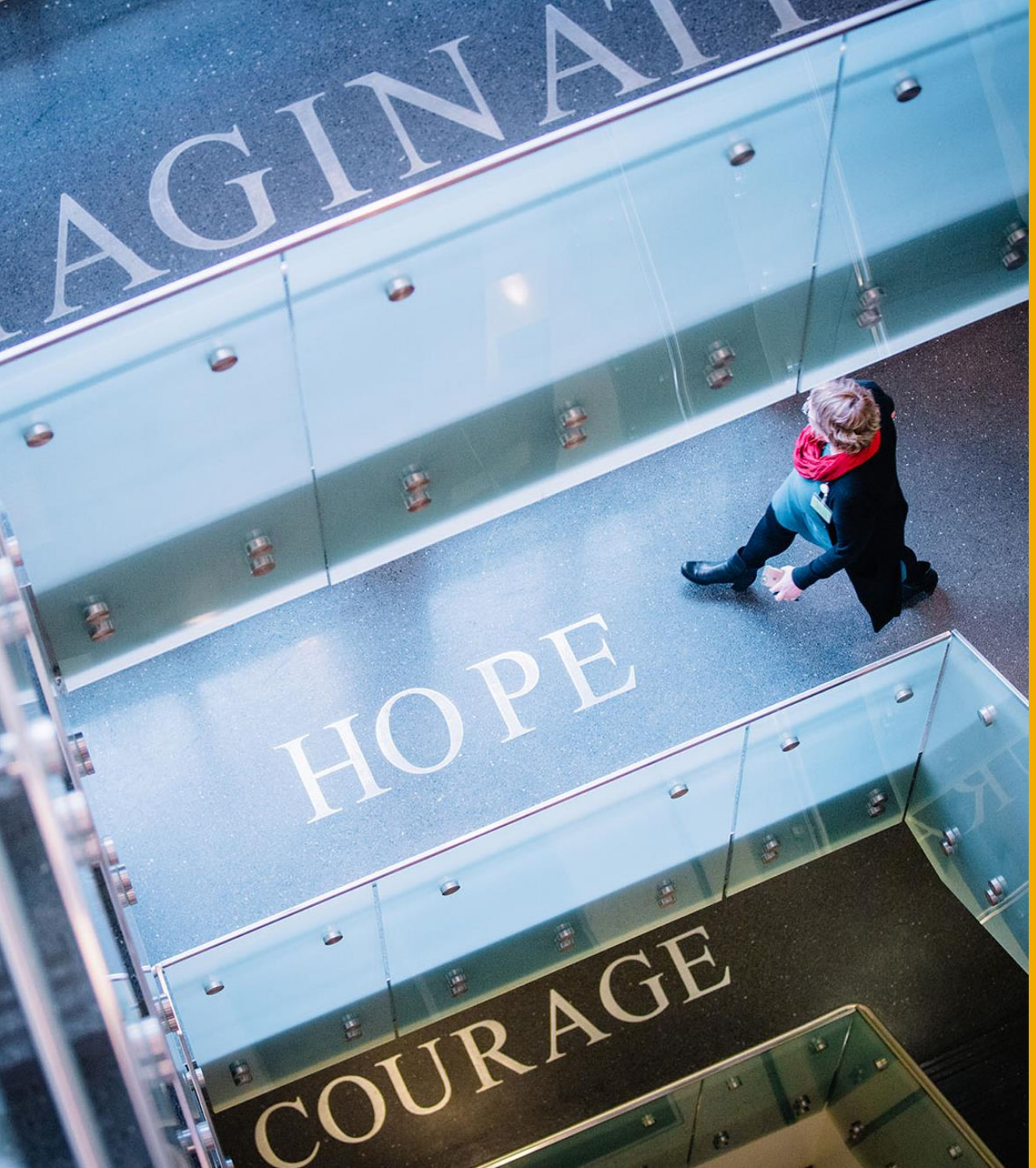

R^2 REMAINS THE STANDARD IN RELAPSED/REFRACTORY FOLLICULAR LYMPHOMA

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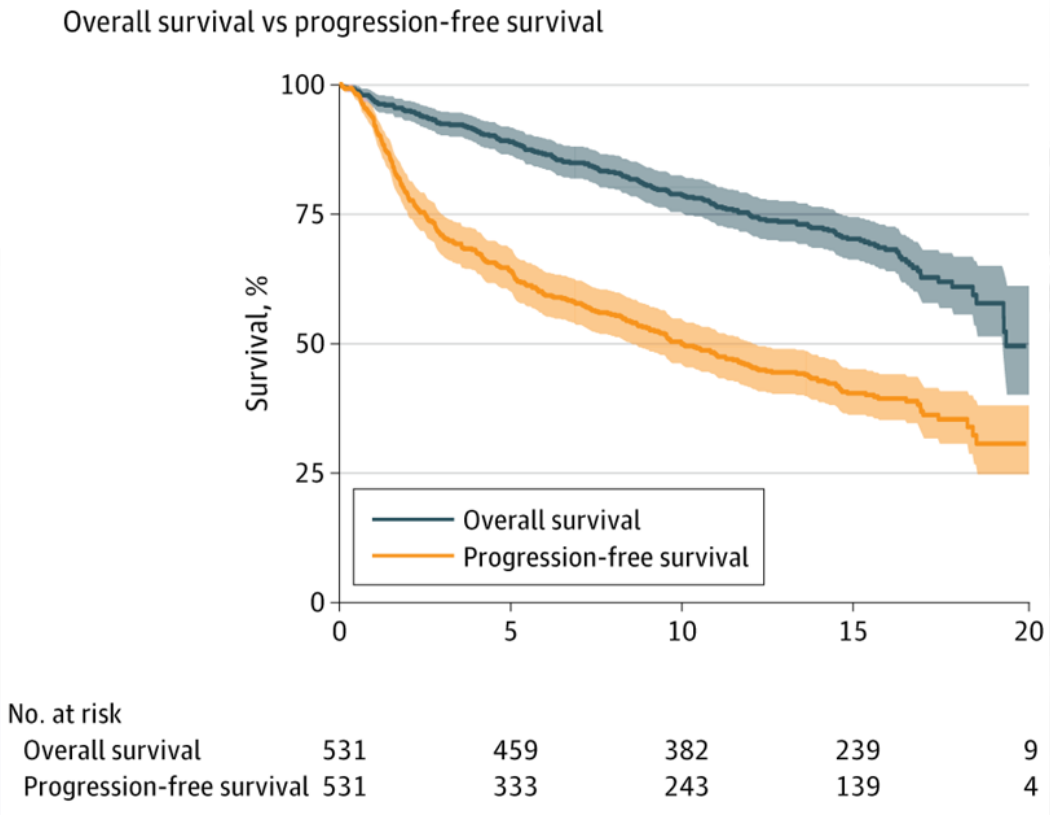
National Cancer Institute-Designated Comprehensive Cancer Center

NCI Designated Comprehensive Cancer Center

Disclosures

None

How do we define success in follicular lymphoma?



