Disclosures

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Polish Lymphoma Research Group

mcm małopolskie centrum medyczne

Uniwersytet Jagielloński Collegium Medicum

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MOR208 anti-CD19 MoAb

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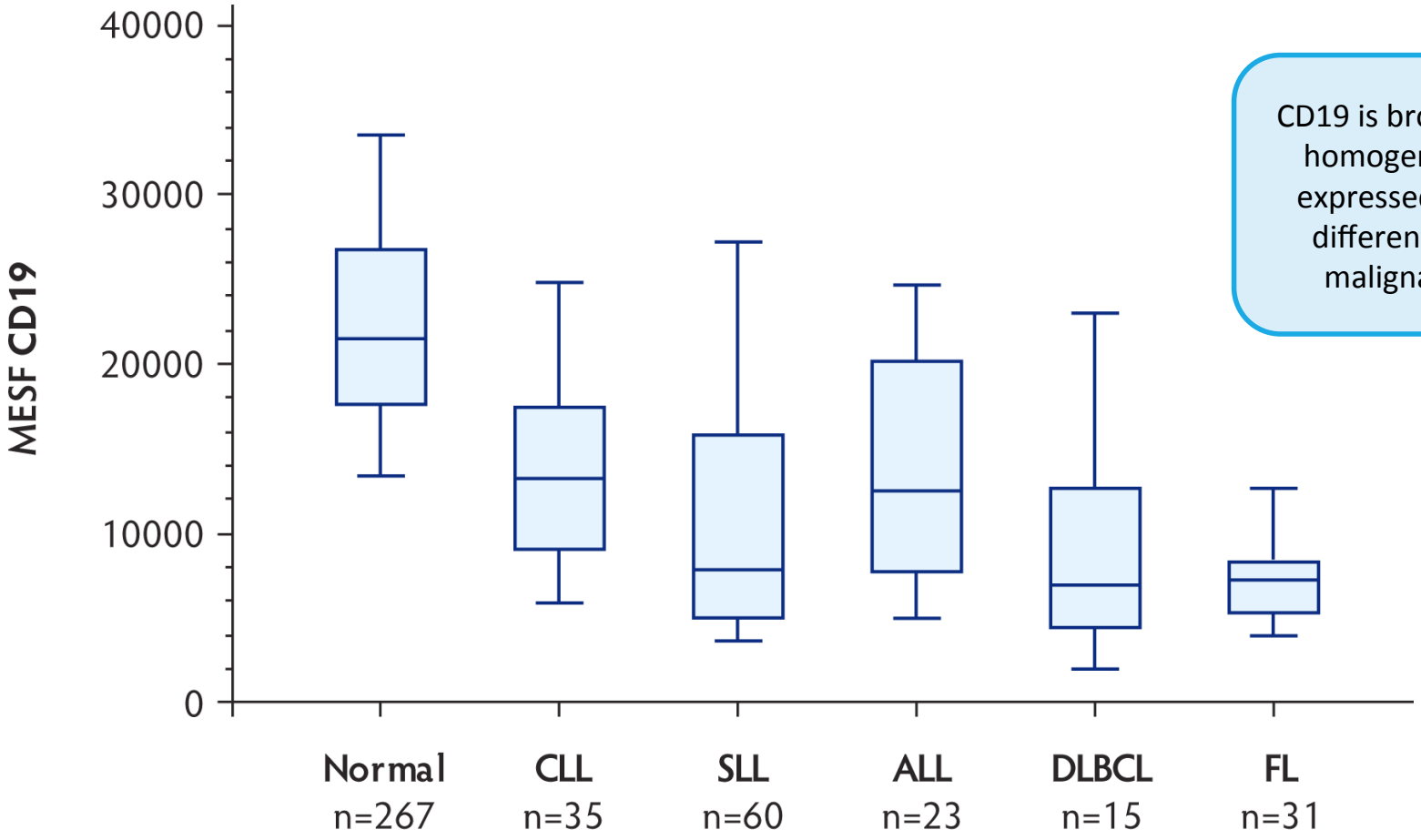
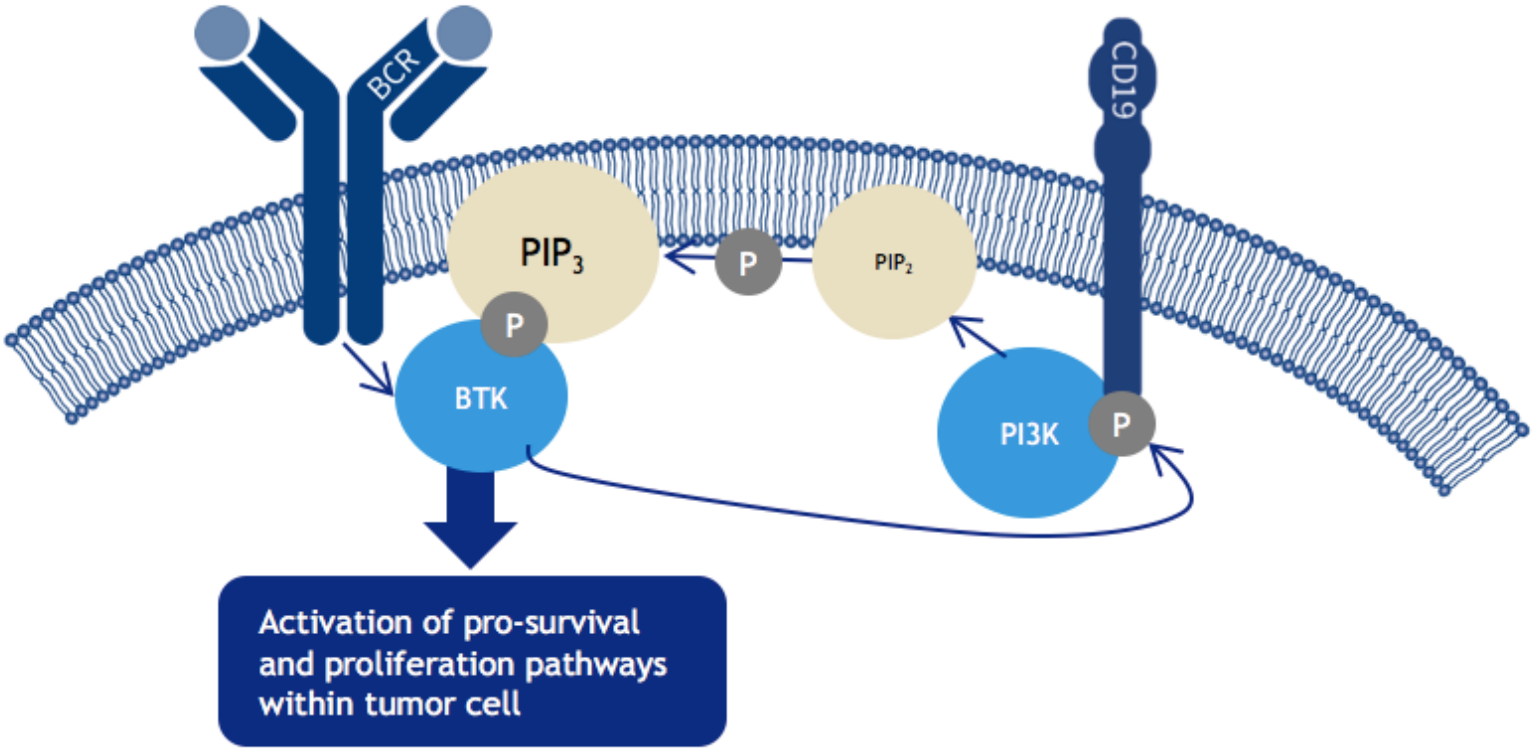
CD19 Expression on B-Cell Tumors



CD19 is broadly and homogeneously expressed across different B-cell malignancies

Modified from Olejniczak SH, et al. Immunol Invest 2006; 35:93-114
Ginaldi L, et al. J Clin Pathol 1998; 51:364-9

CD19 and Tumor Cell Survival

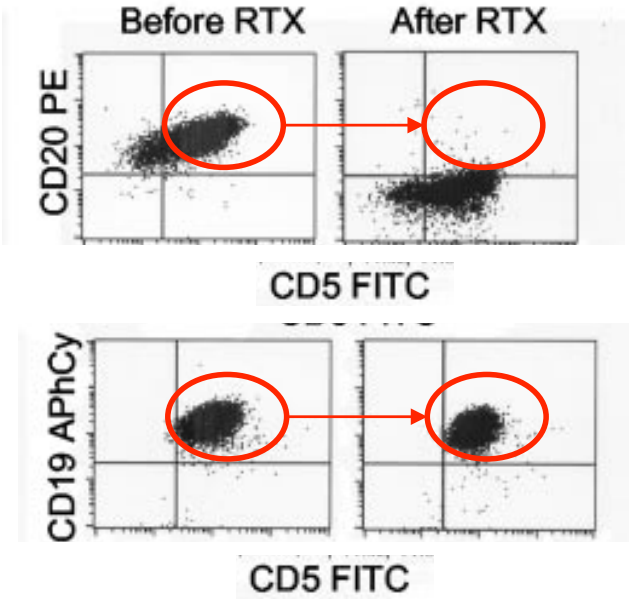


CD19 enhances B-cell antigen receptor signaling by amplification of PI3K and BTK activity

Fujimoto M, et al. Semin Immunol 1998;10:267-77
Fujimoto M, et al. Immunity 2000;13:47-57
Poe JC, et al. J Immunol;2012:2318-25

CD19 expression is preserved on tumour cells

ex vivo analysis of peripheral CLL tumours cells (monotherapy, week 2 of treatment), confirmed by Western Blot



