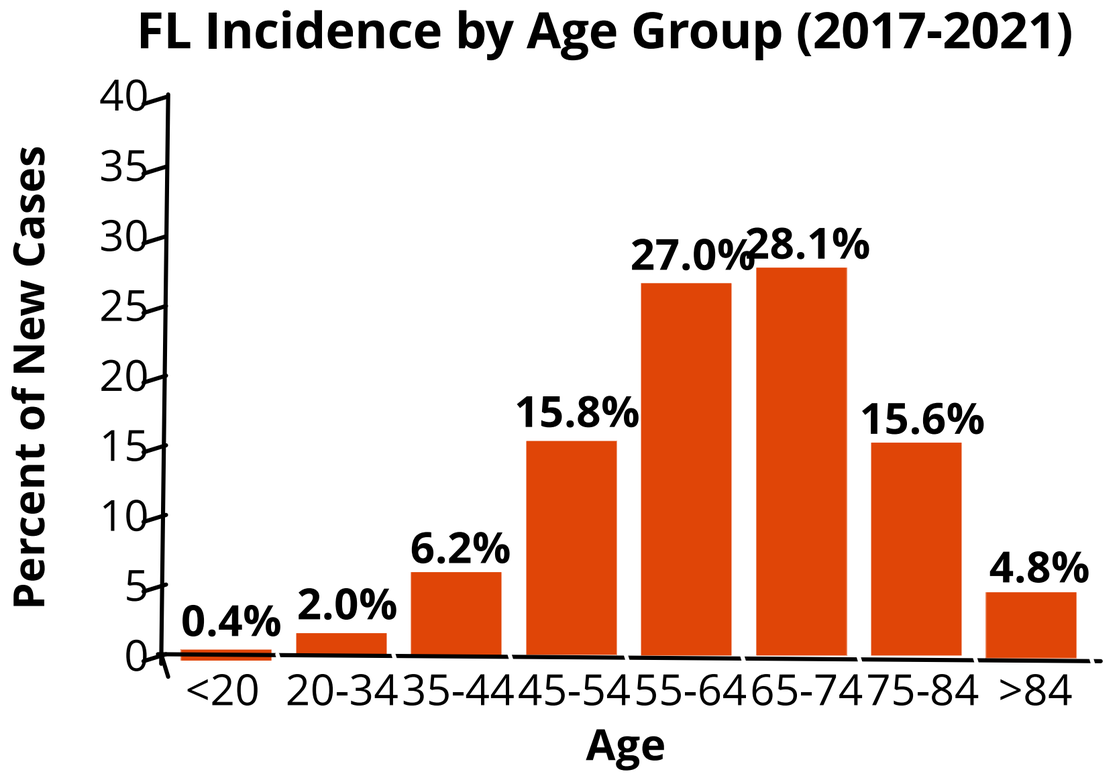
TPH Autólogo en Folicular POD24: No, existen opciones mejores

By Adrián Mosquera

Follicular Lymphoma: Key Principles

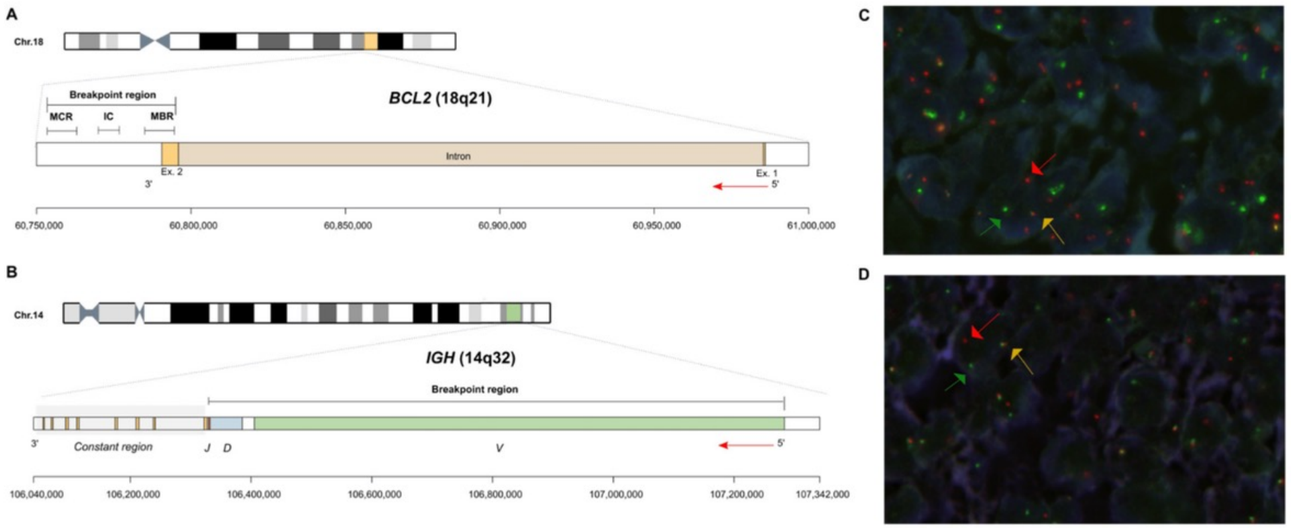
- Indolent and incurable
- Long life expectancy for most patients:
- 5-yr relative survival after diagnosis (90%)
- More common in older adults
  - Median age at diagnosis: 64 yr
  - 8.7% of patients are aged ≤44 yr
- Treatment is primarily based on symptoms rather than stage or biology
- Event-based outcomes can determine prognosis (ie, POD24); however, unable to determine individual prognosis at diagnosis
- Grade, FLIPI and FLIPI-2, molecular assessments imprecise

- **Limited data regarding optimal sequencing**
  - Many new regimens and modalities
  - Lifelong risk for transformation



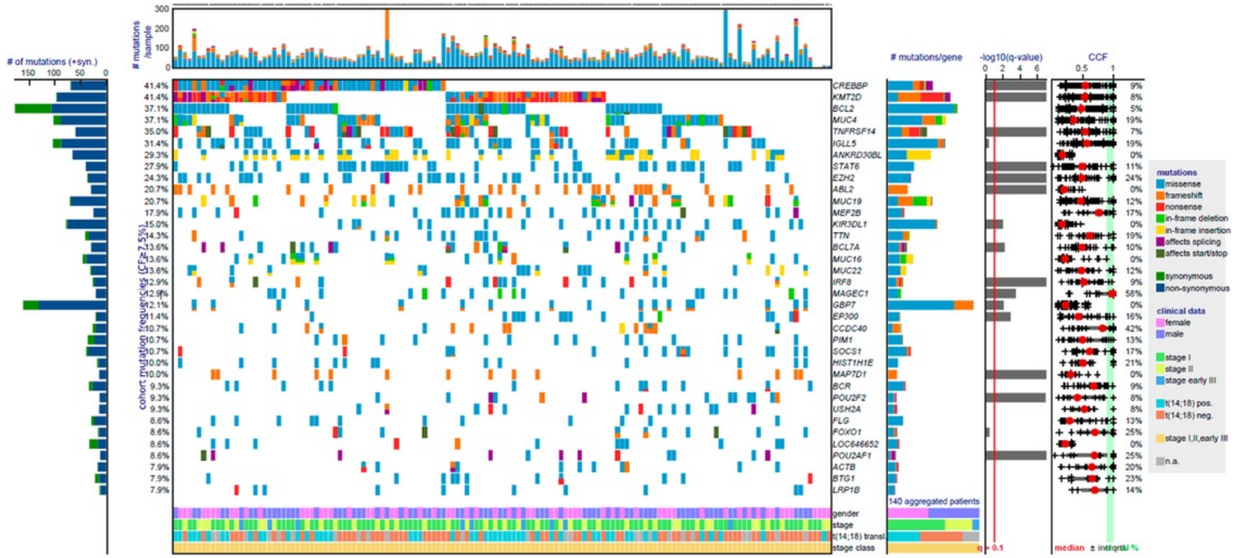
Follicular Lymphoma Is Biologically Complex

Translocation of IGH::BCL2 Breakpoints in FL[1]



t(14;18)(q32;q21) is present in 80%-85% of cases

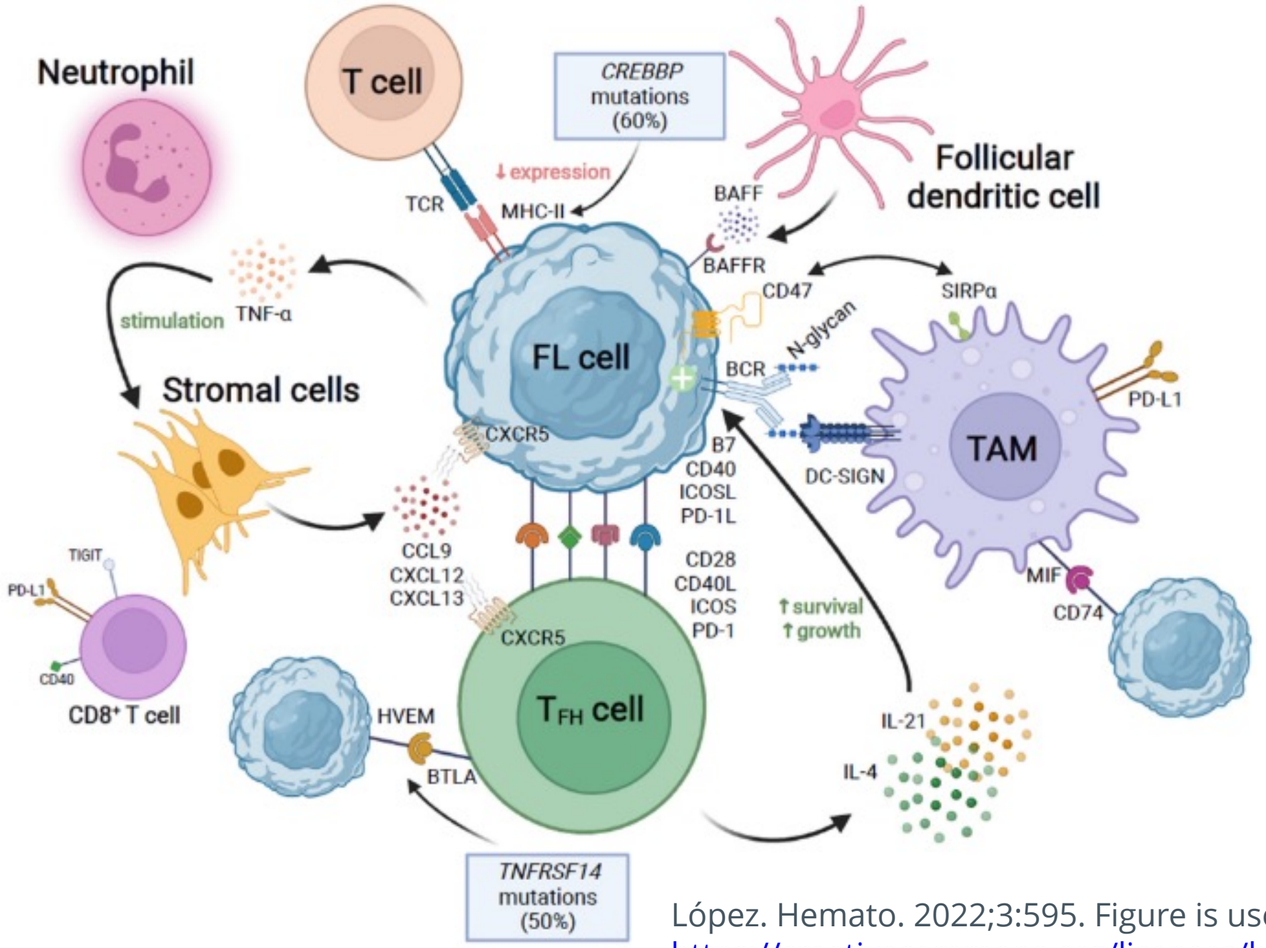
Landscape of Mutations in Intestinal Follicular Lymphoma[2]



BCL2 and *PIM1* mutations are most common

1. López. Hemato. 2022;3:595. Figure is used without changes per https://creativecommons.org/licenses/by/4.0/.
2. Kalmbach. Leukemia. 2023;37:2058. Figure used without changes per http://creativecommons.org/licenses/by/4.0/r.

FL Pathogenesis: Highly Dependent on Tumor Microenvironment



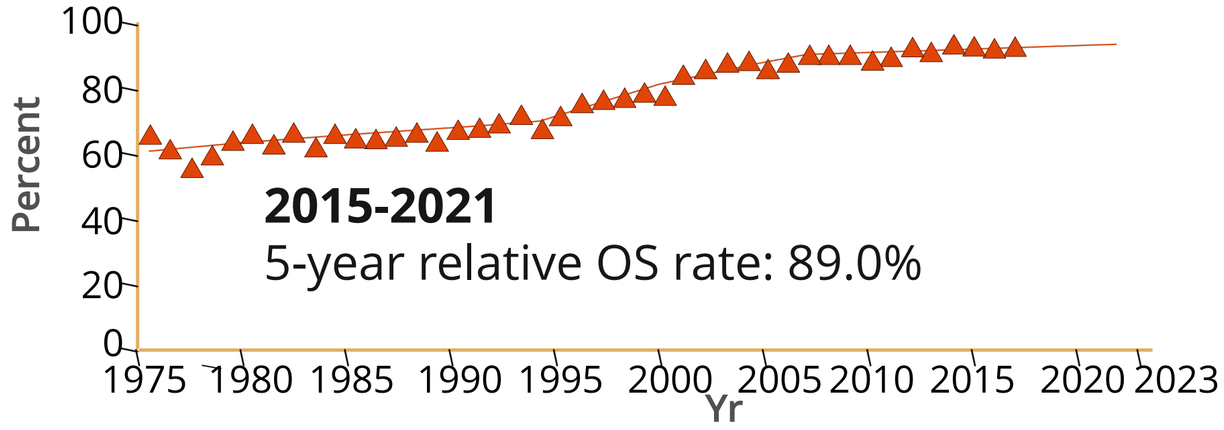
López. Hemato. 2022;3:595. Figure is used without changes per https://creativecommons.org/licenses/by/4.0/.

FL Remains an Important Cause of Death

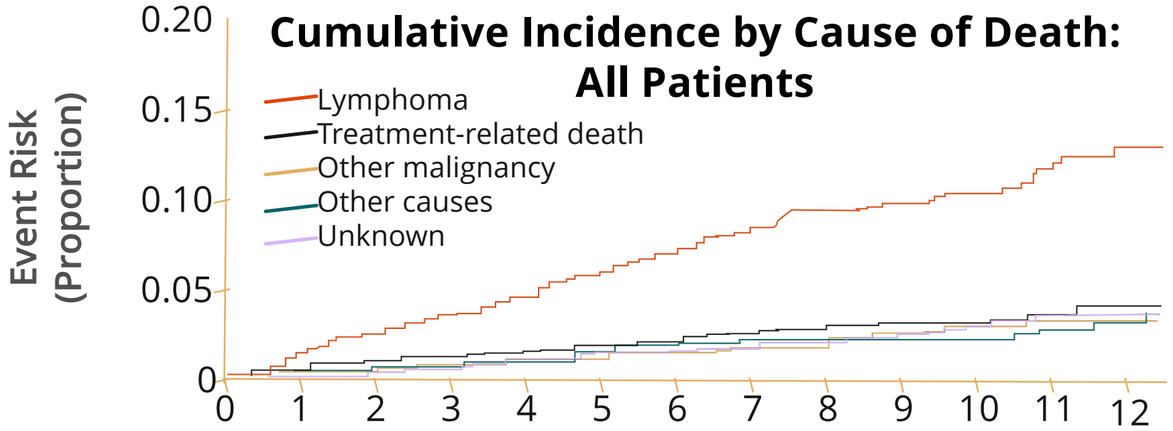
Pooled analysis of newly diagnosed FL in France (2001-2013) and US (2002-2012)

seer.cancer.gov/statfacts/html/follicular.html. Sarkozy. JCO. 2019;37:144.