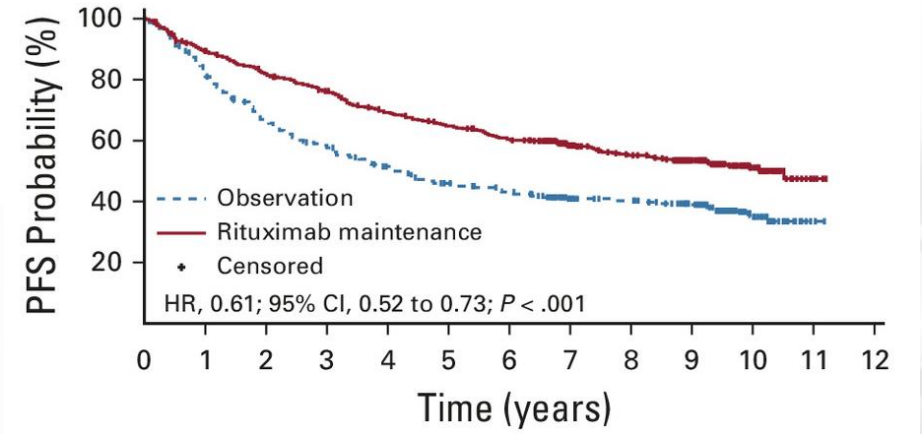
Criteria for successful management:

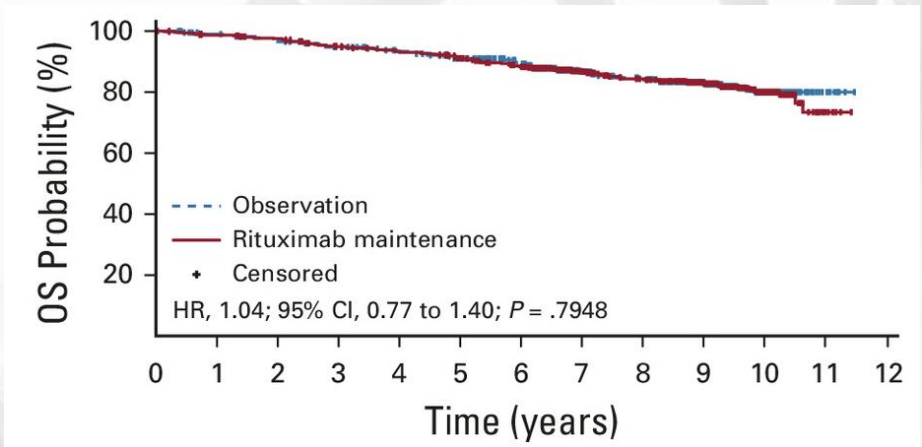
- **Overall survival** — the goal in an incurable disease; not predicted by PFS
- **Symptom management** — durable disease control
- **Toxicity of treatment** — minimize high grade toxicity
- **Deliverability & access** — simple, outpatient, and affordable

