A NEW CORNERSTONE IN IMMUNOMODULATION

KOL hematology event featuring

Guilherme Perini | MD PhD

Stefan K. Barta | MD PhD

Stockholm, June 11, 2026

Disclaimer

This presentation is not a prospectus or other offer document and has not been approved by any regulatory authority in any jurisdiction. The information contained in this presentation has been prepared solely for information purposes. It is not intended for potential investors and does not constitute or form part of, and should not be construed as, an offer or solicitation of an offer to subscribe for or purchase any shares or any other securities in BioInvent International AB ("BioInvent"). This presentation does not purport to contain comprehensive or complete information about the company. Neither shall the presentation or any part of it, nor the fact of its distribution or communication, form the basis of, or be relied on in connection with, any contract, commitment or investment decision in relation thereto. Any decision to invest in any securities of the company should only be made on the basis of a thorough and independent investigation of the company itself and not on the basis of this presentation.

This presentation contains forward-looking statements, which are subject to risks and uncertainties because they relate to expectations, beliefs, projections, future plans and strategies, anticipated events or trends and similar expressions concerning matters that are not historical facts. All statements other than statements of historical fact included in this presentation are forward-looking statements. Forward-looking statements give BioInvent's current expectations and projections relating to its financial condition, results of operations, plans, objectives, future performance and business. These statements may include, without limitation, any statements preceded by, followed by or including words such as "target," "believe," "expect," "aim," "intend," "may," "anticipate," "estimate," "plan," "project," "will," "can have," "likely," "should," "would," "could" and other words and terms of similar meaning or the negative thereof. Such forward-looking statements involve known and unknown risks, uncertainties and other factors, which may cause the actual results, performance or achievements of BioInvent or the industry in which it operates, to be materially different than any future results, performance or achievements expressed or implied by such forward-looking statements. Given these risks, uncertainties and other factors, recipients of this presentation are cautioned not to place undue reliance on these forward-looking statements. The forward-looking statements referred to above speak only as at the date of the presentation. BioInvent will not undertake any obligation to release publicly any revisions or updates to these forward-looking statements to reflect future events, circumstances, anticipated events, new information or otherwise except as required by law or by any appropriate regulatory authority. The information included in this presentation may be subject to updating, completion, revision and amendment and such information may change materially.

BioInvent is under no obligation to update or keep current the information contained in this presentation and any opinions expressed in relation thereto are subject to change without notice. BioInvent make no guarantee, representation or warranty, express or implied, as to the accuracy, completeness or fairness of the information and opinions contained in this presentation, and no reliance should be placed on such information. BioInvent does not accept any responsibility or liability whatsoever for any loss howsoever arising from any use of this presentation or its contents or otherwise arising in connection therewith.

Welcome – Agenda for today

11:45	BioInvent's BI-1206 & BI-1808 in hematology	*Martin Welschof, CEO*
11:50	FL treatment landscape, medical need and future outlook	*Guilherme Perini | MD, PhD*
12:05	BI-1206 in NHL Targeting the resistance to rituximab through FcγRIIB blockade: BI-1206 + rituximab + acalabrutinib shows powerful activity in R/R NHL	*Andres McAllister, CMO*
12:20	BI-1206: Market opportunity in follicular lymphoma (FL)	*Sylvie Ryckebusch, CBO*
12:30	Q&A BI-1206	*All*
12:45	Coffee break (15 mins)	
13:00	CTCL treatment landscape, medical need and future outlook	*Stefan K. Barta | MD, MS*
13:15	BI-1808 in CTCL A novel immunotherapy approach in CTCL: TNFR2 blockade shows durable and meaningful responses	*Andres McAllister, CMO*
13:30	BI-1808: Market opportunity in CTCL	*Sylvie Ryckebusch, CBO*
13:40	Q&A BI-1808	*All*
13:55-14:00	Closing remarks	*Martin Welschof, CEO*

Today's Speakers

Guilherme Perini | MD PhD

Dr. Guilherme Perini is a board-certified hematologist in Brazil, with focus on lymphoid malignancies. He is the current Director of the Department of Excellence in Lymphoid Malignancies in Einstein Hospital Israelita, Sao Paulo, Brazil. He is also the head of Oncology Research in ARO - Academic Research Organization, at Einstein Hospital.
Dr. Perini is currently the principal investigator in >20 clinical trials in Lymphoma and CLL.

Stefan K. Barta | MD MS

Dr. Stefan Barta is a physician scientist focused on lymphoid malignancies. Currently Dr. Barta is directing the T-cell lymphoma program at the University of Pennsylvania and serve as the Executive Officer of the NCI-sponsored Consortium for Advancing Management and Prevention of Cancer in People with HIV (AMC). An active member of the AMC Lymphoma Working group and the ECOG Lymphoma Core Committee. His current research focus is on identifying novel targets for the treatment of T-cell malignancies with a special interest in immunotherapies and cellular therapies, prognostic or predictive biomarkers, as well as treatments for cancer associated with HIV.

Björn Frendéus | CSO
Moderator

Andres McAllister | CMO

Sylvie Ryckebusch | CBO

Martin Welschof

CEO

We are Developing Next-generation IO Therapies Designed to Address One of the Biggest Remaining Unmet Needs in Cancer Treatment

What the opportunity is

Checkpoint inhibitors created a major oncology market

Many patients still fail to respond due to resistance

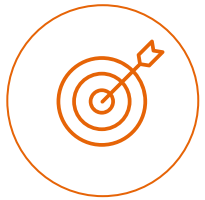
Large pharma seeks differentiated next-generation IO combinations ahead of the PD-1 patent cliff

Why BioInvent

BI-1808 and BI-1206 target immune resistance beyond current therapies

Strong anti-tumor activity with favorable safety profile

Potential to enhance efficacy and durability of existing immunotherapies



Why we are well-positioned

Proprietary human-first platform with in-house manufacturing

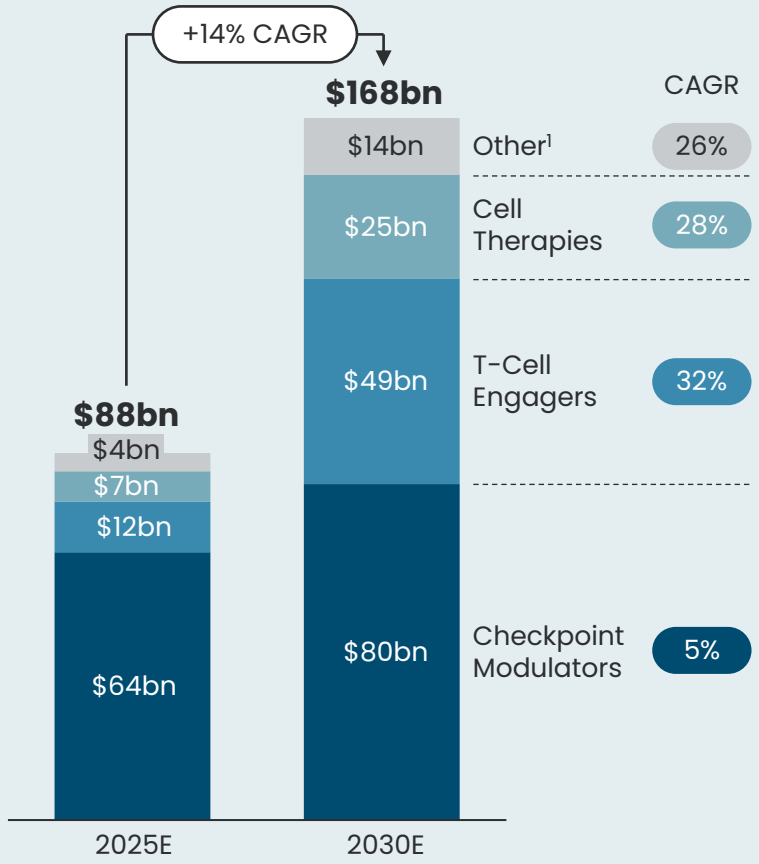
Multiple Phase 2 studies with upcoming readouts

Proven strategic partnerships backed by leading global healthcare investors

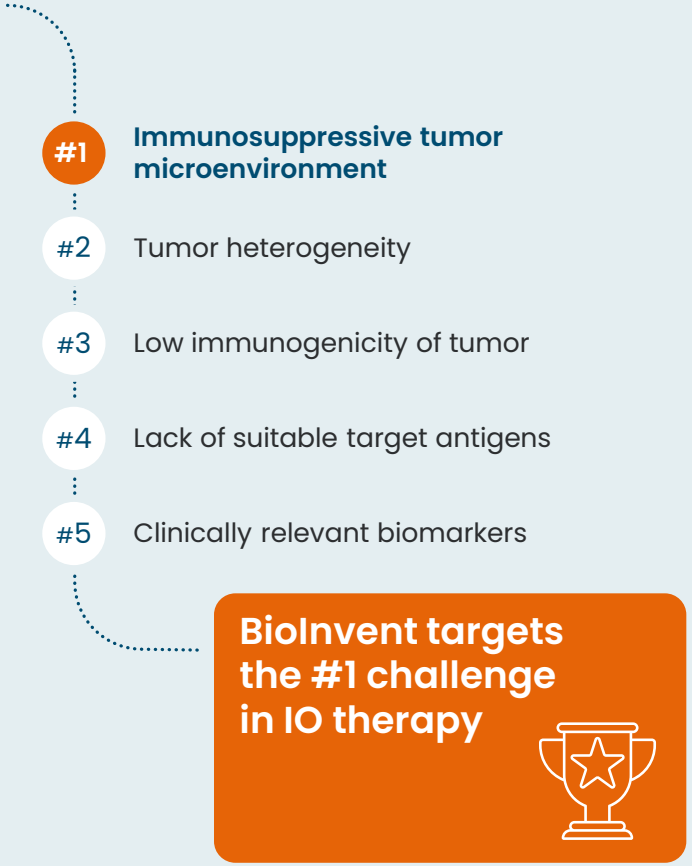
Human biology first. Platform-driven discovery. Breakthrough therapeutics.

The Immuno-Oncology (IO) Market Continues to Grow as Licensing Activity Accelerates

The immuno-oncology market is a $168bn opportunity...



...but there are a few bottlenecks[2]



Notes: 1) Other include cancer vaccines, oncolytic viruses and cytokines, 2) High-Prescriber Survey (March 2025)
Source: GlobalData.

Key insights

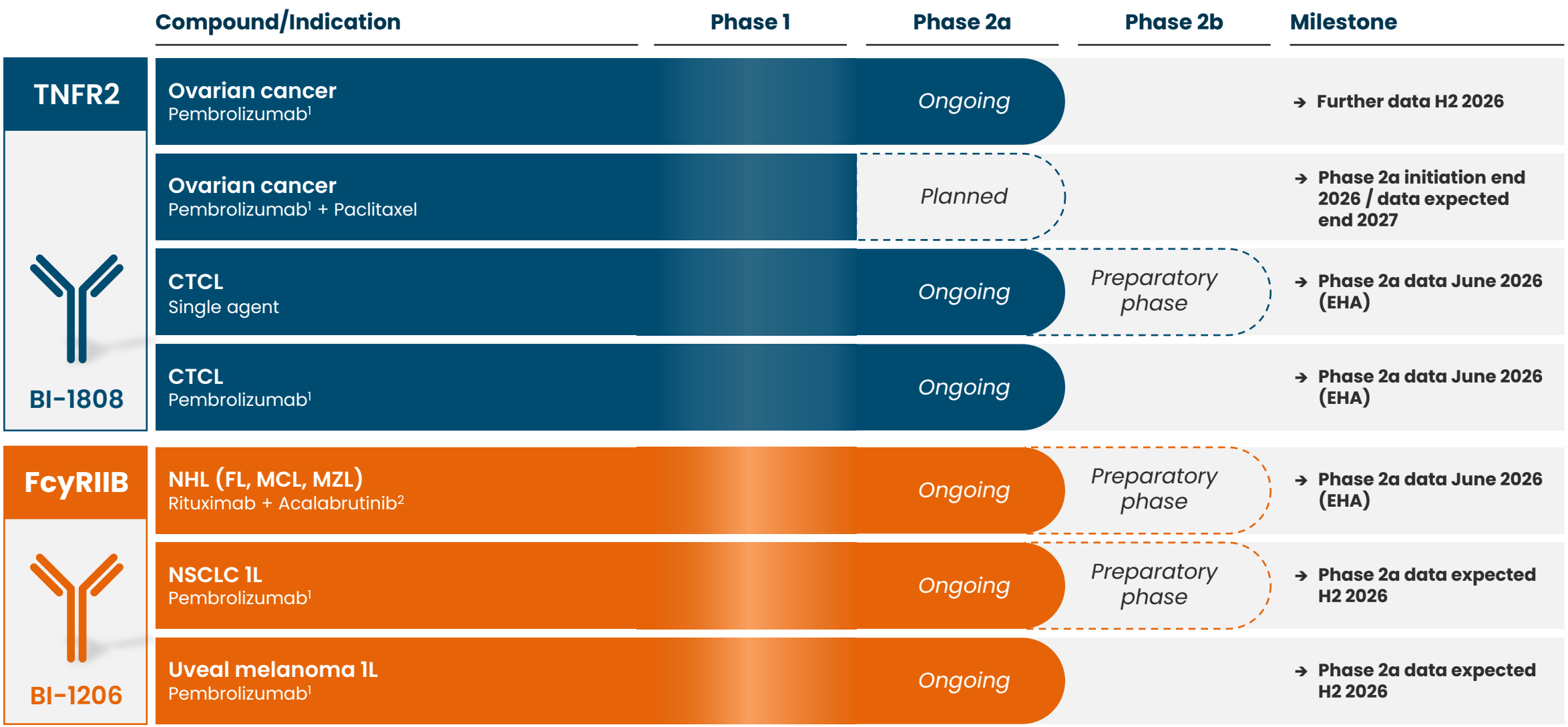
$64bn

Checkpoint Modulators market in 2025. BioInvent's core target market.

$150bn

US & EU IO licensing deal value reached peak levels in 2023, highlighting strong partnering demand

BioInvent has First-in-class Clinical Assets Advancing Across Multiple Indications



1L: First line treatment
CTCL: Cutaneous T-cell Lymphoma, NHL: Non-Hodgkin's Lymphoma, FL: Follicular Lymphoma, MCL: Mantle Cell Lymphoma, MZL: Marginal Zone Lymphoma, NSCLC: Non-small cell lung cancer
Notes: 1) Supply agreement with Merck, 2) Supply agreement with AstraZeneca

Guilherme Perini

MD PhD

FL Treatment Landscape, Medical Need, and Future Outlook

Guilherme Fleury Perini, MD
Head, Center of Excellence in Lymphoid Malignancies
Hospital Israelita Albert Einstein
São Paulo – SP, Brazil
@guiperiniMD

Disclosures:

Speaker’s Bureau: Janssen, Roche, Takeda, Abbvie, BMS, Abbvie, Beigene, Knight, Lilly

Educational Support: Janssen, Takeda, Roche, Abbvie, Dr. Reddys

Advisory Board: Janssen, Abbvie, Astra Zeneca, Roche, Abbvie, Beigene, Knight, Lilly

Research: Janssen, Millenium, Merck, Alnylam, BMS, Beigene, Abbvie, Astra Zeneca, Lilly

FL Facts

- Once considered an uncurable disease, FL is now probably curable in a subset of patients[1]
- First line therapy remains based on Anti-CD20 + Chemotherapy for the majority of patients
- Around 20% of patients have early relapses, now considered one of the most important risk factors for multiple relapses and death[2]

[1]Shadman M, LeBlanc M, Rimsza L, et al. Treatment of Follicular Lymphoma With CHOP and Anti-CD20 Therapy: 15-Year Follow-Up of the SWOG S0016 Trial. JAMA Oncol. 2026;12(4):394–401. doi:10.1001/jamaoncol.2026.0042
[2]Casulo C, Dixon JG, Le-Rademacher J et al. Validation of POD24 as a robust early clinical end point of poor survival in FL from 5225 patients on 13 clinical trials. Blood. 2022 Mar 17;139(11):1684-1693.

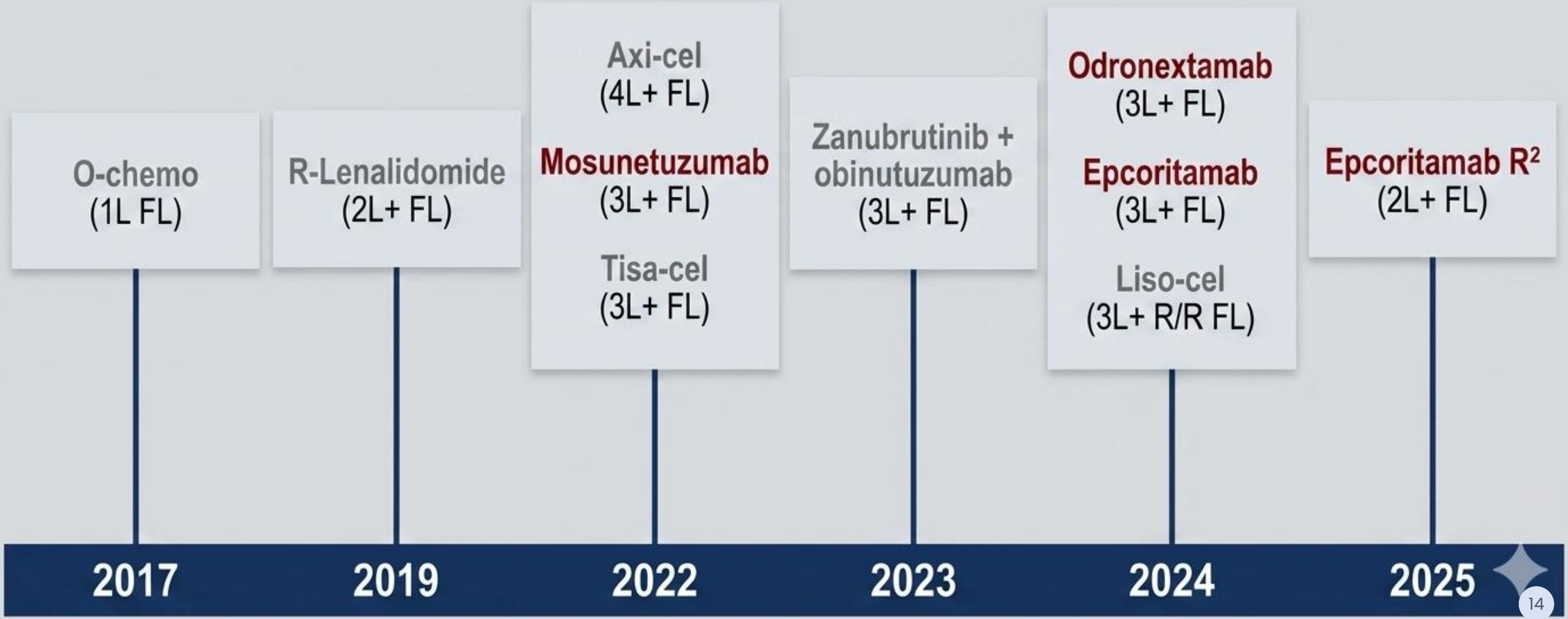
FL Facts

- While first line treatment has not changed in recent years, the treatment landscape of R/R FL has changed substantially

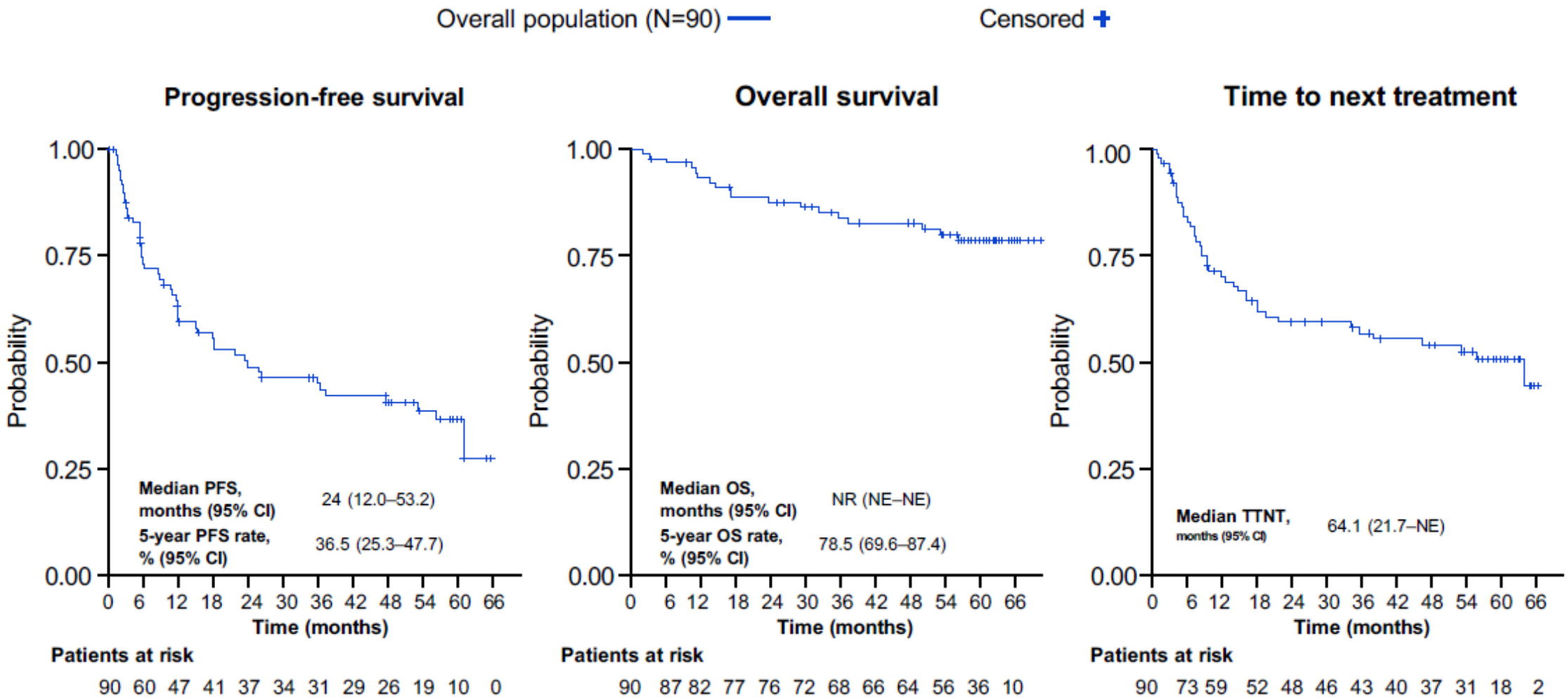
- New agents have changed the way we approach R/R FL:
  - New Monoclonal Antibodies (Tafasitamab)
  - Bispecifics Antibodies (Epcoritamab, Mosunetuzumab and Odronextamab)
  - Small molecules (Zanubrutinib, Golcadomide)
  - CarT therapies (Tisacel, Axicel and Lisocel)

- Toxicity, Access and patient selection is now key in navigating through so many options

Relapsed FL: The “Chemo-Free” Revolution

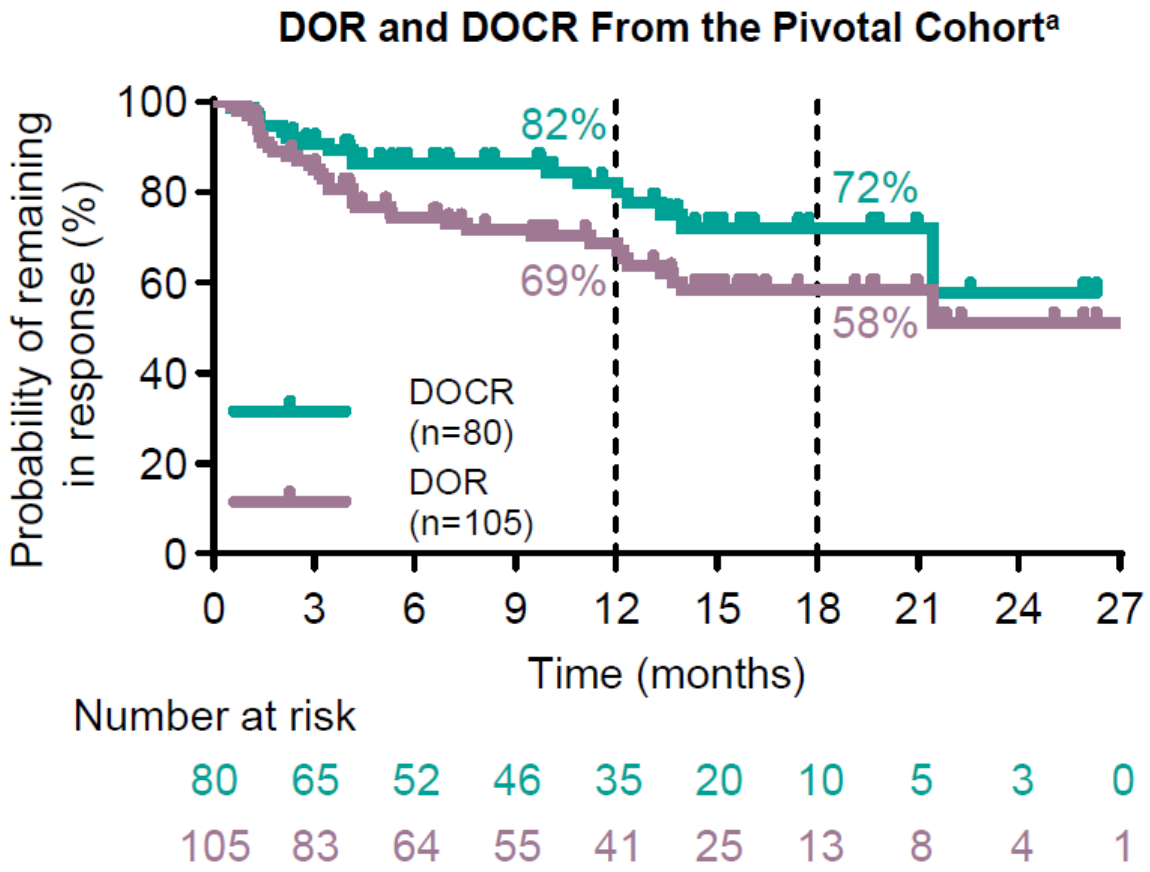


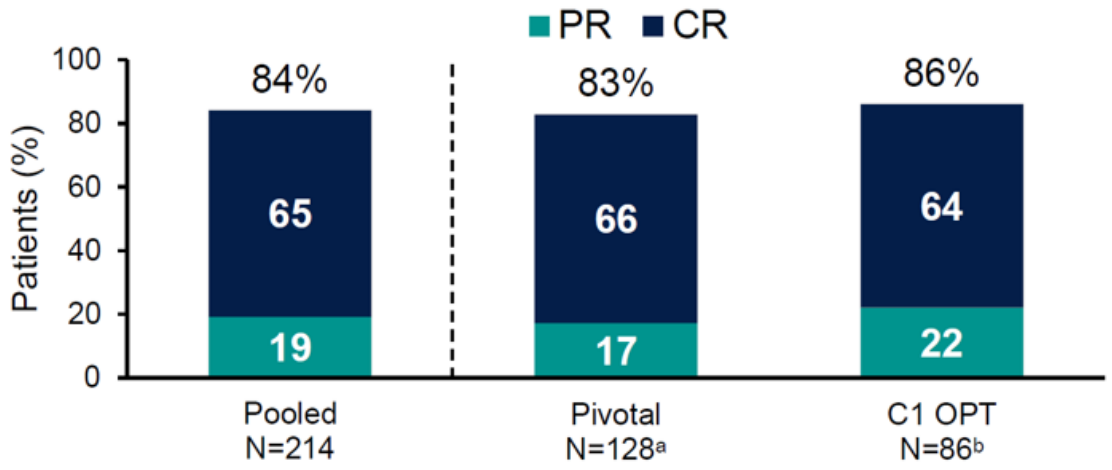
Long-term PFS and favorable OS are achievable with BsAb monotherapy: Mosunetuzumab in 3L+ FL



Budde E, et al. ASH 2025; abstract 5352

Epcoritamab in 2+ Lines FL





Vitolo U et al, EHA 2024

Bispecific antibody combination therapy in R/R FL

Regimen	Trial (Phase)	Patients (R/R FL cohorts)	Treatment duration and administration	Primary endpoint	Study status
Mosunetuzumab-Len	**CO41942** (Phase Ib/II)[1,2]	29[1]	**Mosunetuzumab** (IV/SC) 12 cycles **Len** (oral) 11 cycles[1,2]	Safety[1,2]	Active, not recruiting[2]
Mosunetuzumab-Len versus R-Len	**CELESTIMO** (Phase III)[3]	478[3]	**Mosunetuzumab** (IV) 12 cycles **Len** (oral) 12 cycles[3]	PFS (by IRC)[3]	Active, not recruiting[3]
Odronextamab-Len versus R-Len	**OLYMPIA-5** (Phase III)[4,5]	~352*[4]	**Odronextamab** (IV) 12 cycles **Len** (oral) 12 cycles[4,5]	Safety and PFS (by IRC)[4,5]	Recruiting[4]
Epcoritamab + R-Len	**EPCORE NHL-2** (Phase Ib/II)[6,7]	111[6]	**Epcoritamab** (SC) ≥2 years **Len** (oral) 12 cycles[6,7]	Safety and ORR[6,7]	Active, not recruiting[7]
Epcoritamab + R-Len versus R-Len	**EPCORE FL-1** (Phase III)[8]	549[8]	**Epcoritamab** (SC) 12 cycles **Len** (oral) 12 cycles[8]	ORR and PFS (by IRC)[8]	Active, not recruiting[8]

Results available

Products/indications are investigational and not approved. This slide is for educational purposes only

*Planned enrolment.

1. Morschhauser F, et al. ASH 2021; Oral presentation (abstract #129); 2. NCT04246086. Available at: https://clinicaltrials.gov/study/NCT04246086; 3. NCT04712097. Available at: https://clinicaltrials.gov/study/NCT04712097; 4. NCT06149286. Available at: https://clinicaltrials.gov/study/NCT06149286 5. Vitolo U, et al. ASCO 2023; Abstract (abstract #TPS7094); 6. Falchi L, et al. ASH 2024; Oral presentation (abstract #342); 7. NCT04663347. Available at: https://clinicaltrials.gov/study/NCT04663347; 8. NCT05409066. Available at: https://clinicaltrials.gov/study/NCT05409066.

EPCORE FL-1: Phase 3, Global, Randomized, Open-Label Study

Fixed-Duration: 12 Cycles (28-Day Cycles)

Key eligibility criteria

- Histologically confirmed CD20+ FL
- Grade 1-3a, Stage II-IV
- ≥ 1 prior treatment including anti-CD20 mAb plus an alkylating agent
- Met ≥ 1 GELF criterion

Randomization 1:1

Epcoritamab (48 mg) plus R^2

- **Epcoritamab** (3-SUD cycle 1: QW;[a,b] cycles 2–3, QW; cycles 4–12, Q4W)
- **Rituximab** (375 mg/m^2), 5 cycles (cycle 1, QW; cycles 2–5, Q4W)
- **Lenalidomide** (20 mg), 12 cycles (cycle 1–12, QD, D1-21)

R^2

- **Rituximab** (375 mg/m^2), 5 cycles (cycle 1, QW; cycles 2–5, Q4W)
- **Lenalidomide** (20 mg), 12 cycles (cycle 1–12, QD, D1-21)

Stratification factors

- Disease status:
  - 2L: > or ≤ 2 years since last therapy
  - 3L+: > or < 6 months since last therapy
- Region: US/EU vs Rest of World

- **Dual primary endpoints: ORR per IRC and PFS per IRC**
- Key secondary endpoints: CR rate per IRC, OS, and MRD[c]
- Additional secondary endpoints: DOR, DOCR, TTNLT, safety, and PRO assessments

Data cutoff: May 24, 2025; median follow-up: 14.8 months[d]
Enrollment period: October 2022 - January 2025

[a]Two step-up dosing (SUD) regimens during cycle 1 to mitigate the risk of cytokine release syndrome: either a 2-SUD (0.16 mg on cycle 1 day 1, 0.8 mg on cycle 1 day 8), or 3-SUD (0.16 mg on cycle 1 day 1, 0.8 mg on cycle 1 day 8, 3 mg on cycle 1 day 15) regimen, followed by full dose 48 mg. The 3-SUD regimen was implemented after reduced CRS severity and incidence had been observed in the EPCORE NHL-1 FL trial (NCT03625037).[1] [b]The 24 mg epcoritamab plus R^2 arm was closed to enrollment based on the superior efficacy for the 48 mg dose from EPCORE NHL-2.[2] Only the data for the optimal dose explored (48 mg) are presented here. [c]Minimal residual disease data are forthcoming in a future analysis. [d]The data presented here are from the second planned interim analysis (May 24, 2025) after 78% Information Fraction for PFS had occurred.

1. Vose J, et al. *J Clin Oncol.* 2024;42(16_suppl):7015–7015. 2. Falchi L, et al. *Blood*. 2024;144(Supplement 1):342–342.

