10th POSTGRADUATE

Lymphoma Conference

The therapeutic world of follicular lymphoma is changing rapidly: could it be reasonable to evaluate an update of some parameters such as W&W, FLIPIs score, Deauville score, and POD24?

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Venice,
March 12-13, 2026

Hotel Monaco & Grand Canal

President:
P.L. Zinzani

Disclosures

- **Research funding:** Roche, Genentech, Genmab, AbbVie, Innate Pharma, BeiOne medicines, Astrazeneca
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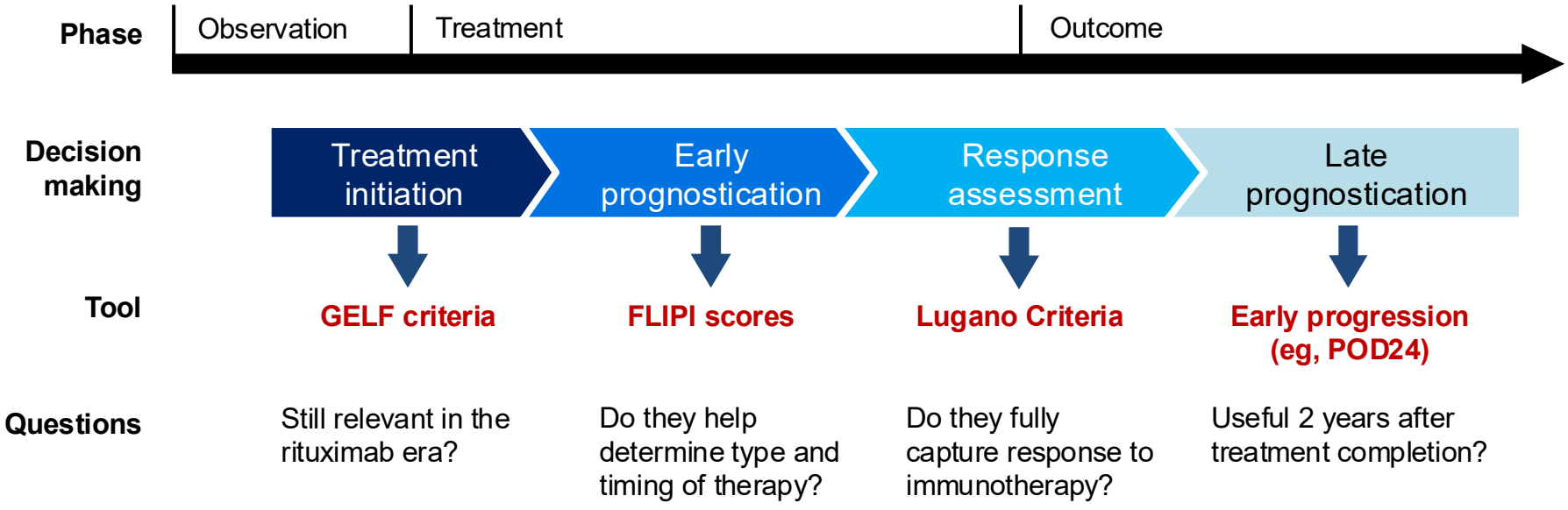
- **Advisory board:** AbbVie, Genentech, Genmab, ADC therapeutics, Johnson & Johnson, Regeneron, Chugai, Bristol Myers Squibb
- **Honoraria:** Roche, Genmab, AbbVie, Kite, Chugai
- **Travel Support:** Genmab, AbbVie, Roche, Kite, Chugai

How do We Currently Support Decision Making in Patients with Follicular Lymphoma?



Treatment initiation

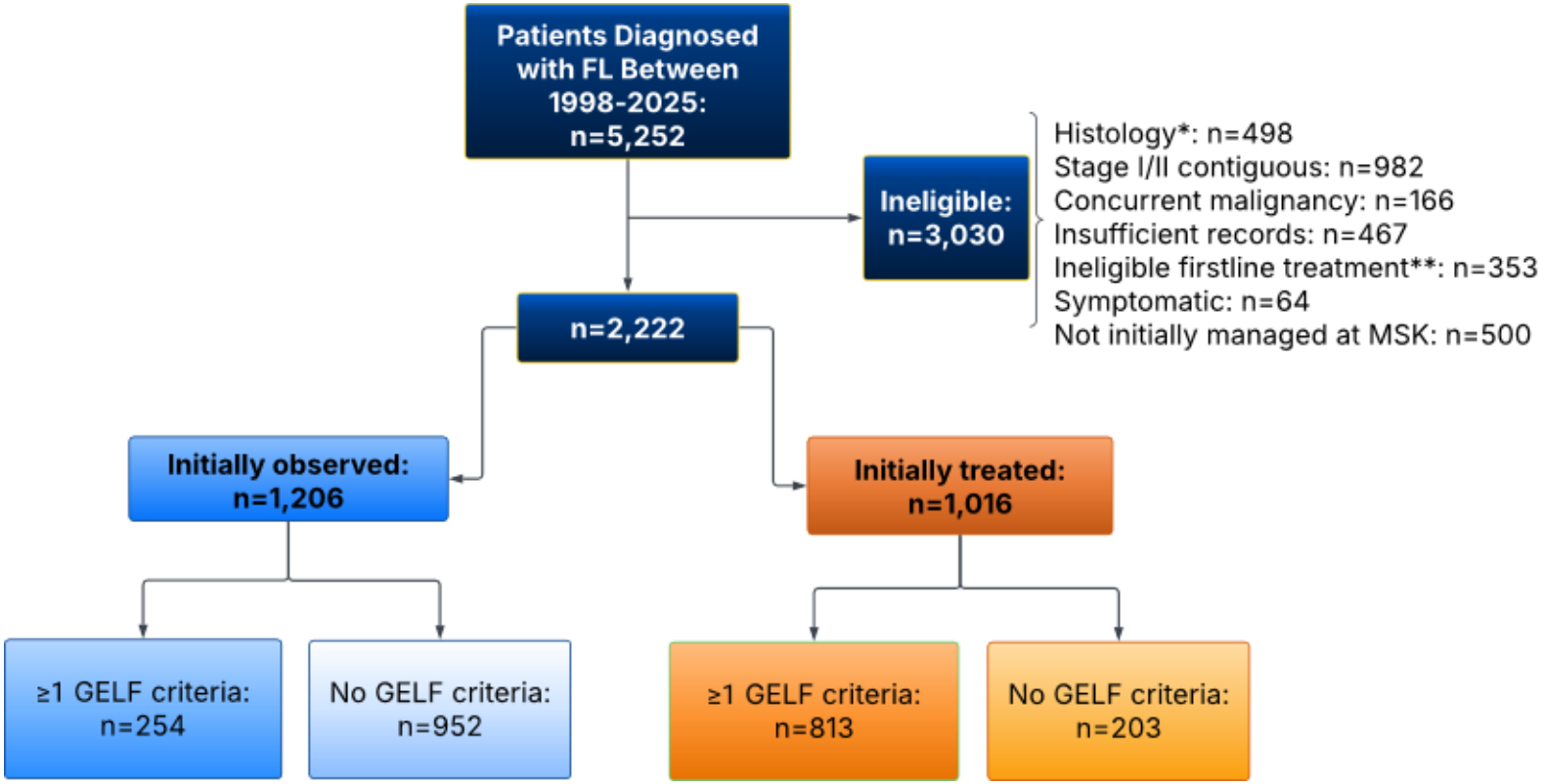
Are traditional GELF criteria still relevant to clinical decision-making in patients with FL?

