deaths,† n (%)	3 (4)	5 (5)	6 (1)	8 (1)	9 (1)	13 (2)
Grade ≥3 neutropenia,‡ n (%)	58 (70)	58 (59)	372 (64)	259 (46)	430 (65)	317 (48)
Any-grade FN on study, n (%)	31 (37)	17 (17)	97 (17)	35 (6)	128 (19)	52 (8)
Any-grade pulmonary AE, n (%)	2 (2)	13 (13)	10 (2)	31 (6)	12 (2)	44 (7)

Evens Hematologica 2022

Sequential BV-AVD approach

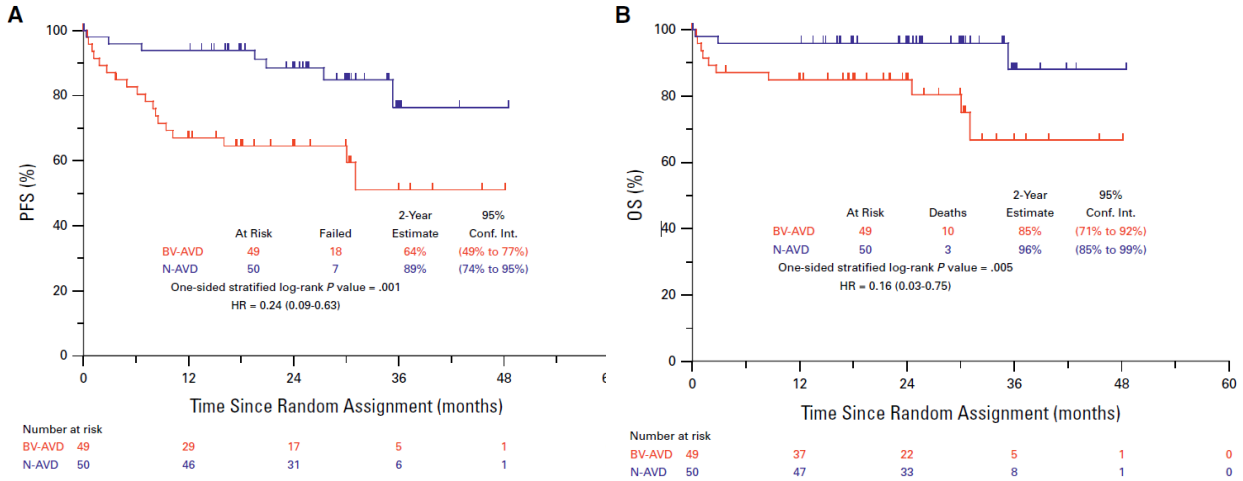


- More favourable toxicity profile
- 2-year PFS 84%
- High CIRS-G and IADL loss do poorer



