Roche Group

Antineoplastic Agent / Anti-CD20/CD3 Humanized Bispecific Antibody

Information Meeting on “LUNSUMIO® for intravenous infusion”

24 March 2025

CHUGAI PHARMACEUTICAL CO., LTD.

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Information regarding pharmaceuticals (including products under development) is included in this presentation, but is not intended as advertising or medical advice.

Please note that Japanese is the preferred language in expression and content, since the official language of this presentation is Japanese.

Agenda

01	Overview of LUNSUMIO® for Intravenous Infusion	NHL Lifecycle Leader, Chugai Pharmaceutical Co., Ltd. **Kenichi Aoki, PhD**
02	A New Treatment Option for Third-line and Beyond for Relapsed or Refractory Follicular Lymphoma　– Lunsumio –	Department of Hematology Oncology, Cancer Institute Hospital, Japanese Foundation for Cancer Research **Dai Maruyama, MD, PhD**

Standard Commodity Classification Number of Japan: 874291

Antineoplastic agent
Anti-CD20/CD3 humanized bispecific monoclonal antibody
Biological product, powerful drug, prescription drug[Note)]

Lunsumio® for Intravenous Infusion 1 mg/30 mg

Listed in the NHI drug price list

Lunsumio
mosunetuzumab

Mosunetuzumab (genetical recombination) injection

Note) Caution – Use only pursuant to the prescription of a physician, etc.

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LUNSUMIO® for Intravenous Infusion 1 mg/30 mg Product Overview

Kenichi Aoki, Ph.D.

NHL Lifecycle Leader
Chugai Pharmaceutical Co., Ltd.

Lunsumio®
mosunetuzumab

Today's Agenda

Lunsumio
mosunetuzumab

- Overview of LUNSUMIO® for Intravenous Infusion 1 mg/30 mg
- Guideline descriptions and clinical positioning
- Clinical trial results

LUNSUMIO® Basic Information

[Brand name]
LUNSUMIO® for Intravenous Infusion 1 mg
LUNSUMIO® for Intravenous Infusion 30 mg

[Generic name]
Mosunetuzumab (genetical recombination)

[Origin of product name]
English name: Lunsumio™

LUN A light from above that brightens the patient through their journey with lymphoma

SUM evoking the power to attack tumors through a total combination, dual targeting of malignant B cell (CD20) and T cell (CD3)

IO for immunotherapy

"LUNA" refers to the Roman goddess of the moon and signifies the moon goddess.
The name embodies the concept of a celestial light that illuminates and supports patients suffering from lymphoma.

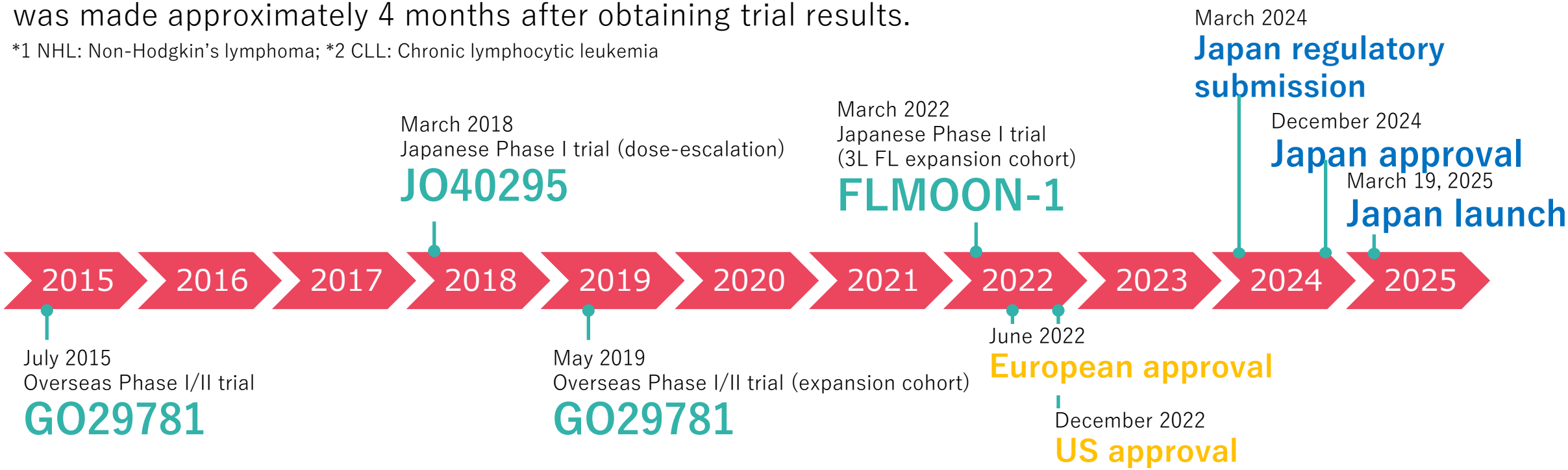
Lunsumio Development Overview

Lunsumio
mosunetuzumab

Lunsumio was originally developed by Genentech, Inc. (USA) and was evaluated in the GO29781 trial, an overseas Phase I/II, multicenter, open-label, dose-escalation, and dose-expansion study initiated in July 2015. This trial targeted patients with relapsed or refractory hematologic malignancies, including B-cell NHL*1 and CLL.*2

In Japan, the FLMOON-1 trial was started in March 2018 to assess the safety, tolerability, pharmacokinetics, anti-tumor efficacy, and immunogenicity of Lunsumio as a monotherapy in patients with relapsed or refractory B-cell NHL. The trial completed patient enrollment within 15 months, and regulatory submission was made approximately 4 months after obtaining trial results.

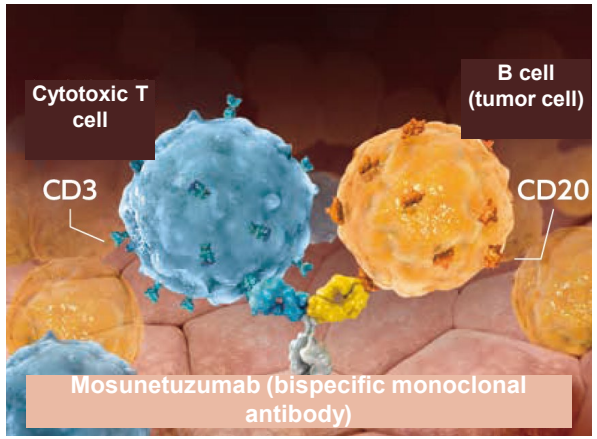
*1 NHL: Non-Hodgkin's lymphoma; *2 CLL: Chronic lymphocytic leukemia



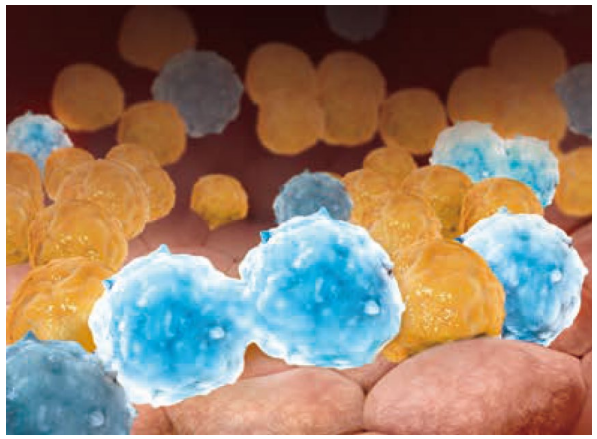
Mechanism of Action of Lunsumio (Mosunetuzumab)

- Mosunetuzumab is a bispecific monoclonal antibody targeting CD20 and CD3.
- CD20 is a cell surface antigen expressed on nearly all B-cell lymphomas, except for pro-B cells and plasma cells.
- Mosunetuzumab is thought to bind to CD3 expressed on T cells and CD20 expressed on B-cell tumors, thereby activating T cells and damaging CD20-positive tumor cells.

Illustrative diagram

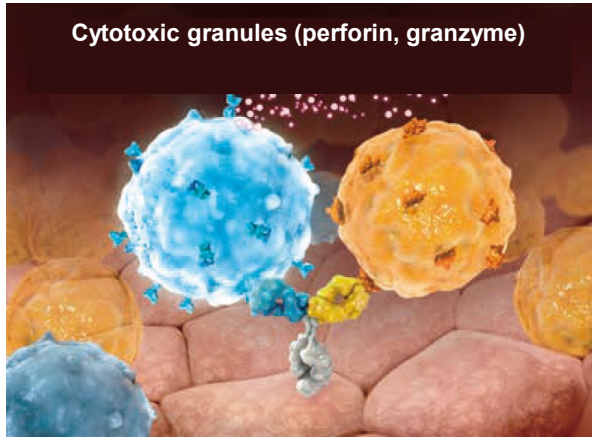


1. Mosunetuzumab simultaneously binds to T cells and B cells (tumor cells).

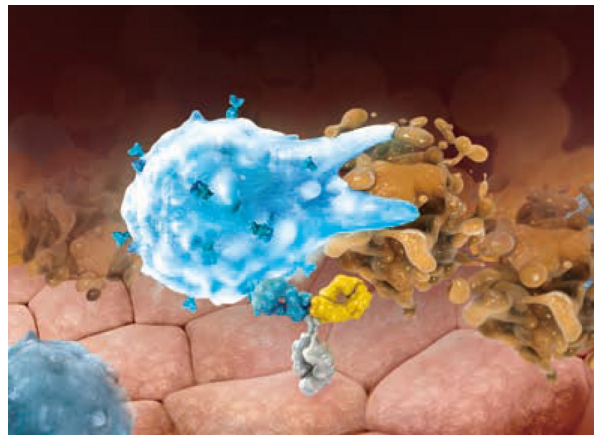


2. Cytokine release mobilizes T cells from the periphery.

3. T cells proliferate at the tumor site.



4. T cell activation triggers downstream signaling and the release of cytotoxic granules such as perforin and granzyme.



5. Tumor cell lysis and apoptosis are induced.

Illustrative diagram

1) Chen DS, et al. Immunity. 2013; 39(1): 1-10. [Conflict of interest: The authors include Genentech employees.]
2) Dieckmann NM, et al. J Cell Sci. 2016; 129(15): 2881-2886.
3) Sun LL, et al. Sci Transl Med. 2015; 7(287): 287ra70. [Conflict of interest: This study was conducted with support from Genentech. The authors include Genentech employees.]
4) Thiery J, et al. Nat Immunol. 2011; 12(8): 770-777.

Indications, Dosage, and Administration

Lunsumio
mosunetuzumab

[Indications]

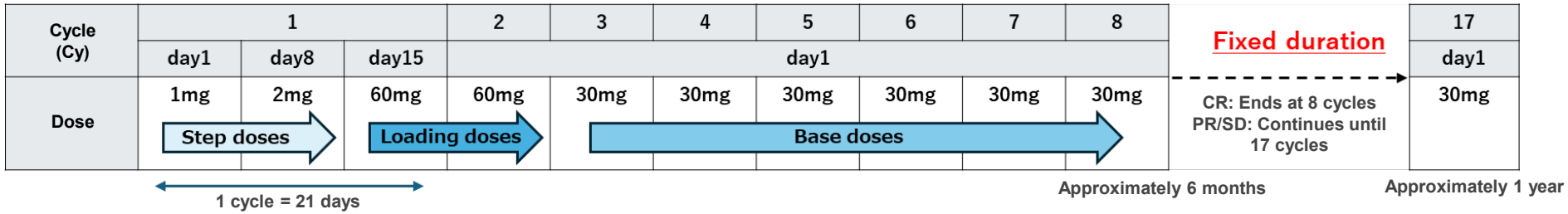
Relapsed or refractory follicular lymphoma

Precautions related to indications

This treatment is intended for **patients who have relapsed or failed to respond to at least 2 standard therapies**, including an anti-CD20 monoclonal antibody.
The drug should be administered to patients diagnosed with Grade 1–3A follicular lymphoma by a pathologist with sufficient experience.

[Dosage and administration]

For adults, mosunetuzumab (genetical recombination) is administered intravenously in 21-day cycles. In the first cycle, 1 mg is administered on Day 1, followed by 2 mg on Day 8 and 60 mg on Day 15. In the second cycle, 60 mg is administered on Day 1. From the third cycle onward, 30 mg is administered on Day 1 of each cycle, continuing up to the eighth cycle.
At the end of the eighth cycle, treatment is discontinued for patients who achieve complete response (CR). However, patients with stable disease (SD) or partial response (PR) continue treatment for up to 17 cycles.



***Fixed duration is a treatment approach developed by Chugai Pharmaceutical, embodying its unwavering commitment to supporting healthcare professionals and patients in the fight against lymphoma over many years.**

CR: complete response, PR: partial response, SD: stable disease

Lunsumio for Intravenous Infusion 1 mg/30 mg Electronic Package Insert, Created in December 2024 (Version 1)

Lunsumio Administration Schedule/Premedication

Lunsumio mosunetuzumab

Cycle 1

Premedication before each administration (Days 1, 8, and 15[*1-3])

- Mandatory: Adequate hydration — From 1–2 days before administration
- Mandatory: Dexamethasone 20 mg (IV) or Methylprednisolone 80 mg (IV) — 1 hour before administration
- Optional: Acetaminophen 500–1,000 mg (PO) and Diphenhydramine hydrochloride 50–100 mg (PO) — 0.5–1 hour before administration

Day 1: Lunsumio 1 mg (1mg) — Administered over 4 hours → Observation[*4]

Day 8: Lunsumio 2 mg (1mg, 1mg) — Administered over 4 hours → Observation[*4]

Day 15: Lunsumio 60mg (30mg, 30mg) — Administered over 4 hours → Observation[*4]

Consider hospitalization based on the patient's condition.

Consider hospitalization based on the patient's condition.

Hospitalization for 48 hours after the initial 60 mg infusion.

Cycle 2

Premedication before each administration[*1-3]

- Optional: Adequate hydration — From 1–2 days before administration
- Mandatory: Dexamethasone 20 mg (IV) or Methylprednisolone 80 mg (IV) — 1 hour before administration
- Optional: Acetaminophen 500–1,000 mg (PO) and Diphenhydramine hydrochloride 50–100 mg (PO) — 0.5–1 hour before administration

Day 1: Lunsumio 60 mg (30mg, 30mg) — If tolerability in Cycle 1 is favorable, the infusion time may be reduced to 2 hours. → Observation[*4]

Cycles 3–8

Premedication before each administration[*1-3]

- Optional: Adequate hydration — From 1–2 days before administration
- Optional: Dexamethasone 20 mg (IV) or Methylprednisolone 80 mg (IV) — 1 hour before administration
- Optional: Acetaminophen 500–1,000 mg (PO) and Diphenhydramine hydrochloride 50–100 mg (PO) — 0.5–1 hour before administration

Day 1: Lunsumio 30 mg (30mg) — If tolerability in Cycle 1 is favorable, the infusion time may be reduced to 2 hours. → Observation[*4]

Cycles 9–17

Premedication before each administration[*1-3]

- Optional: Adequate hydration — From 1–2 days before administration
- Optional: Dexamethasone 20 mg (IV) or Methylprednisolone 80 mg (IV) — 1 hour before administration
- Optional: Acetaminophen 500–1,000 mg (PO) and Diphenhydramine hydrochloride 50–100 mg (PO) — 0.5–1 hour before administration

Day 1: Lunsumio 30 mg (30mg) — If tolerability in Cycle 1 is favorable, the infusion time may be reduced to 2 hours. → Observation[*4]

At the end of Cycle 8

- If CR is achieved → Treatment ends (168 days Approximately 6 months)
- If PR/SD is achieved → Treatment continues (see below)

At the end of Cycle 17

- Treatment ends (357 days Approximately 1 year)

*1 In clinical trials, hydration and other preventive measures for tumor lysis syndrome (TLS) were mandatory during administration in Cycle 1. If the patient was considered at high risk for TLS, hydration and other preventive measures were continued in Cycle 2 and beyond.

*2 In clinical trials, premedication with corticosteroids was mandatory in Cycles 1 and 2, but optional from Cycle 3 onward. If cytokine release syndrome (CRS) was observed, corticosteroid premedication remained mandatory in subsequent cycles until CRS was no longer observed.

*3 In clinical trials, premedication with antipyretic analgesics and antihistamines was administered as needed.

*4 In clinical trials, a 90-minute post-administration observation period was required.

For information regarding medications other than this drug, please refer to the electronic package inserts of each product.

Regulatory evaluation data: overseas Phase I/II clinical trial (GO29781); Regulatory evaluation data: Japanese Phase I clinical trial (JO40295)

Hematologic Cancer Portfolio

Lunsumio mosunetuzumab

- Contributing to the field of hematologic cancers (lymphomas) through the development of Polivy, Lunsumio, and glofitamab.
- Following its initial launch, Lunsumio aims to expand its development and regulatory submissions beyond 1L/2L+ FL, targeting 2L+ aNHL as well.

DLBCL	1L	Polivy +R-CHP POLARIX Trial	August 2022 Indication expansion
DLBCL	1L	Gofitamab + Polivy +R-CHP SKYGLO Trial	Regulatory filing 2027 and beyond (Planned)
aNHL	2L+	Lunsumio + Polivy SUNMO Trial	Regulatory filing 2025 and beyond (Planned)
FL	1L	Lunsumio + Len MorningLyte Trial	Regulatory filing 2027 and beyond (Planned)
FL	2L+	Lunsumio + Len CELESTIMO Trial	Regulatory filing 2026 and beyond (Planned)
FL	3L+	Lunsumio monotherapy Oversea phase I/II Trial, FLMOON-1 Trial	December 2024 Approval

aNHL: Aggressive non-Hodgkin's lymphoma; DLBCL: Diffuse large B-Cell lymphoma; FL: Follicular lymphoma; Len: lenalidomide;
R-CHP: Rituximab, cyclophosphamide, doxorubicin, prednisolone

Lunsumio Characteristics

Lunsumio
mosunetuzumab

- Lunsumio is a bispecific monoclonal antibody targeting CD20 and CD3. It binds to CD3 expressed on T cells and CD20 expressed on B-cell tumors, activating T cells and inducing cytotoxicity against CD20-positive tumor cells.

- Patients who achieve complete response (CR) after 8 cycles of administration will discontinue treatment. Patients with stable disease (SD) or partial response (PR) will continue for a fixed duration of 17 cycles of administration. Lunsumio is the first bispecific monoclonal antibody for lymphoma to adopt a fixed-duration treatment approach, offering a chemo-free alternative.

- Characteristic adverse events include cytokine release syndrome (45.9%) and neurological events [such as immune effector cell-associated neurotoxicity syndrome (0.9%)]. Therefore, appropriate management is required, including premedication with corticosteroids, antipyretic analgesics, and antihistamines, as well as administration of Actemra (tocilizumab) or corticosteroids when symptoms appear.

- Lunsumio is approved in 61 countries and recommended in international treatment guidelines[1)]. Its efficacy has been demonstrated in the overseas Phase I/II trial (GO29781) [2)] and the Japanese Phase I trial (JO40925)[3)]. Based on these findings, Lunsumio is expected to become a beacon (LUN) of hope for patients suffering from relapsed or refractory follicular lymphoma in Japan.

1) National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) B-cell Lymphomas, Version 2, 2025. Available from : https://www.nccn.org
2) Budde E, et al. Blood 2021; 138: 127-130
3) Goto H, et al. Int j Clin Oncol. 2025; 30: 389-396

We want Lunsumio® to be a beacon of hope, ensuring that patients, their partners, and families can stay together and share precious moments for as long as possible.

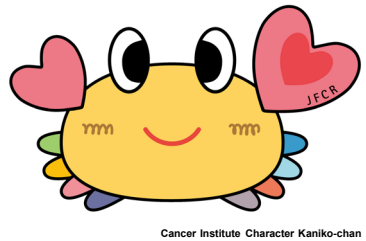
公益財団法人がん研究会
JAPANESE FOUNDATION FOR CANCER RESEARCH

A New Treatment Option for Third-line and Beyond for Relapsed or Refractory Follicular Lymphoma

– Lunsumio –

Dai Maruyama, M.D., Ph.D.