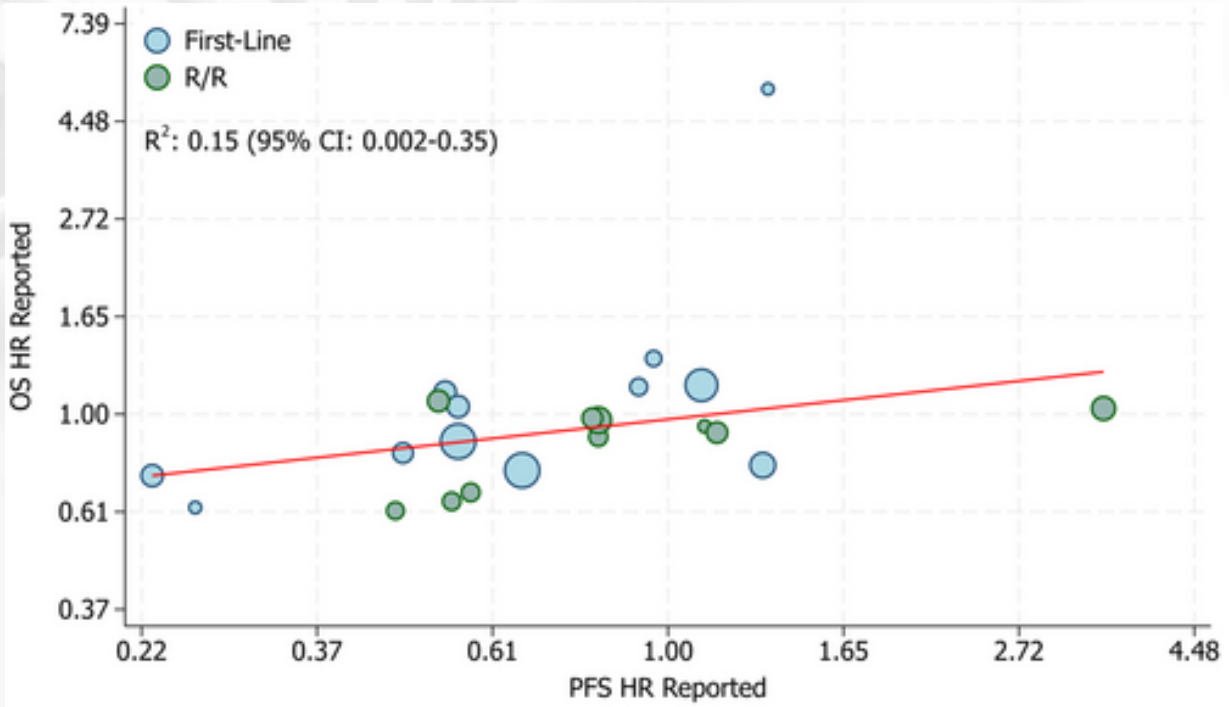
Shadman et al. *JAMA Oncology* 2026

PFS does not predict OS benefit in FL

PRIMA: rituximab maintenance



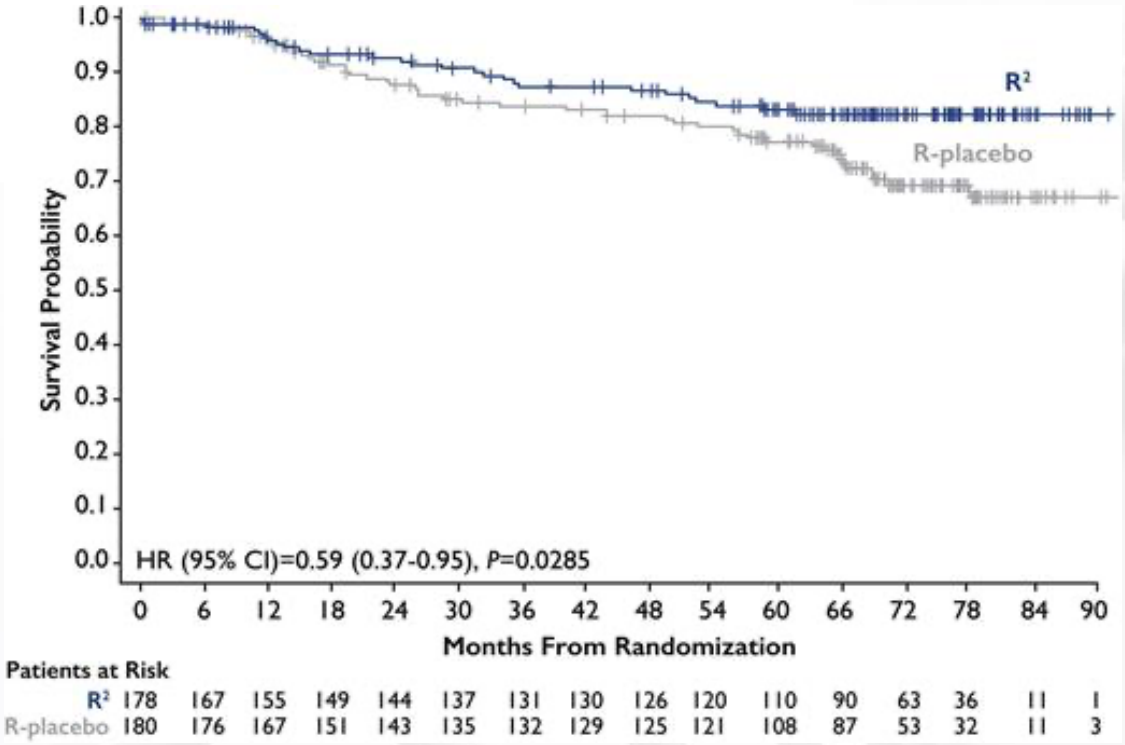




Bachy et al. *JCO* 2019

Milrod et al. *BJHaem* 2024

AUGMENT: R² is effective, easy to administer, and well tolerated



Adverse Event	Lenalidomide + Rituximab (n=176)		Placebo + Rituximab (n=180)	
	All Grades	Grade 3/4	All Grades	Grade 3/4
Neutropenia*	102 (58)	88 (50)	40 (22)	23 (13)
Diarrhea	55 (31)	5 (3)	41 (23)	0
Fatigue	38 (22)	2 (1)	33 (18)	1 (1)
Pyrexia	37 (21)	1 (1)	27 (15)	3 (2)
Leukopenia	36 (20)	12 (7)	17 (9)	3 (2)
Upper respiratory tract infection	32 (18)	2 (1)	23 (13)	4 (2)
Anemia	28 (16)	8 (5)	8 (4)	1 (1)
Headache	26 (15)	1 (1)	17 (9)	0
Infusion-related reaction	26 (15)	4 (2)	24 (13)	0
Thrombocytopenia	26 (15)	4 (2)	8 (4)	2 (1)
Asthenia	24 (14)	2 (1)	19 (11)	1 (1)
Decreased appetite	23 (13)	2 (1)	11 (6)	0
Muscle spasms	23 (13)	1 (1)	9 (5)	1 (1)
Nausea	20 (11)	0	23 (13)	1 (1)
Dyspnea	19 (11)	2 (1)	8 (4)	1 (1)
Rash	19 (11)	2 (1)	7 (4)	1 (1)
