


Kompetenznetz
Maligne Lymphome

Lymphom
Kompetenz
KOMPAKT



**KML-Expert:innen berichten vom
EHA2022 HYBRID**



Prof. Dr. med. Martin Dreyling

Medizinische Klinik III | Klinikum der Universität München

Folikuläres Lymphom (FL)

Offenlegung potentieller Interessenskonflikte

LymphomKompetenz KOMPAKT – EHA 2022 wird in Kooperation mit sechs unterstützenden Firmen durchgeführt.
Meine persönlichen Disclosures betreffen:

Research Support (institution)	Abbvie, Bayer, BMS/Celgene, Gilead/Kite, Janssen, Roche
Employee	-
Major Stockholder	-
Speakers Bureau	-
Speakers Honoraria	Amgen, Astra Zeneca, Bayer, BMS/Celgene, Gilead/Kite, Incyte, Janssen, Novartis, Roche
Scientific Advisory Board	Astra Zeneca, Bayer, Beigene, BMS/Celgene, Genmab, Gilead/Kite, Incyte, Janssen, Lilly/Loxo, Morphosys, Novartis, Roche

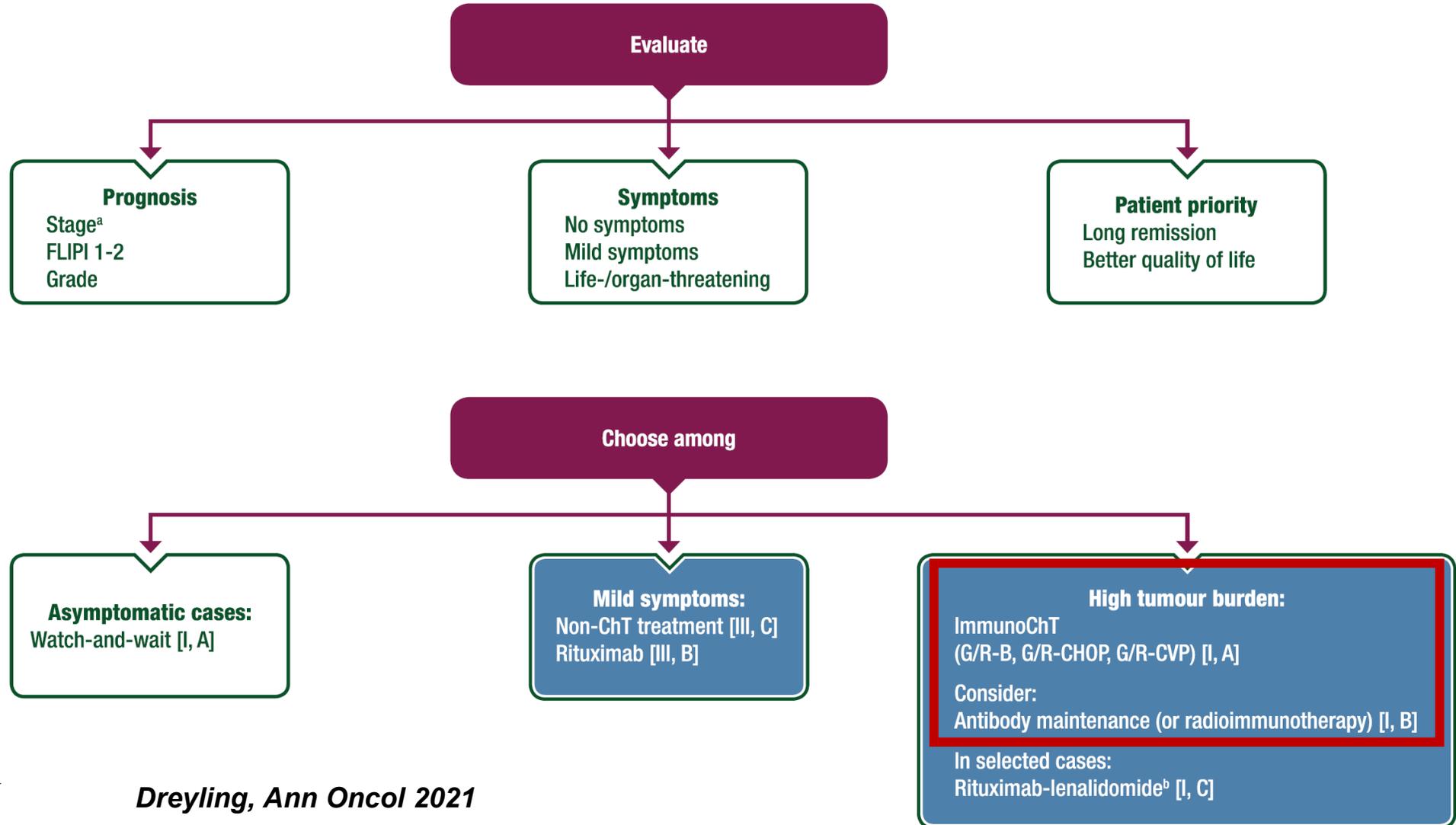
Kapitel 1

Follikuläres Lymphom

Erstlinientherapie

Follicular lymphoma

ESMO/EHA therapeutic algorithm



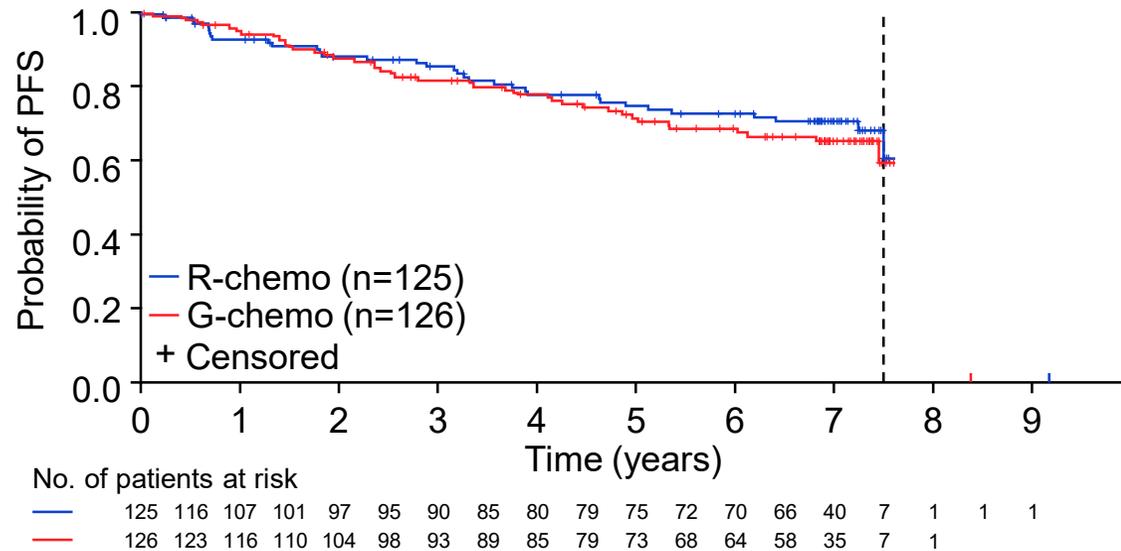
Obinutuzumab plus chemotherapy demonstrates long-term benefit over rituximab plus chemotherapy in patients with previously untreated follicular lymphoma: final analysis of the GALLIUM study

