23rd INTERNATIONAL ULTMANN CHICAGO LYMPHOMA

Can Follicular Lymphoma Be Cured?

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DISCLOSURES

Consulting: BMS, Kite Pharma, Roche/Genentech, Incyte, Abbvie, AstraZeneca, BeOne, Pfizer, Galapagos, Genmab, Ipsen, Ascentage, Janssen, Lava Therapeutics, ADC Therapeutics

Research funding: Roche/Genentech, Abbvie, AstraZeneca, BMS

Case Presentation

52 y/o F with Stage III Follicular lymphoma grade 1-2 (diagnosis: 4/2005)

FLIPI unknown

First line therapy: R-CVP x 6 cycles (completed 9/2005)

Response: Complete response

4/2024: Had CT scan Chest in for pleuritic chest pain, PE ruled out, no LAD

8/2025: Had CT scan A/P for abdominal pain: showed diverticulitis but no LAD

Recent follow up: 2/2026, no clinical signs or symptoms of relapse. CBC, CMP, LDH normal

Is she cured?

What is considered as a cure in Follicular Lymphoma?

- Permanent eradication of disease
- No relapse over a lifetime, without ongoing therapy

What about functional cure?

- Evidence of disease but no clinical relapse during lifetime
- Cause of death unrelated to follicular lymphoma

Evidence of long-term remission in 1L Follicular Lymphoma?

SAKK 35/03

Design

- Symptomatic FL Grades 1-3
- Rituximab weekly x 4 followed by:
  - Short maint: 4 course q 2 months
  - Prolonged maint: q2 months for 5 years

Outcomes

	Treatment-naive patients in need of therapy			
End point	All (N = 97)	Short maintenance (n = 46)	Long maintenance (n = 51)	*P**
EFS				
Median (95% CI), y	5.1 (3.1-7.4)	5.5 (2.1-9.8)	5.0 (2.6-NA)	.924
10-y (95% CI), %	36.3 (26.2-46.5)	34.2 (19.1-49.9)	38.8 (25.5-51.9)	.608
PFS				
Median (95% CI), y	7.4 (4.6-NA)	6.6 (2.1-NA)	7.4 (4.0-NA)	.739
10-y (95% CI), %	42.5.0 (31.4-53.3)	43.9 (27.2-59.3)	42.0 (27.2-56.1)	.869
OS				
Median (95% CI), y	11.0 (NA)	11.0 (NA)	Not reached (NA)	.521
10-y (95% CI), %	83.2 (73.6-89.5)	80.7 (65.0-89.9)	85.3 (71.6-92.7)	.567

Moccia AA et al, Blood Advances 2020, 23:5951-5957

Evidence of long-term remission in 1L Follicular Lymphoma?

PRIMA

Outcome (median f/u: 9 y)	R-CHOP + R maint (2y)
Median PFS	10.5 y
Median TTNLT	NR
Median TTNCT	NR
Median OS	NR