Tumor flare	19 (11)	1 (1)	1 (1)	0
ALT increased	18 (10)	3 (2)	15 (8)	1 (1)

***Febrile neutropenia: 5 patients (3%) with R² vs 1 patient (1%) with placebo + rituximab; all grade 3/4.** Data are No. (%).*

Leonard et al. *JCO* 2019
Leonard et al. *JCO* 2026

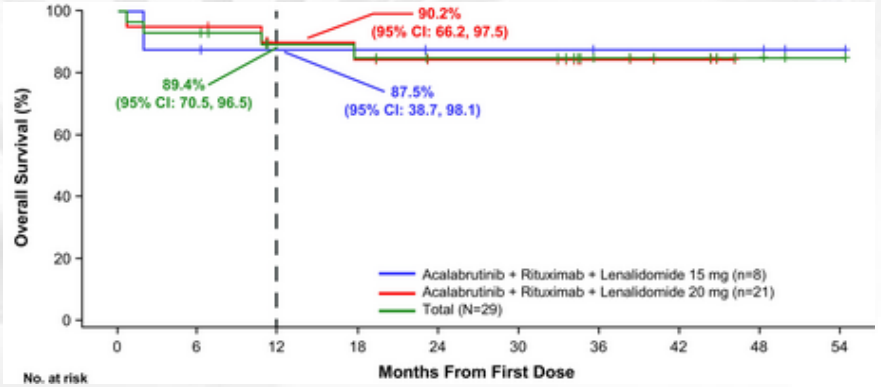
R^2 has performed well against challengers

R-chemo vs R^2

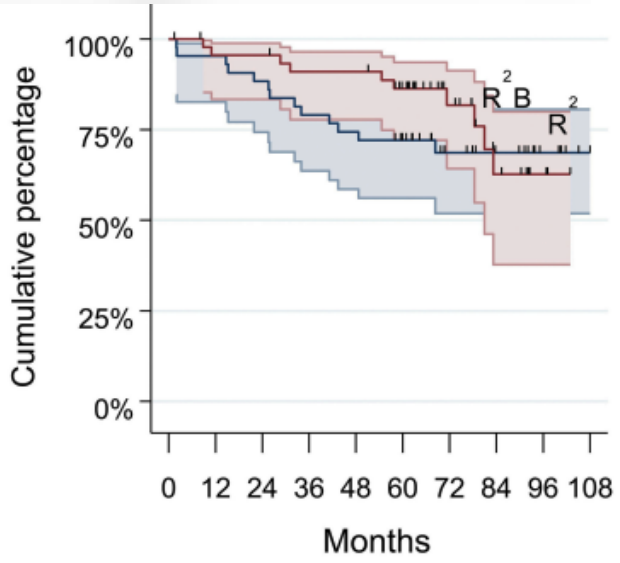
Comparison	Endpoint	R^2 trial(s)	HR (95% CI)	P value
R^2 vs R-CHOP	OS	AUGMENT	**0.77 (0.25–2.43)**	0.660
			0.49 (0.20–1.19)	0.115
	PFS	AUGMENT	**0.93 (0.51–1.71)**	0.827
			0.86 (0.56–1.32)	0.492
		AUGMENT & MAGNIFY	**0.94 (0.52–1.70)**	0.837
			0.94 (0.63–1.42)	0.776
R^2 vs BR	PFS	AUGMENT	**1.20 (0.68–2.13)**	0.532
			1.33 (0.74–2.37)	0.337
		AUGMENT & MAGNIFY	**1.26 (0.70–2.27)**	0.441
			1.10 (0.67–1.81)	0.705

Fox et al. *AJH* 2019
Kersten et al. *Haematologica* 2026
Strati et al. *BJH* 2024

ACE-LY-003 – acalabrutinib-R^2

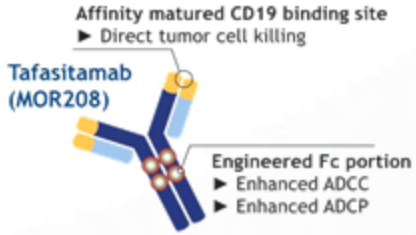


HOVON110 – bendamustine-R^2



ASH 2025: inMIND and EPCORE FL-1

inMIND (n = 548)



