Il Futuro…

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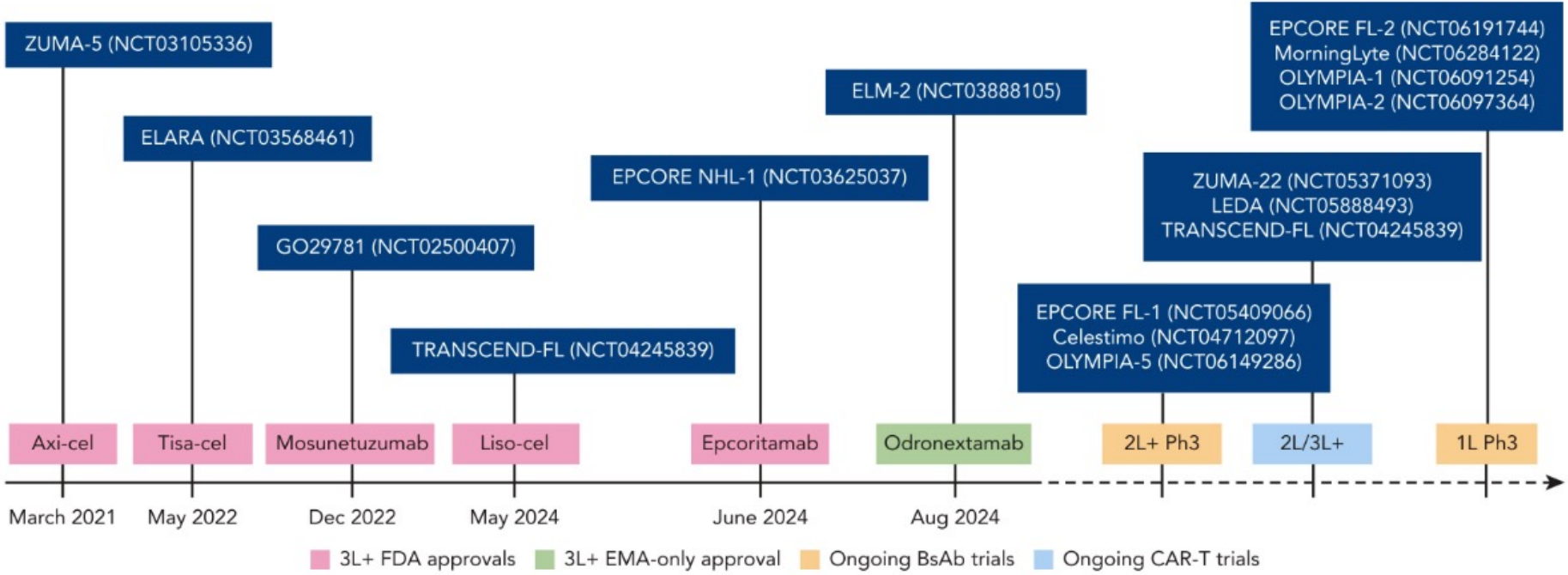
Disclosures of Annalisa Chiarenza

Company name	Research support	Employee	Consultant	Stockholder	Speakers bureau	Advisory board	Other
Roche						X	X
Janssen					X	X	X
Abbvie					X	X	
Gilead						X	
AstraZeneca					X	X	
Takeda						X	
Lilly					X		X
Beigene					X		X

Approvals T-cell-redirecting therapies in Follicular Lymphoma

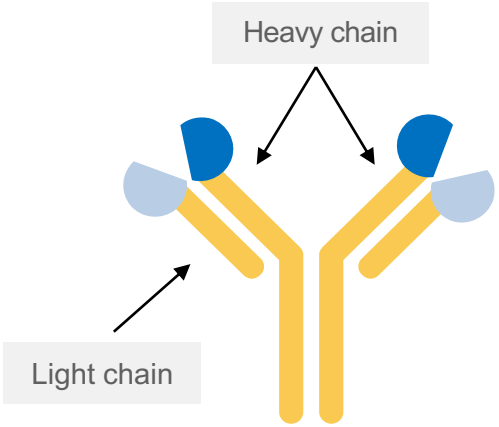


Iacoboni G, Morschhauser F. Blood 2025;145(2):170-175.

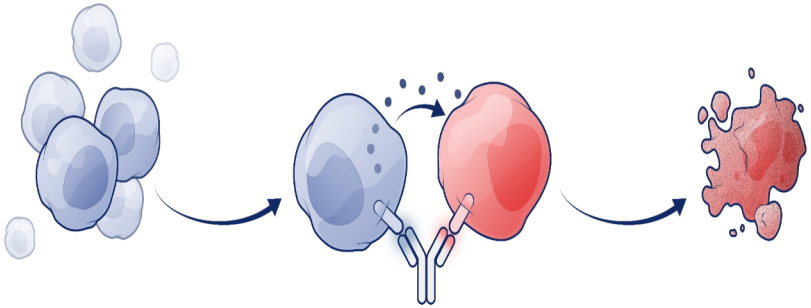
Emerging Therapeutic Innovation in Follicular Lymphoma

- **Novel combinations:**
  - -Humanized bispecific mAb targeting CD20 e CD3 in combination
  - -Novel CD19 monoclonal antibody in combination
- **Earlier access**:
  - -Accelerated approval for relapsed or refractory or earlier access in 1st line therapy
- **New molecules:**
  - -ADC targeting CD19
  - -Humanized bispecific mAb targeting CD19 e CD3

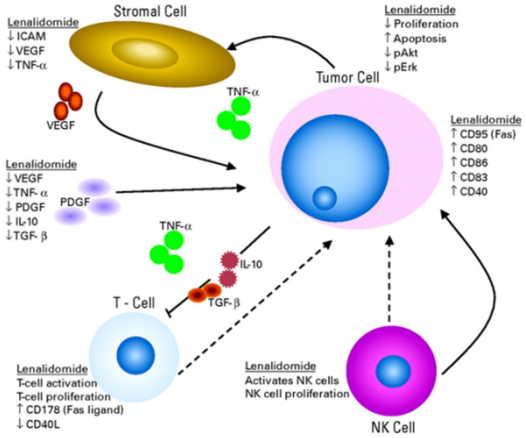
Rational for Drug combinations



CD20-Monoclonal antibody



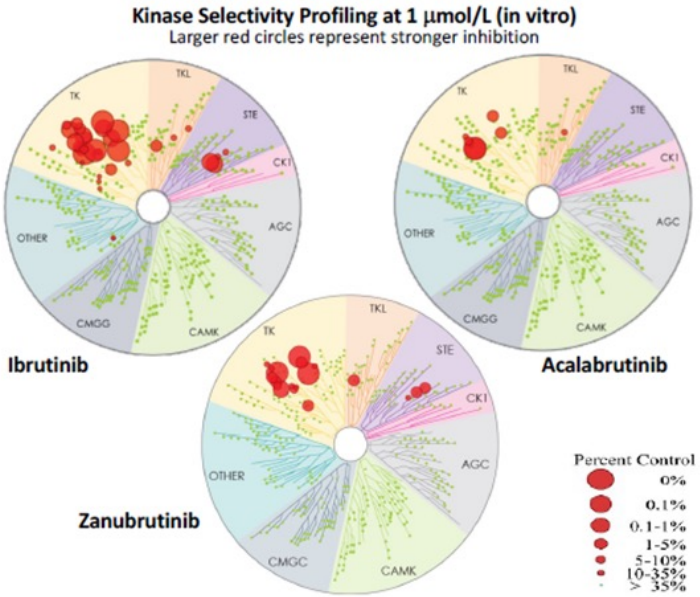
CD20xCD3 Bispecific Antibody

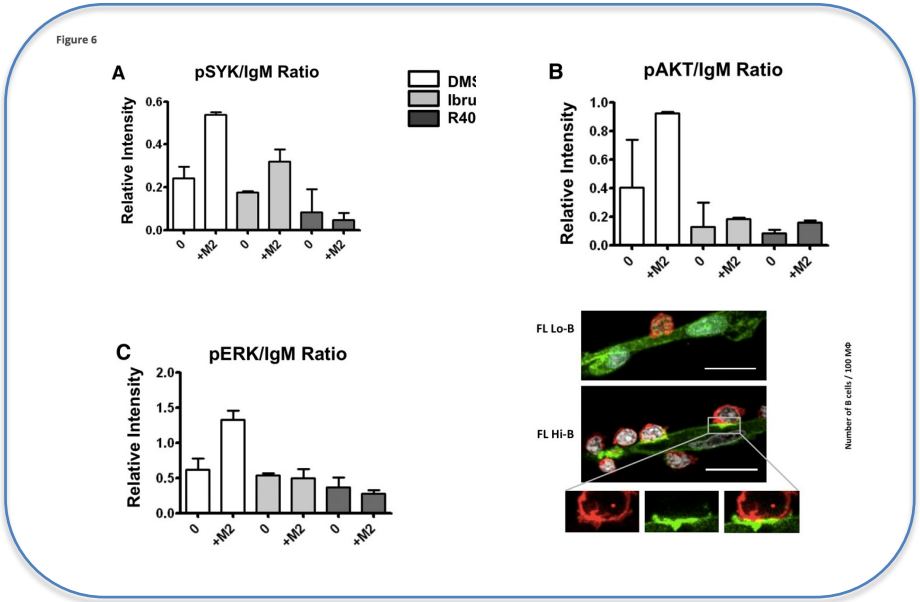


Lenalidomide

Novel combinations

Exploring the Bruton Tyrosine Kinase (BTK) inhibitors in FL

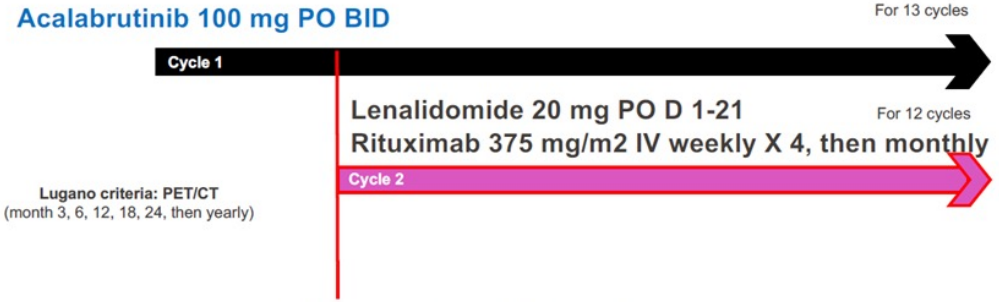




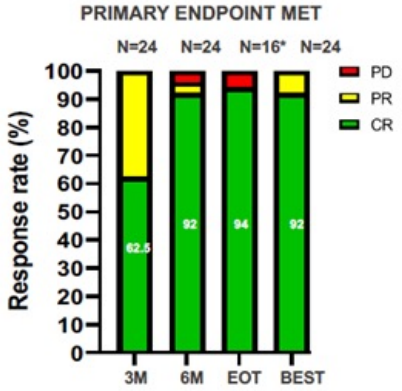
BCR inhibition targets the croosstalk between M2 macrophage and FL cells

Amin R et al. Blood, 13 Aug 2015, 126(16):1911-1920

Acalabrutinib plus Lenalidomide and Rituximab (aR2) in HTB FL

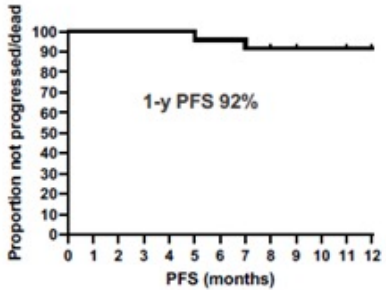


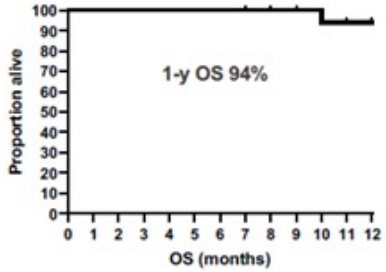
Primary endpoint: CR rate (best response)
Secondary endpoint: safety, 2-year PFS
H0 (R^2): 50%, H1: 80%, α: 0.05, power: 80%; population size: 24