- GELF criteria are still used to determine clinical trial eligibility and, to an extent, need for treatment in routine practice
- Recent studies call into question the role of GELF in therapy initiation decisions:
  - The presence or number of GELF may not impact PFS in observed or treated patients[1]
  - Among observed FL patients, those who met ≥1 treatment criterion did not have an increased rate of therapy initiation vs. those who didn't (44% vs. 42%) during the first 5 years from diagnosis[2]
- More contemporary prognostic tools (FLIPI, FLIPI-2, m-FLIPI, PRIMA-PI, FLIPI24) may better stratify FL disease severity and guide treatment decisions[3-6]

1. Barraclough A et al, *Haematologica*. 2024;109(10):3338-3345; **2.** Khurana A et al, *Blood Cancer J*. 11, 133 (2021); **3.** Solal-Céligny et al. *Blood. 2004;104(5):1258-1265;* **4.** Federico M et al. *J Clin Oncol*. 2009;27(27):4555-4562; **5.** Bachy E et al. *Blood*. 2018 Jul 5;132(1):49-58; **6.** Pastore A, et al. *Lancet Oncol*. 2015;16(9):1111-1122

Grieve C. et al .ASH 2025; Abstract #1008

Study Population

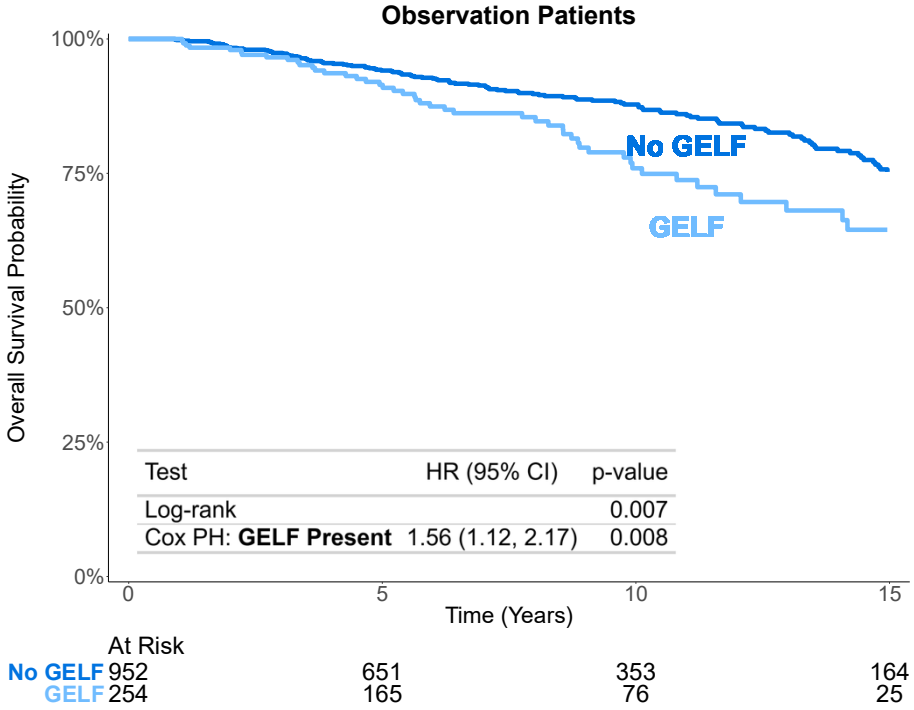


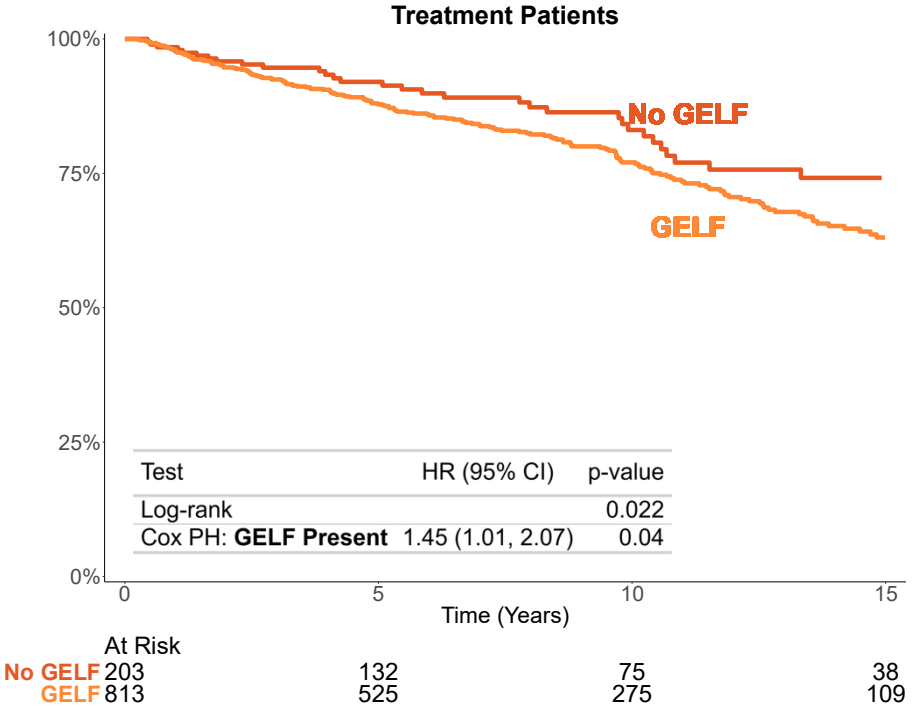
*Composite lymphoma n=23; duodenal-type lymphoma n=57; primary cutaneous FL n=27; pediatric FL n=2; FL in situ n=45; aggressive/transformed disease n=311; histology details missing n=33

**Protocol treatment n=129; chemotherapy only n=28; radiation n=155; surgery n=13; R-lenalidomide n=28

Grieve C. et al .ASH 2025; Abstract #1008

Presence of GELF Criteria Imparted Negative Prognosis Regardless of Initial Management





- Patients with GELF had shorter survival in both study groups; curves diverge sooner in the treatment group

Grieve C. et al .ASH 2025; Abstract #1008

Three GELF Criteria Were Associated with Shorter OS

Characteristic	HR	95% CI	p-value	q-value[1]
B symptoms	1.45	1.02, 2.07	**0.046**	0.12
>3x3 nodes	0.94	0.68, 1.30	0.70	0.75
>7cm mass	1.08	0.81, 1.44	0.60	0.75
Splenomegaly	0.94	0.72, 1.24	0.67	0.75
Lymphocytosis	0.90	0.46, 1.76	0.75	0.75
Cytopenia	2.16	1.45, 3.24	**<0.001**	**0.002**
Serous Effusion	2.06	1.49, 2.83	**<0.001**	**<0.001**
Study Group			0.51	0.75
Observation	—	—		
Treatment	1.10	0.83, 1.45		