Baseline Demographics and Disease Characteristics Were Generally Balanced

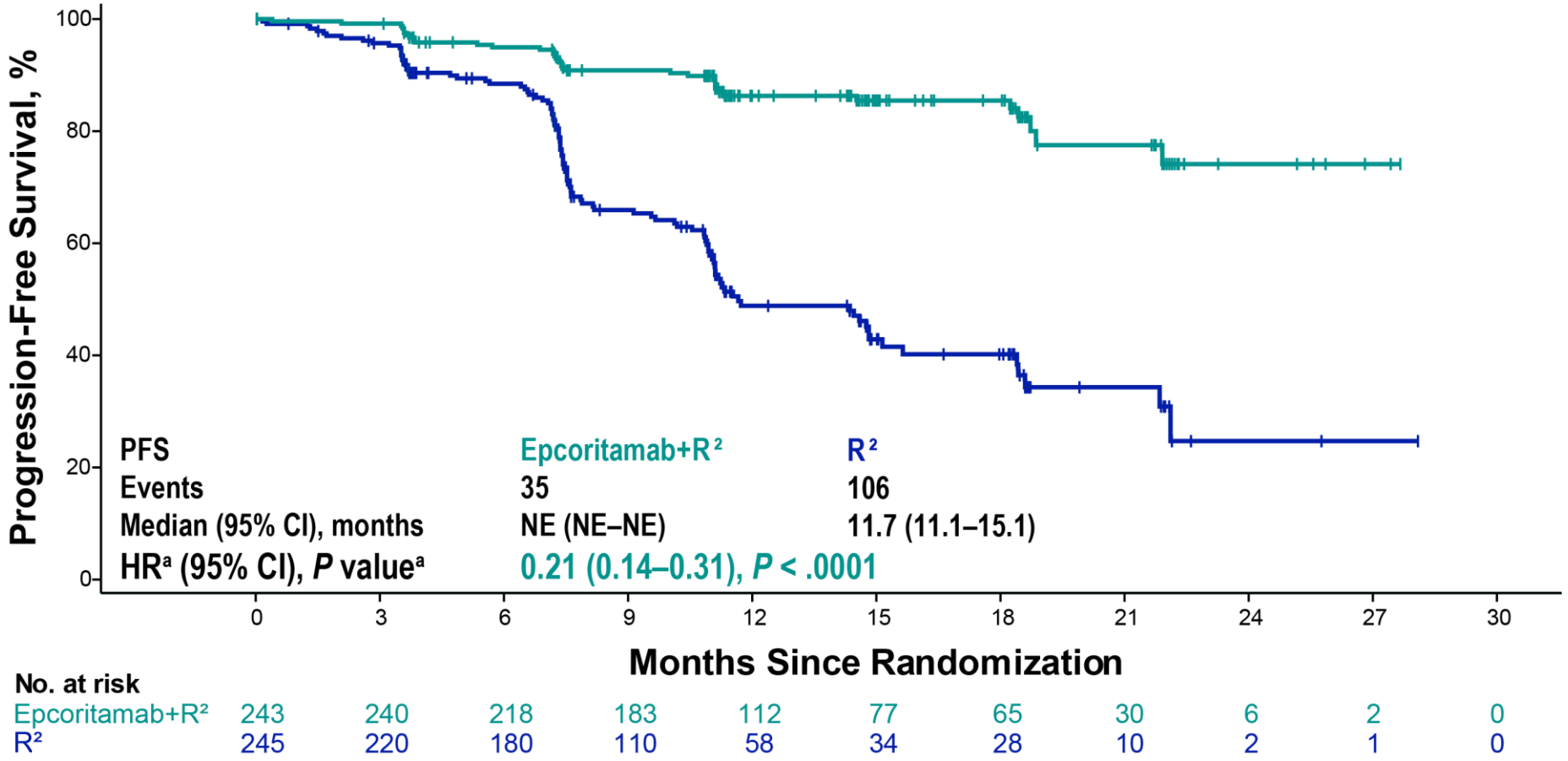
Characteristic	Epcoritamab+R² (N = 243)	R² (N = 245)	Overall (N = 488)
Median age, y (range)	60 (30, 84)	63 (24, 89)	61 (24, 89)
≥ 65, n (%)	88 (36)	106 (43)	194 (40)
Male, n (%)	139 (57)	138 (56)	277 (57)
Race, n (%)			
Asian	63 (26)	54 (22)	117 (24)
Black	6 (2)	2 (< 1)	8 (2)
White	168 (69)	184 (75)	352 (72)
Ethnicity, n (%)			
Hispanic	29 (12)	28 (11)	57 (12)
ECOG, n (%)			
0	166 (68)	170 (69)	336 (69)
1-2	77 (32)	75 (31)	152 (31)
Ann Arbor stage, n (%)			
II	37 (15)	44 (18)	81 (17)
III-IV	206 (85)	201 (82)	407 (83)
FLIPI score, n (%)			
0–1	63 (26)	56 (23)	119 (24)
2	79 (33)	76 (31)	155 (32)
3–5	100 (41)	113 (46)	213 (44)
Bulky disease (≥ 7 cm), n (%)	47 (19)	61 (25)	108 (22)

Treatment History Was Generally Balanced Across Epcoritamab+R² and R²

	Epcoritamab+R² (N = 243)	R² (N = 245)	Overall (N = 488)
Median time from initial diagnosis to randomization, years (range)	4.5 (0.2, 30.3)	5.3 (0.1, 43.0)	5.0 (0.1, 43.0)
Number of prior lines of therapy, median (range)	1 (1, 7)	1 (1, 6)	1 (1, 7)
1, n (%)	145 (60)	141 (58)	286 (59)
2, n (%)	58 (24)	61 (25)	119 (24)
≥ 3, n (%)	40 (16)	43 (18)	83 (17)
Prior anti-CD20 antibody, n (%)	243 (100)	245 (100)	488 (100)
Prior anti-CD20 antibody containing chemotherapy, n (%)	239 (98)	240 (98)	479 (98)
Prior bendamustine in last line, n (%)	53 (22)	47 (19)	100 (20)
Prior R², n (%)	8 (3)	9 (4)	17 (3)
POD24,[a] n (%)	106 (44)	93 (38)	199 (41)
Refractory to 1L therapy, n (%)	86 (35)	81 (33)	167 (34)
Refractory to anti-CD20 antibody, n (%)	104 (43)	103 (42)	207 (42)
Refractory to last line of therapy, n (%)	84 (35)	82 (33)	166 (34)
Double refractory[b]	91 (37)	91 (37)	182 (37)

[a]POD24 is defined as progression of disease ≤ 2 years from the date of initiation of frontline therapy. [b]Double refractory is refractory to prior anti-CD20 therapy and prior alkylator therapy.

Epcoritamab+R² Resulted in Superior PFS per IRC With 79% Risk Reduction



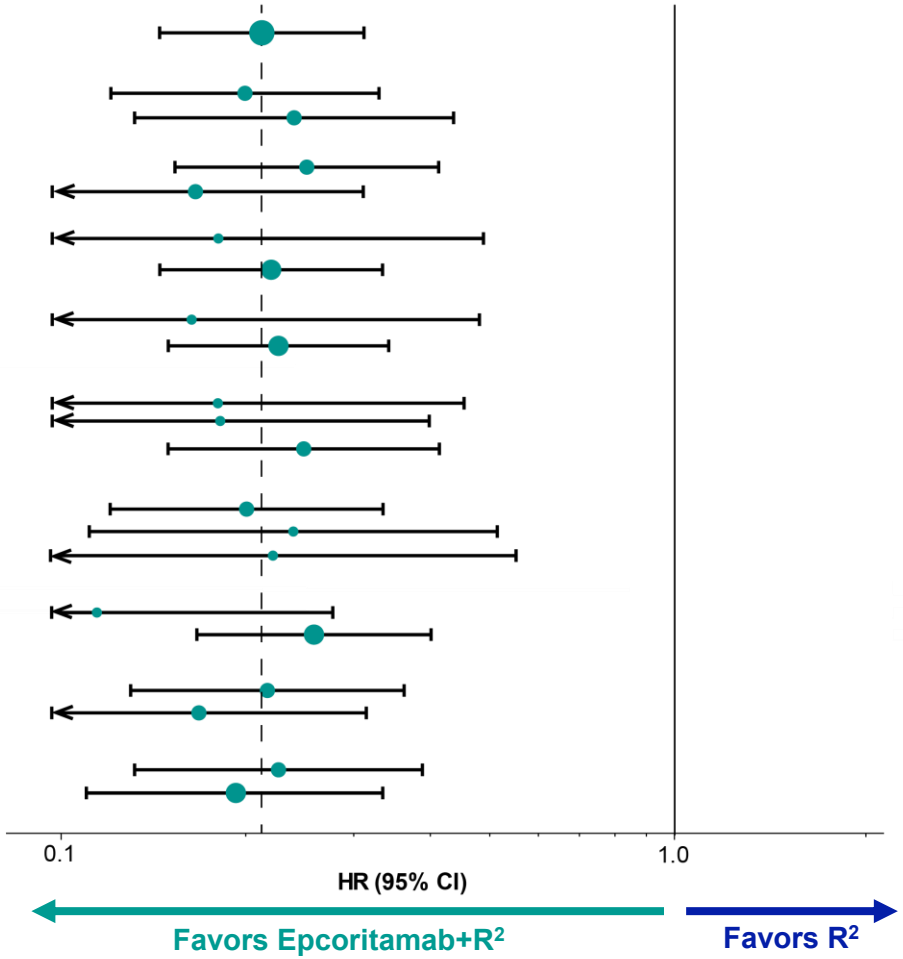
- Concordance rate was 94% for PFS between IRC and investigator assessment
- The estimated 16-month PFS was 85.5% (95% CI: 79.7, 89.7) for epcoritamab+R² and 40.2% (95% CI: 31.8, 48.4) for R²

Median follow-up for PFS: epcoritamab+R² (14.4m), R² (11.5m). The first planned interim analysis (January 10, 2025) achieved statistical significance on PFS, HR 0.21 (95% CI 0.13, 0.33) $P < 0.0001$, with a 1-sided significance level of 0.0023.

[a]Nominal *P* value is based on stratified log-rank test. Hazard ratio is estimated using stratified Cox proportional hazards model. This analysis was performed on the 78% information fraction.

Epcoritamab+R² Demonstrated Favorable PFS Across a Broad R/R FL Population

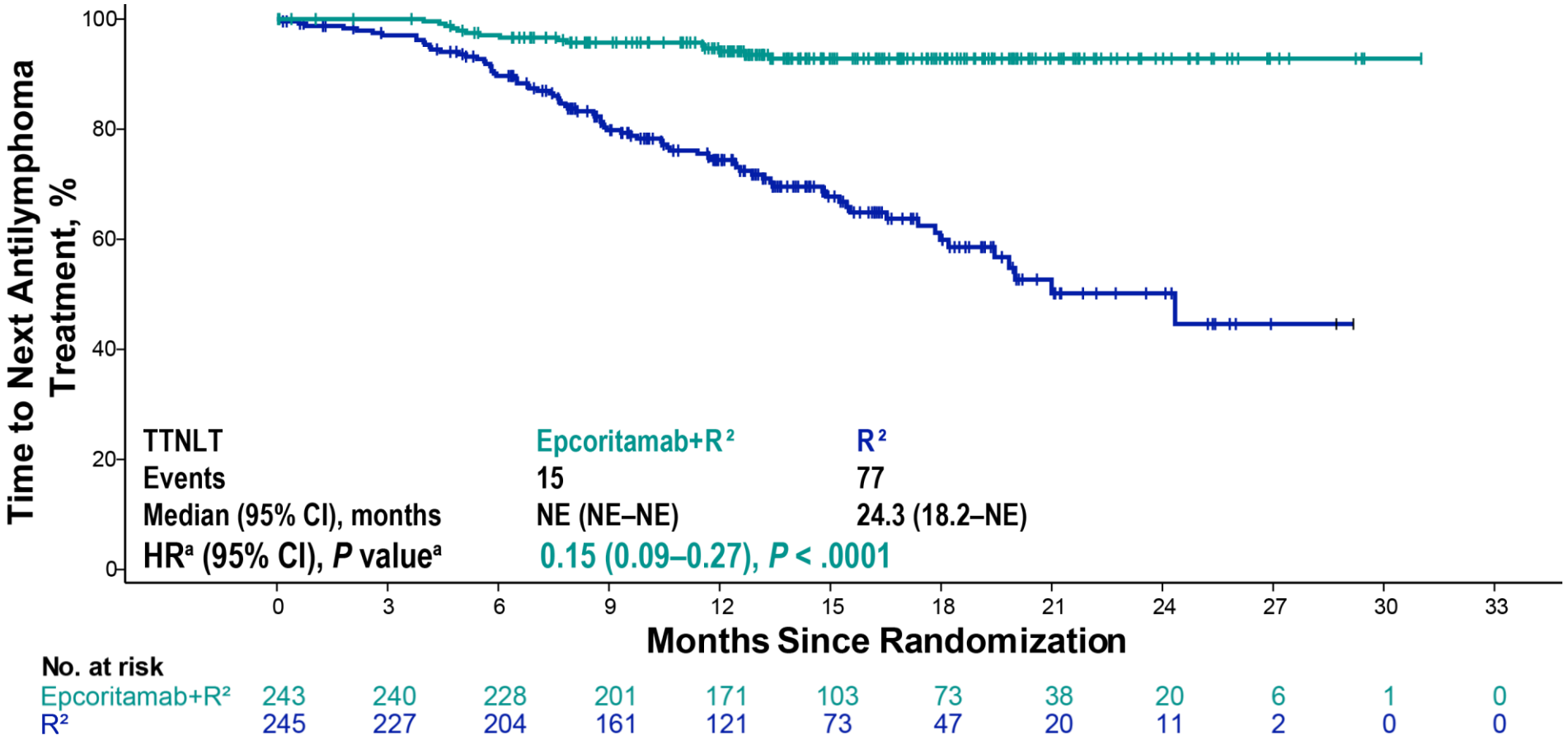
Prespecified Subgroups	Epcoritamab+R² Event/N (%)	R² Event/N (%)	HR (95% CI)
All patients	35/243 (14)	106/245 (43)	0.22 (0.15, 0.32)
Age (years)			
< 65	21/155 (13)	58/139 (42)	0.20 (0.12, 0.33)
≥ 65	14/88 (16)	48/106 (45)	0.24 (0.13, 0.44)
Sex			
Male	23/139 (17)	54/138 (39)	0.25 (0.15, 0.42)
Female	12/104 (12)	52/107 (49)	0.17 (0.09, 0.31)
Region			
US/Western Europe	5/58 (9)	18/60 (30)	0.18 (0.07, 0.49)
Rest of World	30/185 (16)	88/185 (48)	0.22 (0.15, 0.34)
Ann Arbor stage			
II	4/37 (11)	21/44 (48)	0.16 (0.06, 0.49)
III+IV	31/206 (15)	85/201 (42)	0.23 (0.15, 0.35)
FLIPI score at baseline			
0-1	6/63 (10)	19/56 (34)	0.18 (0.07, 0.46)
2	8/79 (10)	30/76 (39)	0.18 (0.08, 0.40)
3-5	21/100 (21)	57/113 (50)	0.25 (0.15, 0.42)
Number of prior lines			
1	20/145 (14)	58/141 (41)	0.20 (0.12, 0.34)
2	9/58 (16)	26/61 (43)	0.24 (0.11, 0.52)
≥ 3	6/40 (15)	22/43 (51)	0.23 (0.09, 0.56)
Bulky disease (≥ 7 cm)			
Yes	6/47 (13)	31/61 (51)	0.12 (0.05, 0.28)
No	28/191 (15)	71/176 (40)	0.26 (0.17, 0.41)
POD24			
Yes	22/106 (21)	47/93 (51)	0.22 (0.13, 0.37)
No	12/131 (9)	54/144 (38)	0.17 (0.09, 0.32)
Double refractory			
Yes	19/91 (21)	47/91 (52)	0.23 (0.13, 0.39)
No	16/152 (11)	59/154 (38)	0.19 (0.11, 0.34)



- Trends in favor of epcoritamab+R² were shown for all prespecified subgroups and ORR, CR, and DOR endpoints

N represents the total number of patients within each category in each arm. Arrows indicate that the confidence interval is extended more than current range. 95% CI is by unstratified Cox proportional hazard model.

Epcoritamab+R² Extended Time to Next Treatment



- At 16 months, 92.8% of patients treated with epcoritamab+R² remained free from new antilymphoma treatment compared with 64.9% of patients treated with R²

Median follow-up for TTNLT: epcoritamab+R² (14.6m), R² (14.1m). TTNLT results are for descriptive purposes only.
[a]Nominal *P* value is based on stratified log-rank test. Hazard ratio is estimated using stratified Cox proportional hazards model.

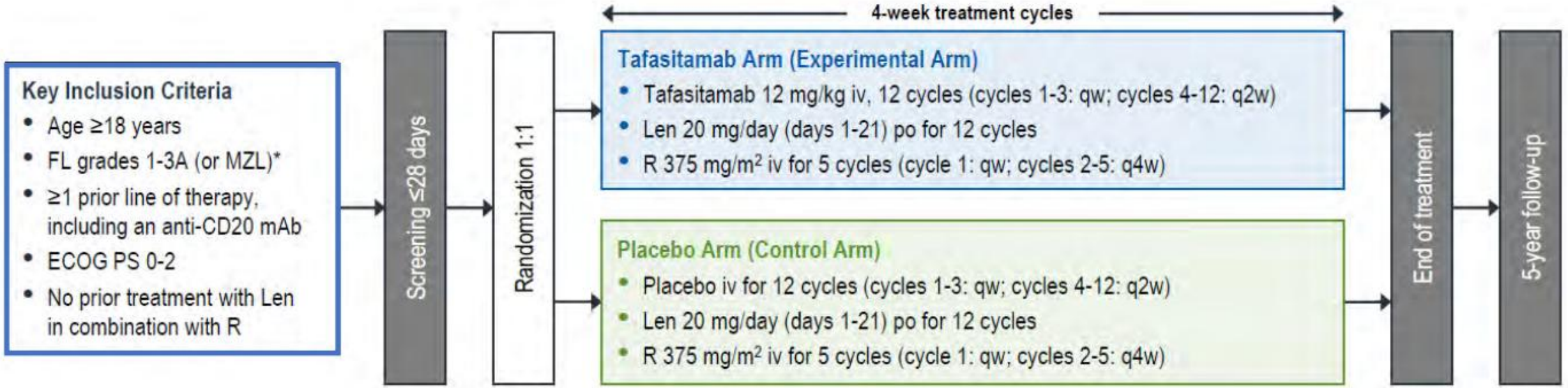
Manageable (?) AEs With No New Safety Signals

Adverse Event, n (%)	Epcoritamab+R^2 (N = 243)		R^2 (N = 238)	
	Any Grade	Grade ≥ 3	Any Grade	Grade ≥ 3
Any adverse event	242 (100)	219 (90)	235 (99)	161 (68)
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 clinical interest > 20%[a,b]				
Infections[c]	188 (77)	81 (33)	125 (53)	37 (16)
Neutropenia	180 (74)	167 (69)	123 (52)	100 (42)
Cytokine release syndrome	85 (35)	-	1 (< 1)	-
Anemia	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)

- Neutropenia was manageable and few patients discontinued any study drug (epcoritamab+R^2, 3%; R^2, 2%)
  - Incidence of febrile neutropenia: epcoritamab+R^2, 6%; R^2, 3%
- Infections were manageable and few patients discontinued any study drug (epcoritamab+R^2, 6%; R^2, 1%)
- Fatal adverse events were rare (epcoritamab+R^2, 2%; R^2, 4%)
- Despite higher rates of AEs in the epcoritamab+R^2 arm, most patients completed the prescribed regimen (median relative dose intensity ≥ 90% for epcoritamab+R^2)

[a]Neutropenia, anemia, pyrexia, rash and COVID-19 are grouped terms comprising multiple clinically related Preferred Terms. [b]This includes the AESI of CRS. [c]Events were in the MedDRA system organ class "Infections and Infestations." No grade 5 infections were reported.

inMIND trial: Phase III RCT in RR FL



Stratification Factors (Patients With FL)

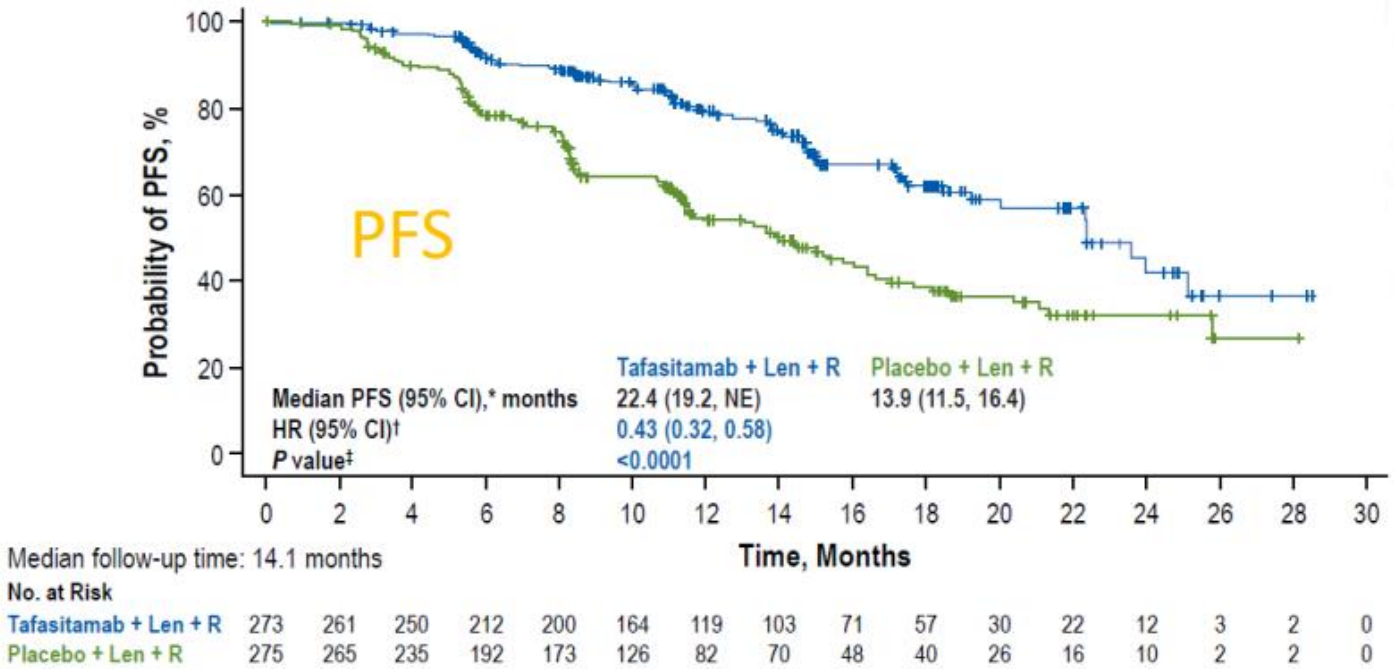
- POD24
- Refractoriness to prior anti-CD20 mAb therapy
- Number of prior lines of therapy (1 or ≥2)

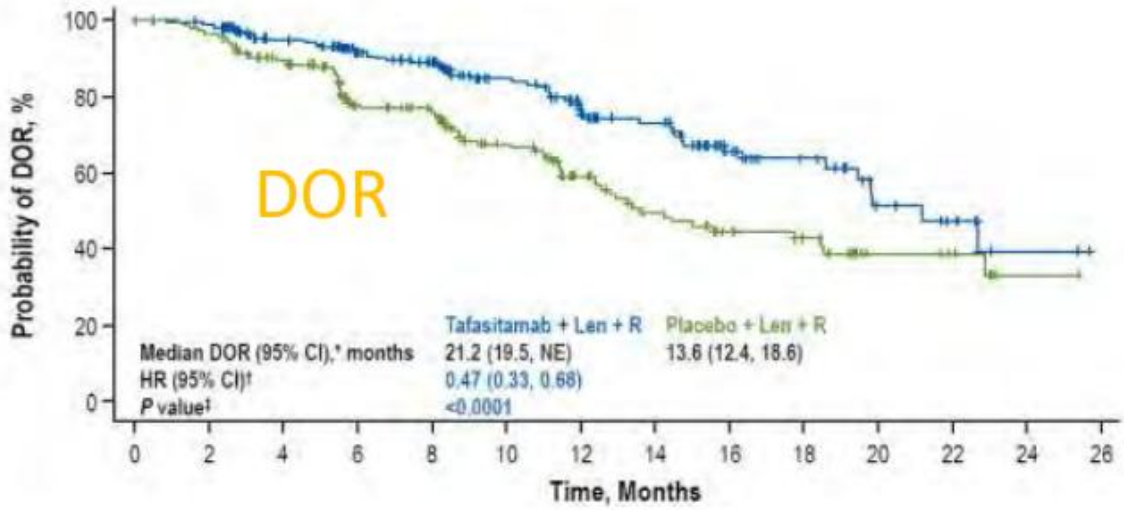
Study Endpoints in FL Population (Investigator Assessed Unless Specified)

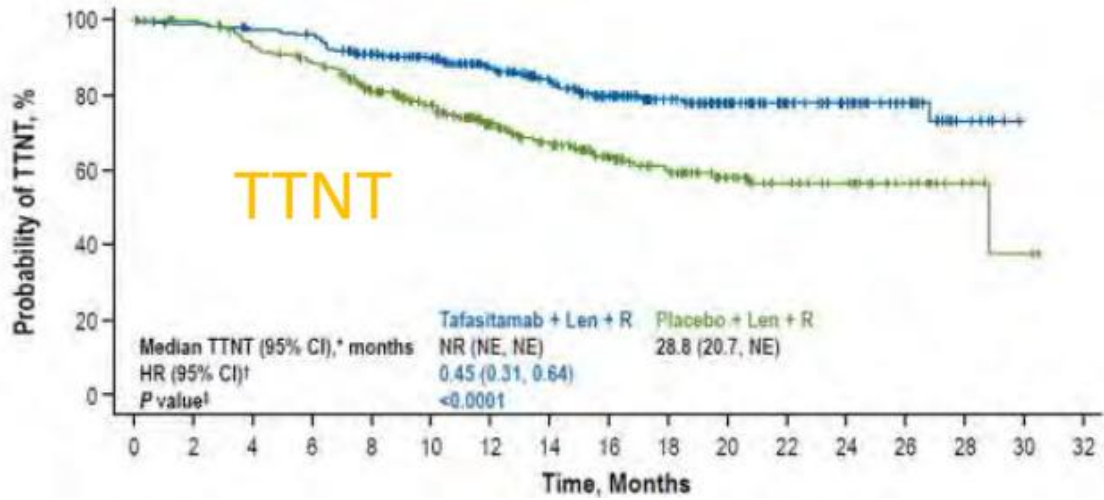
- Primary study endpoint: PFS
- Key secondary: PET-CR rate in the FDG-avid population, OS
- Select other secondary: PFS by IRC, ORR, DOR, safety, QoL, MRD
- Exploratory: TTNT, B-cell recovery, Ig levels, CD19 expression

Sehn et al, Lugano 2025 (Abstract #0028)

Improved PFS, DOR, TTNT with TafaR2







Median FU 14. 1 mo

Sehn et al, Lugano 2025 (Abstract #0028)

Most Frequent Any-Grade TEAEs (≥15% in Any Group)

Preferred Term, n (%)	Tafasitamab + Len + R (n=274)*	Placebo + Len + R (n=272)†	Total (n=546)
Any adverse event	272 (99.3)	270 (99.3)	542 (99.3)
Neutropenia	133 (48.5)	123 (45.2)	256 (46.9)
Diarrhea	103 (37.6)	77 (28.3)	180 (33.0)
COVID-19	86 (31.4)	64 (23.5)	150 (27.5)
Constipation	80 (29.2)	67 (24.6)	147 (26.9)
Rash	60 (21.9)	58 (21.3)	118 (21.6)
Fatigue	58 (21.2)	43 (15.8)	101 (18.5)
Cough	52 (19.0)	47 (17.3)	99 (18.1)
Pyrexia	52 (19.0)	44 (16.2)	96 (17.6)
Muscle spasms	49 (17.9)	49 (18.0)	98 (17.9)
Nausea	49 (17.9)	38 (14.0)	87 (15.9)
Infusion-related reaction	43 (15.7)	41 (15.1)	84 (15.4)
Thrombocytopenia	37 (13.5)	42 (15.4)	79 (14.5)
Pruritus	44 (16.1)	28 (10.3)	72 (13.2)

Sehn et al, Lugano 2025 (Abstract #0028)

ROSEWOOD study design

Key eligibility criteria
- Age ≥18 years
- Grade 1-3A R/R FL
- Previous treatment with ≥2 lines of therapy, including an anti-CD20 antibody and an alkylating agent
- Measurable disease
- ECOG PS of 0-2
- Adequate organ function
- No prior BTK inhibitor

127 sites; 17 countries/regions
Randomized November 2017 to June 2021

Arm A
Zanubrutinib[a] + obinutuzumab[b] (n=145)
Until PD or unacceptable toxicity

Randomization 2:1
Stratification factors
- Number of prior lines of treatment
- Rituximab-refractory status
- Geographic region

Arm B
Obinutuzumab[b] (n=72)
Option to cross over to combination if PD is centrally confirmed or if there is no response at 12 months

Primary endpoint
- ORR by IRC according to Lugano 2014 classification[1]

Other endpoints
- DOR by IRC[c]
- PFS by IRC[c]
- OS[c]
- TTNT
- Safety (AEs)[c]

AE, adverse event; BTK, Bruton tyrosine kinase; DOR, duration of response; ECOG PS, Eastern Cooperative Oncology Group performance status; FL, follicular lymphoma; IRC, independent review committee; ORR, objective response rate; OS, overall survival; PD, progressive disease; PFS, progression-free survival; R/R, relapsed or refractory; TTNT, time to next treatment.
[a] Zanubrutinib was given orally at 160 mg twice daily. [b] Obinutuzumab was given intravenously at 1000 mg in both arms on days 1, 8, and 15 of cycle 1, day 1 of cycles 2-6, and then every 8 weeks up to a maximum of 20 doses. [c] Secondary endpoint.
1. Cheson BD, et al. *J Clin Oncol*. 2014;32(27):3059-3068.

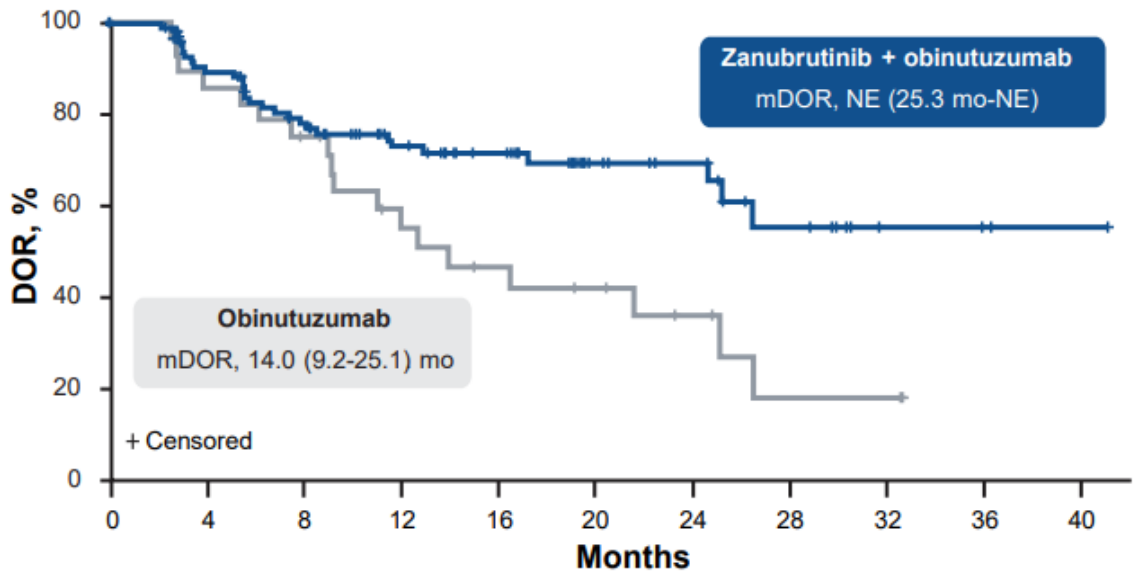
The study population was heavily pretreated and had refractory disease

Characteristics	Zanubrutinib + obinutuzumab (n=145)	Obinutuzumab (n=72)
Age, median (range), years	63.0 (31-84)	65.5 (32-88)
ECOG PS of ≥1, n (%)	59 (40.6)	41 (57.0)
FLIPI score of ≥3, n (%)	77 (53.1)	37 (51.4)
Ann Arbor stage III-IV, n (%)	119 (82.1)	60 (83.3)
Bulky disease (≥7 cm), n (%)	23 (15.9)	12 (16.7)
High LDH level (>ULN), n (%)	49 (33.8)	29 (40.3)
High tumor burden per GELF criteria, n (%)	83 (57.2)	40 (55.6)
No. of prior lines of therapy, median (range)	3 (2-11)	3 (2-9)
Refractory to rituximab, n (%)	78 (53.8)	36 (50.0)
Refractory to most recent line of therapy, n (%)	47 (32.4)	29 (40.3)
PD ≤24 months after starting first line of therapy, n (%)	50 (34.5)	30 (41.7)
Prior therapy, n (%)		
Chemoimmunotherapy	143 (98.6)	71 (98.6)
Anthracyclines	118 (81.4)	57 (79.2)
Cyclophosphamide	136 (93.8)	68 (94.4)
Bendamustine	79 (54.5)	40 (55.6)

ECOG PS, Eastern Cooperative Oncology Group performance status; FLIPI, Follicular Lymphoma International Prognostic Index; GELF, Groupe d'Etude des Lymphomes Folliculaires; LDH, lactate dehydrogenase; PD, progressive disease; ULN, upper limit of normal.