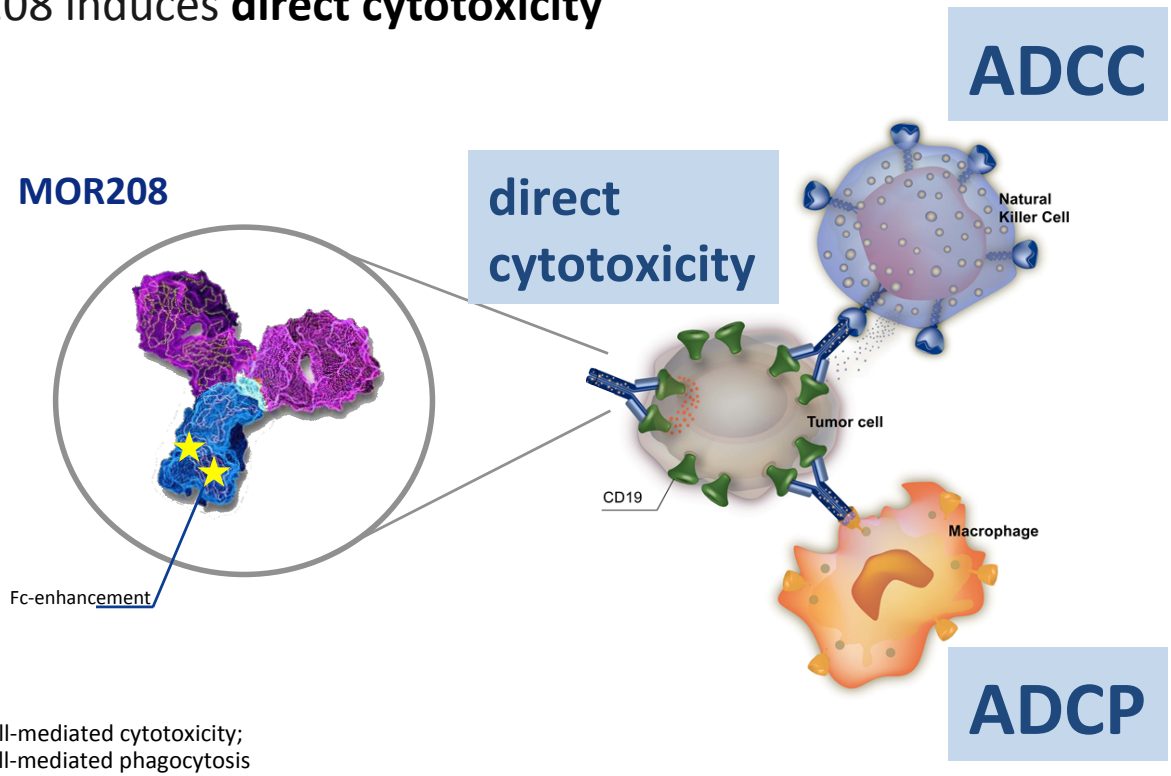
Anti-CD20 treatment might lead to loss of target

Anti-CD19 expression is preserved on tumours cells after therapy

Kennedy et al., 2004
Davis et al., 1999
Taylor et al., 2014
Skarzynski et al 2015

MOR208: An Enhanced CD19 Antibody

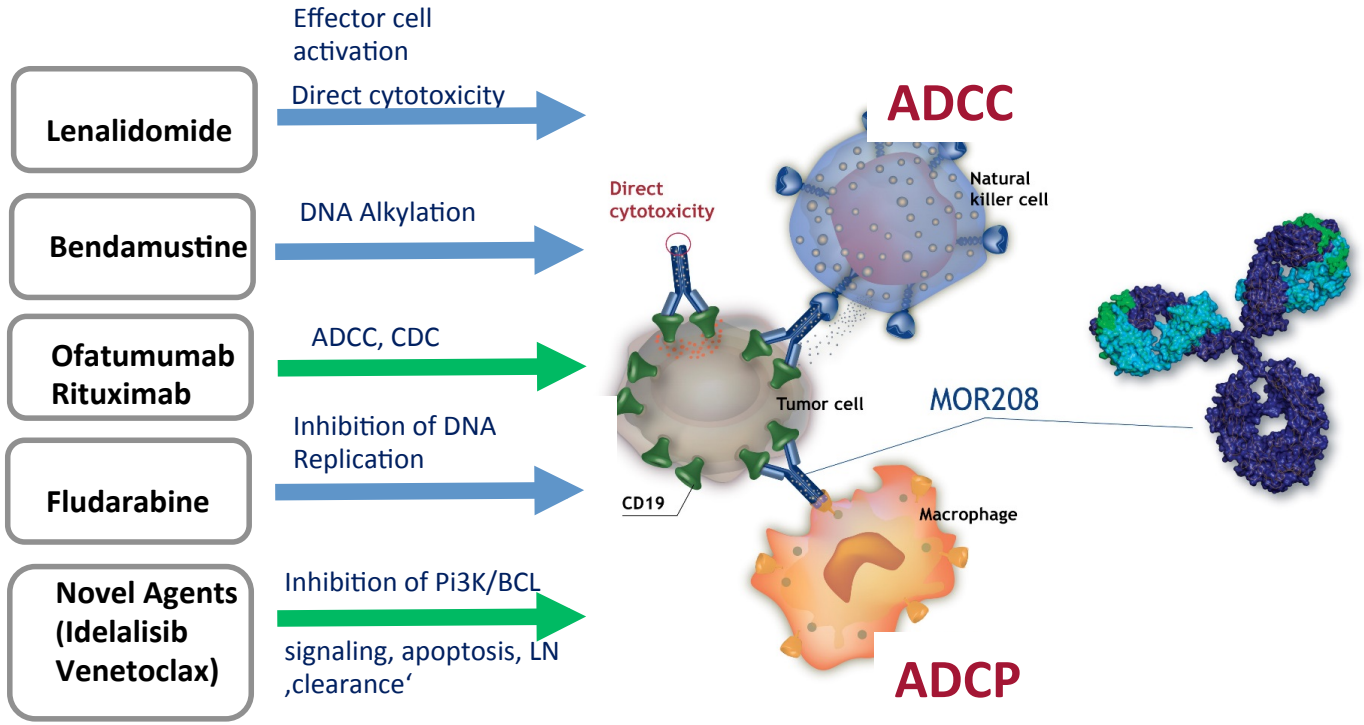
- **MOR208** is an Fc-enhanced monoclonal antibody that targets CD19
- Fc-enhancement of MOR208 leads to a potentiation of **ADCC** and **ADCP**
- MOR208 induces **direct cytotoxicity**



ADCC, antigen-dependent cell-mediated cytotoxicity;
ADCP, antigen-dependent cell-mediated phagocytosis

Horton HM et al. Cancer Res 2008; 68:8049-57

Synergy with all tested B cell therapies



Winderlich et al. ASCO 2012 AND data on file

Phase 1 in R/R CLL – Study design

A Phase 1 Study of MOR208 to Evaluate the Safety, Tolerability, and Pharmacokinetics in Patients With Relapsed or Refractory Chronic Lymphocytic Leukemia (R/R CLL)

- Open-label, multi-dose, single-arm, dose escalation study
- Enrolled 27 heavily pretreated high risk patients suffering from relapsed or refractory CLL
- Primary objective: safety, tolerability, pharmacokinetic profile
- Secondary objective: anti-tumor activity
- Dosing in 6 cohorts:

Dose (mg/kg)	0.3 mg/kg	1 mg/kg	3 mg/kg	6 mg/kg	9 mg/kg	12 mg/kg
No of patients (total n = 27)	1	1	3	3	3	16 (including P2a expansion)

Dosing Scheme:

Woyach JA, et al. Blood 2014;124:3553-60

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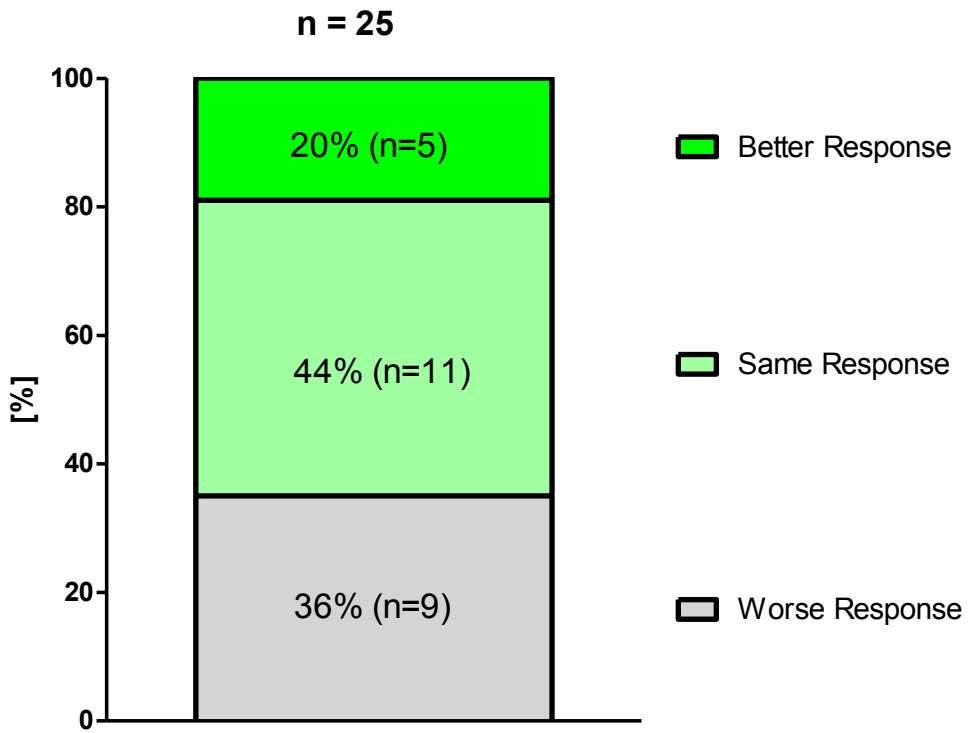
Phase 1 in R/R CLL - Efficacy