[1]False discovery rate correction for multiple testing

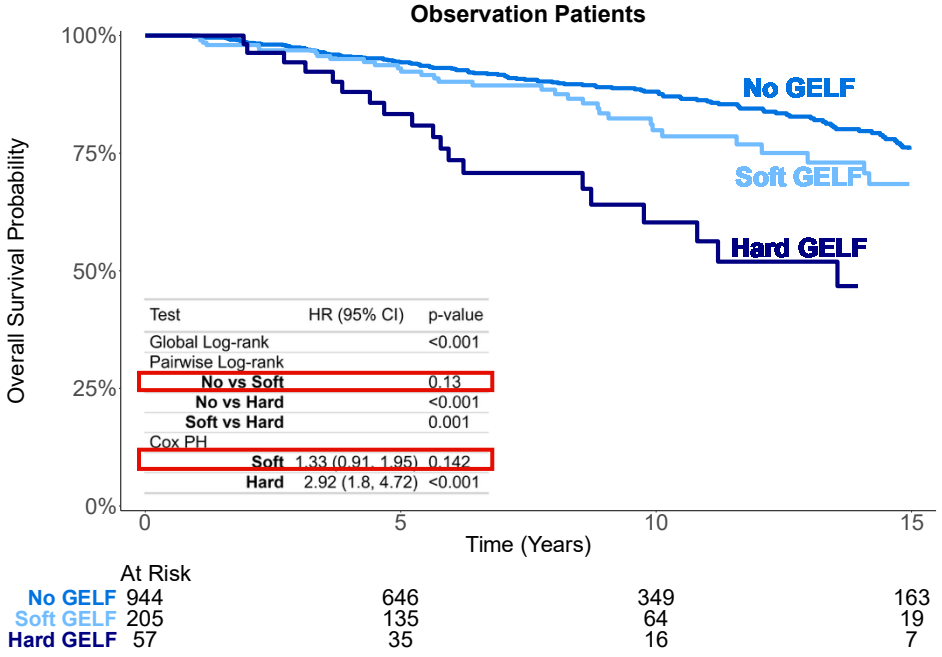
Abbreviations: CI = Confidence Interval, HR = Hazard Ratio

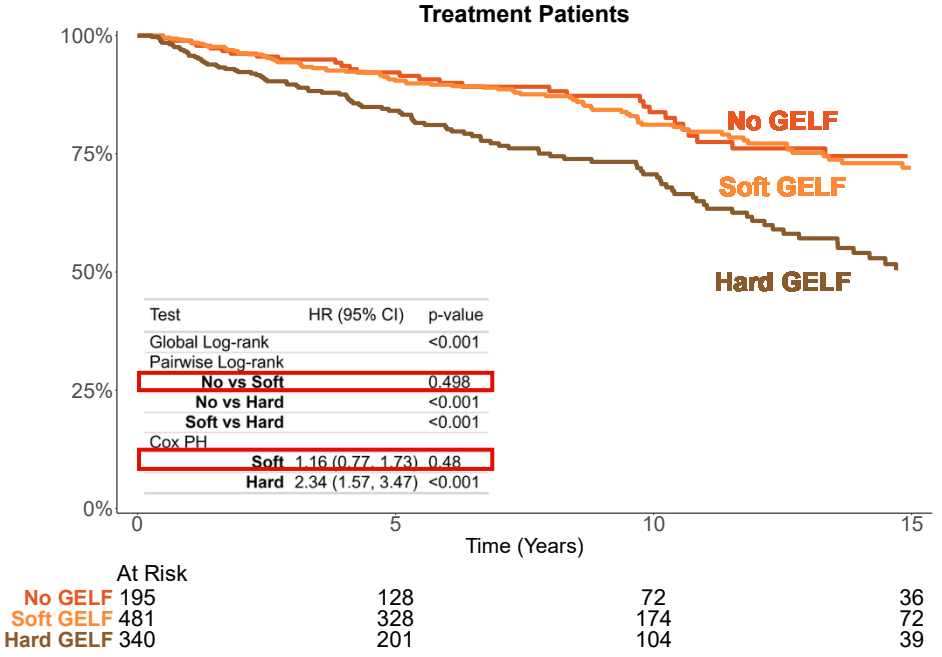
“hard” GELF criteria

“soft” GELF criteria

Grieve C. et al .ASH 2025; Abstract #1008

“Soft” GELF Criteria Did Not Negatively Impact OS in Both Observed and Treated Patients

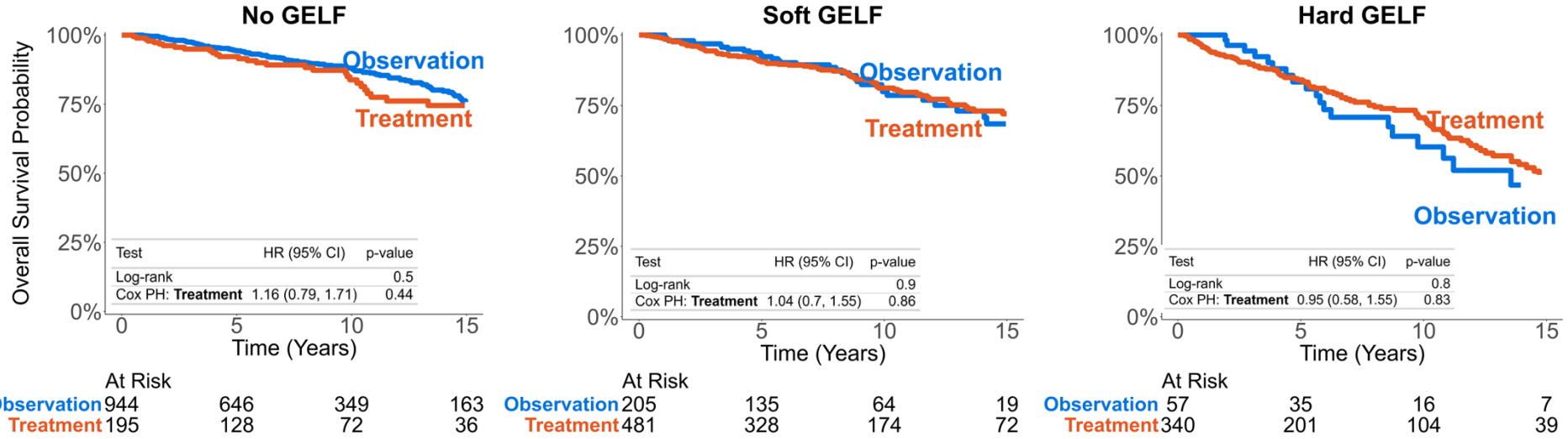




- Patients with soft GELF criteria have similar survival outcomes to those with no GELF at baseline in both study groups
- Those with hard GELF criteria at baseline have significantly shorter overall survival compared to patients without

Grieve C. et al .ASH 2025; Abstract #1008

Observation Was Not Detrimental in Patients with “Soft” GELF Criteria



- **Patients meeting no or “soft” GELF criteria at presentation had similar survival outcomes, regardless of initial approach (observation vs treatment)**
- Among patients meeting hard GELF survival is shorter, but small number of observed patients precludes meaningful comparison