DOR and PFS were longer with zanubrutinib + obinutuzumab

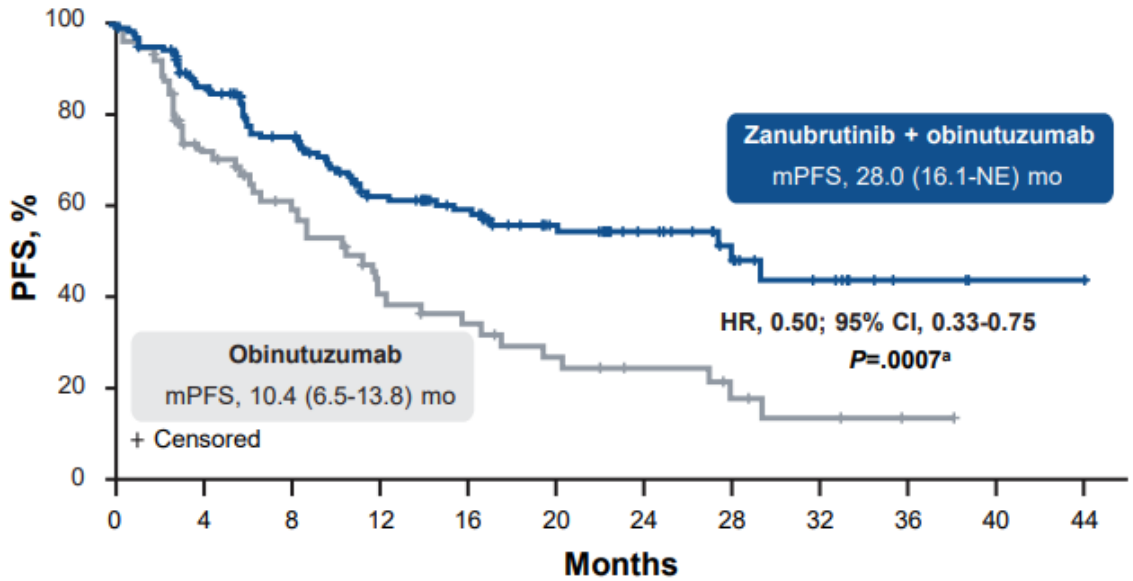
DOR by IRC



No. at risk

Zanubrutinib + obinutuzumab	100	97	82	73	68	59	51	43	40	33	23	21	19	12	10	7	3	3	2	1	1	0
Obinutuzumab	33	29	24	23	20	16	13	11	10	9	8	6	5	3	2	2	2	0				

PFS by IRC



No. at risk

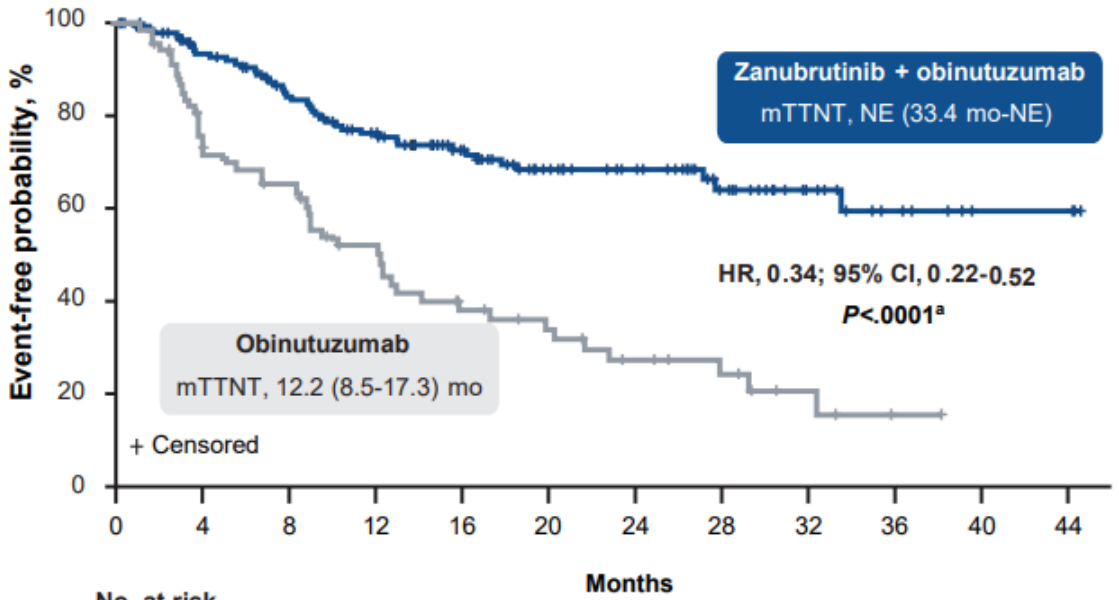
Zanubrutinib + obinutuzumab	145	135	116	96	92	79	67	62	56	45	38	35	25	22	15	10	9	5	3	3	1	1	0
Obinutuzumab	72	63	42	34	30	27	19	16	15	12	11	9	8	8	5	3	3	2	1	1	0		

HR, hazard ratio; IRC, independent review committee; mDOR, median duration of response; mPFS, median progression-free survival; NE, not estimable.

[a] Descriptive 2-sided *P* value.

TTNT and OS were prolonged with zanubrutinib + obinutuzumab

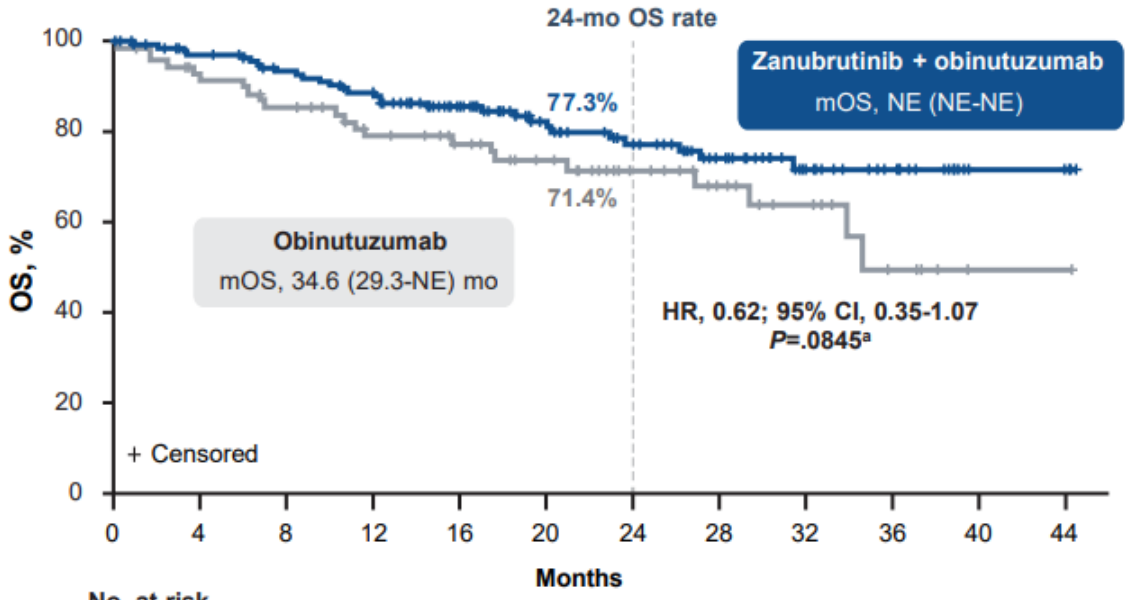
TTNT



No. at risk

Zanubrutinib + obinutuzumab	145	137	125	118	107	98	91	80	71	62	53	47	44	40	29	22	17	12	10	6	3	3	3	0
Obinutuzumab	72	65	49	44	41	32	30	24	20	18	16	13	11	9	8	5	4	2	1	1	0			

OS



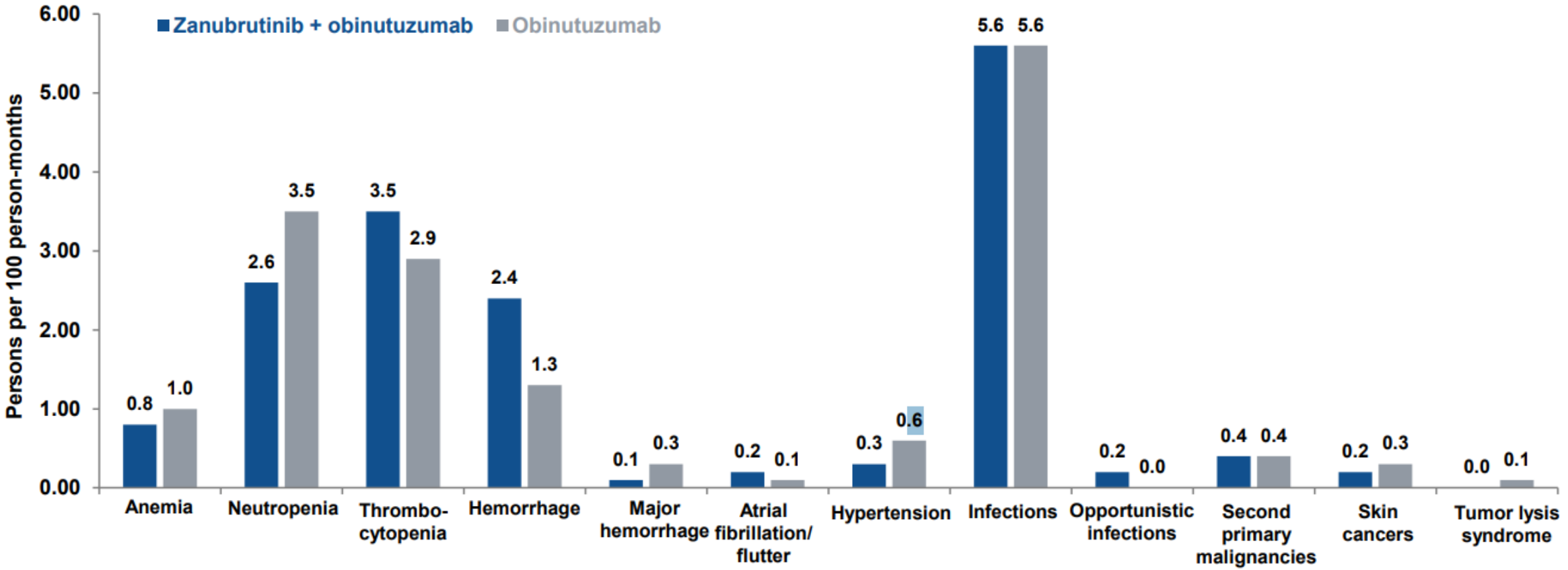
No. at risk

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

HR, hazard ratio; mOS, median overall survival; mTTNT, median time to next treatment; NE, not estimable.
[a] Descriptive 2-sided *P* value.

EAIRs for TEAEs of special interest were similar in both arms, except for any grade hemorrhage

EAIRs for TEAEs of special interest

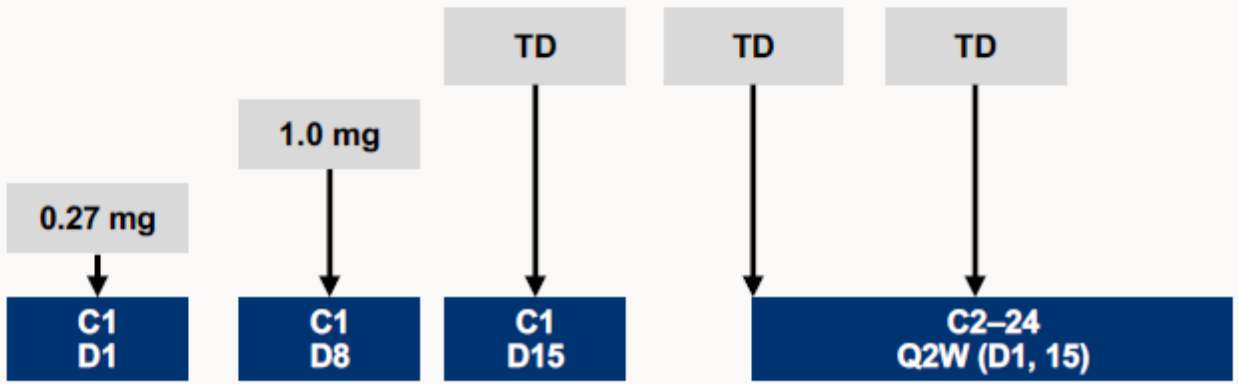


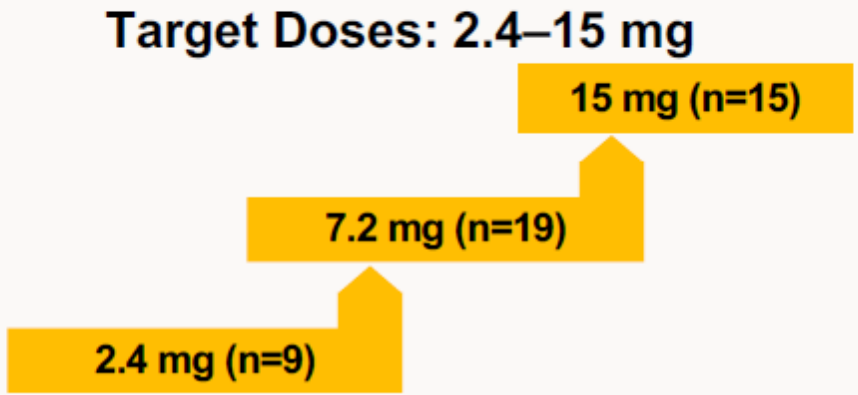
EAIR, exposure-adjusted incidence rate; TEAE, treatment-emergent adverse event.

Surovatamig Phase 1 Study Design

Dosing Regimen

Double SUD (n=43)



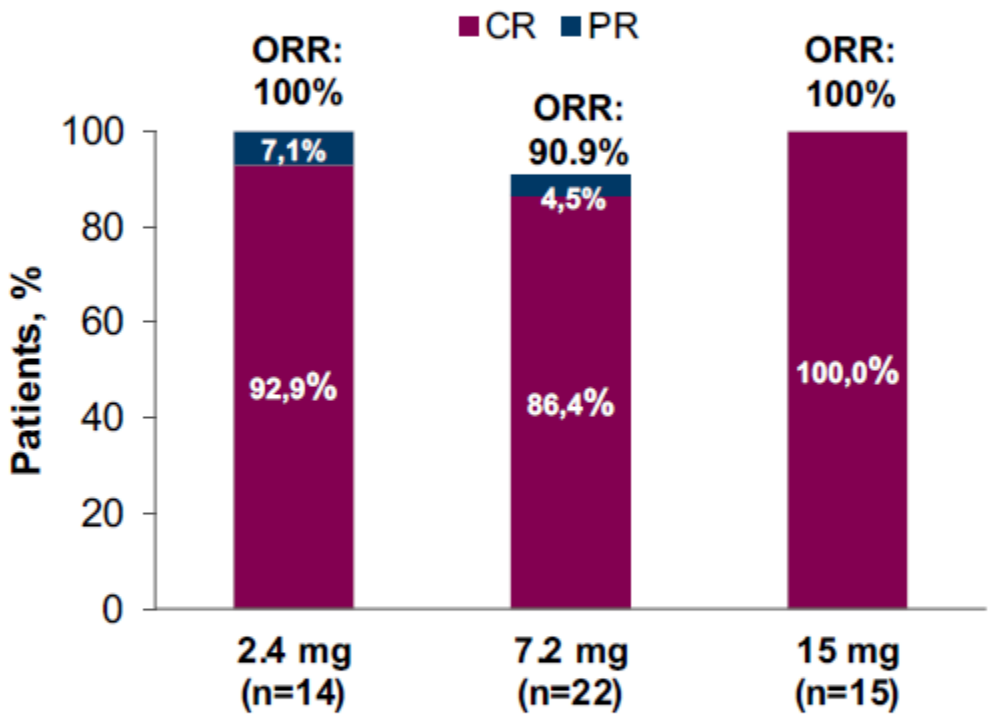


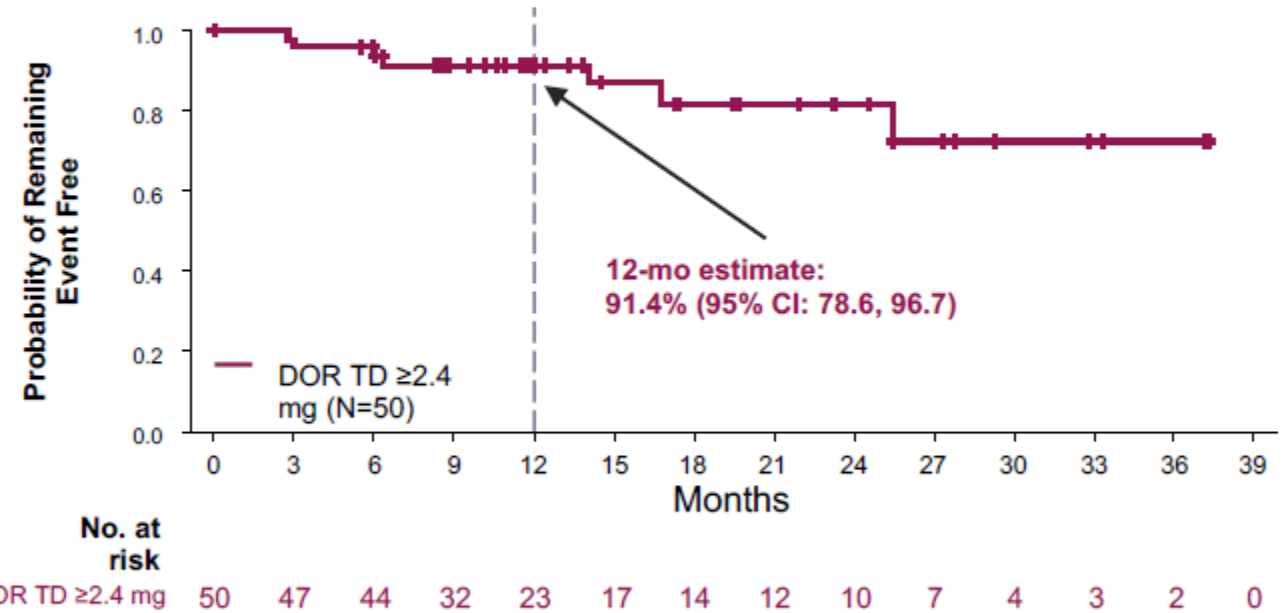
Surovatamig Treatment

- Surovatamig is administered intravenously in fixed-dose escalation, 1SUD, or 2SUD
- Treatment is delivered in 28-day cycles up to 2 years
  - Cycle 1 doses were inpatient
- Patients with CR on 2 consecutive scans may receive surovatamig every 4 weeks after C6
- Premedication with dexamethasone included two 10-mg doses prior to cycle 1 surovatamig doses

NCT04594642; data cutoff: May 19, 2025

High Response Rates Observed at All Target Doses



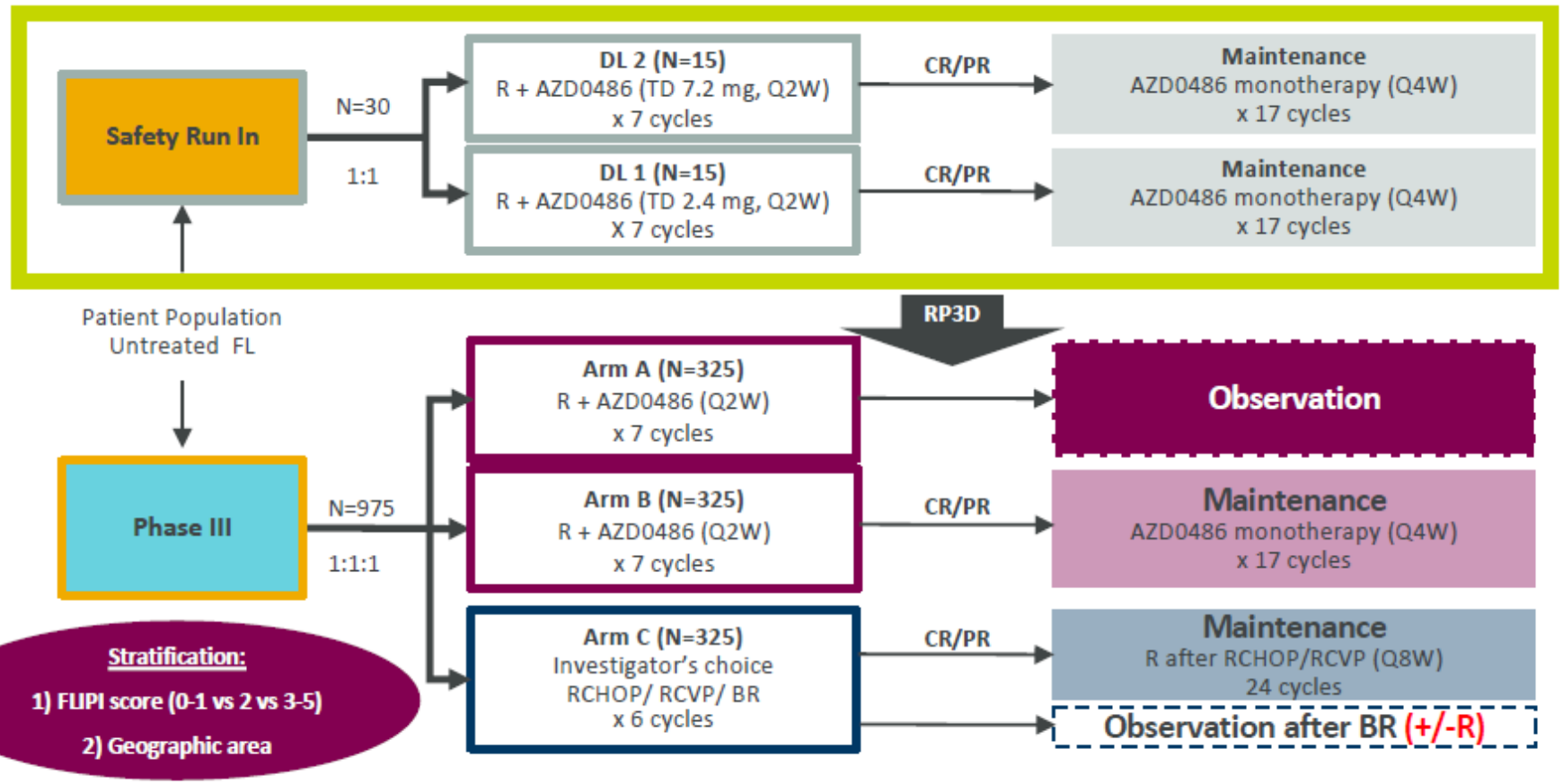


- ORR/CR rate for patients who received ≥2.4 mg was 96%/92%
- In the ITT population, ORR/CR rates were 100%/93%, 87%/83% and 100%/100% in the 2.4-mg, 7.2-mg and 15-mg cohorts, respectively[a]

[a]ITT population includes 1 additional patient who discontinued prior to response assessment due to AE at 7.2 mg TD

- All 8 patients with prior CD20 TCE therapy and/or CD19 CAR T who achieved CR with surovatamig remain in CR
- All 11 patients who completed surovatamig treatment remain in CR off treatment

SOUNDTRACK F1: Phase III Study Design with Safety Run-In



Target population:

- Treatment naïve FL
- Meet GELF criteria

Endpoints:

- **Primary:**
  - Safety Run-in: Safety and tolerability of AZD0486 + R and RP3D determination
  - Phase III: PFS assessed by IRC based on Lugano Response Criteria
- **Secondary:**
  - Safety Run-in: Efficacy (ORR, CRR, CR@EOI, CR30, DoR, PFS, OS), PK/PD/Immunogenicity
  - Phase III: Efficacy (**CR@EOI (Key secondary)**, ORR, CRR,, CR30, DoR, PFS, TTNT, OS), safety, PK/Immunogenicity, PRO, MRD-ve CR rate

B: Bendamustine; CNS: Central nervous system; CR: complete response; CR30: complete response at 30 months; DL: Dose level; DoR: Duration of Response; EOI: end of induction; FL: Follicular Lymphoma; MRD: Minimal residual diseaseORR: Overall response rate; PB: peripheral blood; OS: Overall survival; PFS: progression free survival; PR; partial response; PRO: Patient reported outcome; QxW: every x weeks; R: rituximab; RP3D: recommended Ph3 dose; SOC= standard of care; TD= target dose; TTNT: Time to next treatment

Ongoing randomized studies of bispecific antibody combinations in 1L FL

Regimen	Trial (Phase)	Patients (1L FL cohorts)*	Treatment duration and administration	Primary endpoint	Study status
Mosunetuzumab-Len versus R- / G-chemo	**MorningLyte** (Phase III)[1]	790[1]	**Mosunetuzumab** (SC) 21 cycles **Len** (oral) 11 cycles[1]	PFS (by IRC)[1]	Recruiting[1]
Odronextamab-chemo versus R-chemo	**OLYMPIA-2** (Phase III)[2]	733[2]	**Odronextamab** (IV) **CHOP/CVP** (IV)[2]	Part 1: DLTs and safety Part 2: CR30 (by ICR)[2]	Recruiting[2]
Epcoritamab-R-Len versus R- / G-chemo	**EPCORE FL-2** (Phase III)[3]	1095[3]	**Epcoritamab** (SC) **R** (IV) **Len** (oral)†[3]	CR30 (by IRC) PFS (by IRC)[3]	Recruiting[3]
Surovatamig plus R versus R-chemo	**SOUNDTRACK-F1** (Phase III)[4]	975[4]	**R-surovatamig** (IV) 7 cycles alone (arm A) or + maintenance (ie, 17 cycles) (arm B)	Safety run-in: RP3D safety Phase III: PFS by IRC[4]	Recruiting[4]

Products/indications are investigational and not approved. This slide is for educational purposes only

*Estimated enrollment. †120-week treatment duration

CR30, complete response at 30 months; CVP, cyclophosphamide, vincristine and prednisone; DLT, dose-limiting toxicity; BICR, blinded independent central review; ICR, independent central review; RP3D, recommended Phase III dose.

1. NCT06284122. Available at: https://clinicaltrials.gov/study/NCT06284122;
2. NCT06097364. Available at: https://clinicaltrials.gov/study/NCT06097364;
3. NCT06191744. Available at: https://clinicaltrials.gov/study/NCT06191744;
4. NCT06549695. Available at: https://clinicaltrials.gov/study/NCT06549595.

“We face an era of abundance, and a chaos of choice”

Ayushi Chauan, MD

Future Outlook in FL – My personal Take

- We have improved the overall treatment of FL, including patients with multiple relapses

- However, we may not forget that most patients are not represented in clinical trials:
  - Age/Frailty
  - Comorbidity
  - Access/Infrastructure

- In the end, our patients want only two things: Live LONGER and BETTER

Future Outlook in FL – My personal Take

- Novel agents need to focus on increasing PFS while not compromising QoL or increasing the risk of complications in FL

- As we expect BsAs to move on to earlier lines of therapy, we need to address the post-BsAs scenario, including patients ineligible to CarT

- Chemo-free is not Trouble-Free. Follow up is needed to address long-term toxicities (including secondary neoplasias)

Thank You!

Guilherme Fleury Perini, MD
Einstein Hospital Israelita
Sao Paulo, Brasil
@guiperiniMD
Guilherme.Perini@einstein.br

Andres McAllister

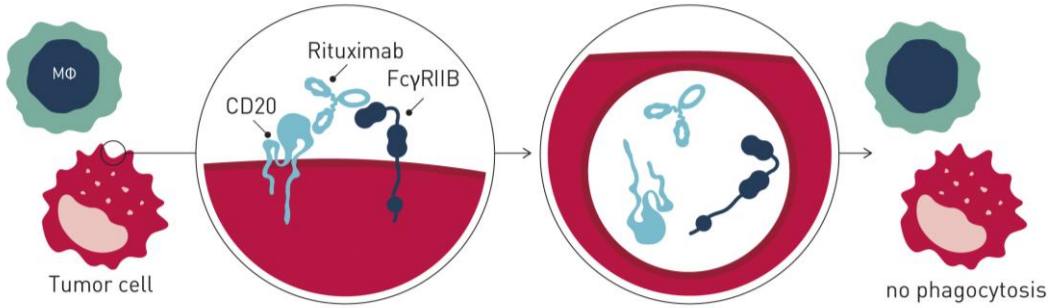
CMO

BI-1206

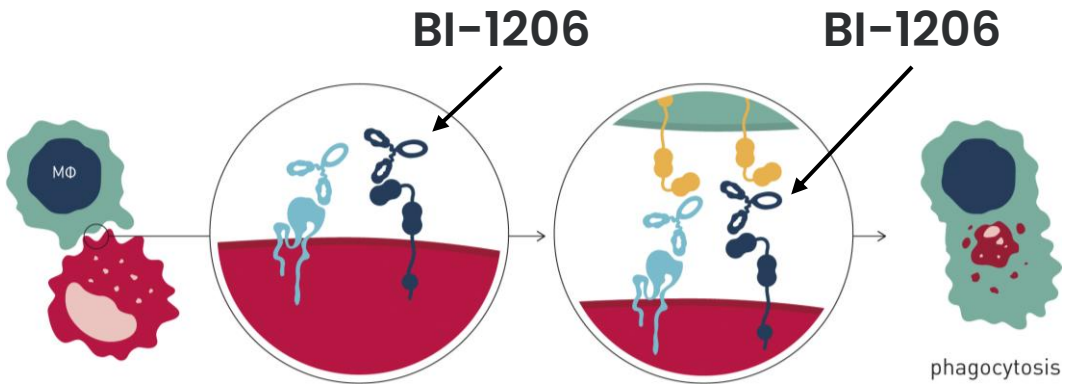
Targeting Resistance to Rituximab Through FcγRIIB Blockade: BI-1206 + Rituximab + Acalabrutinib Shows Powerful Activity in R/R NHL

Mechanism of Action

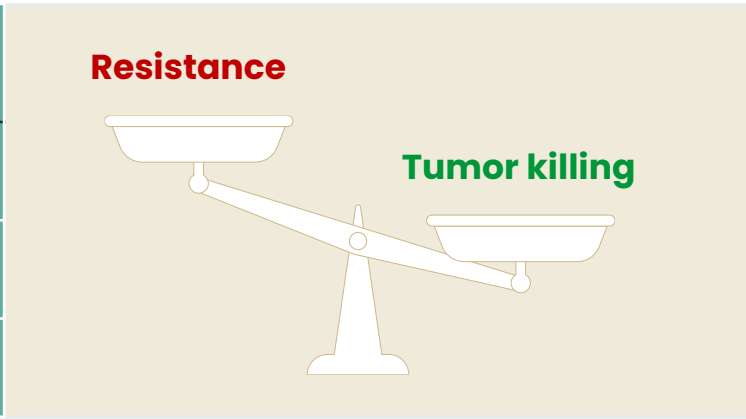
A **FcγRIIB-receptor removes rituximab from CD20 so immune cells can no longer attack the tumor**



B **By blocking the FcγRIIB-receptor, immune cells can kill the tumor**



	CD20 internalization	Activating FcγR-dependent Tumor cell killing
Rituximab	+++	–
Obinutuzumab *(Fc-engineered)*	+	+ (FcγRIIIa)
Rituximab + BI-1206	–	+++ (FcγRI/IIa/IIIa)

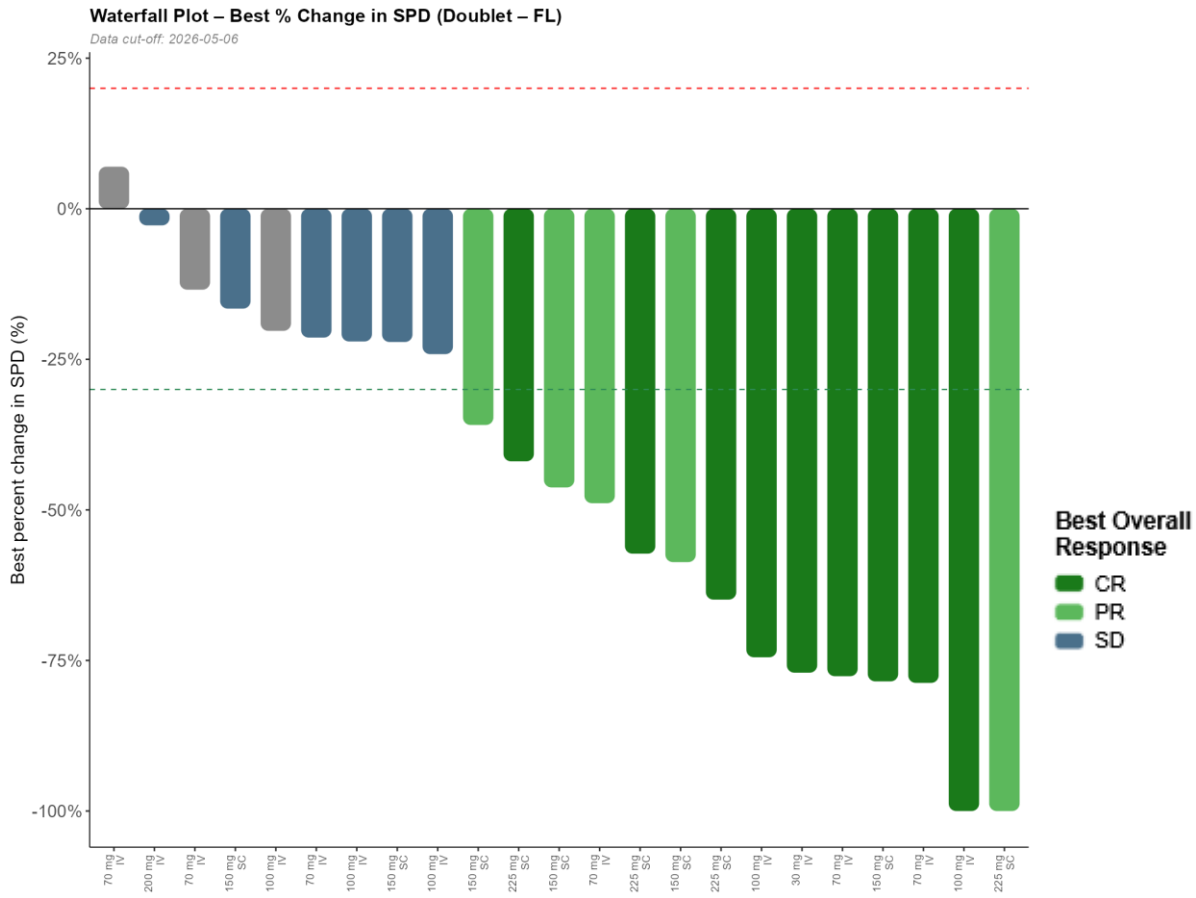


Scientific Rationale in R/R Follicular Lymphoma

Obinutuzumab	ORR 45% ROSEWOOD Study
Obinutuzumab + Zanubrutinib	ORR 69% ROSEWOOD Study
Rituximab + Acalabrutinib	ORR 31%
Rituximab + BI-1206	ORR 59%; CRR - 41%
Rituximab + BI-1206 + Acalabrutinib	BI-1206 can overcome rituximab resistance