Response, n (%)	All patients (N=27)	Patients at recommended dose (12 mg/kg; N=16)
CT criteria*		
CR	0	0
PR	8 (30%)	6 (38%)
SD	17 (63%)	10 (62%)
PD	2 (7%)	0
Physical exam and lab only		
CR	0	0
PR	18 (67%)	12 (75%)
SD	9 (33%)	4 (25%)
PD	0	0

Woyach JA, et al. Blood 2014;124:3553-60

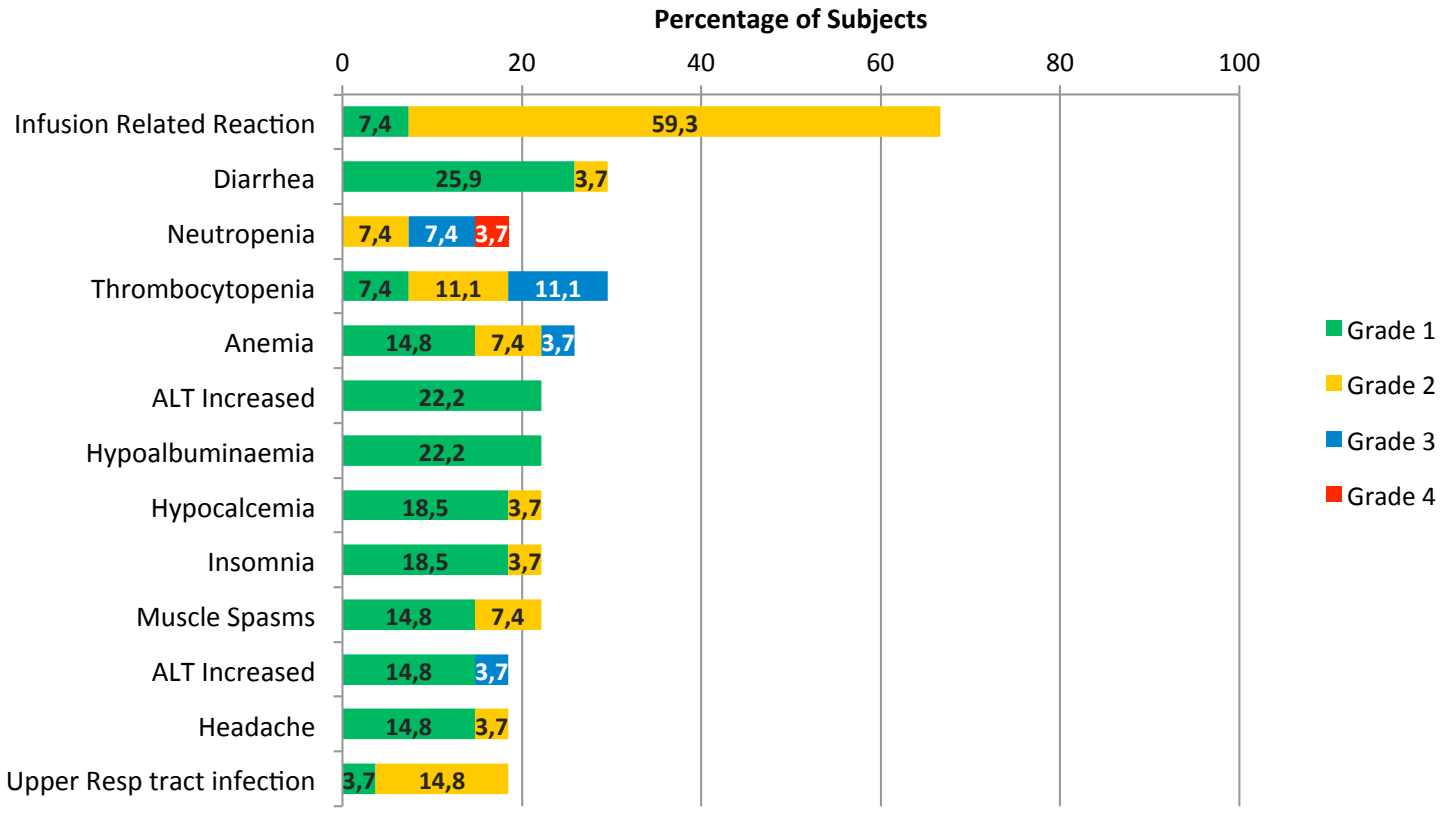
Phase 1 in R/R CLL - Efficacy

Response to MOR208 in comparison to last prior anti-CD20 containing regimen (IWCLL 2008)



Woyach JA, et al. Blood 2014;124:3553-60

Phase 1 in R/R CLL - Safety



Woyach JA, et al. Blood 2014;124:3553-60

ICML 2015 Oral presentation

ASCO 2015 oral presentation

EHA 2016 Oral presentation

ASH 2016 poster presentation

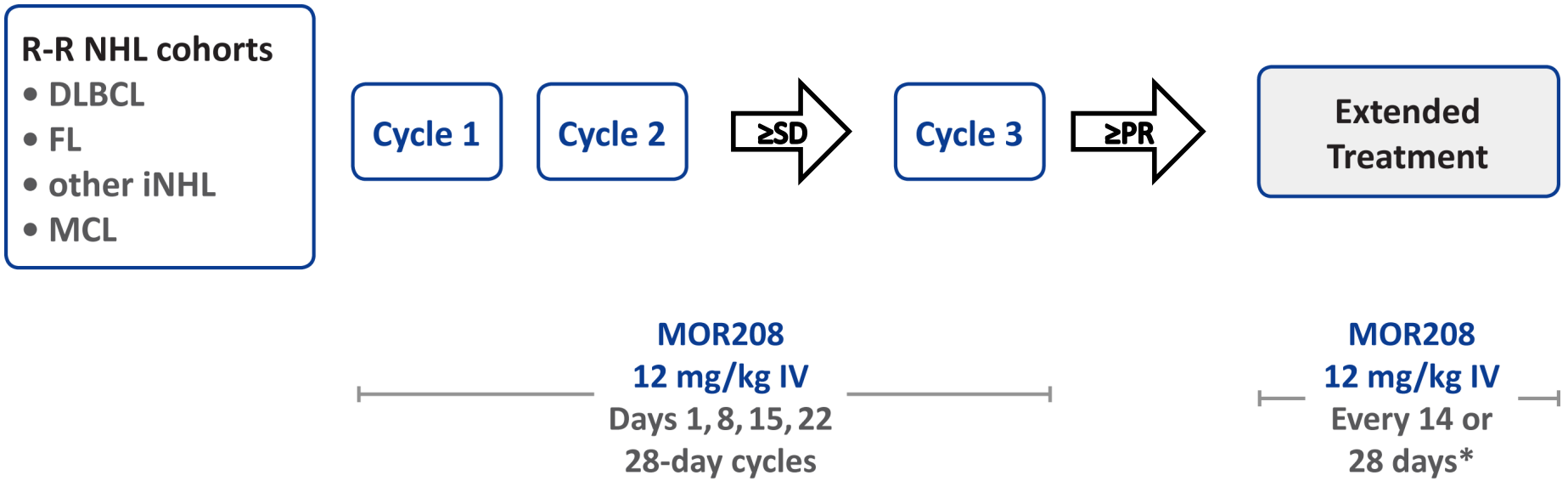
Single-Agent MOR208 in Relapsed or Refractory (R-R) Non-Hodgkin's Lymphoma (NHL): Results from Diffuse Large B-Cell Lymphoma (DLBCL) and Indolent NHL Subgroups of a Phase IIa Study

Wojciech Jurczak,* Pier Luigi Zinzani, Gianluca Gaidano, Andre Goy, Mariano Provencio, Zsolt Nagy, Tadeusz Robak, Kami Maddocks, Christian Buske, Sumeet Ambarkhane, Mark Winderlich, Maren Dirnberger-Hertweck, Jan Endell, Kristie A. Blum

*Jagiellonian University, Kraków, Poland

Study design

Non-randomized phase IIa multicenter study with 2-stage design (NCT01685008)



iNHL, indolent non-Hodgkin's lymphoma; IV, intravenous; PR, partial response; SD, stable disease