5-Year Relative Survival (1975 -2017)

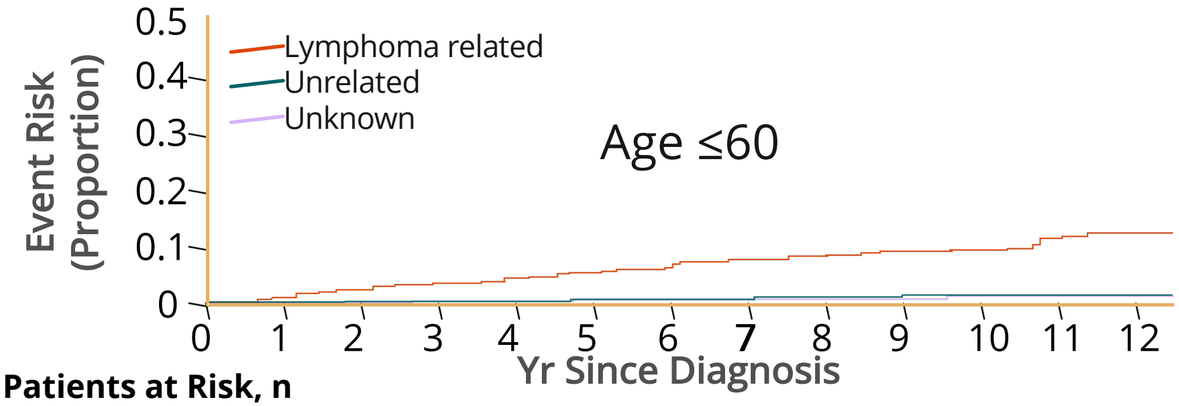


Cumulative Incidence by Cause of Death: All Patients



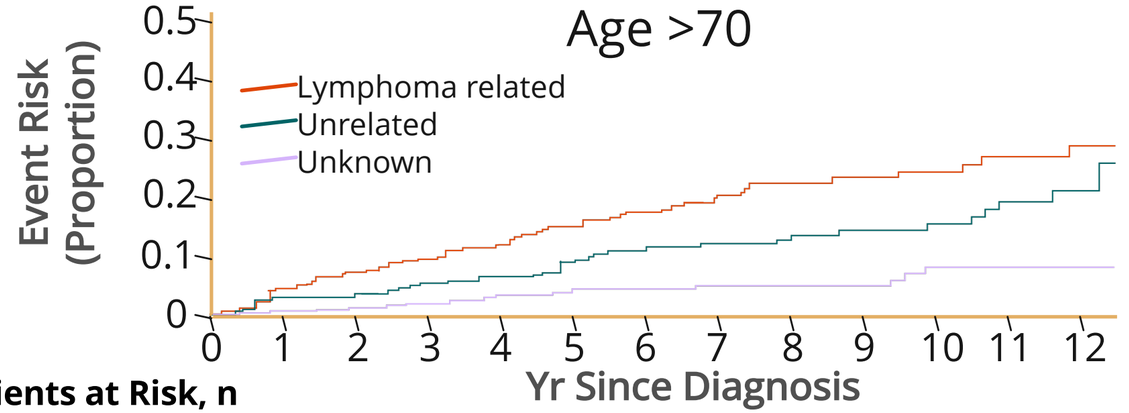
Patients at Risk, n

All	1654	1591	1532	1422	1275	1099	930	759	607	472	348	233	147



Patients at Risk, n

Age <60	916	896	864	807	745	647	559	462
		377	294	223	151	102		

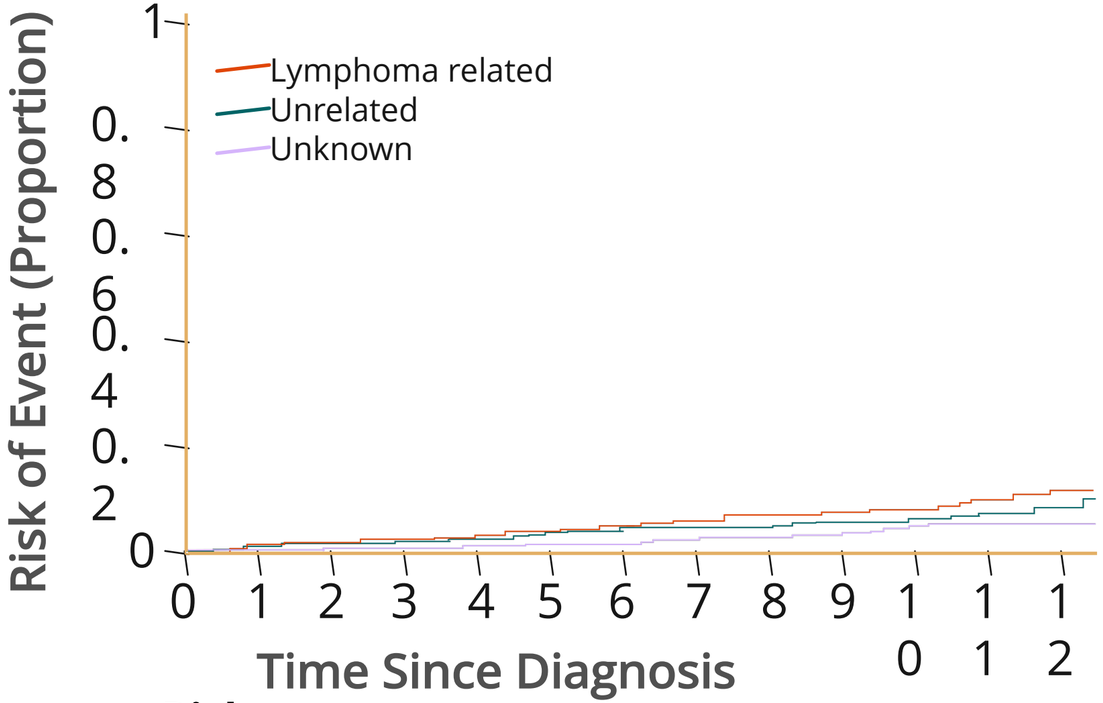


Patients at Risk, n

Age 70+	300	270	256	228	198	160	128	102
		78	62	44	32	14		

FL: Histological Transformation

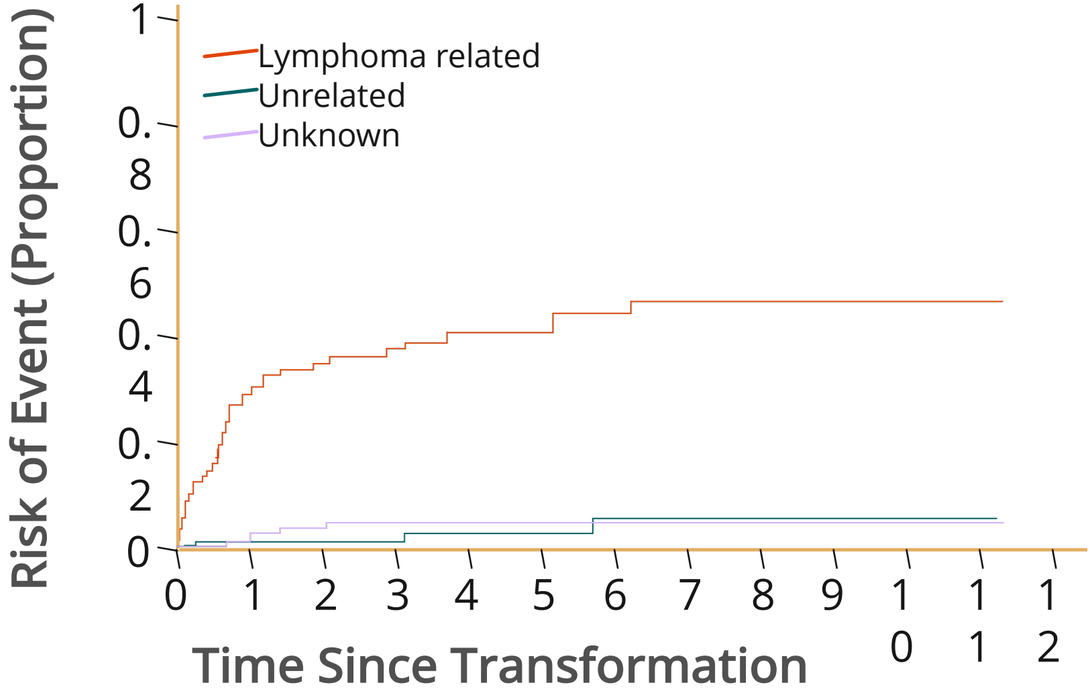
Cumulative Incidence for the Competing Risks of Cause of Death Without FL Transformation



Patients at Risk, n (yr)

No transformation	920	883	854	800	707	598	499
	400	305	247	176	118	65	

Cumulative Incidence for the Competing Risks of Cause of Death With FL Transformation



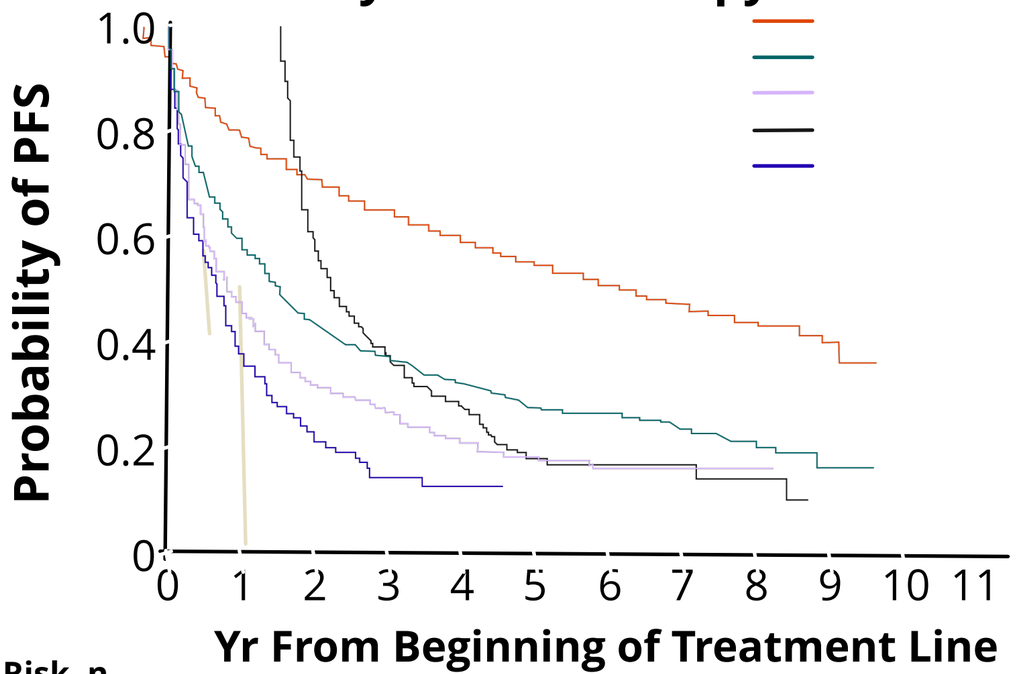
Patients at Risk, n (yr)

Transformation	97	87	80	72	63	54	47	36
		26	22	19	14	9		

Sarkozy. JCO. 2019;37:144.

Survival Decreases by Line of Therapy in the Era of Chemoimmunotherapy

National LymphoCare Study (2004-2007): PFS by Line of Therapy[1]

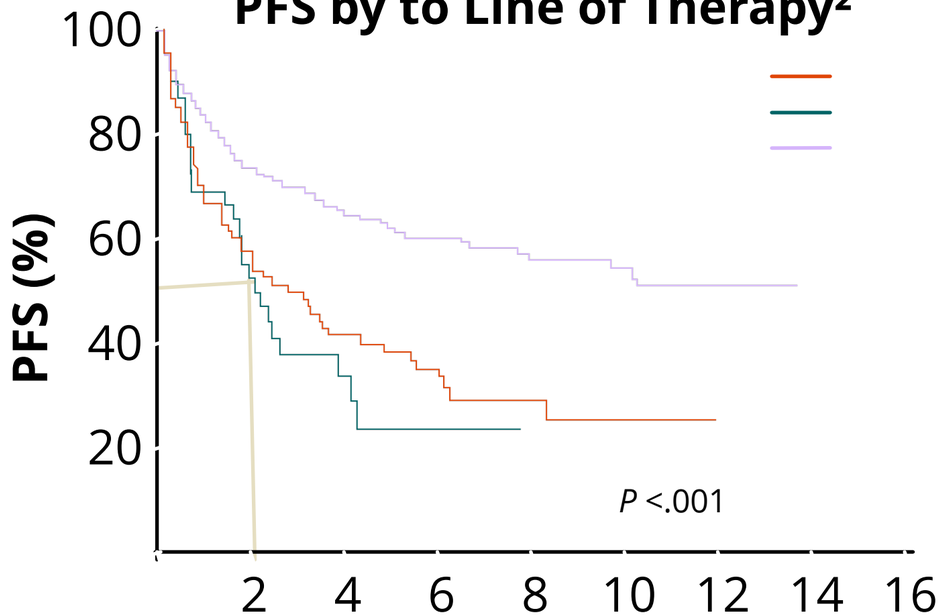


Patients at Risk, n

First line	2429	1916	1602	1381	1202	1035	869	635	329	96	1
Second line	889	489	331	256	199	137	104	57	24	5	0
Third line	438	181	109	78	50	30	18	5	1	0	
Fourth line	229	91	49	24	14	8	3	1	0		
Fifth line	123	42	19	9	5	0					

1. Link. Br J Haematol. 2019;184:660.

Patients Who Received CIT (2001-2014): PFS by to Line of Therapy[2]



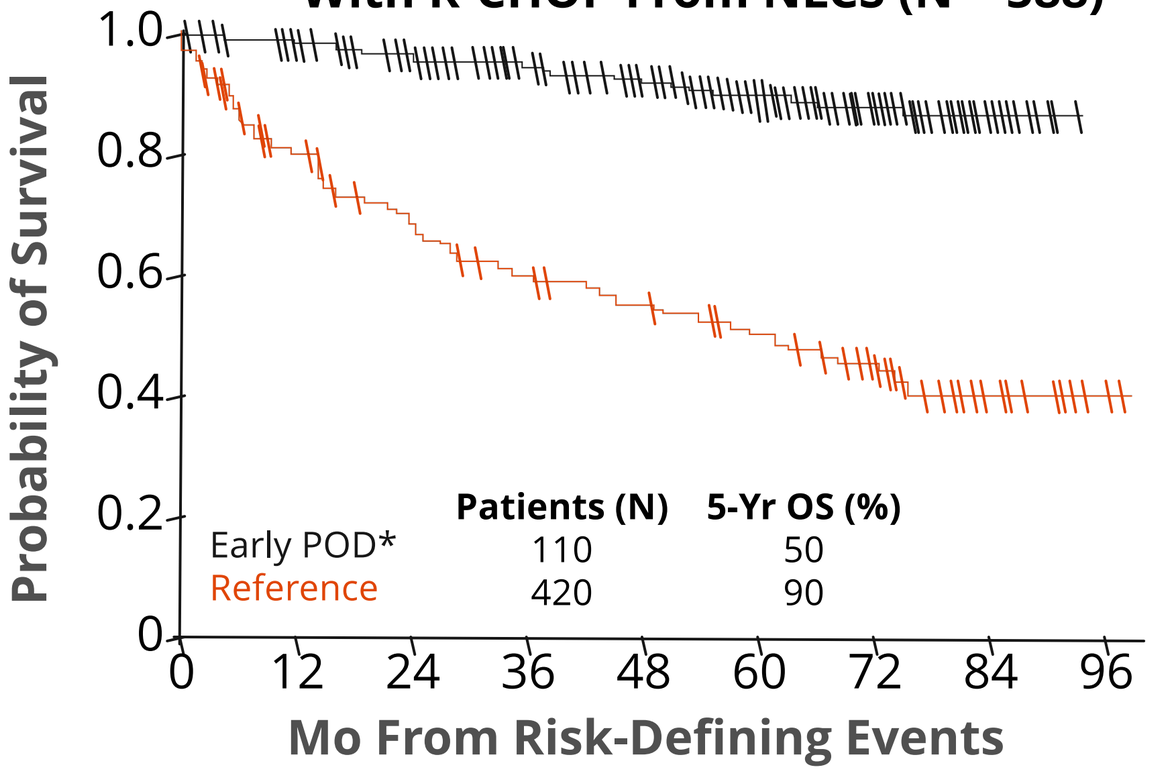
Patients at Risk, n

First line	348	210	148	100	62	31	7	0	0
Second line	111	47	27	20	8	5	0	0	0
Third line	41	19	7	3	0	0	0	0	0

2. Rivas-Delgado. Br J Haematol. 2019;184:753.

Early POD and PET Positivity at End of CIT Predicts Poor Prognosis in Patients With FL

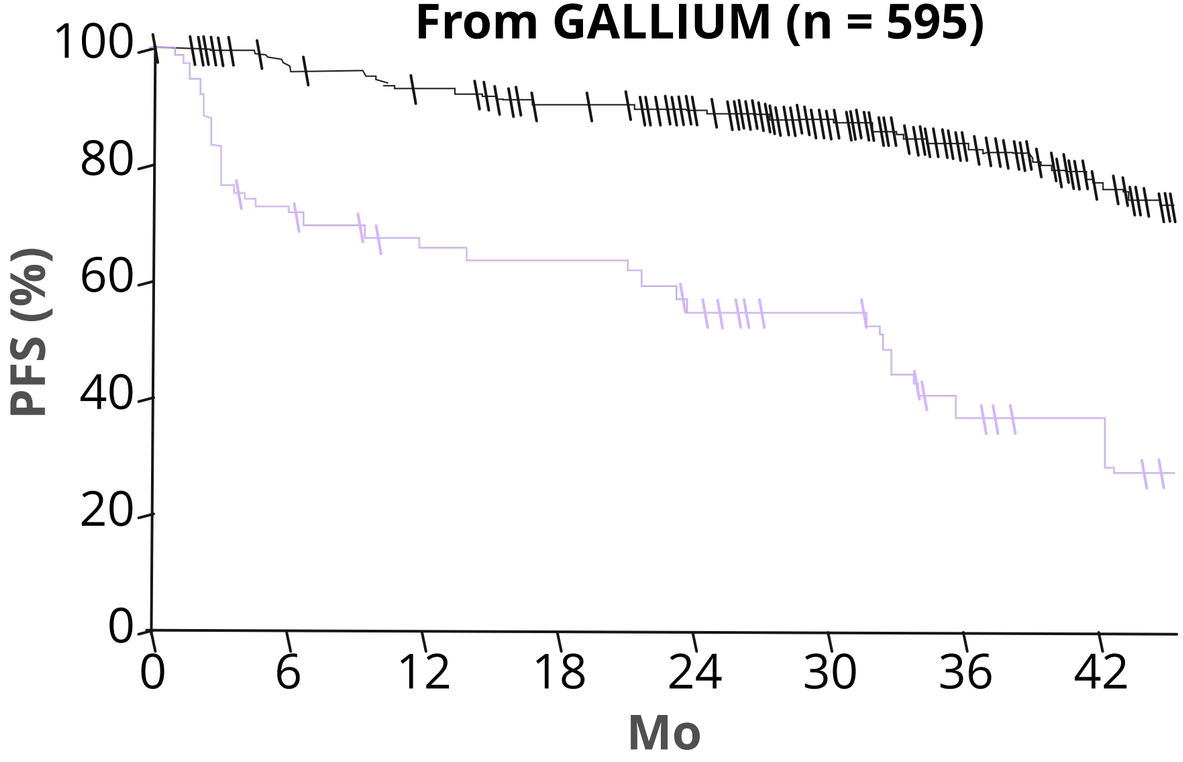
OS of Patients With FL Treated With R-CHOP From NLCS (N = 588)



*Early POD: relapse within 2 yr.
Similar results found for an independent validation set and for first-line R-CVP and R-fludarabine in exploratory analyses.