R/R FL grade 1–3A or MZL; ≥1 prior therapy incl. anti-CD20 mAb; no prior Len+R; ECOG PS 0–2

R 1:1

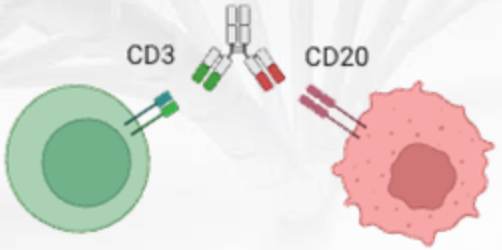
Tafasitamab-R² (n=273)
Tafasitamab 12 mg/kg IV
(C1–3 weekly, C4–12 q2w)
+ Lenalidomide + Rituximab

Control: R² (n=275)
Placebo IV
+ Lenalidomide + Rituximab

Post-treatment follow-up

Sehn et al. Lancet 2026

EPCORE FL-1 (n = 488)



R/R FL grade 1–3A after **anti-CD20 + chemotherapy**; **meets GELF criteria**; ECOG PS 0–2

R 1:1

Epcoritamab-R² (n=243)
Epcoritamab 48 mg SC
(weekly C1–3, q4w C4–12)
+ Rituximab + Lenalidomide

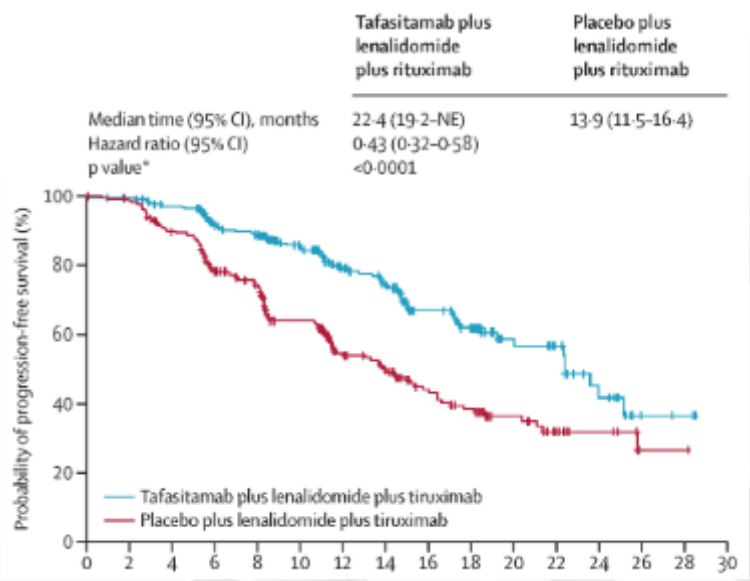
Control: R² (n=245)
Rituximab ×5 cycles
+ Lenalidomide ×12 cycles

Post-treatment follow-up

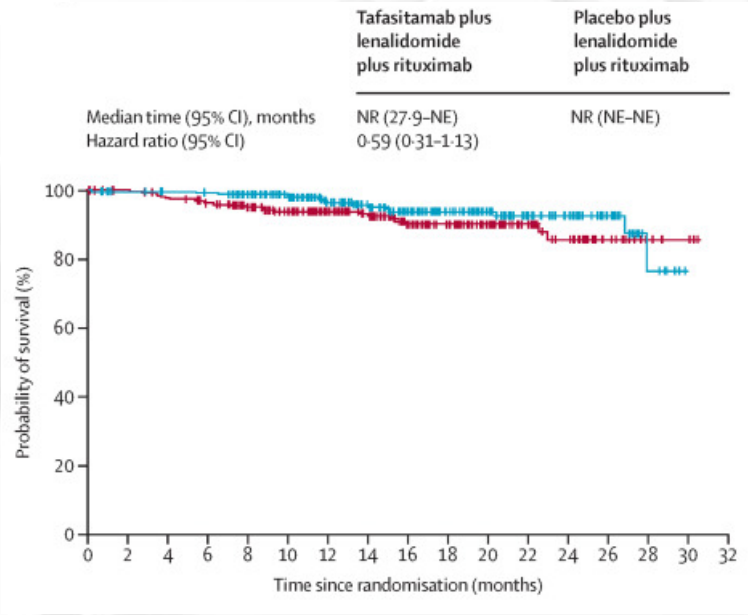
Falchi et al. Lancet 2026 · 24 mg arm (n=61) discontinued