Department of Hematology Oncology,
Cancer Institute Hospital,
Japanese Foundation for Cancer Research



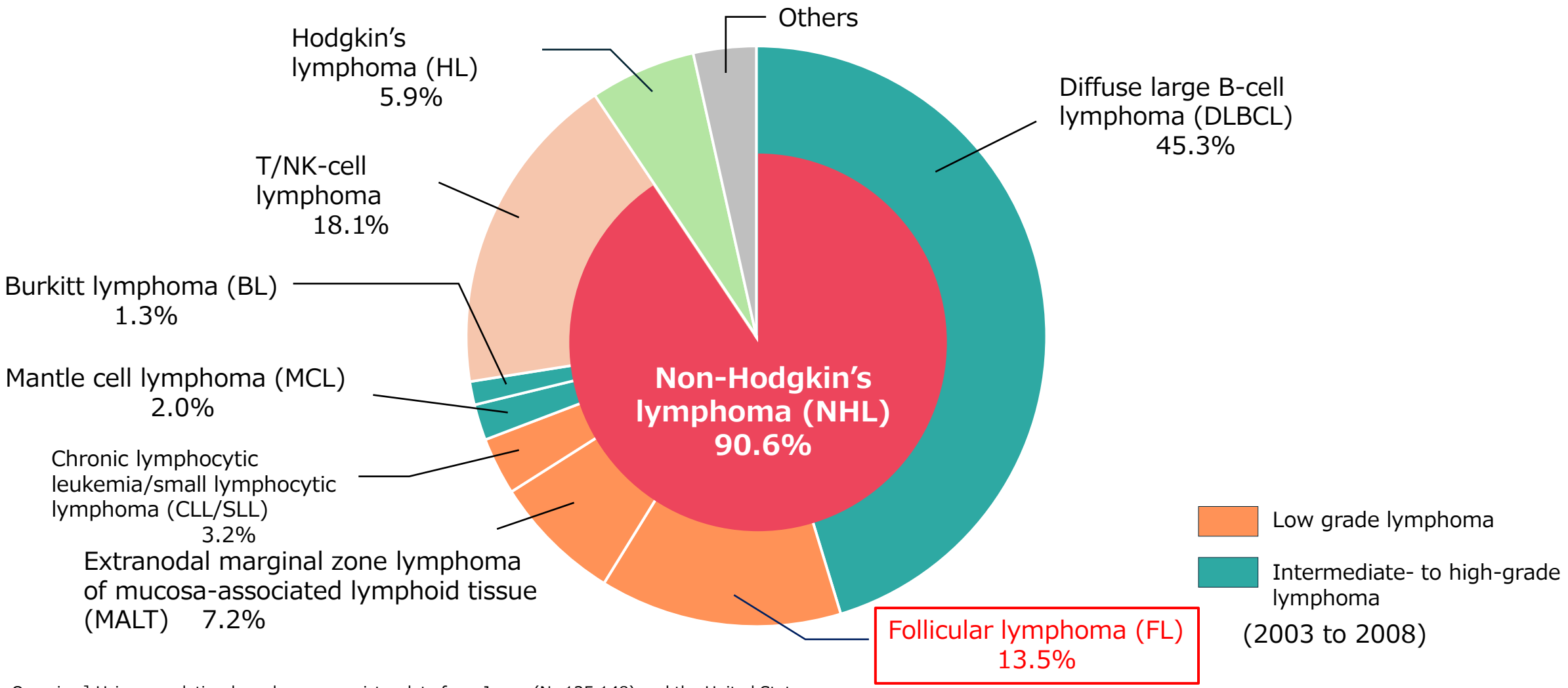
Cancer Institute Character Kaniko-chan

COI Disclosure

Dai Maruyama

Honoraria:	Chugai, Mundipharma, Janssen Pharma, Takeda, Eisai, Celgene, Kyowa Kirin, Ono Pharmaceutical, Nippon Shinyaku, Zenyaku Kogyo, BMS, MSD, AstraZeneca, Sanofi, AbbVie, Genmab
Research funding:	Chugai, Ono Pharmaceutical, Celgene, Janssen Pharma, Mundipharma, Takeda, BMS, MSD, Otsuka, Novartis, Sanofi, Astellas Pharma, Amgen Astellas BioPharma, AbbVie, Eisai, Genmab

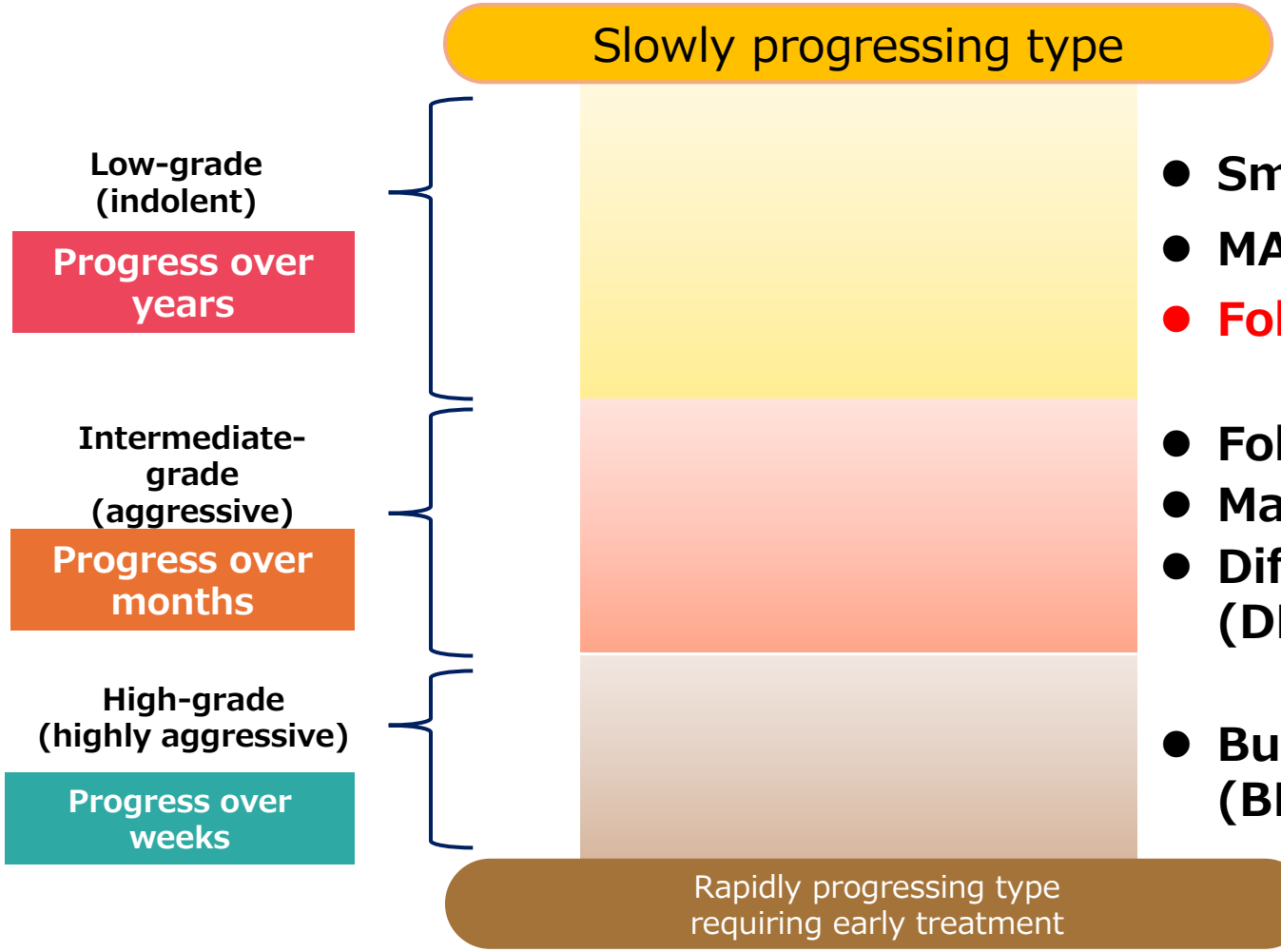
Types of Lymphoma and Proportion of Follicular Lymphoma



[Study Overview] Using population-based cancer registry data from Japan (N=125,148) and the United States (N=172,925), we evaluated trends in incidence rates and annual percent changes of hematologic malignancies (analysis period: 1993-2008).

Chihara D, et al. Br J Haematol 164: 536-545, 2014

Classification by Disease Progression Speed



- **Small lymphocytic lymphoma (SLL)**
- **MALT lymphoma**
- **Follicular lymphoma (FL) [Grade1-3a]**
- **Follicular lymphoma (FL) [Grade3b]**
- **Mantle cell lymphoma (MCL)**
- **Diffuse large B-cell lymphoma (DLBCL)**
- **Burkitt lymphoma (BL)**

Adapted from the Japanese Society of Hematology Clinical Practice Guidelines for Hematologic Malignancy 2024 Edition. Kanehara & Co., Ltd, 2024. http://www.jshem.or.jp/gui-hemali/table.html (Japanese only)(Accessed on March 2025)

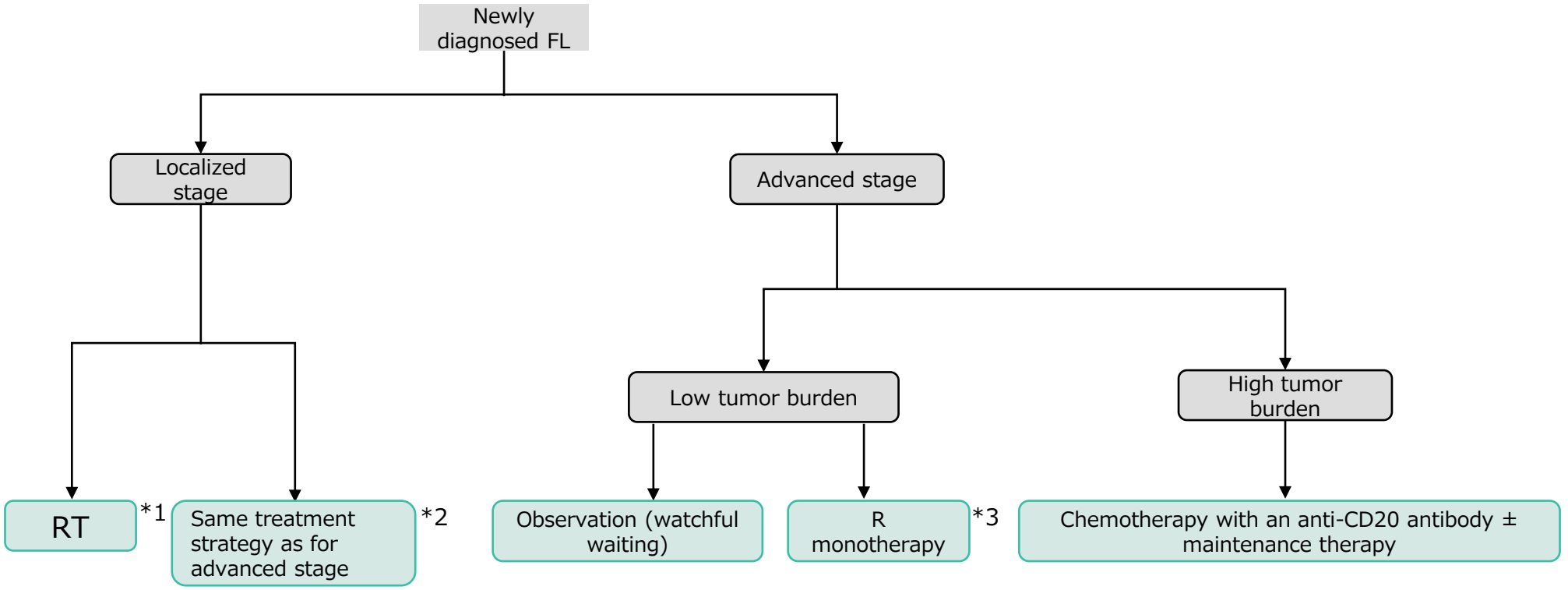
Clinical Characteristics of Follicular Lymphoma

- Accounts for approximately 20% of adult lymphomas, with a higher prevalence in individuals in their 60s.
- A representative type of indolent lymphoma, characterized by slow progression.
- While some patients present with large abdominal masses at diagnosis, many remain asymptomatic.
- At diagnosis, about 80% of patients are in Stage III or higher.
- Additionally, 50% to 60% of patients have bone marrow involvement (Stage IV).
- Primarily involves lymph node lesions, but in some cases, it is confined to the gastrointestinal tract (especially the duodenum).
- B symptoms* and elevated LDH levels are uncommon (≤20%).
- The median survival exceeds 15 years, but curative treatment is challenging in advanced stages.

Prepared by the presenter.

* B symptoms: fever, weight loss, and night sweats (profuse sweating during sleep) that appear as systemic symptoms of lymphoma.

Treatment Algorithm for Newly Diagnosed Follicular Lymphoma

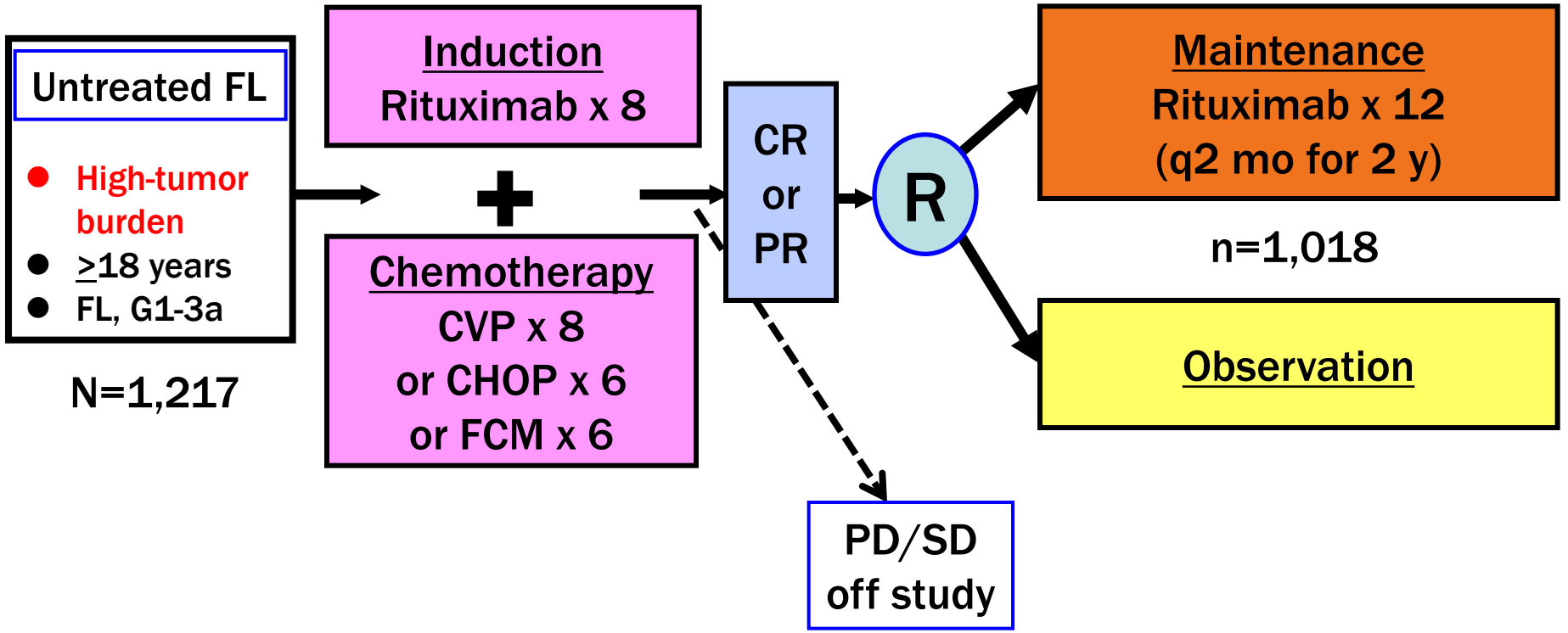


*1 RT: radiotherapy
*2 For localized-stage FL, cases where the risk of radiotherapy outweighs the benefits, such as those with large tumors, abdominal mesenteric involvement in Stage I, or distant lesions in Stage II.
*3 R monotherapy: rituximab monotherapy

Adapted from the Japanese Society of Hematology Clinical Practice Guidelines for Hematologic Malignancy, Version 3.1 (2024 Edition). http://www.jshem.or.jp/gui-hemali/table.html (Japanese only)(Accessed on March 2025)

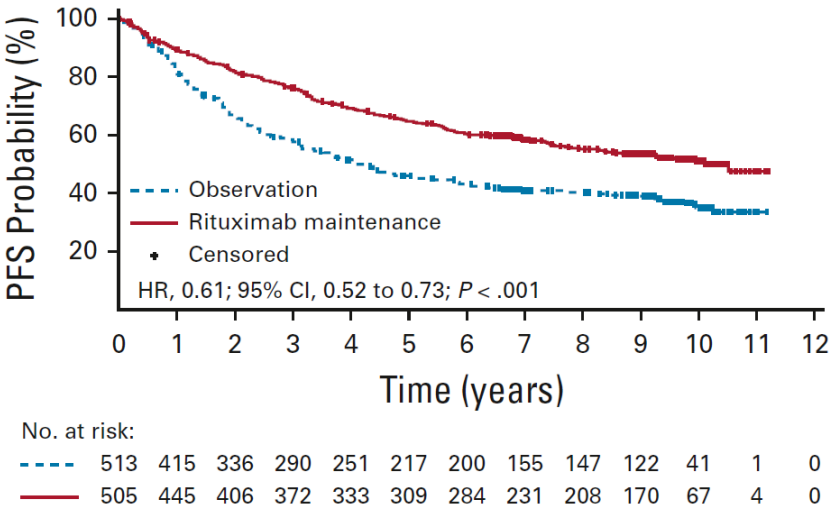
Rituximab Maintenance Therapy for High Tumor Burden Follicular Lymphoma

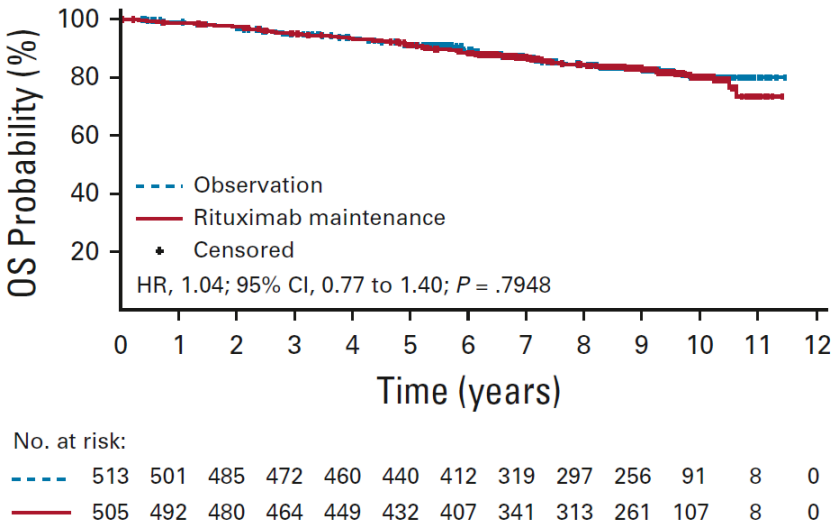
PRIMA: Primary Rituximab and Maintenance



Salles G, et al. Lancet 2011; 377: 42.

9-Year Follow-up Data from the PRIMA Study





- **Median PFS: 10.5 years in the maintenance therapy group vs. 4.1 years in the observation group (HR 0.61, 95% CI 0.52–0.73, P < 0.001)**
- **Median OS: Not reached in either group, with no significant difference. 10-year OS: 80% in both groups.**
- **Serious AE (maintenance therapy group: 21.2%, observation group: 13.4%)**

Bachy E, et al. J Clin Oncol. 2019; 37: 2815.

Obinutuzumab vs Rituximab: GALLIUM Study

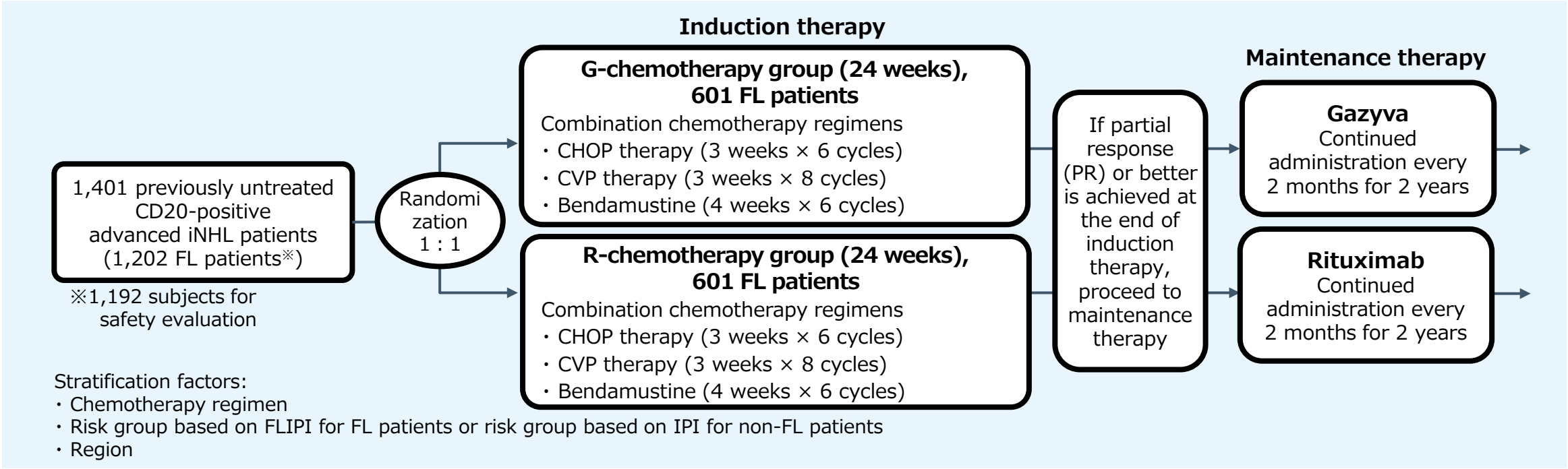
Rituximab	Obinutuzumab
■ Type I antibody	■ Type II antibody
■ Mechanism of action	■ Mechanism of action
➢ Induces complement-dependent cytotoxicity	➢ Weak complement activation
➢ Induces antibody-dependent cytotoxicity	➢ Strongly induces antibody-dependent cytotoxicity
➢ Direct effect on cells leading to apoptosis	➢ Induces non-apoptotic direct cell death

Sehn LH, et al. J Clin Oncol. 2015; 33: 3467.

This drug was approved based on clinical results including domestic Phase I clinical trials, domestic Phase II clinical trials, and international Phase III clinical trials that included Japanese patients. Therefore, the GALLIUM study includes some results for indications that differ from those approved in Japan.

Obinutuzumab vs Rituximab: GALLIUM Study

International, open-label, randomized phase 3 trial



Primary endpoint

- PFS (INV-assessed in FL)

Secondary endpoints and other endpoints

- PFS (IRC-assessed)
- OS, EFS, DFS, DoR, TTNT
- CR/ORR at EOI (+/− FDG-PET)
- Safety

The approved indications for Gazyva are as follows:
- CD20-positive follicular lymphoma
- CD20-positive chronic lymphocytic leukemia (including small lymphocytic lymphoma)

Marcus R, et al. N Engl J Med. 2017; 377: 1331.