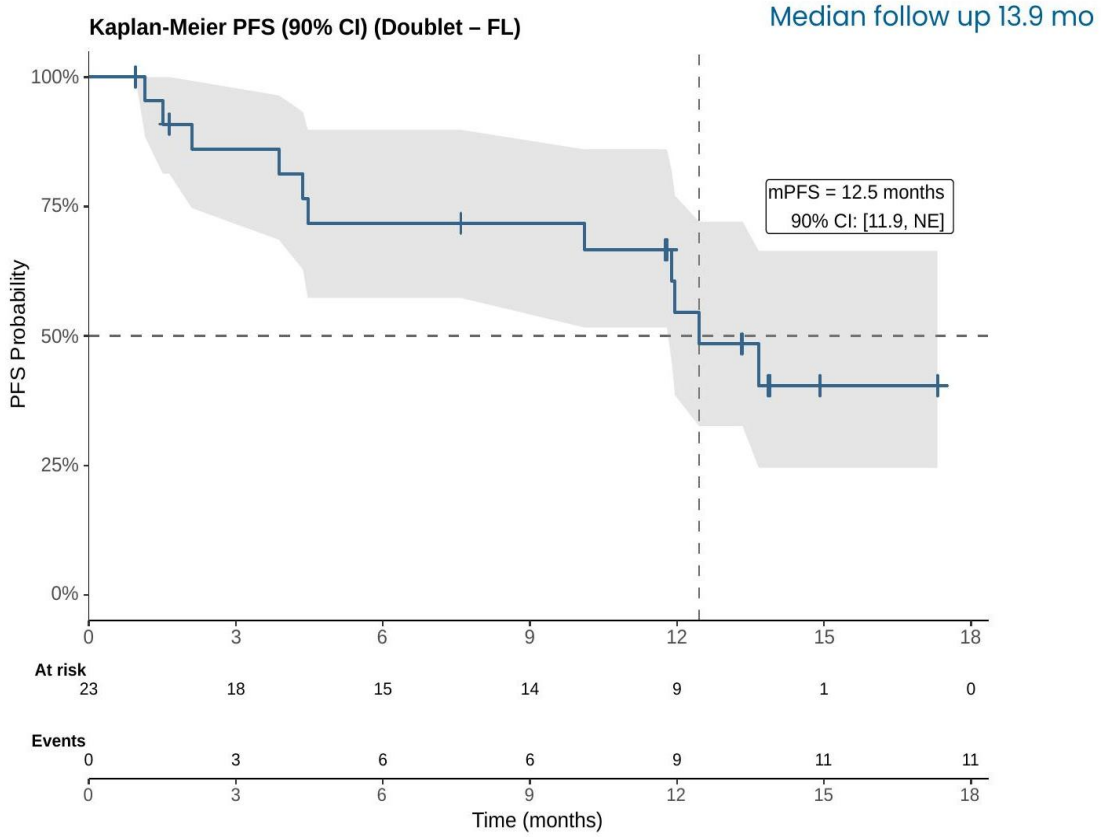
BI-1206 + Rituximab **Doublet** in R/R FL: Deep and Lasting Responses

Response depth (doublet, FL)



Response assessed through FDG-PET according to Lugano criteria (metabolic response)

Median progression-free survival; mPFS 12.5 months *(90% CI: 11.9, NE)*



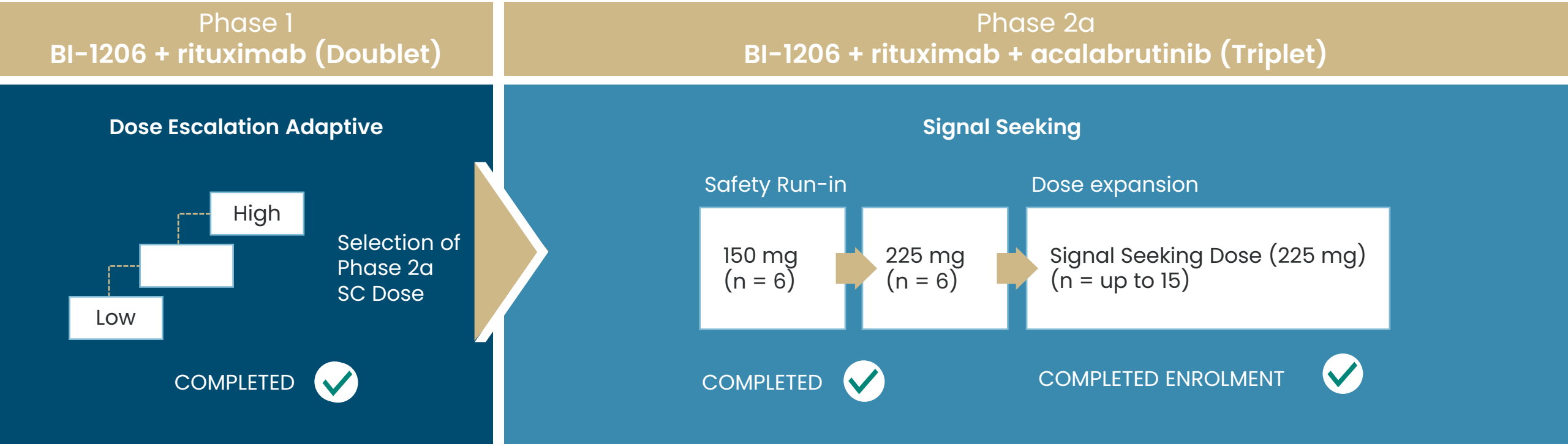
Progression free survival probability in FL subset after treatment with BI-1206+rituximab doublet (Ph1)

Responses are deep and durable: disease control comparable to R2; exceeds obinutuzumab and other agents with similar inclusion criteria

Data cut-off 2026-05-06. R2=rituximab + Revlimid. Response assessed through FDG-PET according to Lugano criteria.
Progression free survival probability in FL subset after treatment with BI-1206 + rituximab doublet in Study 17-BI-1206-02 Ph1.

BI-1206 Clinical Study Overview

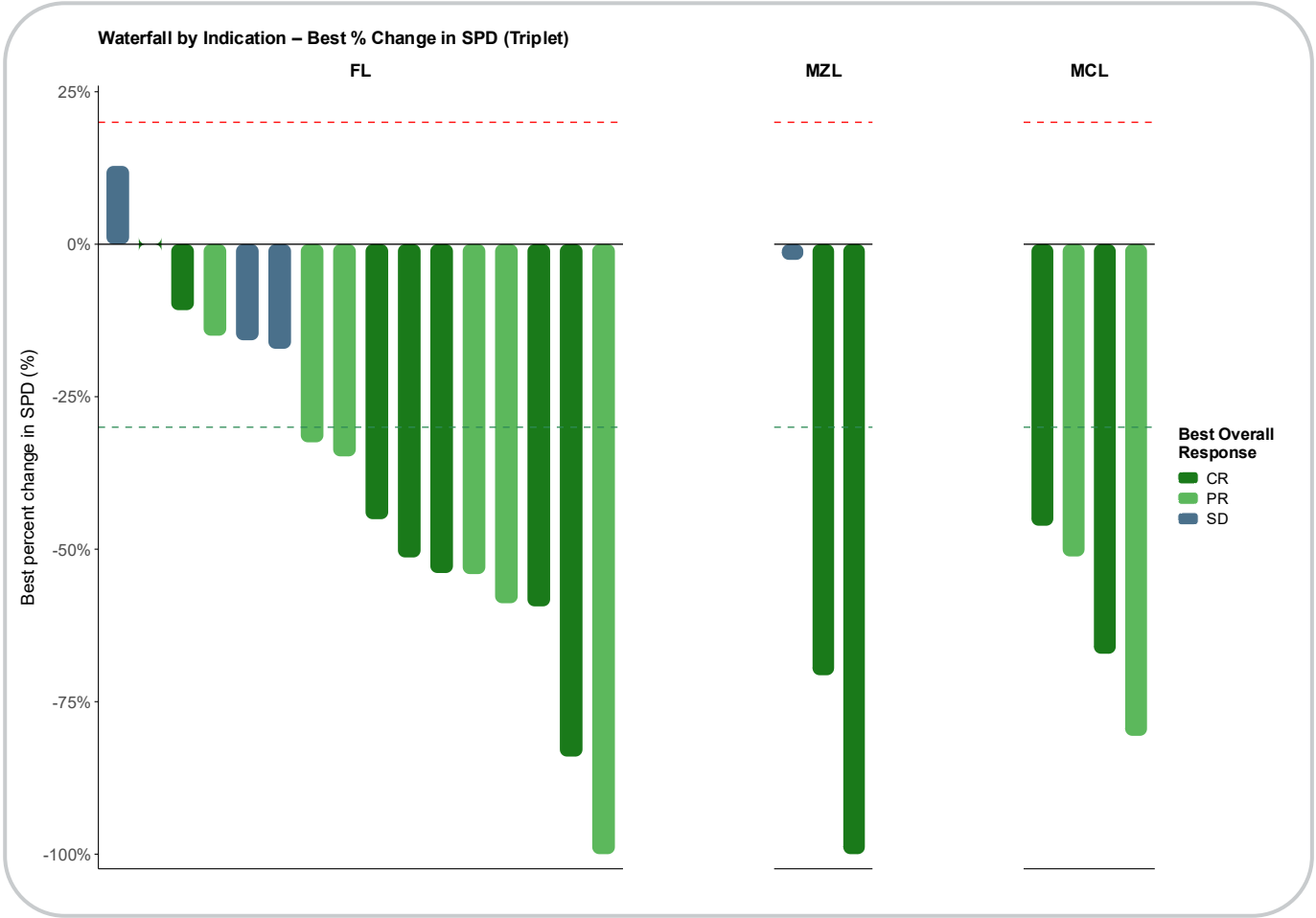
- Phase 1: BI-1206 enhances the activity of rituximab *(next slide)*
- Phase 2a: Adding acalabrutinib to the combination results in impressive efficacy (and Safety!)



Triplet Combination Results in High Response Rates Across NHL Subtype

83% ORR (n=23)	**48%** CRR	**100%** DCR	**81%** ORR in **FL** (n=16)	**44%** CRR in **FL**	**No CRS · No ICANS** No increased infection rate

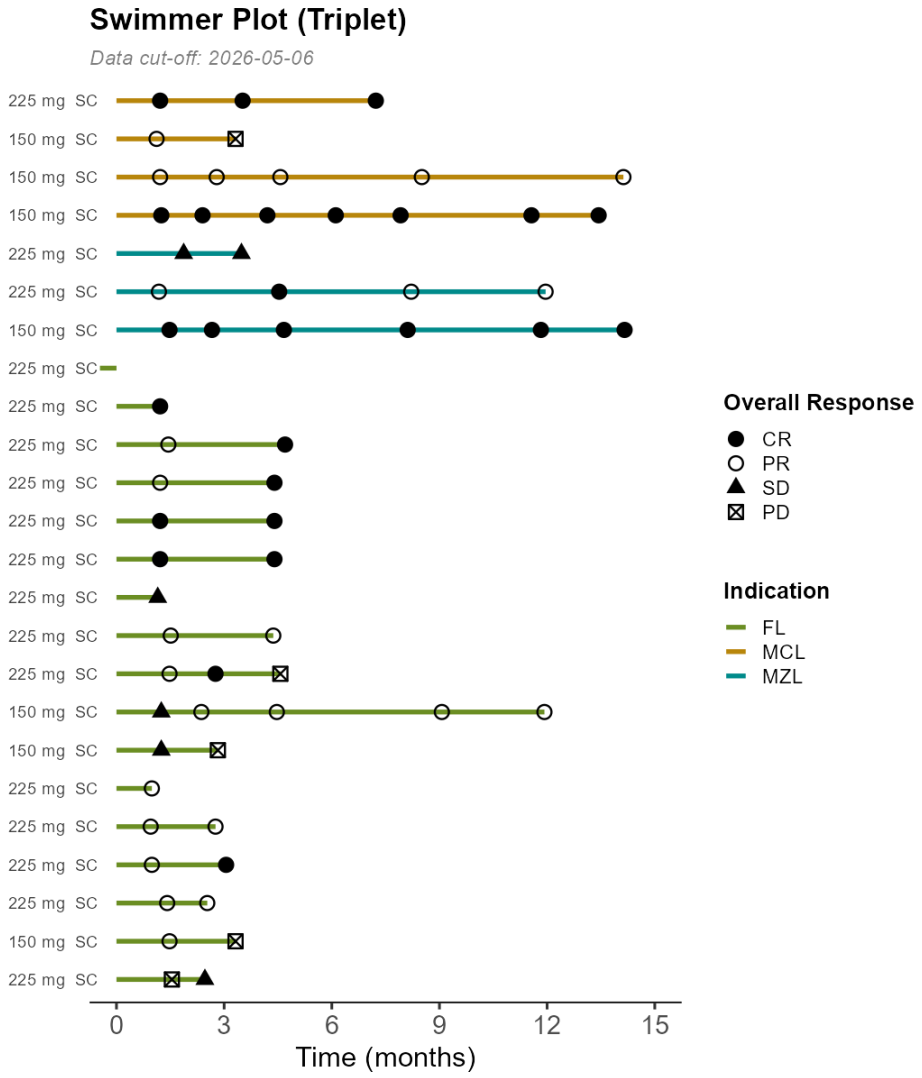
- **ORR of 83%, CRR of 48% and DCR of 100%** (n=23)
- Best Response in 23 evaluable patients:
  - 11 complete responses (CR)
  - 8 partial responses (PR)
  - 4 Patients with stable disease (SD)
- In the **follicular lymphoma (FL) subset (n=16), ORR was 81% and CRR 44%**
- The treatment has been **well-tolerated with no safety or tolerability concerns**
  - No CRS
  - No ICANS
  - No increased rate of infections

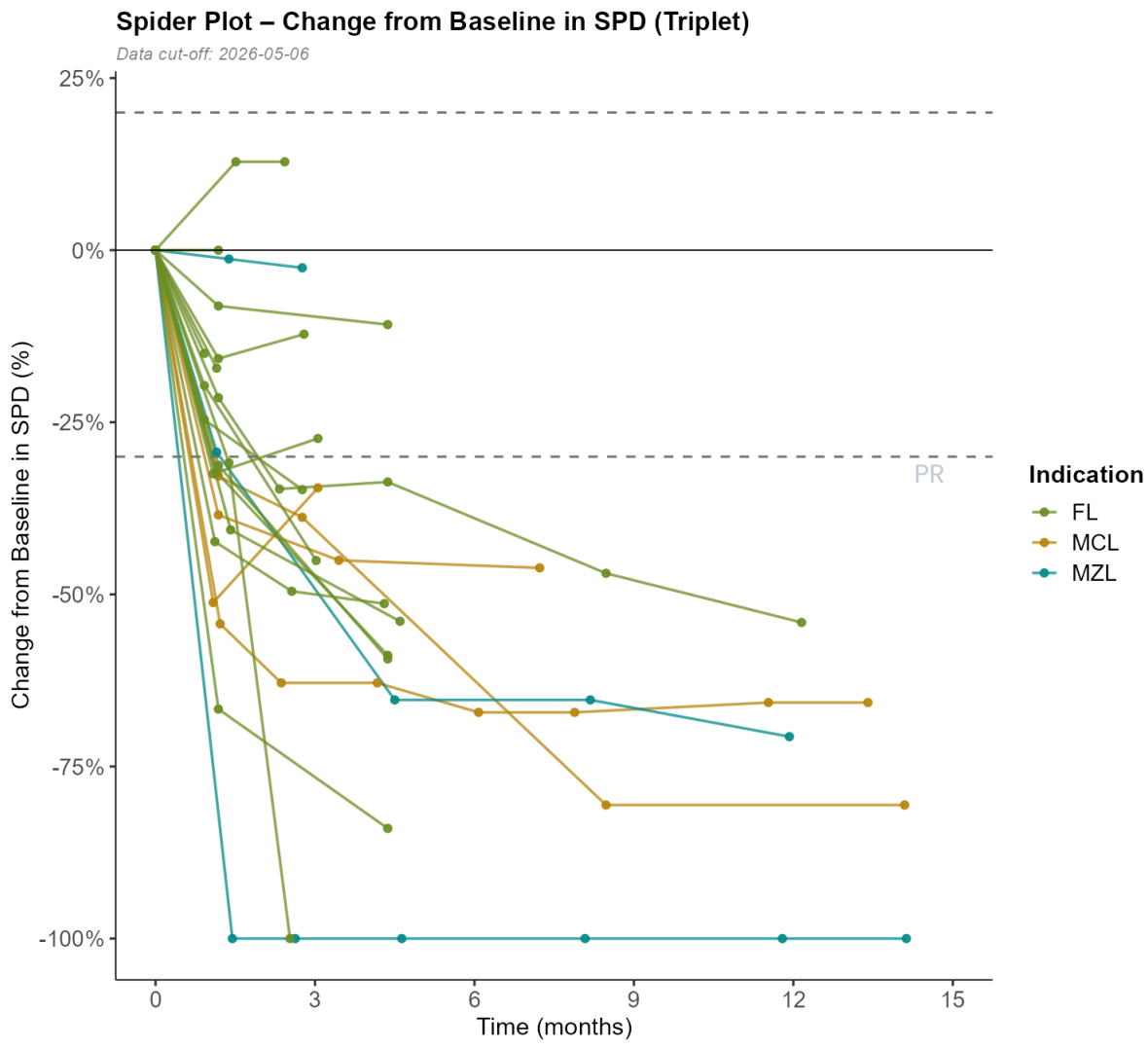


Waterfall plot of BI-1206 + rituximab + acalabrutinib triplet across NHL subtype. Response assessed through FDG-PET according to Lugano criteria (changes in metabolic parameters).

Data cut-off 2026-05-06

BI-1206 + Rituximab + Calquence* **Triplet:** Best Response (FL, MZL, MCL)



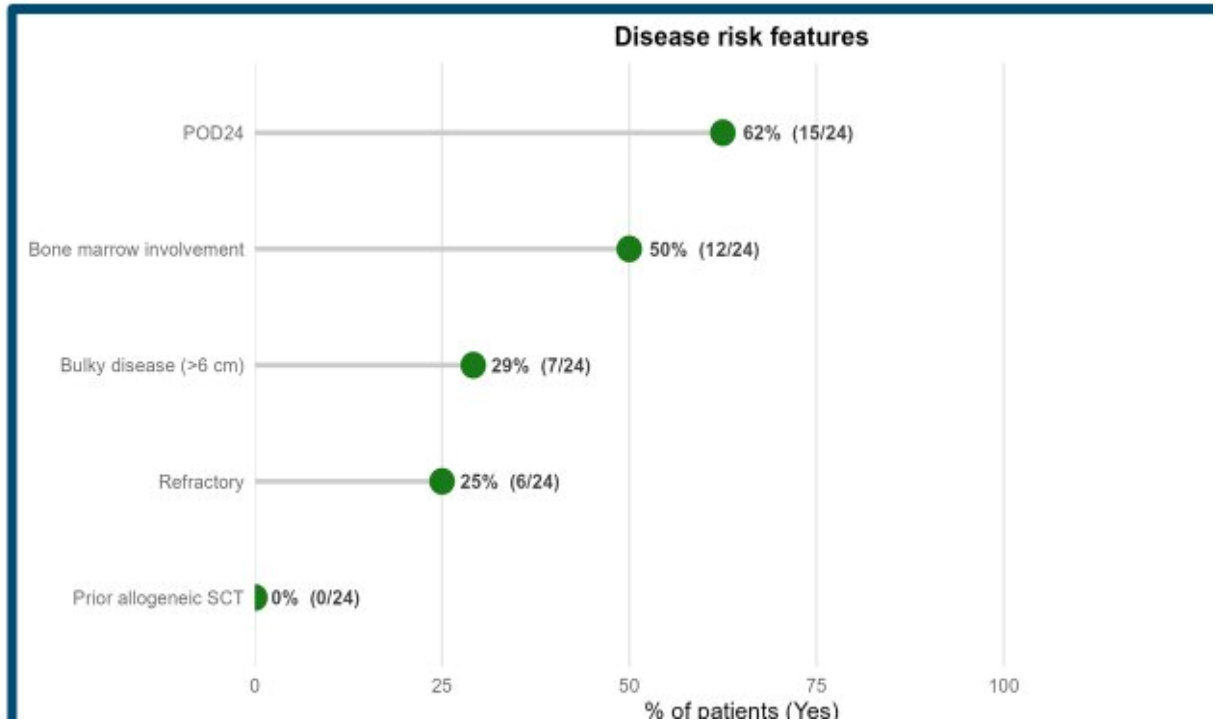


* Acalabrutinib, supplied by AstraZeneca. Data cut-off 2026-05-06

Challenging, Heavily Pretreated Population With High-risk Disease Features

Phase 2a patient population (triplet): n=24

- **Age:** median 53 years old (range 40-84)
- **Three NHL subtypes:** FL (71%), MCL (17%), MZL (12%)
- **62% with POD24*:** a marker of high-risk, aggressive disease
- **25% refractory** to prior therapy; 50% bone marrow involvement
- **83% (n=20) had stage III-IV**



Characteristic	150 mg (n=7)	225 mg (n=17)	Total (n=24)
NHL subtype: FL	3 (43%)	14 (82%)	17 (71%)
NHL subtype: MCL	3 (43%)	1 (6%)	4 (17%)
NHL subtype: MZL	1 (14%)	2 (12%)	3 (12%)
Prior lines: 1	4 (57%)	9 (53%)	13 (54%)
Prior lines: 2	2 (29%)	4 (24%)	6 (25%)
Prior lines: ≥3	1 (14%)	4 (24%)	5 (21%)
Bone marrow involvement	3 (43%)	9 (53%)	12 (50%)
Refractory	**2 (29%)**	**4 (24%)**	**6 (25%)**
POD24*	**3 (43%)**	**12 (71%)**	**15 (62%)**
Prior allogeneic SCT	0 (0%)	0 (0%)	0 (0%)

▲ **High-risk markers**

* Progression of Disease within 24 months. Data cut-off 2026-05-06.

Triplet is Safe and Well-tolerated — No CRS, No ICANS

14%	4%	0	0	0
Treatment-related serious AEs (4/29)	Discontinuation due to drug-related AE	CRS events	ICAN events	Increased infection rate

✓ Low rate of serious AEs

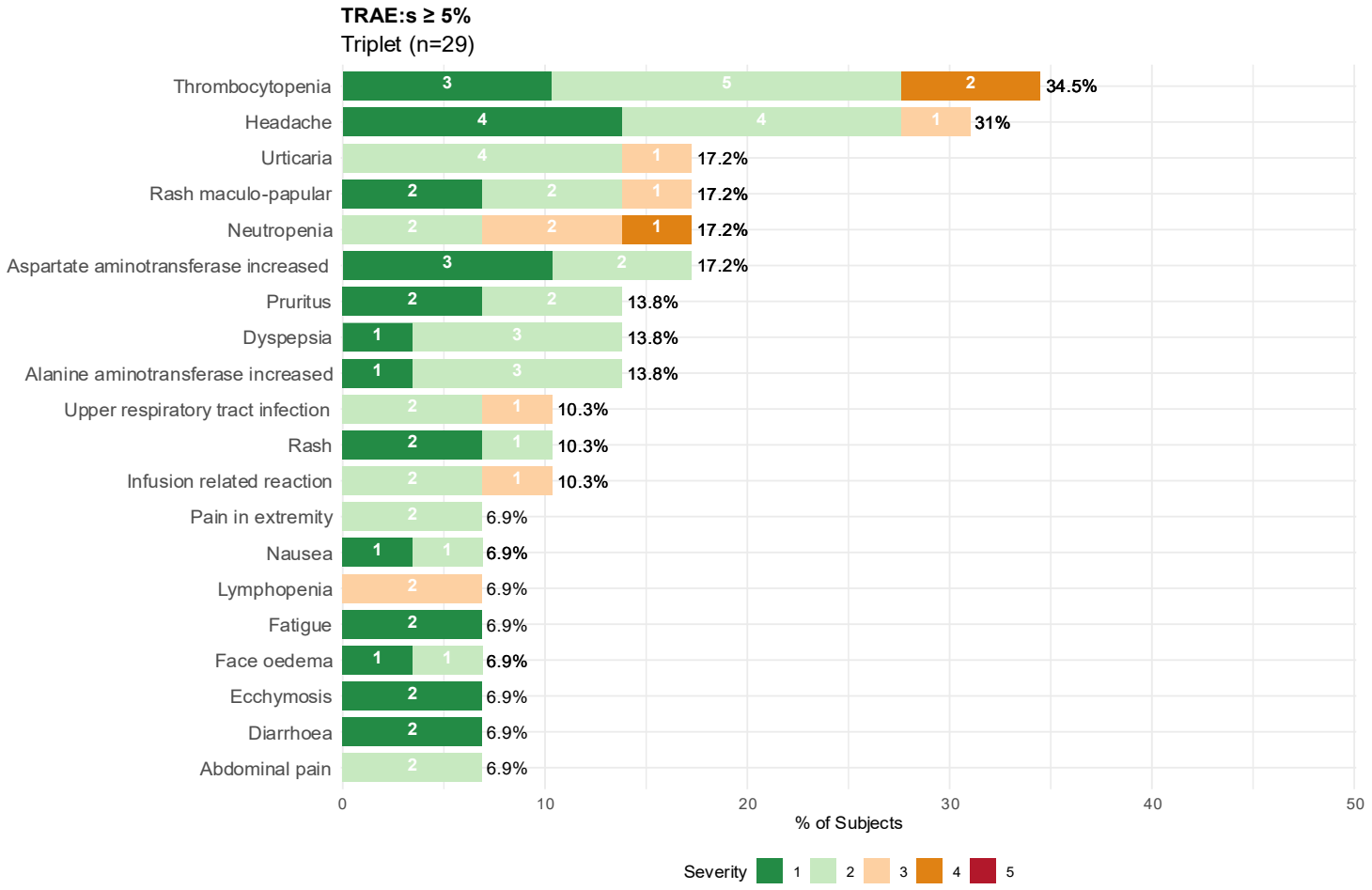
Treatment-related serious AEs observed in 4 (14%) patients. Discontinuation due to drug-related AE in 1 patient only.

✓ Thrombocytopenia was transient

No associated bleeding. Transient in nature with no clinical consequences.

✓ TRAE:s ≥5% shown at right

Most events Grade 1–2. No Grade 4–5 events in top AEs. Favorable profile vs. lenalidomide-based, bispecific antibodies, or any other treatment alternative.



Data cut-off 2026-05-06. n=29 for safety analysis.

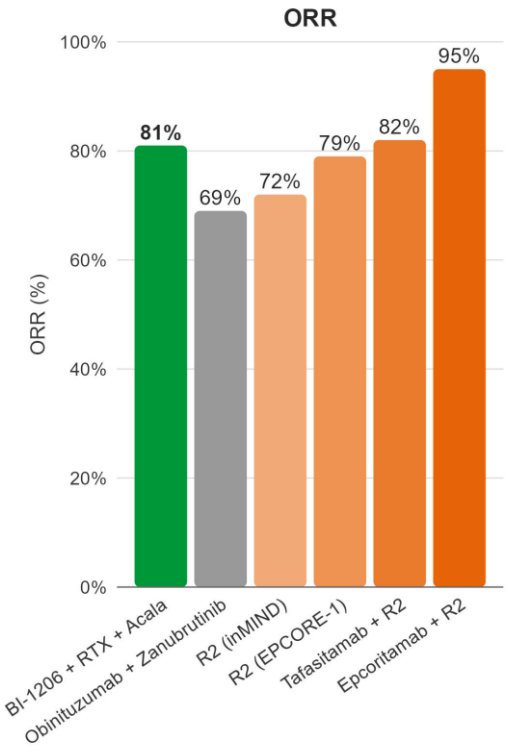
Triplet Regimen Compares Well to Other Treatments in R/R FL

81% ORR — on par with R2 and tafasitamab + R2

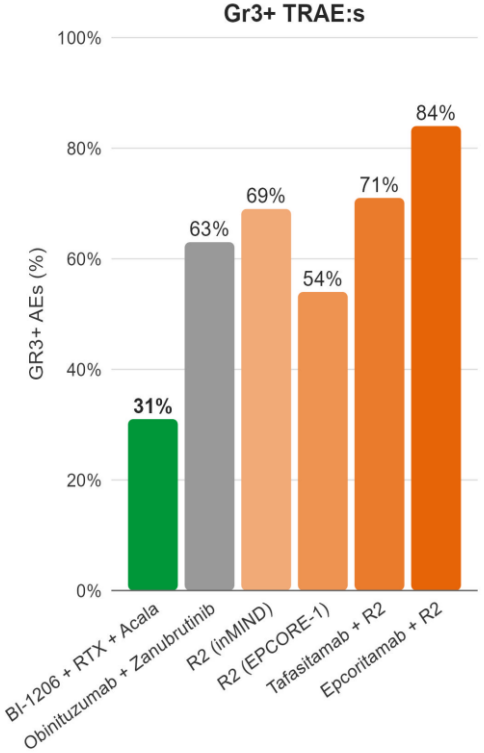
14% Serious AEs vs. 29–56% for comparators

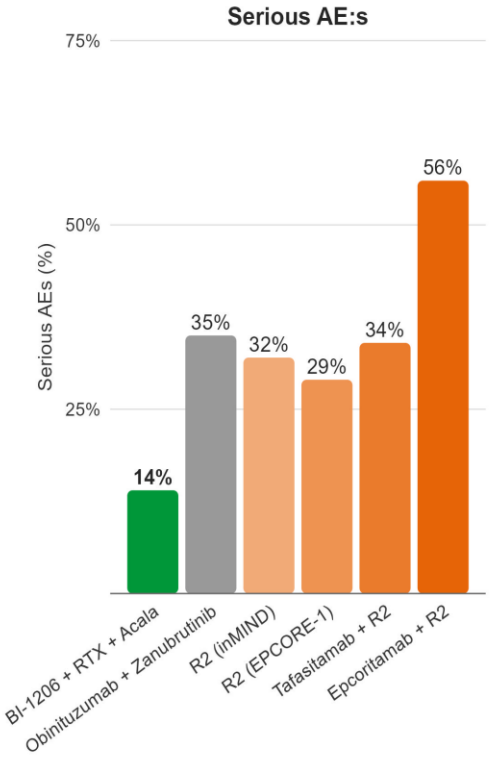
3% TEAE discontinuation vs. 7–19% comparators

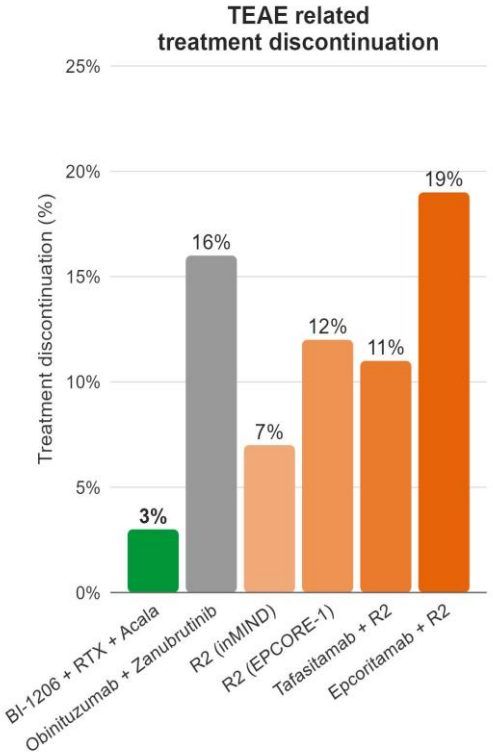
Efficacy



Safety







Zinzani et al. JCO 2023; Strati et al. Br J Haem 2024; Sehn et al. Lancet 2026; Falchi et al. Lancet 2025

Conclusions: BI-1206 + Rituximab + Acalabrutinib (**Triplet**) in FL

81%
ORR in R/R FL

mPFS
not yet assessed
(doublet: ~12.5 mo)

100%
DCR across subtypes

✓ Formidable efficacy in R/R FL

ORR 81%, CRR 44% in FL subset — consistent with established clinical benchmarks (e.g., R2). DCR of 100% across all NHL subtypes.

✓ Unmatched safety and tolerability

No CRS, no ICANS, no increased rate of infections. Treatment-related serious AEs in 14% of patients — favorable vs. alternative regimens.

✓ Durable disease control

mPFS of ~12.5 months with the doublet.
Triplet is likely to provide deeper and longer-lasting responses.