Evens JCO 2018

Nivo-AVD in older adult



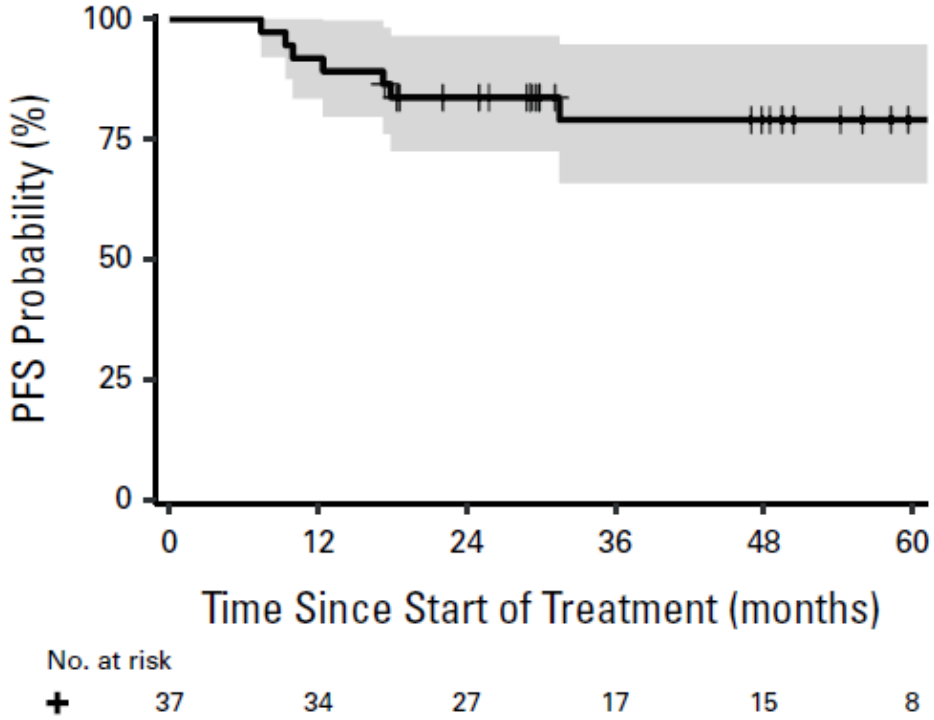


Table: Key Adverse Events by Treatment Arm (Any Grade and Grade ≥3).

	N-AVD (N=48)	Bv-AVD (N=47)		N-AVD (N=48)	Bv-AVD (N=47)	
Adverse Event	Any Grade	Any Grade	p-value[3]	Grade ≥3	Grade ≥3	p-value[3]
Febrile neutropenia	6 (13%)	9 (19%)	0.42	6 (13%)	9 (19%)	0.42
Sepsis	3 (6%)	10 (21%)	0.04	3 (6%)	10 (21%)	0.04
Infections and infestations	9 (19%)	16 (34%)	0.11	3 (6%)	10 (21%)	0.04
Peripheral sensory neuropathy[1]	15 (31%)	31 (66%)	0.001	1 (2%)	5 (11%)	0.11
Peripheral motor neuropathy[2]	4 (8%)	7 (15%)	0.36	0 (0%)	1 (2%)	0.49

- S1826: Nivo-AVD is better efficacy (PFS and OS) and tolerable, less dose reduction/discontinuation
- Phase 1/2 Nivo-AVD well tolerated in highly impaired geriatric population - Median age 66, 82% ADL dependent, 50% high TUG, 40% polypharmacy