Obinutuzumab vs Rituximab: GALLIUM Study

[Analysis Plan]

<Primary endpoint>

- For PFS (investigator-assessed), the superiority of the G-chemotherapy group over the R-chemotherapy group was to be verified using a stratified Log-rank test with combination chemotherapy regimen (CHOP, CVP, bendamustine) and FLIPI-based risk group (low risk, intermediate risk, high risk) as stratification factors. (Significance level at the third interim analysis = 0.012).
- PFS distributions for both groups were estimated using the Kaplan-Meier method, and treatment effect was estimated using a stratified hazard ratio (including 95% confidence interval [CI]) calculated by stratified Cox proportional hazards analysis (stratification factors same as for the primary endpoint).

<Secondary endpoints>

- To control the overall type I error rate at a two-sided 5% level, multiplicity adjustment was performed for the main secondary endpoints. Hierarchical hypothesis testing was conducted in the following order:
  ① PFS in iNHL patients, ② CR rate at the end of induction therapy in FL patients, ③ CR rate at the end of induction therapy in iNHL patients, ④ OS in FL patients, ⑤ OS in iNHL patients, ⑥ ORR at the end of induction therapy in FL patients, and ⑦ ORR at the end of induction therapy in iNHL patients. Subsequent hypothesis tests were evaluated as long as all preceding test results were statistically significant.
  (②, ③, ⑥, and ⑦ were all evaluated without including PET findings). No multiplicity adjustment was made for other secondary endpoints.
- Cochran-Mantel-Haenszel (CMH) test was used to compare CR rates between treatment groups (stratification factors were the same as for the primary endpoint).

<Subgroup Analysis>

- The following subgroup analyses were pre-planned:
  ・Primary and secondary endpoints for Japanese FL patients
  ・Primary endpoint by sex, race, bulky disease (≥7cm), B symptoms, disease stage (Ann Arbor classification), ECOG-PS, ADL, IADL, FLIPI, combination chemotherapy regimen, and region

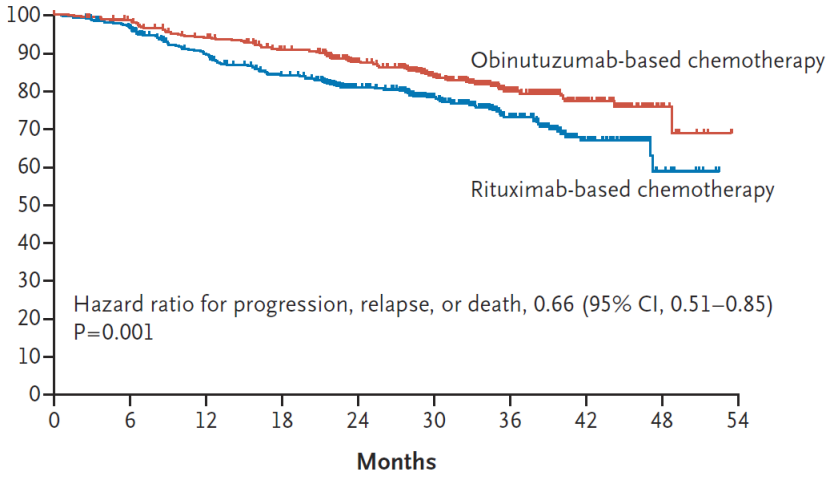
<Exploratory Endpoints>

- PFS for the group achieving CMR at the end of induction therapy and PFS analysis by FLIPI score were pre-planned and estimated using the Kaplan-Meier method. Analysis of CD3-positive and CD4-positive T cell counts by regimen in FL patients was pre-planned.

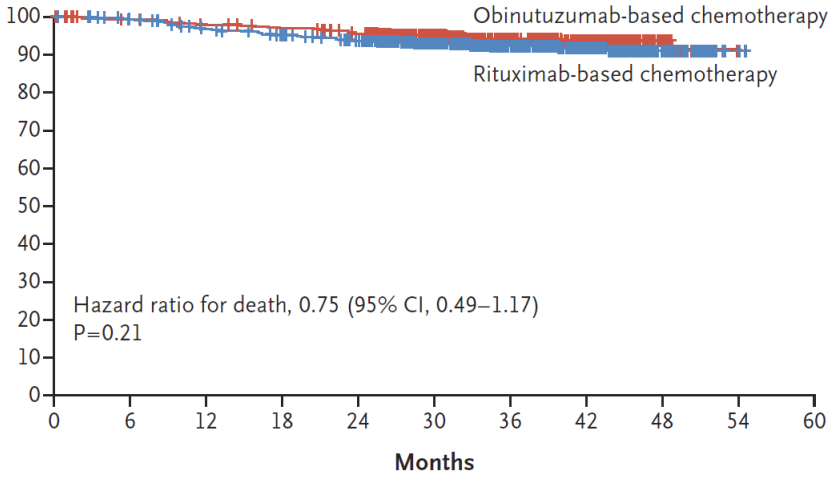
Marcus R, et al. N Engl J Med. 2017; 377: 1331.

Obinutuzumab vs Rituximab: GALLIUM Study

PFS (Primary endpoint)



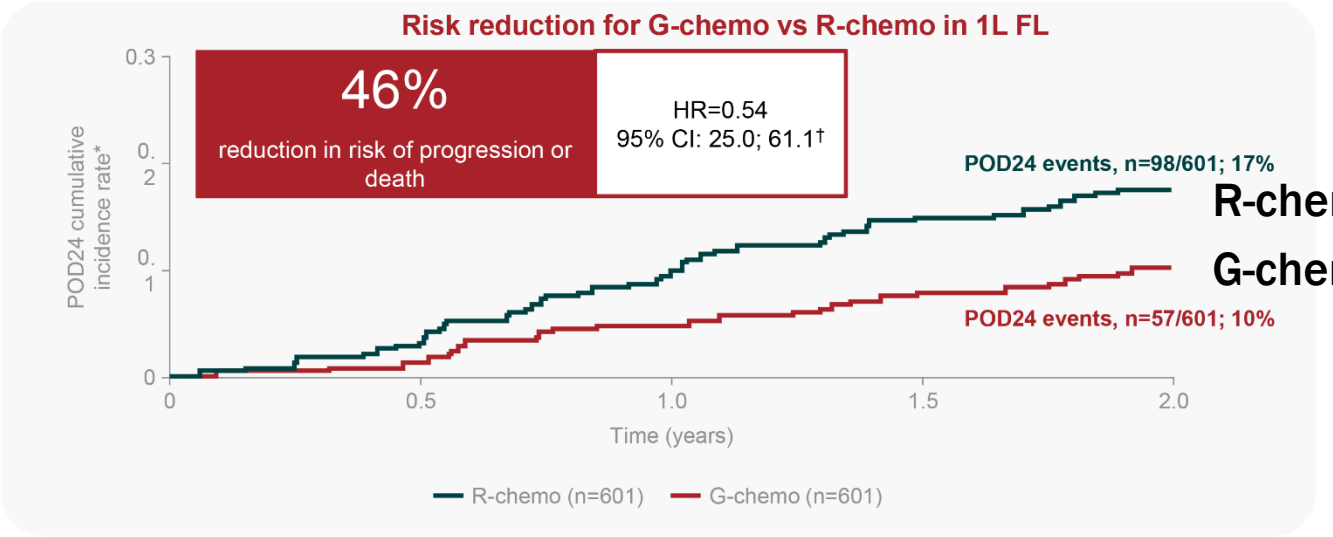
OS (Secondary endpoint)

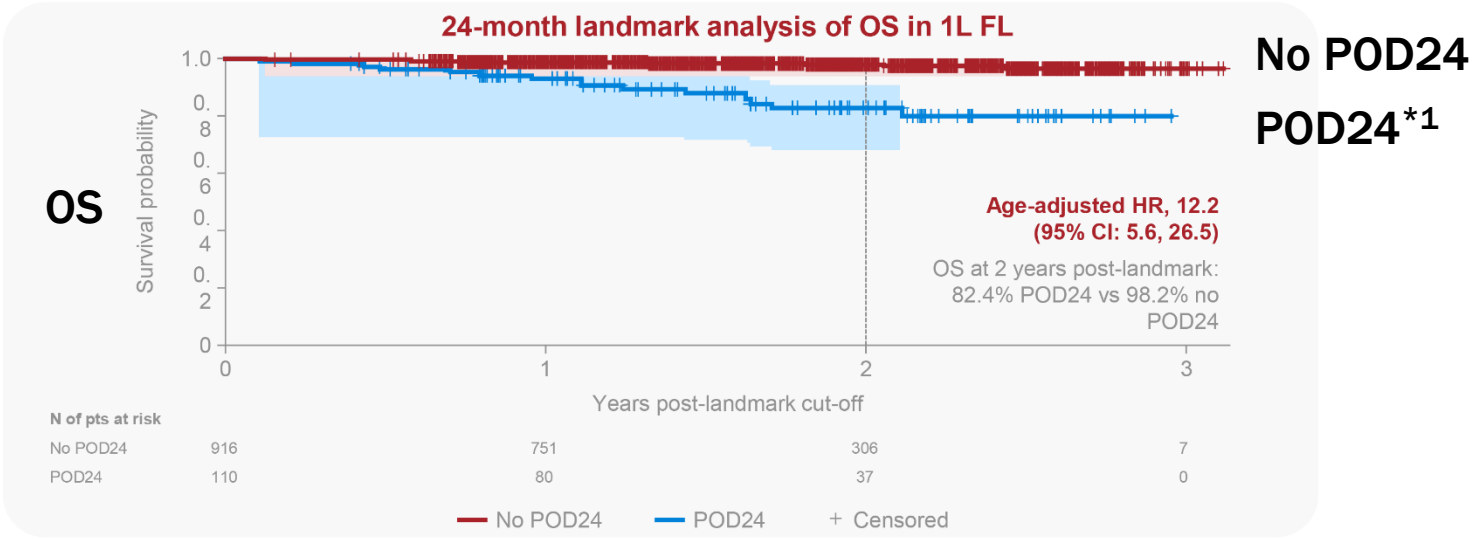


- Median follow-up: 34.5 months
- Overall response rate (obinutuzumab: 88.5% vs. rituximab: 86.9%)
- 3-year PFS (planned interim analysis): Obinutuzumab: 80% vs. rituximab: 73.3% (HR 0.66; 95%CI 0.51-0.85; P=0.001).
- 3-year OS (obinutuzumab: 94% vs. rituximab: 92.4%): No significant difference
- Grade 3–5 AEs (obinutuzumab: 74.6% vs. rituximab: 67.8%)

Marcus R, et al. N Engl J Med. 2017; 377: 1331.

Disease Progression at 24 Months (GALLIUM Study)

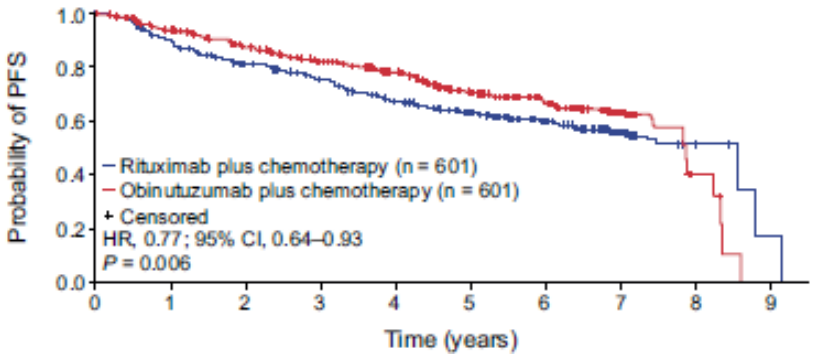


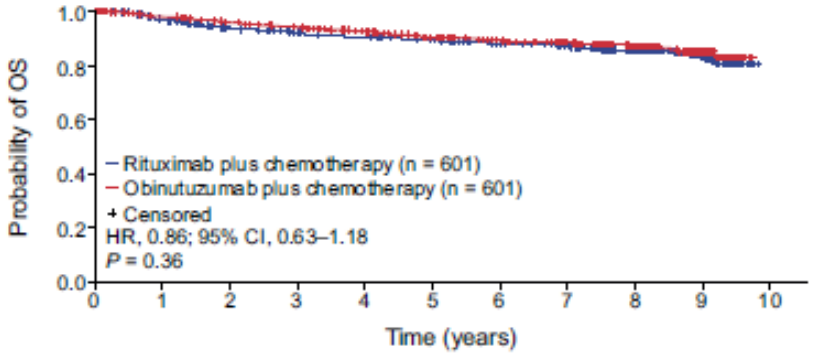


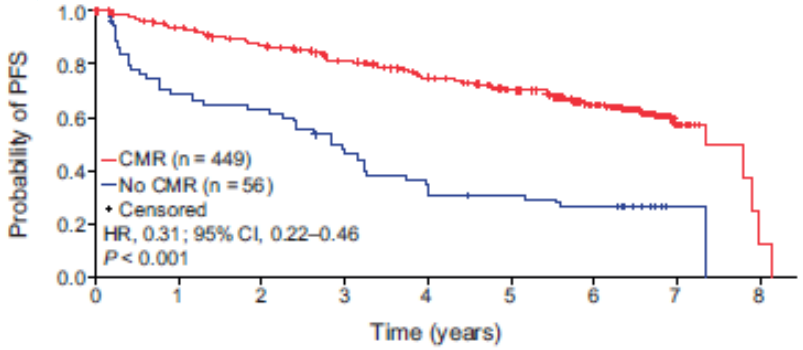
*1 POD24: Progression of disease within 24 months from randomization, or death due to disease progression

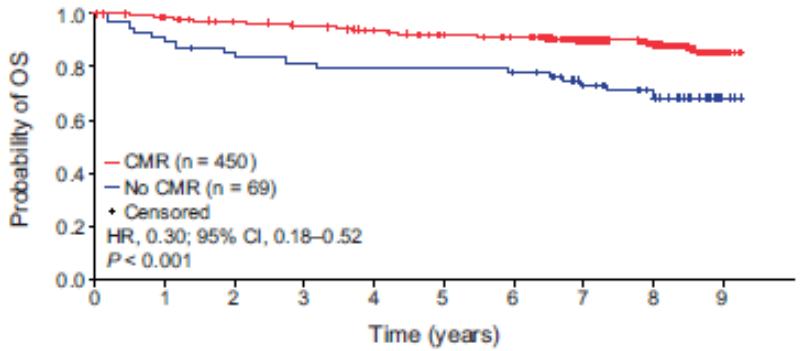
Seymour JF, et al. Haematologica. 2019; 104: 1202.

Final Results of GALLIUM Study









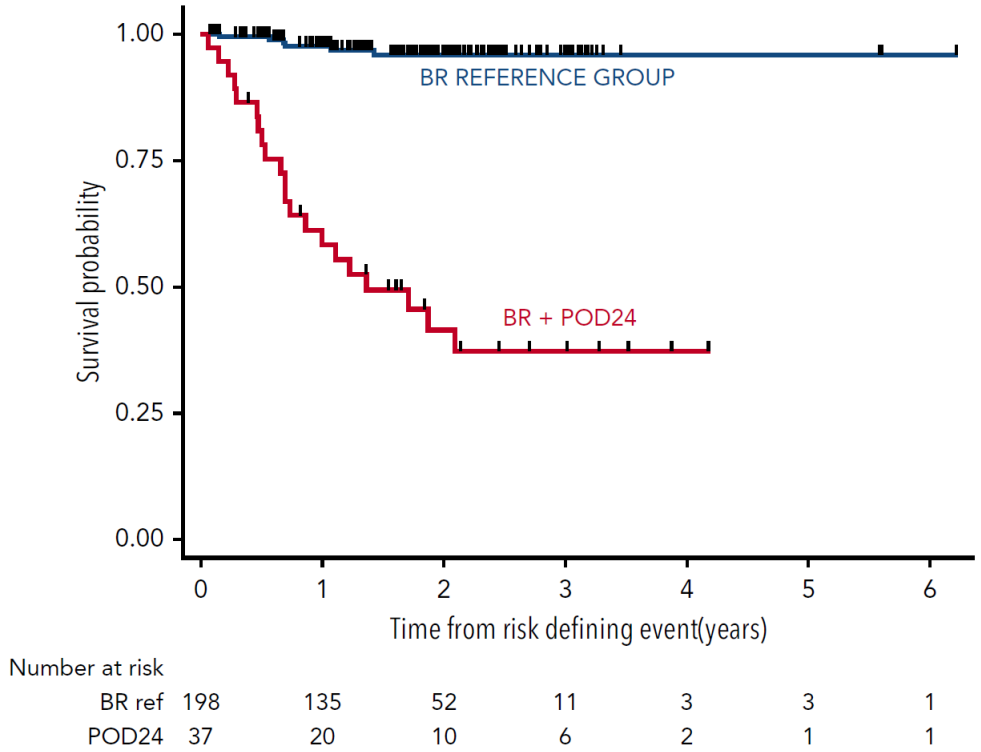
- Median follow-up: 7.9y
- The superiority of PFS in the obinutuzumab group was maintained.
- No significant difference was observed in OS.
- CMR*1 (at EOI*2) was associated with superior PFS and OS compared to No CMR.

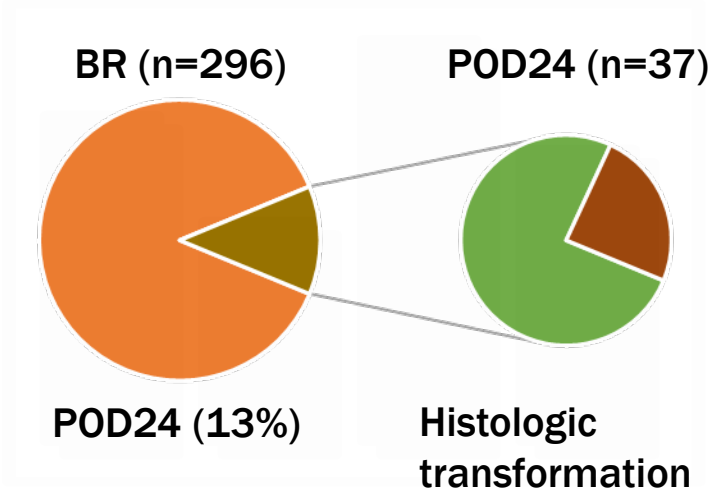
*1 CMR: complete metabolic response
*2 EOI: end of induction

Townsend W, et al. HemaSphere. 2023; 7: 7(e919).

Disease Progression at 24 Months (BR ± R Maintenance Therapy)

Retrospective study at BCCA*2





- Early disease progression within 24 months on BR*1 therapy was associated with poor prognosis.
- The majority (76%) of cases involved histologic transformation.
- The only identified risk factor for POD24 was elevated baseline serum LDH.

*1 BR : Bendamustine and Rituximab
*2 BCCA : British Columbia Cancer Agency

Freeman CL, et al. Blood. 2019, 134: 761.

Relapse or Progression Within 24 Months after Initial Chemotherapy (POD24)

Key Summary Points

Multiple studies have shown increased mortality risk in patients with follicular lymphoma (FL) who have progression of disease within 24 months of initial treatment (POD24) versus those who do not have POD24.

In clinical practice, it is not currently possible to identify individuals who are at increased risk for POD24. Improved tools for risk assessment are needed.

G-chemotherapy appears to reduce the risk of POD24 relative to R-chemotherapy in patients with previously untreated FL, but the impact on overall survival remains unclear.

Treatment strategies for the management of patients with POD24 are not well established. Well-designed studies are needed to determine the role of standard and emerging therapies.

In the absence of treatment standards, reducing the risk of POD24 with effective first-line therapies remains a priority.

Rodgers TD, et al. Oncol Ther 2021; 9: 329.

	High risk FLIPI, %	High risk m7-FLIPI, %	High risk POD24-PI, %
Sensitivity	70-78	43-61	61-78
Specificity	56-58	79-86	67-73

Casulo C, et al. Blood 2019; 133: 1540.

Summary: Newly Diagnosed Follicular Lymphoma

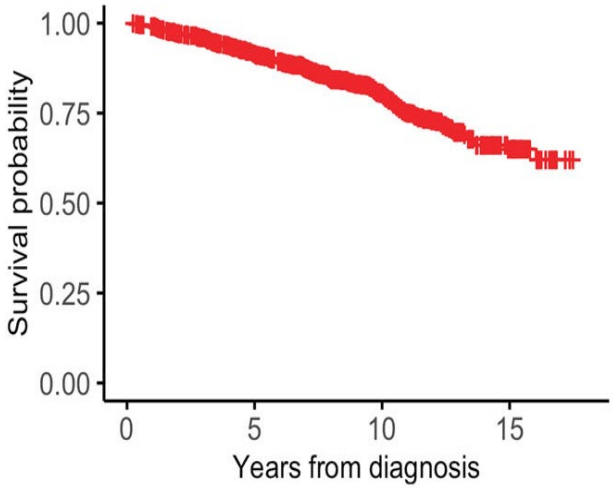
- The standard treatment for previously untreated high tumor burden FL is chemotherapy with an anti-CD20 monoclonal antibody. While long-term disease control is achievable for many patients, FL remains an incurable disease.

- In some patients, POD24 occurs and is recognized as a prognostic factor, particularly affecting OS. However, a first-line treatment that reduces POD24 risk and improves prognosis has not yet been established.