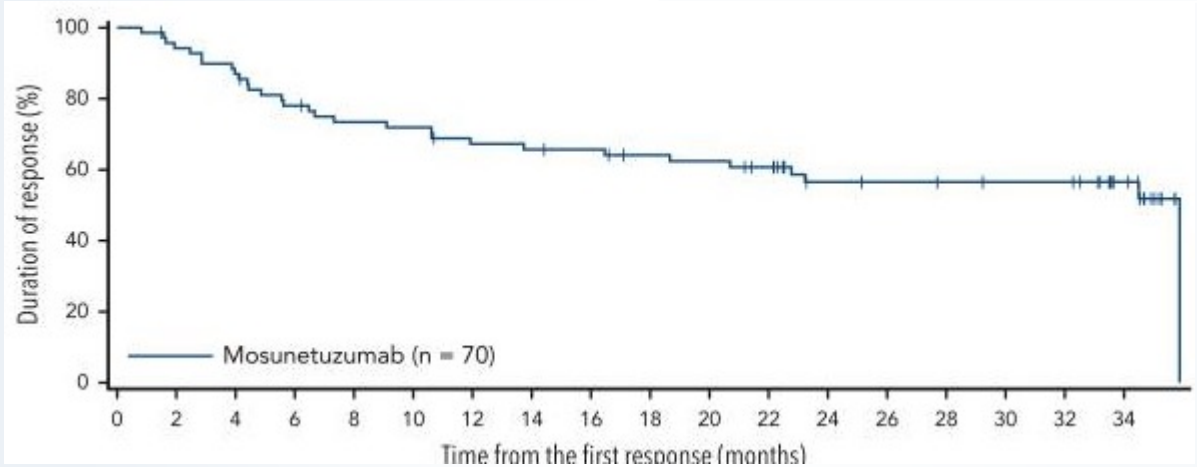
Bachy E et al, JCO 2019, 37: 2815-2824

Evidence of long-term remission in R/R Follicular Lymphoma?

Mosunetuzumab

Characteristic	Incidence
Median prior lines Rx	3 (2-10)
Refractory to prior Rx	69%
POD 24	52%

Outcome (median f/u: 3.1 y)	
Median PFS	24 mo
Median DOR	36 mo
Median DOCR	NR
Median OS	NR



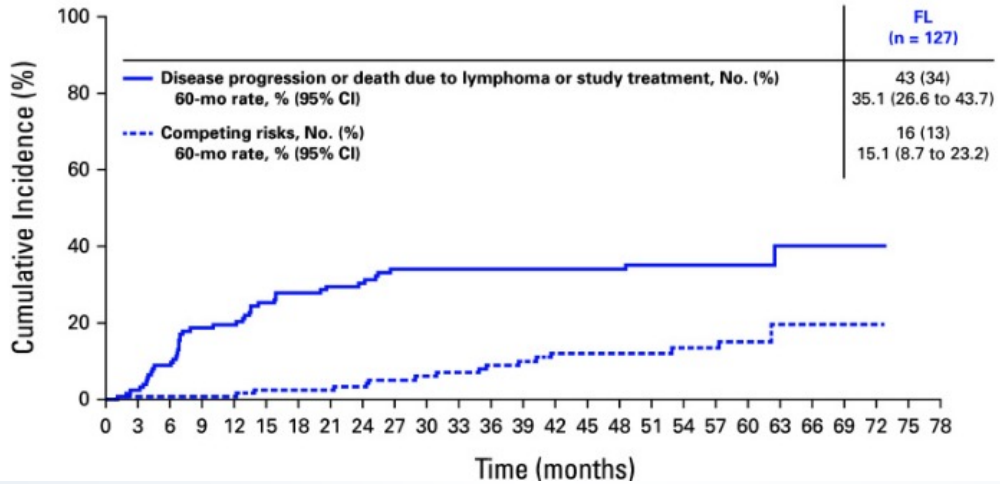
Sehn L et al, Blood 2025, 145(7): 708-719

Evidence of long-term remission in R/R Follicular Lymphoma?

ZUMA 5

Characteristic	Incidence
Median prior lines Rx	3 (1-10)
Refractory to prior Rx	69%
POD 24	56%

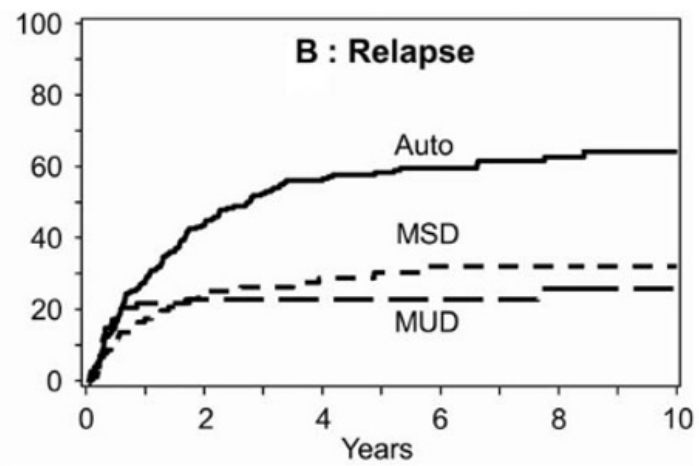
Outcome (median f/u: 5.5 y)	Axicel
Median PFS	57.3 mo
Cumulative incidence of progression	34%
Median lymphoma specific PFS	NR
Median OS	NR