Jurczak et al.: ASCO 2016, EHA 2016

Study objectives

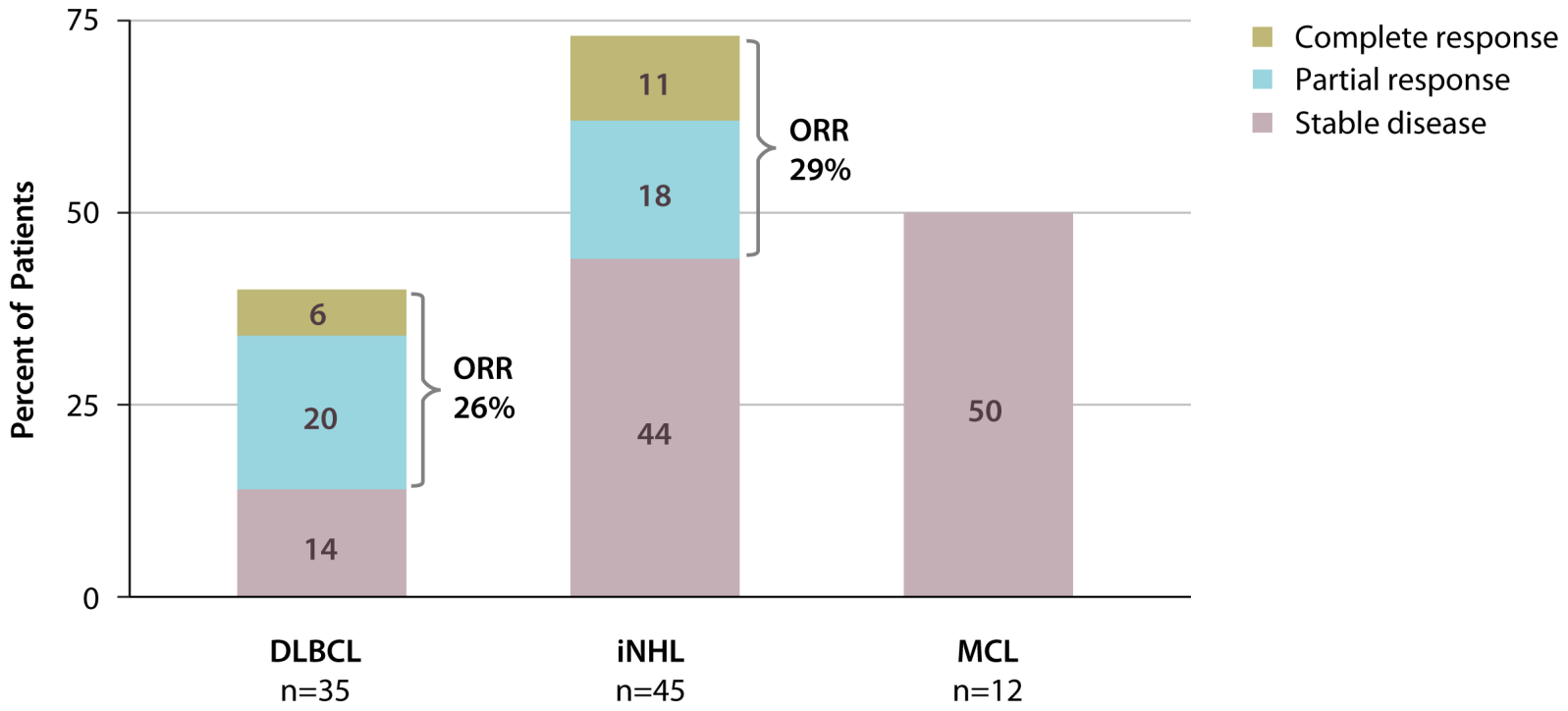
- **Primary objective**
  - ORR in R-R NHL patients who had received at least one prior therapy containing rituximab
- **Secondary objective**
  - Duration of response and PFS
  - Safety and tolerability
  - Pharmacokinetics and pharmacodynamics

Baseline Characteristics

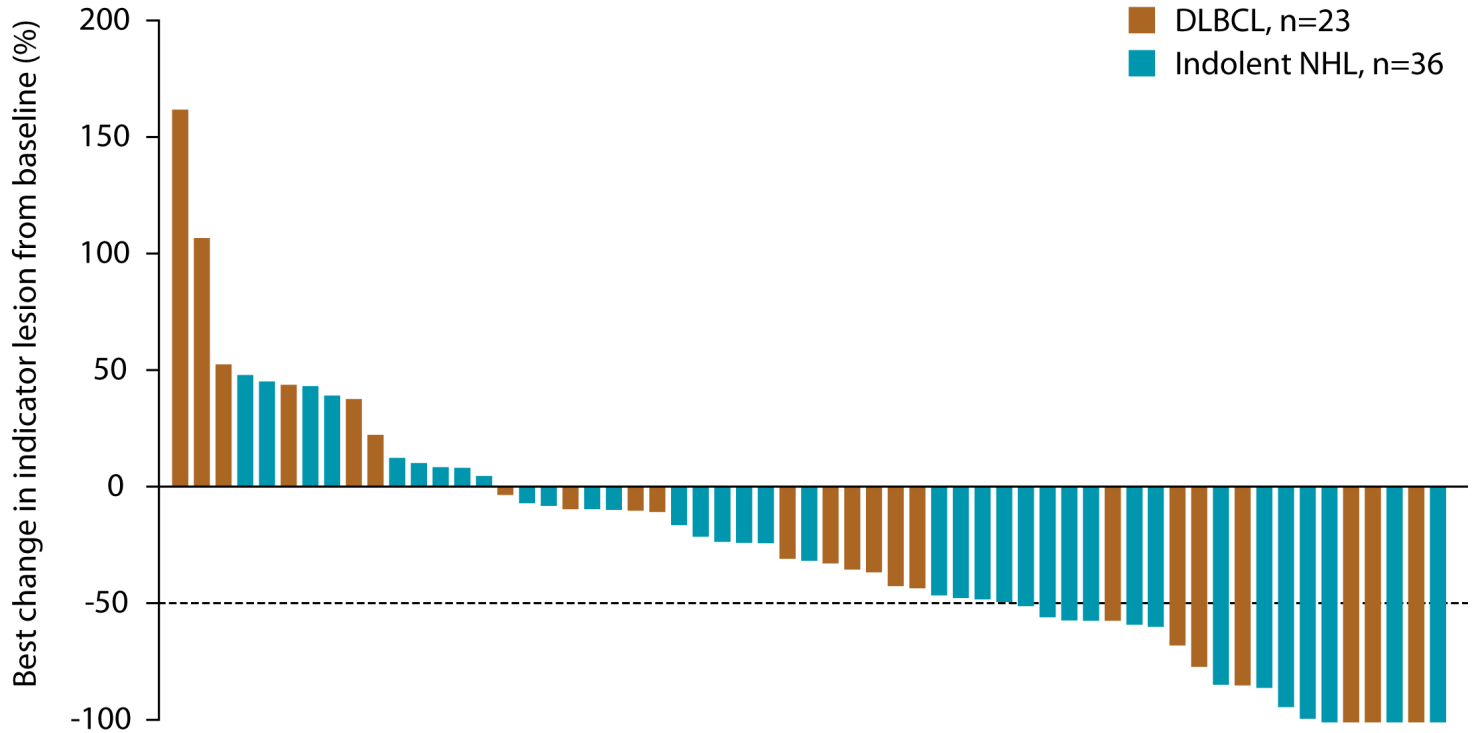
Characteristic, n (%)		DLBCL n=35	iNHL* n=45	MCL n=12	Total n=92
Age, years	Median	71	66	64.5	66.5
Sex	Male	24 (69)	21 (47)	11 (92)	56 (61)
Ann Arbor stage	I-II	4 (11)	5 (11)	1 (8)	10 (11)
	III-IV	30 (86)	40 (89)	11 (92)	81 (88)
	Missing	1 (3)	0	0	1 (1)
ECOG PS	0-1	34 (97)	43 (96)	11 (92)	88 (96)
	2	1 (3)	2 (4)	1 (8)	4 (4)
Prior lines of therapy	1	12 (34)	16 (36)	3 (25)	31 (34)
	2	8 (23)	6 (13)	1 (8)	15 (16)
	≥3	15 (43)	23 (51)	8 (67)	46 (50)
Rituximab refractory	Yes	24 (69)	22 (49)	6 (50)	52 (57)
Last rituximab dose	<6 months	14 (40)	6 (13)	1 (8)	21 (23)
Prior stem cell transplantation	Yes	4 (11)	8 (18)	1 (8)	13 (14)

*Includes follicular lymphoma and other indolent NHLs
Data are n (%) unless otherwise stated. Rituximab refractory was defined as patients who demonstrated less than a partial response or response lasting less than 6 months to a prior rituximab-containing regimen