Rutherford JCO 2025, Herrera NEJM 2024, Torka JCO 2024

BrECADD in older adult (HD21) – phase 2 single arm

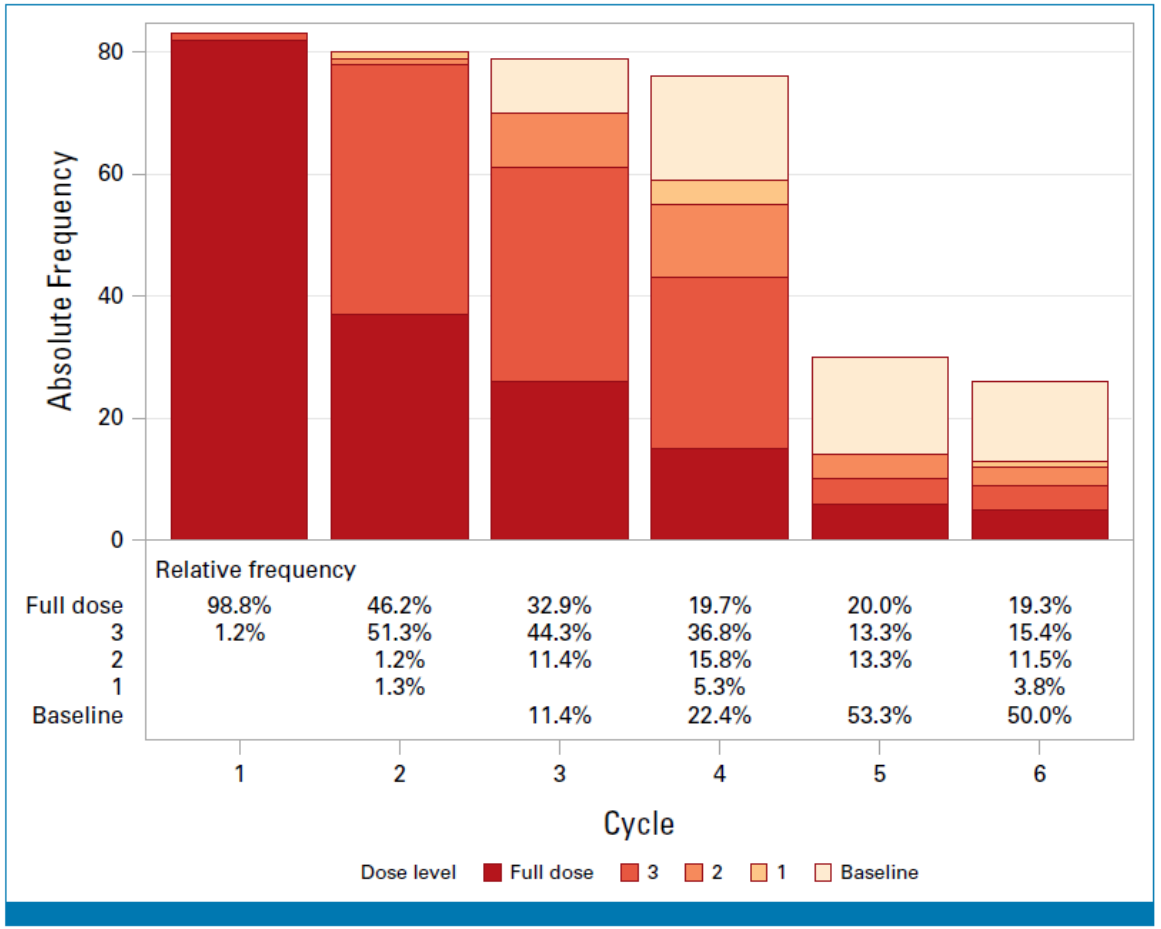


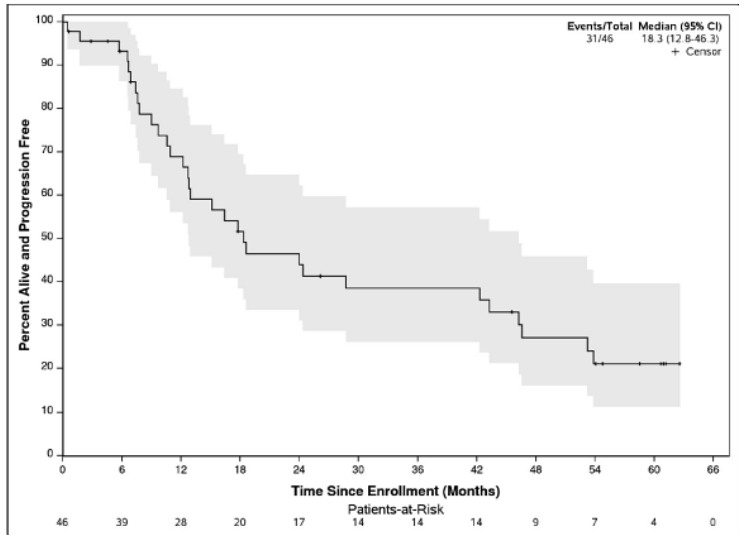
FIG 3. BrECADD dose levels according to cycle. BrECADD, brentuximab vedotin, etoposide, cyclophosphamide, doxorubicin, dacarbazine, and dexamethasone.

CIRS-G sum score	
Mean (SD)	3.7 (2.7)
Median (range)	3 (0-10)
Frailty Index,[a] No. (%)	
0 (fit)	43 (52)
1-2 (unfit)	38 (46)
3 (frail)	2 (2)