Median follow-up 12 months (95% CI,

Phase 2 Trial





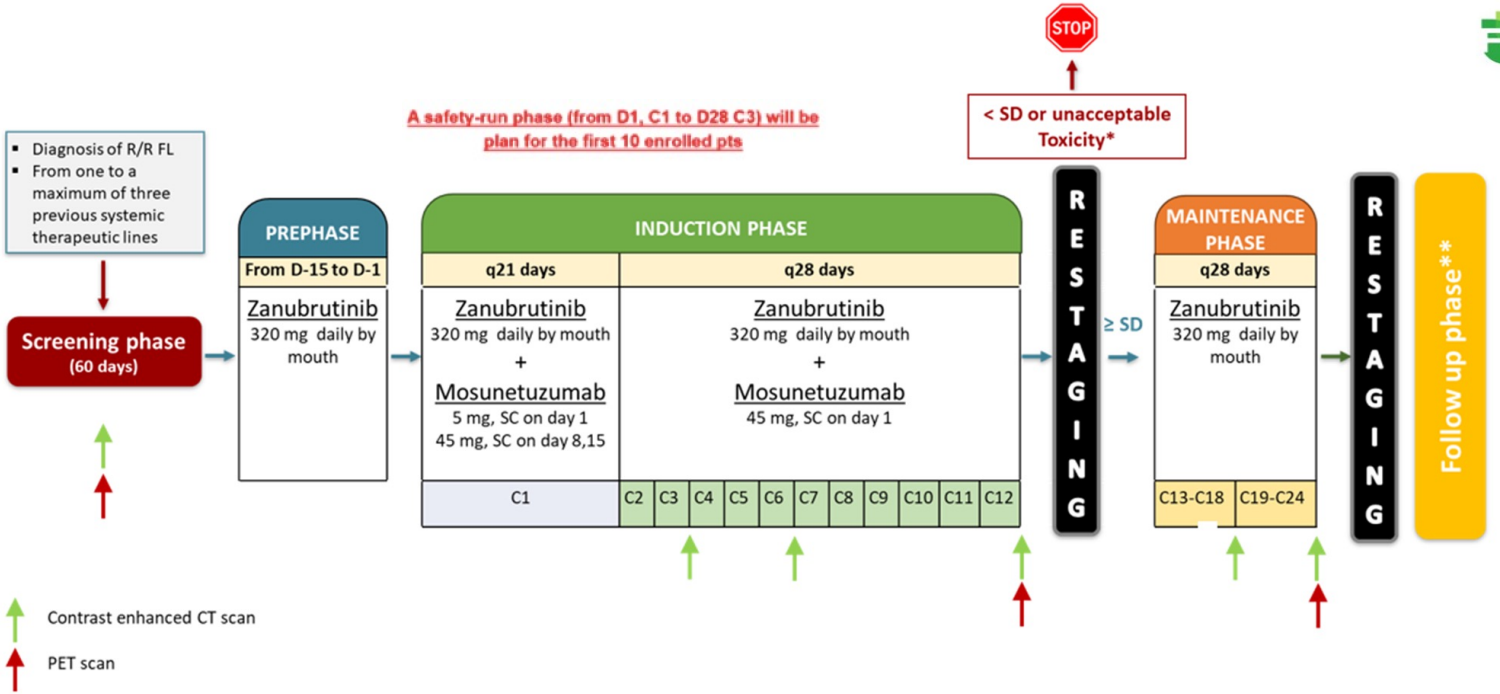
Patients (N=24)	Grade 1-2	Grade 3-4
Neutropenia	8 (33)	10 (42)
ALT elevation	6 (25)	3 (12.5)
AST elevation	6 (25)	2 (8)
Skin rash	7 (29)	2 (8)
Infection	2 (8)	2 (8)
Fatigue	12 (50)	1 (4)
Nausea	2 (8)	1 (4)
Atrial fibrillation	0 (0)	1 (4)

1 patient was diagnosed with localized prostate adenocarcinoma

Patients (N=24)	Grade 1-2	Grade 3-4
Anemia	14 (58)	0 (0)
Thrombocytopenia	13 (54)	0 (0)
Headache	10 (42)	0 (0)
Bruising	6 (25)	0 (0)
Arthralgia	5 (21)	0 (0)
Diarrhea	5 (21)	0 (0)
Infusion-related reaction	5 (21)	0 (0)
Myalgia	5 (21)	0 (0)
Pruritus	5 (21)	0 (0)
Dysgeusia	3 (12.5)	0 (0)
Dizziness	2 (4)	0 (0)
Dry skin	2 (4)	0 (0)
Lymphopenia	2 (4)	0 (0)
Peripheral neuropathy	2 (4)	0 (0)
Sinus bradycardia	2 (4)	0 (0)

Strati P. et al. ICML 2023

MOsunetuzumab and Zanubrutinib in Relapsed/refracTory FL



- **Global, multicenter Phase 2 study**
- **20 Italian** FIL centers and **4 Australian** centers (authorized to use CAR-T therapy or with adequate experience with the use of bispecific monoclonal antibodies)
- **Primary Endpoint**: Complete response rate (**CRR**) at the end of combination therapy (Lugano 2014)

PI: M. Ladetto, S. Luminari

The "Safety Run In" Phase

n = 10 patients

Safety Report

Induction treatment	Grade 1-2		Grade 3		Grade 4	
Hematological events	**n**	**%**	**n**	**%**	**n**	**%**
Neutropenia	0	-	1	10	0	-
Thrombocytopenia	1	10	0	-	0	-
	Grade 1-2		**Grade 3**		**Grade 4**	
Extrahematological events	**n**	**%**	**N**	**%**	**N**	**%**
Gastrointestinal disorders	2	20	0	-	0	-
General disorders and administration site conditions	5	50	0	-	0	-
Immune system disorders	4	40	0	-	0	-
Injury/poisoning/procedural complications	3	30	0	-	0	-
Investigations	1	10	0	-	0	-
Musculoskeletal and connective tissue disorders	1	10	0	-	0	-
Skin and subcutaneous tissue disorders	4	40	0	-	0	-
Vascular disorders	2	20	0	-	0	-

Preliminary Efficacy Report

	Response after 3 cycles			Total
Response 6cy	CR	PR	SD	
CR	2	4	2	**8**
PR	1	1	-	**2**
Total	**3**	**5**	**2**	**10**

After C6 (ORR 8/10, 80% 95%CI 44-97)

Five relevant safety events (4 grade 1-2 CRS, 1 grade 3 neutropenia) occurred, **not exceeding the threshold defined for early stopping**.
The DSMC recommends that the **study proceeds without changes**

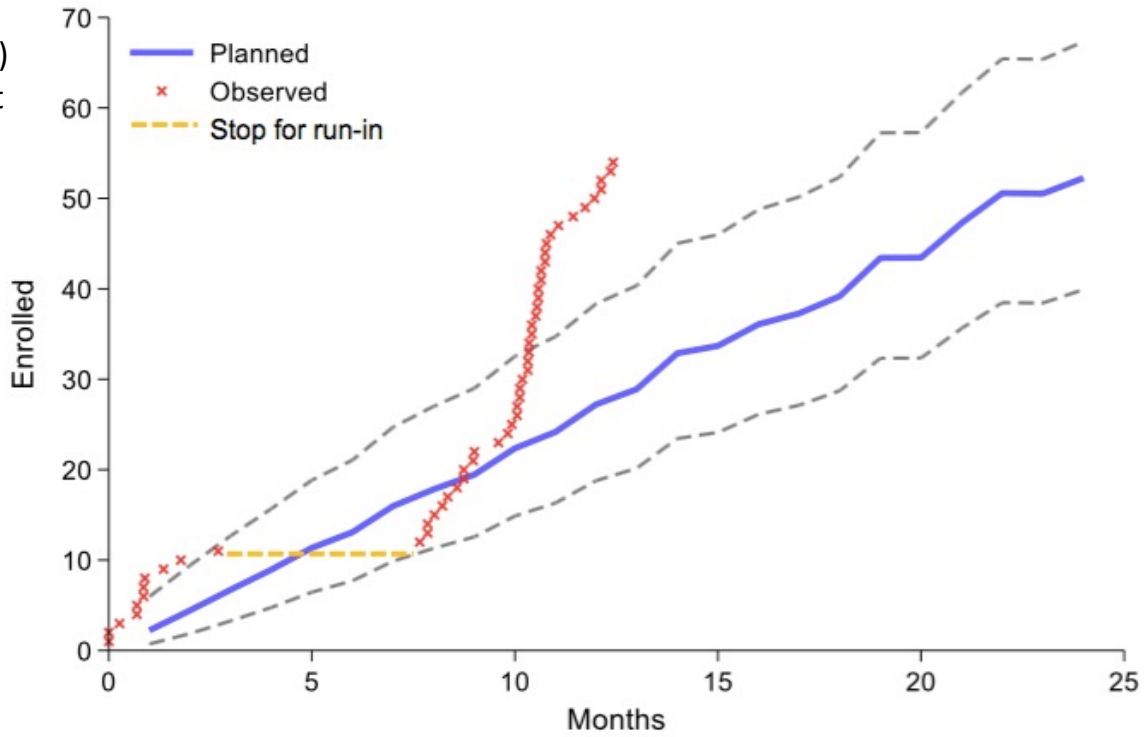
Luminari S. et al. FIL nazionale 2025

Sites Activations and Enrollment Curve

Timeline:

→ 02/10/2024: national EC and AIFA approval
→ 19/12/2024: first site activation (Alessandria)
→ 23/12/2024 to 01/05/2025: enroll.SRI cohort
→ 26/06/2025: last italian site activation
→ 18/08/2025: first autralian sites activation (Adelaide, Melbourne)

Closed enrollment for italian sites (44/55 pts)



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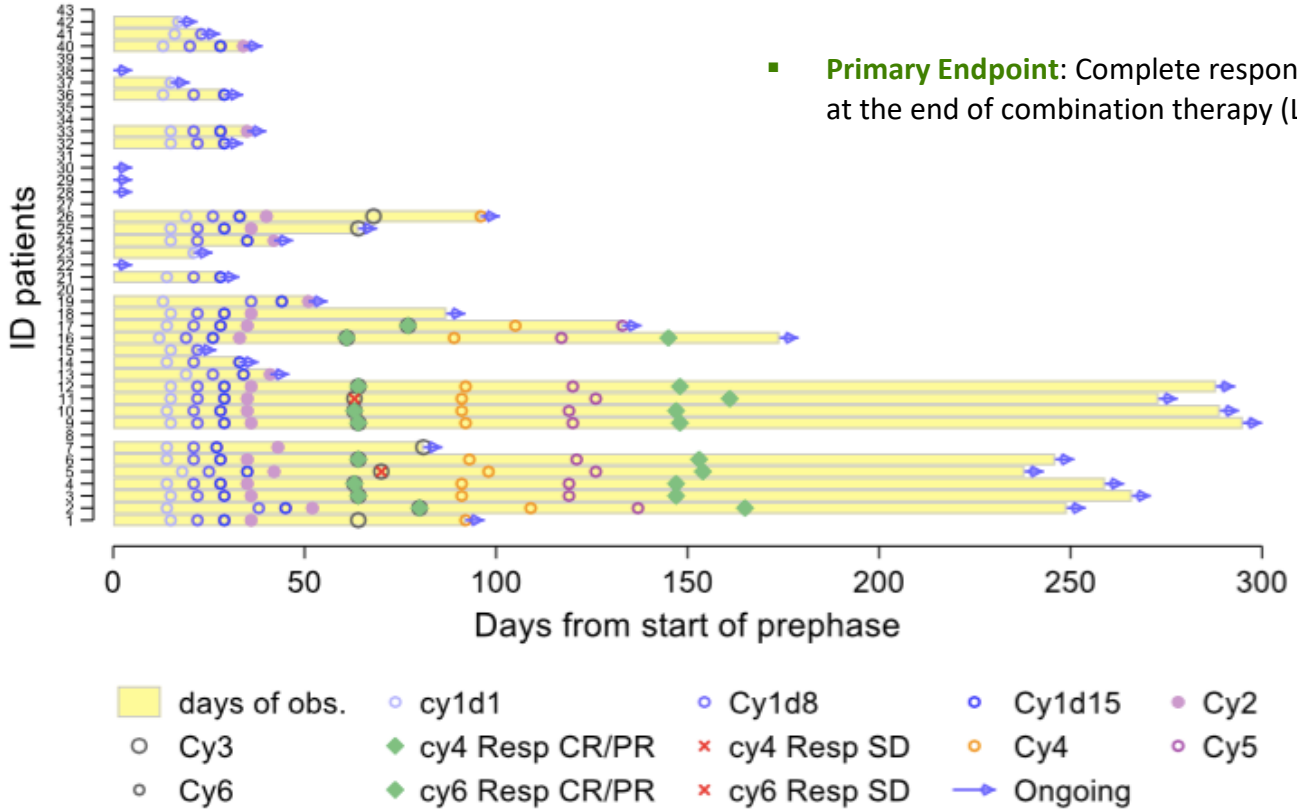
Preliminary Efficacy Analysis All Population (Nov.2025)