Casulo. JCO. 2015;33:2516. Trotman. Lancet Oncol. 2018;19:1530. Nielsen. ASCO 2020. Abstr 8025.

PFS by PET Assessment† at End of CIT From GALLIUM (n = 595)

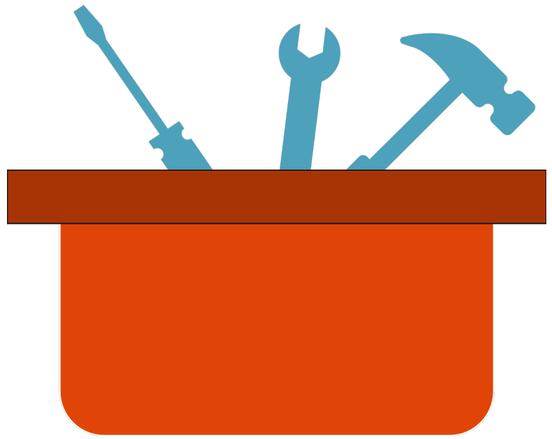


	n	30-Mo PFS, %	72-Mo PFS, %	72-Mo OS, %
CR at 2.5 yr	448	87.4	70.0‡	92.0‖
No CR at 2.5 yr	60	54.9	29.4§	79.6¶

†According to Lugano 2014 criteria.
‡n = 449. §n = 56. ‖n = 450. ¶n = 69.

Treatment Options for R/R FL

Advanced Stage
FL
Grade 1-3a



2L Options

- Chemo + ritux or obin
- Len + ritux or obin
- Tafasitamab + Len + ritux
- Rituximab monotherapy
- Tazemetostat
- Auto-HSCT

On November 18, 2025, the FDA approved epcoritamab + R² for R/R FL based on the results of the EPCORE FL-1 trial. The trial demonstrated superiority of PFS and ORR in the epcoritamab arm (PFS HR: 0.21; *P* <.0001; ORR: 89% vs 74%)*

*Epcoritamab PI. ASH 2025.

3L+ Options

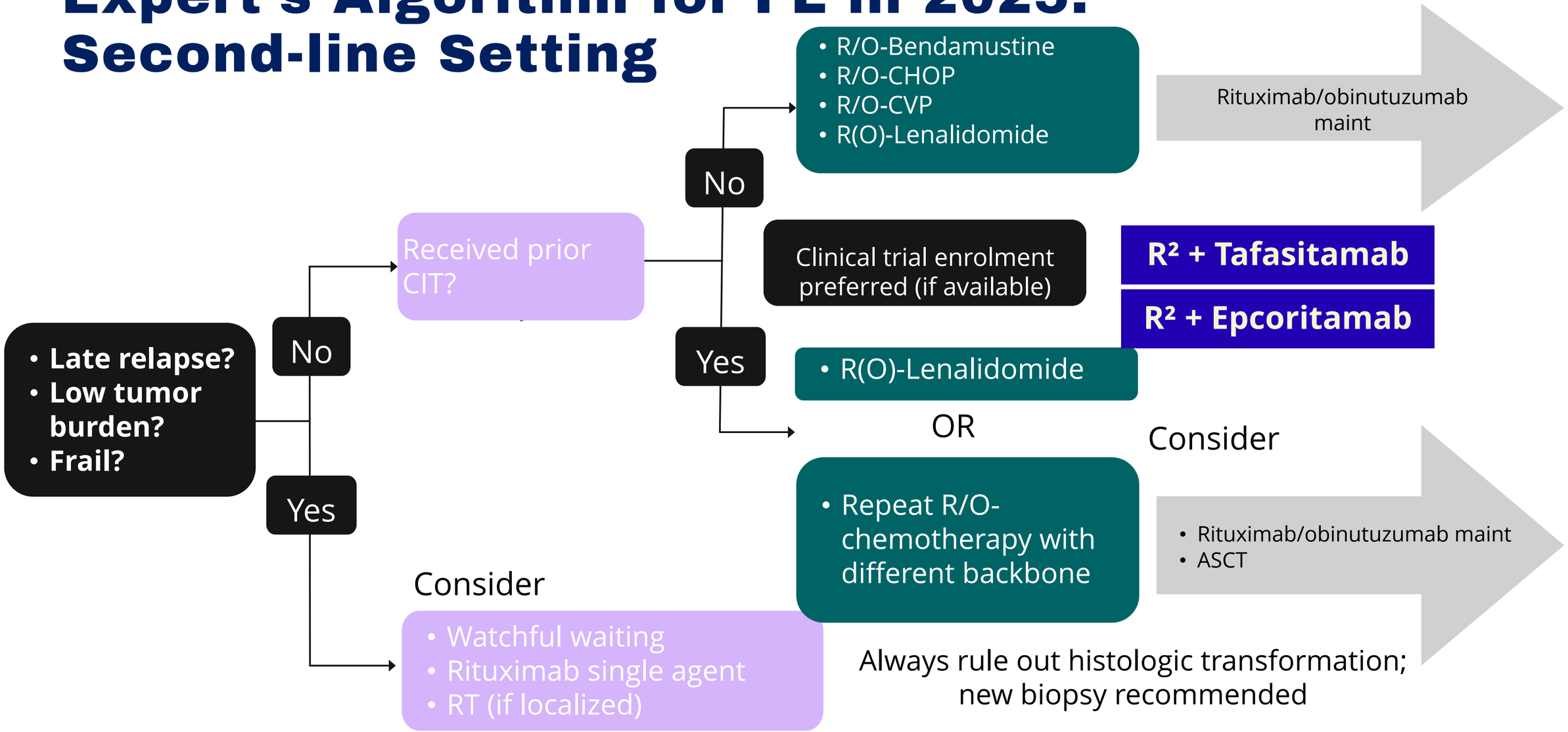
- **Bispecific antibody**
  - Mosunetuzumab
  - Epcoritamab
  - *Odronextamab (not FDA approved)*
- **CAR T-cell therapy**
  - Axi-cel
  - Tisa-cel
  - Liso-cel
- Len + ritux or obin
- Tafasitamab + Len + ritux
- Tazemetostat
- Zanubrutinib + obin
- Allogeneic-HSCT

*EMA authorized.

Key Patient and Disease Factors in Determining Next Therapy

Factor	Comments
Indications	• Does the patient meet the current indications for intensive therapies? • Does the patient meet the criteria for a clinical trial?
Kinetics of disease progression	• Would the patient be able to wait for the logistics of a clinical trial? • Does disease bulk and acuity of symptoms affect choice? • Is there a concern for transformation?
Immediate prior therapy	• What has the patient previously received and what was benefit/tolerance? • How do cytopenias and short duration of response affect next line of treatment?
Transportation	• Does the patient rely on caregivers? • Will the treatment schedule be manageable with caregiver's work schedule? • How far does the patient live from the treatment center?
Non–disease-related comorbidities	• eg, HTN, depression

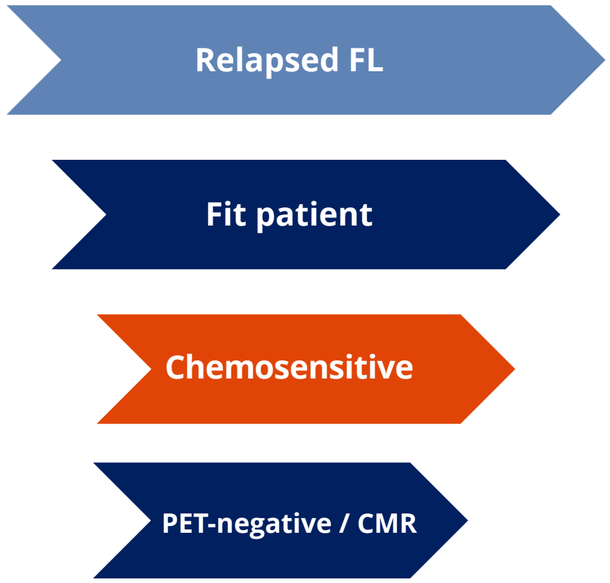
Expert's Algorithm for FL in 2025: Second-line Setting



Leonard. Blood. 2022; 140:561.

Auto-HCT only works in a narrow “sweet spot”

That sweet spot is selected, fit, chemosensitive disease — usually before true refractory biology dominates.



The candidate pool narrows step by step before auto-HCT becomes reasonable.

Where refractory FL clashes with the platform

NOT RESCUE

Auto-HCT consolidates response; it does not create sensitivity where none exists.

BIOLOGY FIRST

PET positivity, rituximab refractoriness, or chemo-refractory disease predict worse outcomes.

SELECTIVE USE

Modern reviews reserve it for highly selected patients, usually in later remission but controlled disease.

Practical framing

- “True refractory” FL often fails before it reaches the transplant sweet spot.
- The more rescue therapy needed to obtain control, the less compelling auto-HCT becomes.
- So the core limitation is biological selection, not just toxicity.

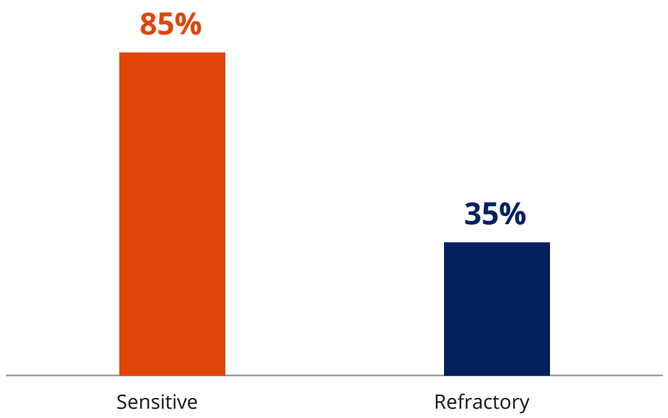
In refractory FL, the main criticism is not that auto-HCT never works — it is that its best biology is not the biology of many real refractory cases.

Refs: Bond 2022

When pre-transplant disease control is weak, outcomes collapse

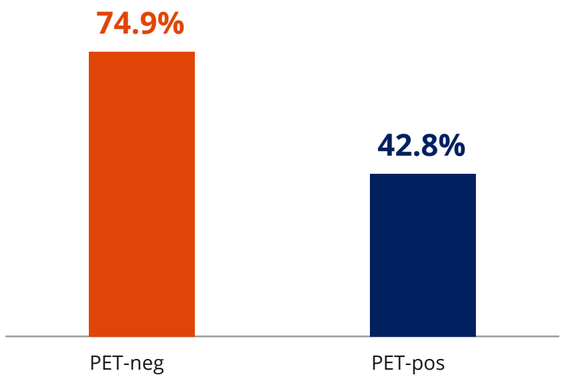
Three different datasets point in the same direction: uncontrolled biology predicts poor post-transplant durability.

3-year PFS after ASCT by rituximab sensitivity



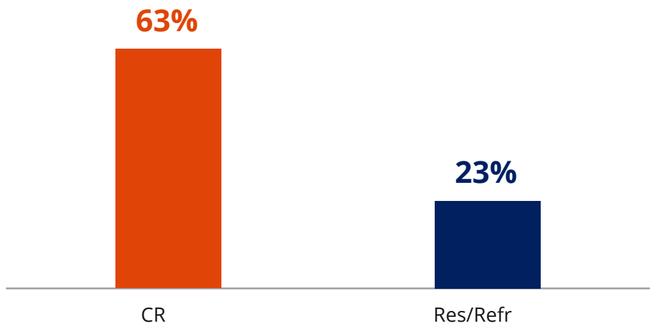
Relapsed FL after ASCT

3-year PFS by PET/CT before ASCT



Deauville threshold ≥3

12-year PFS by disease status at ASCT



Spanish GELTAMO registry

85 → 35

The rituximab-refractory drop is too large to ignore.

PET negativity matters

Even among CT-chemosensitive patients, metabolic positivity still worsens prognosis.

Key message

Auto-HCT is a consolidation tool for controlled disease — not a dependable answer for active refractory FL.

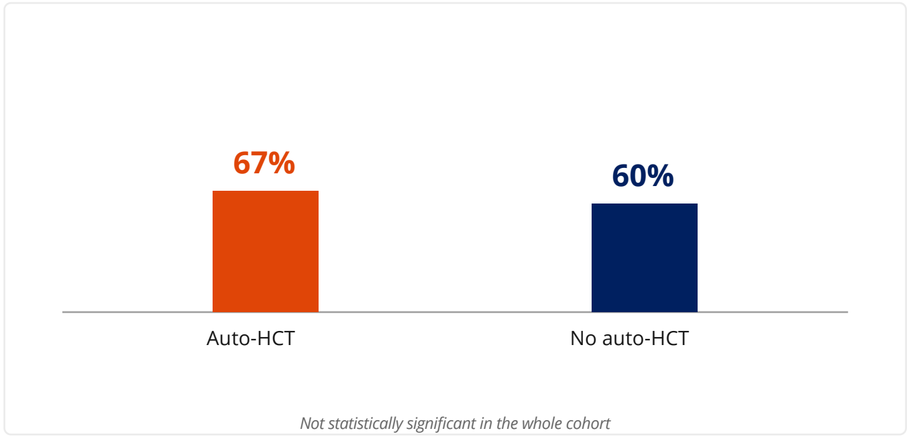
Refs: Phipps 2015; Alcantara 2015; Jiménez-Ubieto 2017

Overall-survival benefit is selection-dependent, not universal

In POD24 / early therapy failure, the headline benefit appears only in the early, best-selected subgroup.

Entire ETF / POD24 cohort

5-year overall survival

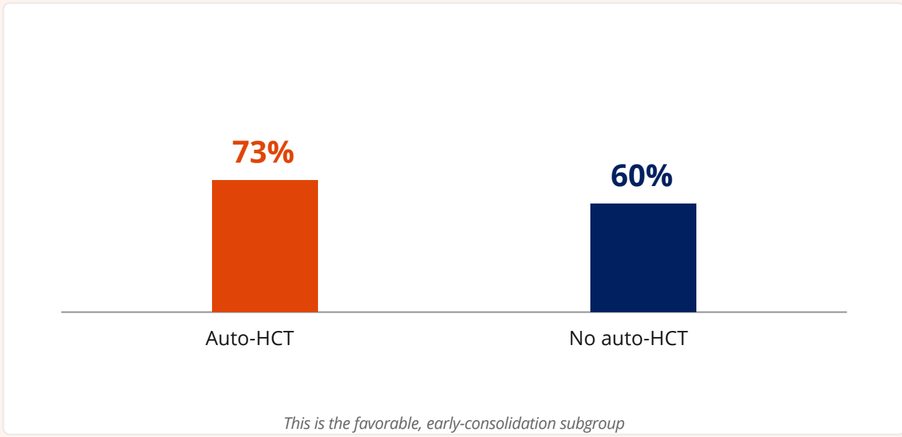


Not statistically significant in the whole cohort

Interpretation: supports selection, not routine use

Only when ASCT was used early

≤ 1 year from ETF



This is the favorable, early-consolidation subgroup

Interpretation: a narrow window, not a blanket rule

Tumor-board framing

If the benefit appears only after early, favorable selection, the argument weakens for patients with genuinely refractory disease later in the course.

Refs: Casulo 2018

The upfront price: severe toxicity is common, and early mortality is real

Acute-toxicity datasets are mostly lymphoma-wide, but they represent the same HDT/ASCT platform used in FL.

Short-term toxicity pattern

- **Mucositis**
- **Febrile neutropenia**
- **Infection / sepsis**
- **GI toxicity**
- **Pneumonitis**
- **Cardiovascular events**

Majority developed severe toxicities

Most frequent grade ≥3 issues in BEAM-AHCT cohorts were febrile neutropenia, GI, infectious, and cardiovascular toxicities.

Useful numbers for the discussion

1.79%
Dahi 2021
100-day NRM (age 60–69)

2.99%
Dahi 2021
100-day NRM (age ≥70)

HR 3.36
Age ≥70 carried more grade ≥3 cardiovascular toxicity.

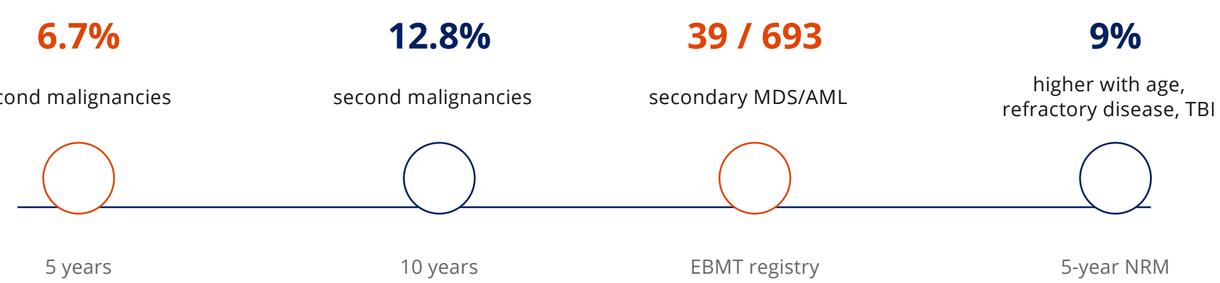
For an indolent lymphoma, this burden matters even before considering whether disease control will actually be durable.