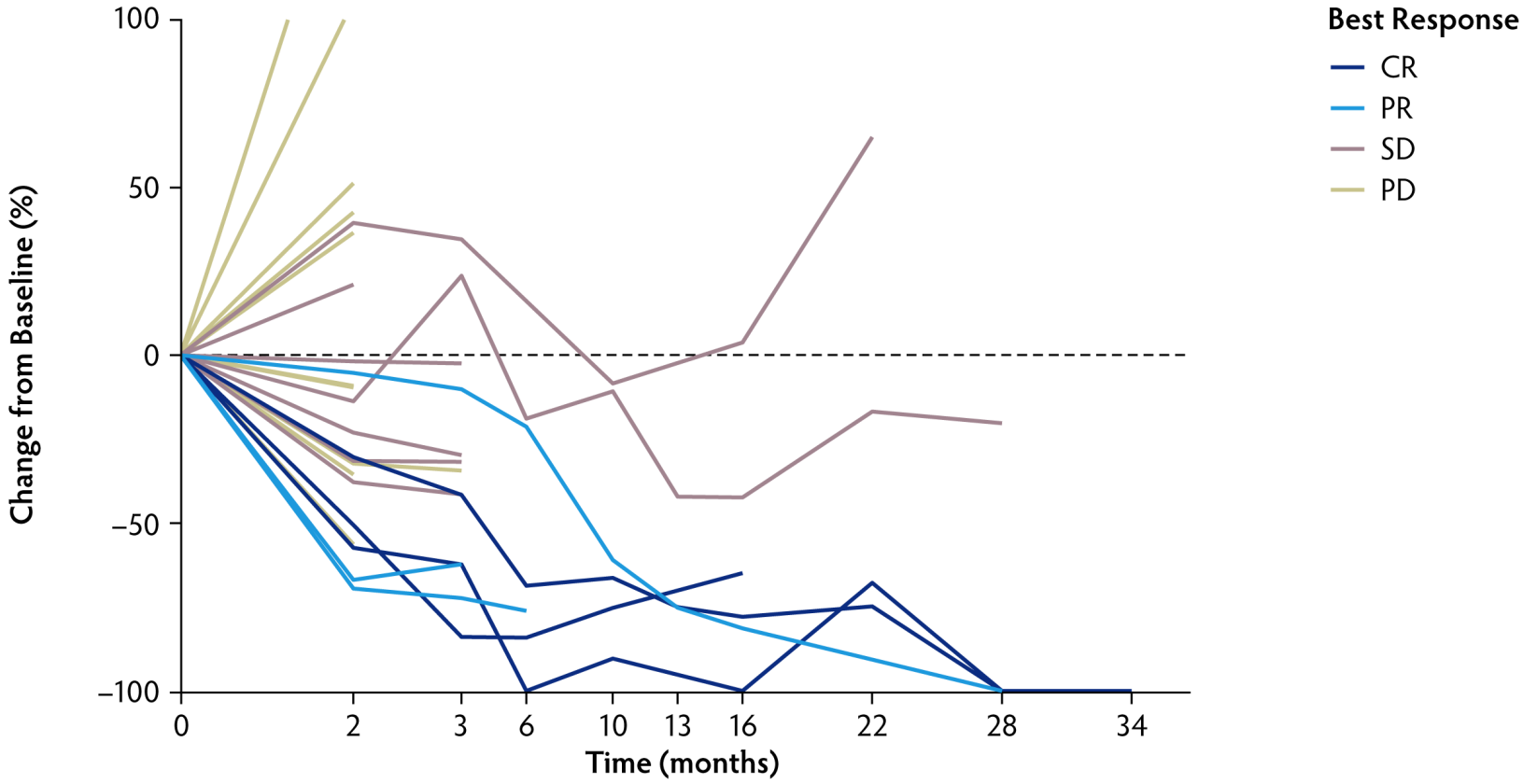
Best Overall Response Rate



Best Tumor Shrinkage

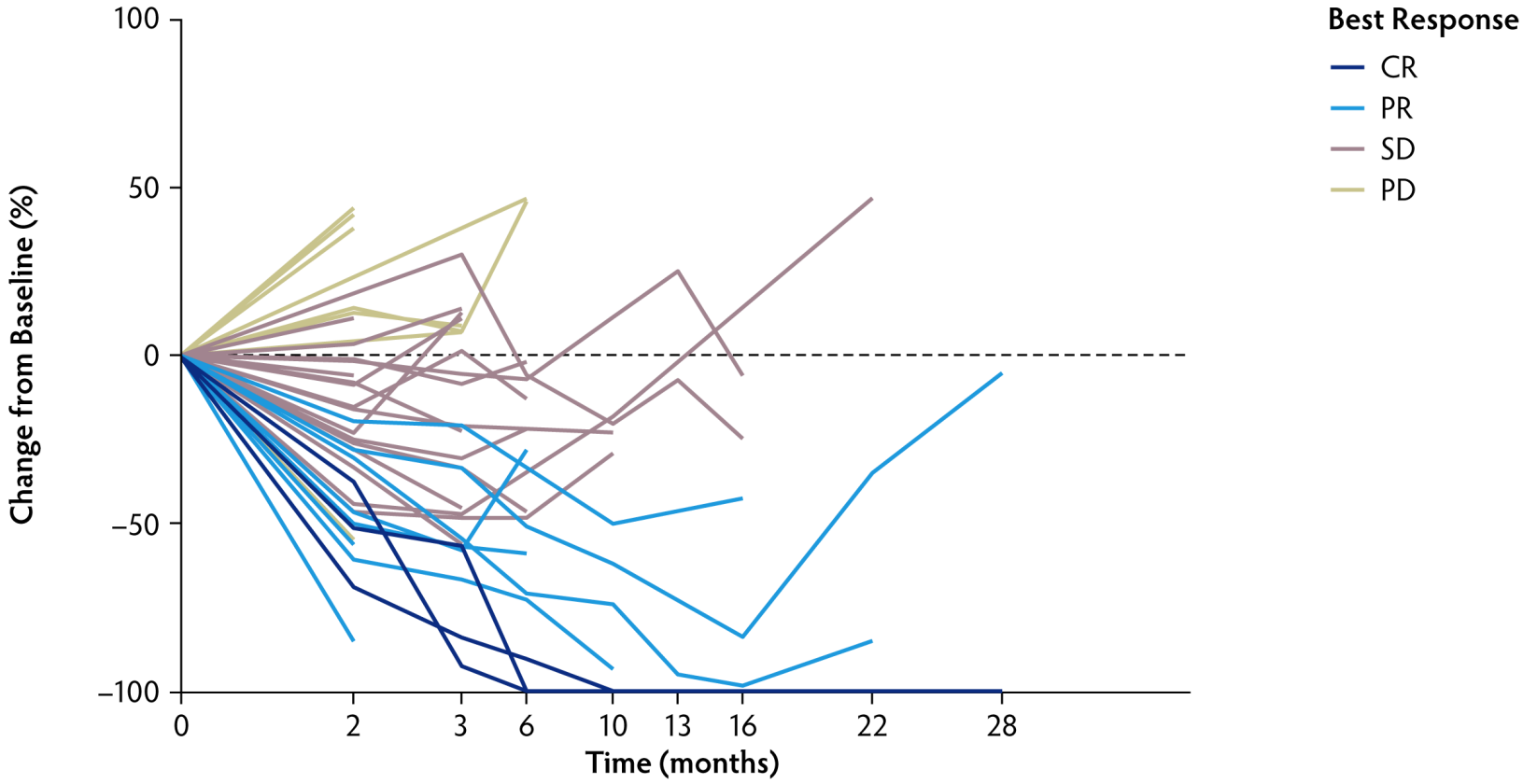


Tumor Shrinkage: DLBCL

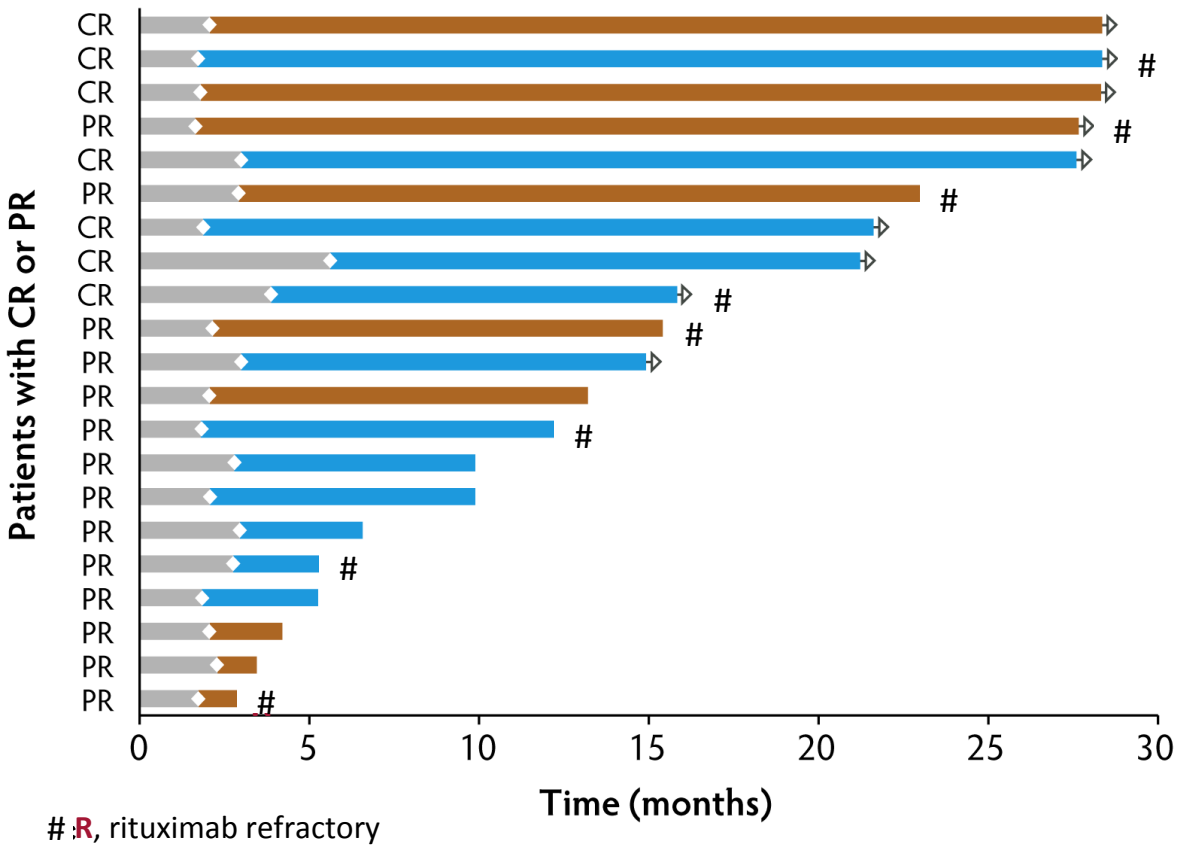


CR, complete response; PD, progressive disease

Tumor Shrinkage: iNHL Subtypes



Timing and Duration of Response



:R, rituximab refractory

DoR, duration of response

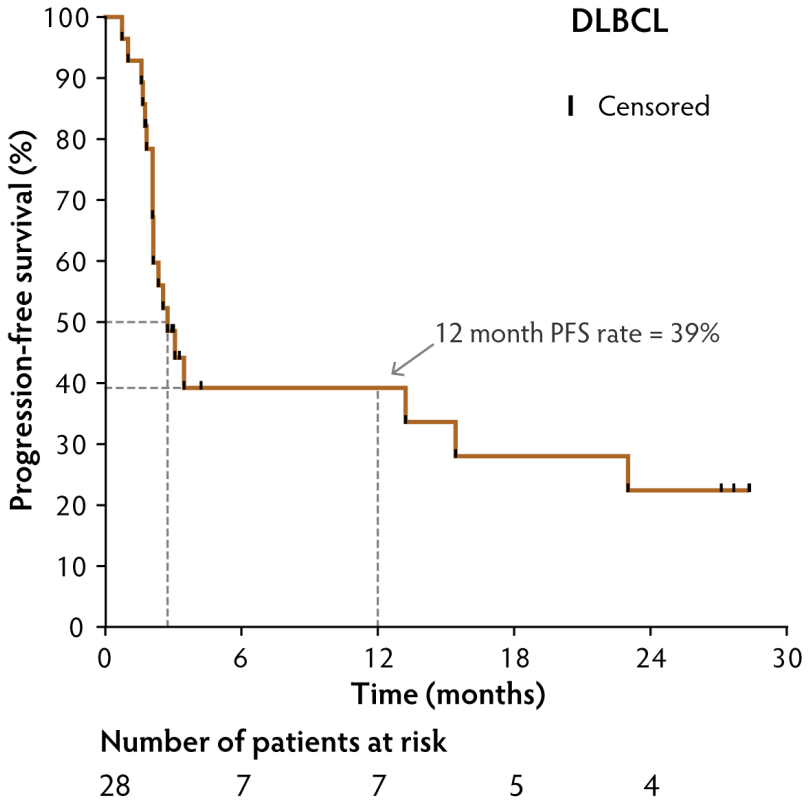
Duration of response

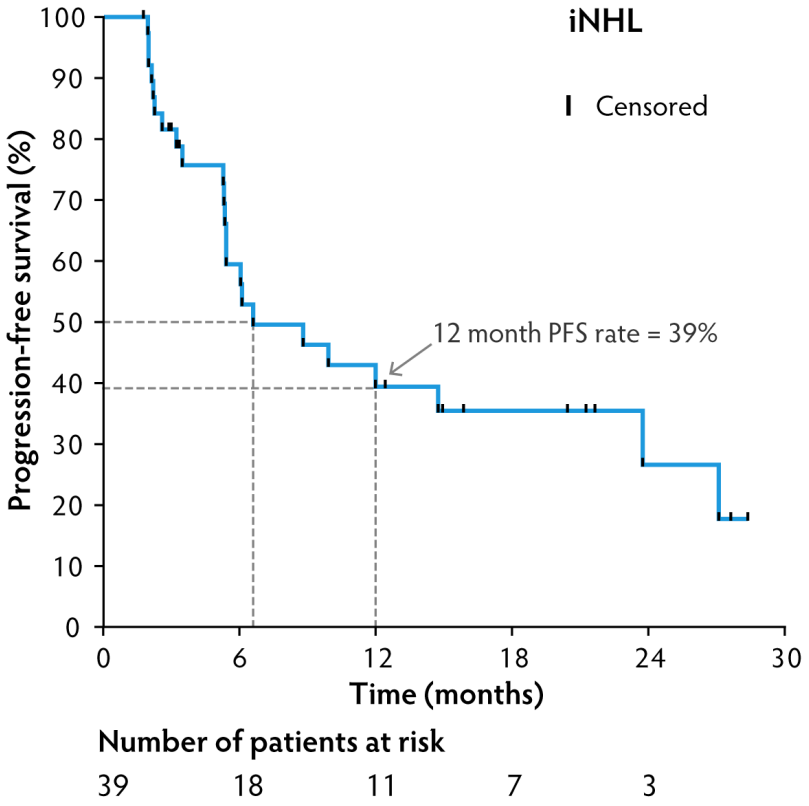
- DLBCL, n=9
- Indolent NHL,* n=12
- Ongoing response, n=9
- Time to response, n=21

* Includes follicular lymphoma and other indolent lymphomas

- 3 DLBCL patients still in remission, longest DoR >26 months, ongoing
- 6 iNHL patients still in remission, longest DoR >26 months, ongoing
- Median DoR 20.1 months in DLBCL and not reached in iNHL

PFS in DLBCL and iNHL Subtypes





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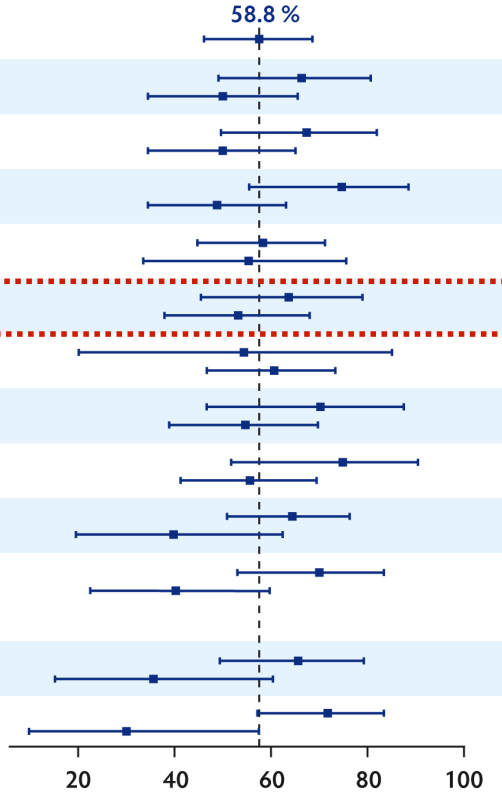
Subgroup Analysis of Disease Control Rate in DLBCL and iNHL Patients

Subgroup		No. of Patients (%)	P Value
Total		80 (100)	