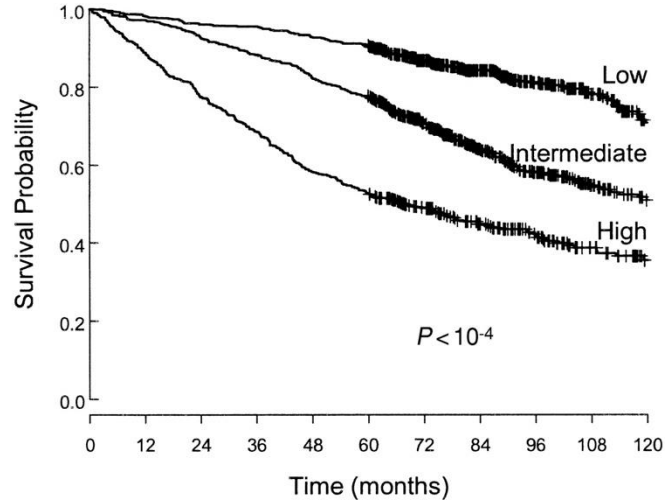
Grieve C. et al .ASH 2025; Abstract #1008

Early prognostication

Courtesy of Dr. M. Maurer

LEGACY MODEL IN FL: FLIPI

- Developed on N=1795 patients diagnosed with FL between 1985 and 1992
- Simple sum of 5 variables
  - Age >= 60
  - Stage III/IV
  - HGB < 12
  - >4 Nodal areas
  - LDH > ULN
- C-statistics (recent datasets)
  - 0.65-0.68 (OS, all patients)



No. of Events											
Low	-	12	25	29	46	60	83	95	106	113	125
Intermediate	-	19	49	79	118	150	192	225	247	255	261
High	-	54	109	152	202	229	245	260	268	274	278

No. at Risk											
Low	641	629	616	612	595	581	450	337	241	157	93
Intermediate	670	651	621	591	552	519	385	263	178	108	68
High	484	430	375	332	282	255	193	139	98	56	33

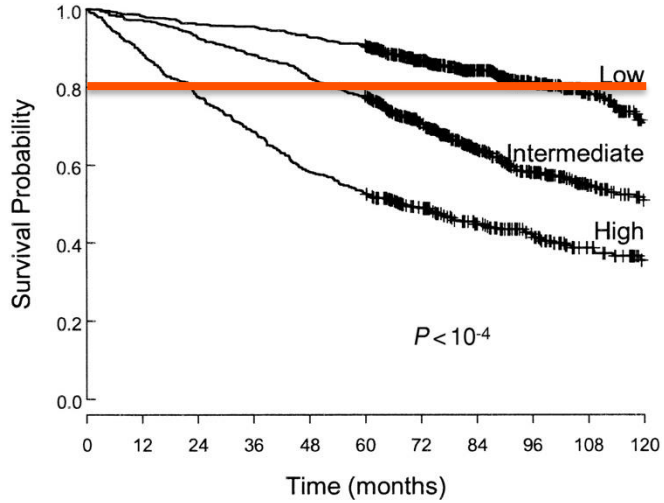
Solal-Celigny et al, Blood 2004

Courtesy of Dr. M. Maurer

LEGACY MODEL IN FL: FLIPI

- Developed on N=1795 patients diagnosed with FL between 1985 and 1992

10-year survival in FL is now 80%



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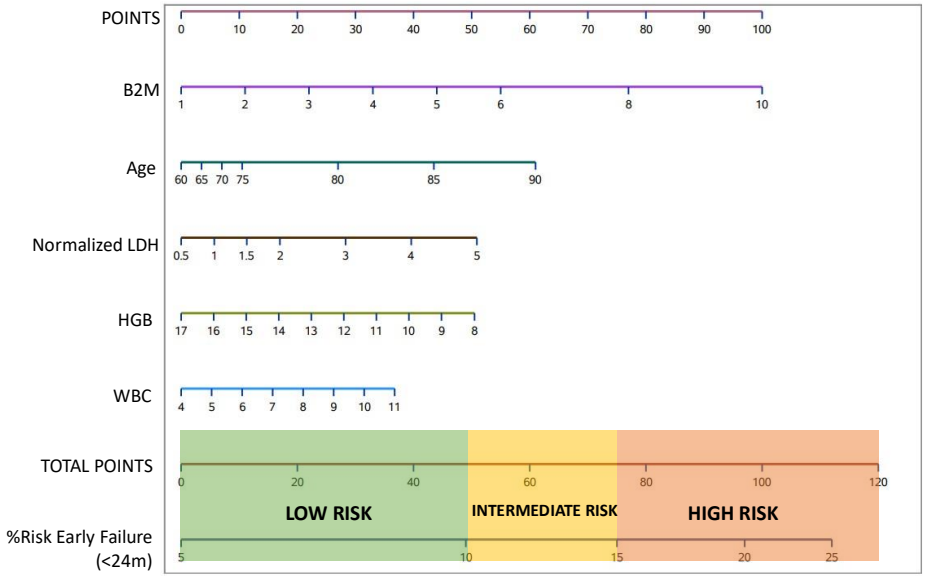
Solal-Celigny et al, Blood 2004
Sarkozy*, Maurer* et al, JCO 2019

Courtesy of Dr. M. Maurer (modified)

FLIPI24 MODEL

- Strategy:
  - **Primary endpoint: EFS24 (e.g. POD24, early transformation or death) in patients receiving immunochemotherapy**
  - Evaluate the model for other outcomes (OS, cause of death) and extend to all patients at diagnosis
- N=3,577 patients form 10 center (EU, North America, and Australia)
- Grade 1-3A and initiated frontline R-CHOP, R-CVP, or B-R or like IC
- Validation in N=6,785 patients from 6 cohorts (internal cohort; Iowa/Mayo SPORE MER; LEO Cohort; GALLIUM, PRIMA, RELEVANCE)



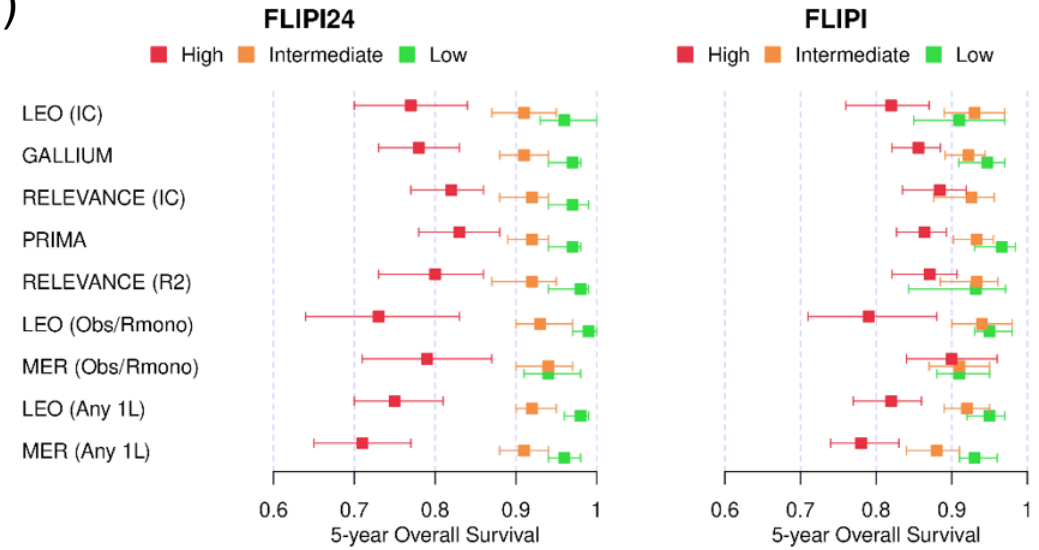
Maurer M et al. J Clin Oncol 2026 Jan 10;44(2):117-128