- **Primary Endpoint**: Complete response rate (**CRR**) at the end of combination therapy (Lugano 2014)



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Earlier access

Epcoritamab with Rituximab-Lenalidomide in Previously Untreated FL: 3-Year Outcomes From EPCORE NHL-2 Arms 6 and 7

Study Design

Key inclusion criteria

Overall

- CD20+ FL
  - Grade 1, 2, or 3A
- ECOG PS 0–2
- Adequate organ function

Arm 6, 1L FL

- 1L FL
- Measurable disease by CT or MRI
- Meet GELF criteria

Arm 7, FL maintenance

- In CR or PR after 1–2 lines of SOC treatment

Data cutoff: Apr 9, 2025

Median follow-up: Arm 6, 36 months[e]; Arm 7, 35 months[f]

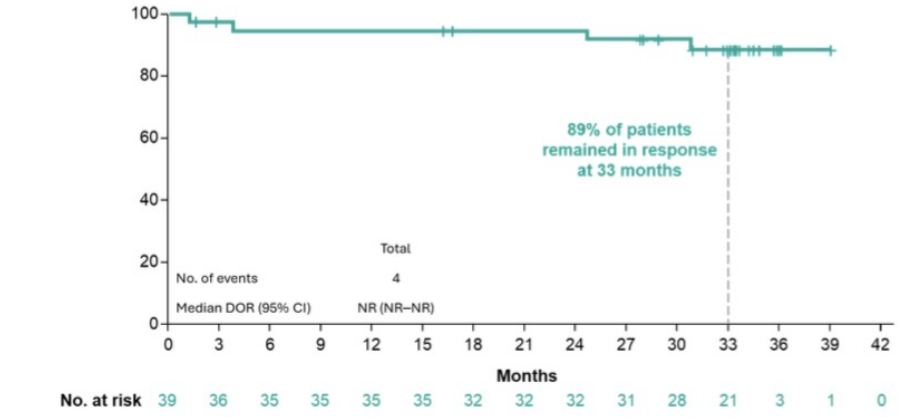
Arm 6 (1L FL) expansion	Arm 7 (FL maintenance after SOC treatment) expansion
Rituximab (IV) 375 mg/m² QW C1, Q4W C2–6 **Lenalidomide (oral) 20 mg** QD for 21 days in C1–12 **Epcoritamab (SC) 48 mg** 2 SUD[a], QW C1–2, Q4W C3+ (28-day cycles); treatment up to 2 years	**Epcoritamab (SC) 48 mg** 2 SUD[a], QW C1 (28 days) Q8W C2–13 (56-day cycles); treatment up to 2 years
Primary endpoint: ORR[b] **Key secondary endpoints:** Safety, DOR, DOCR, PFS, OS, MRD[c] **First patient first visit/last patient last visit** Oct 8, 2021/May 16, 2024	**Primary endpoint:** Safety **Key secondary endpoints:** CR rate,[d] DOCR **First patient first visit/last patient last visit:** Nov 8, 2021/Feb 22, 2024

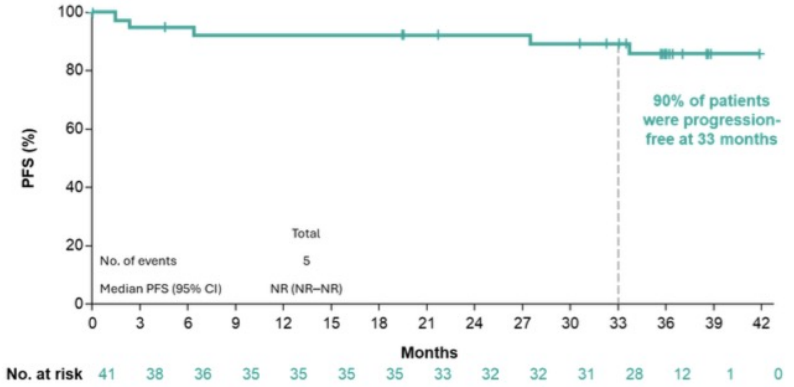
Characteristic	Epcoritamab + R² N = 41
Age, median (range), years	57 (39–78)
Male, n (%)	21 (51)
ECOG PS, n (%)	
0	34 (83)
1	6 (15)
2	1 (2)
Ann Arbor stage, n (%)[a]	
III	9 (22)
IV	28 (68)
FLIPI, n (%)	
0–1	11 (27)
2	14 (34)
3–5	16 (39)
GELF criteria, n (%)	41 (100)
Bulky disease, n (%)[b]	
< 7cm	28 (68)
≥ 7cm	13 (32)
Bone marrow involvement, n (%)	20 (49)
LDH, n (%)[c]	
Normal	31 (76)
Elevated	8 (20)
Beta-2 microglobulin, n (%)[d]	
Normal	22 (54)
High	13 (32)

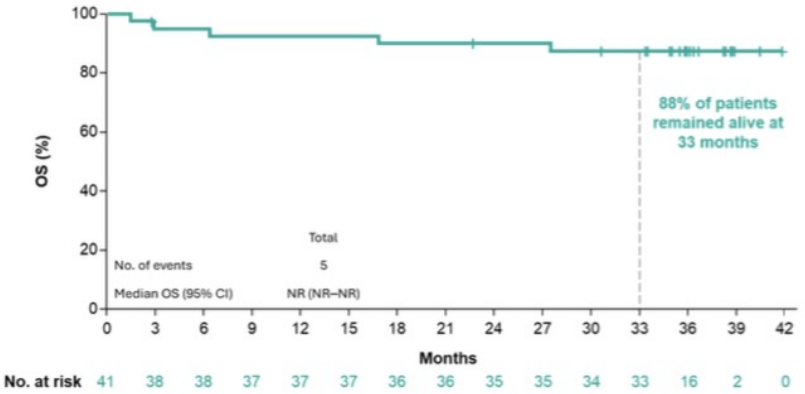
Leslie L. et al. ASH 2025

EPCORE NHL-2 (Arms 6): Efficacy and Long Term Outcome

	Epcoritamab + R² N = 41
Overall response, n (%)	39 (95)
CR	36 (88)
PR	3 (7)
NE[a]	2 (5)







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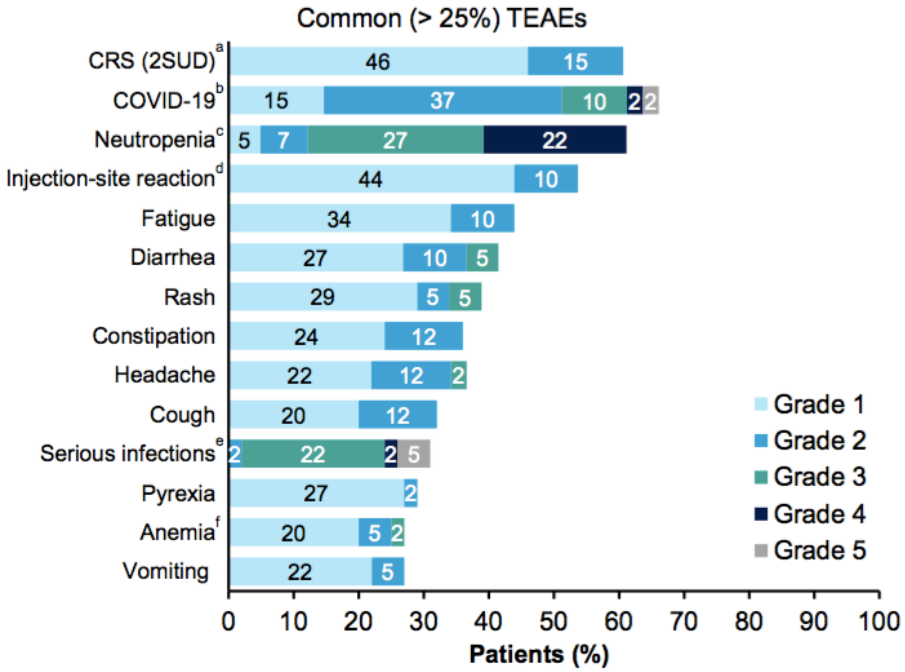
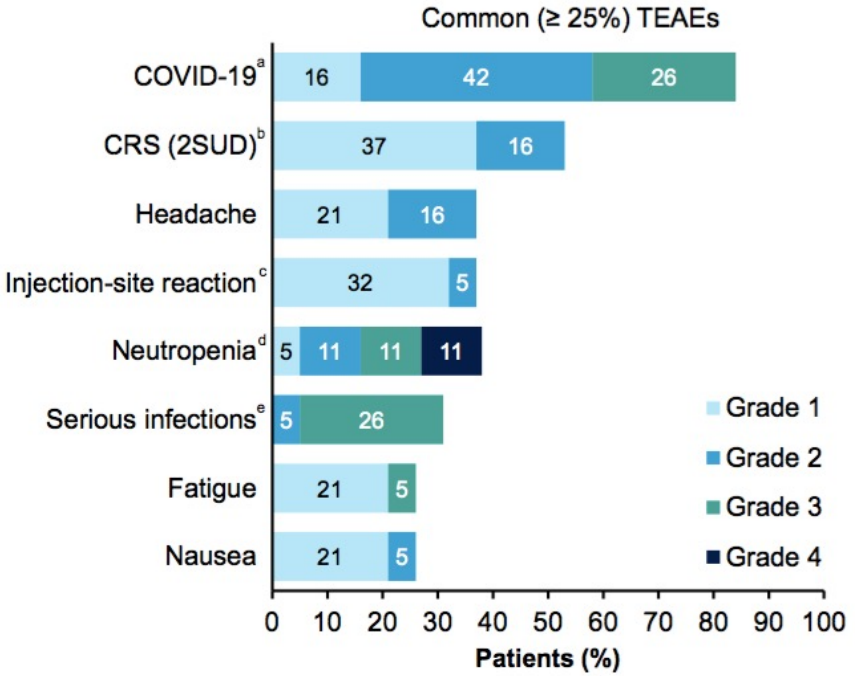
EPCORE NHL-2 (Arms 6 and 7): Safety Report

Arms 6



Arms 7



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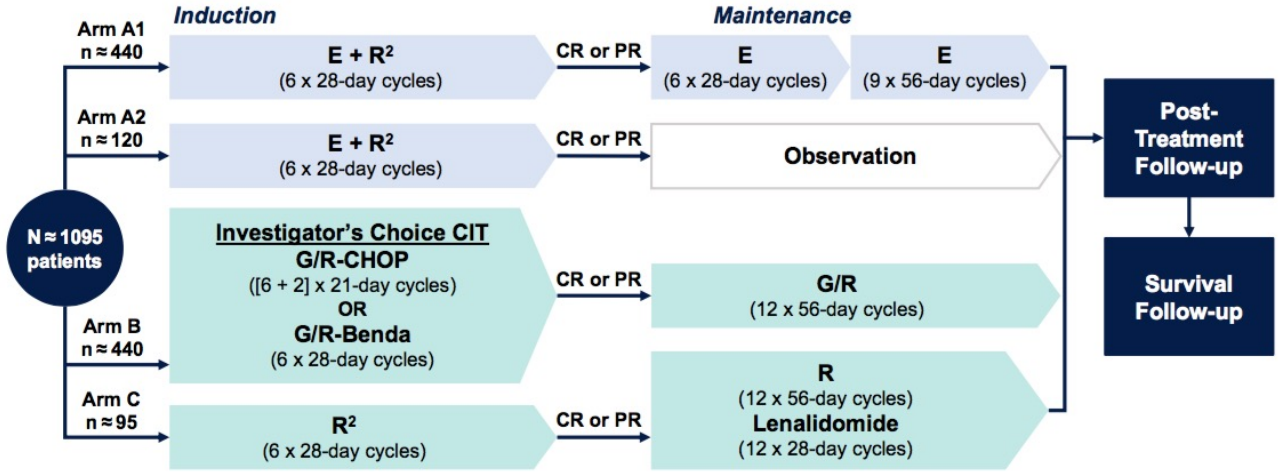
Epcoritamab + R2 vs. Chemoimmunotherapy in Untreated FL
EPCORE FL-2 study

EPCORE FL-2 (NCT06191744)- M22-003 EPCORE global, multicenter, randomized open-label phase 3 trial

Figure 1: Study Design



Benda, bendamustine; CHOP, cyclophosphamide + doxorubicin hydrochloride + vincristine sulfate + prednisone; CIT, chemoimmunotherapy; CR, complete response; E, epcoritamab; G, obinutuzumab; PR, partial response; R, rituximab; R², rituximab and lenalidomide.