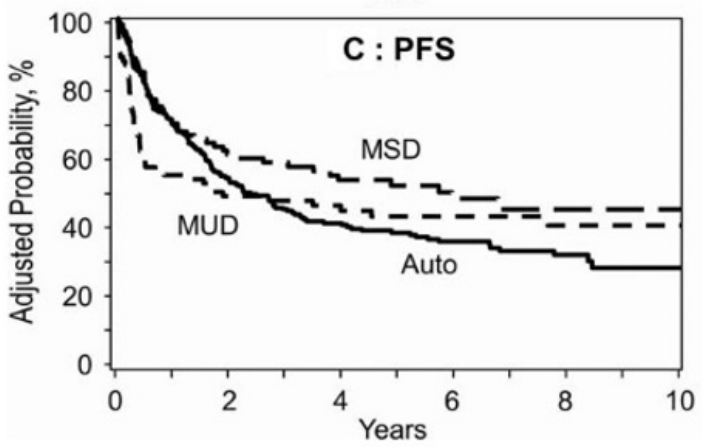
Neelapu S et al, JCO 2025, 43(33): 3573-3577

Evidence of long-term remission in R/R Follicular Lymphoma?

Allogeneic Transplant



The adjusted probability of relapse/progression at 5 years was 31% with MSD and 23% with MUD allo-HCT



The adjusted probabilities of PFS at 5 years for MSD, and MUD cohorts were 52%, and 43%, respectively

Smith S et al, Cancer 2018, 124(12): 2541-2551

Understanding Cure Model

The Concept

A statistical method to estimate what percentage of patients are truly "cured" (not just in long remission) without waiting indefinitely for relapses

How It Works

Compares observed death rates in trial patients vs. expected death rates in general population (from U.S. life tables)

Accounts for background mortality from non-lymphoma causes (heart disease, aging, accidents)

Identifies patients whose survival matches the general population = statistically "cured"

The Mathematical Logic

If we subtract deaths expected from normal aging and other diseases, what percentage of patients have the same death rate as people without lymphoma?

Key Assumptions

Two distinct patient populations exist:

"Cured" patients: Survival follows normal population patterns (lymphoma no longer affects survival)

“Not cured" patients: Remain at risk of lymphoma-related death

SWOG S0016 Trial

Untreated Advanced Stage FL

CHOP x 6 + Rituximab	CHOP x 6 + ^{131}I-Tositumomab

Stratification Factor: β2M Level (Elevated or Not)

- Primary Endpoint: PFS
- No maintenance therapy was used in this study

Shadman, M JAMA Oncology 2026(online)