inMIND: R² vs Tafasitamab-R²

Progression Free Survival



Overall Survival



Serious Adverse Events

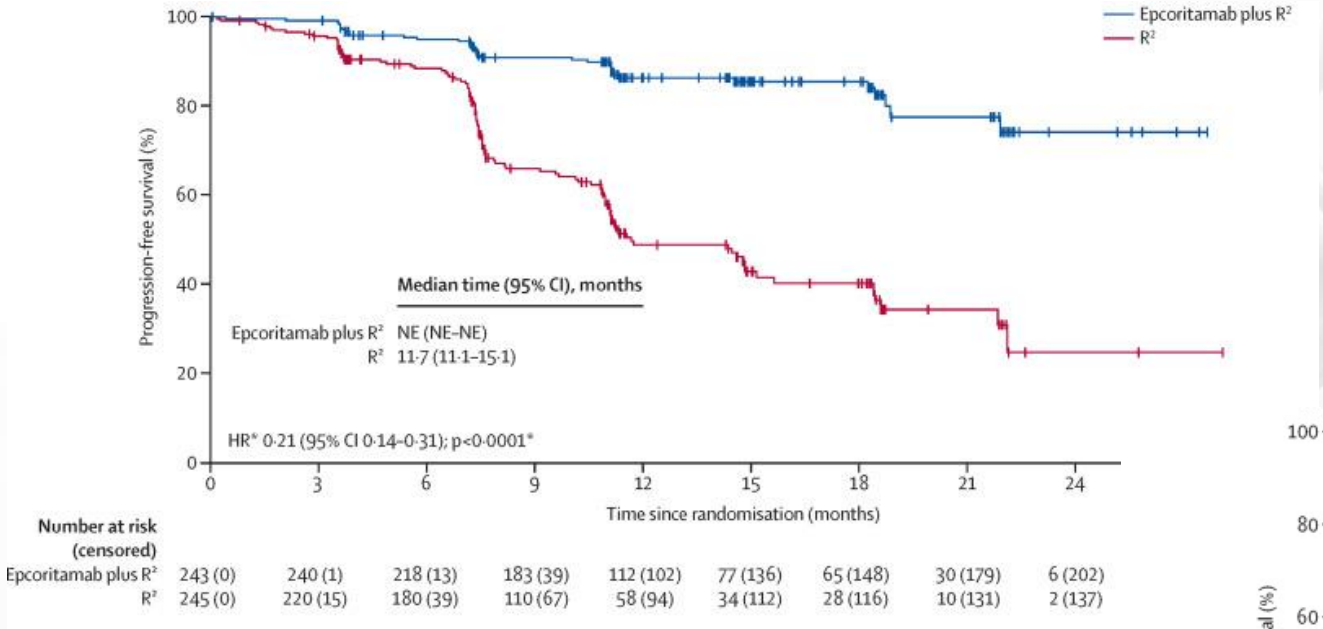
Adverse event	Tafa-R² (n=274)	R² (n=272)	Total (N=546)
Any serious adverse event	99 (36%)	86 (32%)	185 (34%)
Pneumonia	21 (8%)	13 (5%)	34 (6%)
COVID-19	19 (7%)	7 (3%)	26 (5%)
COVID-19 pneumonia	14 (5%)	5 (2%)	19 (3%)
Acute kidney injury	8 (3%)	4 (1%)	12 (2%)
Febrile neutropenia	7 (3%)	6 (2%)	13 (2%)
Pyrexia	4 (1%)	7 (3%)	11 (2%)
Sepsis	3 (1%)	3 (1%)	6 (1%)
Neutropenia	2 (1%)	3 (1%)	5 (1%)
Abdominal pain	0	5 (2%)	5 (1%)
Diarrhoea	0	3 (1%)	3 (<1%)

Tafasitamab targets CD19 and could lead to loss of antigen expression eliminating CAR T-cell therapy as a treatment option

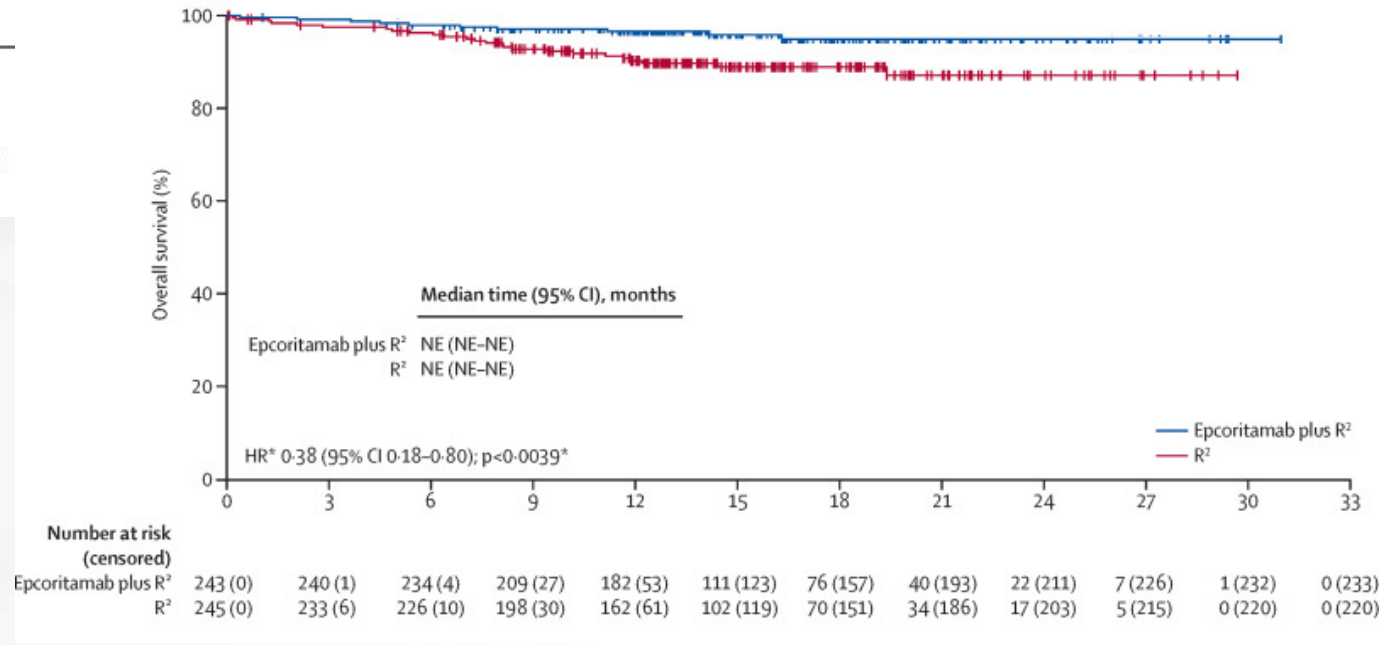
Mildly increased toxicity profile with tafa-R²