Stratification Factors

-FLIPI score (0-1, 2, 3-5)
-Region (US/Europe vs rest of world)
-Investigator's choise (R/G-CHOP, R/G-Benda)

Table 1: Study Endpoints

Primary Endpoints (arm A1 vs arm B)
• CR30[a] by IRC
• PFS[a] by IRC
Key Secondary Endpoints (arm A1 vs arm B)
• OS
• MRD negativity rate
• PROs[b]

Supportative Secondary Endpoints

Safety Endpoints

On going trial…

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Randomized Phase 3 Trials in Untreated FL

TABLE 1 | Selected ongoing BsAbs trials for untreated advanced stage high tumor burden FL patients.

Trial/NCT	Phase	Patient group	Planned enrollment	Experimental arm	Standard arm	Primary endpoint
EPCORE FL2 (NCT06191744)	III	1L	1080	Epcoritamab + R^2, followed by epcoritamab maintenance if CR or PR	R^2 or CIT (O/R-CHOP or O/R-B) + maintenance	CR30 PFS
MorningLyte (NCT06284122)	III	1L (FLIPI 2–5)	790	Mosunetuzumab + lenalidomide	CIT (O/R-CHOP or O/R-B) + maintenance	PFS
OLYMPIA 1 (NCT06091254)	III	1L	446	Odronextamab, followed by odronextamab maintenance if CR or PR	CIT (R-CHOP/CVP/B) + maintenance	CR30
SOUNDTRACK-F1 (NCT06549595)	III	1L	1005	AZD0486 + R	CIT (R-CHOP/CVP/B) + maintenance	PFS

Abbreviations: 1L = first line; AZD0486 = CD19 × CD3 BsAb; B = bendamustine; CHOP = cyclophosphamide, doxorubicin, vincristine, prednisolone; CIT = chemo-immunotherapy; CR = complete response; CR30 = complete response at 30 months; CVP = cyclophosphamide, vincristine, prednisolone; FLIPI = follicular lymphoma international prognostic index; O = obinutuzumab; PFS = progression free survival; PR = partial response; R = rituximab; R^2 = rituximab and lenalidomide.

CAR T cell Randomized Trials in FL

ZUMA-22 (NCT05371093): phase III of axi-cel vs SOC in RR FL

Grade 1-3A FL

POD after 1st line, or > 2 prior line of therapy

SOC: R-CHOP, R-Benda, R-Lena (investigator choice)

Primary endpoint: PFS

LEDA (NCT05888493): phase III of tisa-cel vs SOC in RR FL

Grade 1-3A FL

2 prior line of therapy

SOC: R-CHOP, R-Benda, R-Lena (investigator choice)

Primary endpoint: PFS

New molecules

MorningSun: Mosunetuzumab SC in Previously Untreated FL

Key inclusion criteria

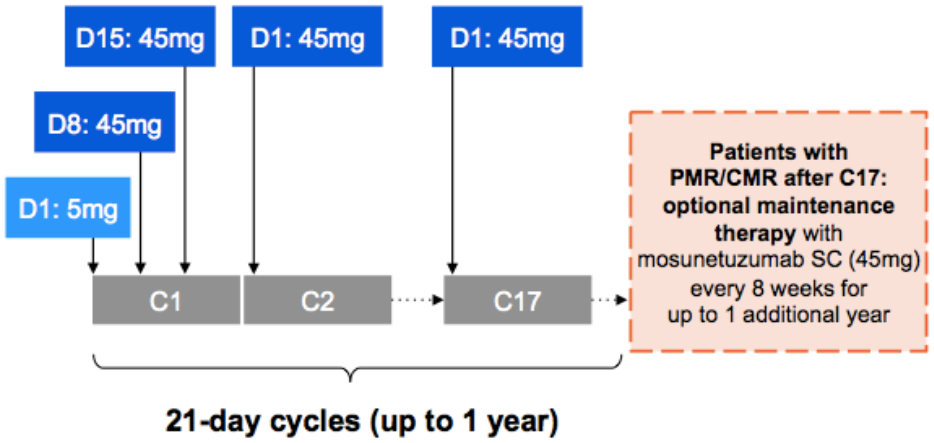
- Previously untreated FL
- HTB by GELF criteria
- ECOG performance status 0–2

CRS mitigation

- Mosunetuzumab SC step-up dosing in C1
- Corticosteroid prophylaxis* was mandatory in C1–2 and optional thereafter
- Hospitalization was not mandatory

Endpoints

- Primary: PFS rate at 24 months
- Key secondary: ORR, DOR, DOCR, safety
- Exploratory analysis of ctDNA levels†

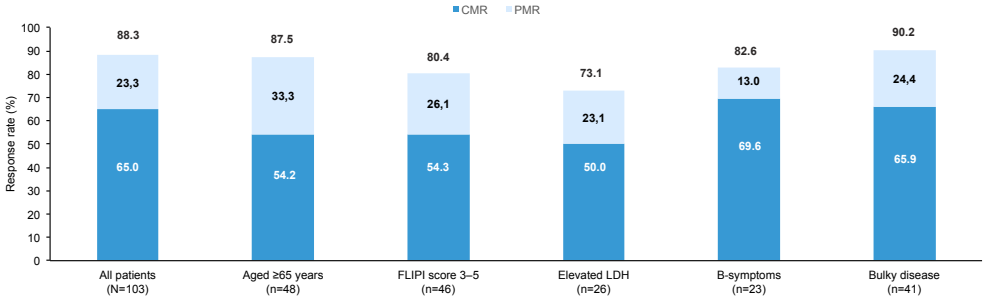


- A total of **82** patients were enrolled from community practices and **21** patients from academic sites

The HTB cohort was enrolled between March 3, 2022, and June 21, 2024. CCOD: February 10, 2025.

Ghosh N. et al, oral presentation ASH 2025; Blood (2025) 146 (Supplement 1): 1020.

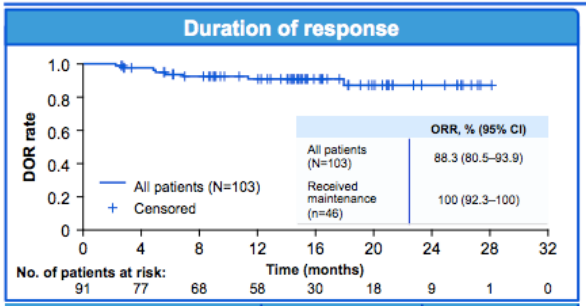
MorningSun Phase 2 study: Response by high-risk subgroup

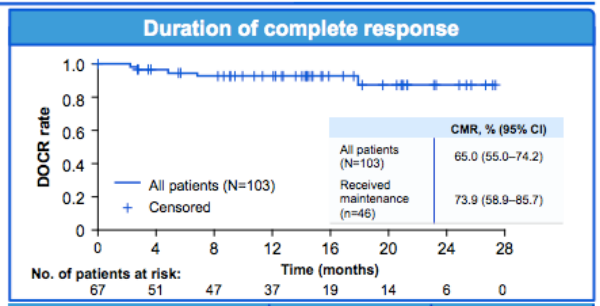


Among patients with a response (n=91), median time to response was 2.7 months (range: 1.2–6.0)

- A total of 68 (66%) patients achieved a PMR/CMR after 17 cycles and were eligible to maintenance treatment
- 46 (44.7%) patients received maintenance treatment, with 15% still receiving maintenance at data cut-off

Median follow-up was 22.3 months





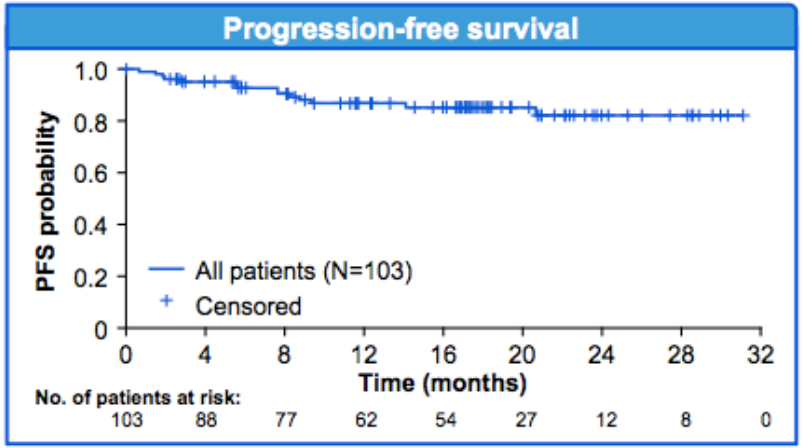
Response rate, % (95% CI)	All patients N=103	Patients who received maintenance treatment n=46
Median DOR, months	NR (NE–NE)	NR (NE–NE)
12-month event-free rate, %	90.9 (81.7–95.6)	100 (100–100)
18-month event-free rate, %	87.2 (74.1–94.0)	94.7 (68.1–99.2)

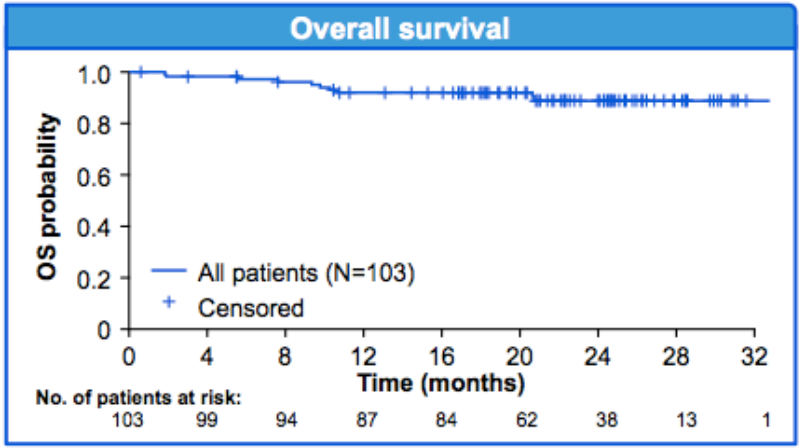
Response rate, (95% CI)	All patients N=103	Patients who received maintenance treatment n=46
Median DOCR, months	NR (NE–NE)	NR (NE–NE)
12-month event-free rate, %	92.7 (81.6–97.2)	100 (100–100)
18-month event-free rate, %	87.2 (68.3–95.2)	91.7 (53.9–98.8)

Ghosh N. et al, oral presentation ASH 2025; Blood (2025) 146 (Supplement 1): 1020.