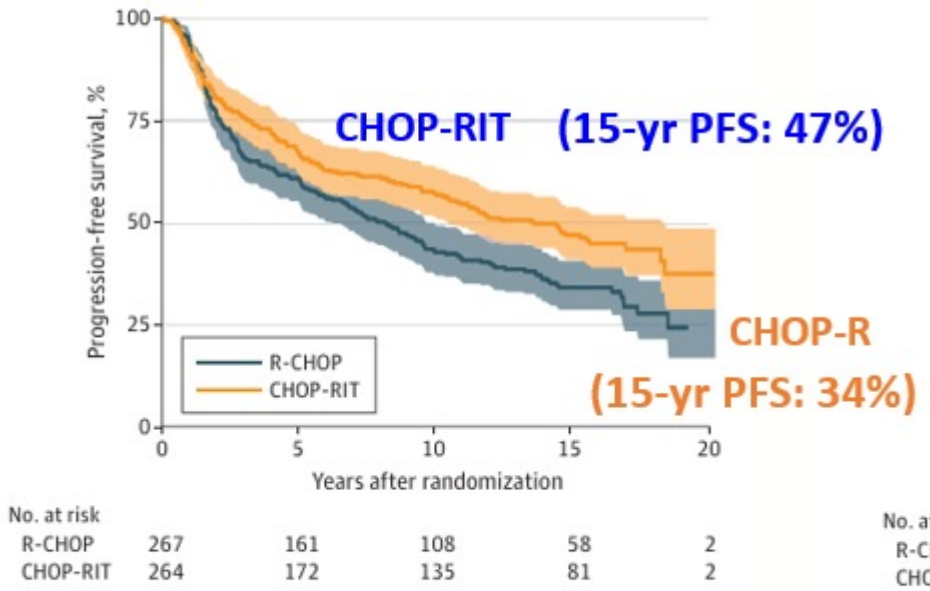
Patient Characteristics

		CHOP-R	CHOP-RIT
Age (Median)		54.5 yr	53.4 yr
Gender (Male)		53%	56%
Race (White)		90%	90%
Elevated β2M		53%	55%
B Symptoms		29%	26%
Bulk (> 10 cm)		24%	26%
BM Involvement		56%	55%
Grade 3		8%	9%
Stage	II	4%	2%
	III	37%	35%
	IV	59%	63%
FLIPI Risk	Low	30%	30%
	Int.	47%	44%
	High	22%	26%

Shadman, M JAMA Oncology 2026(online)