Sehn et al. *Lancet* 2026

EPCORE-FL1: R² vs Epcoritamab-R²



Data are immature and did not reach the threshold for significance



Falchi et al. *The Lancet* 2026

Epcoritamab adds toxicity and reduces accessibility

Adverse Event	Epcoritamab plus R² (n=243)		R² (n=238)	
	Any grade	Grade ≥3	Any grade	Grade ≥3
Any adverse event	**242 (>99%)**	**219 (90%)**	**235 (99%)**	**161 (68%)**
Adverse event related to study drug	236 (97%)	203 (84%)	213 (90%)	129 (54%)
Serious adverse event	135 (56%)	—	69 (29%)	—
Adverse event leading to treatment discontinuation	46 (19%)	—	29 (12%)	—
Epcoritamab	21 (9%)	—	—	—
Rituximab	7 (3%)	—	12 (5%)	—
Lenalidomide	45 (19%)	—	29 (12%)	—
Adverse event of special interest ≥20%				
Infections*	**188 (77%)**	**81 (33%)**	**125 (53%)**	**37 (16%)**
Neutropenia	**180 (74%)**	**167 (69%)**	**123 (52%)**	**100 (42%)**
Cytokine release syndrome	**85 (35%)**	**0**	**1 (<1%)**	**0**
Anaemia	68 (28%)	19 (8%)	41 (17%)	11 (5%)
Thrombocytopenia	67 (28%)	23 (9%)	44 (18%)	15 (6%)
Pyrexia	58 (24%)	1 (<1%)	33 (14%)	3 (1%)
Rash	58 (24%)	19 (8%)	53 (22%)	9 (4%)
COVID-19	54 (22%)	7 (3%)	32 (13%)	4 (2%)

90% grade ≥3 adverse events

More than 2× as many grade ≥3 infections — and 35% CRS

Falchi et al. *The Lancet* 2026

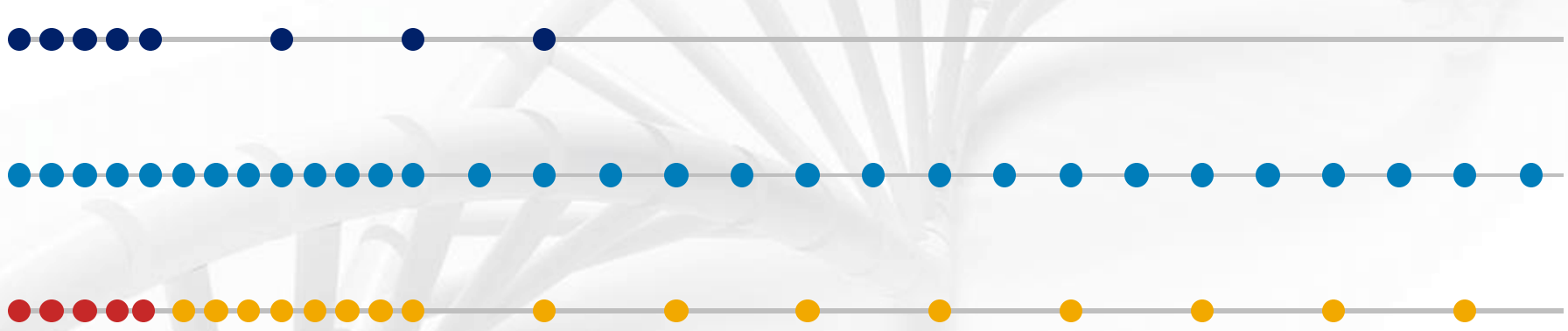
X plus R² is burdensome to administer

Clinic visits across the 12 treatment cycles (each dot = one visit)