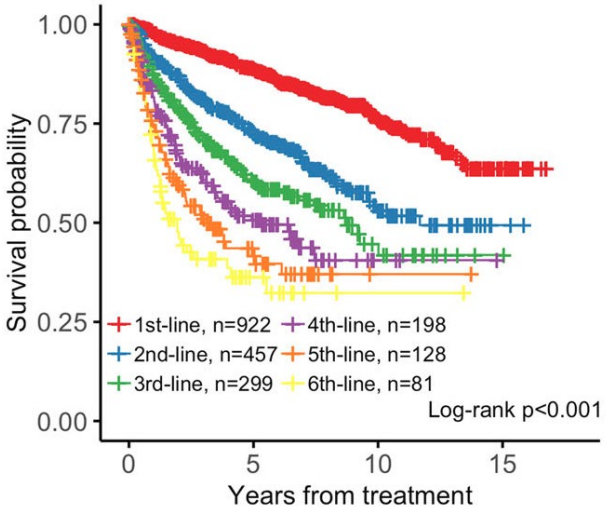
Prognosis of Follicular Lymphoma

FL, G1-3a in MSKCC (1998-2009, N=1088)

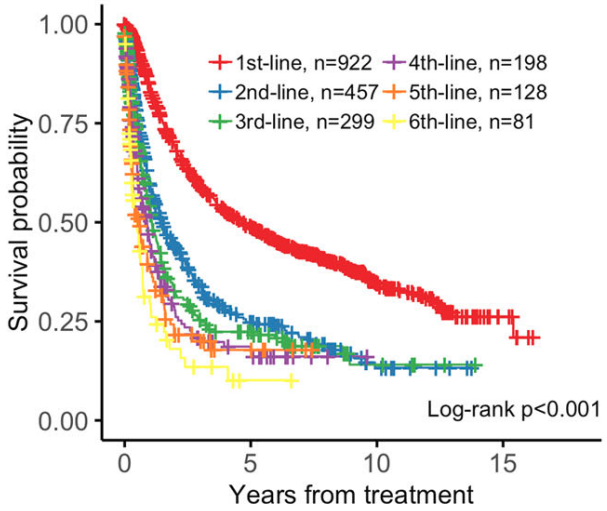
OS for all pts



OS by line of therapy



PFS by line of therapy



- OS: 92% at 5y, 80% at 10y, 65% at 15y.
- Despite an increasing number of treatment options for FL, patient prognosis continues to decline with each successive line of therapy (a major challenge in the treatment of R/R FL).

R/R FL: relapsed/refractory follicular lymphoma

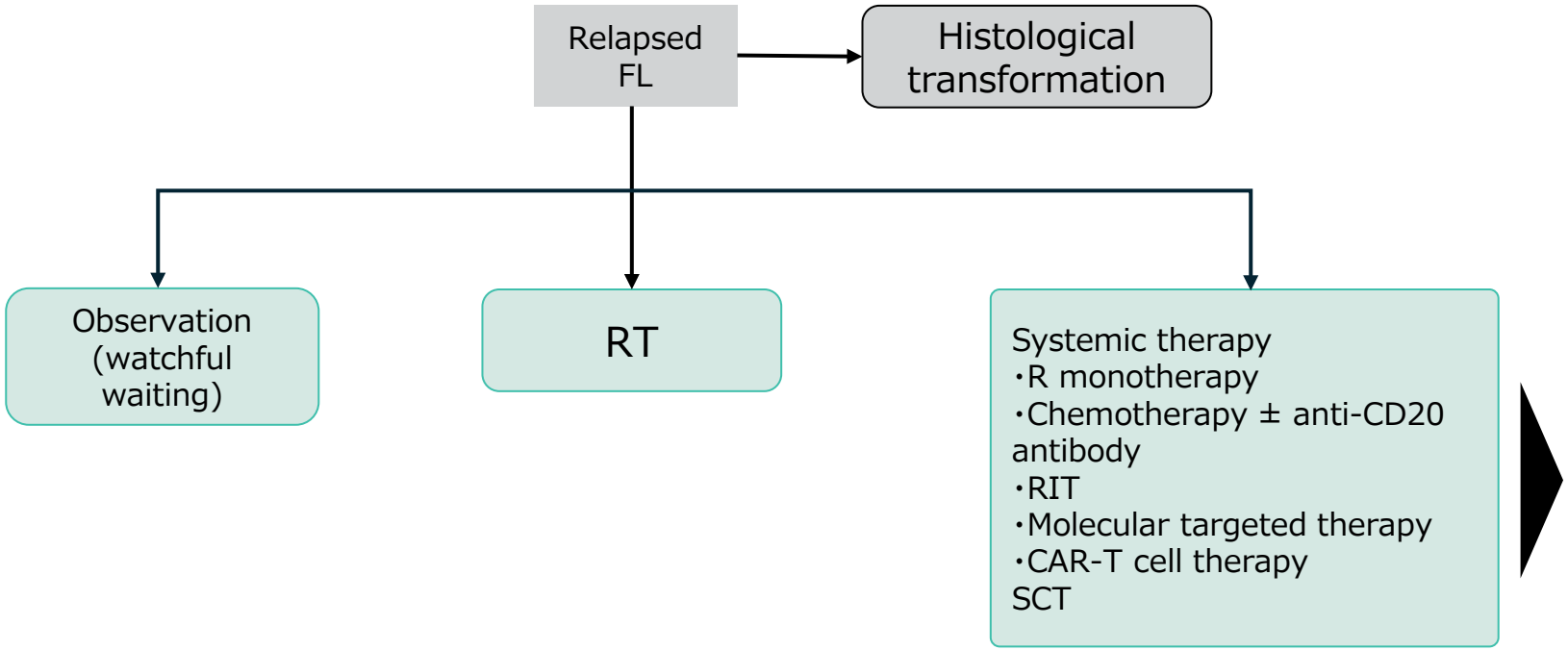
Batlevi C, et al. Blood Cancer J. 2020; 10: 74.

Treatment Options for Relapsed Follicular Lymphoma in Japan

- Watch and wait
- Rituximab alone
- Fludarabine±Rituximab
- Bendamustine±Rituximab or Obinutuzumab
- Rituximab+Lenalidomide
- Tazemetostat (*EZH2* mutation+)
- Radiation therapy (localized disease)
- Radioimmunotherapy (^{90}Y-ibritumomab tiuxetan)
- CAR T-cell therapy (Tisa-cel, Liso-cel)
- Bispecific antibody (Mosunetuzumab, Epcoritamab)
- Stem cell transplantation

Prepared by the presenter.

Treatment Algorithm for Relapsed Follicular Lymphoma



CQ5: What treatment is recommended for relapsed FL?

Recommended grade: Category 2

Various treatment options exist, but no clear superiority has been established.

RT: Radiotherapy
R: Rituximab
RIT: Radioimmunotherapy (RI-labeled antibody therapy)
SCT: Stem cell transplantation
Anti-CD20 antibody: Rituximab (R) or obinutuzumab

Adapted from the Japanese Society of Hematology Clinical Practice Guidelines for Hematologic Malignancy, Version 3.1 (2024 Edition).
http://www.jshem.or.jp/gui-hemali/table.html (Japanese only)(Accessed on March 2025)

CAR-T Cell Therapy for Relapsed or Refractory Follicular Lymphoma

nature medicine

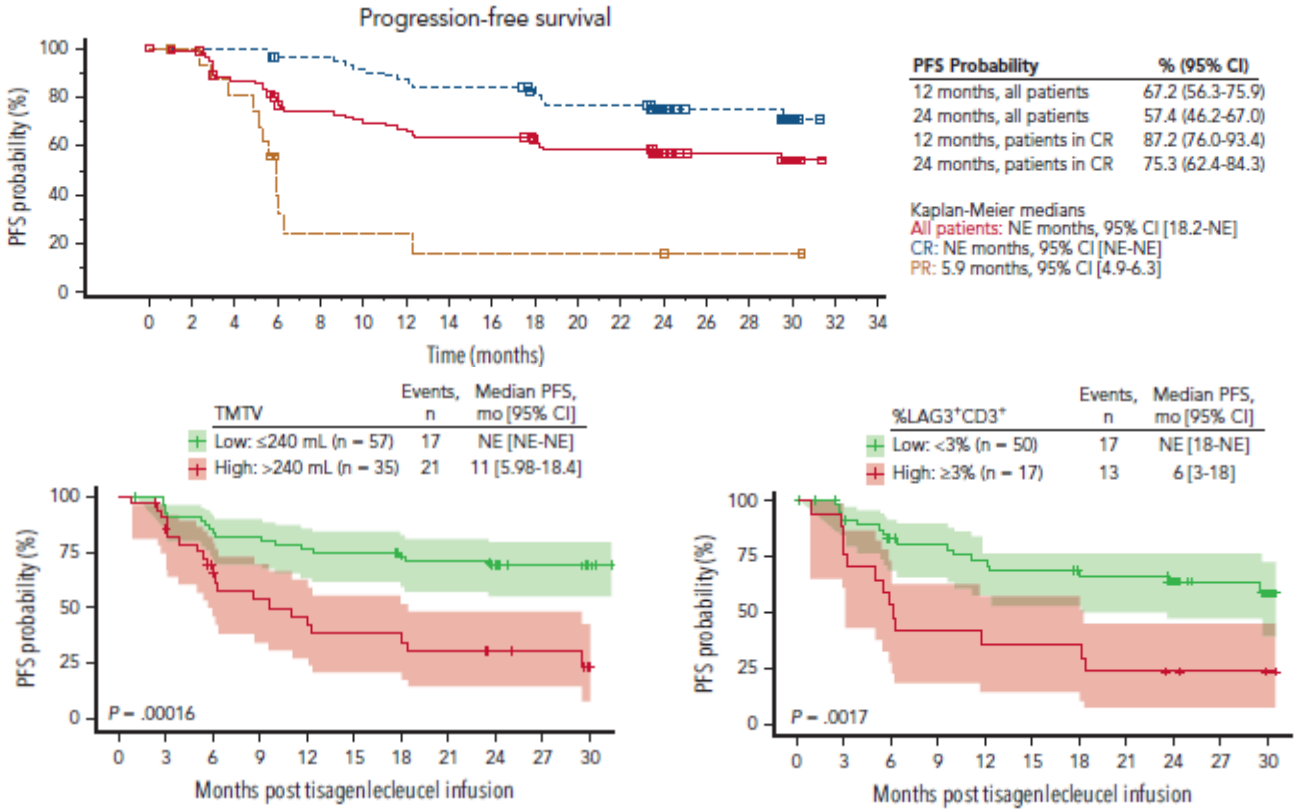
ARTICLES

https://doi.org/10.1038/s41591-021-01622-0

Check for updates

Tisagenlecleucel in adult relapsed or refractory follicular lymphoma: the phase 2 ELARA trial

Fowler NH, et al. Nat Med. 2022; 28: 325.



- Follow-up data for Tisa-cel in 3L+ FL (median: 29 months)
- CR, low TMTV, low LAG3^{+} CD3^{+} exhausted T cells, and high naïve CD8^{+} T cells are associated with a favorable prognosis.

Dreyling M, et al. Blood. 2024; 143: 1713.

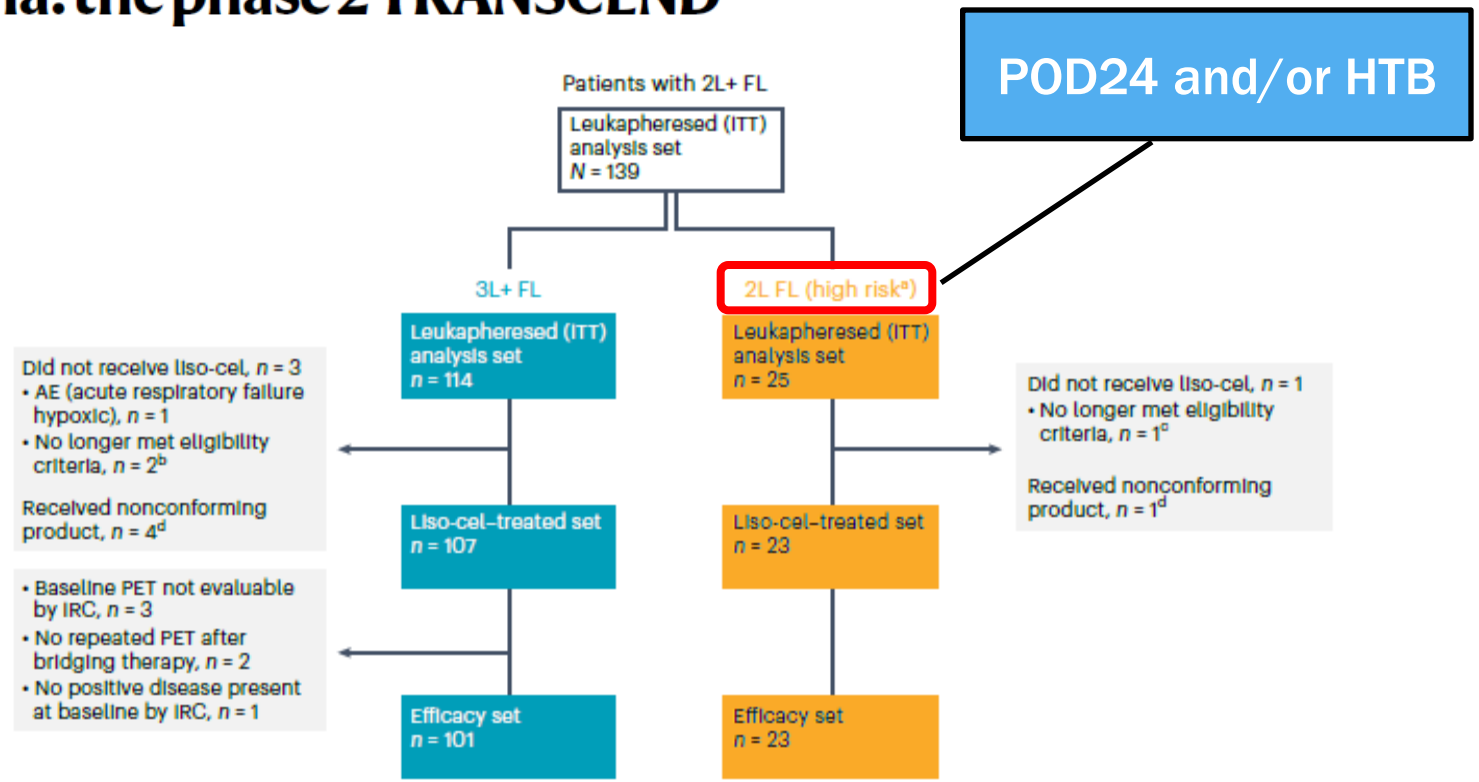
CAR-T Cell Therapy for Relapsed or Refractory Follicular Lymphoma

nature medicine

Article

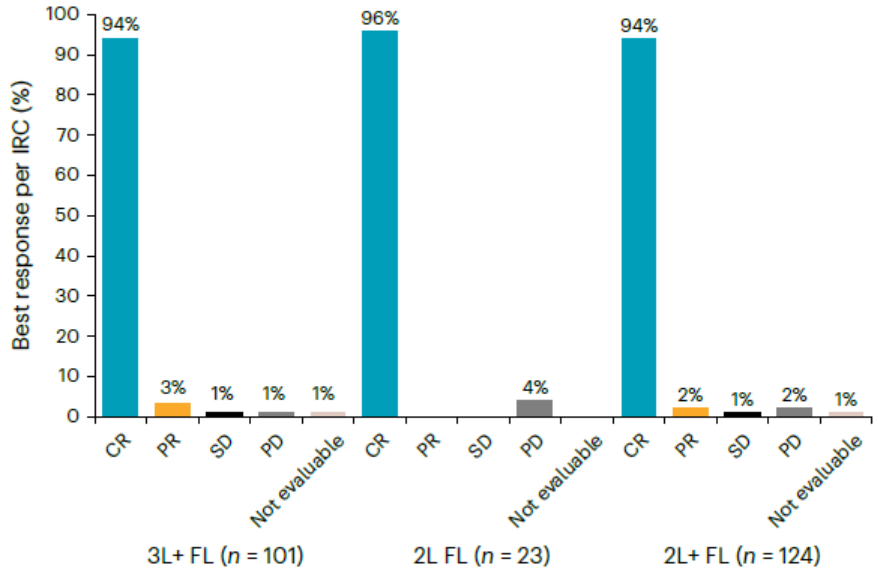
https://doi.org/10.1038/s41591-024-02986-9

Lisocabtagene maraleucel in follicular lymphoma: the phase 2 TRANSCEND FL study

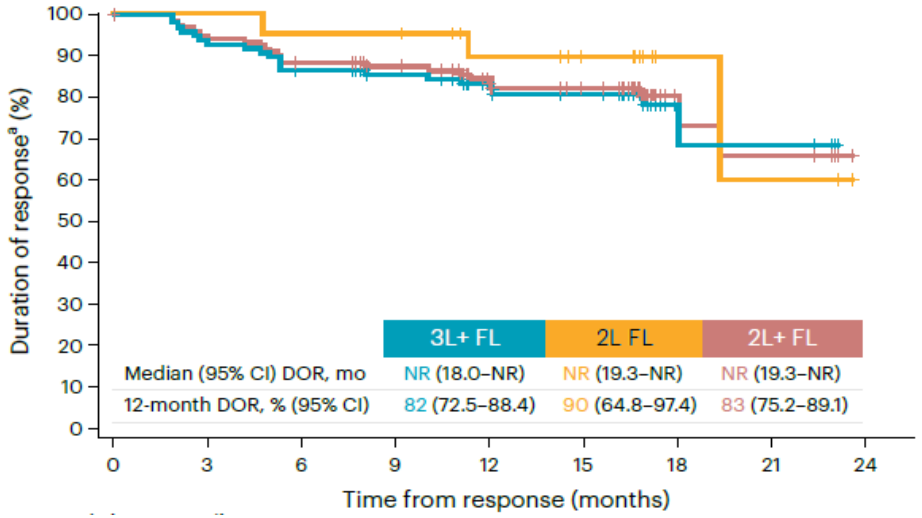


Morschhauser F, et al. Nat Med. 2024; 30: 2199.

CAR-T Cell Therapy for Relapsed or Refractory Follicular Lymphoma



	ORR	CR rate
3L+ FL (*n* = 101)	97% (95% CI: 91.6–99.4) *P* < 0.0001[a]	94% (95% CI: 87.5–97.8) *P* < 0.0001[a]
2L FL (*n* = 23)	96% (95% CI: 78.1–99.9) *P* < 0.0001[b]	96% (95% CI: 78.1–99.9) *P* < 0.0001[b]
2L+ FL (*n* = 124)	97% (95% CI: 91.9–99.1)[c]	94% (95% CI: 88.7–97.7)[c]



- Liso-cel demonstrated a high response rate and durable responses in 2L+ FL, including POD24.

Morschhauser F, et al. Nat Med. 2024; 30: 2199.

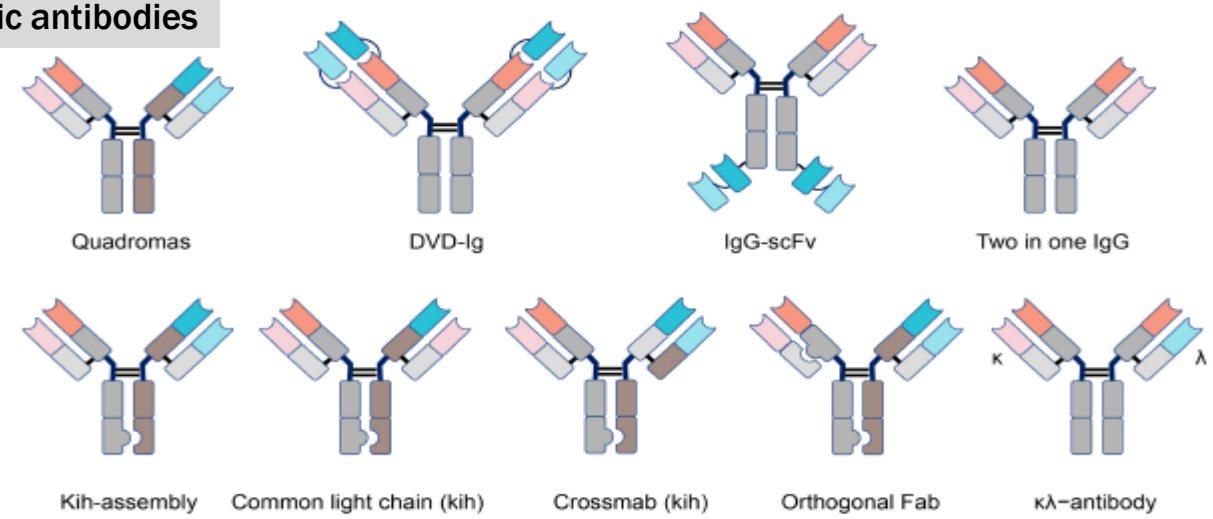
Bispecific Antibody

- Among bispecific agents (including blinatumomab), those with an immunoglobulin-like structure.
- They exert antitumor effects by activating endogenous T cells and directing them toward specific antigens.
- This process is MHC-independent, meaning it does not rely on TCR epitope specificity.
- Advantages of bispecific antibodies: Long half-life, eliminating the need for continuous administration.
- Challenges in the development of bispecific antibody therapies: Requires heterodimerization of heavy and light chains with different antigen-binding specificities, necessitating the avoidance of mismatched assembly/coupling during the manufacturing process.