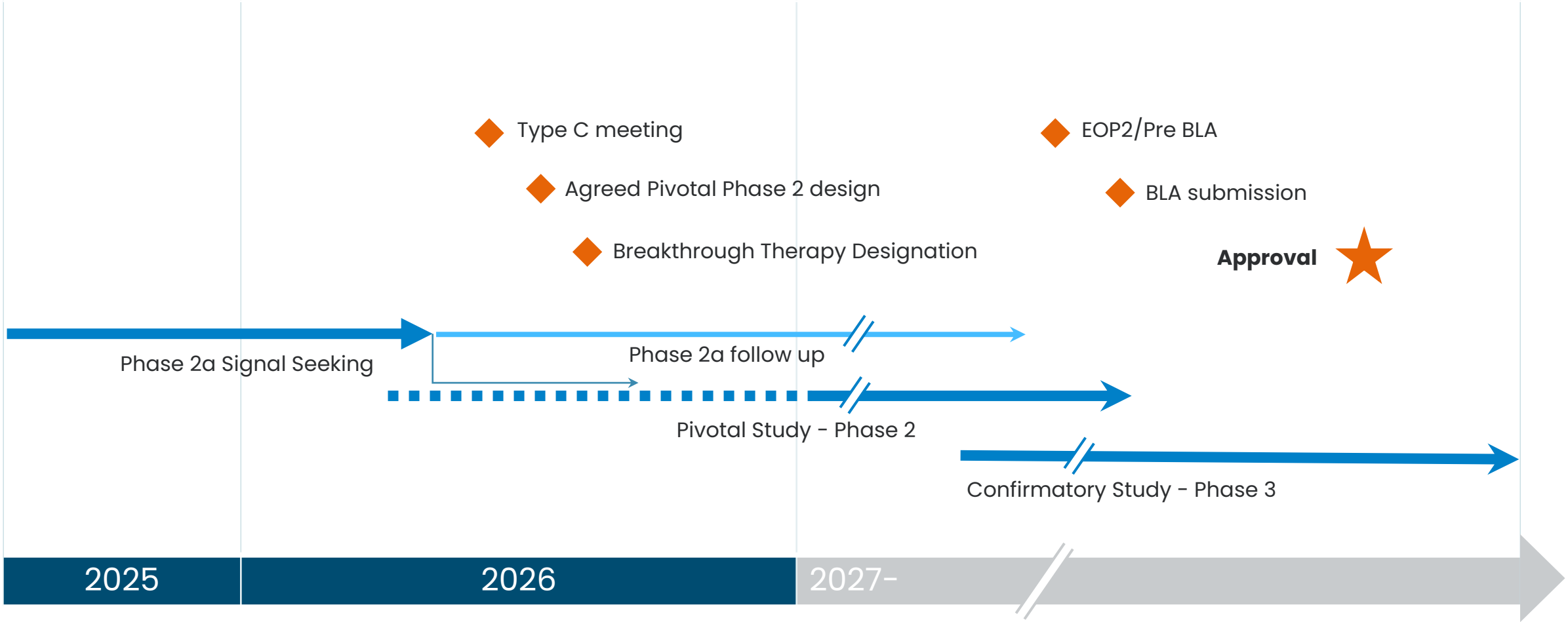
✓ A prominent role in the future treatment landscape

The triplet represents a highly promising therapeutic intervention, adapted to treatment in oncology community practices (approx. 80% of the FL patient population).

Data cut-off 2026-05-06. ORR/CRR/DCR based on FDG-PET (Lugano criteria). mPFS from doublet cohort in FL subset.

BI-1206 in NHL: Combination with Rituximab and Acalabrutinib

Potential Timelines*



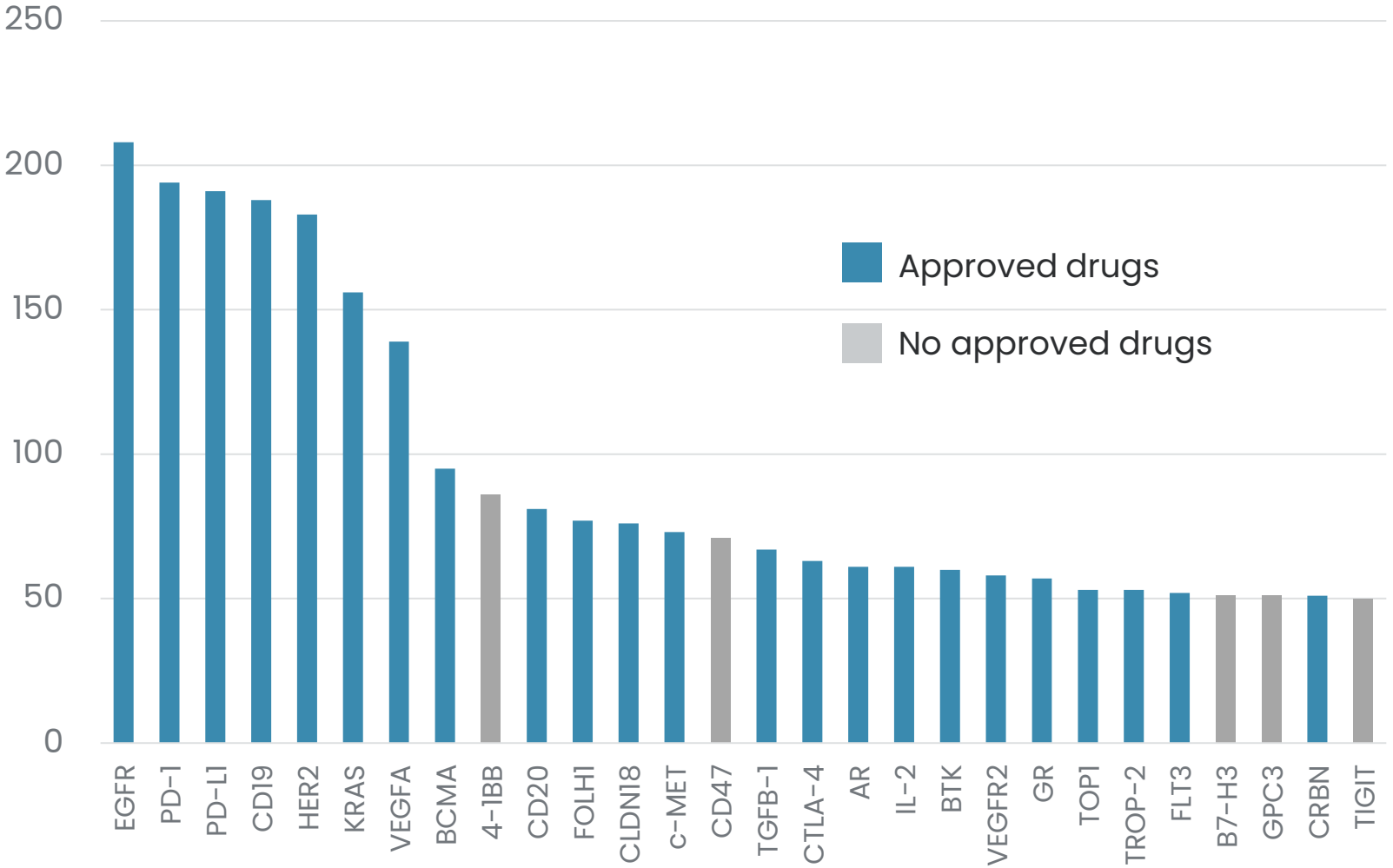
*Depending on partnering discussions and acceptance of development plan by FDA

Sylvie Ryckebusch

CBO

The Oncology Field is Crowded With Me-too Assets

Number of pipeline programs per oncology target in 2024

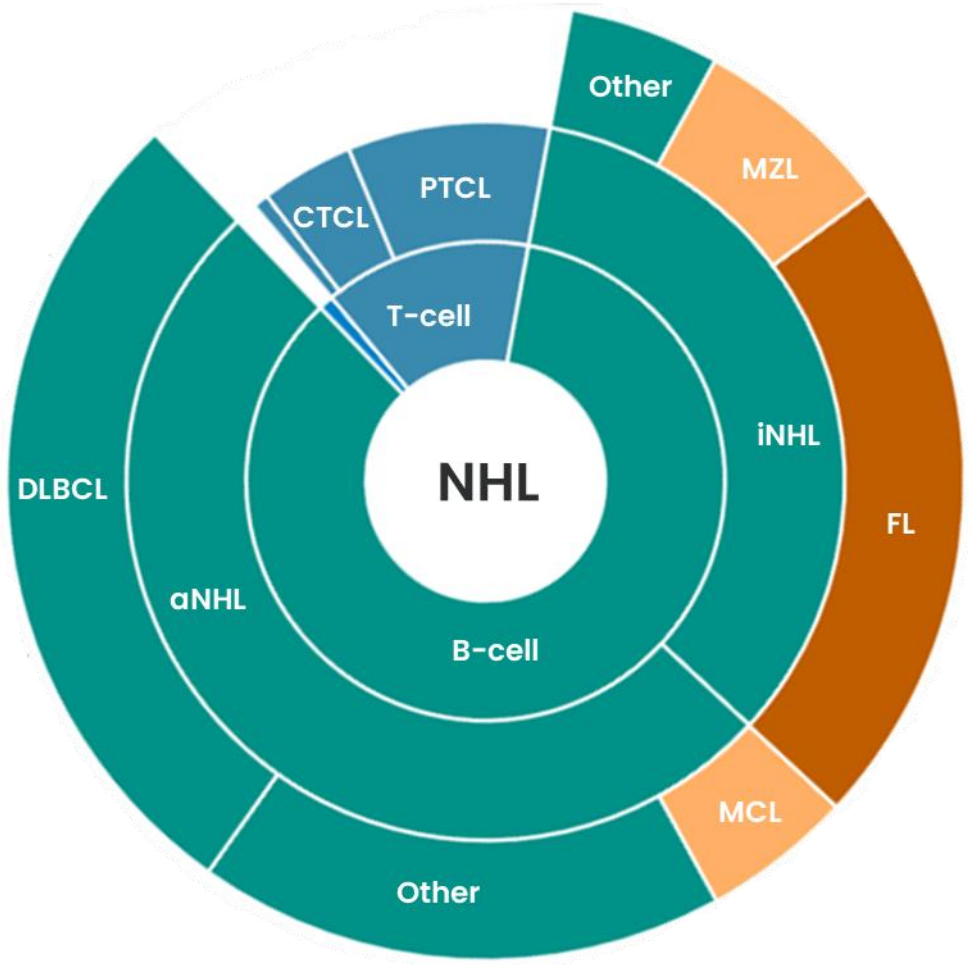


- Dozens of programs are focused on the same targets
- A class failure, such as PI3 kinase, leads to significant value destruction across multiple programs
- FcγRIIB is a rare, unique target

L.E.K Consulting, Citeline Pharmaprojects, January 2025

Follicular Lymphoma: A Large, Growing, Recurring Market

- 60,000 treated patients in US and Europe
- New US + EU cases per year: ~28,500 (CAGR 5%)
- Most frequent indolent NHL subtype
- Median age at diagnosis is 64 years old
- Late line therapies (CAR-T and bispecifics) can be complex to administer and poorly tolerated by increasingly frail patients
- Highest unmet medical need is for safe, convenient, and affordable therapies that provide long duration of remission



Eversana Market Research 2024

BI-1206 Delivers Solid Efficacy With Excellent Tolerability in FL

Phase 2a combo with rituximab + acalabrutinib

81%	44%	100%	3%
ORR	CRR	disease control	discontinuation

- 16 evaluable FL patients, heavily pre-treated
- 7 durable complete responses
- 6 partial responses
- 3 stable disease

- No CRS or neurotoxicity
- Potential for infusion-free administration (subcutaneous BI-1206 and rituximab, oral acalabrutinib)
- FDA Orphan Drug Designation for follicular lymphoma

Cutoff date May 5, 2026

The Need for More Convenient, Safer Treatment in R/R Follicular Lymphoma

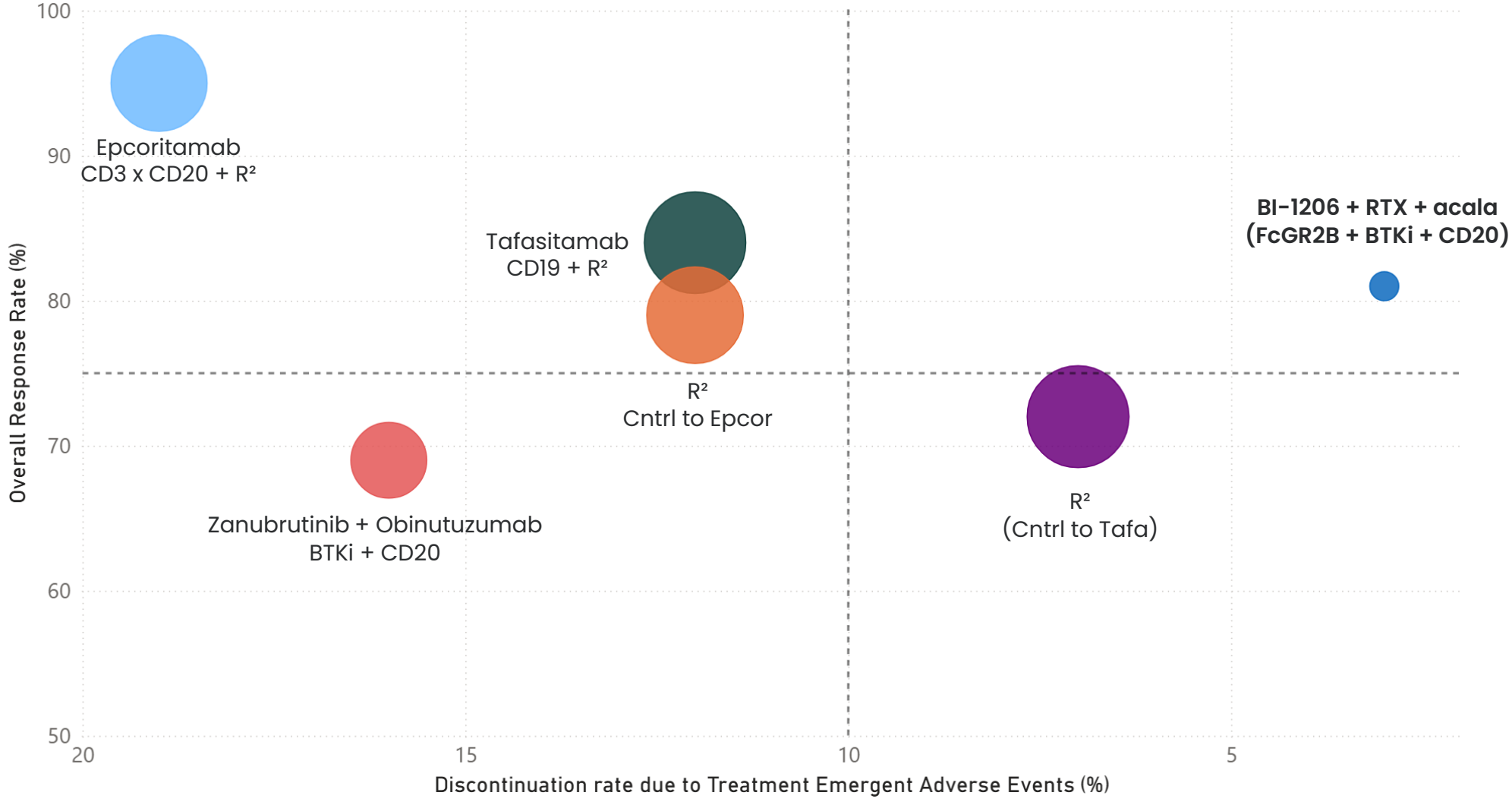
Among second-line options, tolerability and convenience drive commercial success

Treatment class	Toxicities	Other key safety burden	Delivery & setting
Lenalidomide-based (R²)	Grade 3–4 neutropenia, 50%	All-grade infections 63%; cutaneous reactions	2L+ (≥1 prior line) Oral + IV, 12 cycles; ongoing monitoring
Tafasitamab + R² (inMIND)	Grade 3–4 neutropenia (R²-level)	Serious infections 24%; no CRS	2L+ (≥1 prior line) IV + oral, 12 cycles; community or academic
Epcoritamab + R² (EPCORE FL-1)	CRS ~26%, low grade (step-up dosing)	Grade 3–4 neutropenia 69%; grade 3–4 infections 33%	2L+ (≥1 prior line) SC + oral + IV, 12 cycles; step-up dosing; outpatient
BI-1206 triplet	**No CRS, no neurotoxicity**	**14% serious TRAEs; 3% discontinuation**	**2L+ (R/R FL and MZL)** Infusion-free potential (SC + oral); outpatient, community

Cross-trial, not head-to-head. Sources: AUGMENT, inMIND, EPCORE FL-1.

Emerging Results With BI-1206 Triplet Position the Regimen as a Better Tolerated Alternative to R2 and Recently Approved Treatments

Treatments for 2L Follicular Lymphoma



Safety is not Just “Nice to Have” but a Driver of Commercial Success

More cycles per patient

- Low discontinuation means patients complete the intended course rather than dropping out early. That is more cycles billed per patient *and* more of the efficacy actually realized

A larger treatable population

- A safer drug reaches the older, frailer, comorbid patients who are excluded from or poorly served by other therapies — expanding the eligible pool rather than competing for a slice of it.

A broader commercial footprint

- A regimen that requires no step-up dosing or first-cycle hospitalization is deliverable in the community setting where the majority of patients are treated, widening the prescriber base accelerating uptake.

A stronger payer and value case

- Fewer high-grade adverse events, hospitalizations and supportive-care costs improve the cost-effectiveness profile, while higher persistence strengthens the real-world effectiveness — both of which support price and access.

Higher lifetime value per patient

- In a disease treated repeatedly over years, a well-tolerated agent earns repeat use, earlier-line positioning and preserves the quality of life that drives physician and patient preference across the treatment journey.

Many Novel Therapies are Not Well Suited for a Community Environment

% of community physicians who report that novel therapies are **more challenging** to access and administer in the community setting compared to the academic setting

88%

CAR T therapies

59%

Bispecifics

~5000

community hospitals in the US

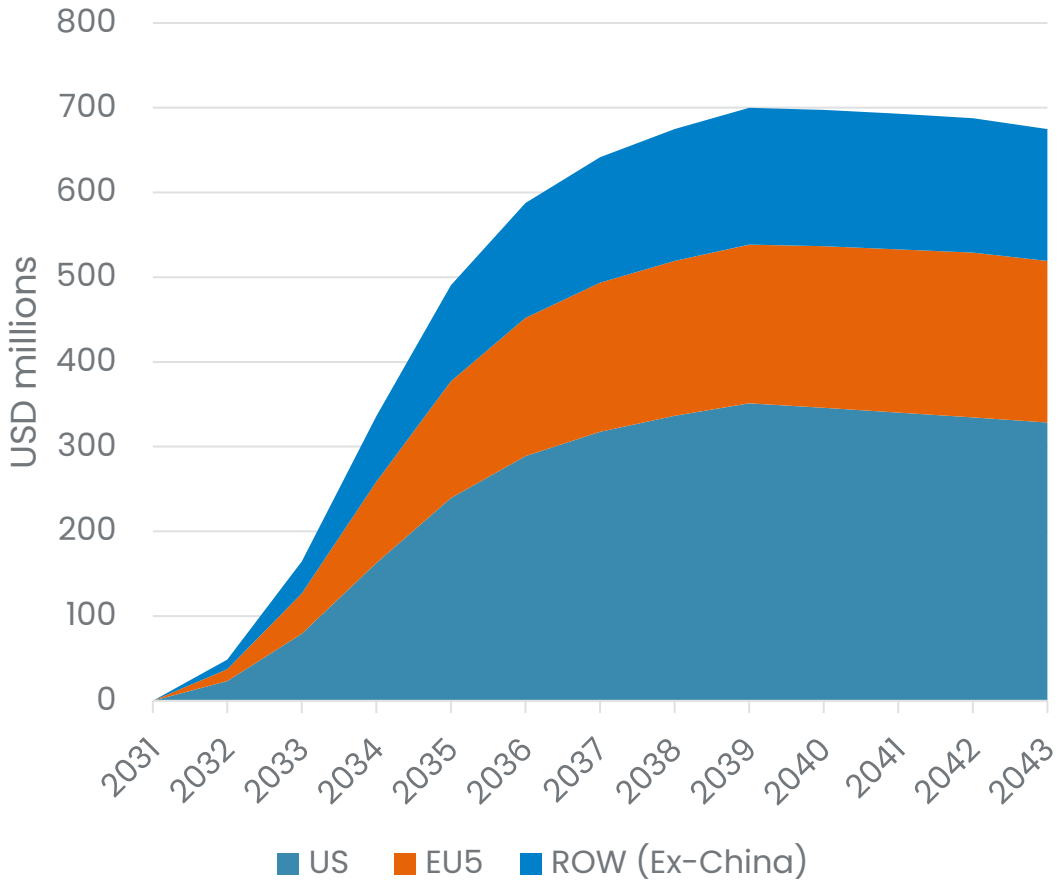
55%

of oncology care is delivered in a community setting

McKesson, Advancing Community Oncology Report, 2025

Peak Global Revenue Potential of ~$700 Million in FL and MZL

Estimated Sales



Assumptions

- BI-1206 + Rituximab + Acalabrutinib in second-line R/R FL and MZL
- 15,000 2L FL patients in US and EU5
- Orphan drug exclusivity of 7 years in US and 10 years in Europe
- US pricing based on premium to Gazyva
- EU pricing 60% discount to US pricing
- Rest of World (ROW) Revenue : Assumption of 30% of the combined US and EU5 revenue streams (excluding China).

Footnotes : *Eversana HCP and Payer Market primary research.

The BI-1206 Opportunity

✓ **New Mechanism**	The only clinical-stage anti-FcγRIIB antibody
✓ **Large Market**	Large and growing patient population with chronic, recurring disease
✓ **Fills Unmet Need in 2L**	Strong, durable efficacy delivered subcutaneously with no CRS or neutropenia
✓ **Safety as Commercial Driver**	Lower discontinuation, broader eligible population, community deliverability, payer-friendly cost profile
✓ **Derisked Path to Approval**	Orphan drug and potential accelerated path to approval

Q & A

Coffee break until 1 pm

Stefan Barta

MD PhD

Penn Medicine

Current Treatment Landscape in Cutaneous T-Cell Lymphomas (CTCL)

Stefan K. Barta, MD, MS

Associate Professor of Medicine

Leader, T-Cell Lymphoma Program

Abramson Cancer Center

University of Pennsylvania

June 11, 2026

Disclosures

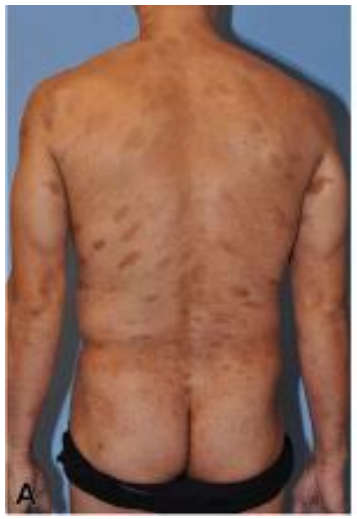
Honoraria/Consultancy: Acrotech, BioInvent, Citius, Daiichi Sankyo, KHK, Secura Bio

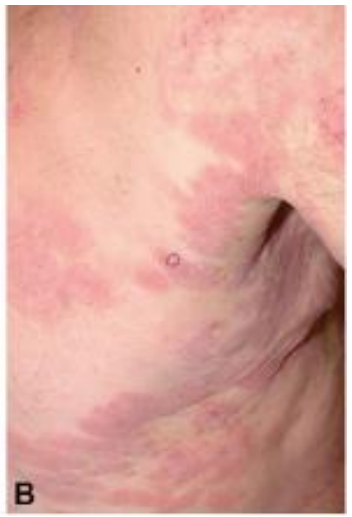
IDMC: Janssen

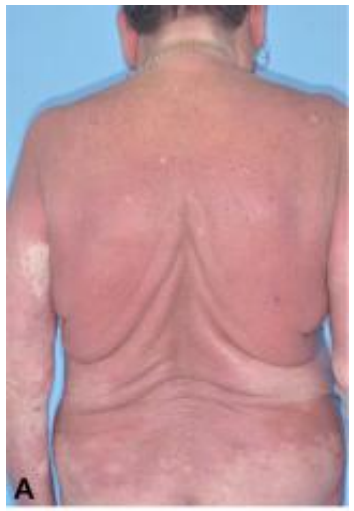
Research support: Vittoria Biotherapeutics

CTCL - Background

- Heterogeneous group of T-cell lymphomas primarily involving the skin
- 3.9% of all NHL; 9.6 cases per million in US
- Majority are Mycosis Fungoides
- Often chronic course
- Unique quality of life issues:
  - debilitating pruritus
  - frequent skin infections







Classification
Cutaneous T-cell and NK-cell lymphomas
Mycosis fungoides
MF variants and subtypes
Folliculotropic MF
Pagetoid reticulosis
Granulomatous slack skin
Sézary syndrome
Primary cutaneous CD30$^+$ lymphoproliferative disorders
Primary cutaneous anaplastic large cell lymphoma
Lymphomatoid papulosis
Adult T-cell leukemia/lymphoma
Subcutaneous panniculitis–like T-cell lymphoma
Extranodal NK/T-cell lymphoma, nasal type
Chronic active EBV infection
Primary cutaneous peripheral T-cell lymphoma, rare subtypes
Primary cutaneous γ/δ T-cell lymphoma
Primary cutaneous aggressive epidermotropic CD8$^+$ cytotoxic T-cell lymphoma (provisional)
Primary cutaneous CD4+ small/medium T-cell lymphoproliferative disorder (provisional)
Primary cutaneous acral CD8$^+$ T-cell lymphoma (provisional)
Primary cutaneous peripheral T-cell lymphoma, NOS

Mycosis fungoides & Sezary syndrome

MF/SS:

- Median age 55-60; M:F 2:1
- 70% caucasian

Table 3. Algorithm for the diagnosis of early MF[15]

Criteria	Major (2 points)	Minor (1 point)
Clinical		
Persistent and/or progressive patches and plaques plus	Any 2	Any 1
(1) Non–sun-exposed location		
(2) Size/shape variation		
(3) Poikiloderma		
Histopathologic		
Superficial lymphoid infiltrate plus	Both	Either
(1) Epidermotropism without spongiosis		
(2) Lymphoid atypia*		
Molecular/biologic: clonal TCR gene rearrangement	NA†	Present
Immunopathologic		
(1) CD2,3,5 less than 50% of T cells	NA†	Any 1
(2) CD7 less than 10% of T cells		
(3) Epidermal discordance from expression of CD2,3,5 or CD7 on dermal T cells		

— indicates not applicable.
*Lymphoid atypia is defined as cells with enlarged hyperchromatic nuclei and irregular or cerebriform nuclear contours.
†Not applicable since it cannot fulfill any major criteria.

Sezary syndrome:

Consensus criteria for the classification as SS requires ***each of the following criteria***:

1) Skin – **One** of the following:

Biopsy is diagnostic of MF/SS **or**

Skin biopsy is compatible/suggestive of MF/SS **plus**:

Biopsy of enlarged lymph node confirming MF/SS **or**

Significant aberrant lymphocyte population in blood with positive TCR clone matching that in skin

2) Erythroderma – Erythema covering ≥80 percent of body surface area.

3) Leukemic blood tumor burden – **Both** of the following:

a) **B2 blood involvement** – B2 blood involvement is currently defined as >1000/uL of Sézary cells or CD4+CD26- or CD4+CD7- lymphocytes.

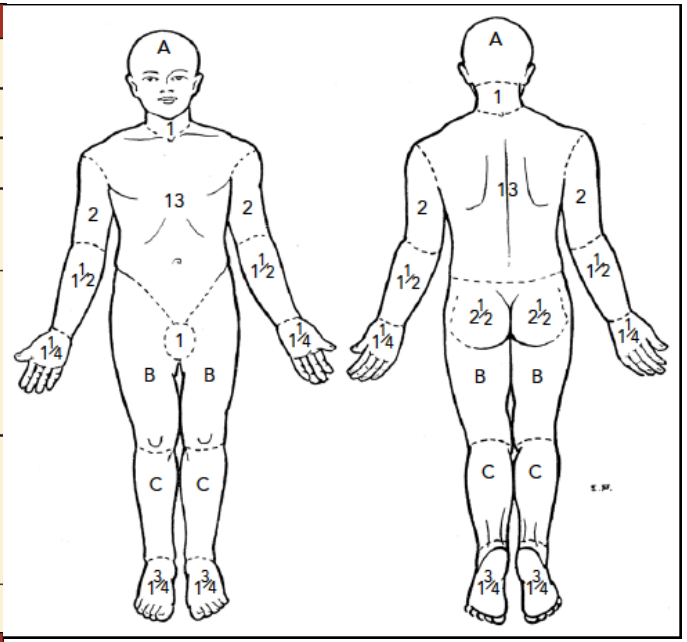
b) ***TCR* clonality** – A clonal *TCR* rearrangement in blood that matches that in skin. Abnormal *TCR* clones in blood that do not match skin can be considered unrelated to the process in the skin and may be related to age

Penn Medicine

Olsen EA, et al. Blood. 2007;110(6):1713. Olsen EA, et al. Blood. 2022;140(5):419; Pimpinelli, N. et al. *Journal of the American Academy of Dermatology 2005:* **53,** 1053-1063

EORTC/ISCL Staging of MF & SS

MF/SS				
Skin (T)	T_0*	Absence of clinically suspicious lesions		
	T_1	Patches, plaques, or papules <10% BSA	T_{1A}	Patch only lesions
			T_{1B}	Plaque/papule+/− patch lesions
	T_2	Patches, plaques, or papules ≥10% BSA	T_{2A}	Patch only lesions
			T_{2B}	Plaque/papule+/− patch lesions
	T_3	One or more tumors ≥1 cm diameter		
	T_4	Confluence of erythema covering ≥80% BSA†		



MF/SS				
Blood (B)§	B_0	B_{0A}	Clone negative **or equivocal**	Absence of significant blood involvement
		B_{0B}	Clone positive **and identical to skin**	
	B_1	B_{1A}	Clone negative **or equivocal**	Low blood tumor burden
		B_{1B}	Clone positive **and identical to skin**	
	B_2	B_{2A}	Clone negative **or equivocal**	High blood tumor burden
		B_{2B}	Clone positive **and identical to skin**	
	Bx	**Bx_A**	**Clone negative or equivocal**	**Unable to quantify blood involvement according to agreed upon guidelines**
		Bx_B	**Clone positive and identical to skin**	

‡Abnormal LNs are those now > 1.5 cm LDi

§Blood staging for MF/SS is defined currently as B_0 = <250/μL of $CD4^+/CD26^-$ or $CD4^+/CD7^-$ cells, B_1= does not meet criteria for B_0 or B_2, and **B_2 = ≥1000/μL of $CD4^+/CD26^-$ or $CD4^+/CD7^-$ cells or other aberrant population of lymphocytes identified by flow cytometry.**

MF/SS			
Nodes (N)‡	N_0	No clinically abnormal LN; no biopsy necessary	
	N_1	N_{1A}	Pathology Dutch grade 1 or NCI LN 0-2: clone negative **or equivocal**
		N_{1B}	Pathology Dutch grade 1 or NCI LN 0-2: clone positive **and identical to skin**
	N_2	N_{2A}	Dutch grade 2, NCI LN3: clone negative **or equivocal**
		N_{2B}	Dutch grade 2, NCI LN3: clone positive **and identical to skin**
	N_3‡ (lymphoma)	N_{3A}	Dutch grade 3-4, NCI LN4: clone negative **or equivocal**
		N_{3B}	Dutch grade 3-4, NCI LN4: clone positive **and identical to skin**
	N_X	Clinically abnormal peripheral or central lymph node but no pathologic determination of representative LN. **Other surrogate means of determining involvement may be determined by Tri-Society consensus**	
Viscera (M)	M_0	No visceral involvement	
	M_{1a}	**BM only involvement**	**Clone positive and identical to skin**
			Clone negative or indeterminate
	M_{1b}	**Non-BM visceral involvement**	**Clone positive and identical to skin**
			Clone negative or indeterminate
	Mx	Visceral involvement is neither confirmed nor refuted by available pathologic **or imaging assessment**	

Staging of MF and SS as per EORTC/ISCL

	T	N	M	B
IA	1	0	0	0,1
IB	2	0	0	0,1
II	1,2	1,2	0	0,1
IIB	3	0-2	0	0,1
III	4	0-2	0	0,1
IIIA	4	0-2	0	0
IIIB	4	0-2	0	1
IVA_1	1-4	0-2	0	2
IVA_2	1-4	3	0	0-2
IVB	1-4	0-3	1	0-2

Olsen EA et. Al., Blood 2022; 140(5):419-437

Penn Medicine

From: **Long-term Outcome of 525 Patients With Mycosis Fungoides and Sézary SyndromeClinical Prognostic Factors and Risk for Disease Progression**

Arch Dermatol. 2003;139(7):857-866. doi:10.1001/archderm.139.7.857

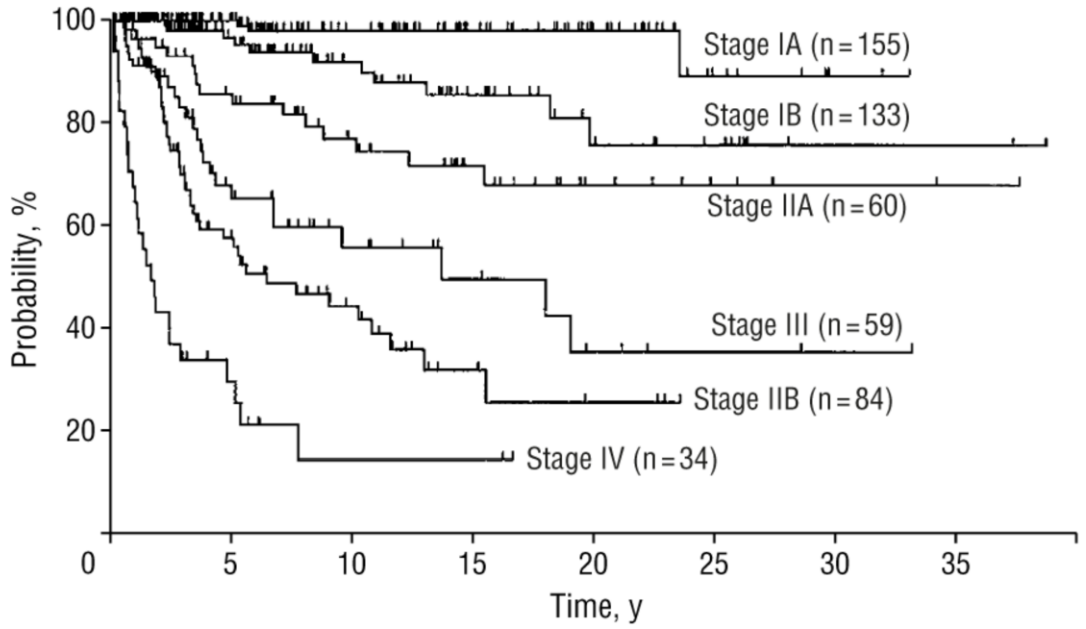


Figure Legend:
Actuarial disease-specific survival of 525 patients with mycosis fungoides and Sézary syndrome according to their clinical stage at diagnosis (stages IA-IV). For stage IA vs IB disease, P = .007; for stage IB vs IIA disease, P = .006; for stage IIA vs IIB disease, P<.001; for stage IIA vs III disease, P = .03; for stage IIB vs III disease, P = .09; and for stage IA-III vs IV disease, P<.001. P values were calculated using the Gehan test.