MorningSun Phase 2 study: Efficacy Results

Median follow-up was 22.3 months





PFS outcomes, (95% CI)	All patients N=103	Patients who received maintenance treatment n=46
Median PFS, months	NR (NE–NE)	NR (NE–NE)
12-month event-free rate, %	86.7 (77.7–92.3)	100 (100–100)
18-month event-free rate, %	85.3 (75.8–91.2)	100 (100–100)

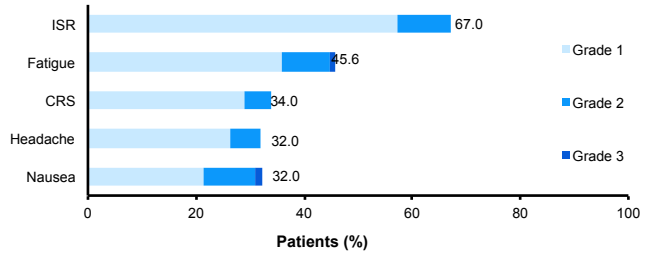
OS outcomes, (95% CI)	All patients N=103	Patients who received maintenance treatment n=46
Median OS, months	NR (NE–NE)	NR (NE–NE)
12-month event-free rate, %	91.9 (84.5–95.9)	100 (100–100)
18-month event-free rate, %	91.9 (84.5–95.9)	100 (100–100)*

CCOD: February 10, 2025. Median follow-up was 22.3 months (95% CI: 20.9–24.1). *One patient died after the 18-month landmark.

Ghosh N. et al, oral presentation ASH 2025; Blood (2025) 146 (Supplement 1): 1020.

MorningSun Phase 2 study: Safety Analysis

Most common (>30%) AEs in all patients



AE summary, n (%)	All patients N=103	Patients who received maintenance treatment n=46
Patients with ≥1 AE	103 (100)	38 (82.6)
Grade 3/4 AE	48 (46.6)	7 (15.2)
Serious AE	37 (35.9)	6 (13.0)
AEs of special interest	29 (28.2)	4 (8.7)
Infections*	81 (78.6)	21 (45.7)
ISR	69 (67.0)	15 (32.6)
CRS (by ASTCT criteria)	35 (34.0)	0
Neutropenia/neutrophil count decreased	23 (22.3)	2 (4.3)
Grade 5 AEs	5 (4.9)†	1 (2.2)‡
AE leading to mosunetuzumab discontinuation	11 (10.7)§	4 (8.7)¶

n (%) unless stated	N=103
Received antimicrobial prophylaxis	46 (44.7)
Any grade infection	81 (78.6)
Grade 1	12 (11.7)
Grade 2	49 (47.6)
Grade 3	13 (12.6)
Grade 4	4 (3.9)
Grade 5*	3 (2.9)
Serious infections	17 (16.5)
Median time from first mosunetuzumab dose to first infection, days (range)	84 (1–624)
Infections resolved, n/n (%)	77/81 (95.1)
Most common infections (≥10%)	
COVID-19/COVID-19 pneumonia†	28 (27.2)
Sinusitis	17 (16.5)
Urinary tract infection	15 (14.6)
Pneumonia	15 (14.6)
URTI	14 (13.6)

Ghosh N. et al, oral presentation ASH 2025; Blood (2025) 146 (Supplement 1): 1020.

Mosunetuzumab SC in Previously Untreated Low Tumor Burden FL

Eligibility

Cohort A1: High-tumor burden[1,2*]

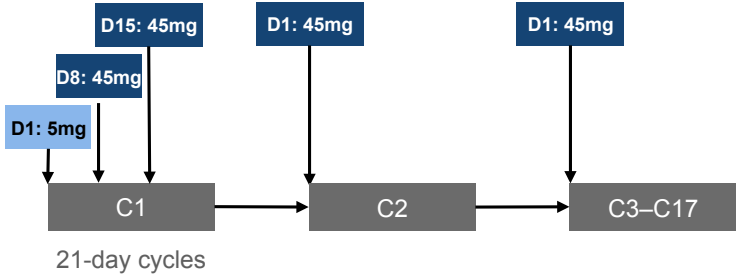
- Previously untreated FL
- Adequate renal function‡
- Histologically confirmed Grade 1–3a FL
- Ann Arbor stage II if bulky (≥7cm maximum in diameter), III, or IV disease
- ECOG PS 0–2

Cohort A2: Low-tumor burden[1,3†]

- Previously untreated FL
- Adequate renal function‡
- Histologically confirmed Grade 1 or 2 FL
- Ann Arbor stage III or IV disease
- ECOG PS 0–2
- Low tumor burden by Groupe d'Études des Lymphomes Folliculaires (GELF) criteria

Mosunetuzumab administration[2,3]

- Cohort A1: Q3W SC administration after step-up dosing for up to 17 cycles (1 year)
  Patients with partial/complete metabolic response at C17 could receive additional maintenance therapy§
- Cohort A2: patients with a CMR at C8 were able to stop therapy; patients with a PMR or SMD continued treatment for 17 cycles



- CRS prophylaxis (dexamethasone premedication) mandatory for first 2 cycles and optional thereafter¶

Endpoints[2,3]

Primary:

- PFS rate at 24 months

Secondary:

- Safety
- PK
- TTNT
- TTR
- DOR
- OS
- ORR

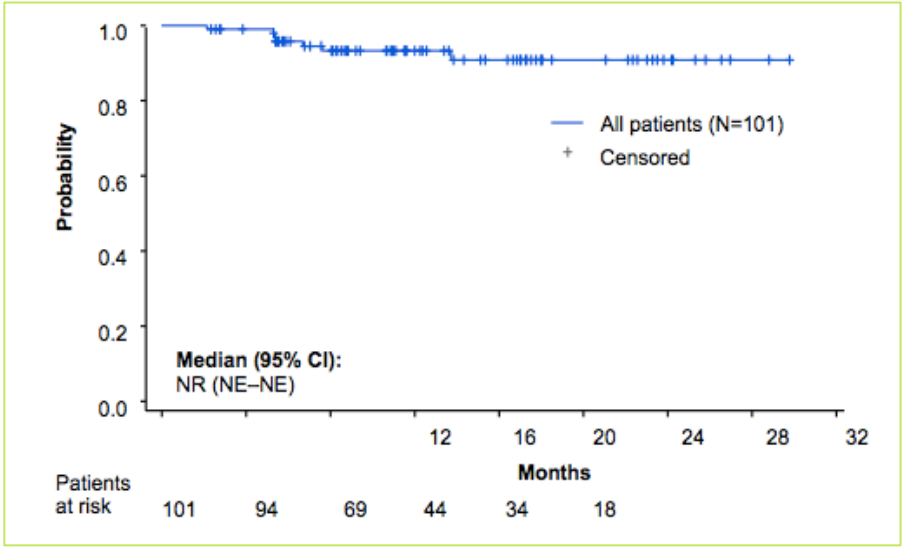
Burke J, et al. ASH 2024; Poster presentation (abstract #P3008).

MorningSun Low Tumor Burden FL (Cohort A2): Efficacy Data

Median follow-up was 13.8 months

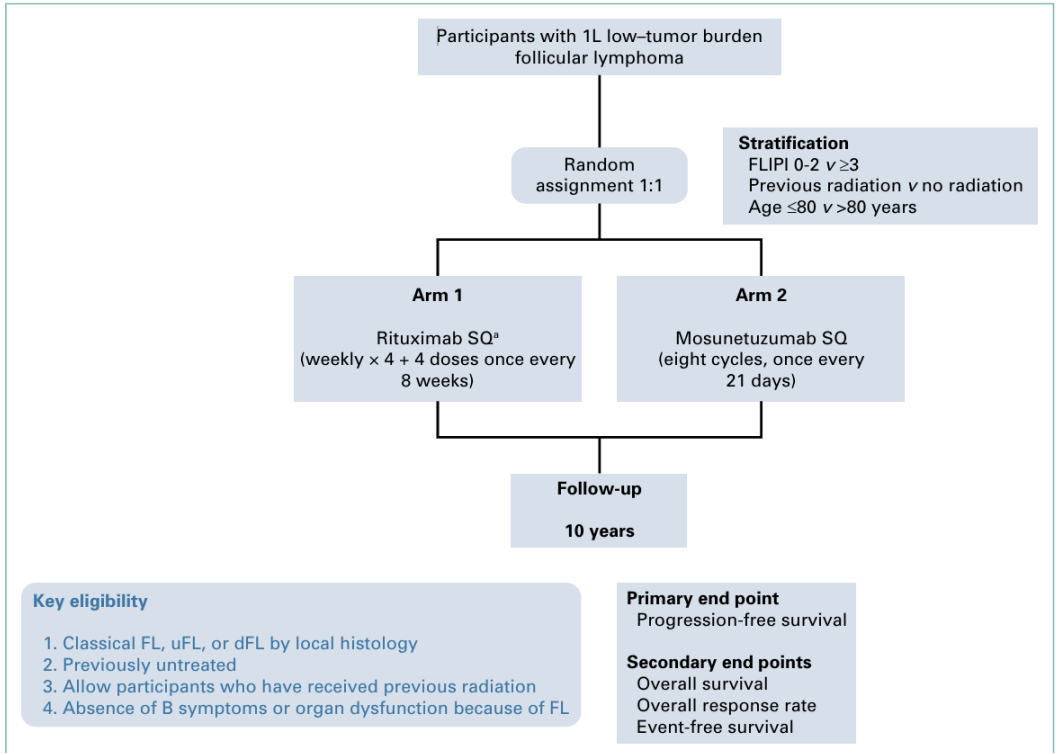
n (%), unless stated	Cohort A2: Low tumour burden n=101[2]
ORR	100 (99.0)
CMR	91 (90.1)
PMR	9 (8.9)
Missing or not done	1 (1.0)
Median TTR, months (range)	2.8 (1.4–8.3)
12-month DOR rate, % (95% CI)	92.0 (82.1–96.6)
12-month DOCR rate, % (95% CI)	95.8 (83.0–99.0)
12-month PFS rate, % (95% CI)	93.1 (85.3–96.9)
12-month OS rate, % (95% CI)	99.0 (93.2–99.9)

PFS[2]



Burke J, et al. ASH 2024; Poster presentation (abstract #P3008). Villasboas JC, et al. ASH 2025; Poster presentation (abstract #1807).

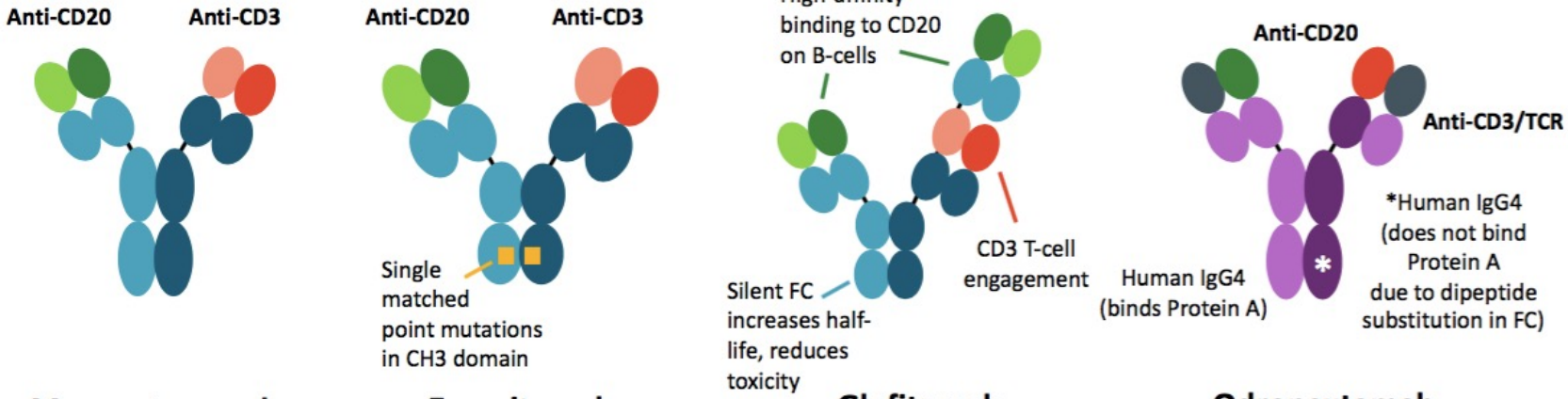
SWOG 2308 Randomized Phase III study for Mosu vs. Rituximab in Low Tumor Burden FL



Gosh N et al. JCO Oncology Adv 2025

CD20xCD3 Bispecific Antibodies: Structure and Function

Humanized mouse IgG1-based mAbs



Mosunetuzumab (IV*) *SC formula under investigation.