William Townsend,¹ Wolfgang Hiddemann,² Christian Buske,³ Guillaume Cartron,⁴ David Cunningham,⁵ Martin JS Dyer,⁶ John G Gribben,⁷ Elizabeth Phillips,⁸ Martin Dreyling,² John F Seymour,⁹ Andrew Grigg,¹⁰ Judith Trotman,¹¹ Tong-Yu Lin,¹² Xiao-Nan Hong,¹³ Dirk Kingbiel,¹⁴ Tina G Nielsen,¹⁴ Andrea Knapp,¹⁴ Michael Herold,¹⁵ Robert Marcus¹⁶

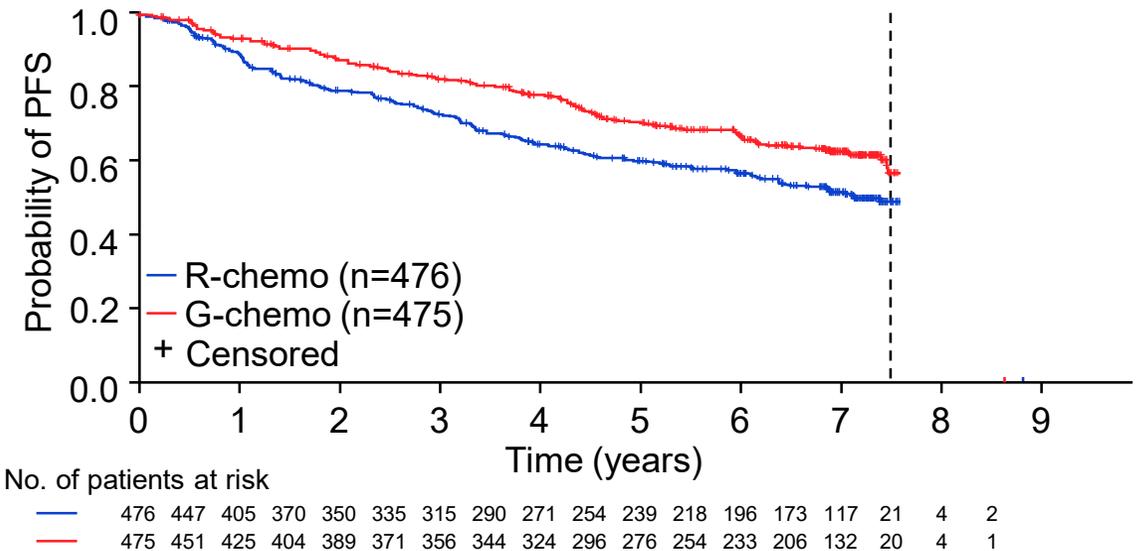
¹Cancer Research UK and UCL Cancer Trials Centre, University College Hospitals London, London, United Kingdom; ²Ludwig-Maximilians-University Hospital Munich, Munich, Germany; ³Universitätsklinikum Ulm, Ulm, Germany; ⁴CHU Montpellier, Montpellier, France; ⁵Royal Marsden Hospital, Sutton, United Kingdom; ⁶Ernest and Helen Scott Haematological Research Institute, University of Leicester, Leicester, United Kingdom; ⁷Queen Mary, University of London, St Bartholomew's Hospital, London, United Kingdom; ⁸University of Manchester, The Christie Hospital and National Institutes of Health Research Manchester Biomedical Research Centre, Manchester, United Kingdom; ⁹Peter MacCallum Cancer Centre, the Royal Melbourne Hospital, and University of Melbourne, Melbourne, Australia; ¹⁰Austin Hospital, Austin, Australia; ¹¹Concord Repatriation General Hospital, University of Sydney, Concord, Australia; ¹²Sun Yat-Sen University Cancer Centre, State Key Laboratory of Oncology in South China, and Collaborative Innovation Centre for Cancer Medicine, Guangzhou, China; ¹³Fudan University Shanghai Cancer Centre, Shanghai, China; ¹⁴F. Hoffmann-La Roche Ltd, Basel, Switzerland; ¹⁵HELIOS-Klinikum Erfurt, Erfurt, Germany; ¹⁶Kings College Hospital, London, United Kingdom

PFS was improved with G- vs R-chemo in the FLIPI 2–5 subgroup

Low risk (FLIPI 0–1)



Intermediate- and high-risk (FLIPI 2–5)