Bispecific T-cell engager (BiTE®)

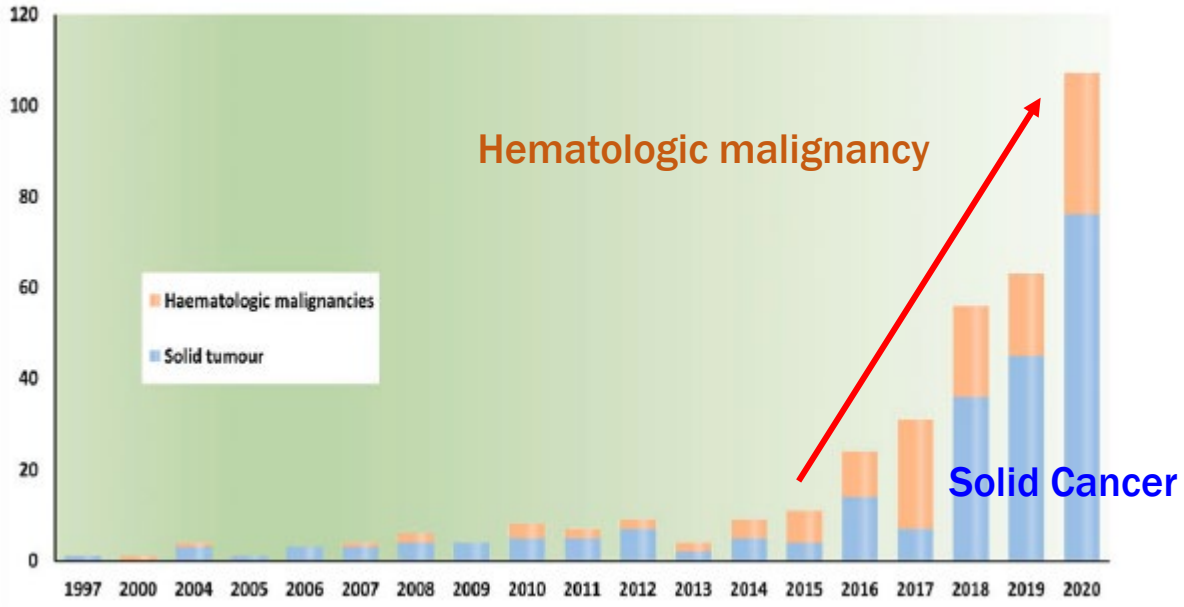
e.g. Blinatumomab

IgG-like bispecific antibodies

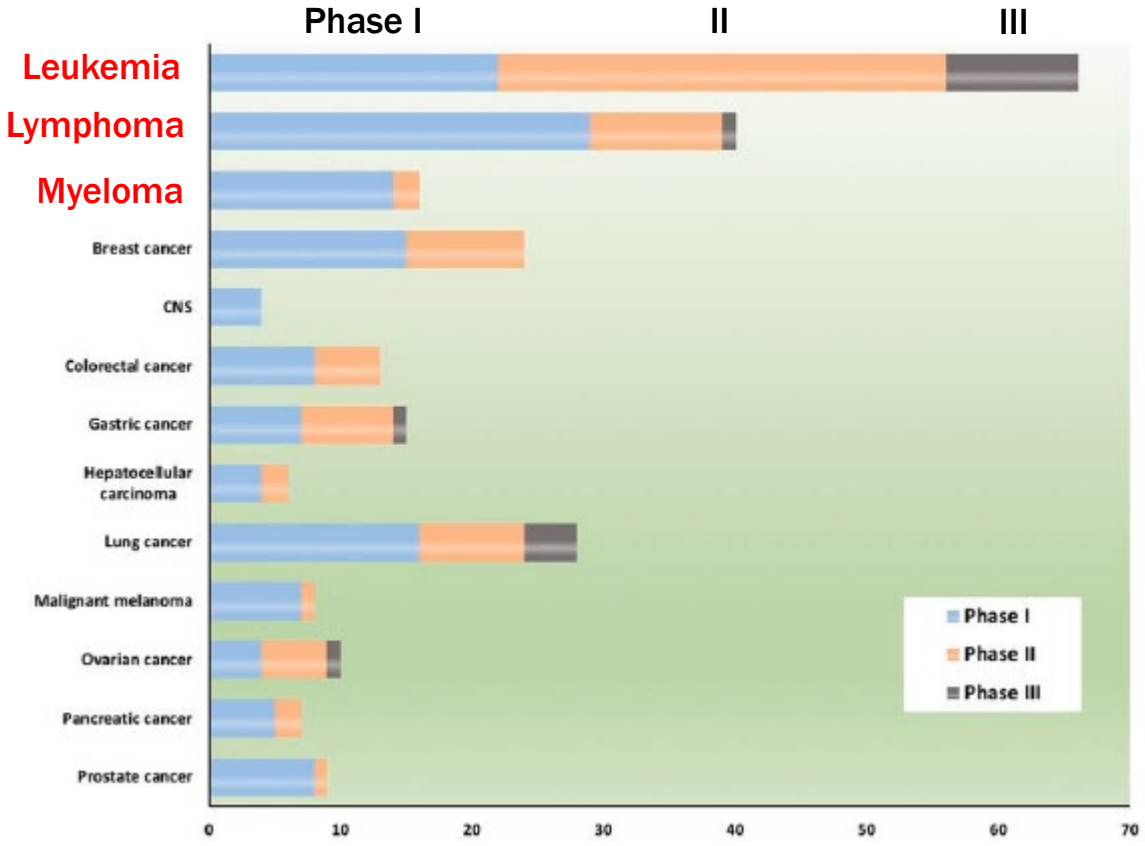


Wang M, et al. Front Biosci (Landmark Ed). 2024; 29: 216.

Development of Bispecific Antibodies



Number of BsAb studies



Number of BsAb studies

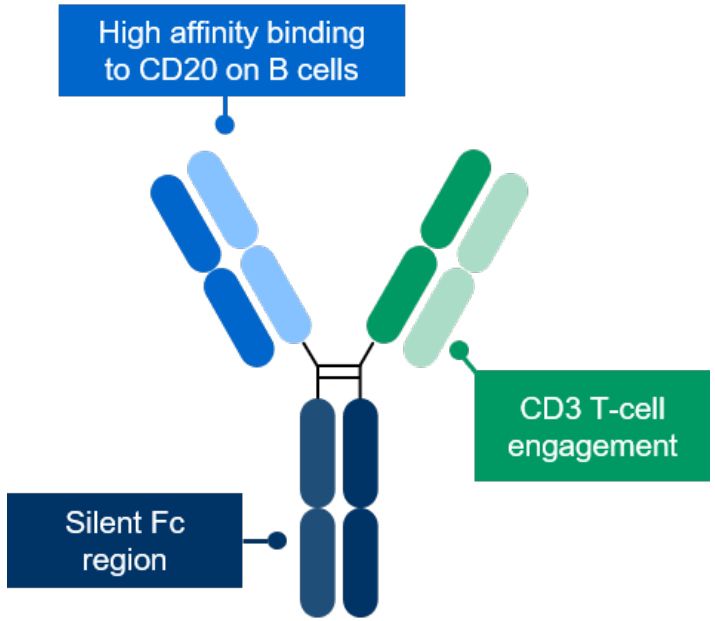
- Clinical trials of bispecific antibodies have rapidly increased.
- Development is notable not only in hematologic malignancies but also in solid tumors.
- As of 2020, the majority of trials were in early-phase (Phase I/II) studies.

Lim SM et al. Cancer Treat Rev. 2021; 99: 102240.

LUNSUMIO (Mosunetuzumab)

- Lunsumio: bispecific monoclonal antibody targeting CD20 and CD3
- Binds to CD3 on T cells and CD20 on B-cell tumors, activating T cells and believed to damage CD20-positive tumor cells[4]
- Off-the-shelf and fixed-duration treatment[4,5]
- Phase I experience (NCT02500407)[5,6]
  - encouraging efficacy and manageable safety in patients with R/R FL and ≥2 prior therapies, including POD24 and double refractory[6]
  - effective CRS mitigation with cycle 1 step-up dosing[6]

***Mosunetuzumab**:*
CD20xCD3 bispecific antibody[4]



1. Rivas-Delgado et al. Br J Haematol 2019;184:753–9、2. Bachy et al. Blood Adv 2021;5:1729–32
3. Seymour et al. Haematologica 2019;104:1202–8、4. Sun et al. Sci Transl Med 2015;7:287ra70
5. NCT02500407、6. Budde LE, et al. Lancet Oncol. 2021; 40（5）: 481-4915

This drug was approved based on the results of the GO29781 and JO40295 studies, which included cohorts conducted outside the approved indications, dosage, and administration. In this presentation, we will show the cohorts conducted under the approved indications, dosage, and administration.

GO29781: Study Design

Single-arm, pivotal Phase II expansion in patients with R/R FL and ≥2 prior therapies

Key inclusion criteria

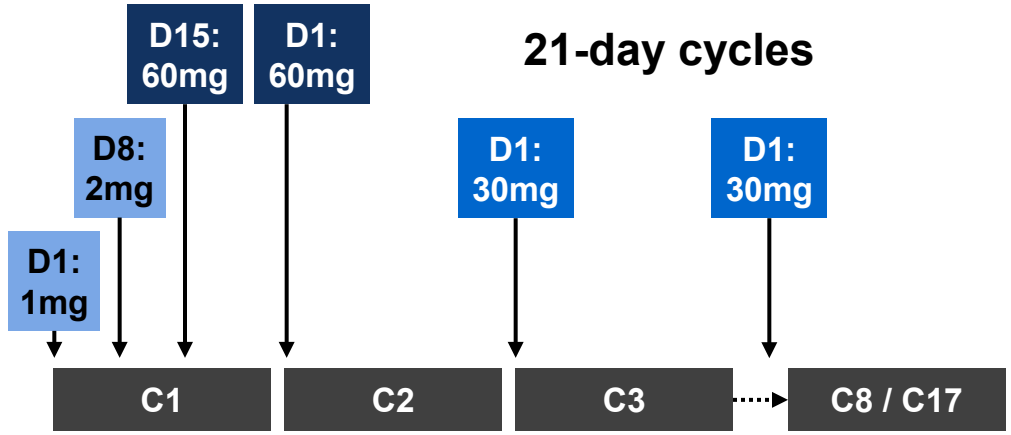
- FL (Grade 1–3a)
- ECOG PS 0–1
- ≥2 prior regimens, including
  - ≥1 anti-CD20 Ab
  - ≥1 alkylating agent

Administration method

- Intravenous infusion
- Step-up dosing (CRS mitigation)
- Fixed-duration (fixed treatment period)
  - At the 8-cycle point (approximately 6 months):

    CR: End of treatment

    PR/SD: Continue up to 17 cycles
- No mandatory hospitalization period



Endpoints

- Primary: CRR [as assessed by Independent Review Facility (IRF)]* – 14% set as threshold CRR based on historical control[1]
- Secondary: ORR, DoR, PFS, safety and tolerability

* Assessment conducted using CT and PET-CT, based on Cheson 2007 criteria2

The approved indication and dosage for Lunsumio are as follows:
- Indications: relapsed or refractory follicular lymphoma
- Dosage and administration:
  For adults, the usual dosage of mosunetuzumab (genetically modified) is administered as an intravenous infusion in 21-day cycles as follows:
  Cycle 1: 1 mg on Day 1, 2 mg on Day 8, and 60 mg on Day 15
  Cycle 2: 60 mg on Day 1
  Cycles 3-8: 30 mg on Day 1 of each cycle
  After 8 cycles, treatment should be discontinued for patients who achieve a complete response. For patients with stable disease or partial response, treatment may be continued for up to a total of 17 cycles.

Dreyling et al. J Clin Oncol 2017;35:3898–905

Cheson et al. J Clin Oncol 2007;25:579–86

Budde LE, et al. Lancet Oncol. 2022; 23 (8):1055-1065.

This study was conducted with the support of F. Hoffmann-La Roche Ltd. and Genentech, Inc.

This publication includes authors who are employees of or have received funding from F. Hoffmann-La Roche Ltd. and Genentech, Inc.

GO29781: Study Design

【Evaluation Items】

Primary Endpoint: Complete Response Rate (CRR) [Independent Review Facility (IRF) Assessment]

Secondary Endpoints: CRR [Investigator Assessment], Overall Response Rate (ORR) [IRF Assessment, Investigator Assessment], Duration of Response (DOR) [IRF Assessment, Investigator Assessment], Duration of Complete Response (DOCR) [IRF Assessment, Investigator Assessment], Progression-Free Survival (PFS) [IRF Assessment, Investigator Assessment], Overall Survival (OS), etc.

【Analysis Plan】

Treatment effects for each evaluation item were assessed using the revised response criteria for malignant lymphoma.
For the primary endpoint of CRR (IRF assessment), results from the ITT population were compared with historical controls using Fisher's exact test. The historical control was set at 14% CRR, based on a foreign Phase II clinical study of copanlisib monotherapy (not approved in Japan) in patients with relapsed or refractory FL1). The threshold CRR was set at 14%. With an expected CRR of 28% for Lunsumio, 80 patients were required to ensure 83% power at a two-sided significance level of 5%. The study protocol pre-specified at least one interim analysis and additional analyses.
An interim analysis was conducted with a data cutoff date of March 15, 2021. As the primary endpoint was achieved, this point was set as the main analysis timepoint, and the previously planned analysis for August 27, 2021, was conducted as an additional analysis.
The 95% CI for CRR was calculated using the Clopper-Pearson method.
The 95% CI for the secondary endpoint of CRR (investigator assessment) was also calculated using the Clopper-Pearson method.
DOR, DOCR, PFS, and OS were estimated using the Kaplan-Meier method, and the 95% CIs for median values were calculated using the Brookmeyer-Crowley method. The 6-month and 12-month DOR, DOCR, PFS, and OS rates were estimated, with 95% CIs calculated using Greenwood's formula.
Subgroup analyses for CRR (IRF assessment) were pre-specified for age, sex, BMI, ethnicity, race, ECOG PS, bulky disease, FLIPI, number of prior treatment regimens, history of R2 therapy, history of CAR-T cell therapy, refractoriness to most recent therapy, refractoriness to anti-CD20 antibodies, refractoriness to alkylating agents, refractoriness to PI3K inhibitors, time since last anti-CD20 antibody treatment, double refractory status, POD24, CD20, and EZH2 gene mutation.

1) Dreyling M, et al. J Clin Oncol. 2017; 35(35): 3898-3905. [Conflict of interest: The authors includes researchers funded by F. Hoffmann-La Roche.]

Approval evaluation data: overseas Phase I/II (GO29781), Budde LE, et al. Lancet Oncol. 2022; 23(8): 1055-1065.

Baseline Patient Characteristics

		N=90
Median age, years (range)		60 (29–90)
Male		55 (61.1%)
ECOG PS	0	53 (58.9%)
	1	37 (41.1%)
Ann Arbor stage	I–II	21 (23.3%)
	III–IV	69 (76.7%)

		N=90
Number of prior lines (range)		3 (2–10)
Prior systemic therapy	Anti-CD20 therapy	90 (100%)
	Alkylator therapy	90 (100%)
	PI3K inhibitor	17 (18.9%)
	IMiD	13 (14.4%)
	CAR-T	3 (3.3%)
Prior ASCT		19 (21.1%)
Refractory to last prior therapy		62 (68.9%)
Refractory to any prior anti-CD therapy		71 (78.9%)
Refractory to any prior anti-CD20 therapy and alkylator therapy (double refractory)		48 (53.3%)
POD24		47 (52.2%)

Cut-off date: August 27, 2021

Budde LE, et al. Lancet Oncol. 2022; 23（8）:1055-1065.

Exposure and Patient Disposition

	N=90
Median duration of follow-up, months (range)	18.3 (2.0–27.5)
Patient disposition	
Completed treatment	54 (60.0%)
Discontinued treatment	36 (40.0%)
Active on retreatment	2 (2.2%)
In follow-up	76 (84.4%)
Discontinued study	12 (13.3%)

	N=90
Number of cycles received*	
<8 cycles	21 (23.3%)
8 cycles	53 (58.9%)
>8 cycles and <17 cycles	5 (5.6%)
17 cycles	11 (12.2%)

Cut-off date: August 27, 2021

Budde LE, et al. Lancet Oncol. 2022; 23（8）:1055-1065.

Complete Response Rate (CRR) and Overall Response Rate (ORR)

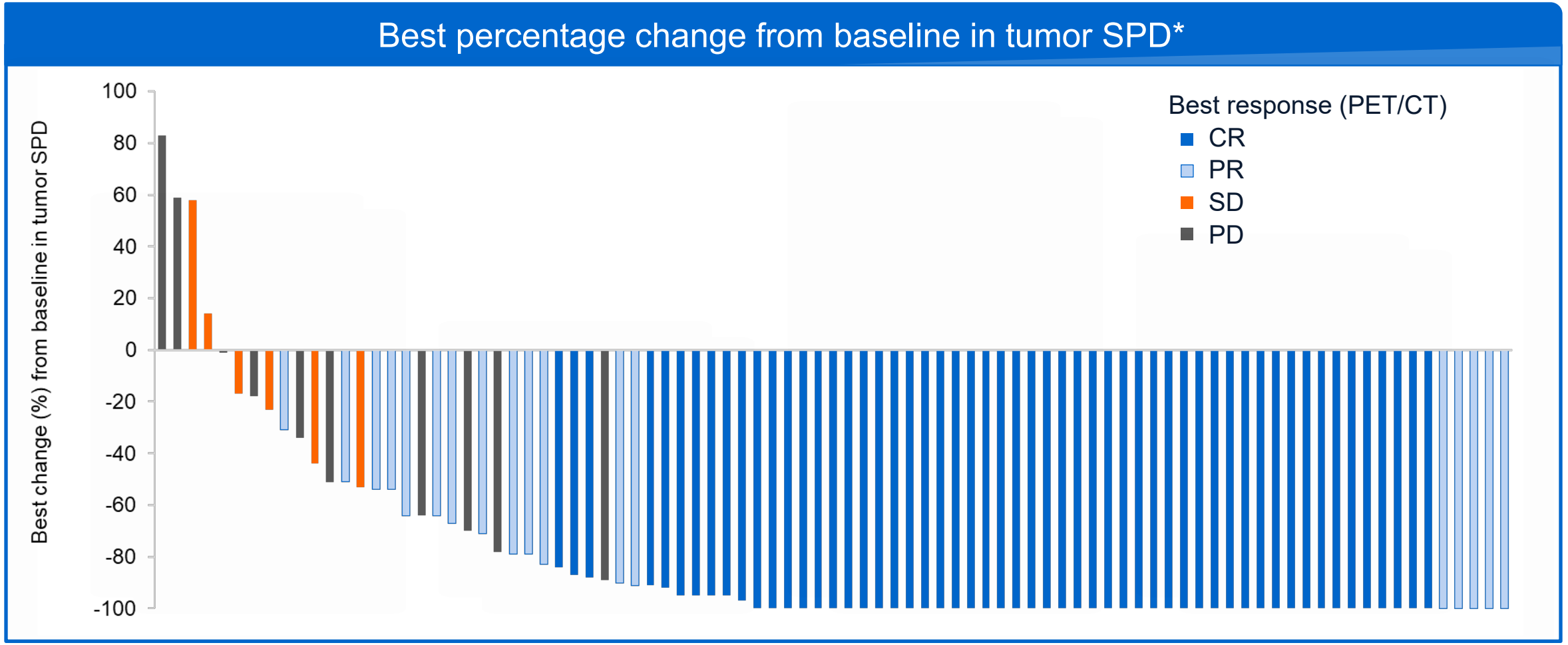
Efficacy endpoint[1]	IRF N (%) [95% CI]	Investigator N (%) [95% CI]	Concordance IRF vs investigator
CR	**54 (60%)** [49%, 70%]	54 (60%) [49%, 70%]	93%
ORR	**72 (80%)** [70%, 88%]	70 (78%) [68%, 86%]	96%

- **60% CR rate significantly greater (p<0.0001)* than 14% historical control CR rate[2]**

*exact binomial test with two-sided alpha level of 5%; CI, confidence interval

1. Cheson et al. J Clin Oncol 2007;25:579–86
2. Dreyling et al. J Clin Oncol 2017;35:3898–905
Budde E, et al. Blood 2021; 138: 127-130

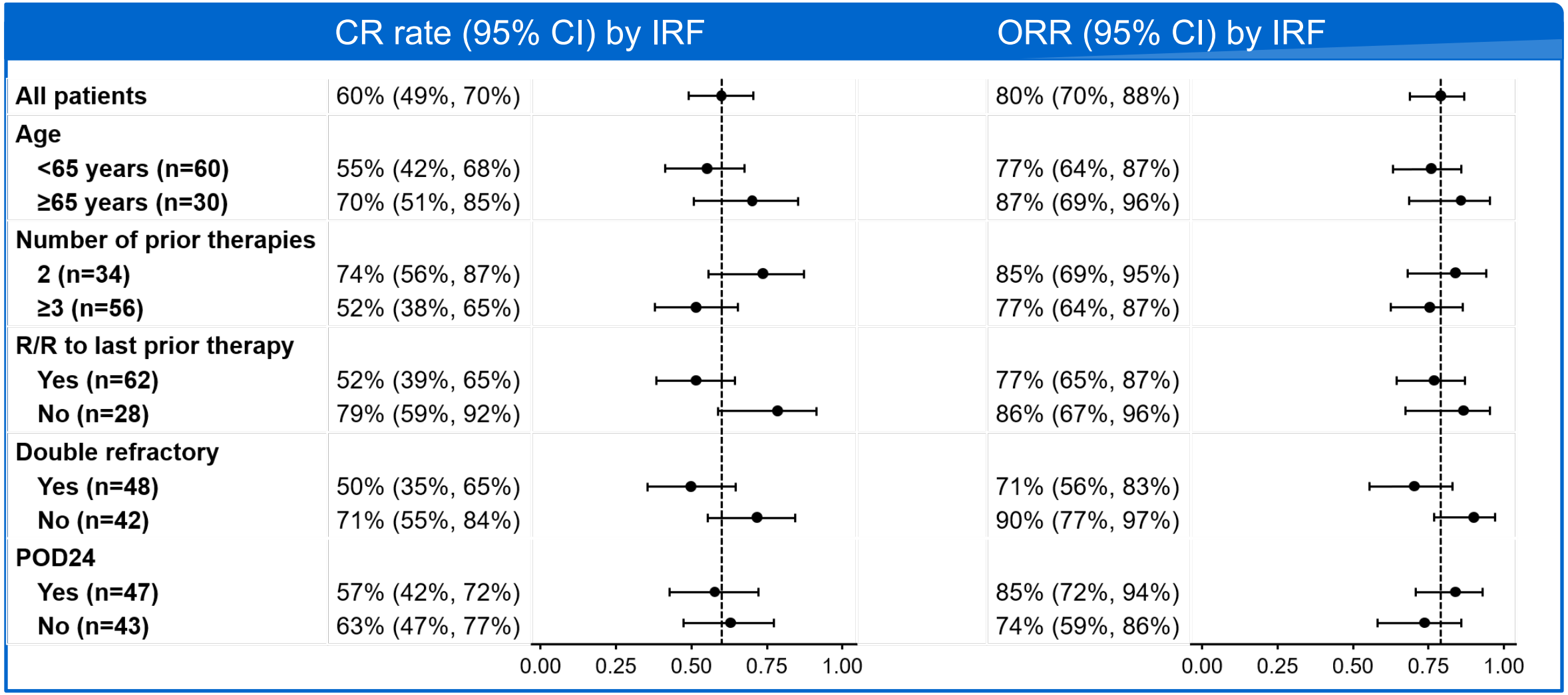
Tumor Shrinkage Effect (Waterfall plot)