Age	< 65 Yr	37 (46)	0.137
	≥ 65 Yr	43 (54)	
Sex	Female	35 (44)	0.116
	Male	45 (56)	
Stage	1 – 3	29 (36)	0.024 *
	4	50 (63)	
Rituximab last dose < 6 m	No	57 (71)	0.797
	Yes	23 (29)	
Rituximab refractory	No	34 (43)	0.352
	Yes	46 (58)	
FCγRIIIa	High affinity	9 (11)	0.721
	Low affinity	55 (69)	
FCγRIIa	High affinity	21 (26)	0.229
	Low affinity	43 (54)	
DoR to most recent treatment	> 12 m	21 (26)	0.124
	≤ 12 m	51 (64)	
Number of prior treatment lines	1 – 3	58 (73)	0.046 *
	> 3	22 (28)	
Prognostic Index (IPI)	Low	38 (48)	0.015 *
	High	29 (36)	
Biomarker			
Baseline NK cell count	> 100 cells/µl	42 (53)	0.029 *
	≤ 100 cells/µl	19 (24)	
Baseline CD16 expression	> 60.000 ABCs	48 (60)	0.003 **
	≤ 60.000 ABCs	16 (20)	



* < 0.05; ** < 0.01

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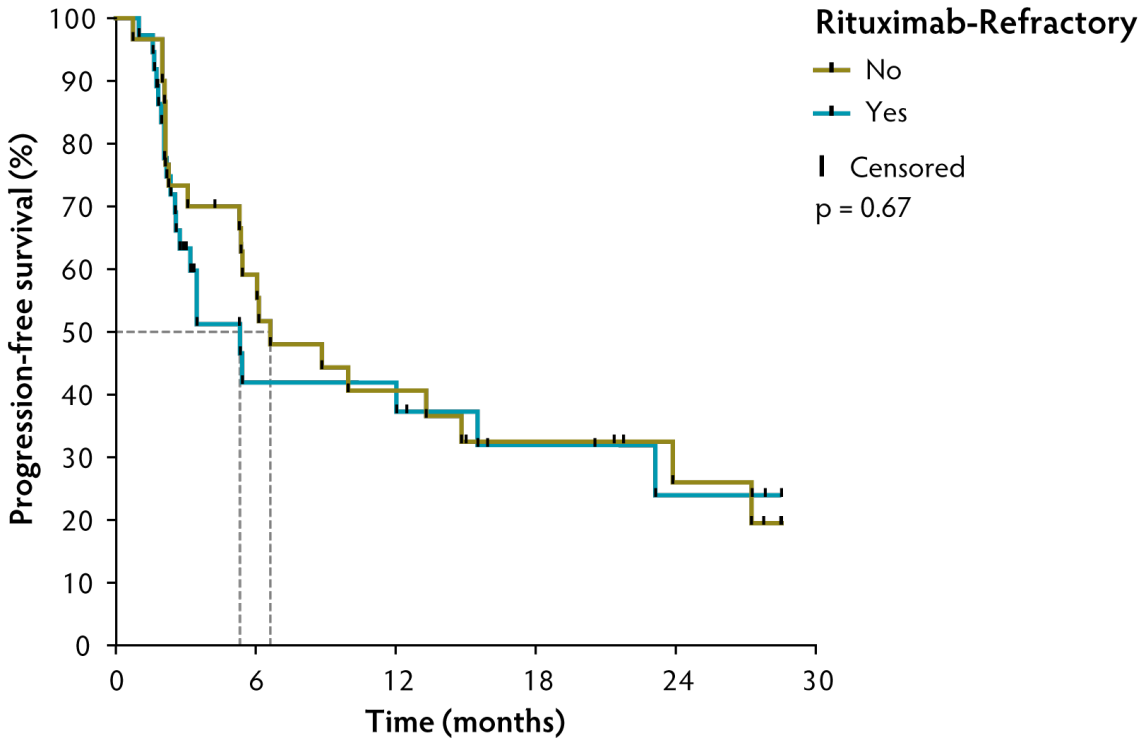
PFS in Rituximab Refractory/Non-Refractory DLBCL and iNHL



Number of patients at risk

Rtx.-Ref. Yes	37	9	8	5	3
Rtx.-Ref. No	30	16	10	7	4

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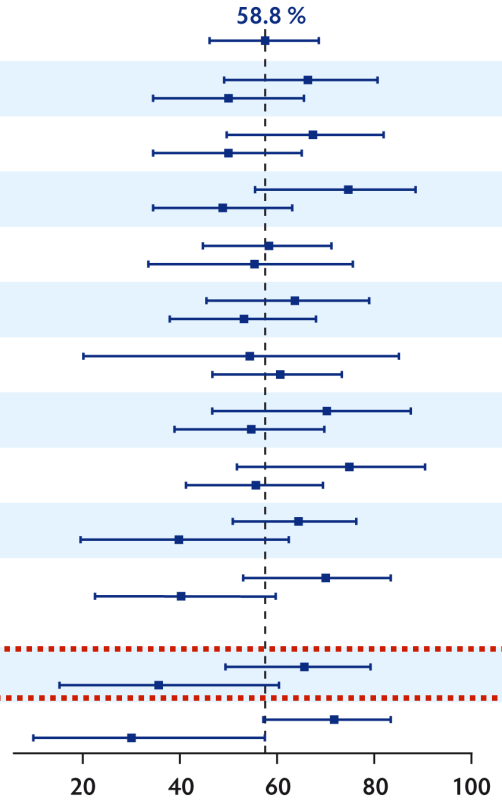