Refs: Bond 2022; Dahi 2021

The long-tail price: second cancers and survivorship burden

Late harm carries extra weight in FL because expected survival can be long even without transplant.

Late-event timeline after auto-HCT



This is the strongest “against” argument in indolent FL

Late toxicities can outlive the early transplant story: therapy-related myeloid neoplasms, second solid cancers, organ sequelae, sexual/fertility issues, and financial toxicity.

What persists beyond relapse-risk curves

- Secondary cancers, especially t-MDS/AML
- Cardiovascular, pulmonary, renal, endocrine, and sexual-health late effects
- Quality-of-life and work/financial consequences
- Need for long-term survivorship follow-up

13-fold

Bhatia 2005

Excess risk of late death vs the general population in long-term auto-HCT survivors.

Refs: Jiménez-Ubieto 2017; Montoto 2007; Majhail 2017; Bhatia 2005

Bottom line for a 2025 discussion

Auto-HCT is a narrow consolidation tool for controlled disease — not a default rescue strategy for biologically refractory follicular lymphoma.

1

Benefit depends on chemosensitivity and PET-negative / metabolically controlled disease before intensification.

2

Acute burden is substantial: mucositis, infection, febrile neutropenia, GI toxicity, cardiovascular toxicity, and measurable early NRM.

3

Late costs are unusually important in FL: second malignancies, t-MDS/AML, organ sequelae, and survivorship toxicity.

Refs: Bond 2022; Phipps 2015; Casulo 2018; Jiménez-Ubieto 2017; Montoto 2007

AUGMENT: R² vs Rituximab Monotherapy in R/R iNHL

Multicenter, placebo-controlled, randomized phase III trial

- **Primary endpoint:** PFS by IRC (2007 IWG criteria without PET)

Stratified by prior rituximab (yes vs no), time since last therapy (≤ vs >2 yr), histology (FL vs MZL)

Adult patients with R/R grade 1-3A FL or MZL; ≥1 prior chemo/immunotherapy; not rituximab refractory (N = 358)

Rituximab 375 mg/m² + **Lenalidomide** 20 mg/day* (n = 178†)

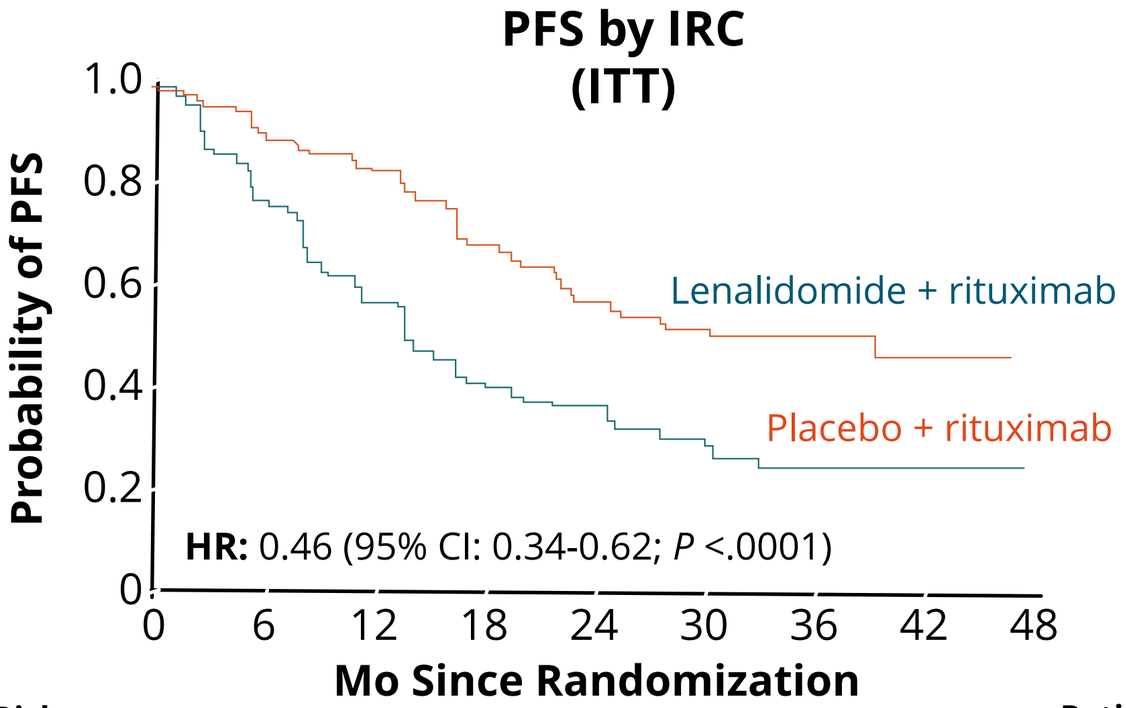
Rituximab 375 mg/m² + **Pbo** (n = 180‡)

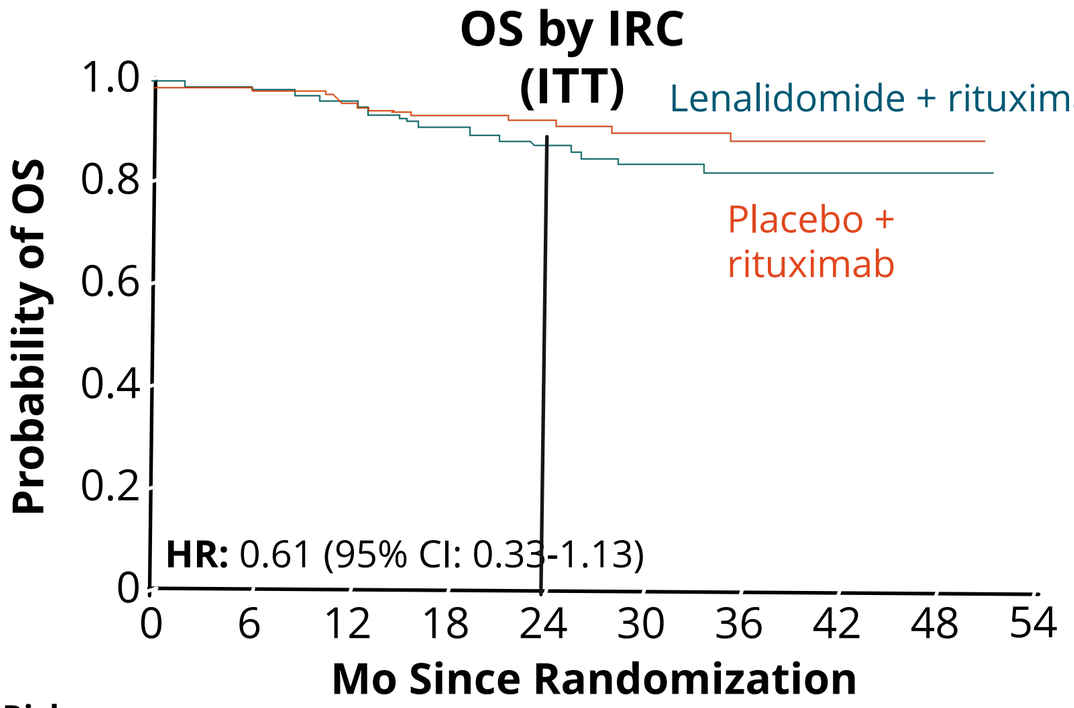
≤12 cycles or until PD, relapse, or intolerability; 5-yr follow-up for OS, SPMs, subsequent treatment, and histologic transformations

Rituximab: Days 1, 8, 15, 22 of cycle 1; Day 1 of cycles 2-5. Lenalidomide: Days 1-21 of 28. Prophylactic anticoagulation recommended for at-risk patients. Growth factor use allowed per ASCO/ESMO guidelines. *10 mg/day if CrCl 30-59 mL/min. **†FL, n = 147; MZL, n = 31. ‡FL, n = 148; MZL, n = 32.**

Leonard. JCO. 2019;37:1188. Leonard. ASH 2022. Abstr 230.

AUGMENT: Survival





Patients at Risk, n

Len + rituximab	178	148	124	91	59	39	20	7	0
Pbo + rituximab	180	132	92	58	40	26	10	4	0

Patients at Risk, n

Len + rituximab	178	167	155	143	122	80	44	15	1	0
Pbo + rituximab	180	176	167	145	116	79	40	14	3	0

- 33% relapsed within 2 yr of initial diagnosis (POD24)
- 50% progressed within 2 yr of most recent tx
- 16% were refractory to most recent tx

Leonard. JCO. 2019;37:1188.

Median follow-up: 28.3 mo.

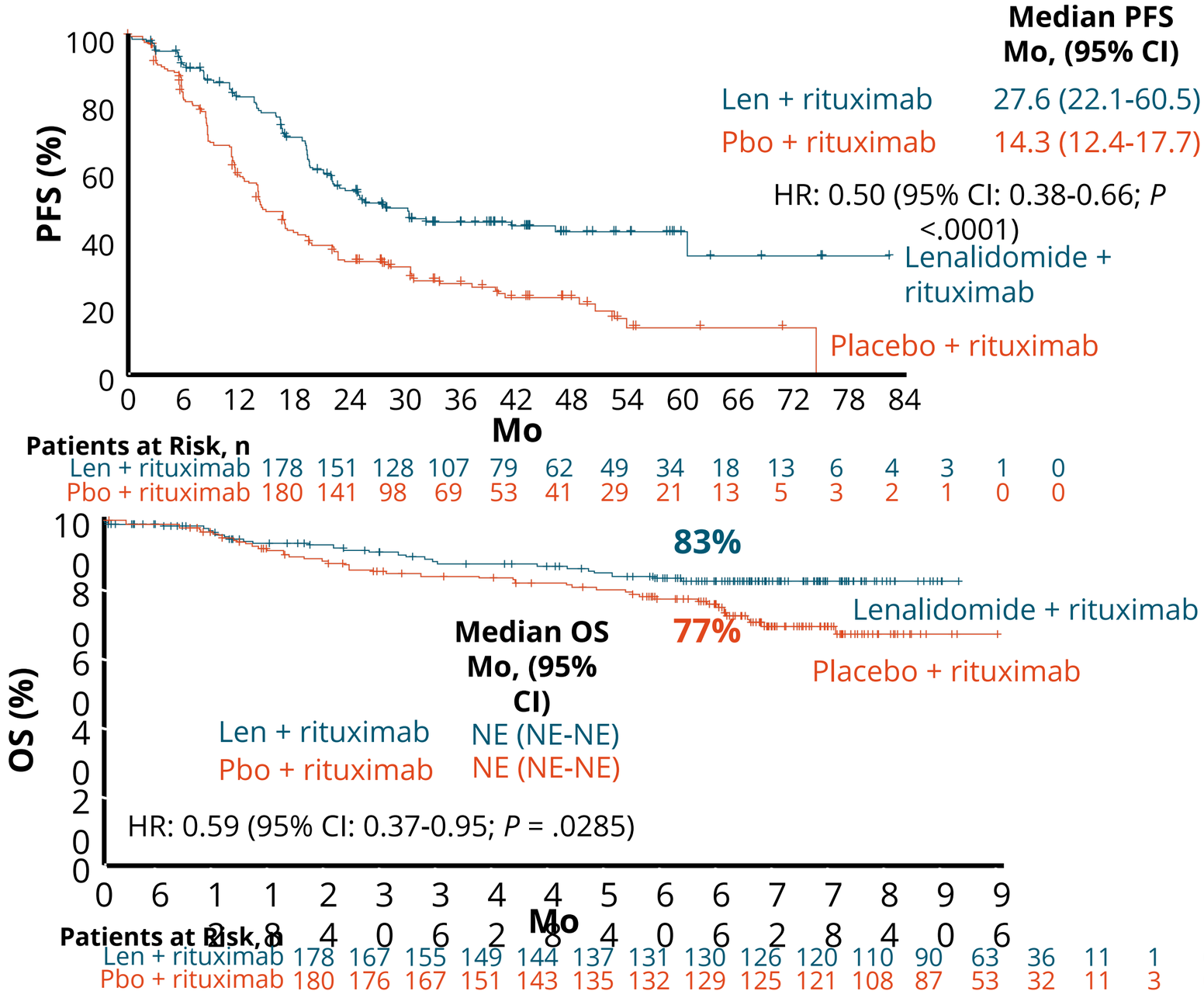
R^2

ORR: 78%; CR 34%
Median DoR: 36.6 mo
Median PFS: 39.4 mo; median OS: NR

AUGMENT: 5-Yr Survival

Median follow-up: 65.9 mo

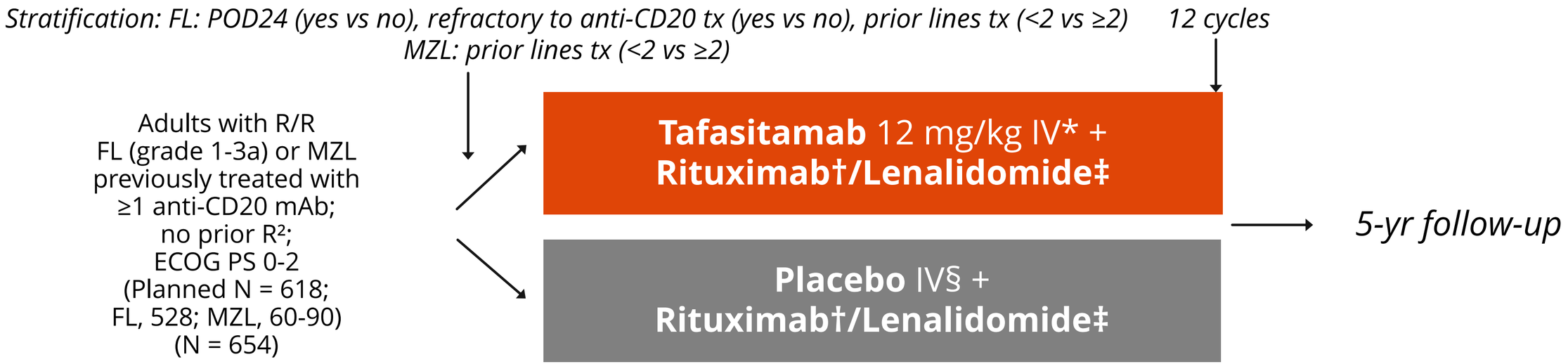
Leonard. ASH 2022. Abstr 230.



InMIND: Tafasitamab + R² vs R² Alone in R/R FL or MZL

Global, double-blind, placebo-controlled, randomized phase III trial
- Tafasitamab: Fc-engineered humanized anti-CD19 mAb

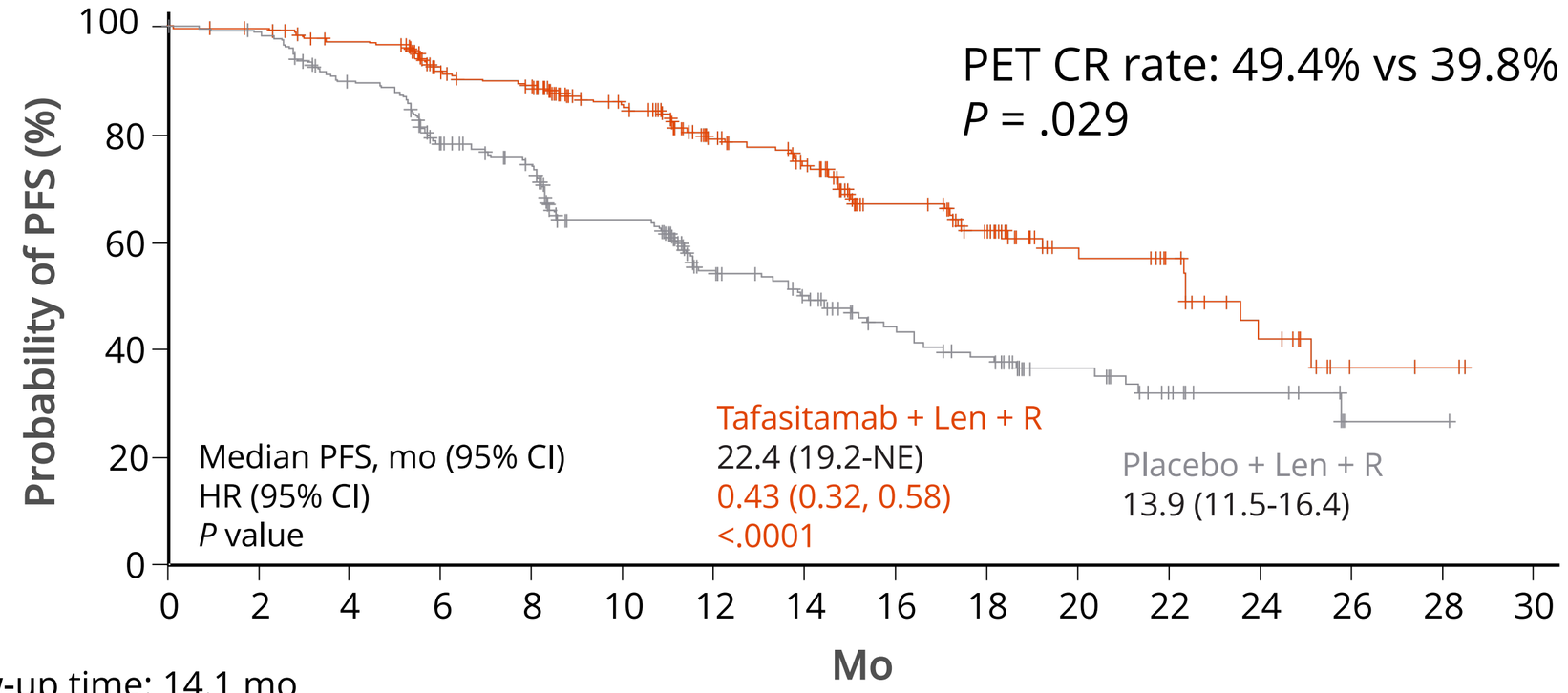
- **Primary endpoint:** PFS by investigator per Lugano 2014 criteria in FL population
- **Key secondary endpoints:** PFS in overall population, PET/CR at EOT and OS in FL population



*Tafasitamab given Days 1, 8, 15, 22 of cycles 1-3 and Days 1, 15 of cycles 4-12 on 28-day cycle.
†Rituximab dosed at 375 mg/m² IV; given on Days 1, 8, 15, 22 of cycle 1, then Day 1 of cycles 2-5.
‡Lenalidomide dosed at 20 mg PO QD given on Days 1-21 for 12 cycles. §Placebo given as 0.9% saline solution IV.