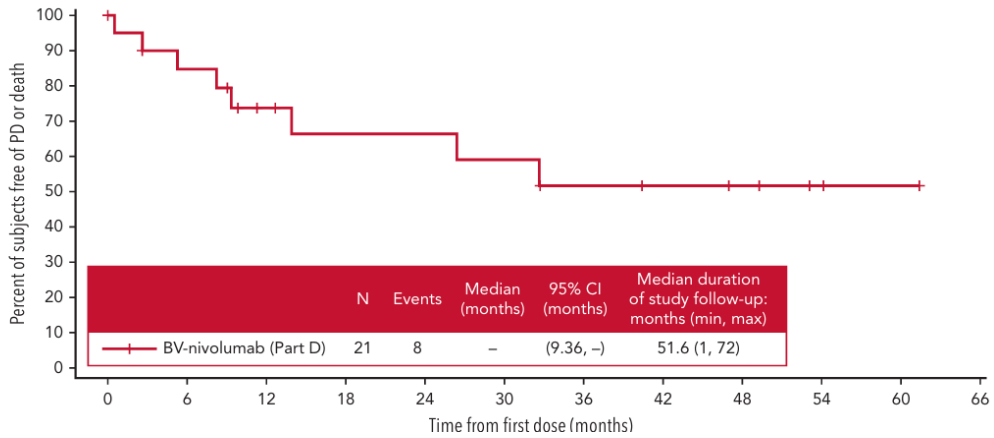
- 83 patients, median age 67 year old (61-75), fitter cohort
- 55% febrile neutropenia
- 2-year PFS/OS 92%
- Dose reduction is very common