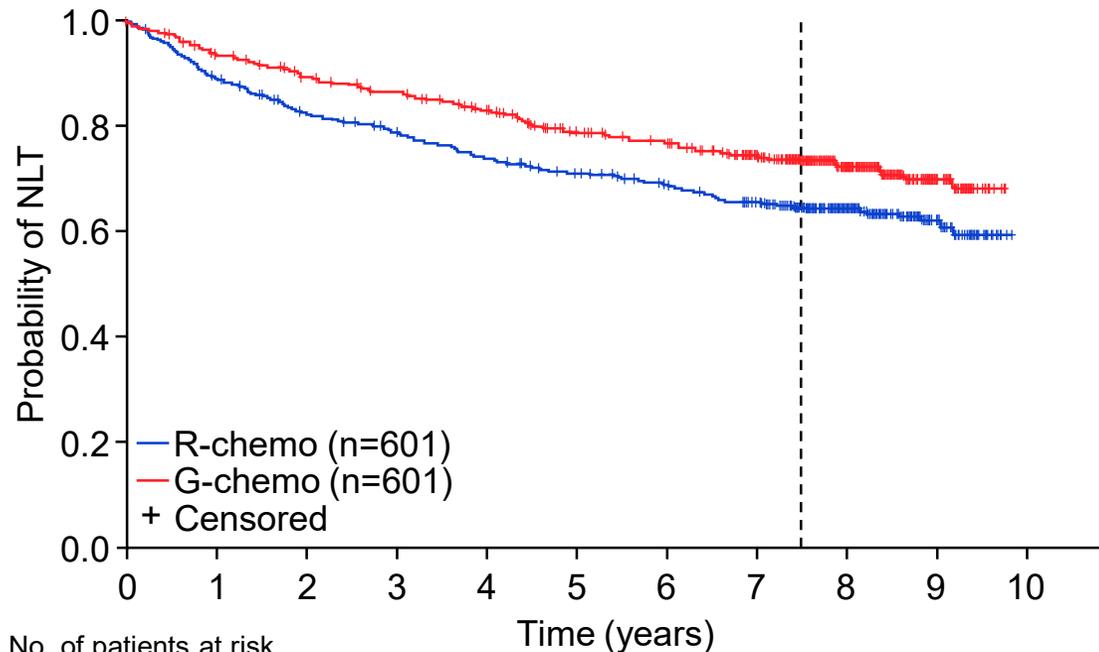
	G-chemo (n=126)	R-chemo (n=125)
7-year PFS, %	65.4	70.9
HR (95% CI)*	1.20 (0.75–1.90)	
P-value	0.45	

	G-chemo (n=475)	R-chemo (n=476)
7-year PFS, %	62.9	51.8
HR (95% CI)*	0.70 (0.57–0.86)	
P-value	<0.001	

*Stratified analysis

Fewer patients had started NLT at 7 years in the G- vs R-chemo arm

TTNLT by INV



TTNLT by INV	G-chemo (n=601)	R-chemo (n=601)
Patients with event, n (%)	160 (26.6)	209 (34.8)
Patients free from NLT at 7 years,* % (95% CI)	74.1 (70.3–77.5)	65.4 (61.4–69.2)
HR (95% CI) [†]	0.71 (0.58–0.87)	
P-value	0.001	

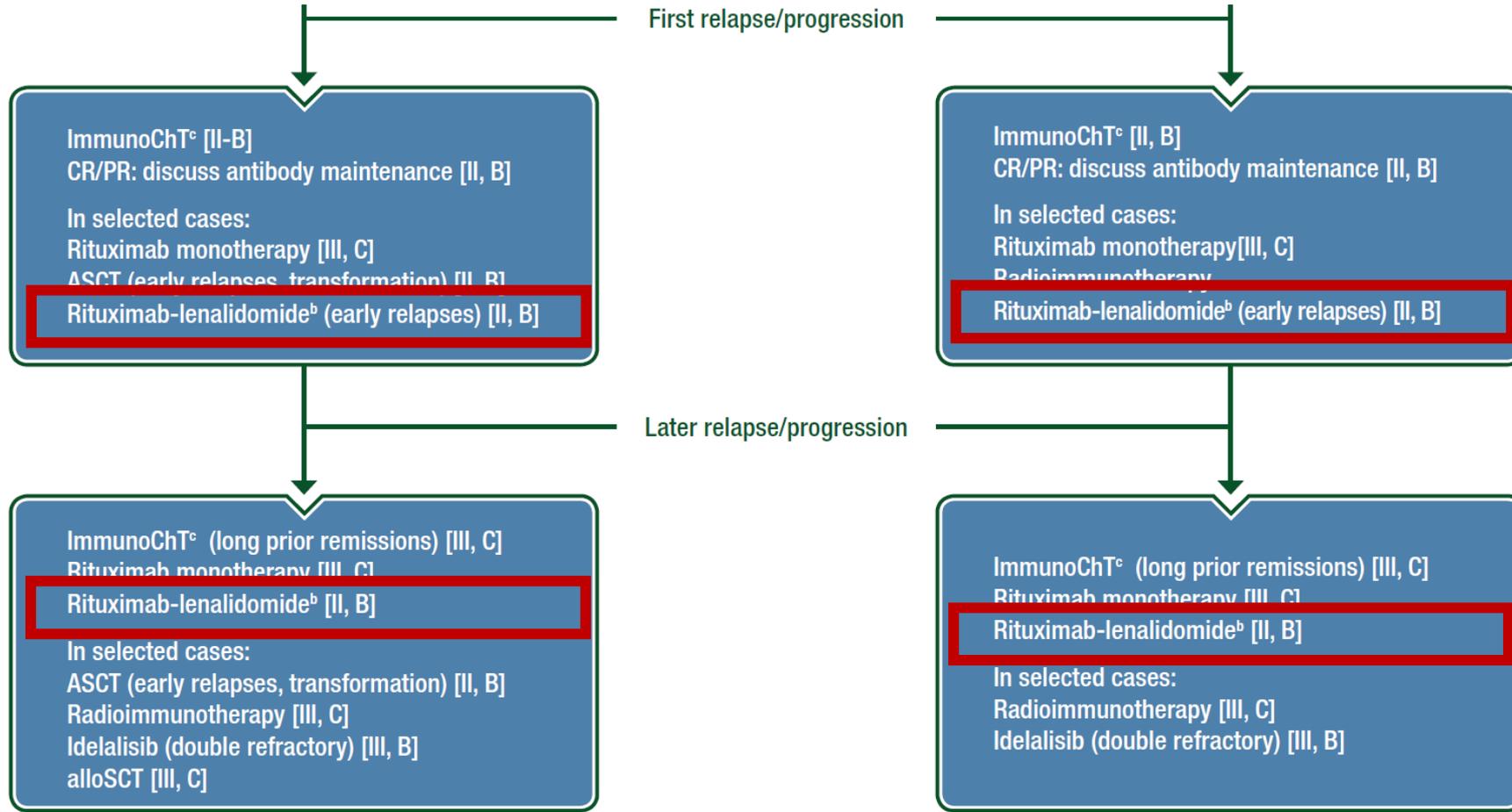
*Patients who were alive and had not started next treatment at 7 years; [†]Stratified analysis NLT, next lymphoma treatment

Kapitel 2

Follikuläres Lymphom **Rezidivtherapie**

Follicular lymphoma

ESMO/EHA therapeutic algorithm



Dreyling, Ann Oncol 2021 March

Abstract #S208

EFFICACY AND SAFETY OF ZANDELISIB ADMINISTERED BY INTERMITTENT DOSING (ID) IN PATIENTS WITH RELAPSED OR REFRACTORY (R/R) FOLLICULAR LYMPHOMA: PRIMARY ANALYSIS OF THE GLOBAL PHASE 2 STUDY TIDAL