Courtesy of Dr. M. Maurer

FLIPI24 MODEL PERFORMANCE

- OS C-statistics (external validation)
  - FLIPI24: 0.72-0.78
    - Superior to FLIPI in every validation dataset
- 3 distinct risk groups across validation datasets

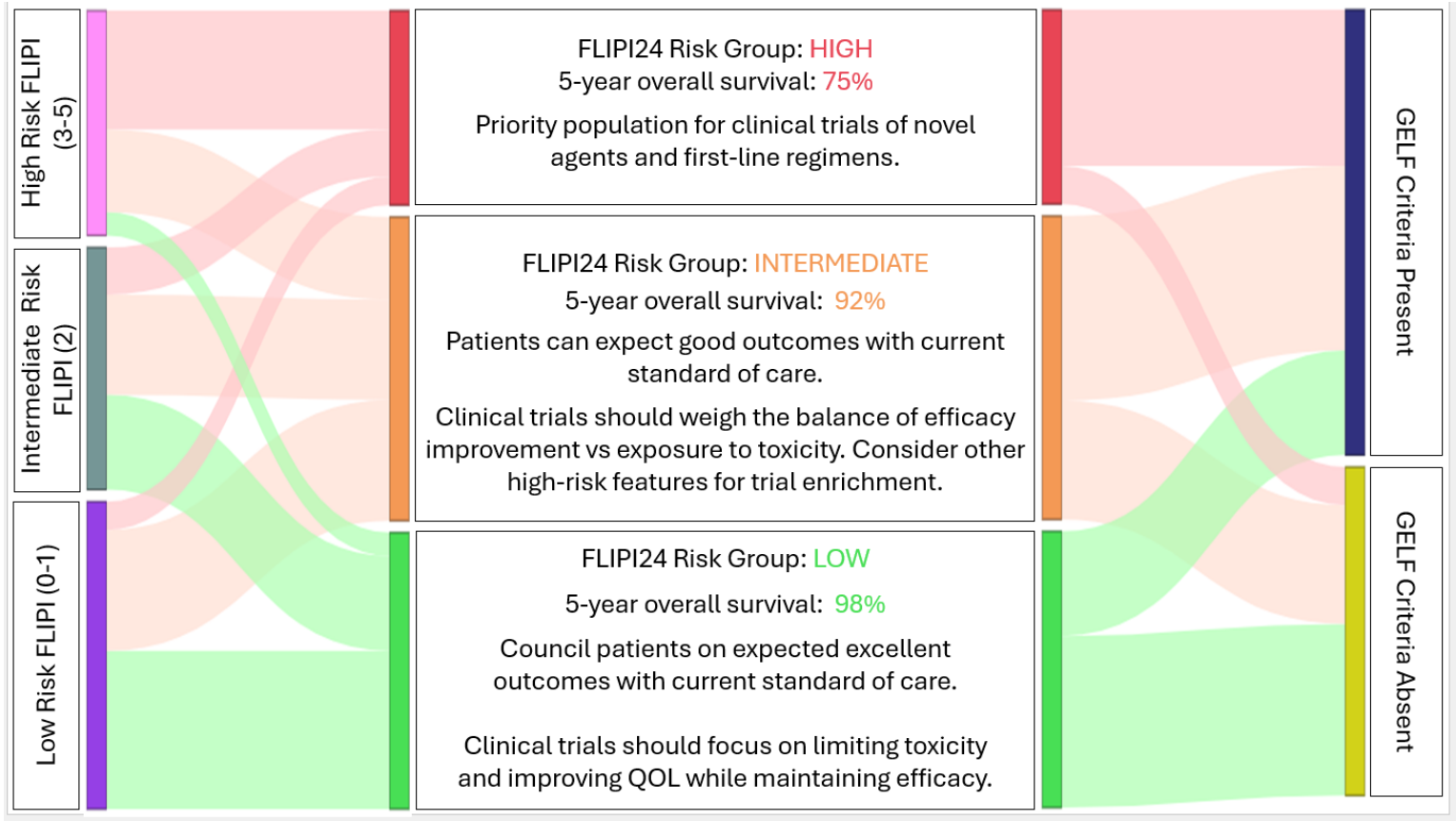
5-year OS in validation datasets



Maurer M et al. J Clin Oncol 2026 Jan 10;44(2):117-128

FLIPI24 VS FLIPI VS GELF

Courtesy of Dr. M. Maurer



Maurer M et al. J Clin Oncol 2026 Jan 10;44(2):117-128

Response assessment

Summary of Lymphoma PET Response Criteria and Their Criticism

Response category	Criteria	Criticism
Complete metabolic response	DS 1-3 in nodes, extranodal sites, marrow (FDG avid Waldeyer's ring, spleen or marrow allowed if clearly reactive)	Subjectivity on "reactive" vs. "disease"
Partial Metabolic response	DS4-5 but decreased vs. baseline	How much decrease is "significant"?
Stable disease	DS4-5 but not significantly decreased vs. baseline	What does "not significantly" mean exactly?
Progressive disease	DS4-5 but increased vs. baseline	PET does not distinguish inflammatory vs. disease-related uptake

Cheson et al. J Clin Oncol 2014

Potential ways to Refine Response Criteria in Patients Treated with Immunomodulators

Response category	Criteria
Complete metabolic response	DS 1-3 in nodes, extranodal sites, marrow (FDG avid Waldeyer's ring, spleen or marrow allowed if clearly reactive)
Partial Metabolic response	DS4-5 but decreased vs. baseline
Stable disease	DS4-5 but not significantly decreased vs. baseline
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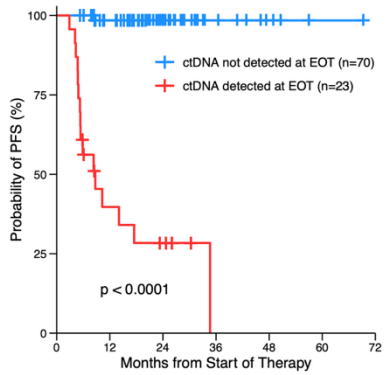
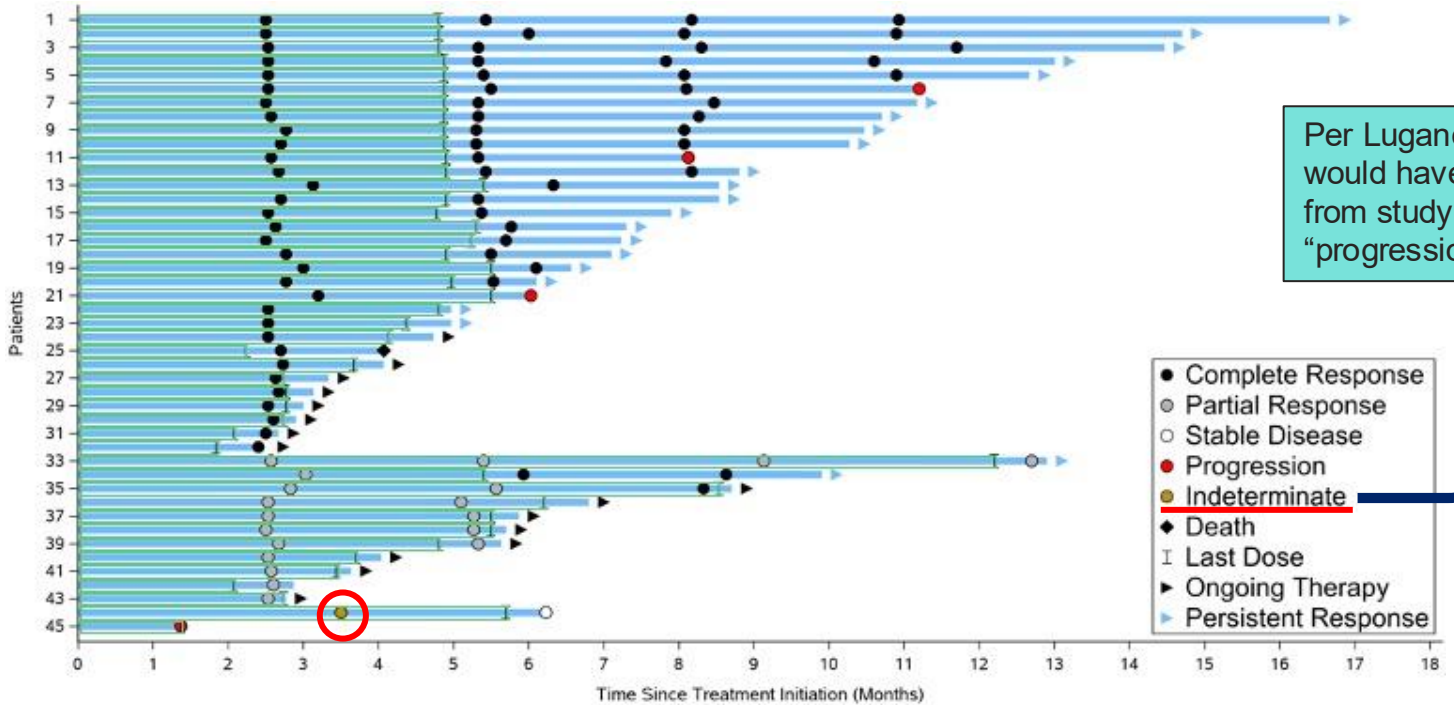