Ferdinandus JCO 2025

Non-anthracycline fit



B



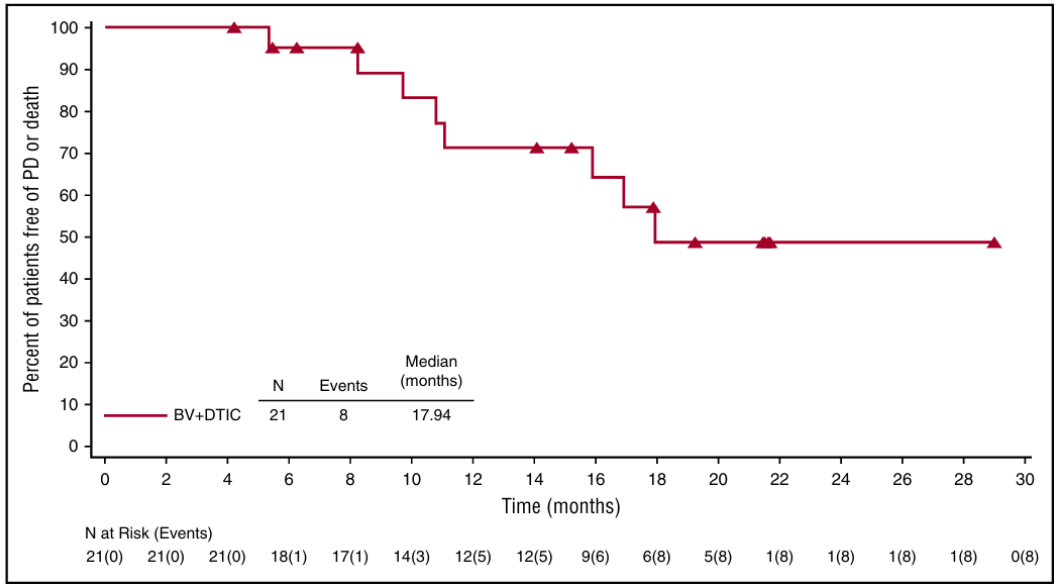


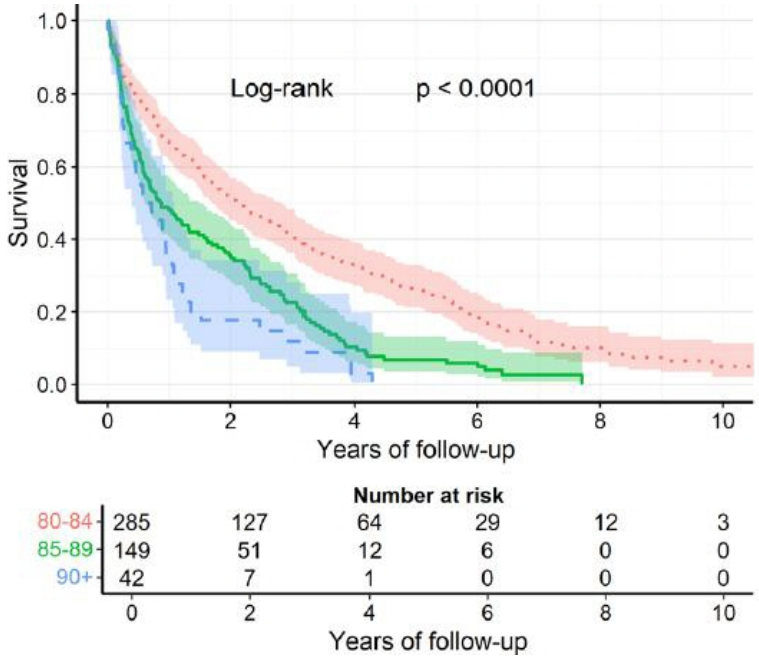
Table 4. Summary of AEs

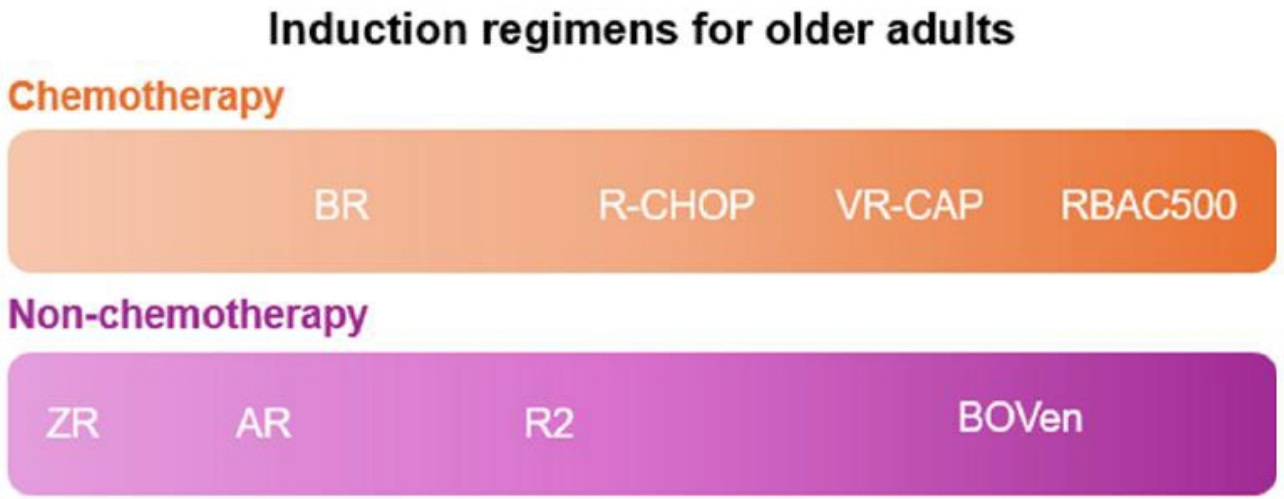
	BV+DTIC (n = 22)	BV+bendamustine (n = 20)
Any TEAE*	22 (100)	20 (100)
Treatment-related AEs	22 (100)	19 (95)
Grade ≥3 AEs	10 (45)	18 (90)
SAEs	4 (18)	13 (65)
AEs leading to treatment discontinuation	12 (55)	12 (60)
Deaths within 30 d of last dose	0	2 (10)†

- 8 cycles of BV-Nivo: not durable on long-term follow up. Median PFS 18 months
- BV-dacarbazine has acceptable efficacy and toxicity. BV-benda is too toxic