Andrew D. Zelenetz¹, Wojciech Jurczak², Vincent Ribrag³, Kim Linton⁴, Graham P. Collins⁵, Javier Lopéz-Jiménez⁶, Nishitha Reddy⁷, Andrea Mengarelli⁸, Tycel Phillips⁹, Gerardo Musuraca¹⁰, Oonagh Sheehy¹¹, Joanne Li¹², Weiming Xu¹², Michel Azoulay¹³, Richard G. Ghalie¹², Pier Luigi Zinzani¹⁴

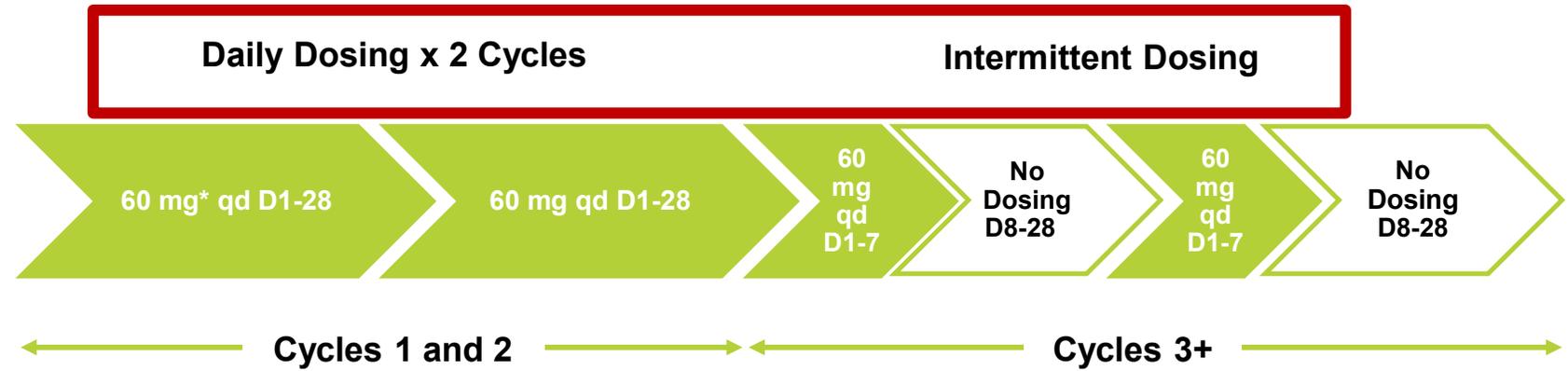
¹Memorial Sloan Kettering Cancer Center, NY, US; ²MSC National Research Cancer Institute, Krakow, Poland; ³Institut Gustave Roussy, Villejuif, France; ⁴Manchester Cancer Research Centre UK; ⁵GenesisCare, Oxford, UK; ⁶Hospital Universitario Ramon y Cajal, Madrid, Spain; ⁷Vanderbilt University, Nashville, US; ⁸Regina Elena National Cancer Institute, Roma, Italy; ⁹University of Michigan Health System, Ann Arbor, US; ¹⁰Istituto Scientifico Romagnolo per lo Studio e la Cura dei Tumori I.R.S.T., Meldola, Italy; ¹¹Belfast Health and Social Care Trust, Belfast, UK; ¹²MEI Pharma, Inc., San Diego, US; ¹³Kyowa Kirin, Princeton US; ¹⁴University of Bologna, Bologna, Italy

Study Design: Open-label, Phase 2 Study

Eligibility

- FL Grade I–IIIA
- PD after ≥ 2 prior therapies, including:
 - Anti-CD20 antibody
 - Alkylating agent
- No prior PI3K inhibitor

Dosing Schema in IS Arm



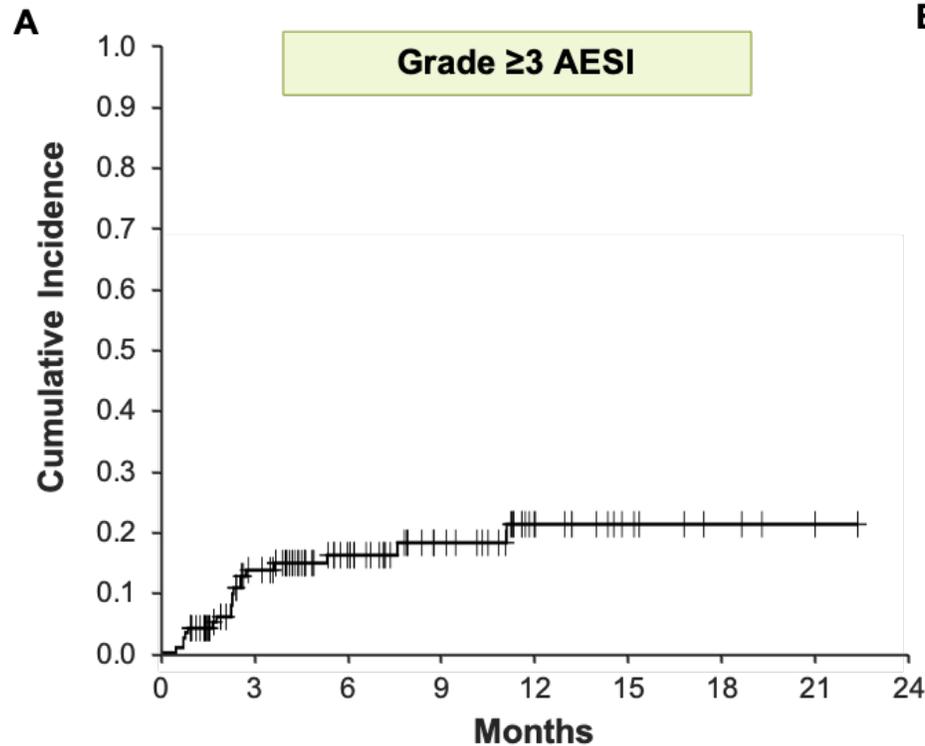
Design

- Continue zandelisib until PD or intolerance
- Initially, randomized trial of continuous daily dosing (CS arm) vs. daily for 2 cycles then ID (IS arm)
- CS arm closed after maturing data from Phase 1b study showed better tolerability and high rate of durable responses on IS