*in all patients with a baseline and ≥1 post-baseline SPD available; PD, progressive disease; SPD, sum of product diameters

Budde E, et al. Blood 2021; 138: 127-130

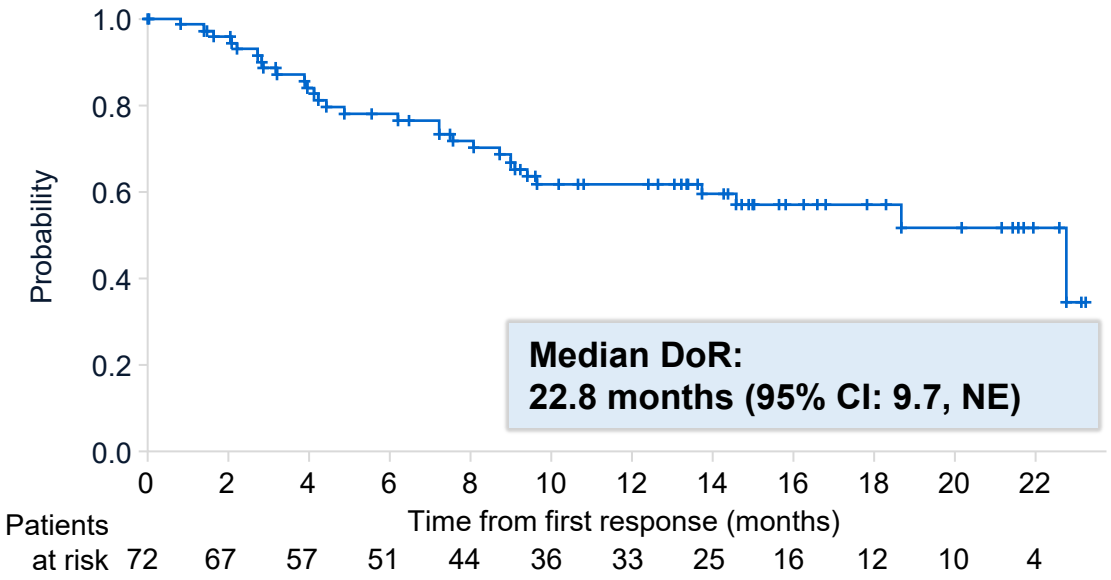
Subgroup Analysis of CRR and ORR in High-risk Populations



Budde LE, et al. Lancet Oncol. 2022; 23（8）:1055-1065.

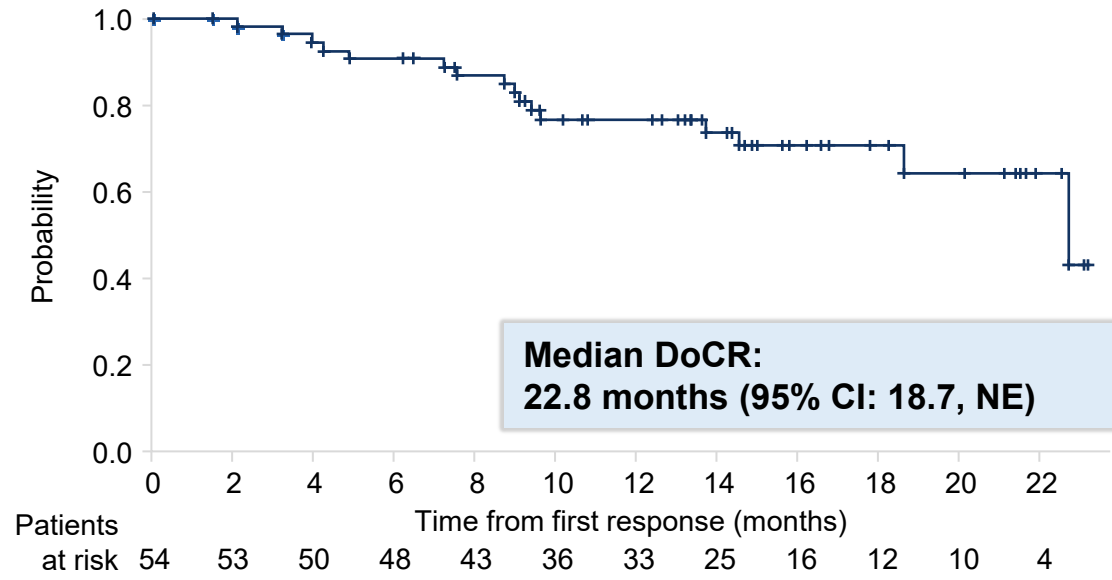
Duration of Response

Duration of response in responders



Median time to first response, mo (range)	1.4 (1.1, 8.9)
12-month event-free rate, % (95% CI)	62% (50%, 74%)
18-month event-free rate, % (95% CI)	57% (44%, 70%)

Duration of response in complete responders



Median time to first CR, mo (range)	3.0 (1.1, 18.9)
12-month event-free rate, % (95% CI)	76% (65%, 88%)
18-month event-free rate, % (95% CI)	70% (57%, 84%)

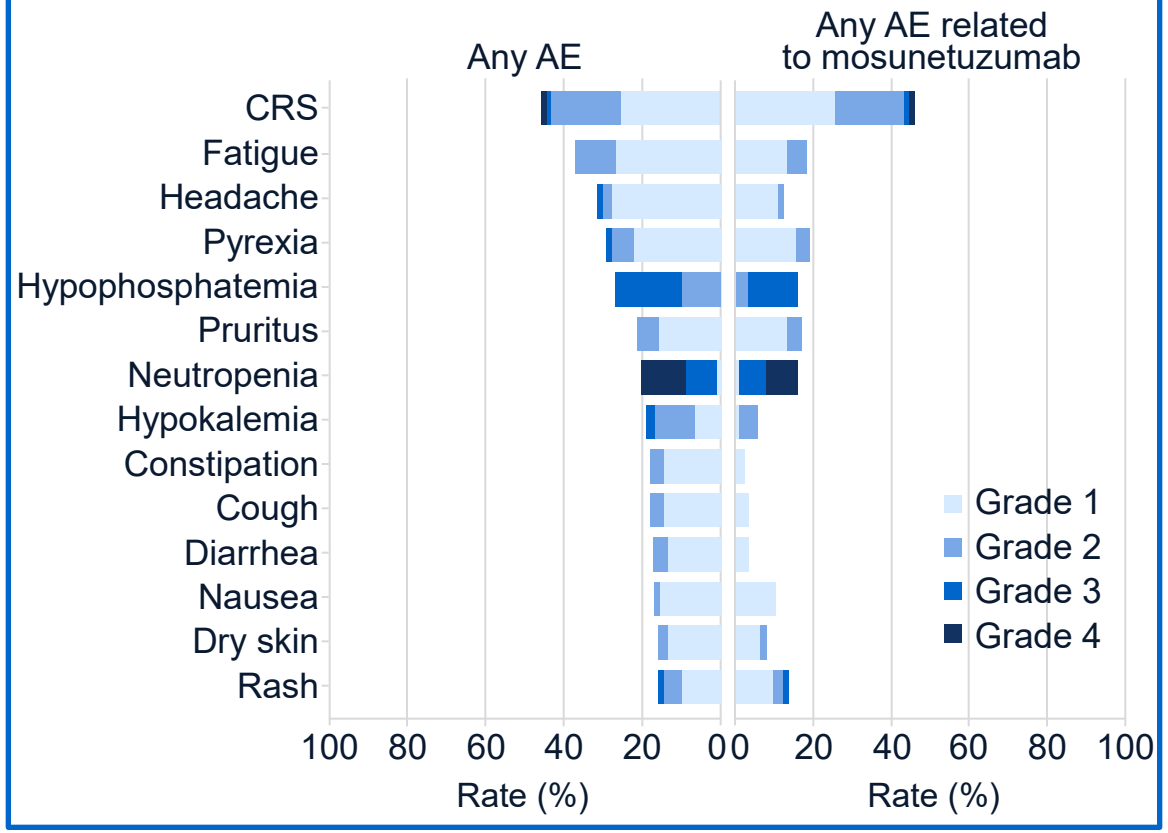
DoRC, duration of response in complete responders; mo, month; NE, not estimable

Budde E, et al. Blood 2021; 138: 127-130

Safety Overview

N (%)	N=90
AE Mosunetuzumab related*	90 (100%) 83 (92.2%)
Grade 3–4 AE Mosunetuzumab related*	63 (70.0%) 46 (51.1%)
Serious AE Mosunetuzumab related*	42 (46.7%) 30 (33.3%)
Grade 5 (fatal) AE Mosunetuzumab related*	2 (2.2%)† 0
AE leading to discontinuation of treatment Mosunetuzumab related*	4 (4.4%)‡ 2 (2.2%)‡

AEs (≥15%) by Gr and relationship with mosunetuzumab



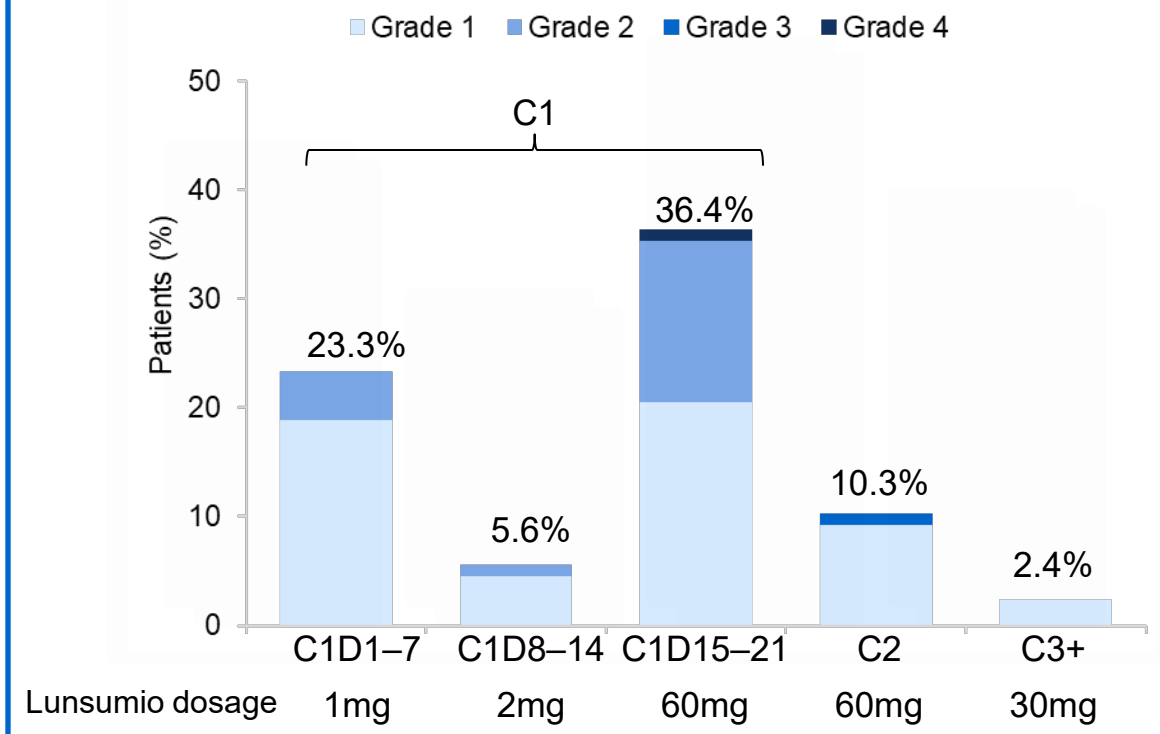
*AE considered related to treatment by the investigator; †mosunetuzumab unrelated: malignant neoplasm progression and unexplained death (1 patient each); ‡mosunetuzumab related: CRS (2 patients); mosunetuzumab unrelated: Esptein-Barr viremia and Hodgkin's disease (1 patient each); AE, adverse event; Gr, Grade

Budde E, et al. Blood 2021; 138: 127-130

Incidence of CRS (Cytokine Release Syndrome)

N (%)	N=90
CRS (全Grade)*	40 (44.4%)
Grade 1	23 (25.6%)
Grade 2	15 (16.7%)
Grade 3	1 (1.1%)
Grade 4	1 (1.1%)†
Median time to onset, hours (range)	
C1D1	5.2 (1.2–23.7)
C1D15	26.6 (0.1–390.9)
Duration until recovery, days (range)	3 (1–29)
Treatment at onset (Corticosteroids)	10 (11.1%)
Treatment at onset (Tocilizumab)	7 (7.8%)

Incidence by Cycle and Grade



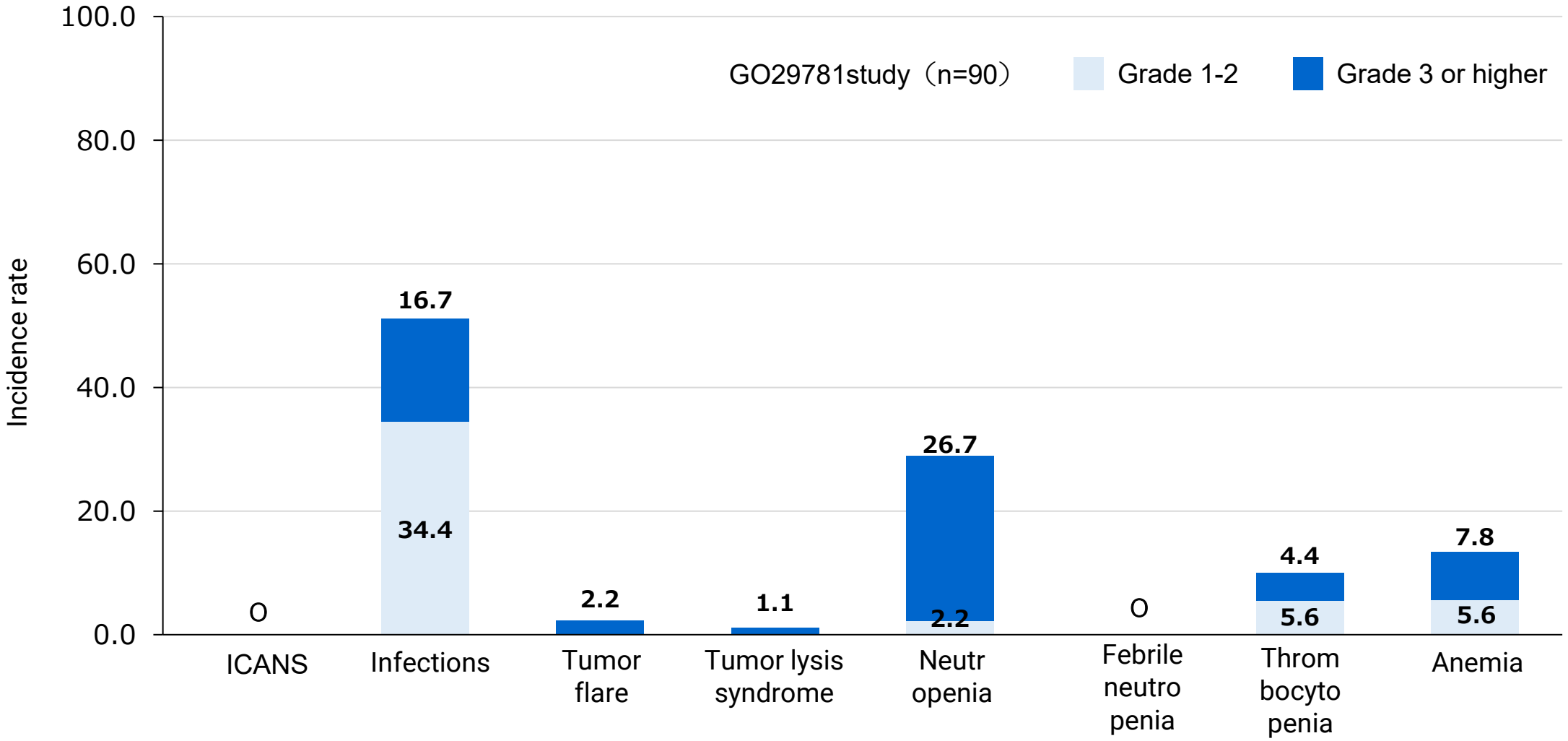
- **CRS was primarily Grade 1-2 and occurred in Cycle 1 (all cases recovered)**

* Evaluated using ASTCT criteria1; † FL case with leukemic transformation

Budde E, et al. Blood 2021; 138: 127-130

1. Lee et al. Biol Blood Marrow Transplant 2019;25:625–38

Other Adverse Effects Requiring Attention

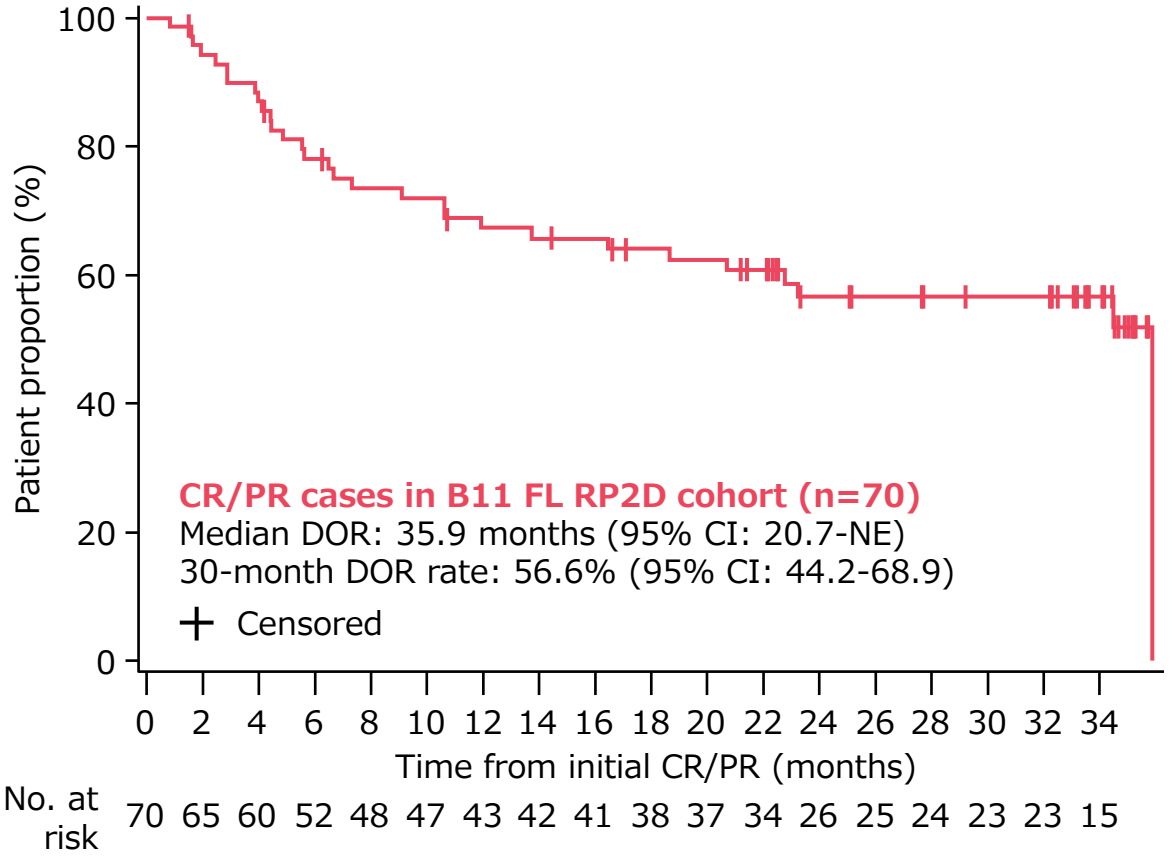


ICANS: Immune Effector Cell-Associated Neurotoxicity Syndrome

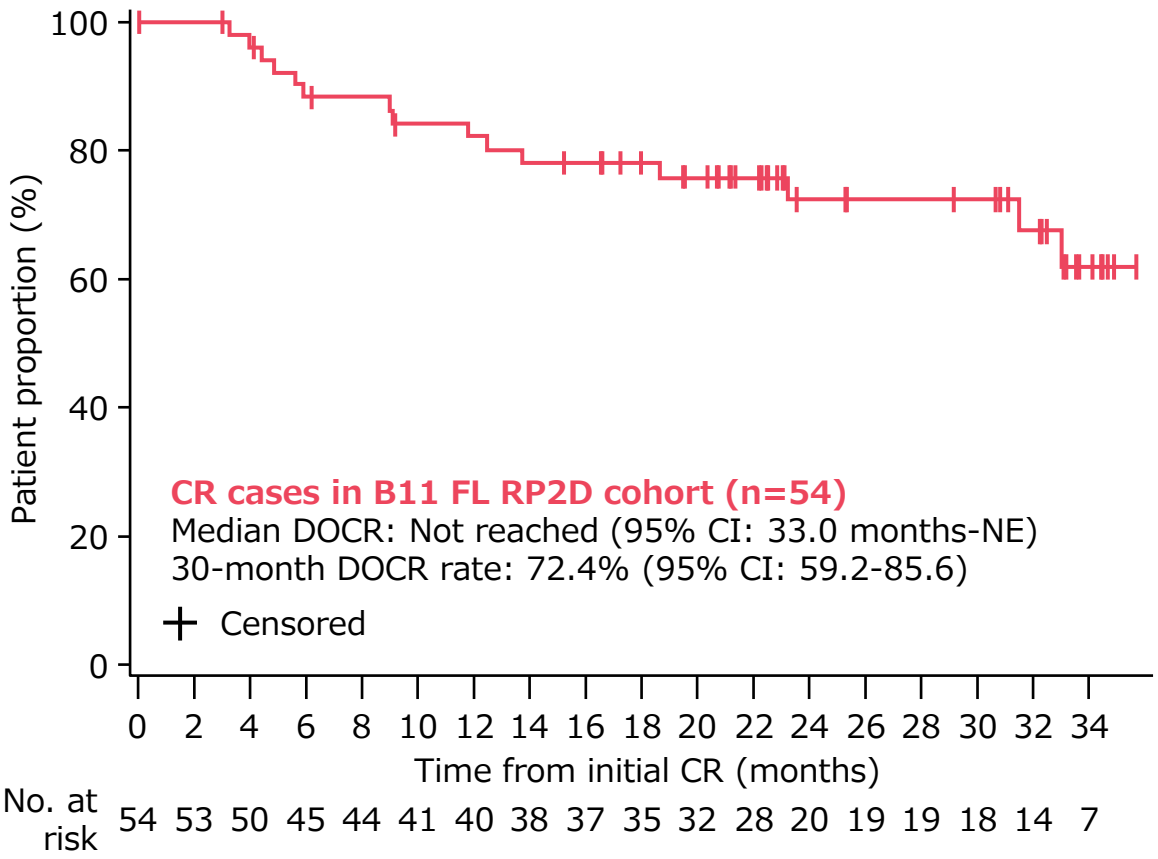
Approval evaluation data: overseas Phase I/II (GO29781)