FDA accelerated approval: 3L+ R/R FL

Epcoritamab (SC)

FDA full approval: monotherapy 3L+ FL and 2L+ in combo with R2

Glofitamab (IV)

FDA accelerated approval: 3L+ LBCL arising from FL

Odronextamab (IV)

EU approval: 2L+ R/R FL

Mosunetuzumab PI; Epcoritamab PI; Glofitamab PI; Blair HA. Drugs. 2024;84:1651-1658; Falchi. Blood. 2023;141:467.

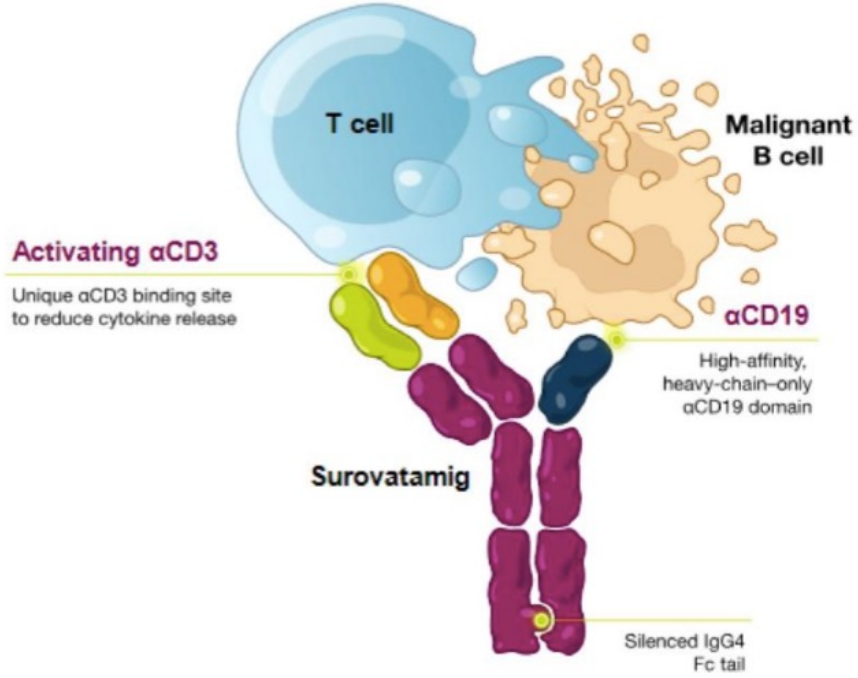
Surovatamig (AZD-0486)

- **-IgG4** fully human **CD19xCD3** bispecific TCE, yielded high response rates with tolerable safety in patients with heavily pretreated FL in a phase 1 study

- Surovatamig is administered by IV infusion every 2 weeks (+1, +15) on 28-day cycles for up 2 year

- Phase 1 dosing regimen for cycle 1:
  -fixed-dose escalation
  -1SUD
  -2SUD

- After 6 cycle: Q4W schedule for pts in CR



Malik-Chaudhry HK, et al. mAbs. 2021;13:1890411. Hou JZ, et al. Blood. 2024;144:341-43.

Surovatamig Phase 1b study in in RR Follicular Lymphoma

Key Eligibility Criteria

- Adults with R/R B-NHL
- CD19+ by flow cytometry or IHC
- ≥2 prior lines of therapy
- measurable lesion
- No active CNS disease
- No leukemic presentation
- ECOG PS ≤2
- Prior anti-CD19 therapies, CAR T-cells, and anti-CD20 TCE allowed

Endpoints

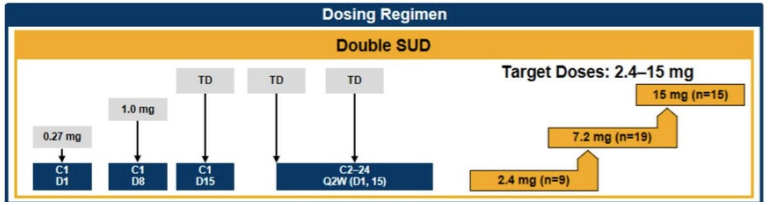
Primary
- Safety/tolerability
- MTD/RP2D
- PK

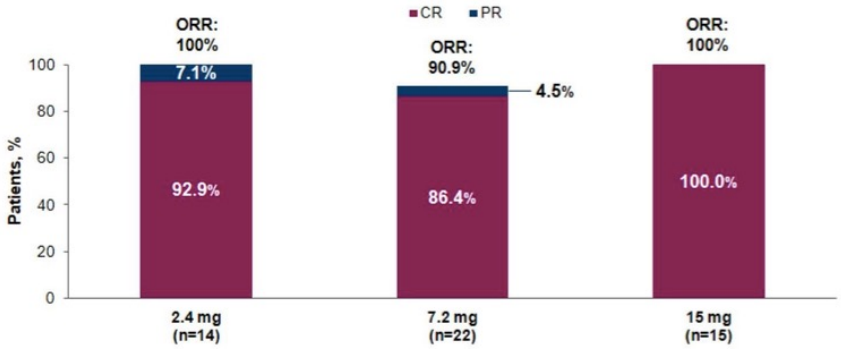
Secondary
- Antitumor activity

Characteristic	N=61[a]
Age, median (range), y	63 (33–86)
ECOG PS 2, n (%)	2 (3)
Ann Arbor stage III–IV, n (%)	49 (80)
CD20-negative disease at study entry, n (%)	10 (16)
Bulky disease,[b] n (%)	13 (21)
POD24, n (%)	22 (36)
Median prior lines of therapy (range)	3 (2–11)
3–4 lines, n (%)	27 (44)
≥5 lines, n (%)	9 (15)
Refractory to last line of therapy,[c] n (%)	32 (52)
Prior types of treatment, n (%)	
R-CHOP	37 (61)
Lenalidomide	26 (43)
CD19-directed CAR T	7 (11)
CD20 TCE	5 (8)
Allogeneic or autologous SCT	3 (5)

Devata. et al. EHA 2024 (Abstr # P1131). ASH 2025 oral presentation

Three-year Follow-up of the Phase 1 First-in-Human study (FL cohort)





61 patients received ≥1 dose of surovatamig

20 patients discontinued treatment:
- Disease progression (n=8)
- Physician decision (n=4)
- AEs (n=3)
- Withdrawal by patient (n=2)
- Treatment delay (n=1)
- Other (n=2)

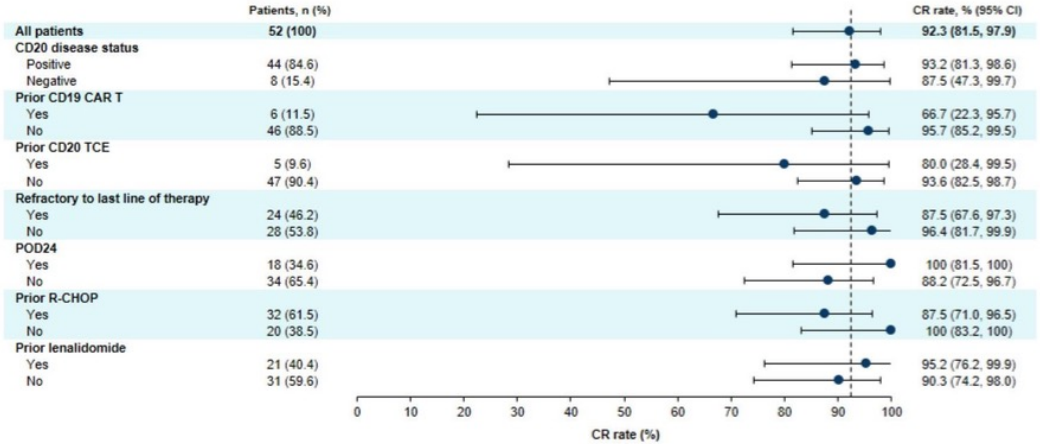
11 patients completed 24 cycles treatment

and

30 patients remain on treatment

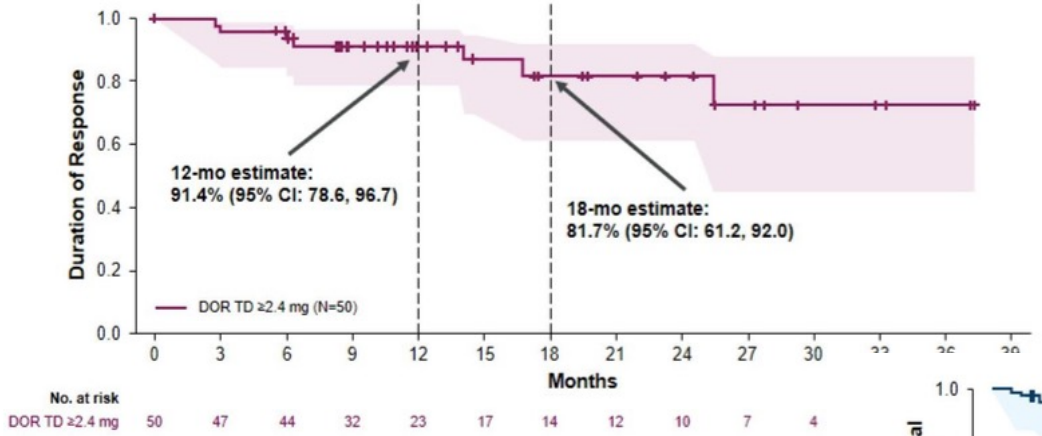
- Median study follow-up for TDs ≥2.4 mg: 16 mo (range 1–40)

- ORR/CR rate for patients who received ≥2.4 mg was 96%/92%



Jing-Zhou Hou. et al. ASH 2025

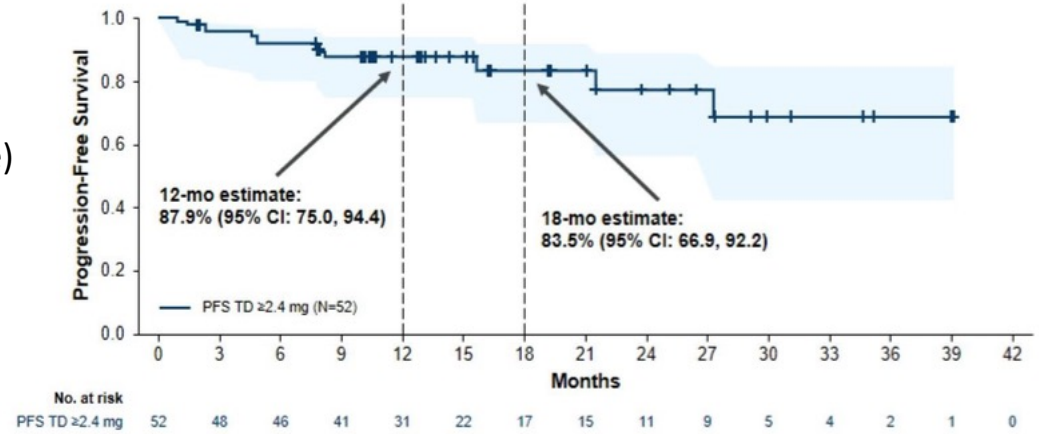
Durable Responses in Heavly pretreated FL patients



Including patients with prior CD20 TCE and/or CD19 CAR T

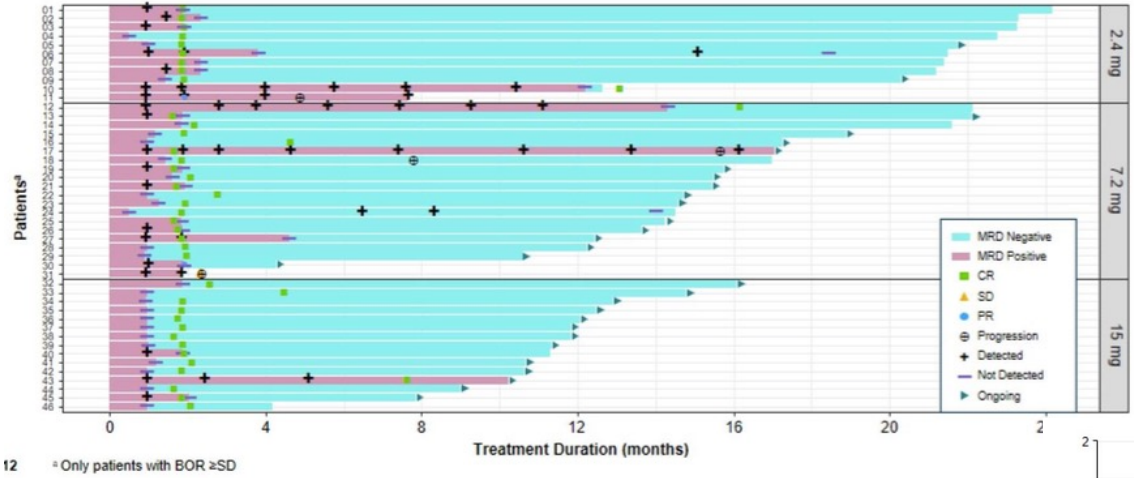
DOR: 91.4% and 81.7% (12 mo and 18 mo estimate)