- **IR1:** ≥50% increase in SPD in first 12 weeks
- **IR2:** <50% increase in SPD with
  - New lesion(s)
  - ≥50% increase in PPD of a lesion or set of lesions at any time during treatment
- **IR3:** Increase in FDG uptake without a concomitant increase in lesion size meeting criteria for PD

Cheson et al. J Clin Oncol 2014

Is the Lugano 2014 adequate to adjudicate response? Mosunetuzumab in 1L FL: MITHIC-FL1

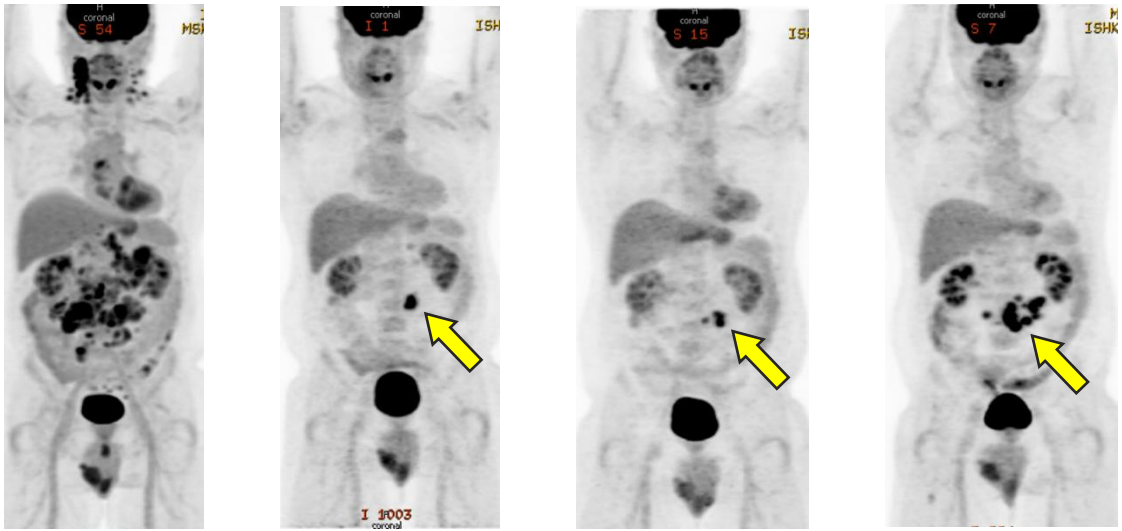


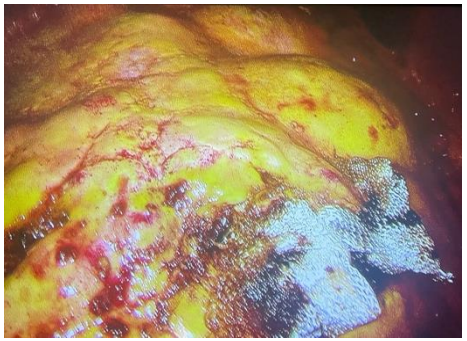
Per Lugano 2014, this patient would have been removed from study due to disease "progression"

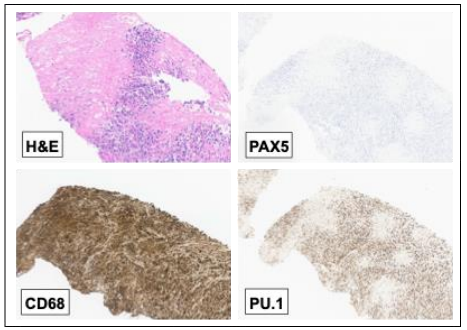
NOTE: Patients who achieved complete response after 8 cycles discontinued therapy; those who achieved partial response, continued therapy for up to 17 cycles.