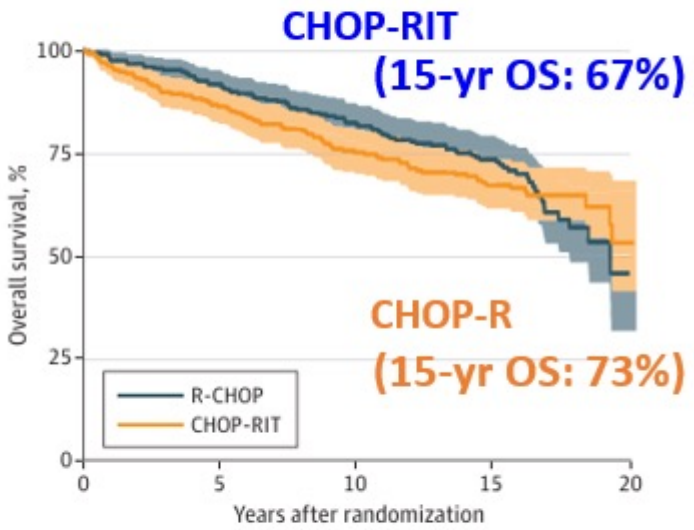
PFS and OS

PFS



No. at risk					
R-CHOP	267	161	108	58	2
CHOP-RIT	264	172	135	81	2

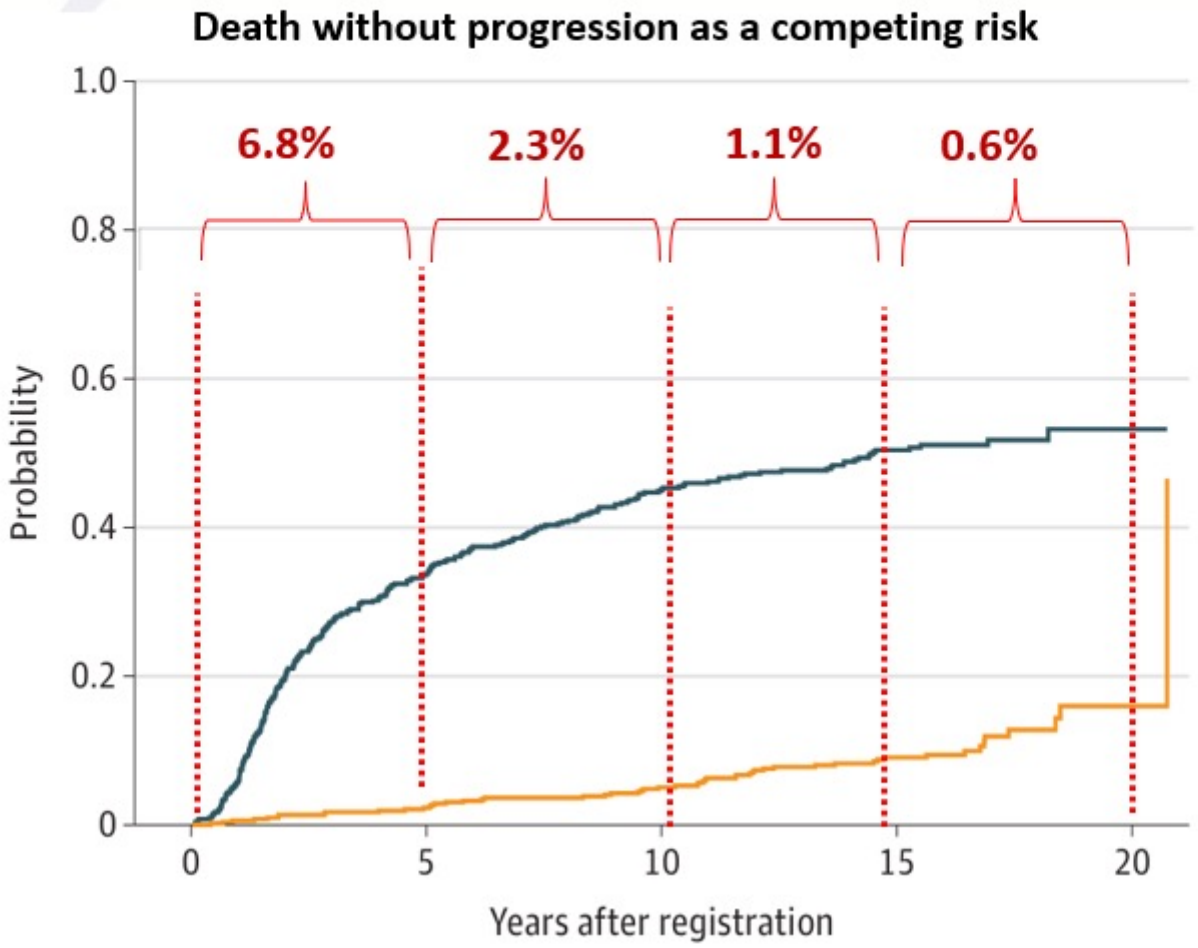
OS



No. at risk					
R-CHOP	267	238	201	122	4
CHOP-RIT	264	221	181	117	5

Shadman, M JAMA Oncology 2026(online)

Cumulative Incidence of Progression



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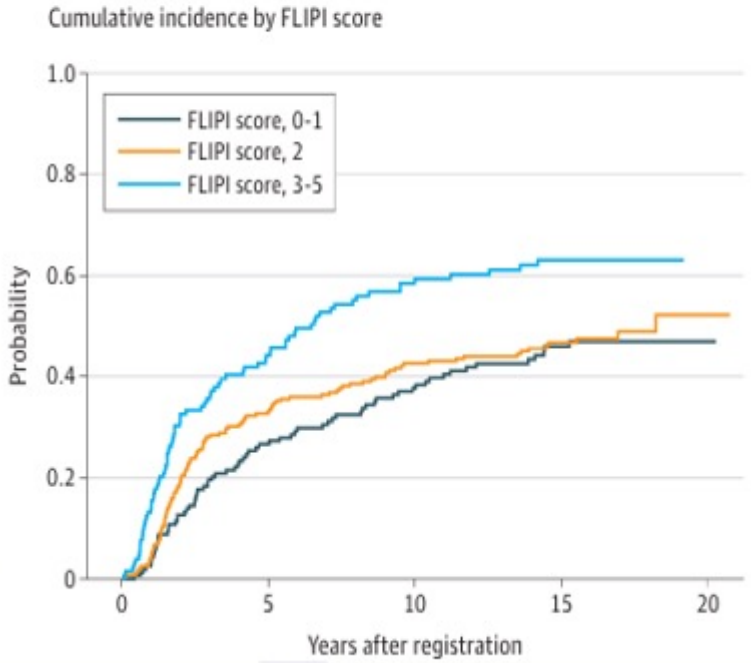
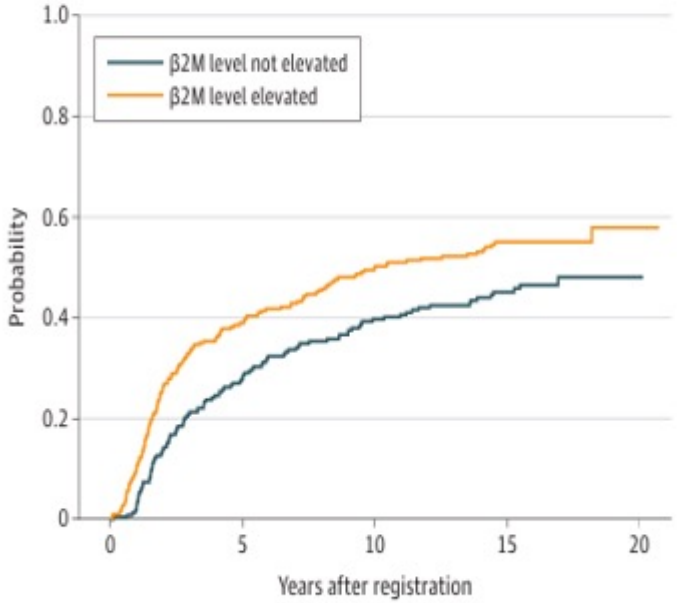
Cumulative incidence of progression by FLIPI and β2M