Friedberg Blood 2017, Friedberg Blood 2024, Cheson Blood Adv 2025

Older adult with Mantle Cell Lymphoma

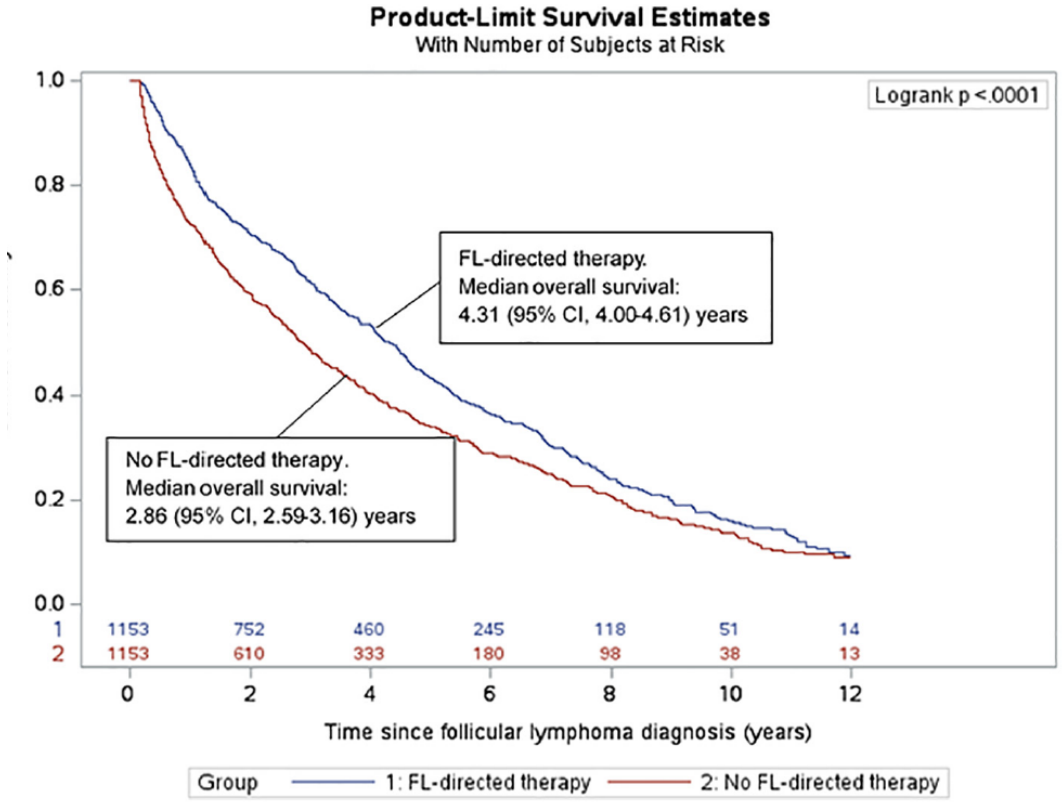




- Consider BR for now
- R-Acalabrutinib/R-Zanubrutinib are promising to avoid chemotherapy.