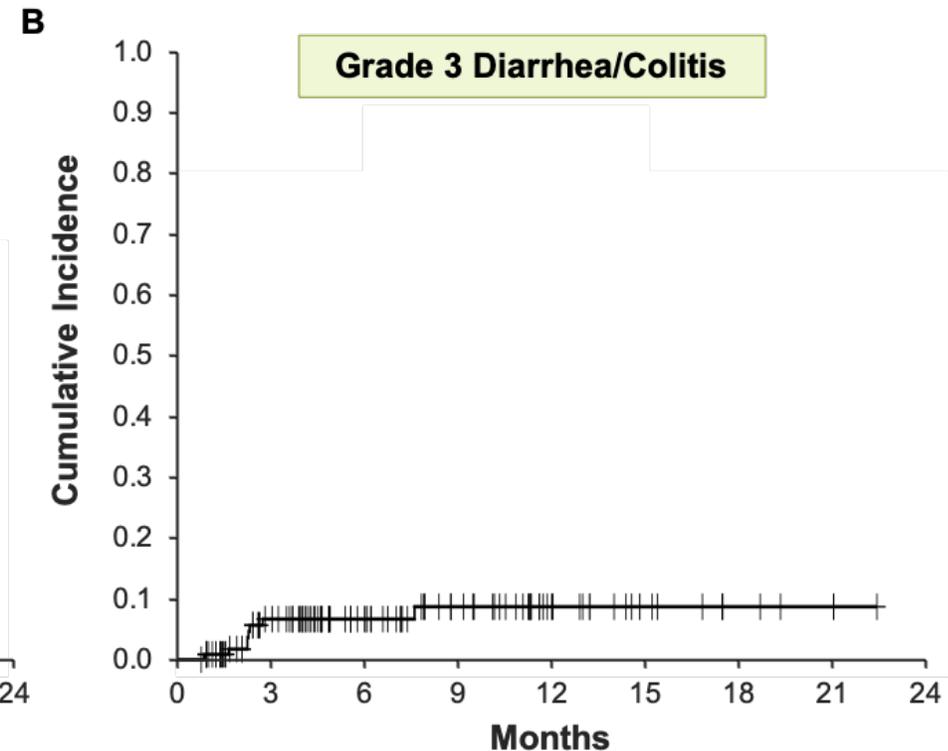
Clinicaltrials.gov Identifier: #NCT03768505

Time to Grade 3 AEsIs

Cumulative Incidence of (A) Grade ≥ 3 AEsI or (B) Grade 3 Diarrhea/Colitis



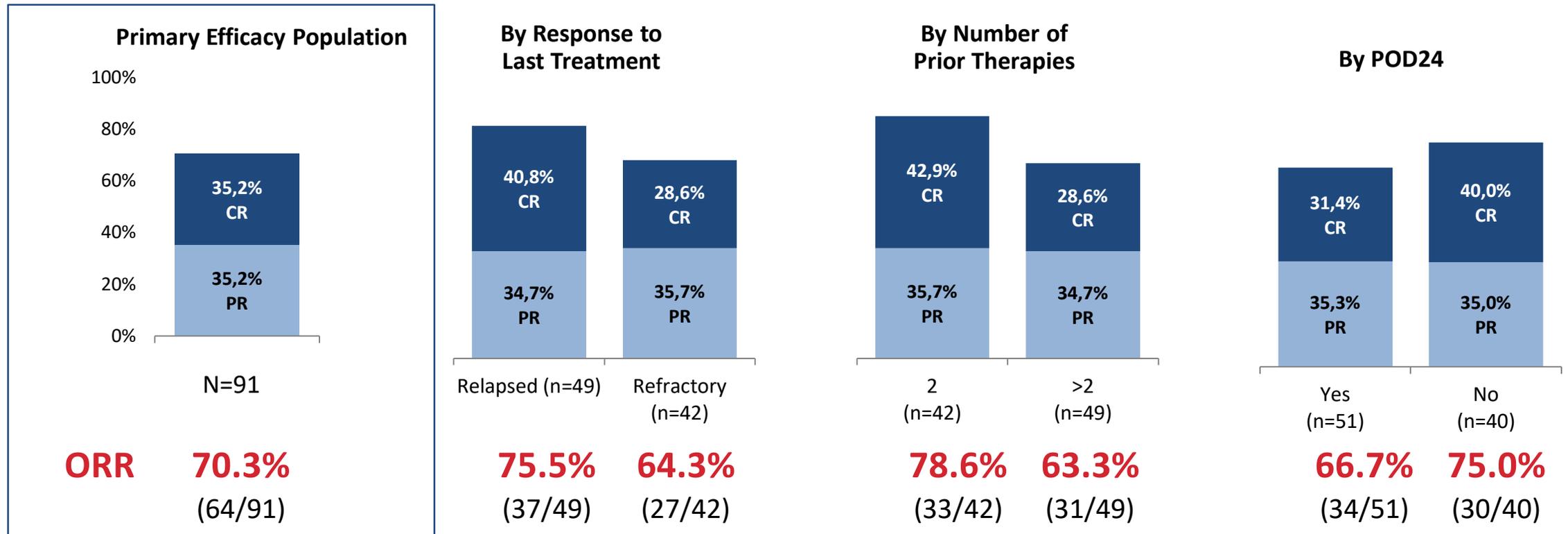
No. at risk: 121 84 54 34 17 8 4 2 0



No. at risk: 121 89 57 37 19 9 4 2 0

- Grade 3 AEsIs occurred primarily in Cycles 1-3

Overall Response Rates



- Responses occurred early:
 - 87.5% (n=56) of all responses at end of Cycle 2
 - 75.0% (n=24) of CRs at end of Cycle 4
- Disease control (CR+PR+SD): 85% (77/91)
- Follow-up is immature to accurately estimate DoR

Zanubrutinib plus obinutuzumab versus obinutuzumab monotherapy in patients with relapsed or refractory follicular lymphoma: primary analysis of the phase 2 randomized ROSEWOOD trial