Falchi et al. ASH 2023. Abstract #604

Utility of LYRIC criteria as a complement to the Lugano criteria: A case study







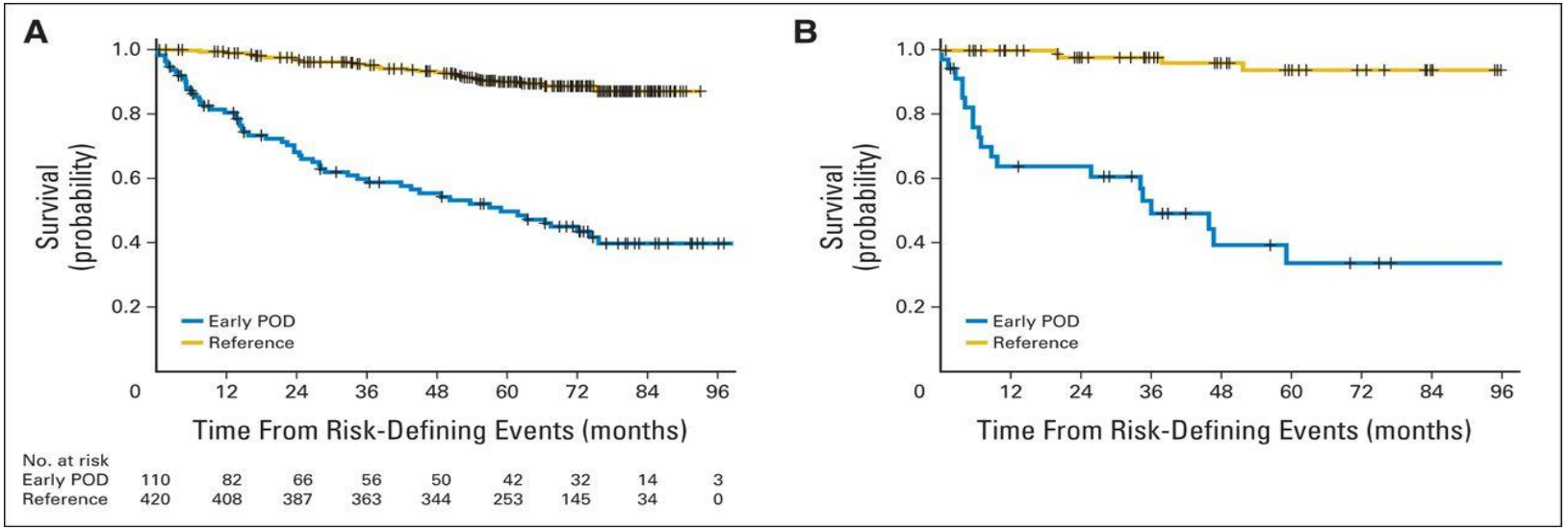
Mosunetuzumab

Baseline | 6 months | 12 months | 18 months | 19 months

Falchi et al. ASH 2024. Abstract #340

Late prognostication

Is early progression is associated with shorter survival in a retrospective study without systematic use of PET/CT and limited information on subsequent therapies

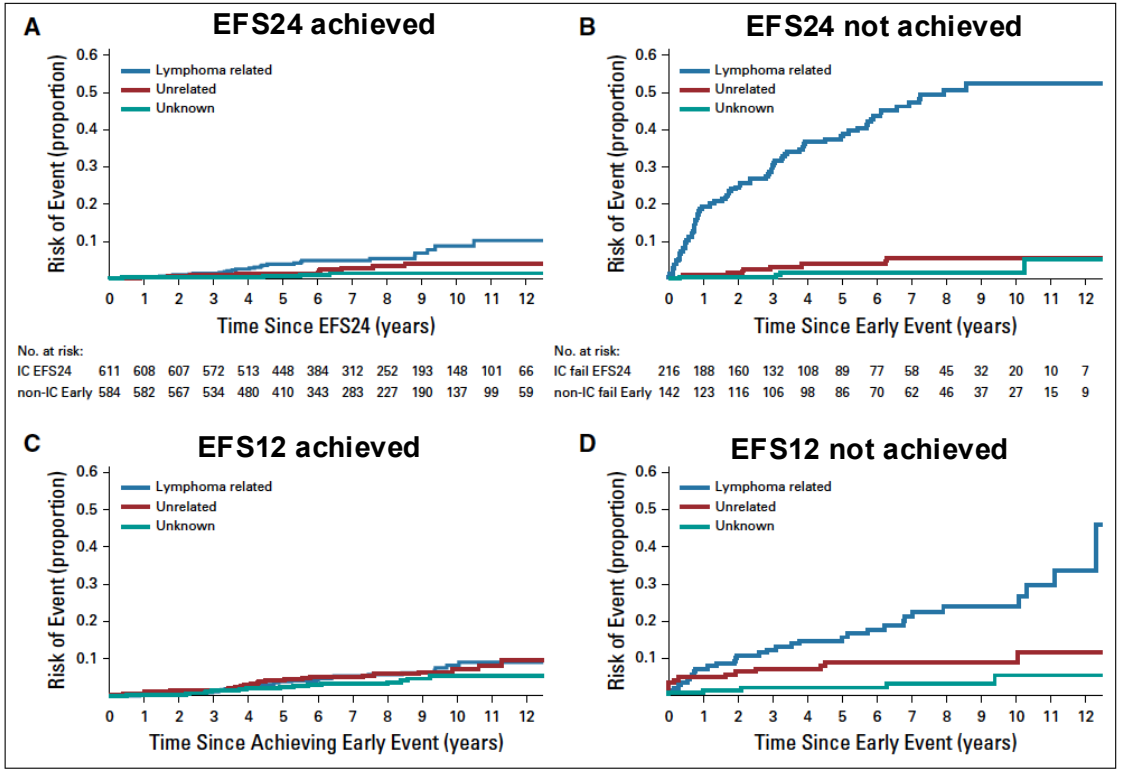


Casulo C et al. JCO 2015;33:2516-2522

Lymphoma is a major cause of death in patients with early events after chemoimmunotherapy…

Pts treated **with** immunochemotherapy

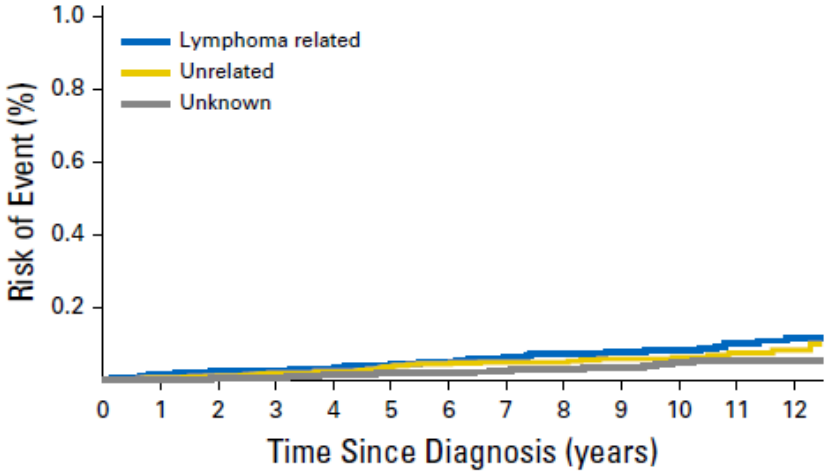
Pts treated **without** immunochemotherapy



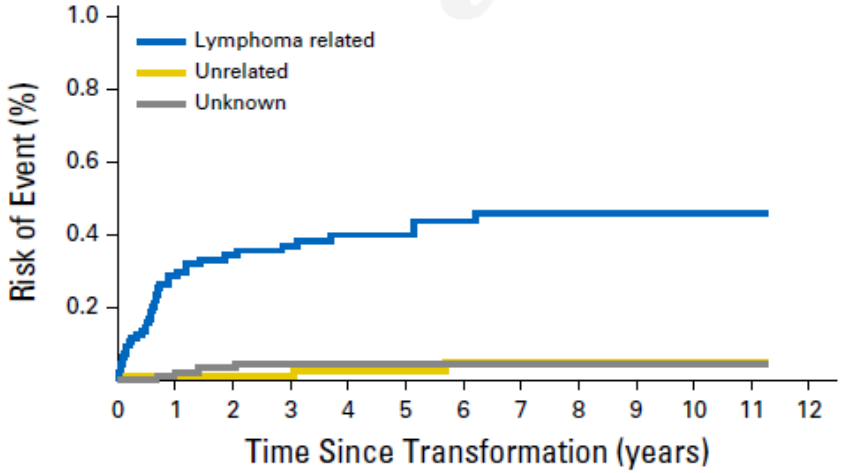
Sarkozy C, *et al*. *J Clin Oncology* 2019; **37**:144–152.