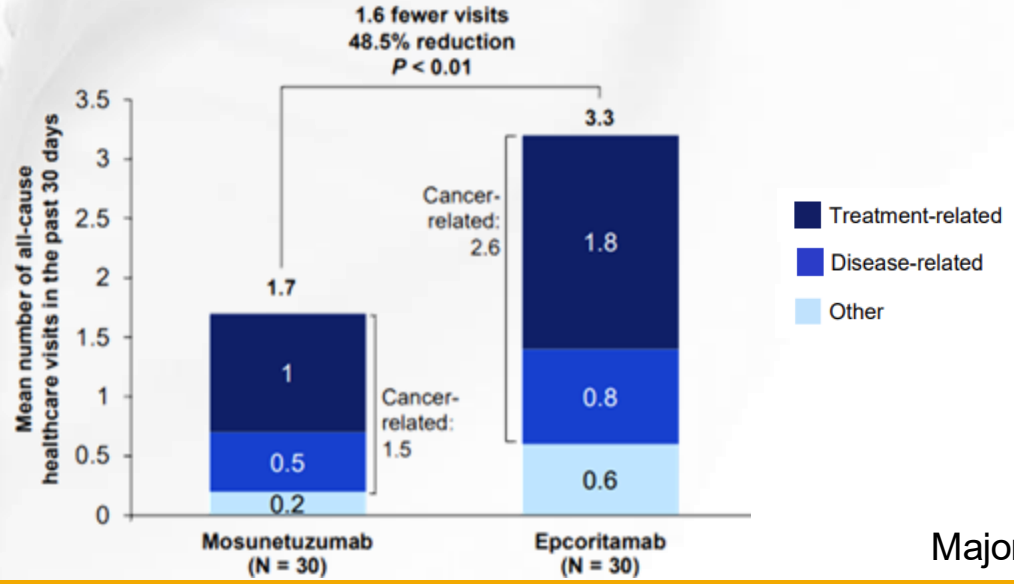
R²
≈ 8 clinic visits

Tafasitamab-R²
≈ 30 clinic visits

Epcoritamab-R²
≈ 21 visits · early doses CRS-monitored



Both newer regimens require roughly 3–4× more clinic visits than R² — and epcoritamab's early doses (red) require CRS monitoring.



Major et al. *The Oncologist* 2026

Final Scorecard: R² remains the balanced choice

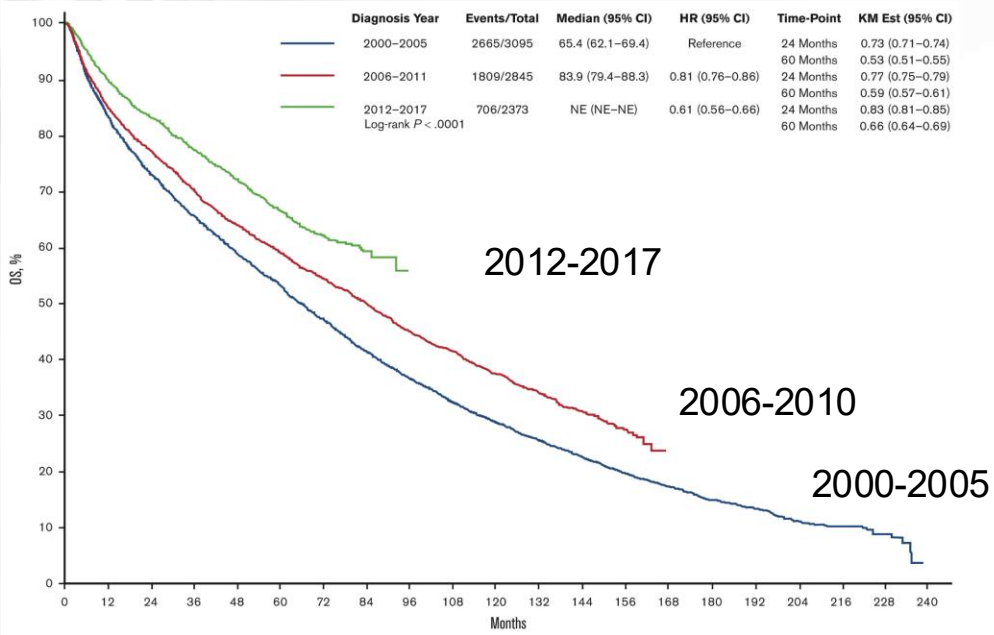
Measure	R² (standard)	Tafasitamab-R² (inMIND)	Epcoritamab-R² (EPCORE FL-1)
Overall survival	Proven — 5-yr OS 83% in AUGMENT	Immature; no significant benefit yet	Immature, trend towards benefit
Progression-free survival	---	HR 0.43	**HR 0.21 (largest benefit)**
High grade toxicity	Manageable, few serious side effects	Similar to R²	**More cytopenias, high grade infections, and CRS risk**
Administration & access	Oral + IV rituximab; most simple	Adds over 20 IV infusions visits over 12 cycles	Adds ~15 visits + CRS monitoring
Other factors	---	May affect CD19 expression and candidacy for future CAR T-cell therapy	Alternative BiTE with less burdensome administration schedule is available
Financial cost*	≈ $130K (backbone)	≈ $320K (+$190K)	**≈ $580K (+$450K)**

**Approximate US cost using generic lenalidomide + rituximab biosimilar over ~12 cycles; the lenalidomide + rituximab backbone is shared by all three regimens.*

Favorable Intermediate Unfavorable

Conclusions

- Follicular lymphoma is an indolent disease with good long term survival outcomes
- R^2 is an **effective, safe, and easy to administer regimen** and remains an excellent option for patients with relapsed/refractory FL
- More intensive regimens, including tafa-R^2 and epcor-R^2, **add toxicity and treatment burden** without an established improvement in OS outcomes
- Selected fit and highly motivated patients are good candidates for more intensive therapy, but for most R/R FL patients R^2 should remain the standard



Chihara et al. *Blood Neoplasia* 2025