From: **Long-term Outcome of 525 Patients With Mycosis Fungoides and Sézary SyndromeClinical Prognostic Factors and Risk for Disease Progression**

Arch Dermatol. 2003;139(7):857-866. doi:10.1001/archderm.139.7.857

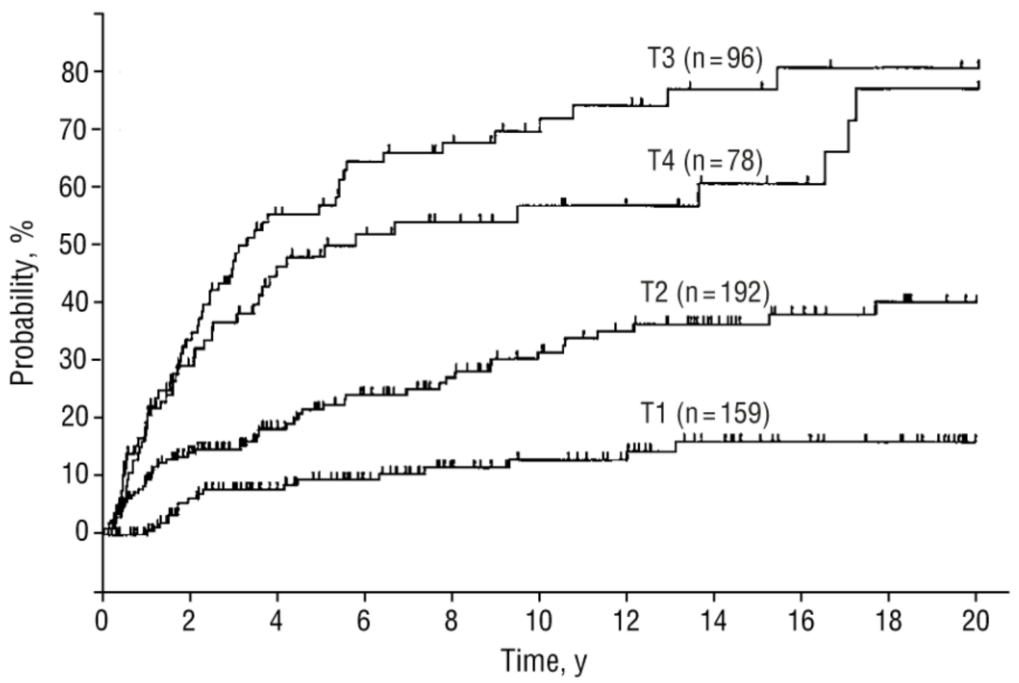


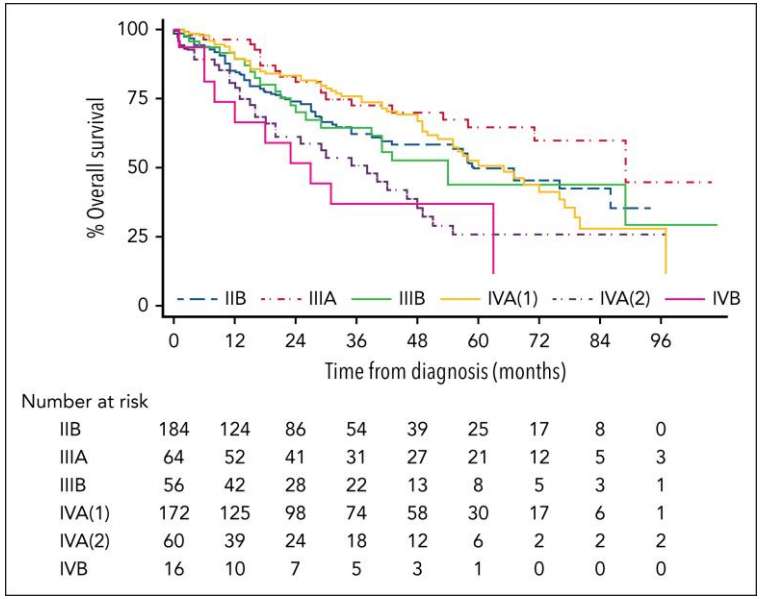
Figure Legend:
Risk for disease progression by Kaplan-Meier analysis for 525 patients with mycosis fungoides and Sézary syndrome according to their T classification at diagnosis. Disease progression was defined as progression to more advanced TNM and B classifications or clinical stage or death due to MF. For T1 vs T2 disease, P<.001; for T2 vs T3 or T4 disease, P<.001; and for T3 vs T4 disease, P = .48. P values were calculated using the Gehan test.

Stage Progression in Mycosis Fungoides According to Initial Stage

Initial Stage	Total	Remained same stage	Progressed to higher stage	Progressed to		
				IB	IIB	III/IV
Stage IA	N=552	N=412	N=140 (25%)	N=50 (9%)	N=47 (8%)	N=43 (8%)
Stage IB	N=556	N=396	N=160 (29%)	-	N=83 (15%)	N=77 (14%)
Overall Early Stage	N= 1,108	N=808	N=300 (27%)			
Stage IIB	N=78	N=44	N=34 (43%)	-	-	N=34 (43%)
Median follow up = 14.5 years (range 1-35 years)						

Quaglino et al. *Cancer 118: 5830-5839, 2012*

The CLIPI for advanced cutaneous lymphoma enables precise risk stratification



Number at risk

IIB	184	124	86	54	39	25	17	8	0
IIIA	64	52	41	31	27	21	12	5	3
IIIB	56	42	28	22	13	8	5	3	1
IVA(1)	172	125	98	74	58	30	17	6	1
IVA(2)	60	39	24	18	12	6	2	2	2
IVB	16	10	7	5	3	1	0	0	0

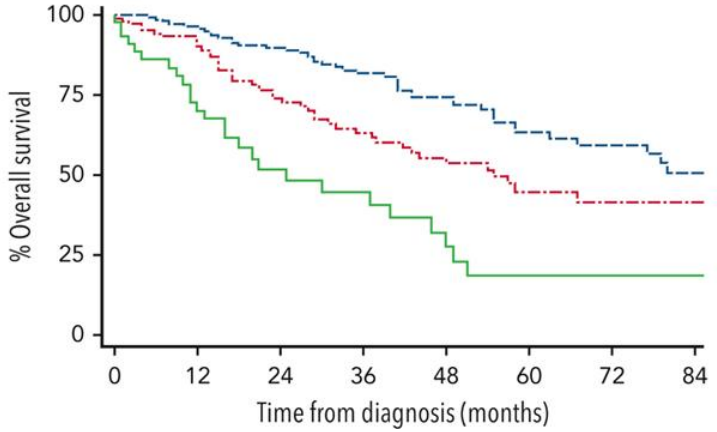
Prognostic Factors To Stratify Patients Into Risk Groups:

1. Age >60 years
2. Raised lactate dehydrogenase (LDH)
3. N3 node status
4. Large cell transformation

Low-risk (0-1 Risk Factors)

Intermediate-risk (2 Risk Factors)

High-risk (3-4 Risk Factors)



	Hazard ratio (95% CI)	*P* value
Age >60 y (vs 60 and under)	2.39 (1.65-3.47)	<.001
Male	1.15 (0.83-1.59)	.415
LDH above upper limit	1.43 (1.04-1.96)	.029
Follicular MF	0.87 (0.56-1.35)	.541
LCT (vs those which were not)	1.58 (1.06-2.37)	.025
N3 vs not N3 (including Nx)	1.98 (1.29-3.04)	.002
B2 (vs B0 and B1)	0.90 (0.61-1.32)	.585
Bx (vs B0 and B1)	1.18 (0.81-1.72)	.386

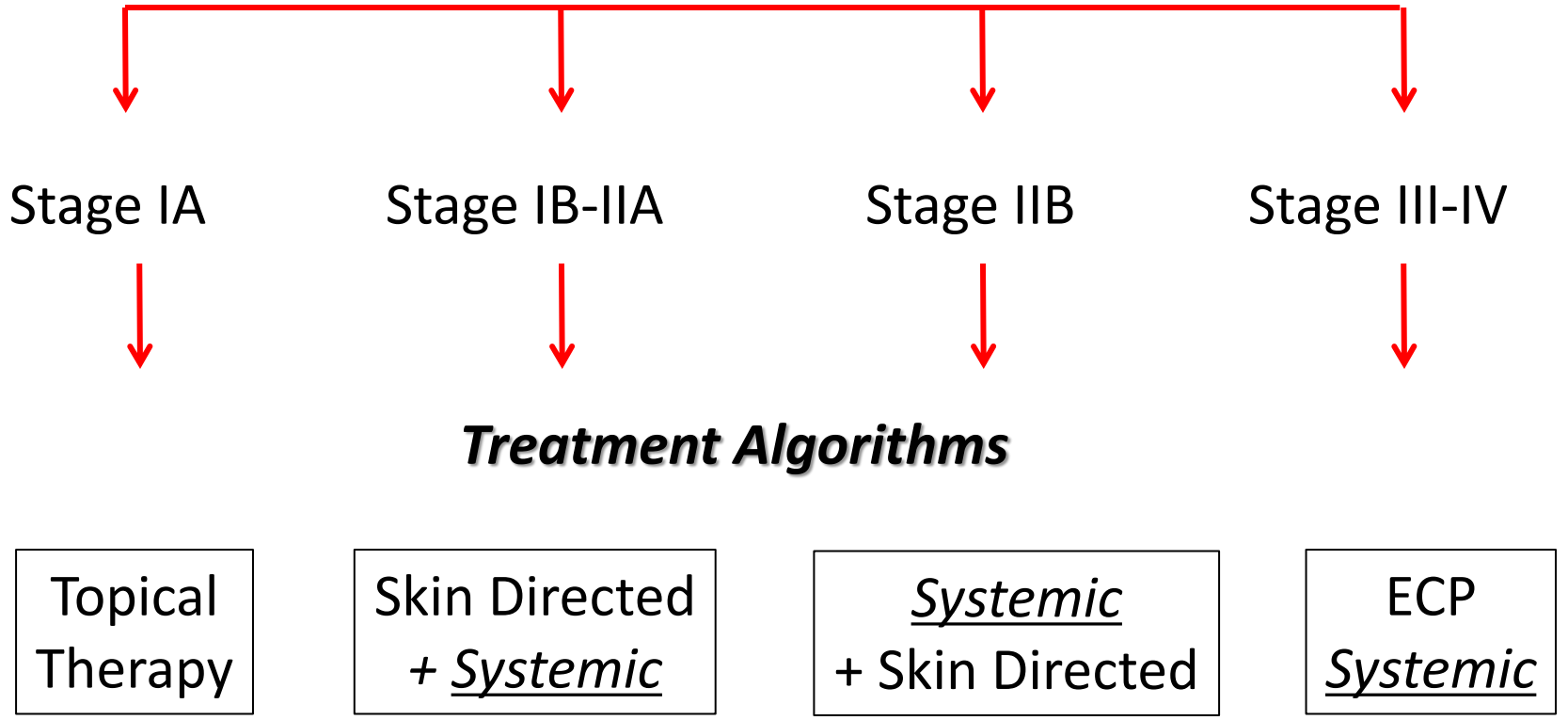
	PROCLIPI cohort			Retrospective cohort		
	Low, %	Intermediate, %	High, %	Low, %	Intermediate, %	High, %
OS at 12 mo (95% CI)	95.8 (90.9-98.1)	90.1 (82.3-94.5)	70.1 (53.2-81.9)	91.9 (88.7-94.2)	85.9 (81.3-89.5)	76.4 (65.8-84.1)
OS at 24 mo (95% CI)	89.7 (83.2-93.8)	72.6 (62.4-80.5)	51.8 (34.4-66.7)	83.3 (79.0-86.8)	71.2 (65.2-76.4)	50.7 (39.0-61.2)
OS at 36 mo (95% CI)	81.8 (73.7-87.5)	63.1 (51.9-72.4)	44.4 (27.2-60.3)	73.1 (67.6-77.8)	60.1 (53.3-66.3)	37.0 (26.0-48.0)
OS at 48 mo (95% CI)	74.2 (65.0-81.4)	53.5 (41.7-64.0)	27.5 (12.5-44.9)	65.6 (59.3-71.2)	43.6 (35.7-51.1)	33.6 (22.9-44.7)
OS at 60 mo (95% CI)	63.3 (52.6-72.3)	44.7 (32.2-56.4)	18.3 (6.2-35.5)	62.0 (55.3-68.0)	39.4 (31.4-47.3)	21.2 (11.7-32.6)
Median OS (95% CI), mo	86 (not calculable)	55 (not calculable)	25 (16-46)	Not reached	42.8 (37.8-49.8)	24.4 (18.9-32.8)
Median disease specific survival (95% CI), mo	Not reached	89 (not calculable)	48 (not calculable)	Not reached	49.8 (not calculable)	27.2 (21.7-57.5)

Scarisbrick JJ, et al. Blood (2025) 146 (14): 1687–1692.

Penn Medicine

Mycosis Fungoides/Sezary Syndrome – General Approach

Diagnosis, Workup and Staging



Treatment Choices

Early stage:

Skin directed therapies, e.g.

- Topical steroids
- UV therapy (NBUVB, PUVA)
- Radiation
- Other topical agents

+/- Systemic therapies, e.g.

- Retinoids
- Interferon
- Low dose methotrexate

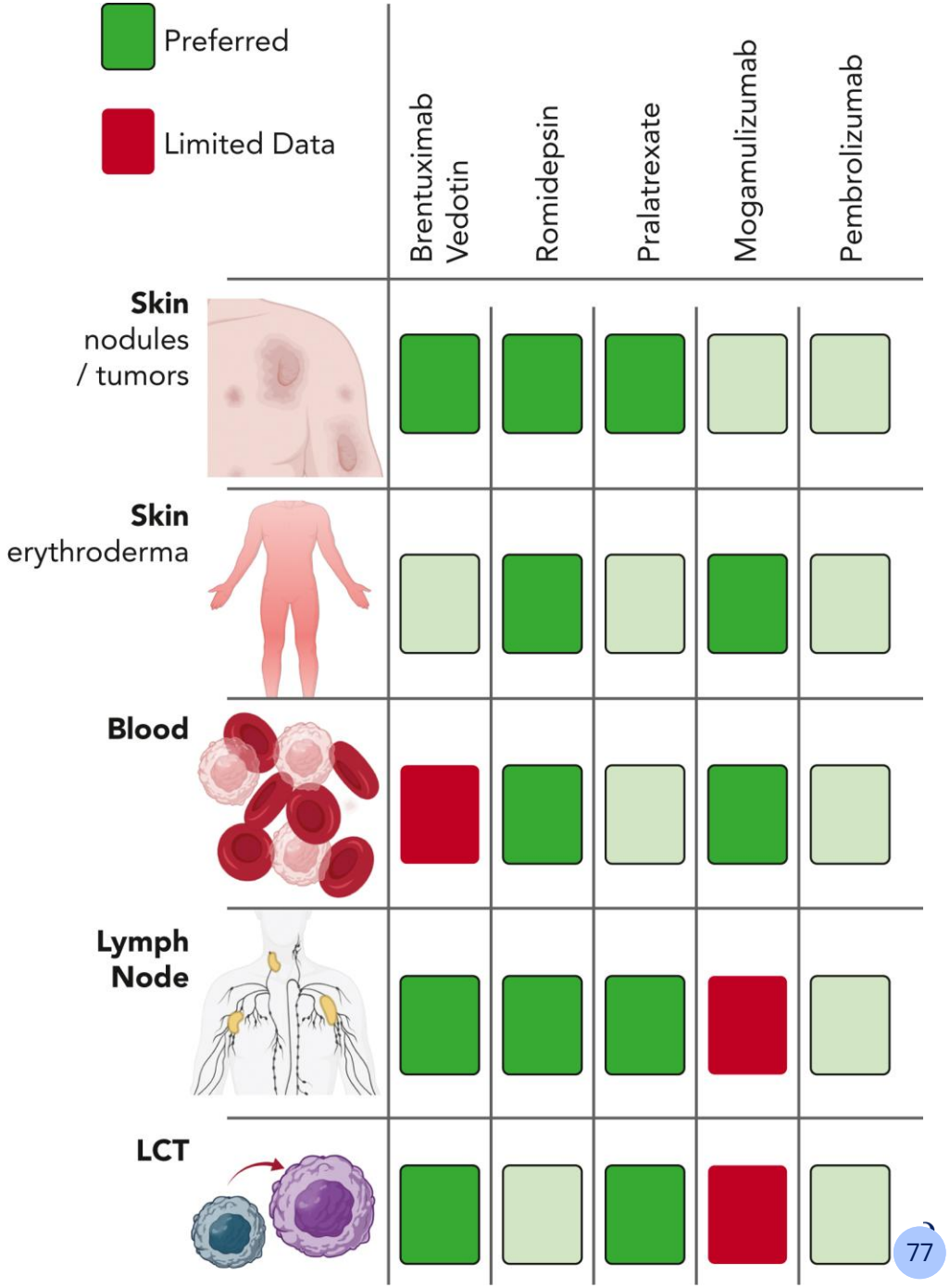
Advanced stage:

Skin directed therapies +

Systemic therapies based on the affected "compartment"

Extracorporeal photopheresis

Allogeneic hematopoietic transplant in very select situations



Khodadoust MS, Mou E, Kim YH. EA et. Al., Blood 2023. 141(7):695-703

Aggressive upfront treatment does not improve survival

1784 THE NEW ENGLAND JOURNAL OF MEDICINE Dec. 28, 1989

A RANDOMIZED TRIAL COMPARING COMBINATION ELECTRON-BEAM RADIATION AND CHEMOTHERAPY WITH TOPICAL THERAPY IN THE INITIAL TREATMENT OF MYCOSIS FUNGOIDES

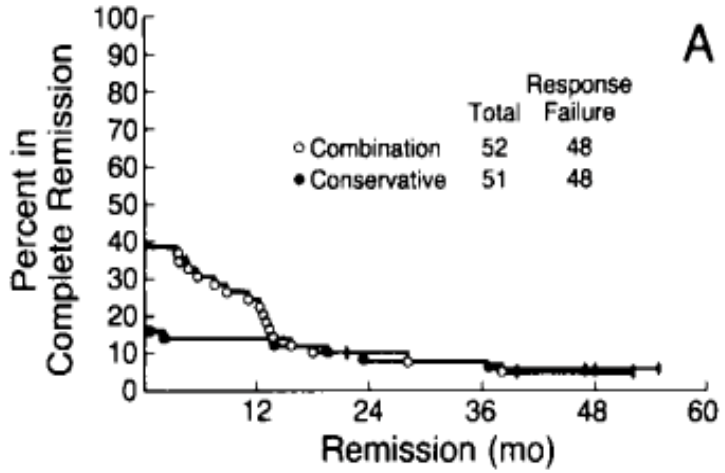
Frederic J. Kaye, M.D., Paul A. Bunn, Jr., M.D., Seth M. Steinberg, Ph.D., Joyce L. Stocker, R.N., Daniel C. Ihde, M.D., A.B. Fischmann, M.D., Eli J. Glatstein, M.D., Geraldine P. Schechter, M.D., Ruby M. Phelps, B.A., Francine M. Foss, M.D., Harry L. Parlette III, M.D., Michael J. Anderson, M.D., and Edward A. Sausville, M.D., Ph.D.

Abstract Mycosis fungoides is a T-cell lymphoma that arises in the skin and progresses at highly variable rates. Nonrandomized studies have suggested that early aggressive therapy may improve the prognosis in this usually fatal disease. We studied 103 patients with mycosis fungoides, who, after complete staging, were randomly assigned to receive either combination therapy, consisting of 3000 cGy of electron-beam radiation to the skin combined with parenteral chemotherapy with cyclophosphamide, doxorubicin, etoposide, and vincristine (n = 52) or sequential topical treatment (n = 51). The prognostic factors were well balanced in the two groups.

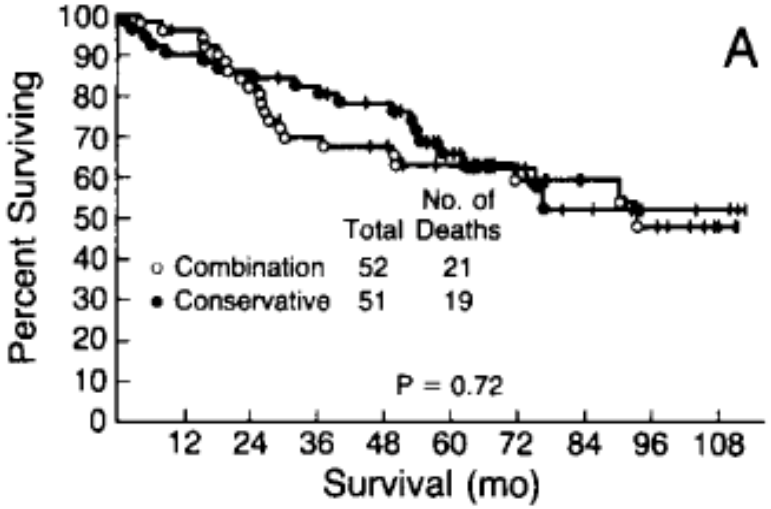
Combined therapy produced considerable toxicity: 12 patients required hospitalization for fever and transient neutropenia, 5 had congestive heart failure, and 2 were later found to have acute nonlymphocytic leukemia. Patients receiving combined therapy had a significantly higher rate of complete response, documented by biopsy, than patients receiving conservative therapy (38 percent vs. 18 percent; P = 0.032). After a median follow-up of 75 months, however, there was no significant difference between the treatment groups in disease-free or overall survival.

We conclude that early aggressive therapy with radiation and chemotherapy does not improve the prognosis for patients with mycosis fungoides as compared with conservative treatment beginning with sequential topical therapies. (N Engl J Med 1989; 321:1784-90.)

<u>Current paradigm:</u>
Conservative sequential approach

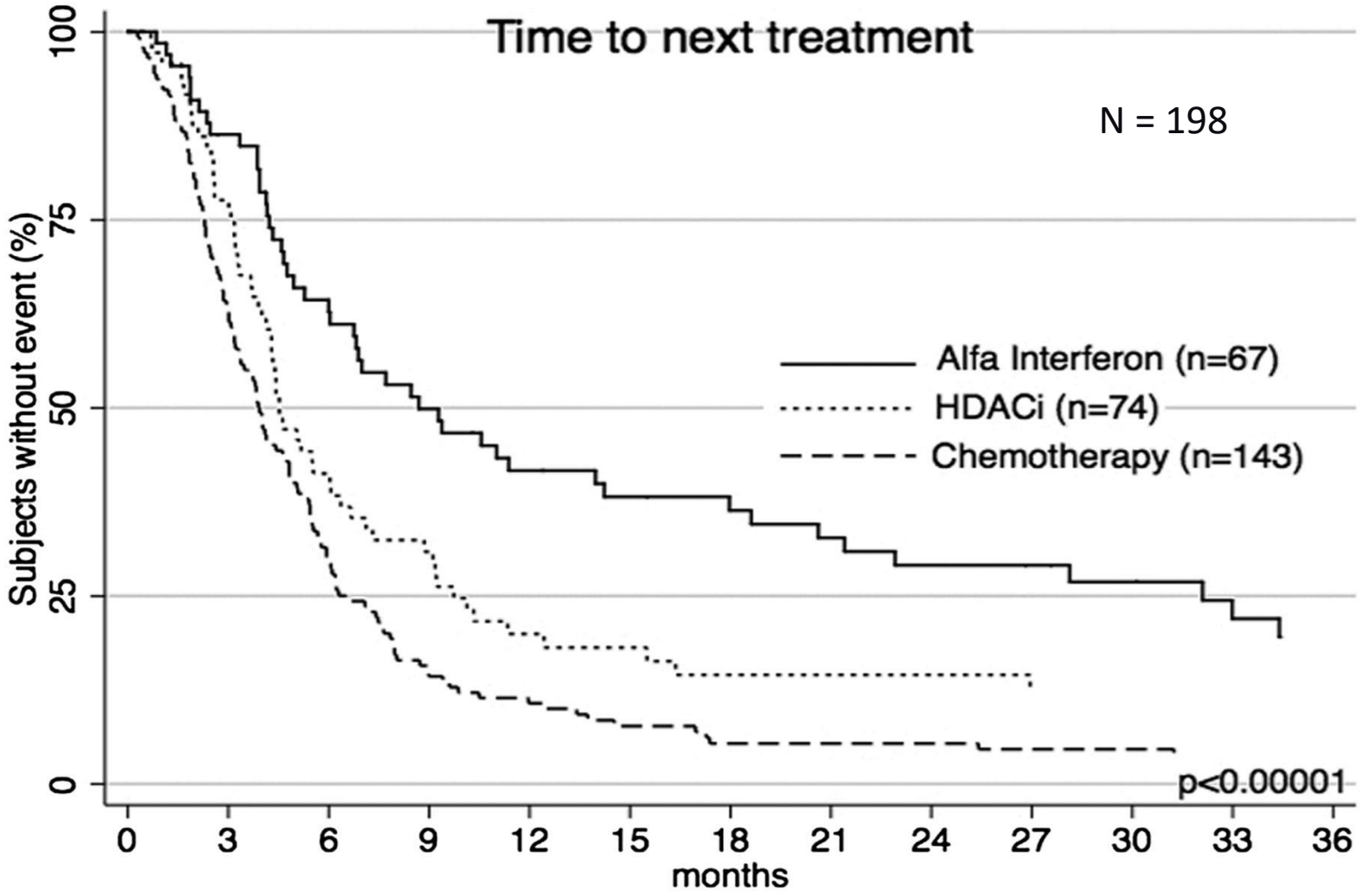


Disease-free survival



Overall survival

Retrospective comparison of systemic therapies at Peter MacCallum Cancer Center



Hughes et al. Blood 125: 71-81, 2015

Penn Medicine

Table 1. Systemic Therapy for MF and SS

Trial	Regimen/Dose		Disease Stage and Number of Patients	ORR	Median PFS
ALCANZA trial (phase III RCT)[a,30]	Brentuximab vedotin (1.8 mg/kg every 3 weeks; up to 16 3-week cycles)		Stage IA–IVB MF (n=48)	65% (10% CR)	17 mo
	Oral methotrexate (5–50 mg once per week) for up to 48 weeks or Oral bexarotene (300 mg/m^2 once per day) for up to 48 weeks		Stage IA–IVB MF (n=49)	16%	4 mo
MAVORIC trial (phase III RCT)[b,31]	Mogamulizumab (1 mg/kg intravenously on a weekly basis for the first 28-day cycle, then on days 1 and 15 of subsequent cycles)		Stage IB–IVA (n=186)	28% (23% by IR)	8 mo (7 mo by IR)
	Vorinostat (400 mg daily)		Stage IB–IVA (n=186)	5% (4% by IR)	3 mo (4 mo by IR)
Phase II and III[32]	Bexarotene	300 mg/m^2/d	Stage IA–IIA (n=28)	54%	
		>300 mg/m^2/d	Stage IA–IIA (n=15)	67%	
Phase II and III[33]	Bexarotene	300 mg/m^2/d	Stage IIB–IVB (n=56)	45%	
		>300 mg/m^2/d	Stage IIB–IVB (n=38)	55% (13% CR)	
Phase IIB[35]	Vorinostat (400 mg daily)		Stage IB–IVA (n=74)	30%	
Phase II[38]	Romidepsin (14 mg/m^2 as a 4-hour IV infusion on days 1, 8, and 15 of each 28-day cycle for up to 6 cycles)		Stage IB–IVA (n=96)	34% (6% CR)	
PDX-010 (dose-escalation study)[40]	Pralatrexate (15 mg/m^2, weekly for 3 out of 4 weeks)		Stage IB–IVA (n=29)	45%	Not reached
Phase II[44]	Alemtuzumab (IV 30 mg)		Stage III or IV (n=22)	55% (32% CR)	
Trial of low-dose SC alemtuzumab[45]	Alemtuzumab (SC 10 mg maximum per administration)[45,c]		SS (n=14)	86% (21% CR)	Median survival (35 mo)
Phase II (CITN-10)[49]	Pembrolizumab (2 mg/kg IV, every 3 weeks)		Stage IIB–IVB (n=24)	38%	65% (1-year PFS rate)

Abbreviations: CR, complete response; IR, independent review; IV, intravenous; MF, mycosis fungoides; LCT, large cell transformation; ORR, overall response rate; PFS, progression-free survival; RCT, randomized controlled trial; SC, subcutaneous; SS, Sézary syndrome.
[a]Patients with SS were excluded from ALCANZA trial; median follow-up 23 months.
[b]Patients with LCT of MF were excluded from MAVORIC trial; median follow-up 17 months.
[c]SC alemtuzumab at lower doses given for shorter duration based on Sézary cell levels was associated with a more favorable toxicity profile.