Pahnke BCJ 2025, Munoz Leuk Lymphoma 2024

Older adult with Follicular Lymphoma



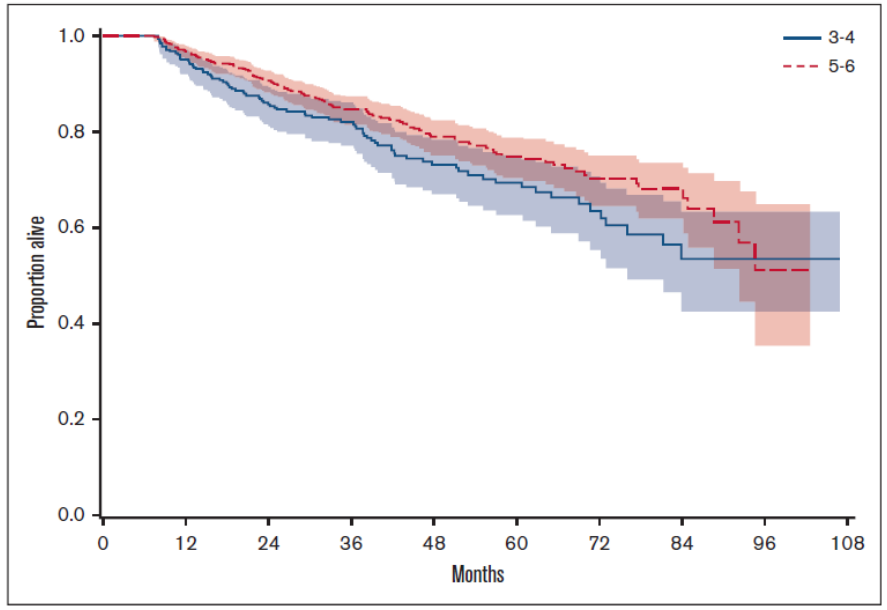
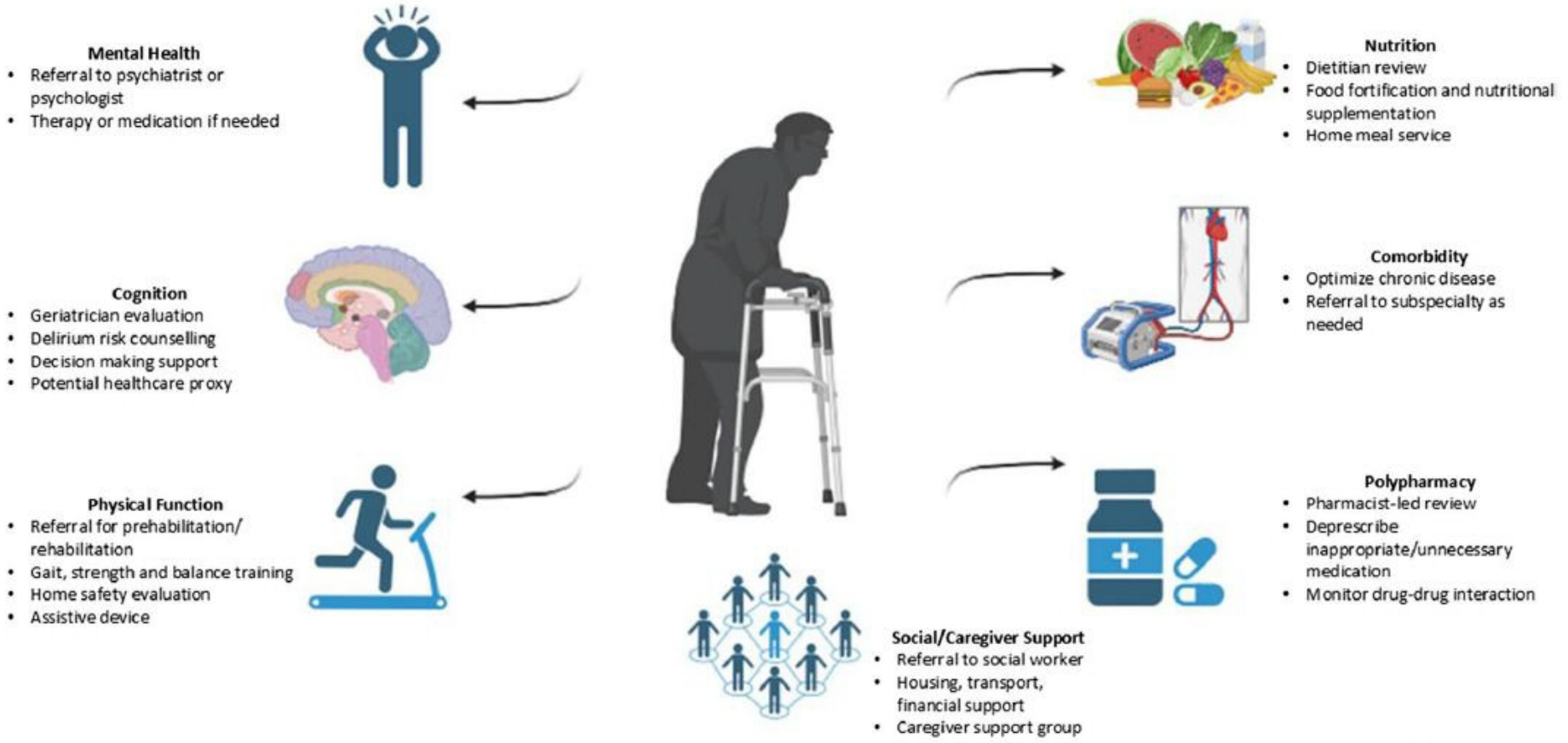


Figure 2. Overall survival by number of cycles.

- Consider treatment even in those advance age (80s) – single rituximab+/- len or low dose BR
- Optimal BR cycles in elderly (median age 75)

Albarmawi JGO 2020, Strouse Blood Neo 2024



- Multi-dimensional approach to support older adults with lymphoma
- Geriatric assessment – allow targeted intervention
- Seems a lot of effort (can do simple one) but it is meaningful because lymphoma is “SO TREATABLE”

L Ng et al Curr Treatment Options Oncol 2025