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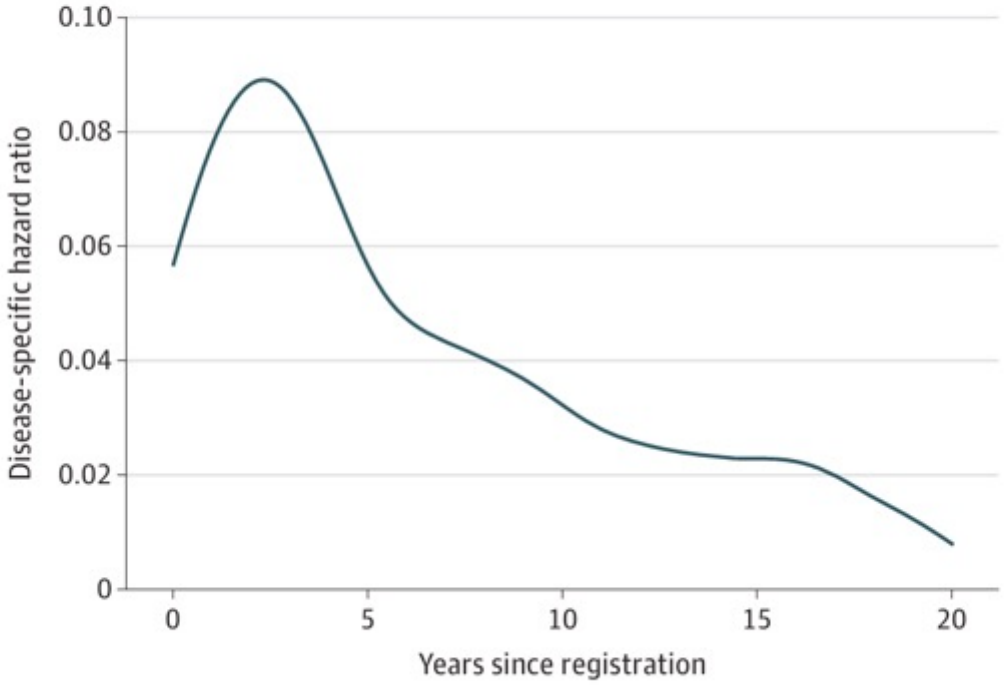
Hazard Curve



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Cure Model Validation

Relapse rate declines over time

- Years 0-5: 6.8% annual relapse rate
- Years 10-15: 1.1% annual relapse rate
- >6-fold reduction in relapse suggests that the patients who have not relapsed by 10 years are likely cured

Mortality matching to general population

- Death rates in long-term survivors match expected background mortality

Consistency across prognostic groups

- Patients with low FLIPI or low beta2 microglobulin had lower relapse

Cause of Death

	CHOP + I-131 (n=264)			CHOP + Rituximab (n=267)		
Cause of Death						
Medical issues other than cancer	**17**	**6.4%**	3	**23**	**8.6%**	2
Transplant complications	0	0		3	1.1%	
lymphoma	**40**	**15.2%**	1	**31**	**11.6%**	1
Second malignancies	**19**	**7.2%**	2	**15**	**5.6%**	3
unknown	10	3.8%		12	4.5%	
Total	87	32.9%		84	31.5%	