…but histological transformation drives most lymphoma-related deaths

Without transformation

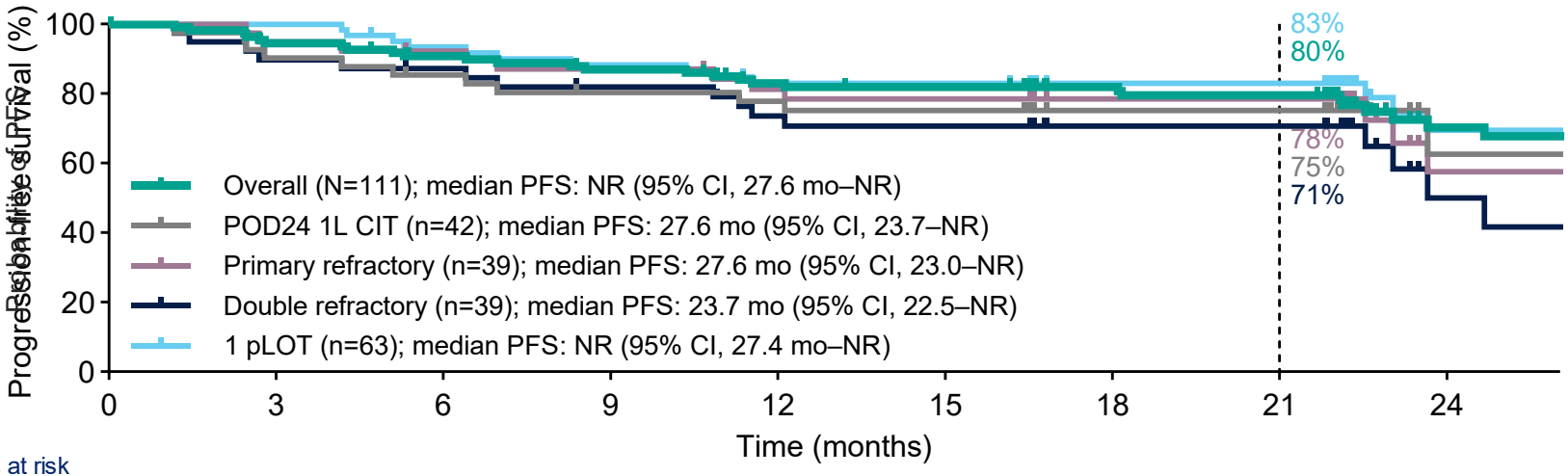


With transformation



Sarkozy C et al, JCO 2019

POD24 is not associated with shorter PFS in 2L+ FL treated with epcoritamab +R²



Patients at risk

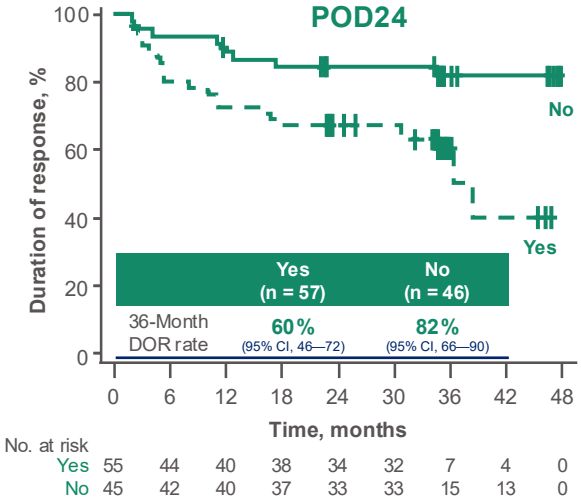
Overall	111	102	95	90	82	80	68	66	29
POD24 1L CIT	42	37	34	31	30	29	21	21	5
Primary refractory	39	37	35	32	28	27	22	22	7
Double refractory	39	35	33	30	26	25	18	18	6
1 pLOT	63	61	55	52	45	45	38	38	13

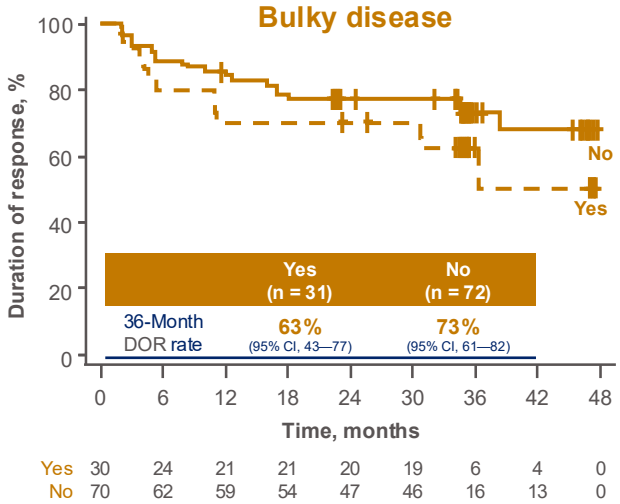
Data cutoff: May 15, 2024. PFS is among the full analysis population. Median follow-up for PFS: 22.3 months.

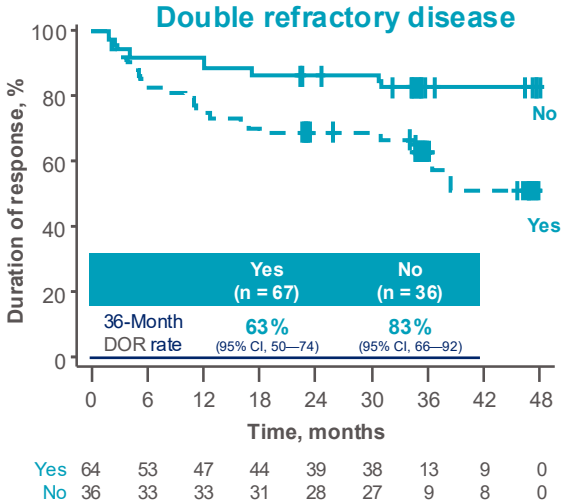
Falchi et al. Blood. 2025 Nov 27;146(22):2629-2640.

PFS rates *may* be lower in patients with 3L+ FL and high-risk features (incl. POD24) treated with liso-cel

DOR







36-Month PFS rate

POD24 (n = 57)	No POD24 (n = 46)	Bulky disease (n = 31)	No bulky disease (n = 72)	Double refractory (n = 67)	Not double refractory (n = 36)
58% (95% CI, 43—70)	80% (95% CI, 65—89)	61% (95% CI, 41—75)	71% (95% CI, 58—80)	60% (95% CI, 47—71)	83% (95% CI, 66—92)

Median DOR was not reached across all these subgroups except patients with POD24 (38.5 months [95% CI, 31.0—NR]).

Revisiting Decision-Making Tools in the Management of Follicular Lymphoma: Conclusions

- **GELF criteria: no longer adequate to determine the need for treatment.**
  - FLIPI24 may be a temporary substitute but needs validation with T-cell based immunotherapy
- **FLIPI24 outperforms historical FLIPI and may be important to inform the choice of 1st line treatment**
  - Potential to determine need for early intervention vs. watchful waiting
- **The 2014 Lugano criteria alone do not fully capture responses following T-cell based immunotherapy, LYRIC helps (in part)**
  - A revised classification that accounts for newer immunotherapies modalities is warranted
  - Is there a future where MRD is incorporated in the response criteria?
- **The predictive role of early progression (eg, POD24) is controversial.**
  - Limited (if any) role in the era of T-cell based immunotherapy

Memorial Sloan Kettering
Cancer Center