Sehn. ASCO 2022. Abstr TPS7583. NCT04680052.

inMIND: PFS by Investigator Assessment (Primary Endpoint)



Median follow-up time: 14.1 mo

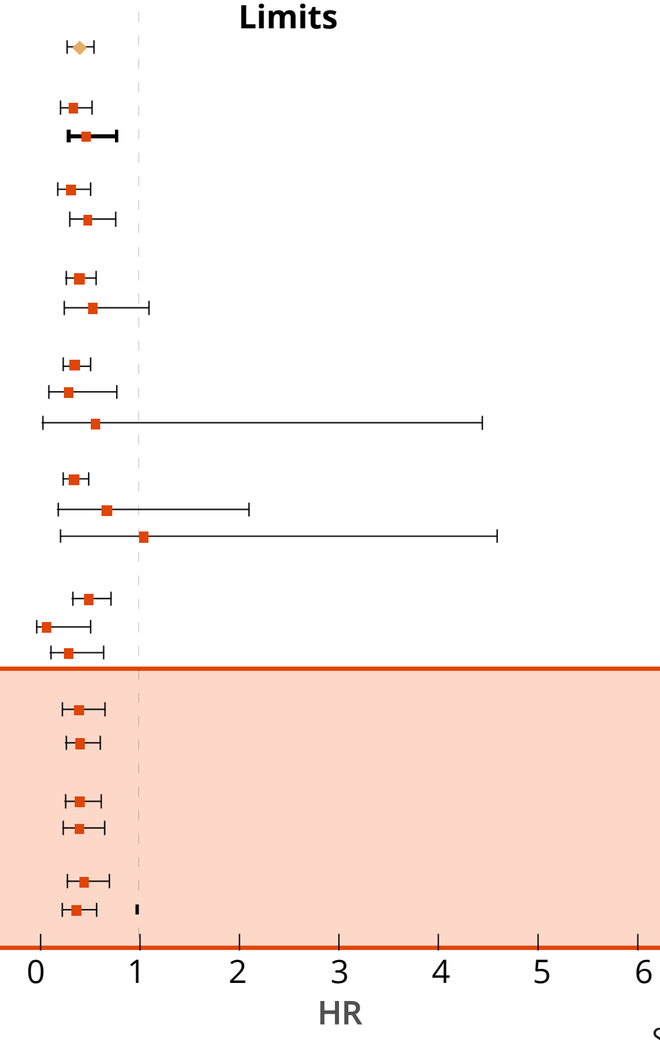
Patients at Risk, n																
Tafasitamab + Len + R	273	261	250	212	200	164	119	103	71	57	30	22	12	3	2	0
Placebo + Len + R	275	265	235	192	173	126	82	70	48	40	26	16	10	2	2	0

Significant improvement in PFS was observed with tafasitamab

Sehn. ASH 2024. Abstr LBA-1.

inMIND: Prespecified Subgroup Analysis of PFS

Subgroup	Tafasitamab + Len + R # Events/# Patients Censored	Placebo + Len + R # Events/# Patients Censored	HR (95% CI)
All patients	75/198	131/144	0.43 (0.32-0.58)
Sex			
Mal	40/110	78/71	0.38 (0.26-0.56)
Femal e	35/88	53/73	0.51 (0.33-0.80)
Age group 1			
<65 yr	29/108	69/70	0.35 (0.23-0.55)
≥65 yr	46/90	62/74	0.53 (0.35-0.80)
Age group 2			
<75 yr	55/164	102/119	0.44 (0.31-0.61)
≥75 yr	20/34	29/25	0.58 (0.30-1.12)
Race			
White	61/158	106/113	0.40 (0.29-0.55)
Asian	11/29	21/21	0.34 (0.14-0.81)
Other/missin g	3/11	4/10	0.60 (0.08-4.41)
Ethnicit y			
Not Hispanic or Latino/a	62/166	112/114	0.39 (0.28-0.53)
Hispanic or Latino/a	8/23	10/14	0.71 (0.24-2.10)
Other/missin g	5/9	9/16	1.07 (0.25-4.56)
Geographic region			
Europe	52/124	88/105	0.53 (0.38-0.76)
North America	8/30	11/13	0.12 (0.02-0.55)
Rest of the world	15/44	32/26	0.33 (0.16-0.68)
POD24			
Yes	29/56	52/36	0.43 (0.27-0.69)
N	46/142	79/108	0.45 (0.31-0.65)
Refractory to prior anti-CD20			
Yes	45/73	68/47	0.44 (0.30-0.65)
N	30/125	63/97	0.44 (0.28-0.68)
Number of prior lines			
1 line	36/110	61/86	0.48 (0.32-0.74)
≥2 lines	39/88	70/58	0.41 (0.28-0.61)

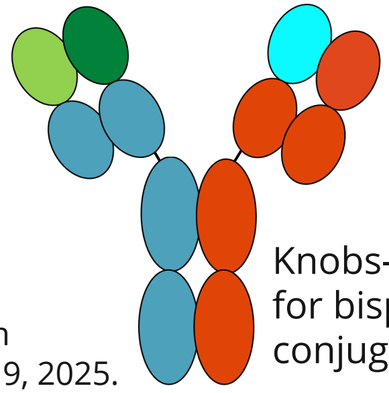


Sehn. ASH 2024. Abstr LBA-1.

Bispecific Antibodies Approved or in Development for FL

Mosunetuzumab (IV and*SC)

Anti-CD20 Anti-CD3



*Mosun SC formulation approved on December 19, 2025.

Knobs-into-holes for bispecific Ab conjugation

FDA approved: 3L+ R/R FL

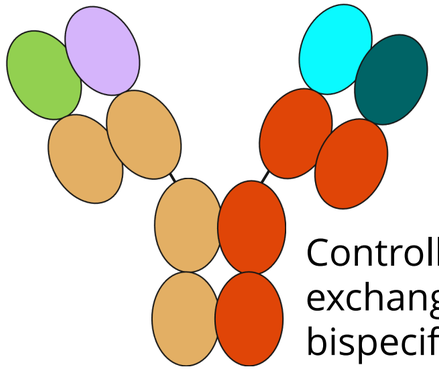
EMA approved

IgG1

Fc silencing mutation (Fsm): N297G

Epcoritamab (SC)

Anti-CD20 Anti-CD3



Controlled Fab arm exchange for bispecific Ab conjugation

FDA approved: 3L+ R/R FL

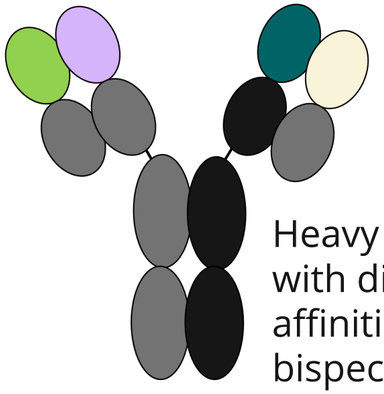
EMA approved

IgG1

Fsm: L234F, L235E, D265A

Odronextamab (IV)

Anti-CD20 Anti-CD3



Heavy chains with different affinities for bispecific Ab conjugation

EMA approved

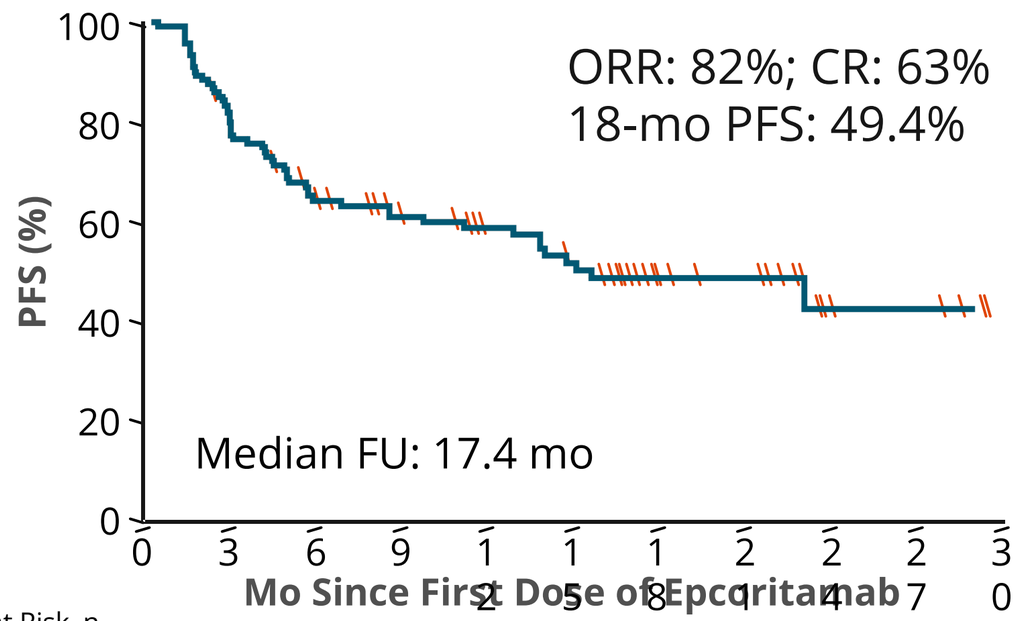
IgG4

Fsm: Modified IgG4 (no FcγRIII binding)

Falchi. Blood. 2023;141:467. Mosunetuzumab PI. Epcoritamab PI. Assouline. ASH 2025. Abstr 5353.

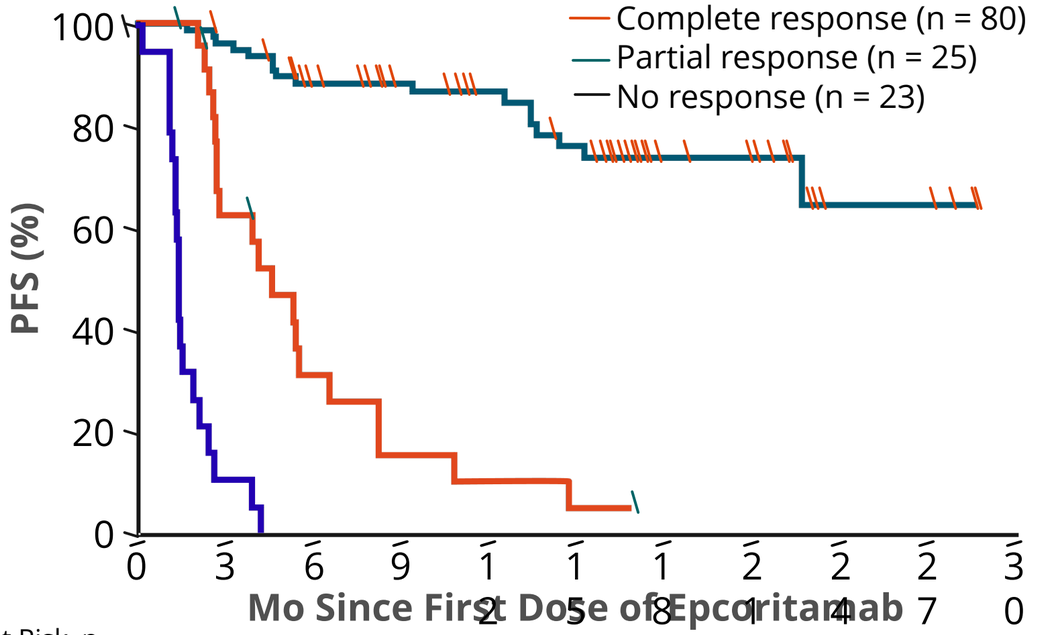
EPCORE NHL-1: Phase II Trial of Epcoritamab in Patients With R/R FL After ≥2 Prior LoT

PFS (Overall Population)



Patients at Risk, n (number censored)											
Pivotal cohort	128 (0)	90 (10)	67 (19)	57 (26)	43 (38)	35 (40)	14 (60)	12 (62)	4 (69)	4 (69)	0 (73)

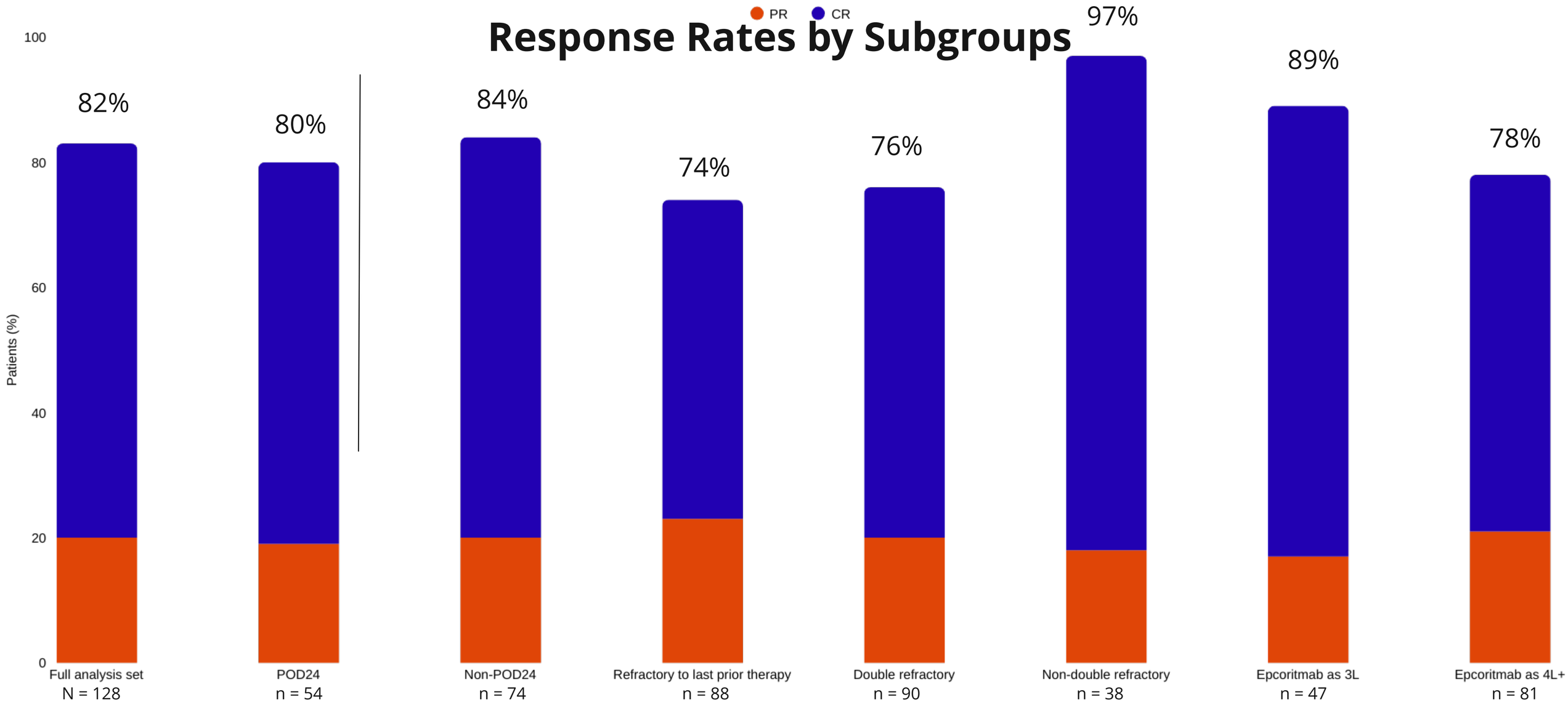
PFS (by Response)



Patients at Risk, n (number censored)											
Complete response	80 (0)	75 (2)	61 (10)	54 (17)	41 (29)	34 (31)	14 (50)	12 (52)	4 (59)	4 (59)	0 (63)
Partial response	25 (0)	13 (4)	6 (5)	3 (5)	2 (5)	1 (5)	0 (6)	0 (6)	0 (6)	0 (6)	0 (6)
No response	23 (0)	2 (4)	0 (4)	0 (4)	0 (4)	0 (4)	0 (4)	0 (4)	0 (4)	0 (4)	0 (4)