Penn Medicine

Mehta-Shah N, et al. NCCN Guidelines Insights: Primary Cutaneous Lymphomas, Version 2.2020. J Natl Compr Canc Netw. 2020 May;18(5):522-536

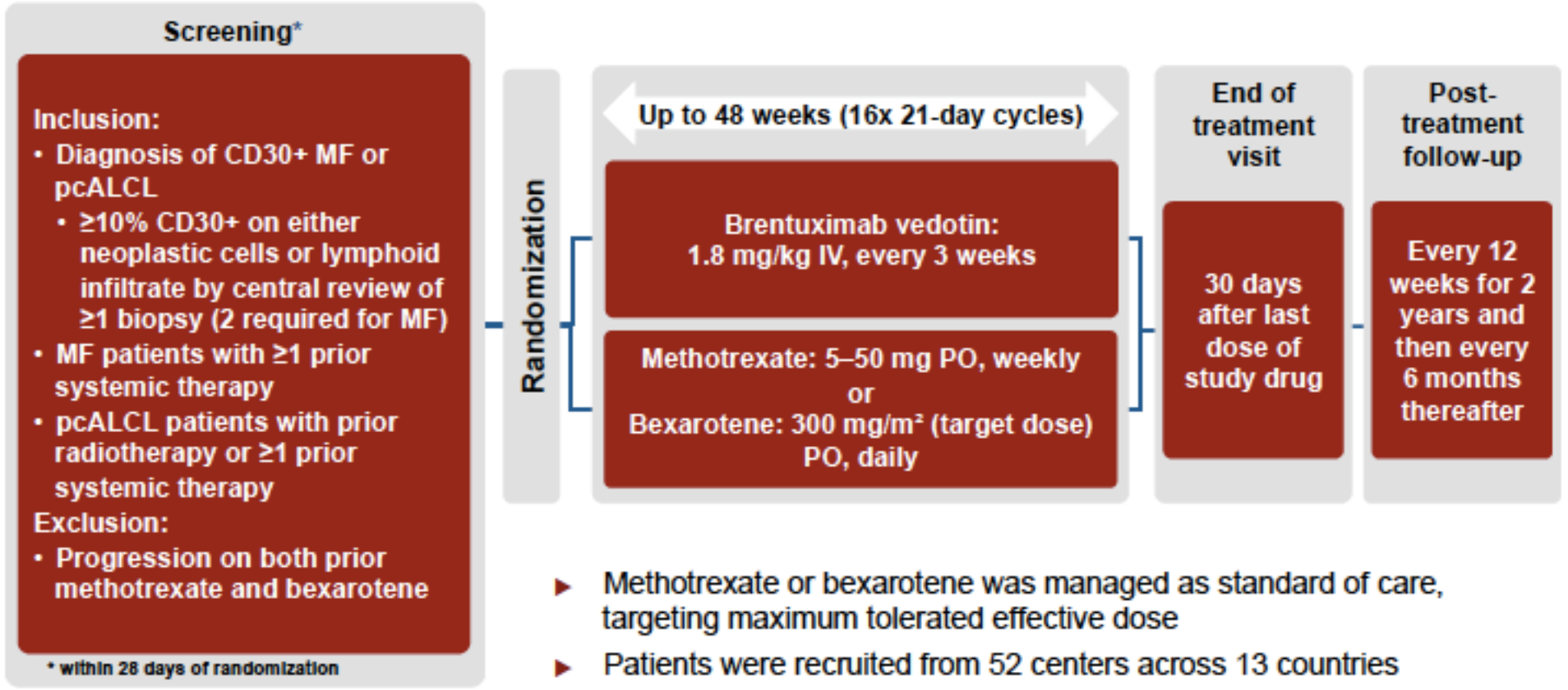
Table 2 Treatment by Compartment

Compartment	Therapy	Compartment - Specific Response	Progression Free Survival	AEs	References
Epidermal skin	Bexarotene	30%-45%	Unknown	Hypertriglyceridemia, hypothyroidism, rash, and headache	Duvic 2001[41]
	Brentuximab vedotin	68%	16.1 months	Neuropathy (50%), nausea (38%), fatigue (34%), and diarrhea (32%)	Prince 2017[10]
	Liposomal doxorubicin	73%	Unknown	lymphopenia (53%)	Falkenhain-Lopez 2022[40]
	Methotrexate	30%	Unknown	Cytopenias, liver disease	Zackheim 2003[33]
	Mogamulizumab	42%	Unknown	Infusion-related reactions (32%), diarrhea (23%), fatigue (22%), drug rash (20%)	Kim 2018[9]
	Romidepsin	34%	Unknown	Nausea (73.2%), fatigue (57.7%), thrombocytopenia (56.3%), and anemia 52.1%	Piekarz 2009[30]
	Vorinostat	30%	Unknown	Diarrhea (49%), fatigue (46%), and nausea (43%)	Olsen 2007[29]
Dermal Skin	Bexarotene	30-45%	Unknown	Hypertriglyceridemia, hypothyroidism, rash, and headache	Duvic 2001[42]
	Liposomal doxorubicin	73%	Unknown	Lymphopenia (53%)	Falkenhain-Lopez 2022[40]
	Pralatrexate	50%	Unknown	Mucositis (48%), fatigue (41%), nausea (31%), and fluid retention (28%)	Horwitz 2012[36]
	Romidepsin	34%	Unknown	Nausea (73.2%), fatigue (57.7%), thrombocytopenia (56.3%), and anemia 52.1%	Piekarz 2009[30]
Blood	Brentuximab vedotin	43%	10 months	Neuropathy (50%), nausea (38%), fatigue (34%), and diarrhea (32%)	Papadavid 2021[18]
	Liposomal Doxorubicin	38%	Unknown	Lymphopenia (53%)	Falkenhain-Lopez 2022[40]
	Mogamulizumab	68%	Unknown	Infusion-related reactions (32%), diarrhea (23%), fatigue (22%), drug rash (20%)	Kim 2018[9]
	Romidepsin	Some blood clearance	Unknown	Nausea (73.2%), fatigue (57.7%), thrombocytopenia (56.3%), and anemia 52.1%	Piekarz 2009[30]
Nodes	Brentuximab vedotin	62%	Unknown	Neuropathy (50%), nausea (38%), fatigue (34%), and diarrhea (32%)	Papadavid 2021[18]
	Pralatrexate	60%	Unknown	Mucositis (48%), fatigue (41%), nausea (31%), and fluid retention (28%)	Horwitz 2012[36]
	Romidepsin	18%	Unknown	Nausea (73.2%), fatigue (57.7%), thrombocytopenia (56.3%), and anemia 52.1%	Piekarz 2009[30]
Viscera	Brentuximab vedotin	Unknown	Unknown	Neuropathy (50%), nausea (38%), fatigue (34%), and diarrhea (32%)	
	Liposomal Doxorubicin	100%	Unknown	Lymphopenia (53%)	Falkenhain-Lopez 2022[40]
	Romidepsin	30%	Unknown	Nausea (73.2%), fatigue (57.7%), thrombocytopenia (56.3%), and anemia 52.1%	Piekarz 2009[30]

Brazel D and Pinter-Brown L. Clinical Lymphoma, Myeloma and Leukemia 2023. 23(6):401–9

ALCANZA trial

ALCANZA: a randomized, open-label, phase 3 trial of brentuximab vedotin vs physician's choice (methotrexate or bexarotene) in patients with CD30+ CTCL

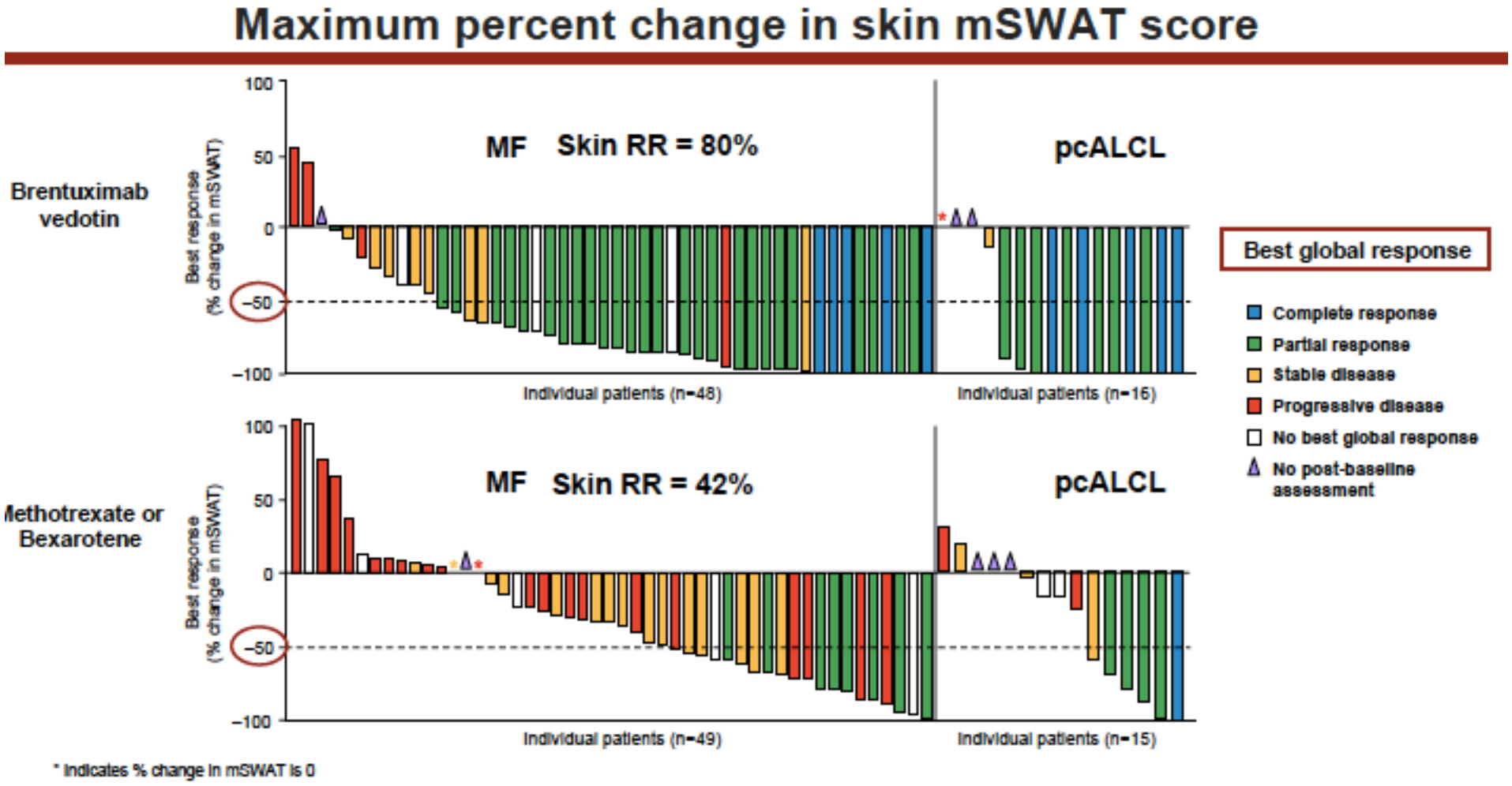


- Methotrexate or bexarotene was managed as standard of care, targeting maximum tolerated effective dose
- Patients were recruited from 52 centers across 13 countries

IV, intravenously; PO, orally

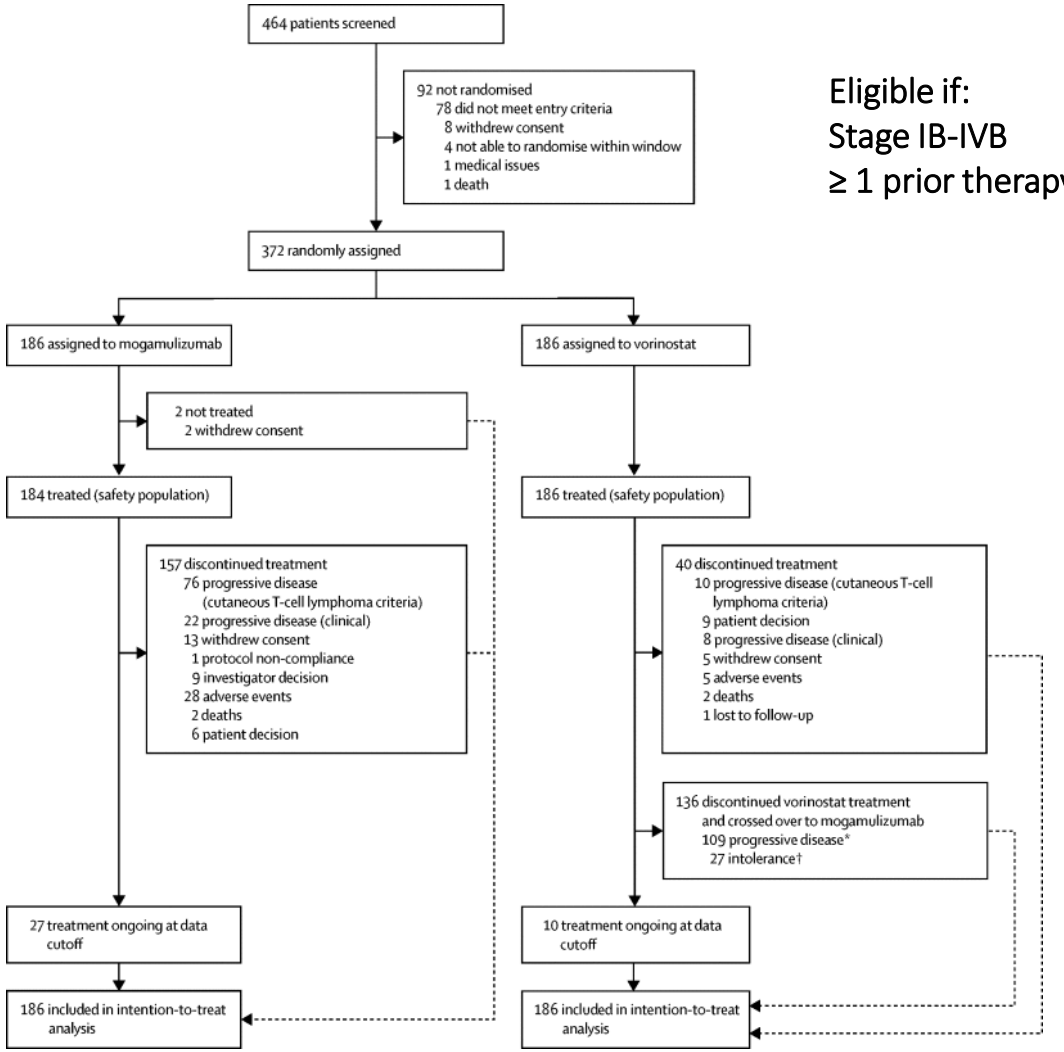
Slide courtesy of Youn Kim

ALCANZA - Efficacy

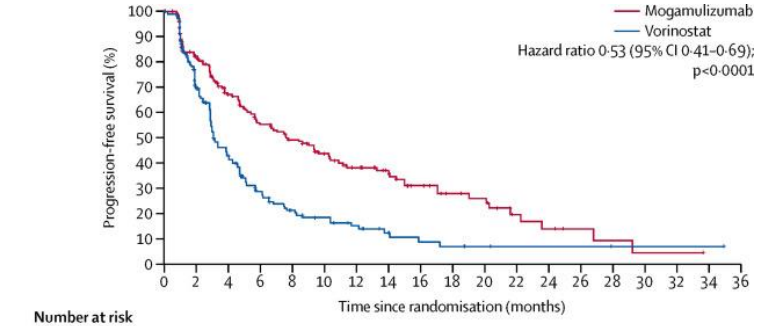


Slide courtesy of Youn Kim

MAVORIC trial: Mogamulizumab vs Vorinostat in MF/SS

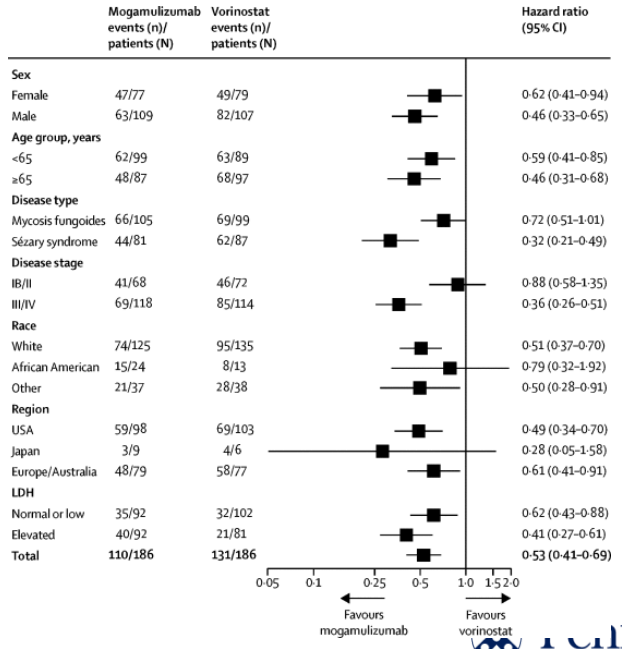


Eligible if:
Stage IB-IVB
≥ 1 prior therapy



Number at risk (number censored)

Mogamulizumab	186 (0)	138 (16)	100 (30)	77 (36)	65 (40)	50 (49)	39 (53)	32 (59)	22 (64)	16 (68)	14 (69)	7 (73)	5 (73)	3 (75)	2 (75)	1 (75)	1 (75)	0 (76)	0 (76)
Vorinostat	186 (0)	111 (23)	61 (33)	36 (39)	23 (43)	18 (45)	13 (47)	8 (50)	5 (51)	4 (51)	3 (52)	2 (53)	2 (53)	2 (53)	1 (54)	1 (54)	1 (54)	1 (54)	0 (55)

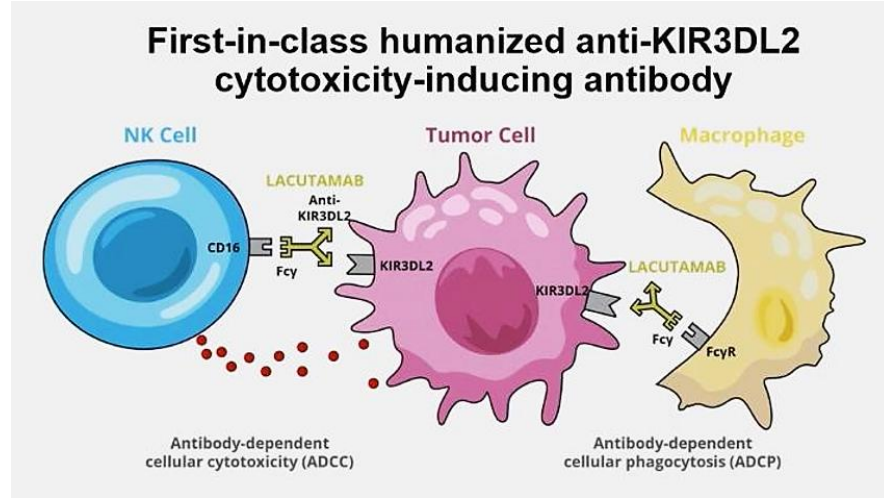


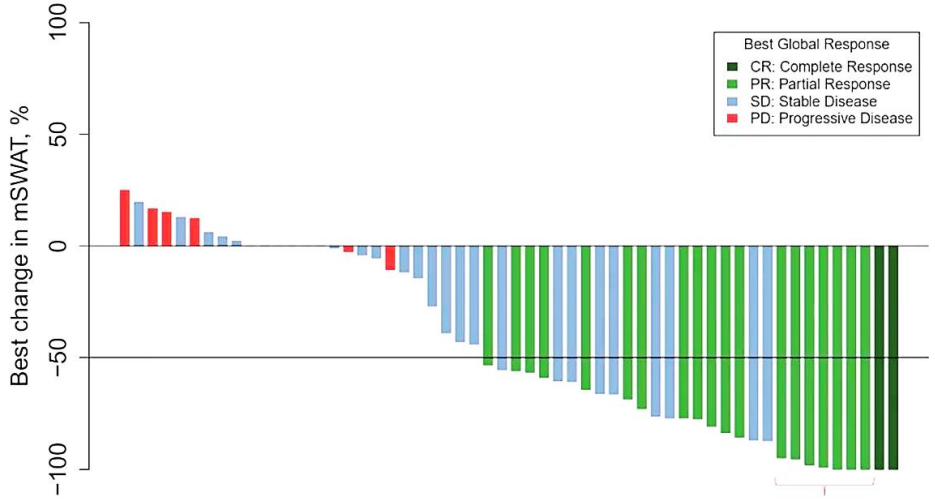
Kim YH et al. Lancet Oncol 2018; 19(9):1192-1204

Lacutamab for Sezary Syndrome – Ph2 TELLOMAK

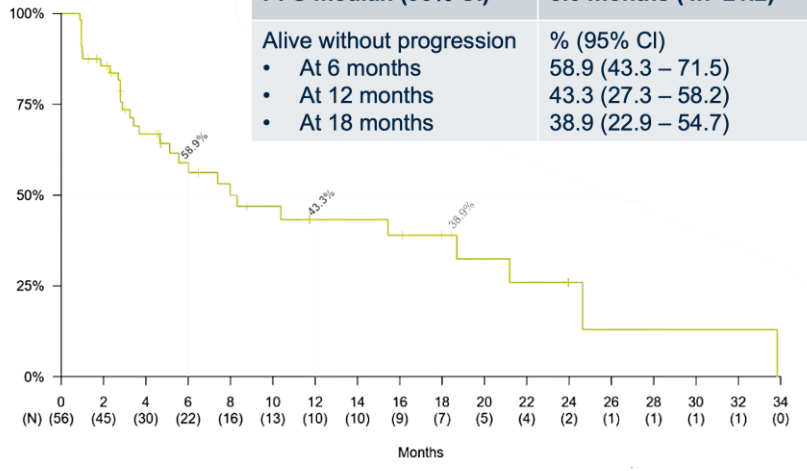
	Best Global Response N=56	Best Response in Skin N=56	Best Response in Blood N=56	Best Response in LN N=46*
Best Response, N (%)				
• CR	2 (3.6)	5 (8.9)	15 (26.8)	3 (6.5)
• PR	19 (33.9)	21 (37.5)	12 (21.4)	6 (13.0)
• SD	28 (50.0)	27 (48.2)	24 (42.9)	28 (60.9)
• PD	7 (12.5)	3 (5.4)	5 (8.9)	5 (10.9)
• NE	0	0	0	4 (8.7)
ORR% [95%CI]	**37.5%** [26.0-50.6]	**46.4%** [34.0-59.3]	**48.2%** [35.7-61.0]	**19.6%** [10.7-33.2]

Sezary Syndrome ≥2 prior systemic therapies. Must include Mogamulizumab as prior therapy.





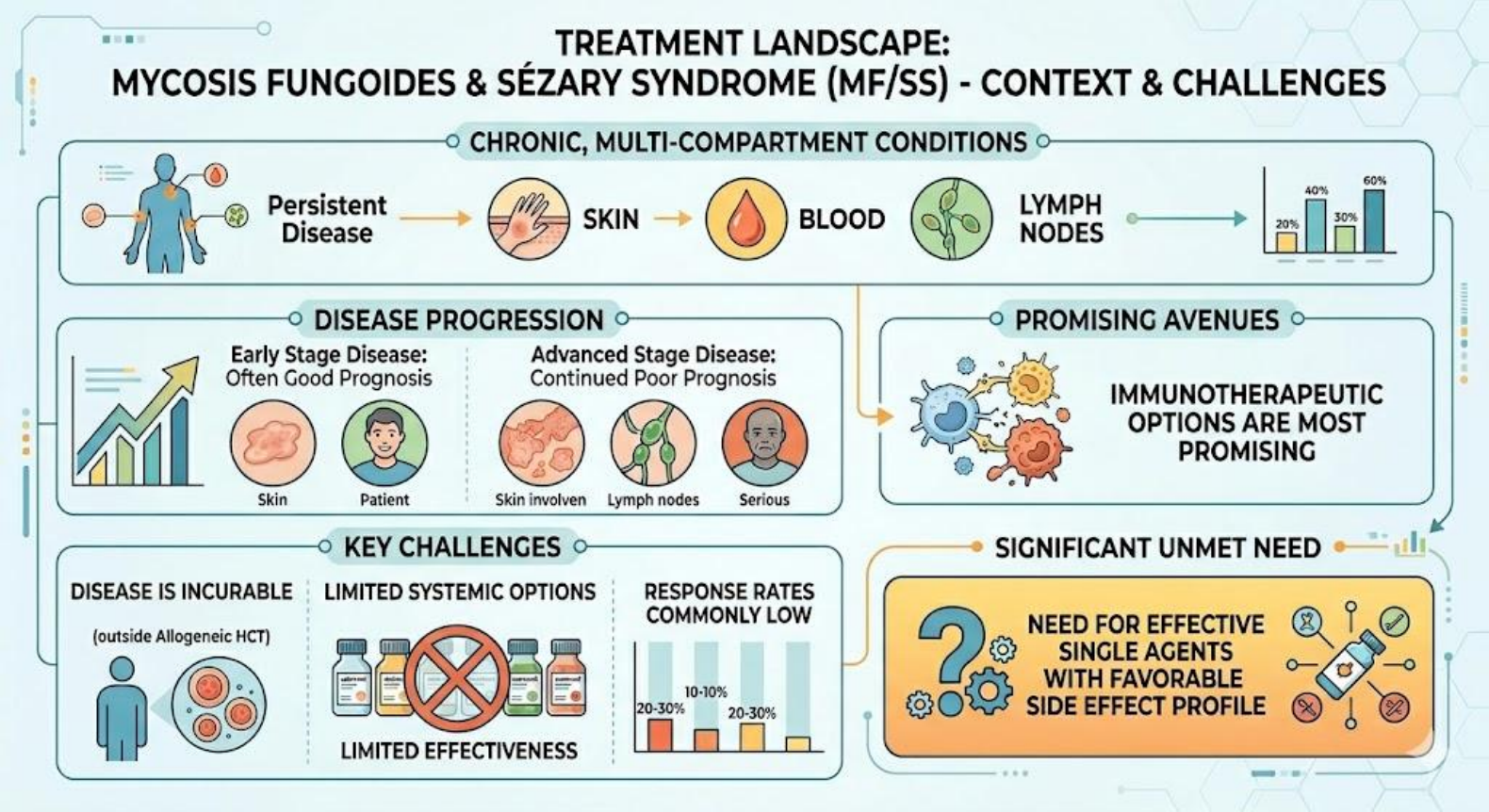
Progression Free Survival (PFS)	
PFS median (95% CI)	**8.0 months (4.7-21.2)**
Alive without progression	% (95% CI)
• At 6 months	58.9 (43.3 – 71.5)
• At 12 months	43.3 (27.3 – 58.2)
• At 18 months	38.9 (22.9 – 54.7)



Battistella M, et al. Blood (2024) 144 (Supplement 1): 1609.

Data cut-off (DCO): May 1, 2023

Summary and Conclusions



Mycosis Fungoides and Sezary Syndrome are chronic conditions that affect multiple compartments.

While patients with early-stage disease can do well, advanced stage disease continues to have a poor prognosis.

The disease remains incurable outside of an allogeneic hematopoietic cell transplant.

Several single agents are approved for MF/SS but response rates are commonly low and effective systemic treatment options remain limited.

Immunotherapeutic options have been most promising in MF/SS.

There remains a significant need for effective single agents with a favorable side effect profile.


Penn Medicine

Andres McAllister

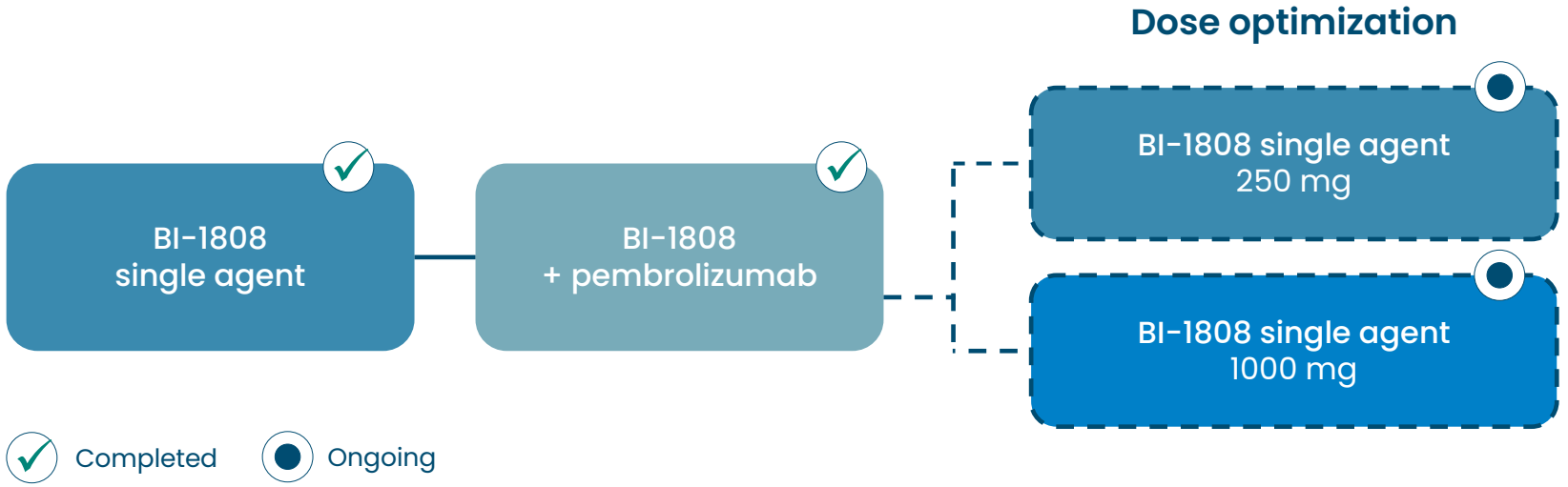
CMO

BI-1808

A Novel Immunotherapy Approach in CTCL: TNFR2 Blockade Shows Meaningful Responses

BI-1808 Clinical Phase 1/2a Study Overview

- Safety and preliminary efficacy currently investigated in CTCL patients (sub-cohort of the ongoing Phase 2a clinical trial)
- 20 patients enrolled for BI-1808 1000 mg as single agent every third week (Q3W)
- Followed by 10 patients treated with the combination of BI-1808 and pembrolizumab
- Currently enrolling 10 vs 10 patients evaluating BI-1808 at 250 mg vs 1000 mg Q3W as single agent



BI-1808 in CTCL: Background & Single Agent Results

Background

- **Cutaneous T-cell lymphomas (CTCL)** are rare non-Hodgkin's lymphomas from malignant skin-homing T cells; most common subtypes are mycosis fungoides (MF) and Sézary syndrome (SS)
- **Outcomes for advanced CTCL remain poor**, with limited 20%–60% 5-year survival
- **TNFR2 has emerged as a pathogenic driver in CTCL** through increased expression in malignant CD4+CD26- cells
- **BI-1808, an IgG1 mAb targeting TNFR2**, blocks ligand engagement and induces:
  - FcγR-mediated depletion of regulatory T cells
  - Activation of myeloid cells promoting proinflammatory changes in the tumor microenvironment
  - Enhanced intratumoral CD8+ T-cell activity
- **BI-1808 demonstrates clinically relevant immune activation and disease control**
- **Combination with pembrolizumab** was explored since TNFR2-mediated immune modulation may enhance sensitivity to PD-1 blockade

BI-1808 Single Agent

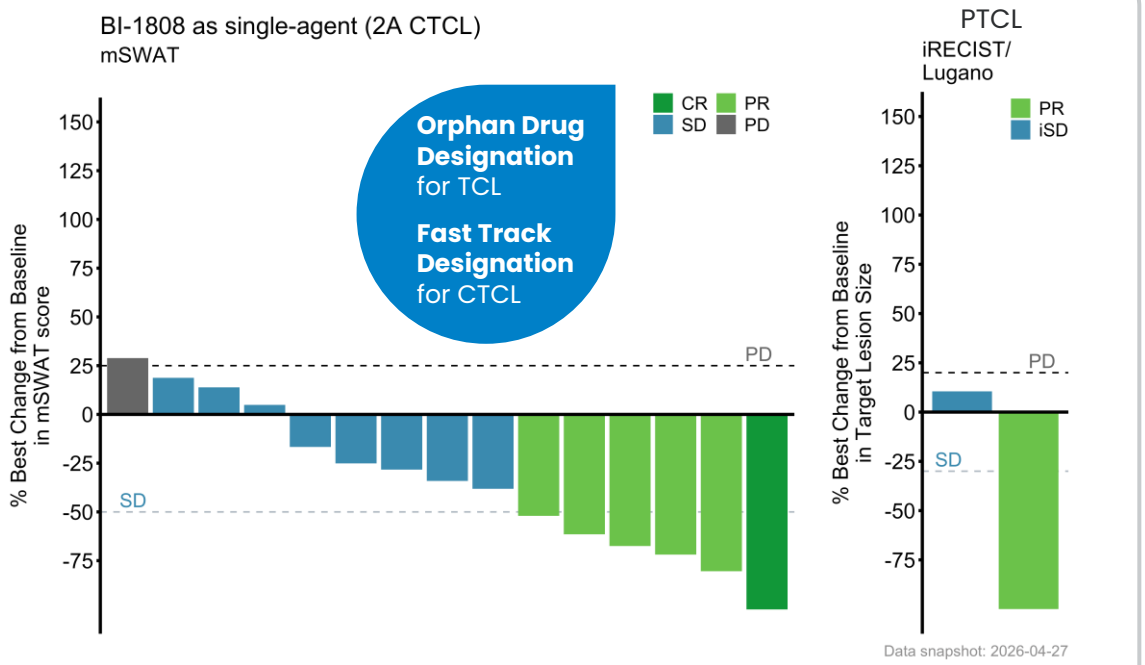
40%	**93%**	**1 CR**
ORR	**DCR**	**ongoing 2+ yrs**
5 confirmed PRs	8 patients SD	SS patient

- The signal-seeking portion of the study has been **fully enrolled**.
- **20 patients with advanced stage CTCL** received 1000 mg BI-1808 as single-agent Q3W (12 MF, 8 SS).
- **15 CTCL subjects were mSWAT evaluable**; 1 SS patient exhibited complete response (CR) lasting 2 years to date and ongoing.
- **5 patients (3 MF, 2 SS)** exhibited confirmed partial response (PR), corresponding to an ORR of 40%. 8 patients exhibited SD as best clinical response, corresponding to a DCR of 93%.
- **Two enrolled PTCL patients were evaluable.** 1 subject exhibited PR, and the other SD as best response.