PFS: 87.9% and 83.5% (12 mo and 18 mo estimate)



Jing-Zhou Hou. et al. ASH 2025

MRD Negativity Correlated With Durable Responses



Rapid Clearance of ctDNA in the Majority of Patients

(ctDNA assessed by PhasED-Seq)

- **95% of patients in CR had undetectable MRD**
- 12-mo PFS estim: 97% for undetectable MRD pts

Jing-Zhou Hou. et al. ASH 2025

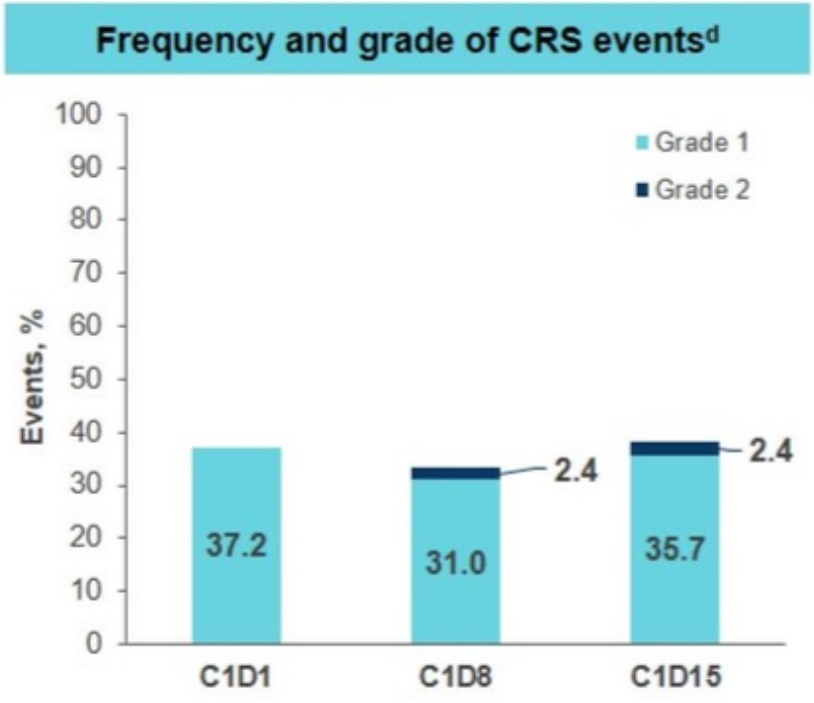
Surovatamig (AZD-0486) in RR Follicular Lymphoma: Safety Analysis (I)

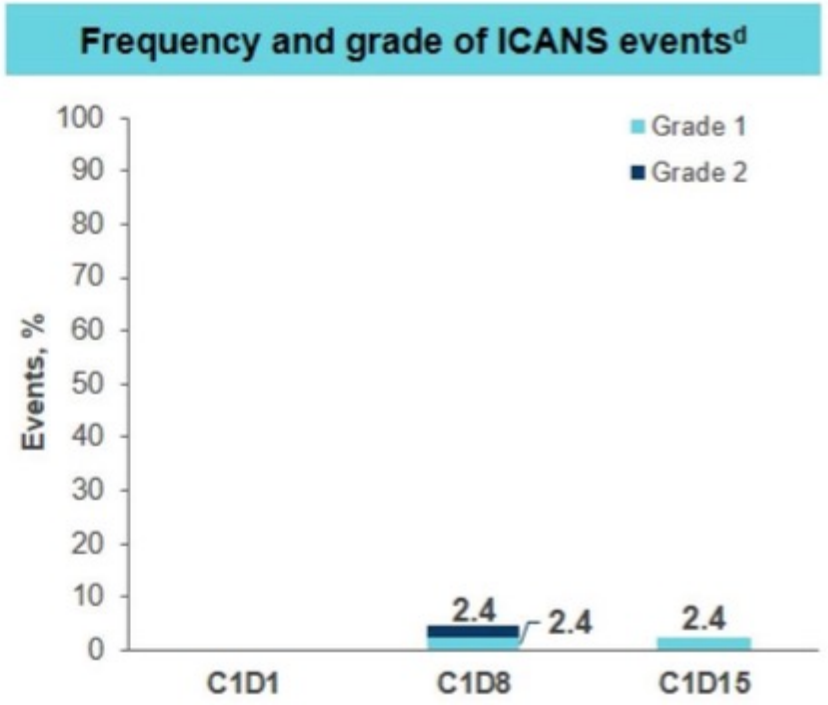
Most common AEs (≥20%), n (%)	Any grade	Grade 3	Grade 4
CRS	35 (57)	0	0
COVID-19	20 (33)	2 (3)	0
Headache	20 (33)	0	0
Nausea	19 (31)	0	0
Diarrhea	18 (30)	0	0
Cough	17 (28)	1 (2)	0
Fatigue	15 (25)	1 (2)	0
Neutropenia	14 (23)	9 (15)	3 (5)
Hypogammaglobulinemia	14 (23)	0	0
Hypertension	13 (21)	5 (8)	0

- Infections occurred in 43 (70%) of patients (grade 3/4: n=8 [13%]; grade 5: n=2 [3%])
- The most common infections: COVID-19, upper respiratory tract infection, pneumonia, sinusitis, nasopharyngitis, rhinitis, and UTI.

Jing-Zhou Hou. et al. ASH 2025

Surovatamig (AZD-0486) in RR Follicular Lymphoma: Safety Analysis (II)



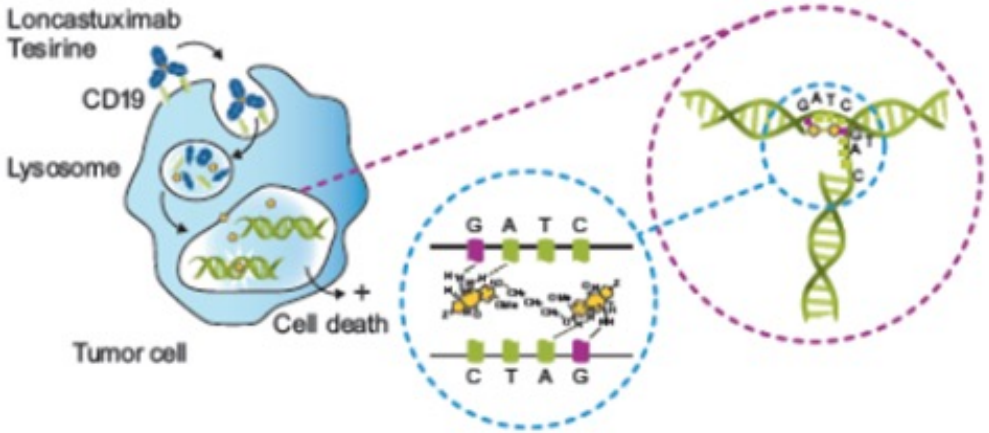


2SUD

No CRS and no ICANS events occurred after cycle 1

Jing-Zhou Hou. et al. ASH 2025

Loncastuximab tesirine (CD19-directed ADC)



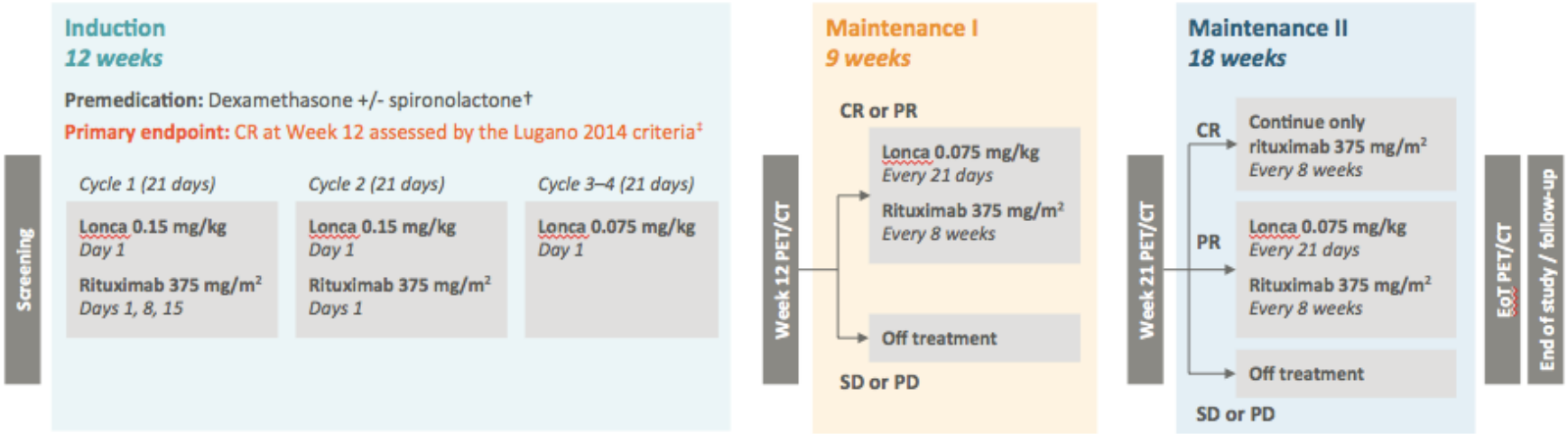
- A humanized monoclonal anti-CD19 Ab conjugated to a pyrrolobenzodiazepine (PBD) dimer toxin
- Lotis-1 study: Showed activity in 14 patients with FL Lotis-1 (**ORR 78,6%, CR 64%, PR 14%**)
- Preclinical data indicated synergistic activity between rituximab-induced cytotoxicity and Lonca in follicular lymphoma xenografts

Hamadani M et al. Blood (2021) 137 (19): 2634–2645. Ryan et al. *Blood* 2017

Loncastuximab tesirine in combination with Rituximab in RR FL

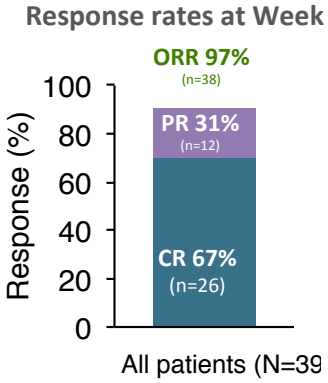
Eligibility*
- Adult patients
- Histologically confirmed follicular lymphoma (grade 1, 2, or 3A) per 2016 WHO classification
- Previously treated with ≥1 line of systemic therapy
- Presenting with POD24 after the 1L treatment