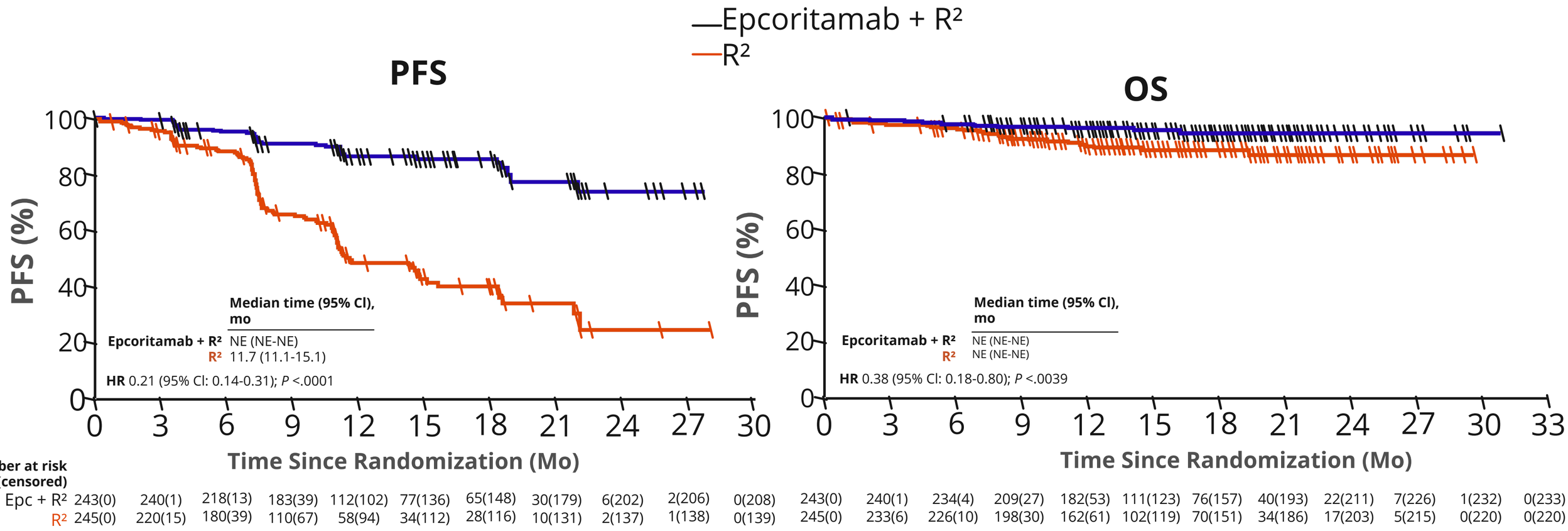
Linton. Lancet Haematol 2024;11:E593

EPCORE NHL-1: Efficacy of Epcoritamab in R/R FL



Linton. Blood. 2023;142:1655. Linton. ASH 2023. Abstr

EPCORE FL-1: PFS and OS With Epcoritamab + R² vs R² in Patients With R/R FL



Number at risk (censored)

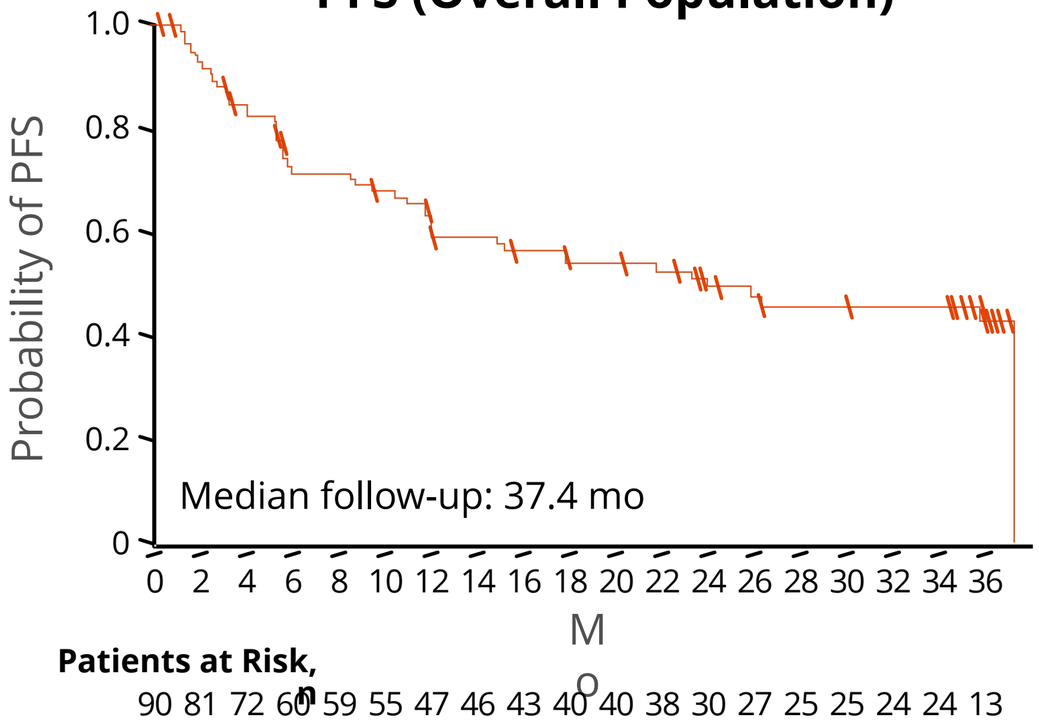
Epc + R²	243(0)	240(1)	218(13)	183(39)	112(102)	77(136)	65(148)	30(179)	6(202)	2(206)	0(208)	243(0)	240(1)	234(4)	209(27)	182(53)	111(123)	76(157)	40(193)	22(211)	7(226)	1(232)	0(233)
R²	245(0)	220(15)	180(39)	110(67)	58(94)	34(112)	28(116)	10(131)	2(137)	1(138)	0(139)	245(0)	233(6)	226(10)	198(30)	162(61)	102(119)	70(151)	34(186)	17(203)	5(215)	0(220)	0(220)

Falchi. Lancet. 2025;S0140-6736:25:02360-8

Mosunetuzumab in R/R FL: 3-Yr Update

- **INV-assessed CR rate: 60.0% (95% CI: 49.1-70.2)**

PFS (Overall Population)

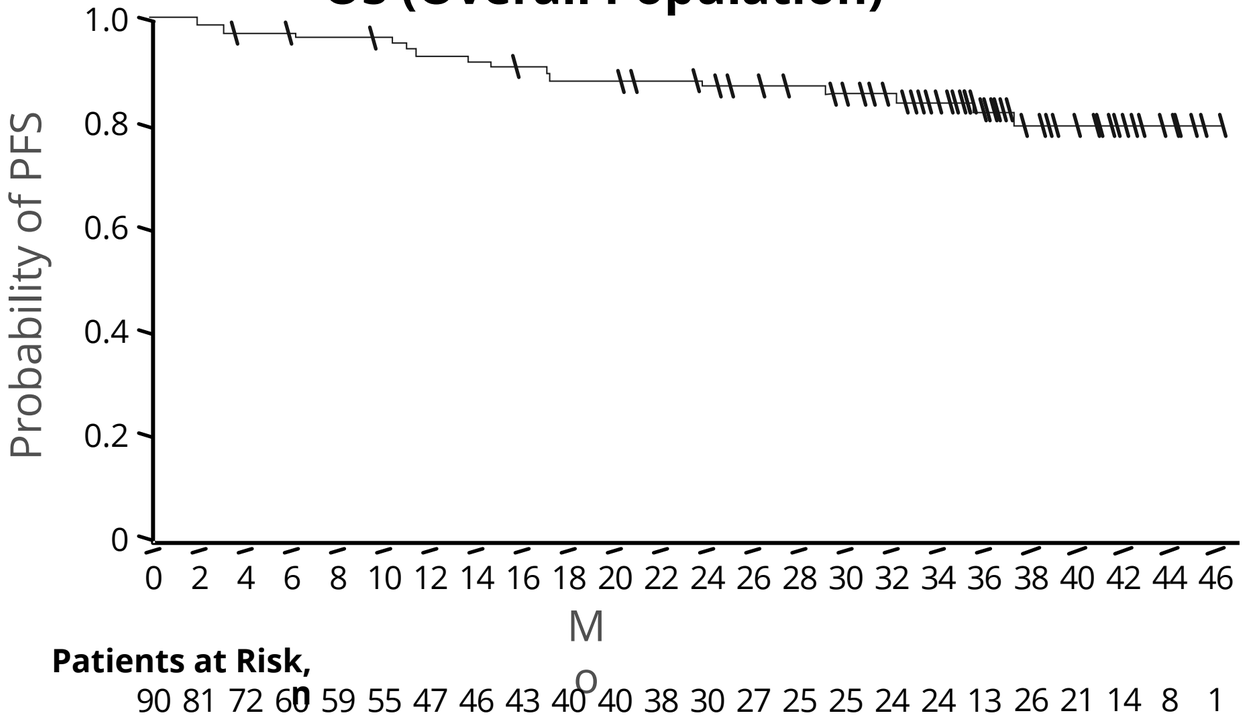


Patients at Risk, n

90 81 72 60 59 55 47 46 43 40 40 38 30 27 25 25 24 24 13

Outcome, Mo (95% CI)	Mosunetuzumab (n = 90)
Median PFS	24.0 (12.0-NR)
36-mo PFS	43.2 (31.3-55.2)

OS (Overall Population)



Patients at Risk, n

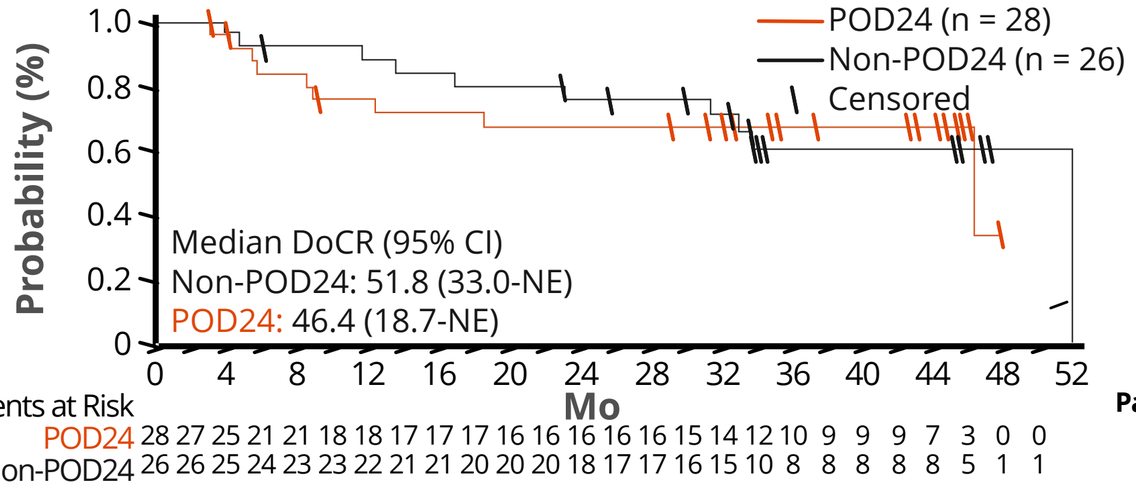
90 81 72 60 59 55 47 46 43 40 40 38 30 27 25 25 24 24 13 26 21 14 8 1

Outcome, Mo (95% CI)	Mosunetuzumab (n = 90)
Median OS	NR (NE-NE)
36-mo OS	82.4 (73.8-91.0)

Sehn. Blood. 2025;145:708

Mosunetuzumab in High-risk Subgroups of FL

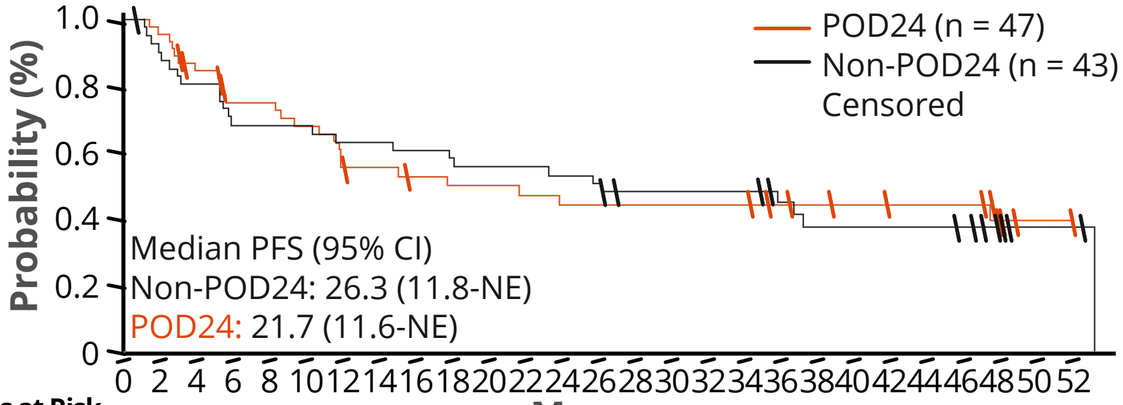
DoCR By Subgroup



Patients at Risk

POD24	28	27	25	21	21	18	18	17	17	17	16	16	16	16	16	15	14	12	10	9	9	9	7	3	0	0
Non-POD24	26	26	25	24	23	23	22	21	21	20	20	20	18	17	17	16	15	10	8	8	8	8	8	5	1	1

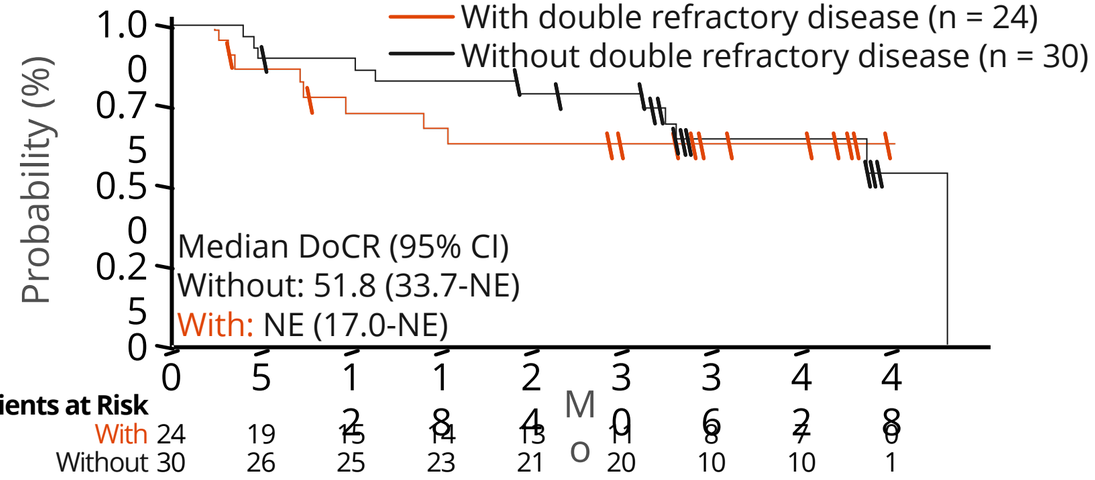
PFS By Subgroup



Patients at Risk

POD24	47	44	38	31	31	28	22	21	19	18	18	17	16	16	16	16	16	16	14	13	12	11	11	11	6	1	0
Non-POD24	43	37	33	29	28	27	25	25	24	23	22	22	21	21	17	17	17	17	13	11	11	11	11	10	5	2	2