Mosunetuzumab in R/R FL; 3-year Follow-up Data

DOR



DOCR

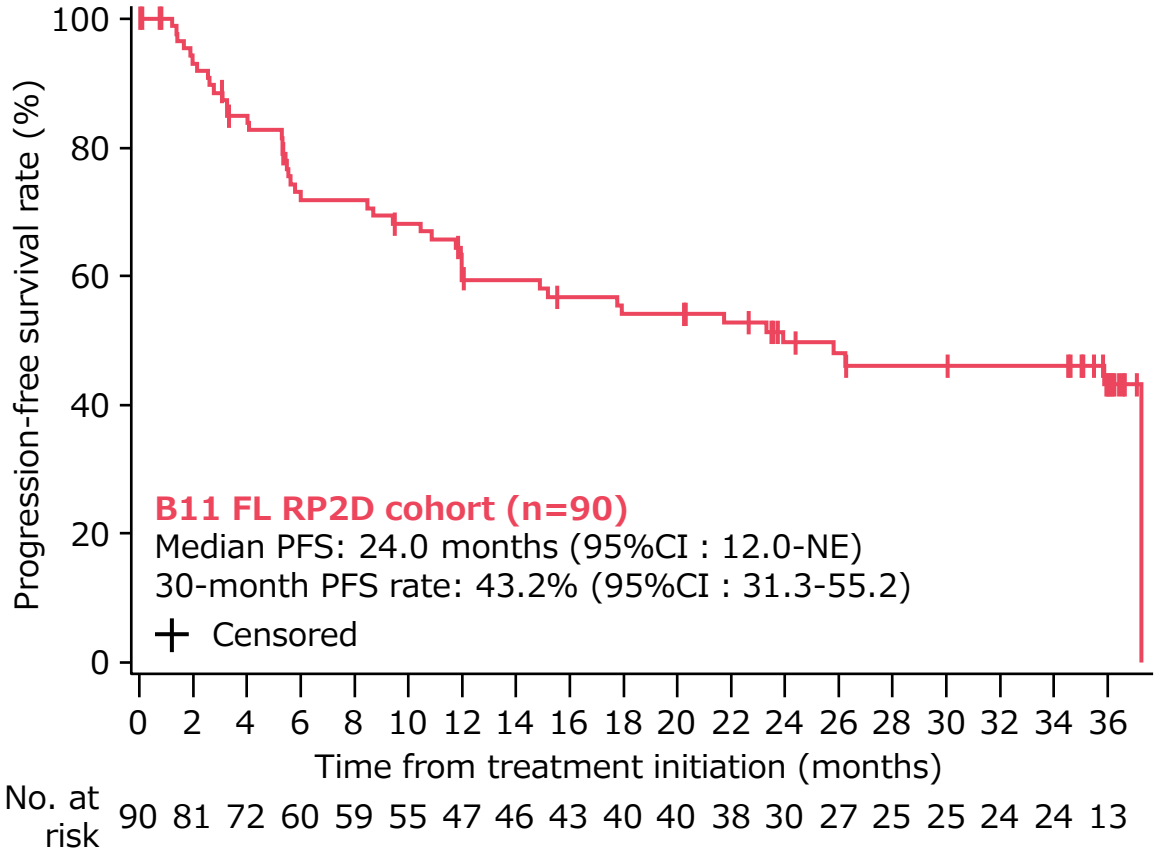


At additional analysis (data cutoff date: May 2, 2023),
Median observation period: 37.4 months (range: 2-48)

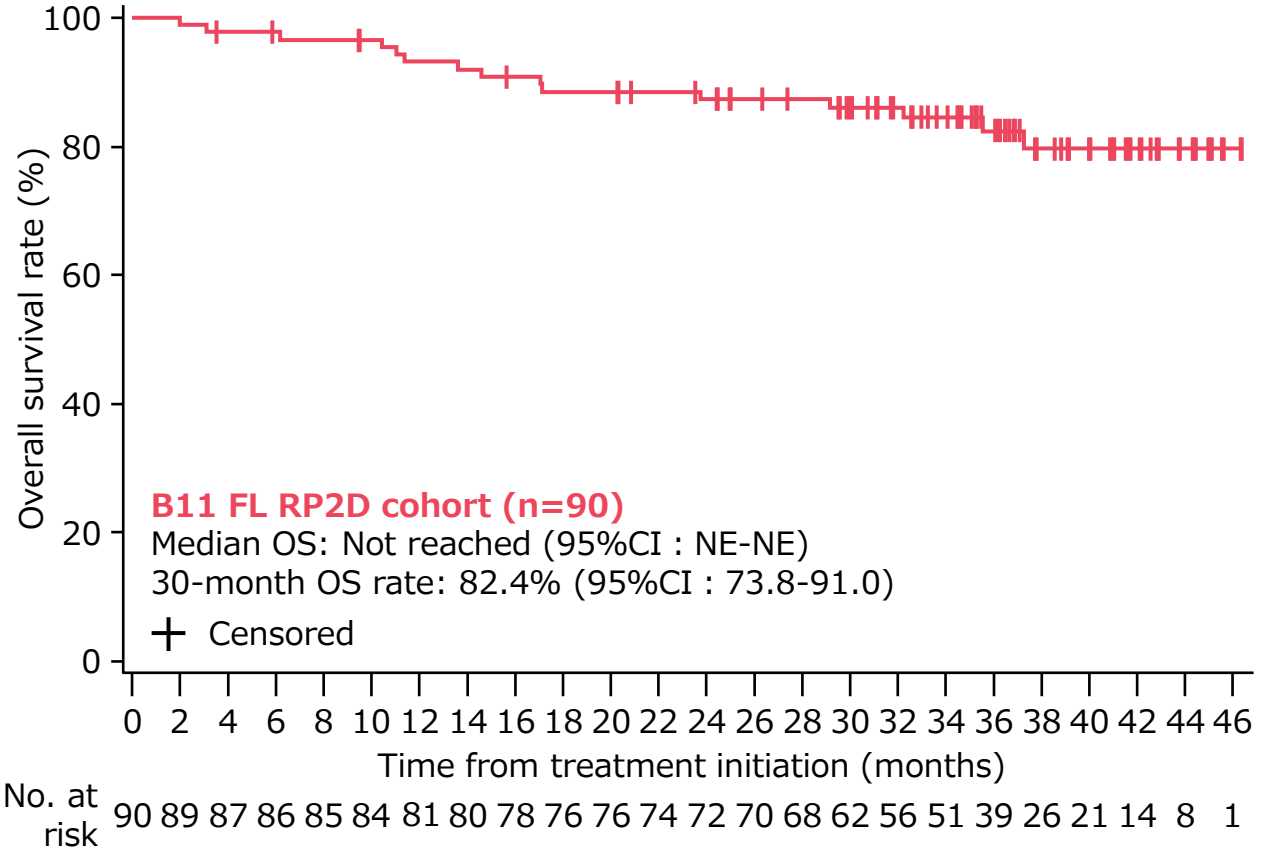
Sehn LH, et al. Blood. 2025; 145(7):708-719
This study was conducted with support from F. Hoffmann-La Roche Ltd. and Genentech, Inc.
This publication includes authors who are employees of F. Hoffmann-La Roche Ltd. and Genentech, Inc., or who received funding from these companies.

Mosunetuzumab in R/R FL; 3-year Follow-up Data

PFS



OS



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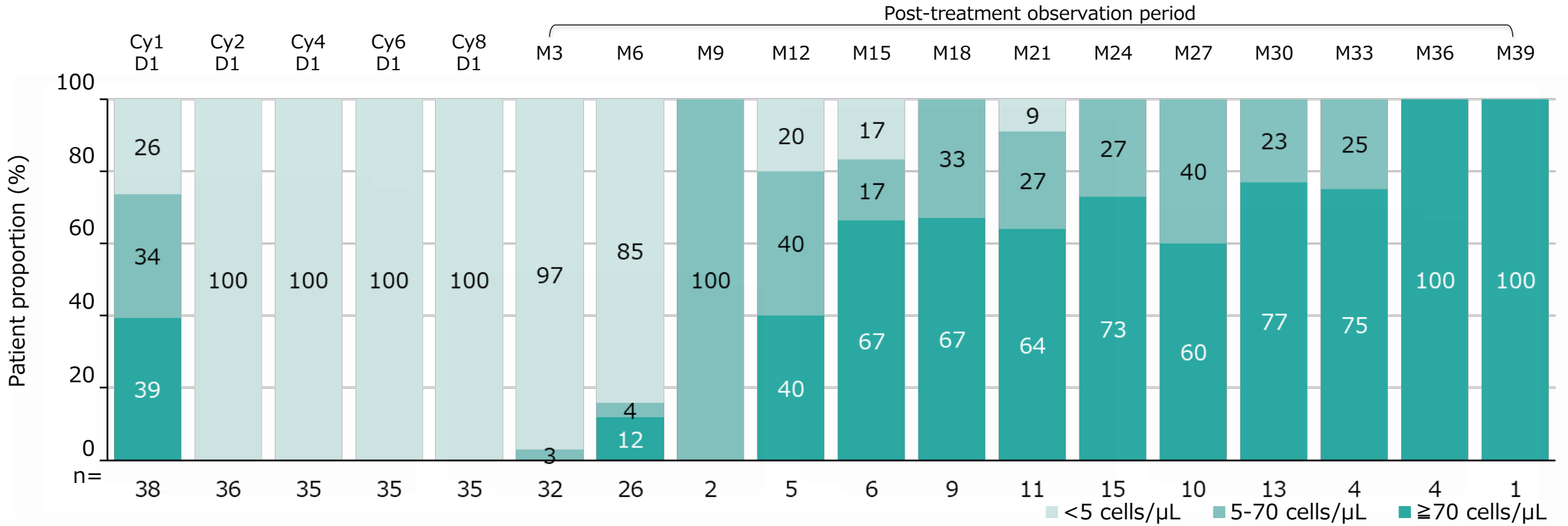
B-Cell Depletion and Recovery (GO29781 Trial: 3-Year Follow-up Data)

Peripheral blood B-cell depletion (<5 cells/μL) was observed in all patients with CR by the start of Cycle 2.

The median time to B-cell recovery (≥5 cells/μL) was 18.4 months after completing Cycle 8 (95% CI: 12.8–25.0). The median time to recovery to the lower limit of normal (≥70 cells/μL) was 25.1 months after completing Cycle 8 (95% CI: 19.0–NE).

CD19-Positive B-Cell Dynamics in Patients with CR



Additional analysis (data cutoff: May 2, 2023)
Median follow-up: 37.4 months (range: 2–48 months)

Sehn LH, et al. Blood. 2024: blood. 2024025454. [Conflict of interest: This study was supported by F. Hoffmann-La Roche and Genentech. The authors includes employees of and researchers funded by F. Hoffmann-La Roche, Genentech.]

Japanese Phase I Study (FLMOON-1 [JO40295 Expansion Cohort])

【Purpose】 To evaluate the efficacy and safety of Lunsumio monotherapy in patients with relapsed or refractory follicular lymphoma.

【Participants】 19 patients with relapsed or refractory FL who have received two or more prior systemic therapy
(ITT population, efficacy and safety analysis set: 19 patients)

【Methods】 Lunsumio was administered 1 mg on day 1, 2 mg on day 8, and 60 mg on day 15 of the first cycle, and 60 mg on day 1 of the second cycle. From the third cycle onwards, 30 mg was administered on day 1.
One cycle was defined as 3 weeks, and treatment was continued for up to 8 cycles.
At the end of 8 cycles, patients who achieved CR discontinued treatment, and patients who achieved PR/SD continued treatment for up to a total of 17 cycles.

Patients with relapsed or refractory FL (n=19)

Main inclusion criteria:
- Histologically confirmed CD20-positive, Grade 1-3A
- 18 years of age or older
- ECOG PS 0-1
- Treatment history of 2 or more regimens of systemic lymphoma therapy including anti-CD20 targeted therapy and alkylating agents

In case of CR, treatment is discontinued; in case of PR/SD, treatment is continued up to 17 cycles

Cycle (3 weeks)	1			2	3			8						17
	Day 1	Day 8	Day 15	Day 1	Day 1			Day 1						Day 1
Lunsumio dosage	1mg	2mg	60mg	60mg	30mg			30mg						30mg

Step doses → Loading doses → Base doses

Premedication: Administered before each dose
- Adequate hydration (starting 1-2 days before) (mandatory for cycle 1, continue for cycle 2 and beyond if high risk of tumor lysis syndrome)
- Corticosteroid (1 hour before): Dexamethasone 20mg (IV) or Methylprednisolone 80mg (IV) (mandatory for cycles 1 and 2, as needed for cycle 3 and beyond)
- Antipyretic analgesic (0.5-1 hour before): Acetaminophen 500-1,000mg (PO) (as needed)
- Antihistamine (0.5-1 hour before): Diphenhydramine hydrochloride 50-100mg (PO) (as needed)

Approval evaluation data: Japanese Phase I study (JO40295), Goto H, et al. Int J Clin Oncol. 2024.
This study was conducted with support from Chugai Pharmaceutical Co., Ltd. This publication includes authors who are employees of Chugai Pharmaceutical Co., Ltd. and F. Hoffmann-La Roche Ltd., as well as authors who received funding from Chugai Pharmaceutical Co., Ltd.

Japanese Phase I Study (FLMOON-1 [JO40295 Expansion Cohort])

【Evaluation Items】

Primary Endpoint: Complete Response Rate (CRR) [assessed by Independent Review Facility (IRF)]

Secondary Endpoints: CRR [investigator assessment], Overall Response Rate (ORR) [IRF assessment, investigator assessment],Duration of Response (DOR) [IRF assessment, investigator assessment], Duration of Complete Response (DOCR) [IRF assessment, investigator assessment],Progression-Free Survival (PFS) [IRF assessment, investigator assessment], Overall Survival (OS), etc.

【Analysis Plan】

Treatment effects for each evaluation item were assessed using the revised response criteria for malignant lymphoma.
For the primary endpoint of CRR (IRF assessment), a historical control of 14% CRR was set based on a foreign phase II clinical trial of copanlisib monotherapy (not approved in Japan) in patients with relapsed or refractory FL[1)]. The threshold CRR was set at 14%. The null hypothesis that CRR is less than 14% would be rejected if the lower limit of the 90% CI for CRR (IRF assessment) exceeded the threshold CRR of 14%. The sample size was determined to ensure a power of 94.4% at a one-sided significance level of 5%, with an expected CRR of 46.9%.
The 90% CI for CRR was calculated using the Clopper-Pearson method.
The 95% CI for CRR (investigator assessment), a secondary endpoint, was also calculated using the Clopper-Pearson method.
DOR, DOCR, PFS, and OS were estimated using the Kaplan-Meier method, and the 95% CI for the median was calculated using the Brookmeyer-Crowley method. The 6-month DOR, DOCR, PFS, and OS rates were estimated, and their 95% CIs were calculated using Greenwood's formula.
Subgroup analyses for CRR (IRF assessment) and ORR (IRF assessment) were pre-specified for age, sex, ECOG PS, bulky disease, FLIPI, number of prior treatment regimens, history of R² therapy, history of CAR-T cell therapy, refractoriness to most recent therapy, refractoriness to anti-CD20 antibody, refractoriness to alkylating agents, double refractory status, and POD24.

1) Dreyling M, et al. J Clin Oncol. 2017; 35(35): 3898-3905. [Conflict of interest: The authors includes researchers funded by F. Hoffmann-La Roche.]

Approval evaluation data: Japanese Phase I study (JO40295), Goto H, et al. Int J Clin Oncol. 2024.

Baseline Patient Background

		N=19
Median age [range], years		72 (58–80)
Male		9 (47.4%)
ECOG PS	0	17 (89.5%)
	1	2 (10.5%)
Ann Arbor Classification	I–II	3 (15.8%)
	III–IV	16 (84.2%)

		N=19
Number of prior treatment regimens (range)		3 (2–5)
Types of prior treatments	Anti-CD20 antibody	19 (100%)
	Alkylating agent	19 (100%)
	PI3K inhibitor	17 (18.9%)
	IMiD	1 (5.3%)
	CAR-T	1 (5.3%)
History of prior treatment with autologous stem cell transplantation		0 (0.0%)
Refractory to most recent treatment		9 (47.4%)
Refractory to any anti-CD antibody		8 (42.1%)
Refractory to anti-CD20 antibody and alkylating agent (double refractory)		8 (42.1%)
POD24		5 (26.3%)

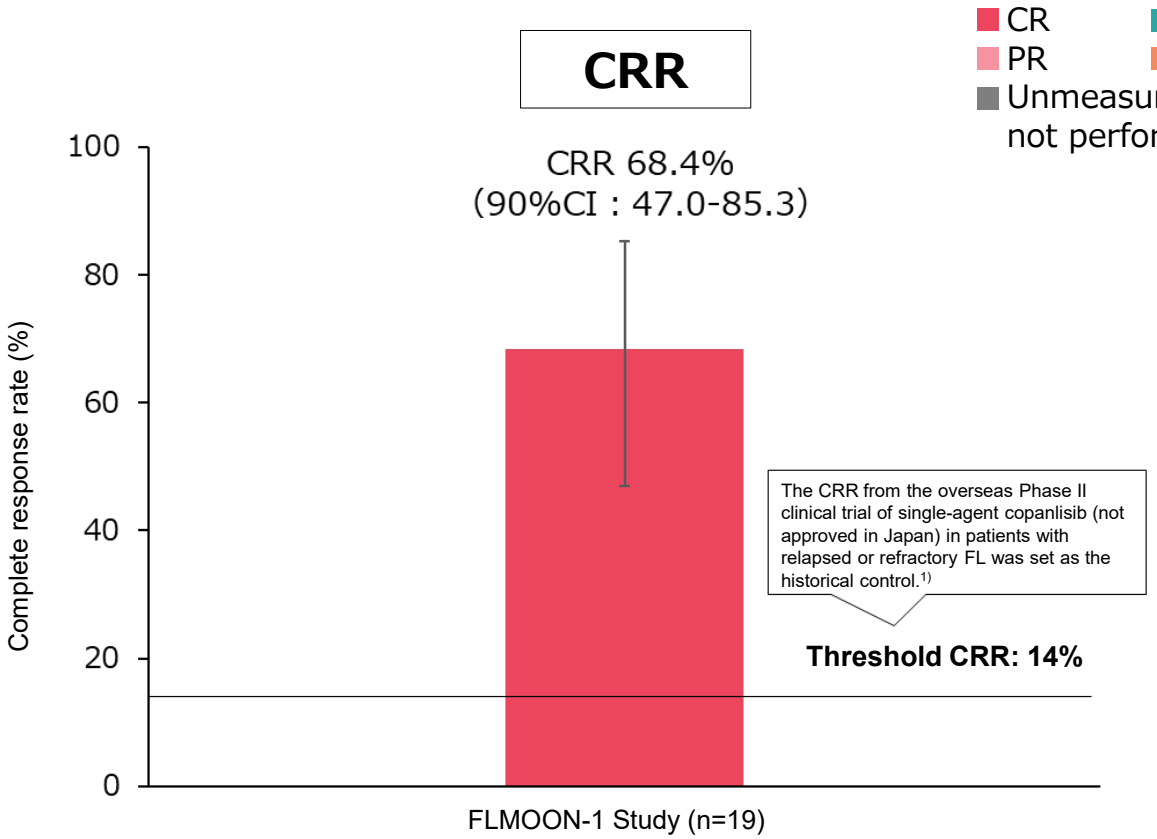
SPD: Sum of Product of Diameters

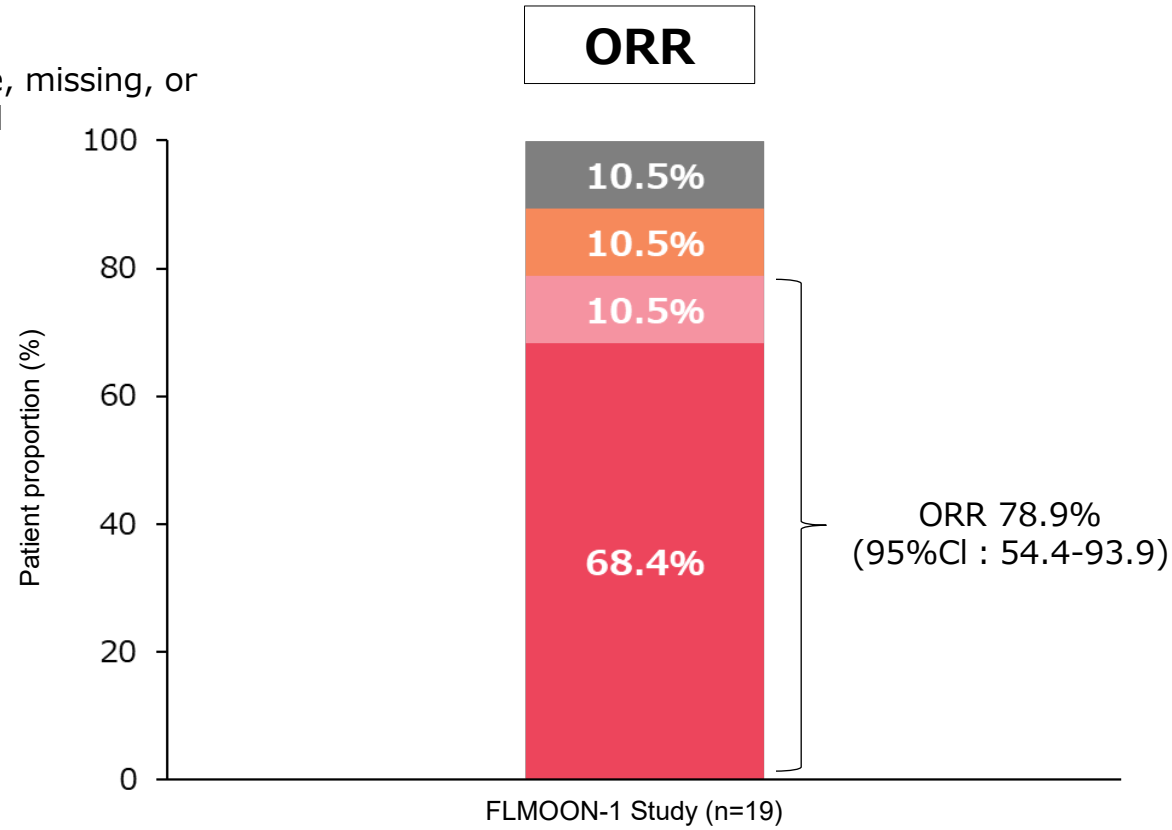
At the time of primary analysis (data cutoff: October 13, 2023)
Median follow-up: 7.95 months (range: 0.1–17.1 months)

Approval evaluation data: Japanese Phase I study (JO40295), Goto H, et al. Int J Clin Oncol. 2024.