Pier Luigi Zinzani, MD, PhD¹; Jiří Mayer, MD²; Rebecca Auer, MRCP, FRPath, PhD³; Fontanet Bijou, MD⁴; Ana C. de Oliveira, PhD⁵; Christopher R. Flowers, MD, MS, FASCO⁶; Michele Merli, MD⁷; Krimo Bouabdallah, MD⁸; Peter S. Ganly, BMBCh, PhD⁹; Roderick Johnson, MD¹⁰; Sam Yuen, MBBS, FRACP, FRCPA¹¹; Edwin Kingsley, MD¹²; Gayane Tumyan, DMSc, MD, PhD¹³; Sarit E. Assouline, MD, MSc, FRCPC¹⁴; Elena Ivanova, PhD¹⁵; Pil Kim, PhD¹⁶; Jane Huang, MD¹⁶; Richard Delarue, MD¹⁵; and Judith Trotman, MBChB, FRACP, FRCPA^{17,18}

¹Institute of Hematology "Seràgnoli", University of Bologna, Bologna, Italy; ²Department of Internal Medicine-Hematology and Oncology, Masaryk University and University Hospital, Brno, Czech Republic; ³St. Bartholomew's Hospital, Barts Health NHS Trust, London, United Kingdom; ⁴Institut Bergonié, Bordeaux, France; ⁵Institut Català d'Oncologia (ICO) Hospital Duran I Reynals, Hospital, Barcelona, Spain; ⁶Department of Lymphoma/Myeloma, MD Anderson Cancer Center, Houston, TX, USA; ⁷Hematology, University Hospital "Ospedale di Circolo e Fondazione Macchi" - ASST Sette Laghi, University of Insubria, Varese, Italy; ⁸Hôpital Haut-Lévêque, CHU Bordeaux, Pessac, France; ⁹Department of Haematology, Christchurch Hospital, Christchurch, New Zealand; ¹⁰St. James's University Hospital Trust, Leeds, United Kingdom; ¹¹Calvary Mater Newcastle, Waratah, NSW, Australia; ¹²Comprehensive Cancer Centers of Nevada, Las Vegas, NV, USA; ¹³Department of Chemotherapy of Hemoblastosis, Blokhin Russian Cancer Research Center, Moscow, Russian Federation; ¹⁴Jewish General Hospital, Montreal, Canada; ¹⁵BeiGene Switzerland GmbH, Basel, Switzerland; ¹⁶BeiGene (Beijing) Co., Ltd., Beijing, China and BeiGene USA, Inc., San Mateo, CA, USA; ¹⁷Concord Repatriation General Hospital, Concord, NSW, Australia; and ¹⁸Department of Haematology, University of Sydney, Concord, NSW, Australia

Saturday, June 4, 2022, 8:00 AM-11:00 AM CDT; 3:00 PM-4:30 PM
Hematologic Malignancies—Lymphoma and Chronic Lymphocytic Leukemia

TEAEs (Safety Analysis Set)

TEAE, %	Zanubrutinib plus obinutuzumab N=143		Obinutuzumab N=71	
	Any grade	Grade ≥3	Any grade	Grade ≥3
Patients with at least 1 TEAE	92.3	53.8	88.7	47.9
Thrombocytopenia or platelet count decreased	34.3	14.0	23.9	7.0
Neutrophil count decreased or neutropenia	27.3	22.4	25.4	19.7
Diarrhea	16.1	2.8	16.9	0.0
Fatigue	14.0	1.4	11.3	0.0
Constipation	13.3	0.0	7.0	0.0
Cough	11.9	0.0	11.3	0.0
Pyrexia	11.2	0.0	19.7	0.0
Dyspnea	10.5	1.4	9.9	0.0
Anemia	9.1	4.2	9.9	5.6
Nausea	8.4	0.0	12.7	0.0
Pruritus	7.0	0.0	9.9	0.0
Infusion-related reaction	2.8	0.7	9.9	4.2
TEAEs of special interest				
Atrial fibrillation and flutter	2.1	0.7	1.4	0.0
Hypertension	3.5	0.7	4.2	1.4
Hemorrhage	26.6	1.4	8.5	0.0
Major hemorrhage	1.4	1.4	1.4	0.0
Infections	47.6	18.9	36.6	12.7
Second primary malignancies	6.3	3.5	2.8	0.0
Tumor lysis syndrome	0.0	0.0	1.4	1.4

- Most common any grade and grade ≥3 toxicities in Arm A were heme toxicities
- Other toxicities were similar between Arm A and Arm B
- There were no unexpected safety findings associated with Arm A

TEAE, treatment-emergent adverse event.

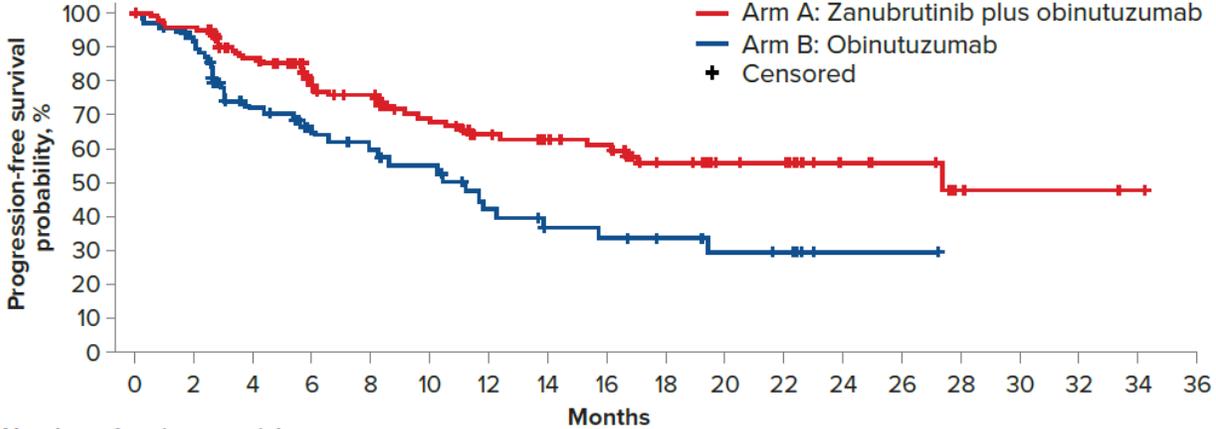
Disease Response by Independent Central Review

Response by ICR	Zanubrutinib plus obinutuzumab N=145	Obinutuzumab N=72
ORR, % (95% CI)	68.3 (60.0, 75.7)	45.8 (34.0, 58.0)
Risk difference, % (95% CI)	22.0 (8.3, 35.8)	
2-sided <i>P</i> value	0.0017	
BOR, n (%)		
CR	54 (37.2)	14 (19.4)
PR	45 (31.0)	19 (26.4)
SD	25 (17.2)	14 (19.4)
Nonprogressive disease	3 (2.1)	4 (5.6)
PD	13 (9.0)	15 (20.8)
Discontinued prior to first tumor assessment	4 (2.8)	6 (8.3)
NE	1 (0.7)	0 (0.0)
Complete response rate, % (95% CI)	37.2 (29.4, 45.7)	19.4 (11.1, 30.5)
2-sided <i>P</i> value	0.0083	

BOR, best overall response; CI, confidence interval; CR, complete response; ICR, independent central review; NE, not evaluable; ORR, overall response rate; PD, progressive disease; PR, partial response; SD, stable disease.