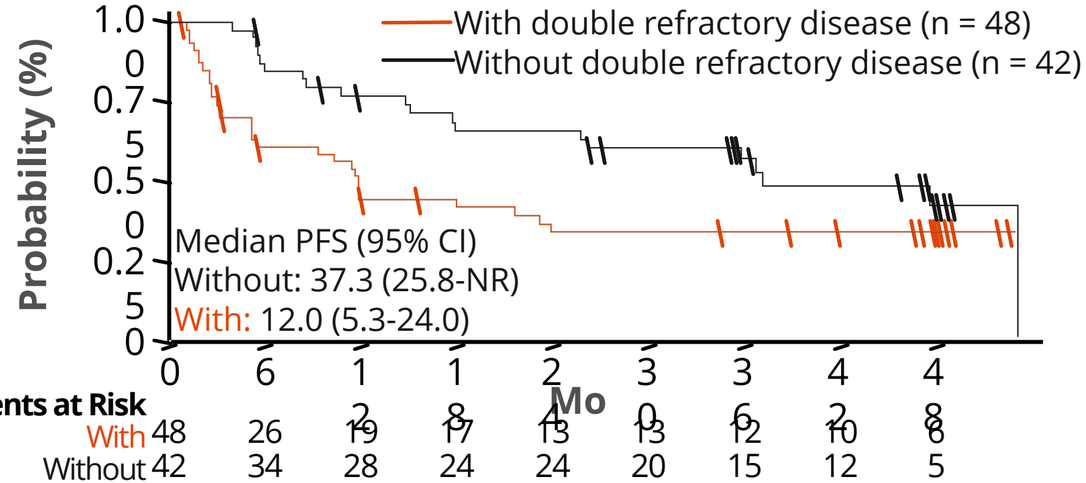
DoCR



Patients at Risk

With	24	19	15	14	13	11	8	7	0
Without	30	26	25	23	21	20	10	10	1

PFS in Patients With Double Refractory Disease



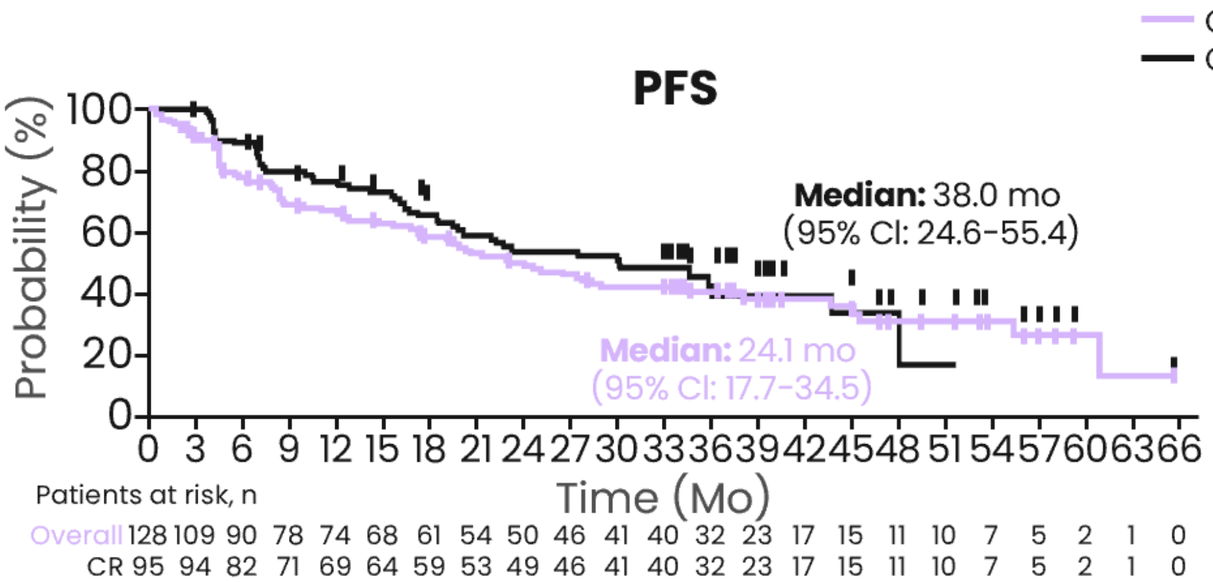
Patients at Risk

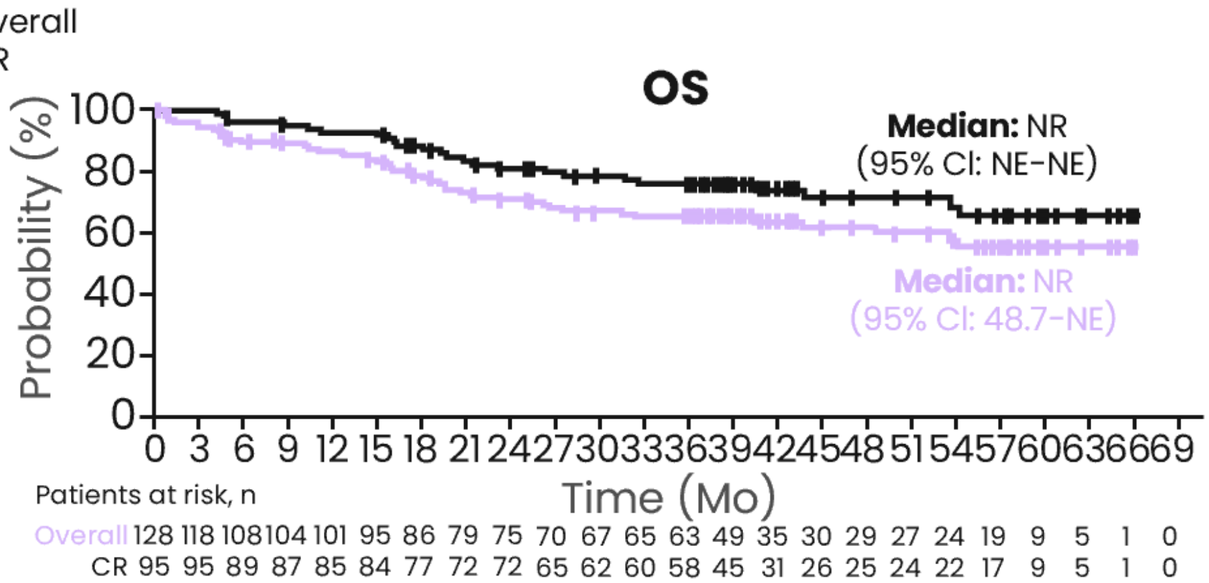
With	48	26	19	17	13	13	12	10	6
Without	42	34	28	24	24	20	15	12	5

Cheah. EHA 2025. Abstr

ELM-2: Efficacy of Odronextamab in R/R FL

- **ORR** in the overall population = **80.5%** (95% CI: 72.5-86.9)





PFS Rate, % (95% CI)	N = 128	CR (n = 95)
24 mo	50.0 (40.4-58.9)	63.1 (51.9-72.4)
36 mo	40.8 (31.4-49.9)	52.5 (41.1-62.6)

OS Rate, % (95% CI)	N = 128	CR (n = 95)
24 mo	70.1 (60.9-77.6)	80.1 (70.3-87.0)
36 mo	64.3 (54.7-72.4)	75.2 (64.7-82.9)

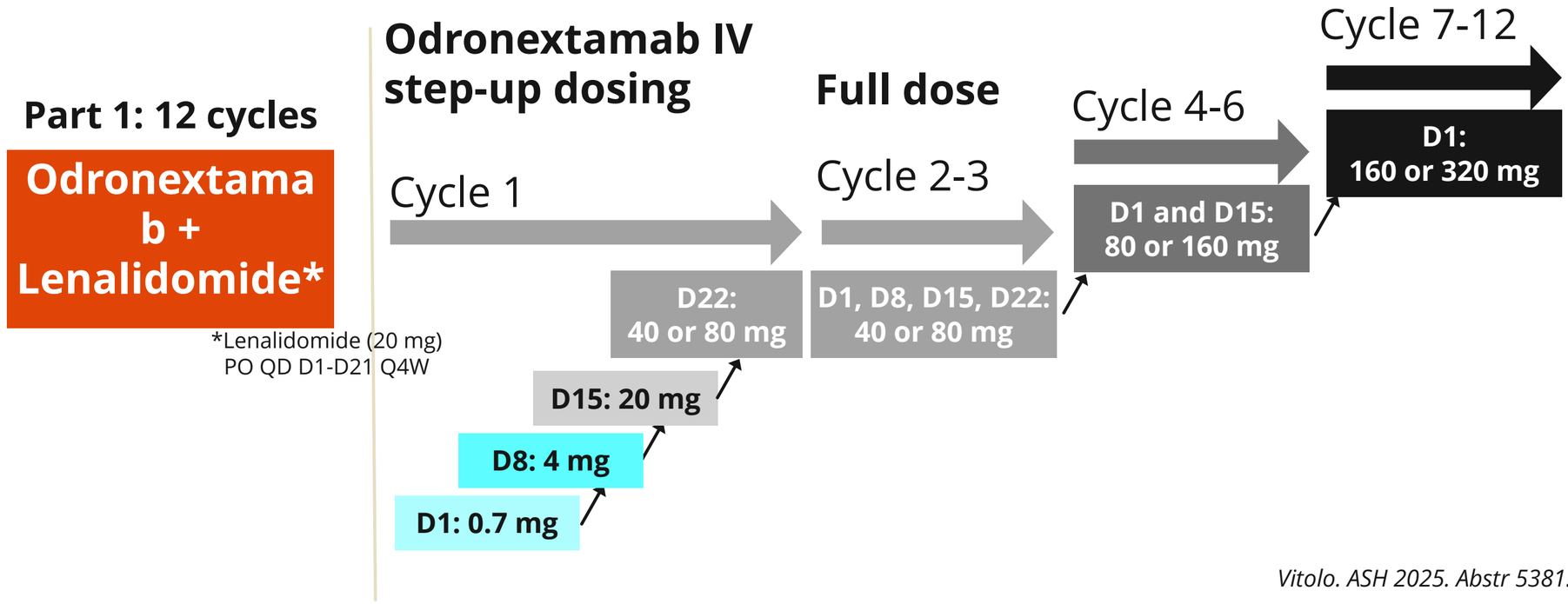
Bisneto. ASH 2025. Abstr 3588.

OLYMPIA 5: Odro + Len in R/R FL After ≥1 Prior LoT Safety Lead-in Results

Randomized, phase III, open-label, multicenter study

- **Primary endpoints:** DLT incidence, TEAEs
- **Secondary endpoints:** PK, immunogenicity, INV-assessed ORR, CR, and DoR

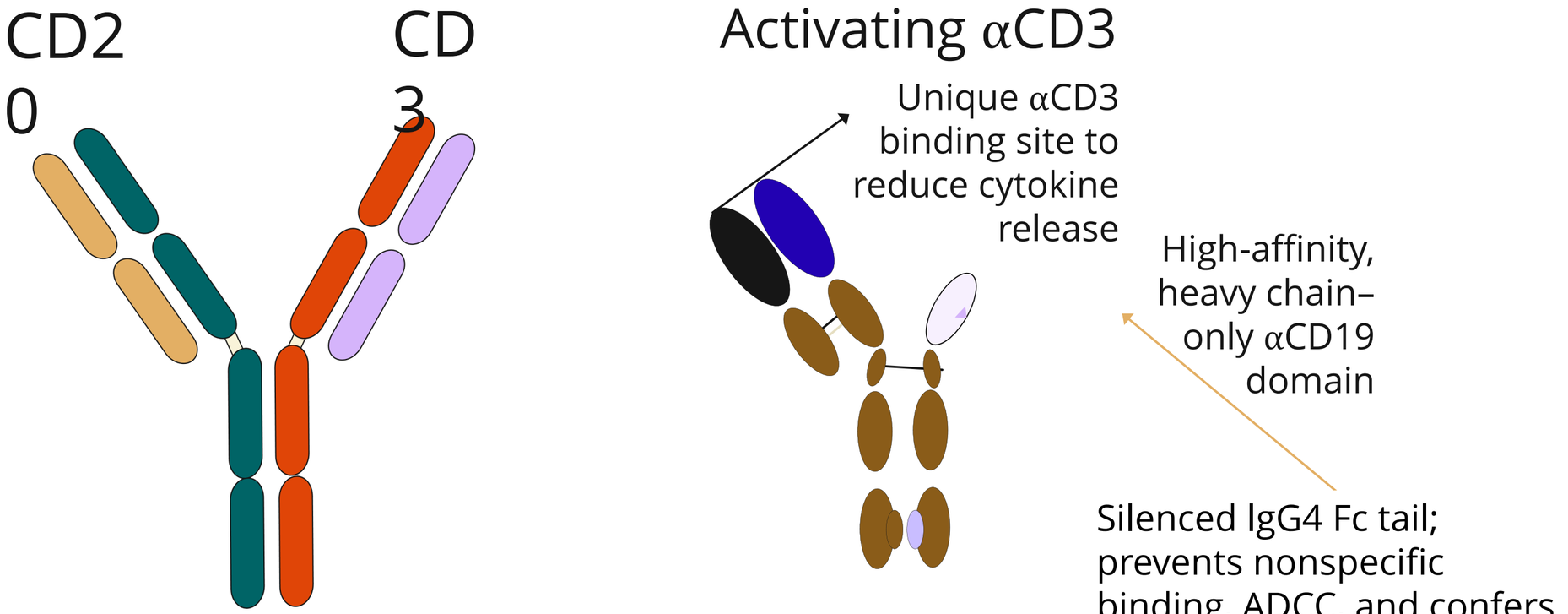
Adults with FL grade 1-3A; R/R after ≥1 line of tx; ECOG PS ≤2; adequate organ function; No CNS disease or pathology; No prior lenalidomide or CD20 x CD3 BsAb in past 6 mo
(N = 32)



Vitolo. ASH 2025. Abstr 5381.

Key Differences Between Investigational and Approved Bispecific Antibodies

- CD20 vs CD19 targeting bispecific antibodies

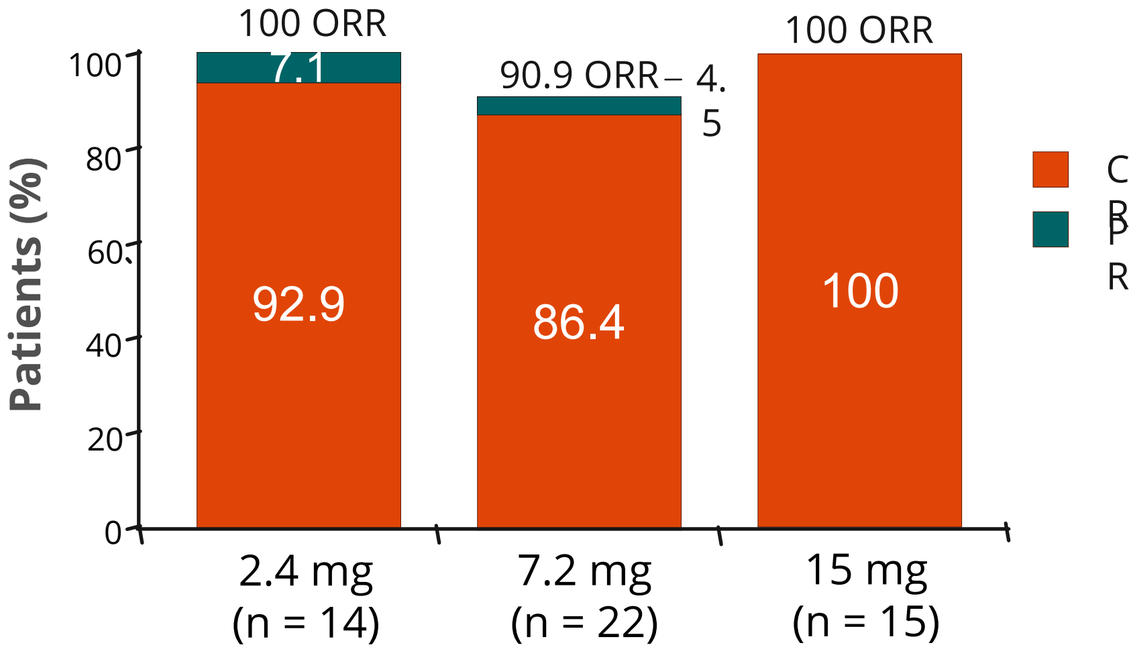


Hambleton. Expert Opin Investig Drugs. 2025;34:245.

Phase I Study of Surovatamig: FL Cohort

- Median follow-up for TD ≥2.4 mg:
- 16 mo (range: 1-40)
- Durability of response for TD ≥2.4 mg (n = 50):
  - 12-mo DoR rate: 91.4% (95% CI: 78.6-96.7)
  - 18-mo DoR rate: 81.7% (95% CI: 61.2-92.0)

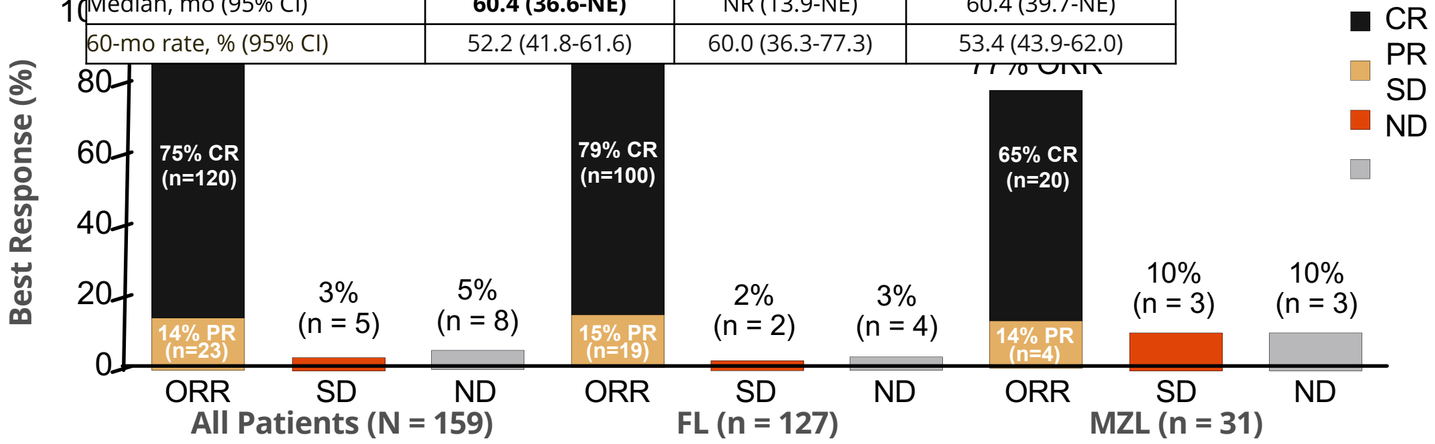
- High response rates observed at all TDs - 2.4 mg
- ORR/CR rate for patients who received - 2.4 mg was 96/92%



Hou. ASH 2025. Abstr 1005.