Shadman, M JAMA Oncology 2026(online)

Conclusions: S0016

- 15-year follow-up suggests a subset of patients with advanced-stage FL may achieve cure with CHOP-based CIT (without maintenance)
- Relapse rates decline over time, supporting the presence of a plateau consistent with cure fraction

Shadman, M JAMA Oncology 2026(online)

S2308: Rationale: Quest for a cure in low tumor burden FL

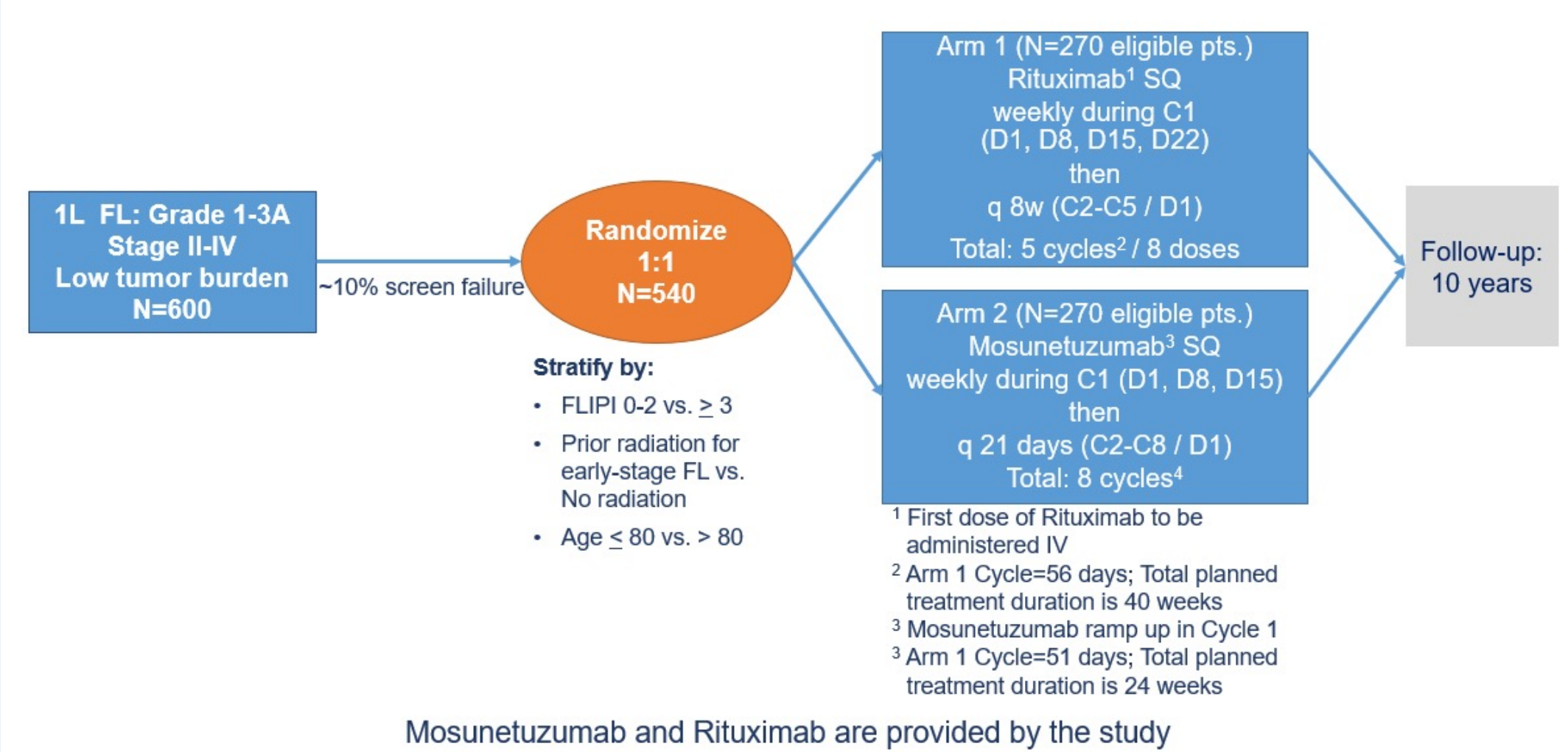
Allogeneic transplant which harnesses the potential of donor T cells is a known curative modality on FL but at a cost of Transplant related mortality and morbidity