Selected Secondary Efficacy Endpoints

Progression-Free Survival by ICR

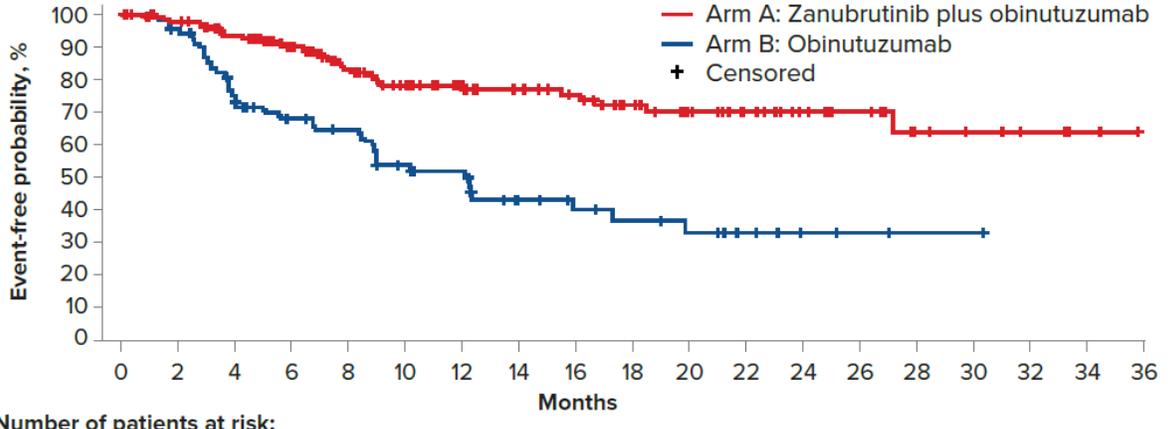


Number of patients at risk:

Arm A	145	135	111	83	76	56	46	40	37	27	19	18	10	8	3	2	2	1	0
Arm B	72	63	39	29	26	23	16	12	11	9	7	6	1	1	0				

Median PFS, months (95% CI):
 27.4 (16.1, NE) Arm A vs 11.2 (6.5, 15.7) Arm B

Time to Next Antilymphoma Treatment



Number of patients at risk:

Arm A	145	137	124	110	89	74	62	53	48	40	32	26	20	14	8	6	4	2	0
Arm B	72	65	49	40	36	28	25	16	13	11	9	6	3	2	1	1	0		

Median TTNT, months (95% CI):
 NE (21.1, NE) Arm A vs 12.1 (8.3, 19.8) Arm B

CI, confidence interval; DOR, duration of response; ICR, independent central review; NE, not evaluable; PD, progressive disease; PFS, progression-free survival.

Kapitel 3

Follikuläres Lymphom **Immuntherapie**



EFFICACY AND SAFETY OF A THIRD GENERATION CD20 CAR-T (MB-106) FOR TREATMENT OF RELAPSED/REFRACTORY FOLLICULAR LYMPHOMA (FL)

Mazyar Shadman^{1,2} , Cecilia Yeung² , Mary Redman ² , Sang Yun Lee² , Dong Hoon Lee² , Susan Ra² , David Qian² , Chaitra Ujjani¹ , Bruce Dezube³ , Christina Poh^{1,2} , Edus H. Warren^{1,2} , Aude Chapuis^{1,2} , Damian Green^{1,2} , Andrew Cowan^{1,2} , Ryan Cassaday^{1,2} , Hans-Peter Kiem^{1,2} , Victor Chow^{1,2} , Jordan Gauthier^{1,2} , Cameron Turtle^{1,2} , Ryan Lynch^{1,2} , Stephen Smith^{1,2} , Ajay Gopal^{1,2} , David Maloney^{1,2} , Brian Till^{1,2}

1- University of Washington, Seattle WA 2- Fred Hutchinson Cancer Center, Seattle WA, 3-Mustang Bio, Worcester , MA



RESULTS: PATIENT CHARACTERISTICS

N	28
Age, median (range)	61.8 (44.7-81.3)
> 65, n(%)	7 (25%)
> 80, n(%)	2 (7%)
Female sex, n(%)	10 (55.5%)
Stage at initial diagnosis	
1-2	2 (11%)
3-4	16 (89%)
Histologic grade at diagnosis	
1-2	11 (61%)
3A	5 (28%)
Prior lines of treatment (range)	5 (1-12)
History of transformation	3 (17%)
POD24	12 (67%)
Prior CD19 CAR-T	1 (5.5%)