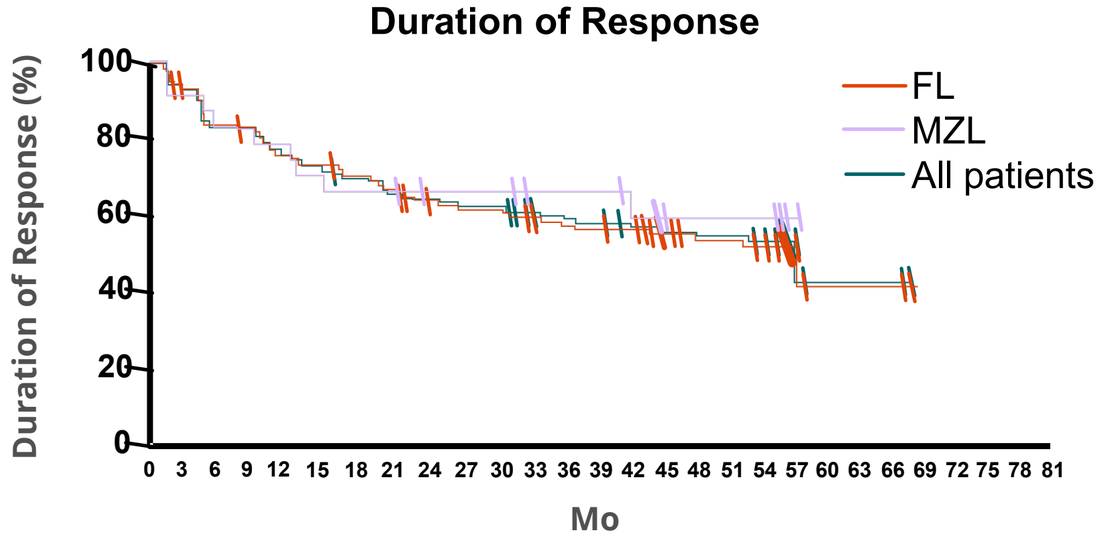
ZUMA-5: Axicabtagene Ciloleucel in FL & MZL

Estimated DoR	FL (n = 127)	MZL (n = 31)	All Pts (N = 159)
Median, mo (95% CI)	**60.4 (36.6-NE)**	NR (13.9-NE)	60.4 (39.7-NE)
60-mo rate, % (95% CI)	52.2 (41.8-61.6)	60.0 (36.3-77.3)	53.4 (43.9-62.0)



Median follow-up: 64.6 mo (range: 32.3-81.4)
FL (n = 127): 65.7 (56.7-81.4)
MZL (n = 31): 55.8 (32.3-76.4)

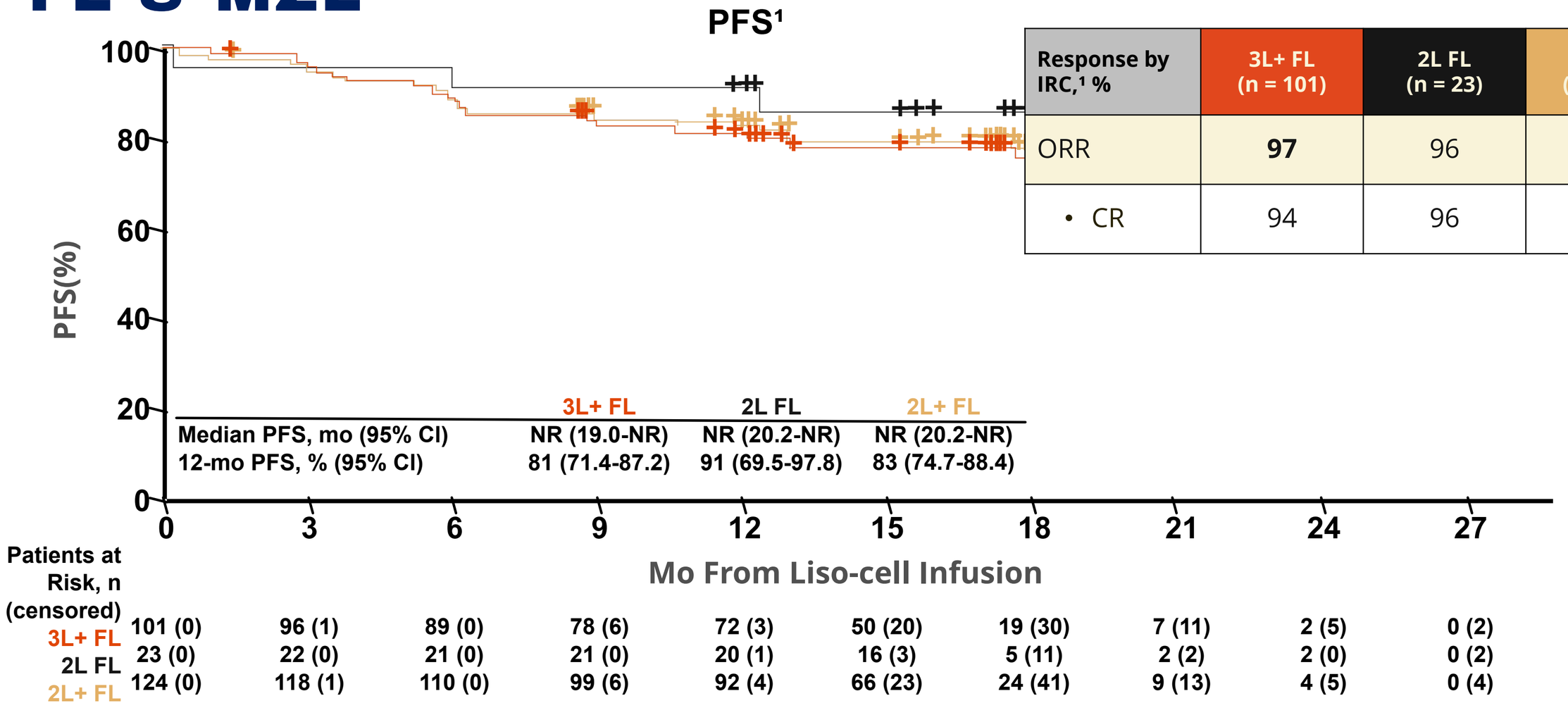
- n = 87 (55%) of patients alive without needing next treatment
- Ongoing response rate:
  - 44% (FL: 43%; MZL: 48%)
  - 58% of patients with CR maintained CR with median DoCR of 60.5 mo (95% CI: 60.4-NE)



Estimated TTNT	FL (n = 127)	MZL (n = 31)	All Patients (N = 159)
Median, mo (95% CI)	**NR (37.8-NE)**	NR (12.1-NE)	NR (38.6-NE)
60-mo rate, % (95% CI)	54.0 (44.8-62.3)	50.9 (31.5-67.5)	53.3 (45.0-60.9)

Neelapu. JCO. 2025;43:3573. Neelapu. ASH 2024. Abstr 864.

TRANSCEND FL: Lisocabtagene Maraleucel in FL & MZL

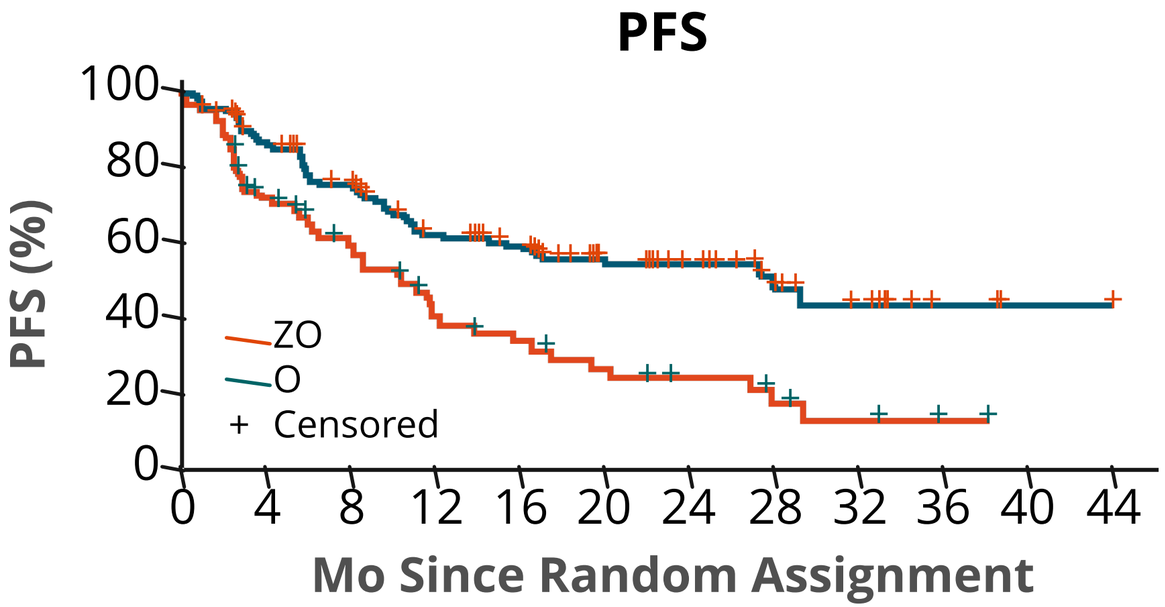


Response by IRC,[1] %	3L+ FL (n = 101)	2L FL (n = 23)	2L+ FL (n = 124)
ORR	**97**	96	97
• CR	94	96	94

3-yr updated mPFS in 3L+ FL (n = 103): NR (95% CI: 39.4-NR); 36-mo PFS rate: 68% (95% CI: 58-76)[2]

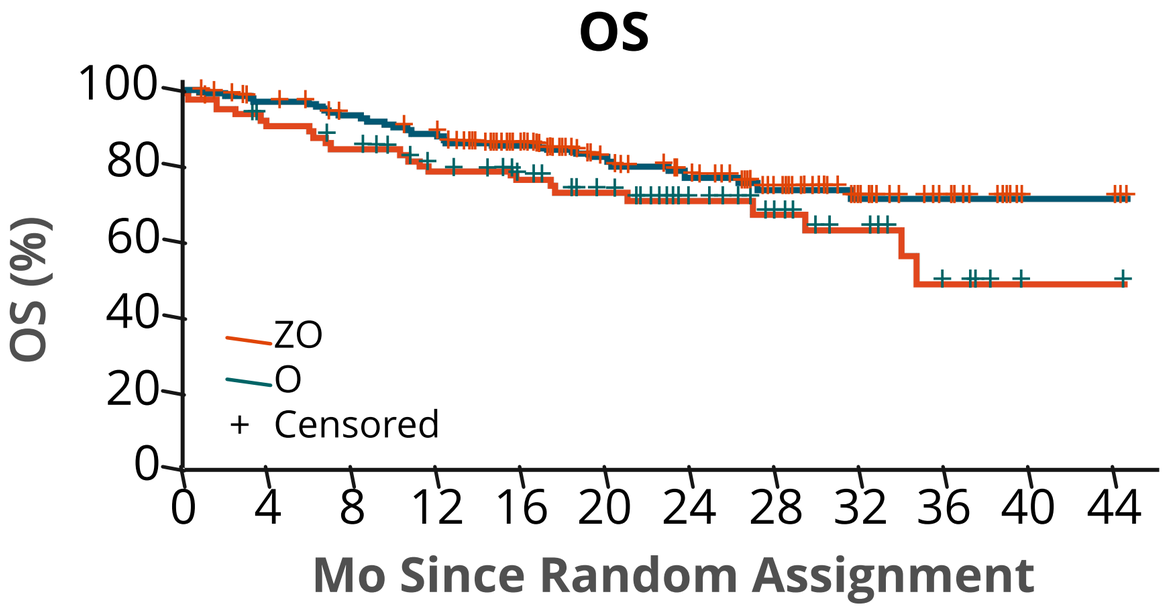
1. Morschhauser. Nat Med. 2024;30:2199. 2. Ahmed. ASH 2025. Abstr 467.

ROSEWOOD: Next-Generation BTK Inhibitor Zanubrutinib With Obinutuzumab in R/R FL



Patients at Risk, n

ZO	145	135	116	96	92	79	67	62	56	45	38	35	25	22	15	10	9	5	3	3	1	1	0
O	72	63	42	34	30	27	19	16	15	12	11	9	8	8	5	3	3	2	1	1	0		



Patients at Risk, n

ZO	145	139	133	129	123	119	113	102	92	81	70	62	56	51	41	33	26	20	17	11	4	4	3	0
O	72	67	63	62	57	54	49	48	43	39	36	32	25	23	18	14	13	8	5	3	1	1	1	0

Ongoing phase III MAHOGANY trial is evaluating zanubrutinib + obinutuzumab vs R² in patients with R/R FL after ≥1 line of systemic therapy including an anti-CD20 mAb (NCT05100862)

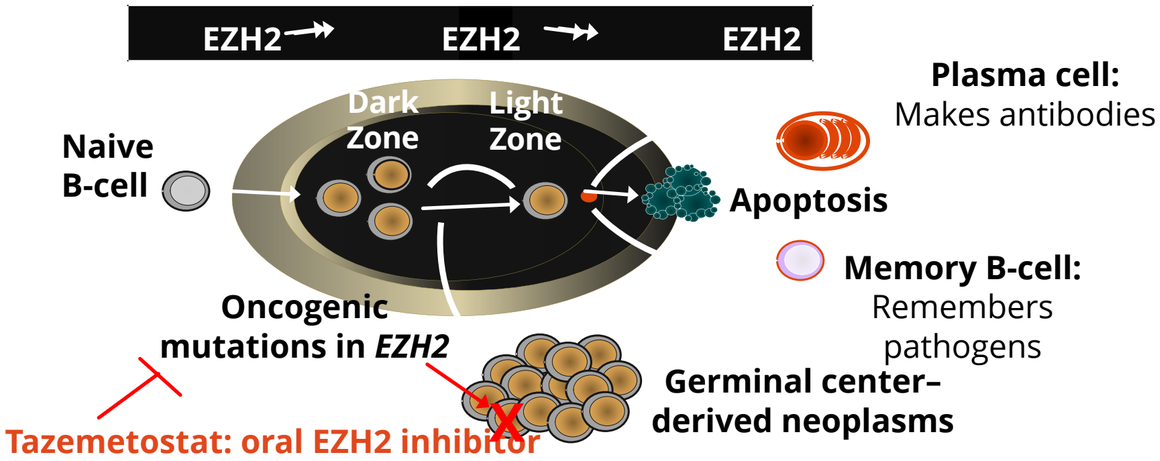
Zinzani. JCO. 2023;41:5107.

Novel Approaches for R/R NHL

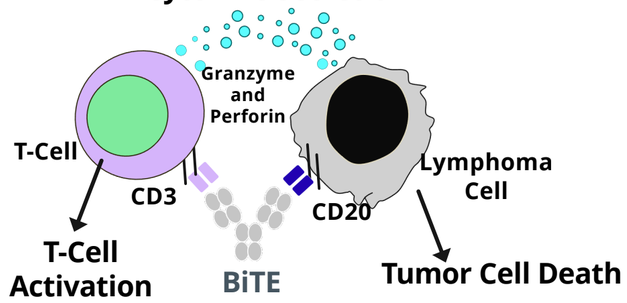
Gan. Biomark Res. 2018;6:10. Falchi. Blood. 2023;141:467. Ran. Eur J Med Chem. 2022;229:114009. Barankiewicz. Cancers. 2022;14:4492.

Tazemetostat MoA

Germinal Center Reaction



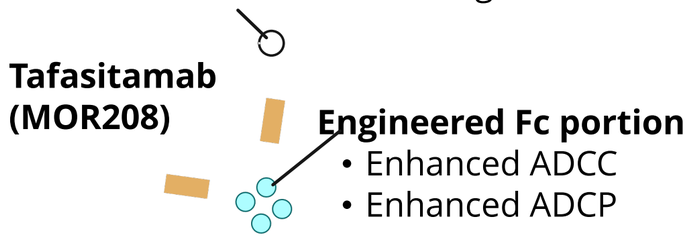
Bispecific T-Cell Engager (BiTE) Antibodies: MoA



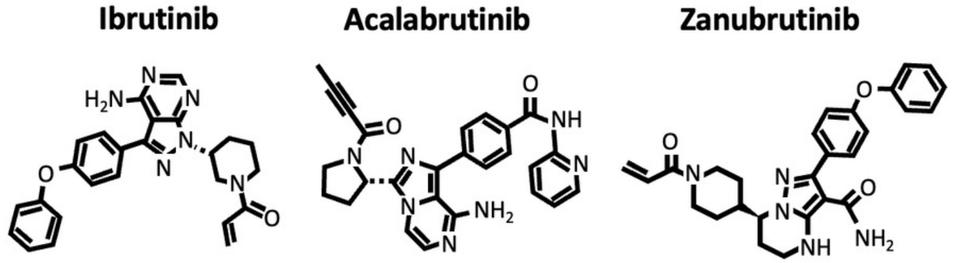
Tafasitamab MoA

Affinity matured CD19 binding site

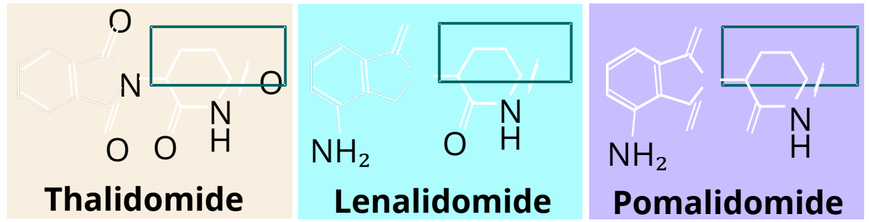
- Direct tumor cell killing



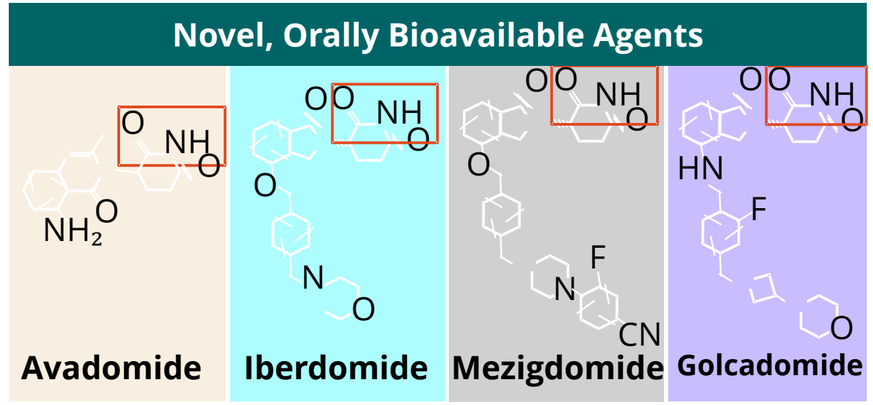
Covalent BTK Inhibitors



IMiDs and CELMoDs



Novel, Orally Bioavailable Agents



Conclusions

- The number of therapeutic options for patients with R/R FL is increasing
- It is important to consider patient characteristics, disease behavior, prognostic indicators, goals of therapy, and patient preferences before treatment selection
- It is also important to consider response type and duration of response to last therapy
- For optimal treatment sequencing:
  - Weigh benefit vs toxicity
  - Biomarkers to guide treatment selection are greatly needed

Thanks!

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