* < 0.05; ** < 0.01

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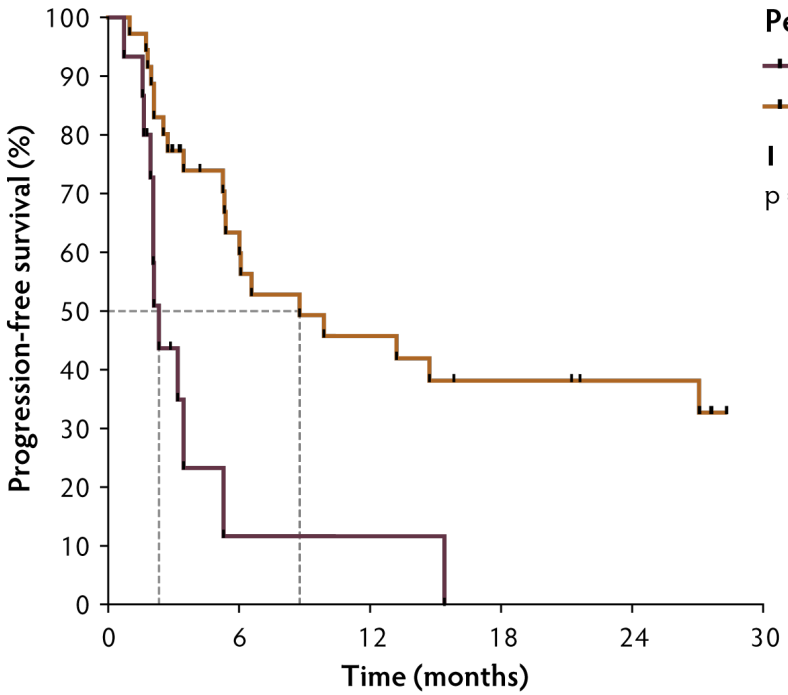
PFS in DLBCL and iNHL Patients
with High and Low Peripheral NK Cell Count at Baseline



Number of patients at risk

≤ 100 NK cells/µl	15	1	1	0	0
> 100 NK cells/µl	36	18	12	9	7

Safety Profile

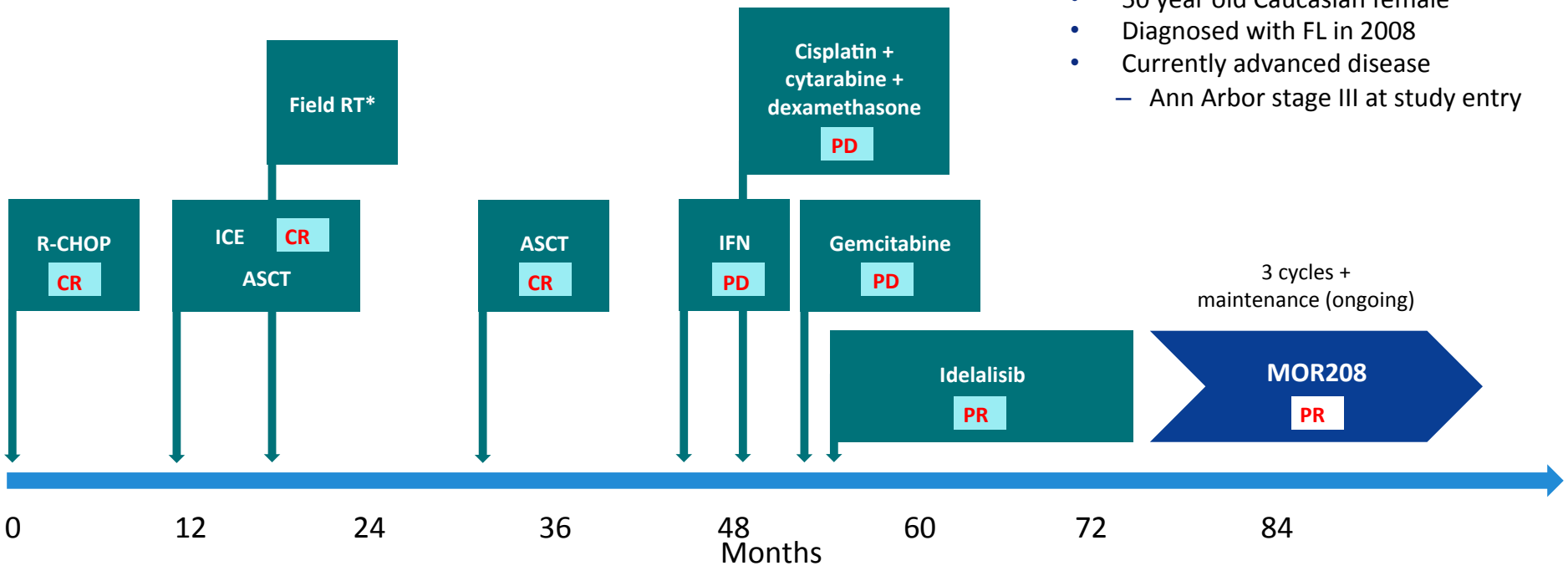
Grade ≥3 TEAEs,* n (%)	DLBCL n=35	iNHL† n=45	MCL n=12	Total n=92
Any‡	19 (54)	14 (31)	4 (33)	37 (40)
Hematological¥				
Neutropenia	6 (17)	2 (4)	0	8 (9)
Thrombocytopenia	2 (6)	1 (2)	1 (8)	4 (4)
Anemia	3 (9)	0	0	3 (3)
Non-Hematological¥				
Dyspnea	2 (6)	1 (2)	1 (8)	4 (4)
Pneumonia	3 (9)	0	0	3 (3)
Fatigue	1 (3)	1 (2)	0	2 (2)
Hypokalemia	1 (3)	1 (2)	0	2 (2)
Infections and Infestations#	5 (14)	1 (2)	0	6 (7)
Infusion-related reactions,* n (%)	**DLBCL n=35**	**iNHL† n=45**	**MCL n=12**	**Total n=92**
Any	**4 (11)**	**5 (11)**	**2 (17)**	**11 (12)**
Grade 1/2	4 (11)	4 (9)	2 (17)	10 (11)
Grade 4	0	1 (2)	0	1 (1)

Data are number of patients (%); *Treatment emergent adverse events (TEAEs) according to MedDRA preferred term (PT); ‡TEAEs including PT disease progression; ¥TEAEs of grade ≥3 reported in two or more patients overall; #TEAEs according to MedDRA system organ class; †includes follicular lymphoma and other iNHLs

There were no treatment-related deaths

FL Case Study 1

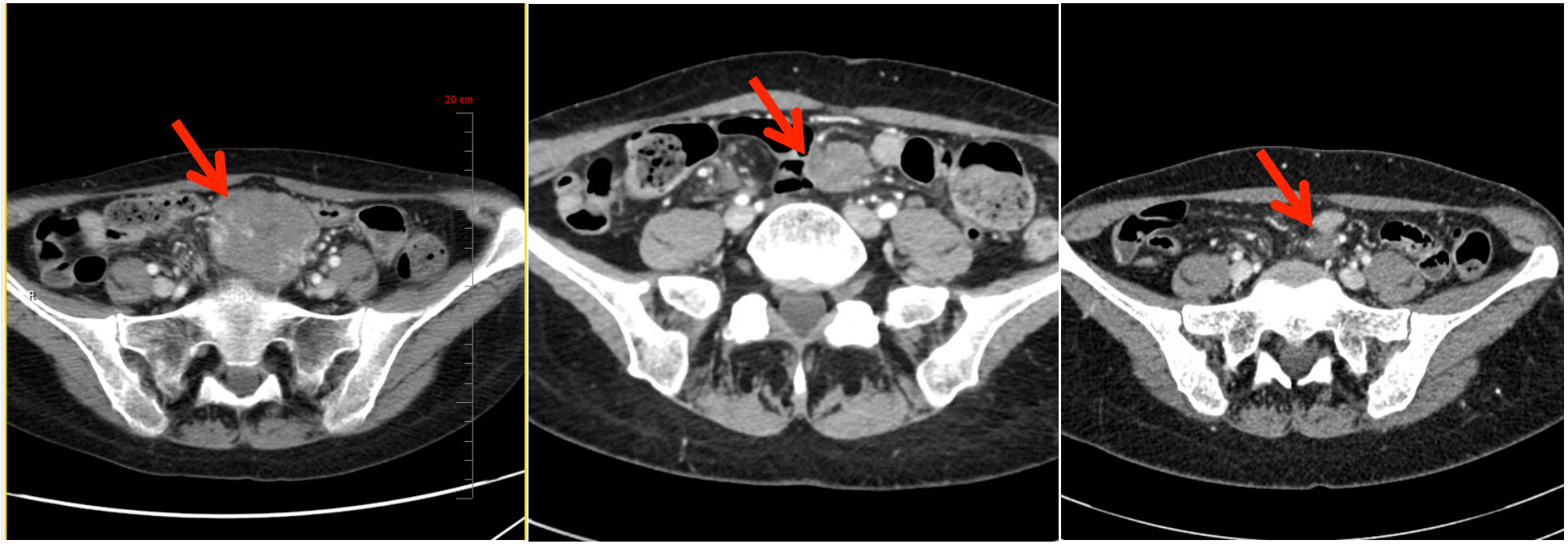
- 50 year old Caucasian female
- Diagnosed with FL in 2008
- Currently advanced disease
  - Ann Arbor stage III at study entry



Patient has remained responsive to MOR208 for over 15 months

*Field radiotherapy (RT) of spinal chord (D6, D11); best response unknown
ASCT, autologous stem-cell transplant; ICE, ifosfamide, carboplatin, etoposide; IFN, interferon; R-CHOP, rituximab plus cyclophosphamide, doxorubicin, vincristine and prednisone