Due to the presence of healthier T cells in treatment naïve patients, the early use of the CD20/CD3 bispecific antibody, mosunetuzumab in low-tumor burden follicular lymphoma has the potential to cure follicular lymphoma and lead to better long-term outcomes compared to rituximab

Proposed Advantages of Mosunetuzumab[1]	
Efficacy	High CR rate, durable responses
Toxicity	Lower incidence and lower grade of CRS compared to CAR T, very low incidence of ICANs
Access	Outpatient use, subcutaneous route, off the shelf, fixed duration therapy

1. Ghosh N JCO Oncology Advances 2025:2(1) e2500037

S2308: Randomized Phase III Study of Mosunetuzumab vs Rituximab in Low Tumor Burden Follicular Lymphoma



Ghosh N JCO Oncology Advances 2025:2(1) e2500037

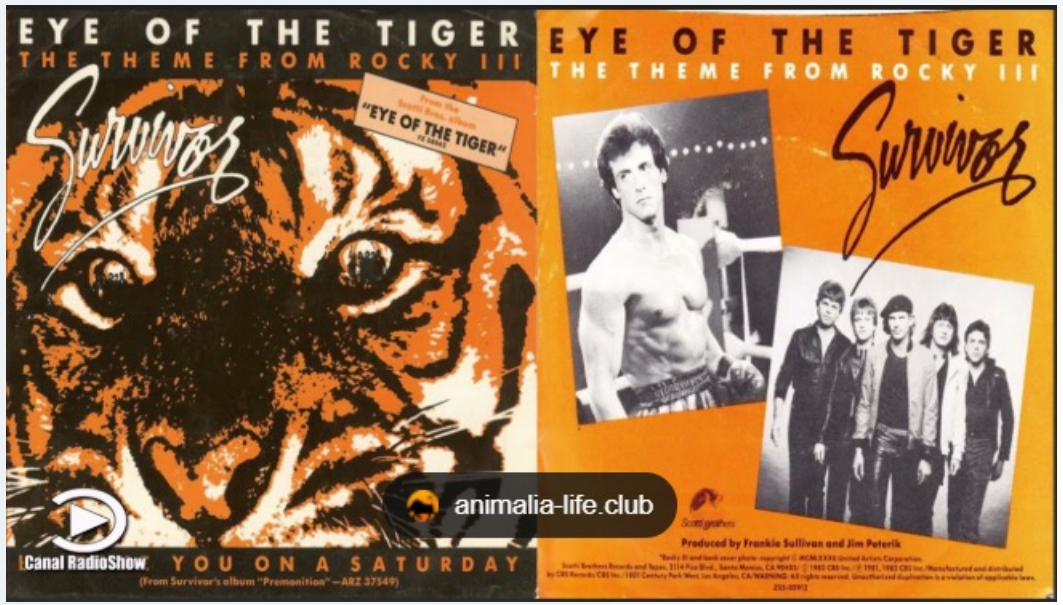
What percentage of patients can expect long term remission with RCHOP as 1L therapy for Follicular lymphoma

- 20%
- 34%
- 50%
- 75%

Conclusions

- Follicular lymphoma is curable in a subset of patients
- Approximately 40% of patients are in remission 10 years after 1L rituximab for low tumour burden disease
- Approximately one third of patients are in remission 15 years after 1L RCHOP
- Allogeneic transplantation has been curative modality in R/R FL
- Modern immunotherapies such as CAR T and T cell engaging bispecific antibodies have demonstrated durable remissions in R/R FL
- S2308 is a trial testing if fixed duration bispecific antibody can be potentially curative when used as first line therapy in low tumor burden FL

Fun Fact



"It's the eye of the tiger, it's the thrill of the fight
Risin' up to the challenge of our rival"

October 12, 2023, Chicago