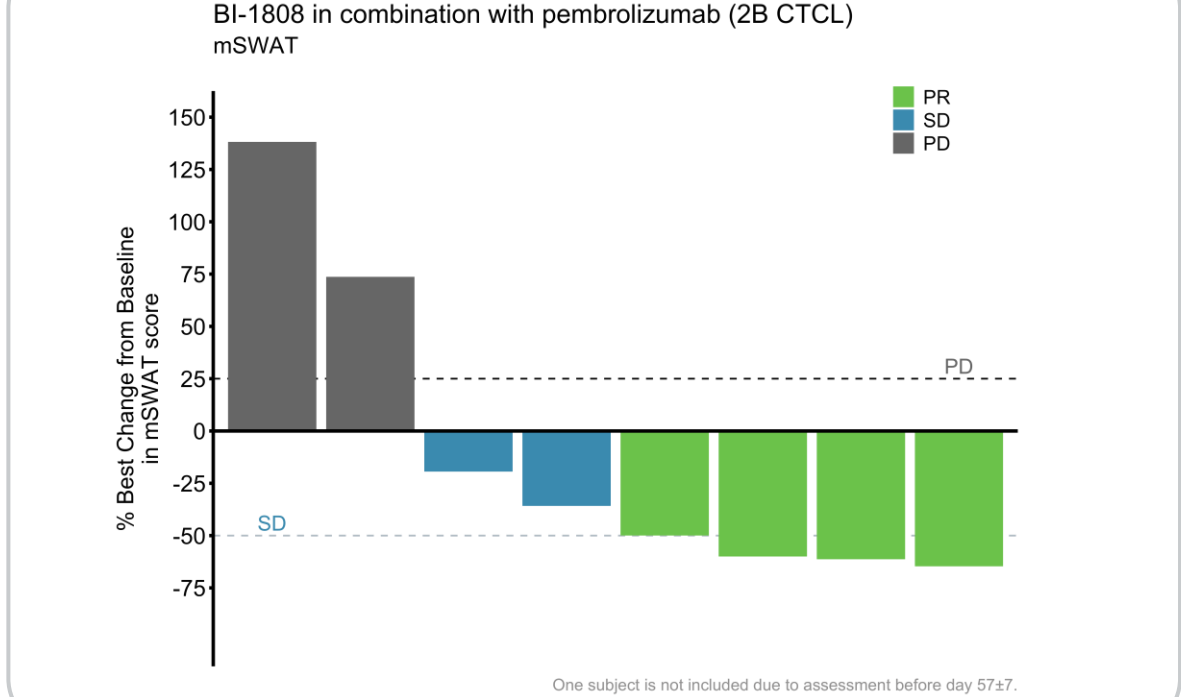
BI-1808 Shows Promising Efficacy in CTCL (and PTCL)

EHA 2026 poster Phase 2a monotherapy & combination data

Single Agent (2A CTCL) — mSWAT



+ Pembrolizumab (2B CTCL) — mSWAT



40%	**93%**	**1 CR**	**50%**	**75%**	**4 PR**
ORR	**DCR**	**SS ongoing 2+ yrs**	**ORR**	**DCR**	
5 PRs + 1 CR	15 evaluable pts		4 PRs	8 evaluable pts	

CTCL: Cutaneous T-cell Lymphoma, PTCL: Peripheral T-cell Lymphoma | Data snapshot: 2026-04-27

Patient Characteristics

Heavily pretreated

patient population

33%

prior mogamulizumab exposure

47%

of patients had SS

Characteristic	Level	Mono	Combo	Total
N		**15**	**8**	**23**
Age, years	Median (range)	68 (27–77)	60 (43–72)	64 (27–77)
Sex	F	5 (33%)	3 (38%)	8 (35%)
	M	10 (67%)	5 (62%)	15 (65%)
CTCL subtype	MF	8 (53%)	5 (62%)	13 (57%)
	SS	7 (47%)	3 (38%)	10 (43%)
ECOG status	0	8 (53%)	2 (25%)	10 (43%)
	1	7 (47%)	6 (75%)	13 (57%)
Stage at initial diagnosis	Unk.	1 (7%)	1 (12%)	2 (9%)
	IB	5 (33%)	1 (12%)	6 (26%)
	IIA	1 (7%)	0 (0%)	1 (4%)
	IIB	3 (20%)	1 (12%)	4 (17%)
	IIIB	2 (13%)	1 (12%)	3 (13%)
	IV	3 (20%)	4 (50%)	7 (30%)
mSWAT at baseline	Median (range)	46 (4–109)	55 (20–137)	50 (4–137)
Prior systemic therapies, n	Median (range)	**3 (2–9)**	**6.5 (1–14)**	**4 (1–14)**
Prior mogamulizumab		**5 (33%)**	**4 (50%)**	**9 (39%)**
Prior pembrolizumab		4 (27%)	0 (0%)	4 (17%)
Prior brentuximab vedotin		3 (20%)	3 (38%)	6 (26%)
Prior romidepsin		2 (13%)	1 (12%)	3 (13%)

Data snapshot: 2026-04-27

BI-1808 Well Tolerated as Single Agent and in Combination

Single Agent — Monotherapy CTCL+PTCL (n=23)

9% Gr3+ TRAEs

13% Treatment-related SAEs

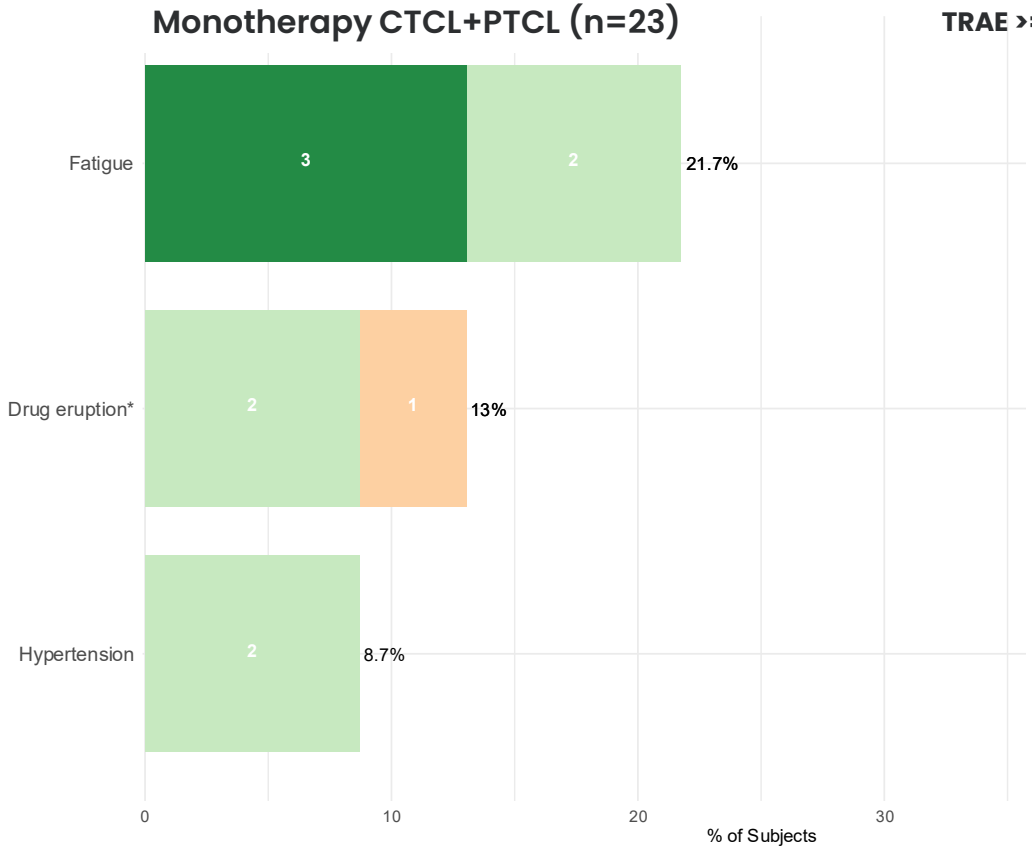
4% TRAE → discontinuation

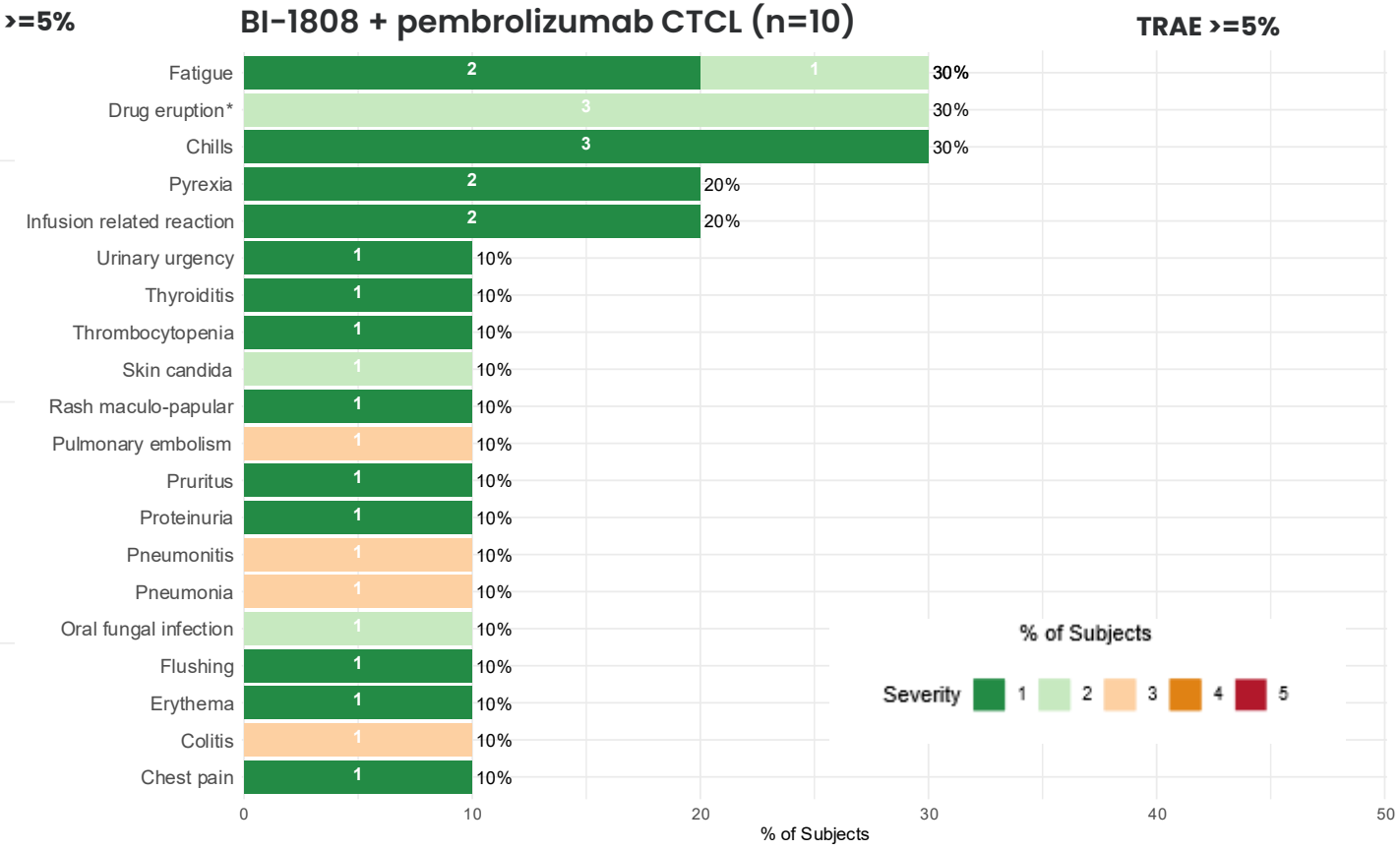
+ Pembrolizumab — Combination CTCL (n=10)

40% Gr3+ TRAEs

30% Treatment-related SAEs

10% TRAE → discontinuation





*drug eruption: worsening of cutaneous symptoms (erythema, pruritus) shortly after first dose

Conclusions

Novel therapeutic strategy

TNFR2 blockade is a powerful new therapeutic strategy in CTCL, combining direct tumor targeting with robust immune reactivation

Competitive efficacy

Efficacy rivals current treatments while driving robust, targeted immune activation — including Treg depletion and CD8+ T-cell influx into the skin

Deep & durable responses

BI-1808 achieved objective responses across MF and SS: a complete response ongoing >2 years, confirmed partial responses, and a high rate of durable disease stabilization (DCR 93%)

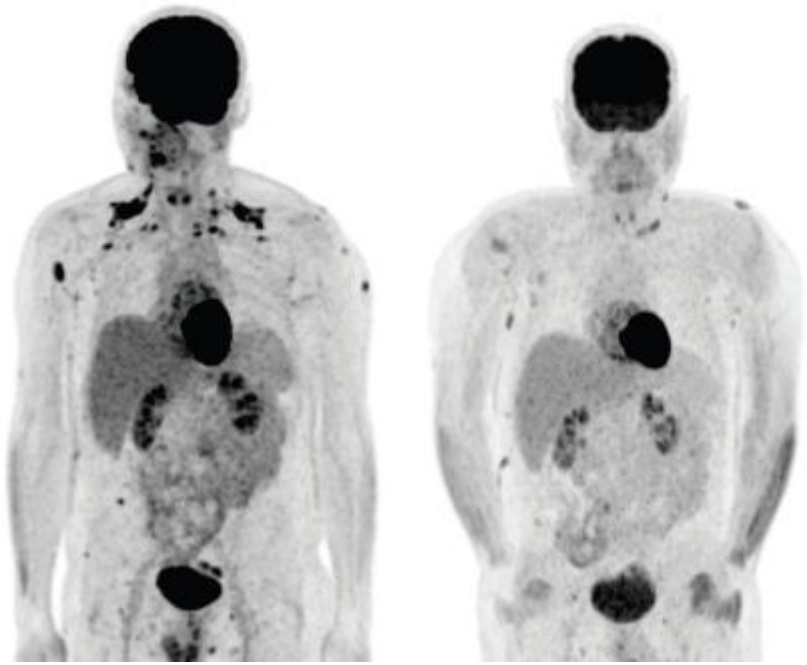
Favorable safety profile

BI-1808 stands out for its low rate of severe side effects (Gr3+ TRAE 9%) — well tolerated as single agent and in combination with pembrolizumab

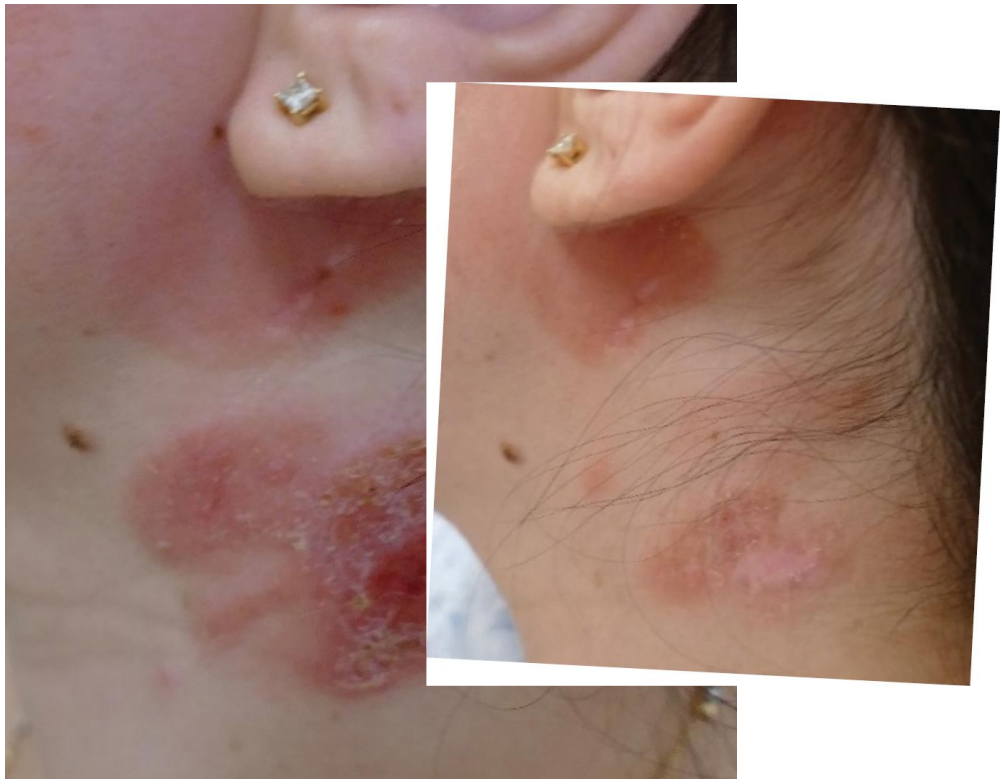
Impressive Responses Were Observed in Heavily Pre-treated Patients with PTCL or CTCL Treated with BI-1808 Monotherapy

Case Studies

PTCL Patient (stage IV, 6 prior lines of treatment)	**CTCL Patient** (stage IIb MF, 5 prior lines of treatment)

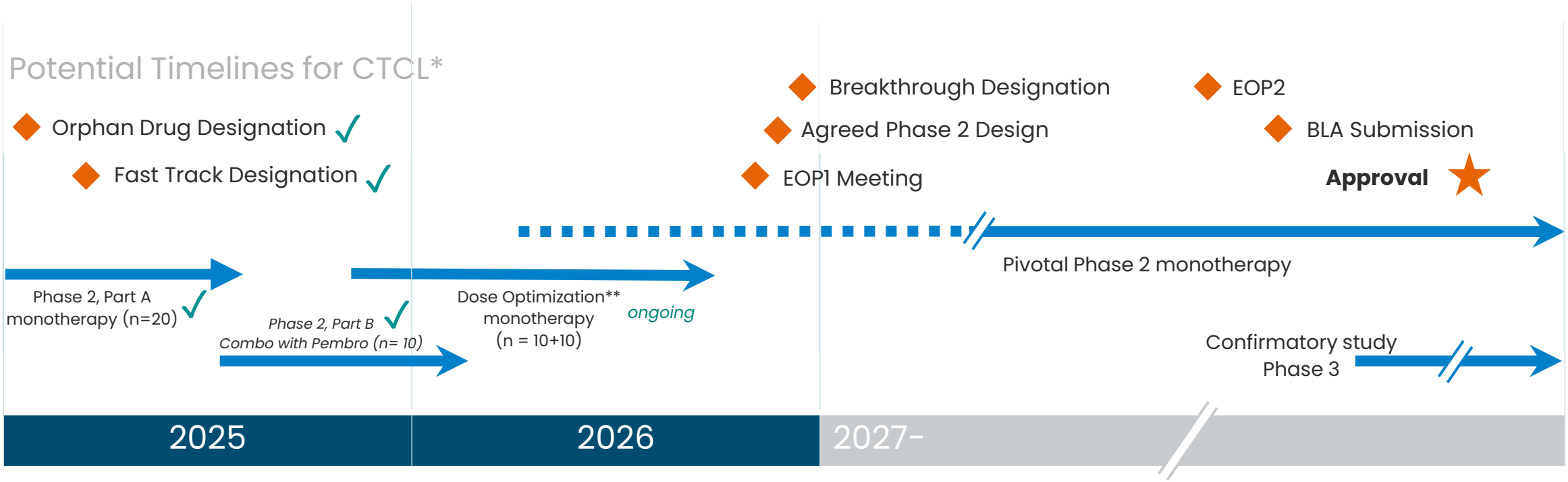


Baseline Week 9



Baseline Week 21

BI-1808 Potential Path to Approval – US



* Depending on partnering discussions and acceptance of development plan by FDA
** Clinical study protocol approved in the US

Sylvie Ryckebusch

CBO

Rare-disease Oncology: A Faster, De-risked Path to Value

Smaller, faster trials, strong incentives, and premium pricing

Rare-disease oncology as market entry strategy

Faster, smaller trials

Accelerated approval on response rate — not large randomized survival trials

Strong incentives

7 years' US / 10 years' EU market exclusivity, tax credits and fee waivers

Premium pricing, light footprint

High margins on a concentrated, academic-center prescriber base

Limited competition

Few new mechanisms reach CTCL — under-innovated, not saturated

A proven path to value

Adcetris (brentuximab vedotin)

- Accelerated approval in 2011 in rare relapsed Hodgkin lymphoma / ALCL on two single-arm trials (~160 patients)
- Expanded across lymphomas → Seagen acquired by Pfizer for ~$43B (2023)

Poteligeo (mogamulizumab)

- Orphan approval in CTCL
- ~$300M global net sales and still growing (19% YoY)

BI-1808 is already on this path — FDA Fast Track (CTCL) and Orphan Drug Designation (CTCL + PTCL)

BI-1808 is the Most Advanced TNFR2 Antibody

Validated new *immunotherapy* mechanism of action

#1

The most advanced TNFR2 antibody in development — a first-mover position with little competition

BI-1808 mechanism of action

Depletes suppressive Tregs	Removes a key brake on anti-tumor immunity in the tumor microenvironment
Drives effector T-cell infiltration	Expands CD8+ T cells as observed directly in the skin lesions
Reprograms the immune environment	Immune infiltration detected in the skin

A new mechanism with potential as a platform across multiple tumor types, including both T cell lymphomas and solid tumors

CTCL is a Rare but Devastating Disease With High Unmet Need

~70% of CTCL patients have mycosis fungoides

55-60 years median age at diagnosis

~96% of CTCL patients relapse

6-12 months between relapses, shortening over time

~30% present with or progress to advanced-stage disease

~3 years median survival of patients with advanced disease

Dobos et al., Cancers 2020; Talpur et al., Clin Cancer Res 2012; Agar et al., JCO 2010; Alberti-Violetti et al., CLML 2015; Eversana market research 2026

Clinician Interviews Confirm the Need for New Treatment Options

Toxicities and low efficacy limit current treatments in MF, the largest patient subset

"Within a few years, we exhaust everything you can find even in NCCN guidelines and beyond. And then we have to go back and recycle these drugs."

Hemato-oncologist, US

"I have many patients who can't sleep [because of the itch]. The skin is torn apart. Itchiness, sleep, pruritus relief — that's all I care about."

Hemato-oncologist, US

"The very high unmet need is in Mycosis Fungoidis (MF). Mogamulizumab is not a good option in these patients."

Dermatologist, France

"30% of patients get a severe rash from mogamulizumab and we have to discontinue it."

Hemato-oncologist, US

"We don't have too many drugs to play with.— and brentuximab vedotin is often limited by severe peripheral neuropathy."

Hemato-oncologist, UK

"There is really no cookbook approach to MF. There's this throw-the-kitchen-sink approach depending on what's worked in the past."

Dermatologist, US

Eversana primary market research, 2026

Existing Treatment Classes in CTCL are Suboptimal Both With Respect to Efficacy and Tolerability

Treatment class	Example	Status	Strongest setting	Key limitation
Skin-directed / phototherapy	Topical, PUVA, RT	1L, early stage	Early skin disease	Not for advanced / systemic disease
HDAC inhibitors	Vorinostat, romidepsin	Approved	—	Low ORR, short responses; poorly tolerated
Anti-CCR4 mAb	Mogamulizumab	Approved 2018	Sézary / blood	Weaker in MF; severe rash; not curative
Anti-CD30 ADC	Brentuximab vedotin	Approved 2017	CD30+ MF (~30%)	Biomarker-gated; neuropathy; black box
Fusion toxin	Lymphir	Approved	Heavily pre-treated	36% ORR; excludes stage IV; capillary-leak warning
Allo-SCT	—	Curative intent	Fit, select patients	Only potential cure; high morbidity

BI-1808 Delivers Durable, Well-tolerated Single-agent Activity

Phase 2a monotherapy, CTCL cohort

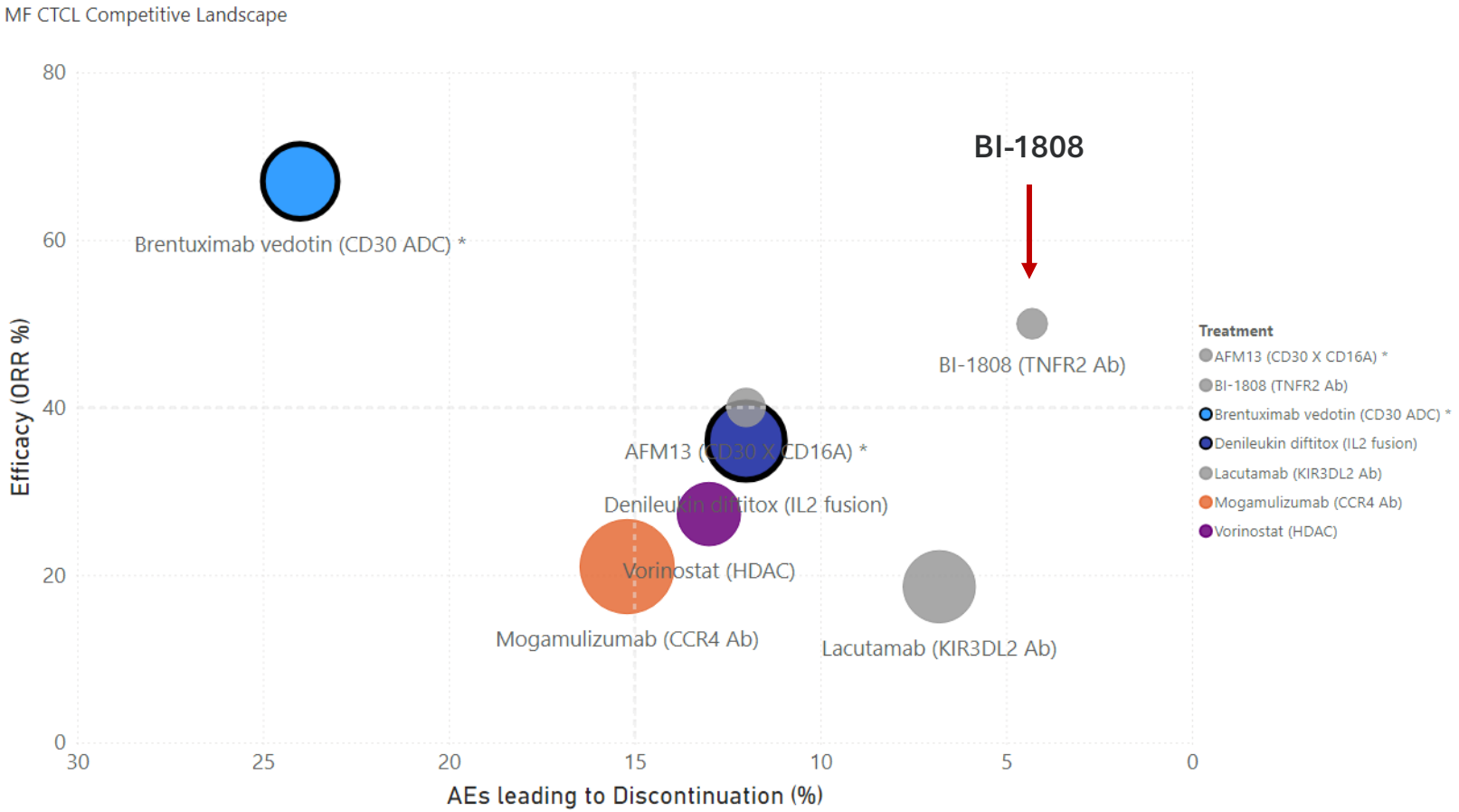
40%	93%	9%	4%
ORR	disease control	Grade 3 AEs	discontinuation

- 15 evaluable CTCL patients (20 enrolled), heavily pre-treated
- 1 complete response in Sézary syndrome — ongoing beyond two years
- 5 partial responses (3 MF, 2 SS) and 8 with stable disease
- Immune activation observed early: Treg depletion, CD8+ T-cell and granzyme B influx into the skin
- Very well tolerated — only one patient discontinued for a treatment-related event
- FDA Fast Track (CTCL) and Orphan Drug Designation (CTCL + PTCL)

BI-1808 Phase 2a (NCT04752826), data cutoff 27 Apr 2026

BI-1808 is Differentiated Where it Matters Most: Mycosis Fungoides

MF represent the majority of CTCL patients (~70%), and where incumbents are weakest



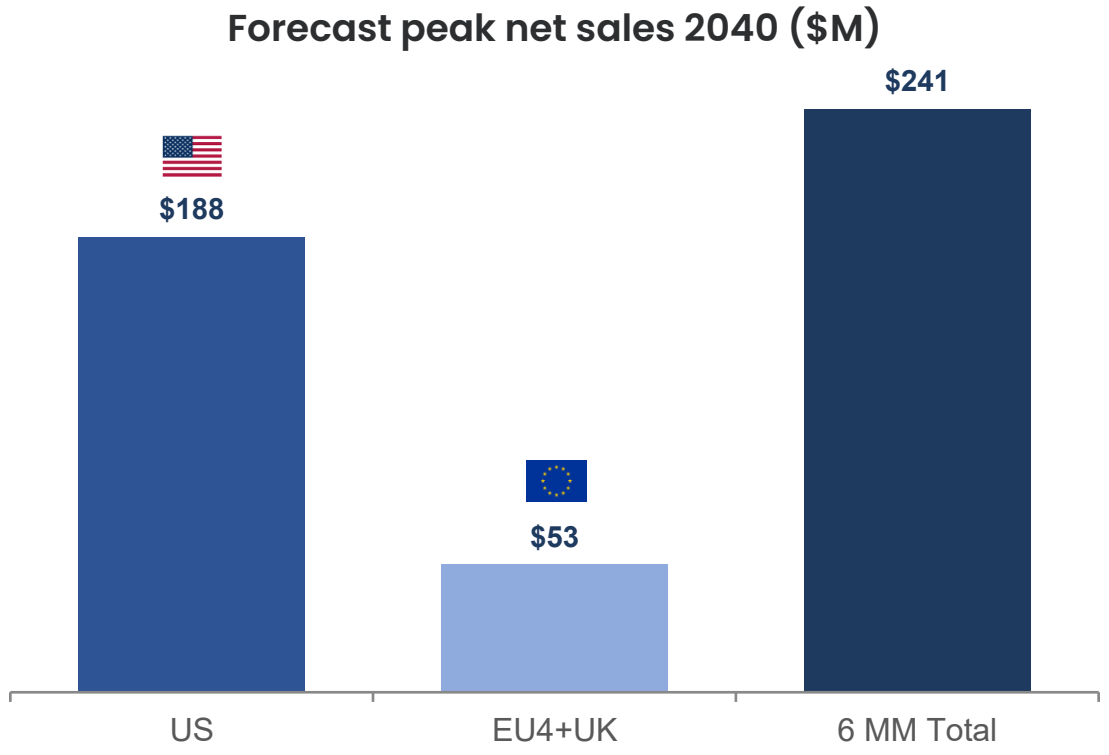
- Higher efficacy in MF than all other treatments except for brentuximab (30% of patients, black box warning)
- No biomarker restriction
- Best-in-class tolerability with only 4% discontinuation

* Biomarker-selected subpopulation; Bubble size represents number of patients in reported dataset; Colored bubbles are approved treatments; Grey bubbles are unapproved treatments; Dark outline signifies black box warning

BI-1808 in CTCL is a Focused Orphan Opportunity With Fast Path to Market

Assumptions

- Positioned as a 2L+ systemic option in intermediate-stage MF/SS,
- Upside potential in earlier stages as evidence matures
- Accelerated approval supported by Fast Track + Orphan designations with US launch in 2030
- ~5,600 drug treated 2L+ patients in 6MM
- Orphan premium pricing $65,000/mo in US; 60% discount in EU



Market benchmark the anti-CCR4 CTCL antibody mogamulizumab reached ~$300M global net sales in FY2025, still growing by 19% YoY — the market tolerates premium orphan antibodies.

Poteligeo figure = anti-CCR4 orphan CTCL antibody, FY2025 global net sales (Kyowa Kirin); USD converted at ~¥150/$. Shown as a market-validation benchmark, not a forecast input.

The BI-1808 Opportunity

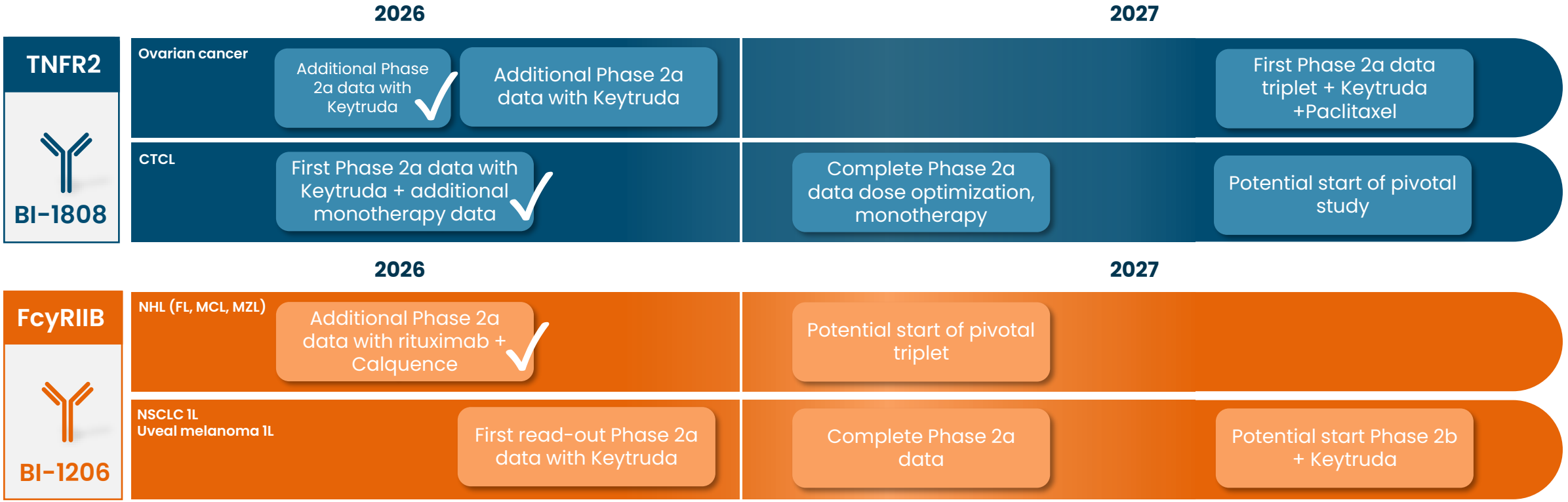
Wins where it matters	Superior efficacy in MF — the ~70% majority where incumbents are weakest
Best in Class Tolerability	9% Grade 3 AEs and only 4% discontinuation; resolves skin symptoms and preserves QoL
Long-Lasting Responses	Complete response in Sézary ongoing past two years; active even after mogamulizumab
First-in-Class, Fast Path	Most advanced TNFR2 antibody; FDA Fast Track and Orphan Drug
Expansion Opportunities	Platform potential across many indications, including solid tumors

Q & A

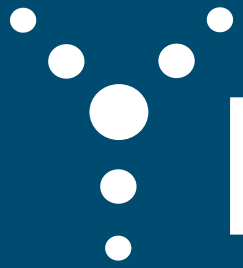
Key Expected Milestones

2026–2027

Key Expected Milestones 2026-2027



1L: First line treatment
CTCL: Cutaneous T-cell Lymphoma, NHL: Non-Hodgkin's Lymphoma, FL: Follicular Lymphoma, MCL: Mantle Cell Lymphoma, MZL: Marginal Zone Lymphoma, NSCLC: Non-small cell lung cancer



BioInvent

Unleashing Immunity To Fight Cancer

www.bioinvent.com

Appendix