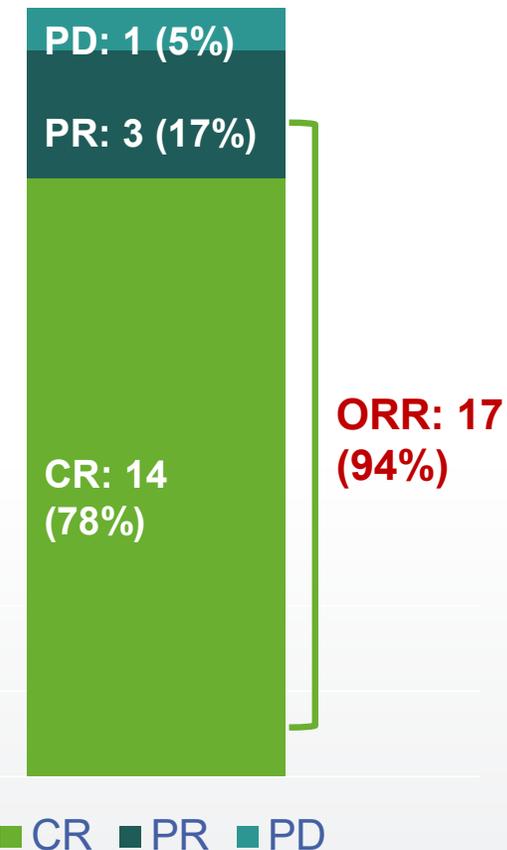
RESULTS: ADVERSE EVENTS IN FL PATIENTS IN FIRST 28 DAYS

N=18 AEs	Grade				
	1	2	3	4	Any
CRS	4 (22%)	1 (5.5%)	-	-	5 (27.5%)
ICANS	-	-	-	-	0 (0%)
Lymphopenia	-	-	2 (11%)	16 (89%)	18 (100%)
Neutropenia	-	-	6 (33%)	11 (61%)	17 (94%)
Anemia	-	4 (22%)	7 (39%)	-	11 (61%)
Thrombocytopenia	-	3 (17%)	-	2 (11%)	5 (28%)
Febrile Neutropenia	1 (5.5%)	-	2 (11%)	-	3 (16.5%)
Skin infections	-	1 (5.5%)	-	-	1 (5.5%)
Bacteremia	-	-	1 (5.5%)	-	1 (5.5%)
Pneumonia	-	1 (5.5%)	-	-	1 (5.5%)
CMV reactivation	-	-	1 (5.5%)	-	1 (5.5%)

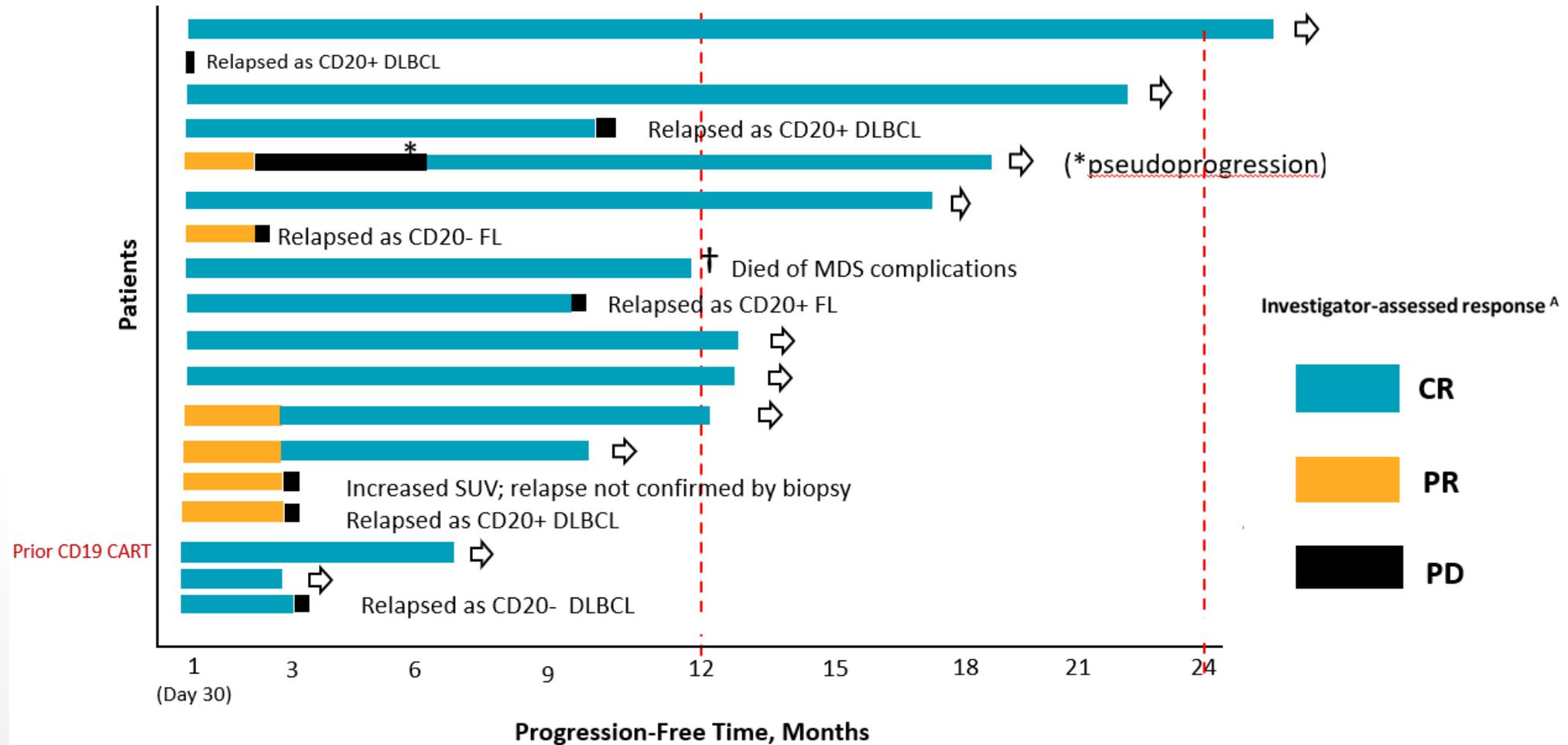
RESULTS: EFFICACY (FL)

Best Responses
N=18

Histology	Best Response by Lugano PET criteria †	All dose levels	Dose level 0 (n=1)	Dose level 1 (n=2)	Dose level 2 (n=4)	Dose level 3 (n=8)	Dose level 4 (n=3)
			1 x 10 ⁵ cells/kg	3.3 x 10 ⁵ cells/kg	1 x 10 ⁶ cells/kg	3.3 x 10 ⁶ cells/kg	1 x 10 ⁷ cells/kg
FL (n=18)	ORR, n(%)	17/18 (94%)	1	1	4	8	3
	CR, n(%)	14/18 (78%)	1	1	2	7	3
	PR, n (%)	3/18 (17%)	-	-	2	1	-
	SD, n (%)	-	-	-	-	-	-
	PD, n (%)	1/18 (5%)	-	1	-	-	-



RESULTS: DURATION OF RESPONSE (FL PATIENTS ONLY)



^A Evaluated according to Lugano 2014 criteria.¹

Relapsed follicular lymphoma

Therapy: Role of immunotherapy?



Follicular lymphoma

GLA Studien 2022



Relapse



GLA/European MCL Network Acknowledgements



Die Kurzpräsentationen sind online unter

www.lymphome.de/eha2022

Für den Inhalt verantwortlich:

Prof. Dr. med. Martin Dreyling

Klinikum der Universität München



Das Informationsprojekt wird unterstützt von den Firmen:



A Sandoz Brand



Diese hatten keinen Einfluss auf die Inhalte.