CRR (IRF assessment, primary endpoint) / ORR (IRF assessment, secondary endpoint)

In the FLMOON-1 Trial, the CRR (IRF assessment) was 68.4% (90% CI: 47.0–85.3), with the lower limit of the 90% CI exceeding the threshold CRR (14%). The ORR (IRF assessment) was 78.9% (95% CI: 54.4–93.9).





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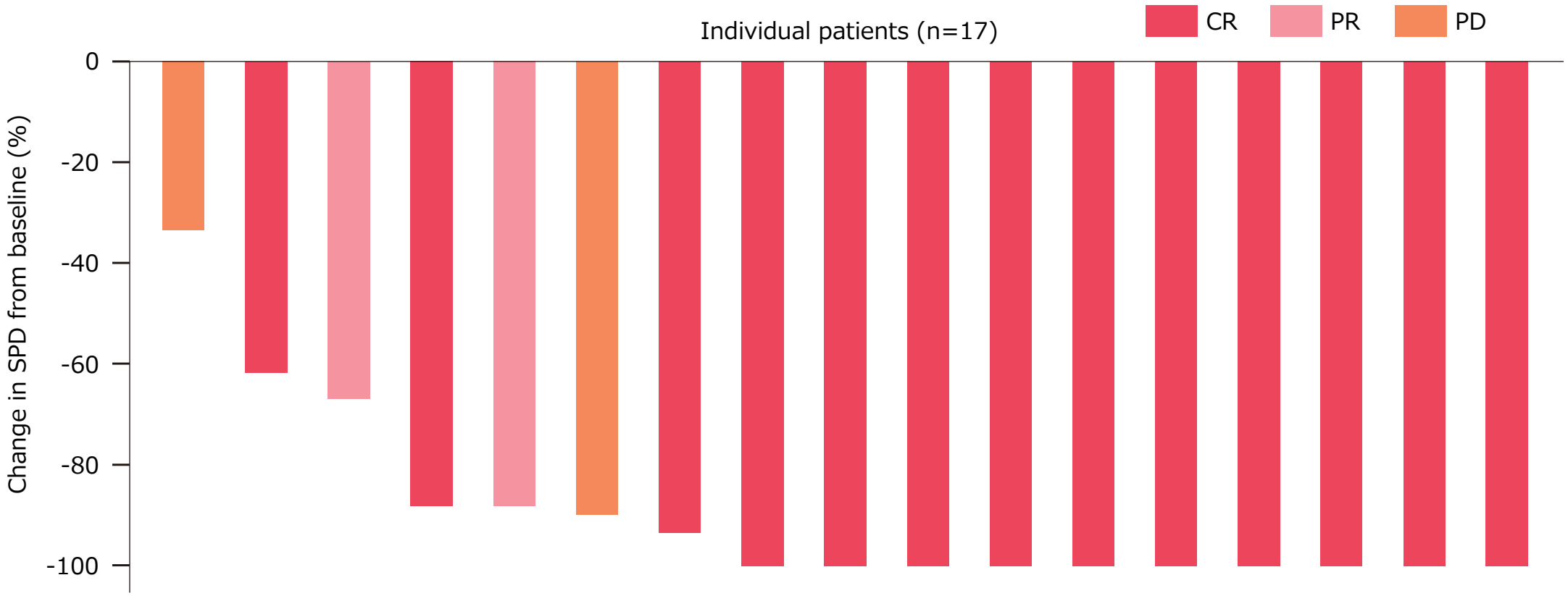
1) Dreyling M, et al. J Clin Oncol. 2017; 35(35): 3898-3905. [Conflict of interest: The authors includes researchers funded by F. Hoffmann-La Roche.]
Approval evaluation data: Japanese Phase I study (JO40295), Goto H, et al. Int J Clin Oncol. 2024.

Tumor Shrinkage Effect (Waterfall plot)

Tumor shrinkage was observed in all 17 patients* (100%) with available post-treatment imaging evaluations.

*Excluding 2 patients who had no tumor evaluation after baseline and no efficacy assessment.



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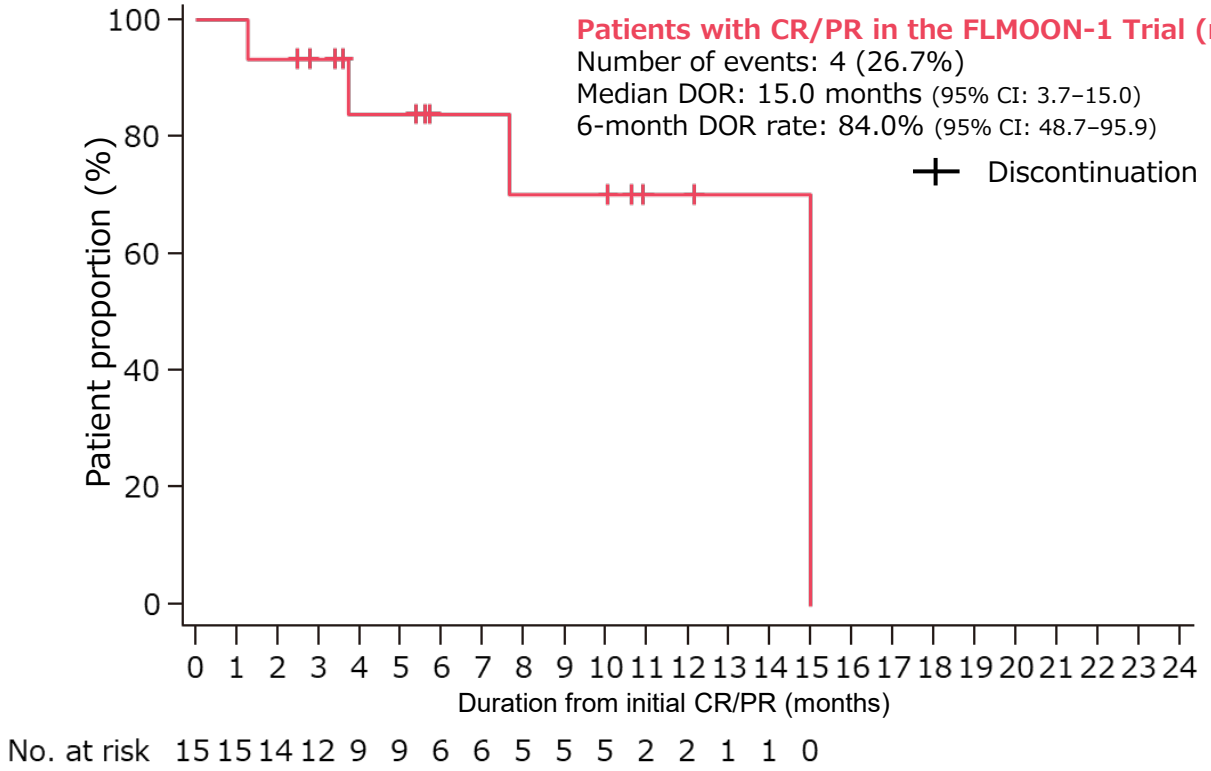
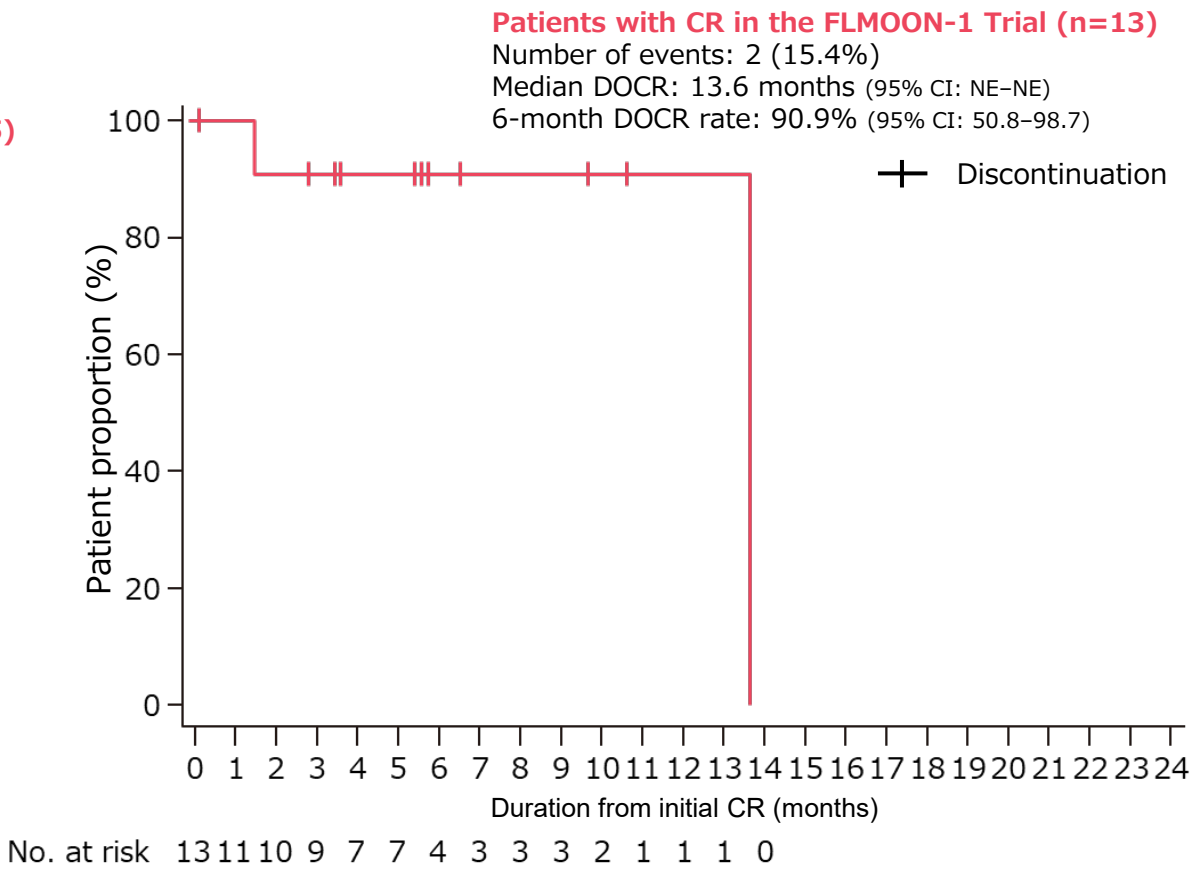
Median follow-up: 7.95 months (range: 0.1–17.1 months)

Approval evaluation data: Japanese Phase I study (JO40295), Goto H, et al. Int J Clin Oncol. 2024.

DOR (IRF assessment, secondary endpoint) / DOCR (IRF assessment, secondary endpoint)

In the FLMOON-1 Trial, the median DOR (IRF assessment) was 15.0 months (95% CI: 3.7–15.0), and the 6-month DOR rate was 84.0% (95% CI: 48.7–95.9). The median DOCR (IRF assessment) was 13.6 months (95% CI: NE–NE), and the 6-month DOCR rate was 90.9% (95% CI: 50.8–98.7).





At the time of primary analysis (data cutoff: October 13, 2023)
Median follow-up: 7.95 months (range: 0.1–17.1 months)

Approval evaluation data: Japanese Phase I study (JO40295), Goto H, et al. Int J Clin Oncol. 2024.

Main Adverse Events (≥15%)

	FLMOON-1 Trial (n=19)	
	All grades	Grade 3 or higher
Number of subjects with adverse events	18 (94.7%)	17 (89.5%)
Lymphocyte count decreased	13 (68.4%)	13 (68.4%)
Cytokine release syndrome (CRS)	9 (47.4%)	1 (5.3%)
AST increased	6 (31.6%)	2 (10.5%)
ALT increased	6 (31.6%)	2 (10.5%)
Neutrophil count decreased	5 (26.3%)	5 (26.3%)
Rash	5 (26.3%)	0
Infusion-related reaction	4 (21.1%)	2 (10.5%)
Hyperglycemia	4 (21.1%)	2 (10.5%)
Constipation	4 (21.1%)	0
Pruritus	4 (21.1%)	0
White blood cell count decreased	3 (15.8%)	3 (15.8%)
Blood bilirubin increased	3 (15.8%)	1 (5.3%)
Erythema multiforme	3 (15.8%)	1 (5.3%)
Nausea	3 (15.8%)	0
Herpes zoster	3 (15.8%)	0

At the time of primary analysis (data cutoff: October 13, 2023)
Median follow-up: 7.95 months (range: 0.1–17.1 months)

MedDRA ver. 20.1、CTCAE ver.4.03

Approval evaluation data: Japanese Phase I study (JO40295), Goto H, et al. Int J Clin Oncol. 2024.

Serious Adverse Events

	FLMOON-1 Trial (n=19)
Serious Adverse Event	7 (36.8%)
Cytokine release syndrome (CRS)	2 (10.5%)
Pneumonia viral	1 (5.3%)
Hepatic function abnormal	1 (5.3%)
Pancreatitis acute	1 (5.3%)
Small cell lung cancer	1 (5.3%)
Neurotoxicity (ICANS)*	1 (5.3%)
Erythema multiforme	1 (5.3%)

MedDRA ver. 20.1
*Although reported as neurotoxicity based on MedDRA ver. 20.1 at the time of reporting, the physician-reported event name was ICANS, so it is categorized as ICANS.

At the time of primary analysis (data cutoff: October 13, 2023)
Median follow-up: 7.95 months (range: 0.1–17.1 months)

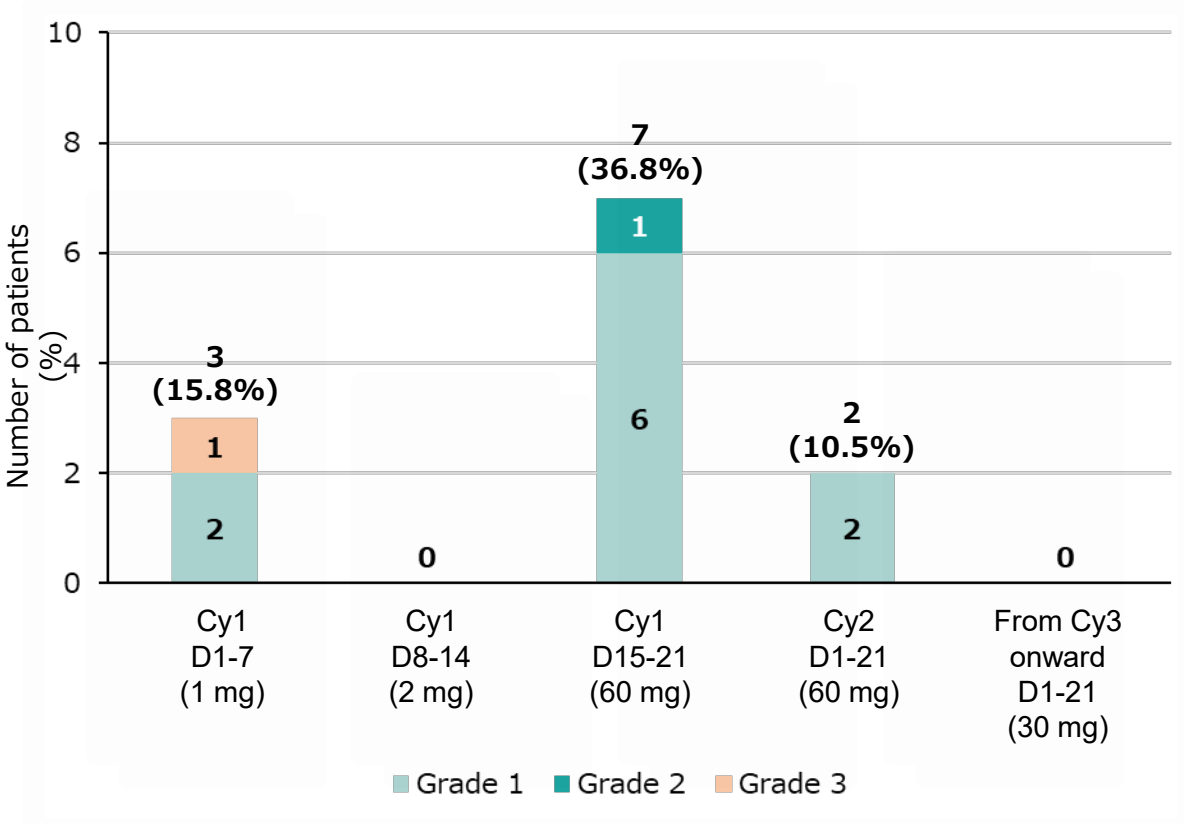
Approval evaluation data: Japanese Phase I study (JO40295), Goto H, et al. Int J Clin Oncol. 2024.

CRS Occurrence (Cytokine Release Syndrome)

In the FLMOON-1 Trial, CRS* was observed in 9/19 patients (47.4%), with 1 case (5.3%) being Grade 3 or higher, and 2 cases (10.5%) were considered serious. The median time to first occurrence of CRS was 16 days (range: 1 to 17 days). The median time to recovery from CRS was 4 days (range: 2 to 9 days).

	FLMOON-1 Trial (n=19)
CRS	9 (47.4%)
Grade 3 or higher CRS	1 (5.3%)
Serious CRS	2 (10.5%)
CRS leading to discontinuation	0
CRS leading to interruption	1 (5.3%)
Time to first occurrence Median [range], days	16 [1-17]
Time to recovery Median [range], days	4 [2-9]

*Includes events categorized under MedDRA PT as "cytokine release syndrome," "cytokine storm," "shock," "macrophage activation," "hemophagocytic lymphohistiocytosis," "capillary leak syndrome," "capillary permeability increased," "cytokine abnormal," and "cytokine test."
The grade of adverse events is in accordance with the consensus of the American Society for Transplantation and Cellular Therapy (ASTCT).



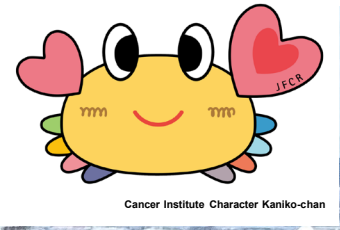
At the time of primary analysis (data cutoff: October 13, 2023)
Median follow-up: 7.95 months (range: 0.1–17.1 months)

Approved evaluation data: Japanese Phase I study (JO40295)

Summary: Relapsed Follicular Lymphoma and Expectations for Lunsumio

- Multiple new treatments are being developed for relapsed/refractory FL, but the treatment outcomes worsen with each subsequent line of therapy.
- Lunsumio, as an anti-CD20/CD3 bispecific antibody, was approved for the first time in Japan for 3L+ relapsed/refractory FL (grade 1–3A) (approved on December 27, 2024).
- Although it involves a fixed treatment duration, long-term durable responses were shown, regardless of the presence of POD24* events, and toxicity was manageable.
- Lunsumio is one of the promising treatment option for 3L+ relapsed/refractory FL.

Thank you for your attention.



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INNOVATION BEYOND IMAGINATION

CHUGAI PHARMACEUTICAL

A member of the Roche group