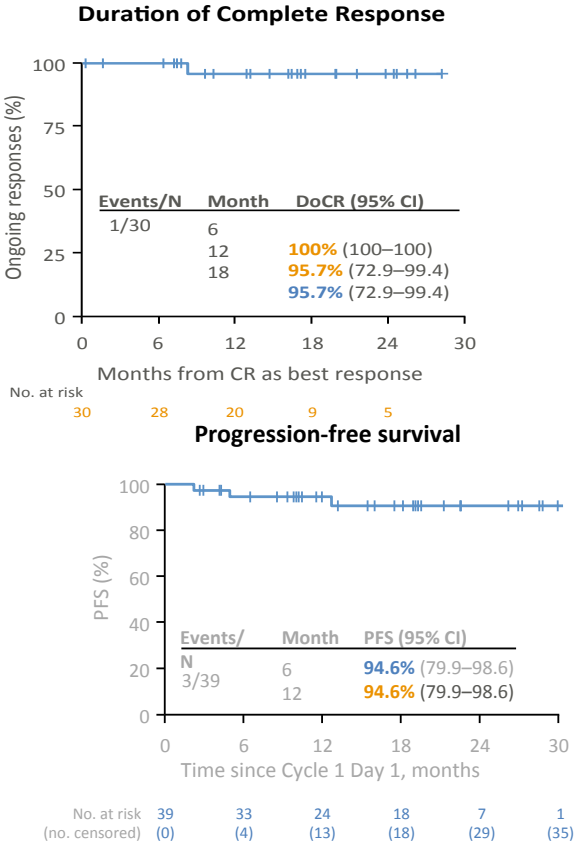
Phase 2 Trial

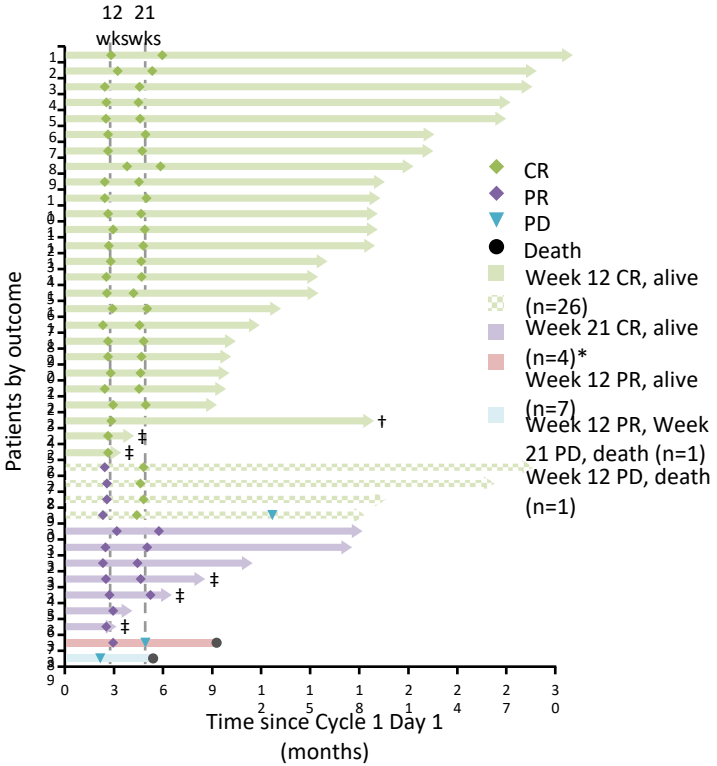


Alderuccio et al. Lancet Haematol 2024:12:e23-34.

Response rate to Loncastuximab plus Rituximab



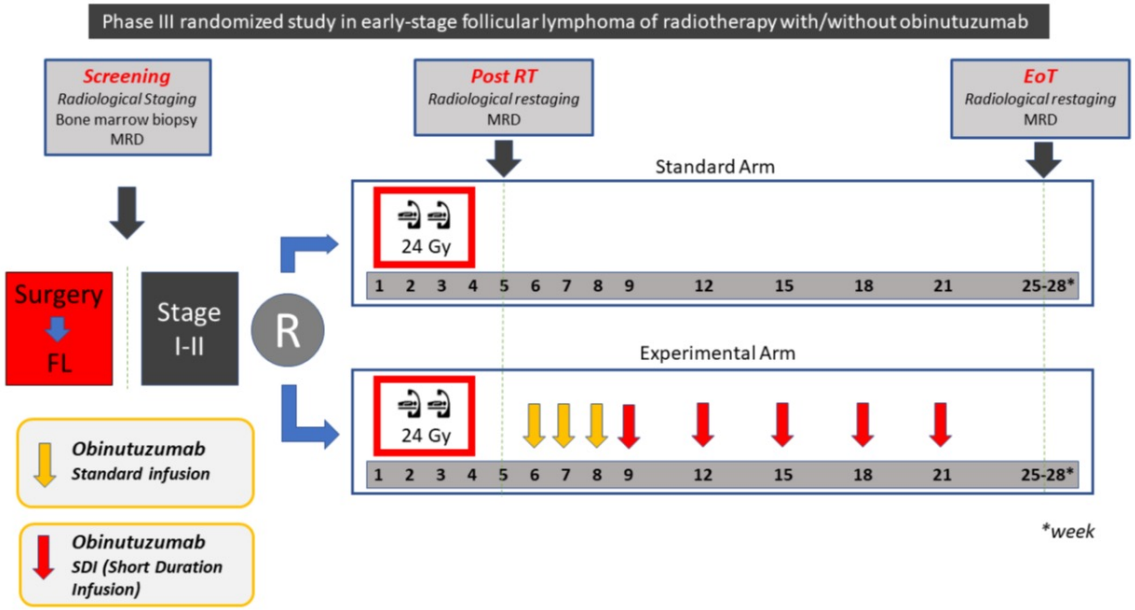




Alderuccio et al. Lancet Haematol 2024:12:e23-34.

FIL-GAZEBO in Early Stage FL

An open-label, randomized phase III trial comparing local radiotherapy alone or combined with Obinutuzumab in early stage Follicular Lymphoma: the **GAZEBO** Trial from the Fondazione Italiana Linfomi

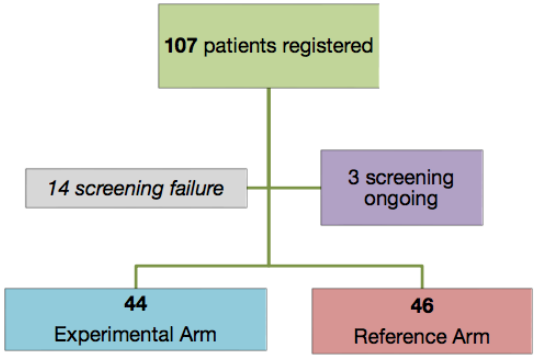


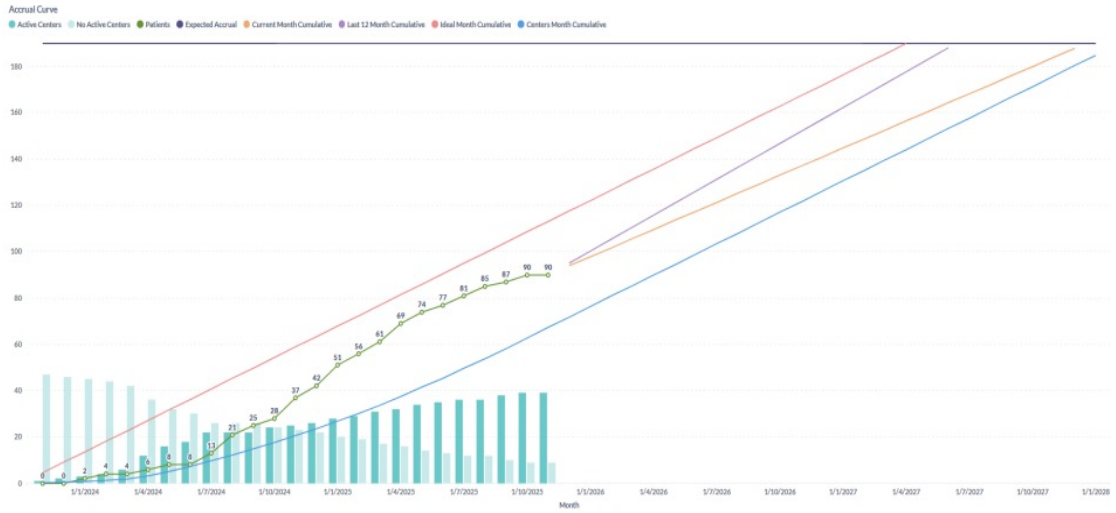
PI: A. Pulsoni, A. Pilippi

FONDAZIONE ITALIANA LINFOMI

Sites Activations and Enrollment Curve

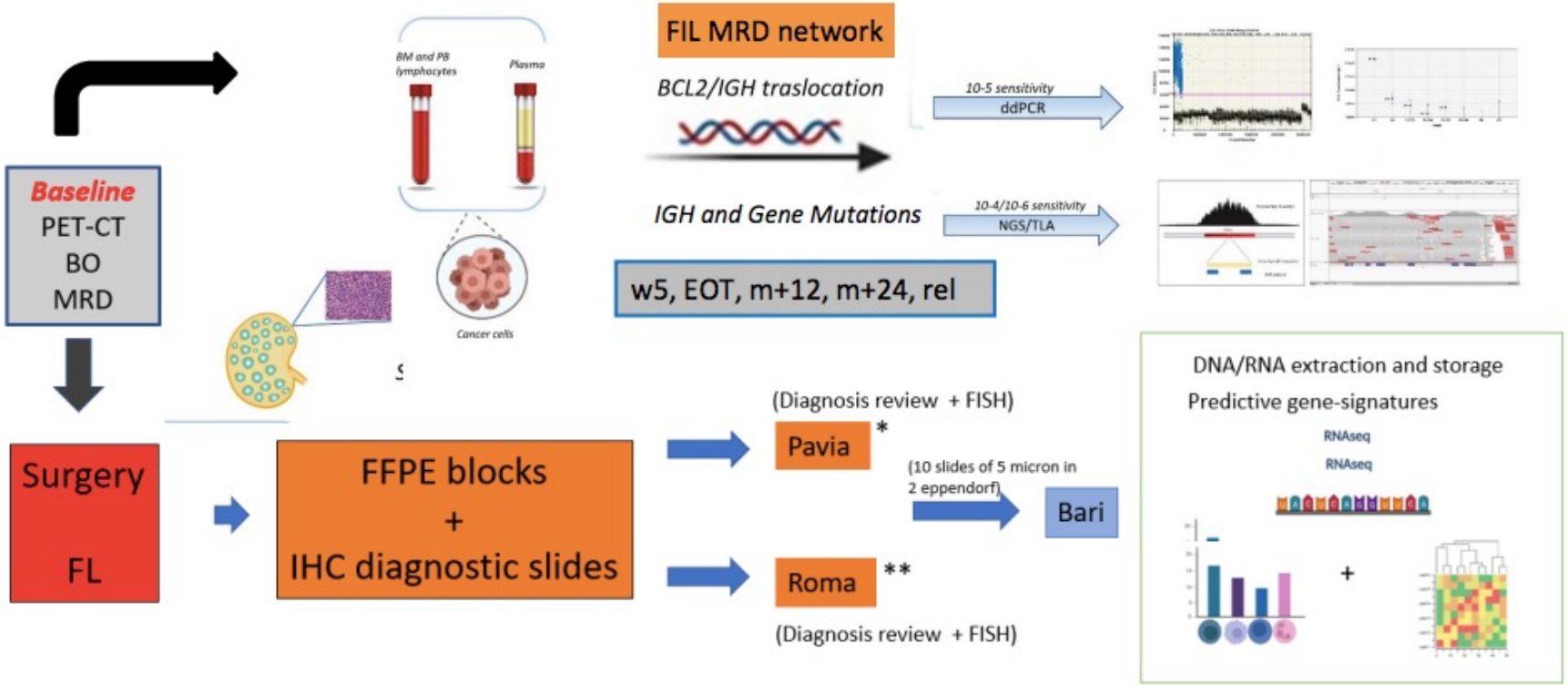
- **Multicenter Phase 3 study**
- **50 Italian** FIL centers and **190 patients** (95 by arm)
- **Primary Objective**: superiority of PFS for the combination for radiotherapy plus obinutuzumab (experimental arm) vs. radiotherapy alone (standard arm)





PI: A. Pulsoni, A. Pilippi

BIO-GAZEBO: Explorative Biological Studies



PI: A. Pulsoni, A. Pilippi

Goals For The Future

- Improve outcomes (high-risk patients)
- Reduce toxicity
  - acute (elderly)
  - long term complications (young)
- Upfront identification high risk patients (POD24, transformation)
- Upfront identification very low risk patients
- Better incorporation of biomarkers and tools for risk stratification
- Risk-adapted approach (PET driven, MRD adapted)
- Consider patient preferences and needs

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Annalisa Chiarenza
Michele Merli
Marzia Varettoni
Luca Arcaini
Alessandro Pulsoni

Commissione studi biologici e biostatistici

Commissioni imaging, commissione radioterapisti, etc

Gruppo statistici

Uffici studi FIL

“As the landscape evolves, there is a growing need to shift toward precision-based treatment decisions, potentially guided by underlying disease biology.”

Grazie per l’attenzione