FL Case Study 1

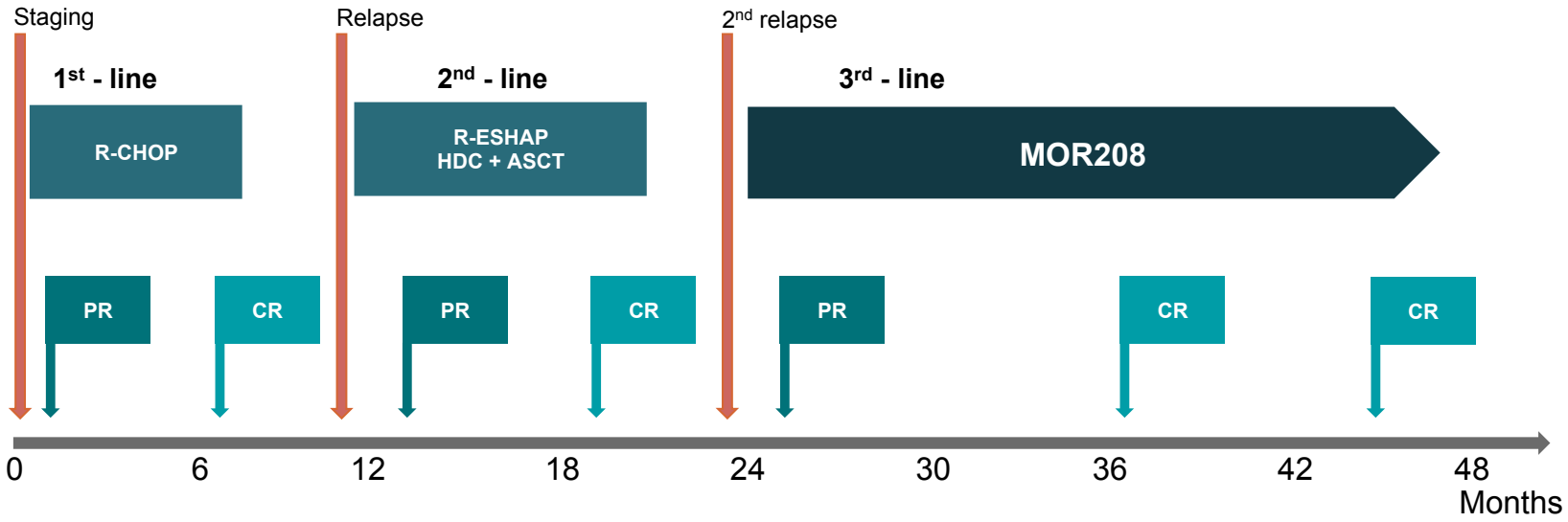


Mesenteric nodal mass 1

Cycle 1 | Cycle 2 | Follow-up 2

DLBCL Case study 2

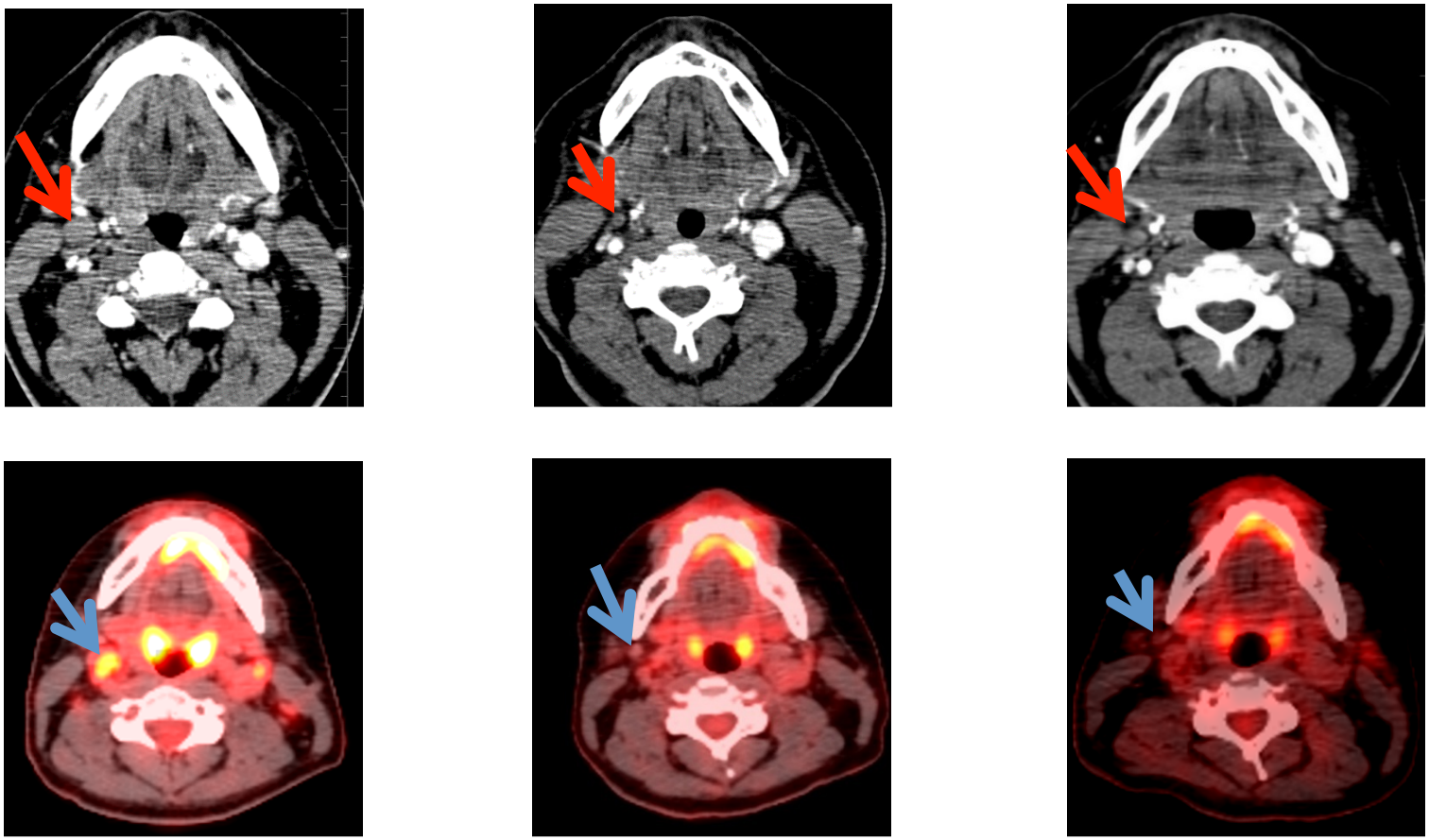
- 35-yrs old Caucasian male diagnosed with Stage III (Ann Arbor) DLBCL in 2011



R-CHOP: rituximab, cyclophosphamide, doxorubicin, vincristine, prednisone
R-ESHAP: rituximab, etoposide,methylprednisolone, cisplatin, and cytarabine
HDC: high dose chemotherapy
ASCT: Autologous Stem Cell Transplantation
PR: partial response
CR: complete response

Jurczak W. et al., J Med Case Reports, 2016

DLBCL Case study 2



Cervical nodal mass 1

Cycle 1 | Follow-up 2 | Follow -up 4

Jurczak W. et al., J Med Case Reports, 2016

COSMOS

A Phase II, Two-Cohort, Open-Label, Multicenter Study to Evaluate the Efficacy and Safety of **MOR208** Combined with **Idelalisib** or **Venetoclax** in Patients with Relapsed or Refractory CLL/SLL Previously Treated with Bruton's Tyrosine Kinase (BTK) Inhibitor (**COSMOS**: **C**LL patients assessed for **O**RR & **S**afety in **MO**R208 **S**tudy)

CLL/SLL Patients

- Relapsed or refractory disease while receiving a BTK inhibitor therapy
- Single-agent or combination therapy with a BTK inhibitor for at least one month must be the patient's most recent prior anticancer therapy
- Age ≥18 years
- ECOG 0 – 2
- Patients with transformed CLL/SLL or Richter's syndrome are excluded

→ **MOR208 + Idelalisib** — Cohort A

→ **MOR208 + Venetoclax** — Cohort B

Abbreviations: CLL = chronic lymphocytic leukaemia; SLL = small lymphocytic lymphoma; BTK = Bruton's tyrosine kinase

Summary and Conclusions

MOR208 showed encouraging single-agent activity in R-R DLBCL and R-R iNHL

- ORR: 26% in DLBCL and 29% in iNHL
  - Target lesion shrinkage also observed in patients with stable disease (5/6 DLBCL and 14/17 iNHL)
- Long-lasting responses in DLBCL and iNHL
  - 12 month PFS rate: 39% in DLBCL and iNHL
  - Longest responses: >26 months in DLBCL and iNHL
- MOR208 efficacious in patients with rituximab-refractory disease
- MOR208 well tolerated, also in long-term treatment

MOR208 is currently being studied for the treatment of R-R DLBCL in:

- A phase II trial in combination with lenalidomide (L-MIND)
- A phase II/III trial in combination with bendamustine (B-MIND)

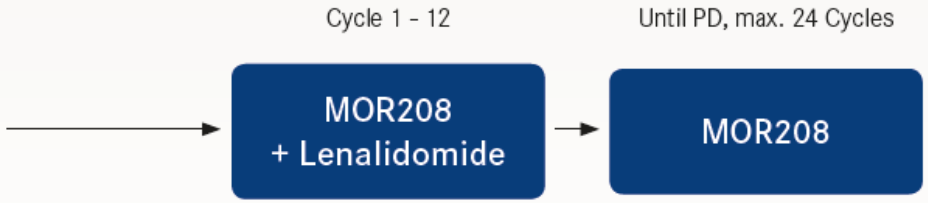
L-MIND

A Phase II, Single-Arm, Open-Label, Multicentre Study to Evaluate the Safety and Efficacy of **MOR208 combined with Lenalidomide** in Patients with Relapsed or Refractory Diffuse Large B-Cell Lymphoma (R-R DLBCL)

Relapsed/Refractory Diffuse Large B-Cell Lymphoma (R/R DLBCL)

- Patients after failure of ASCT or not eligible for HDC and ASCT
- At least one prior regimen included an anti-CD20 antibody
- 1-3 prior regimen
- ECOG 0 to 2

N=80



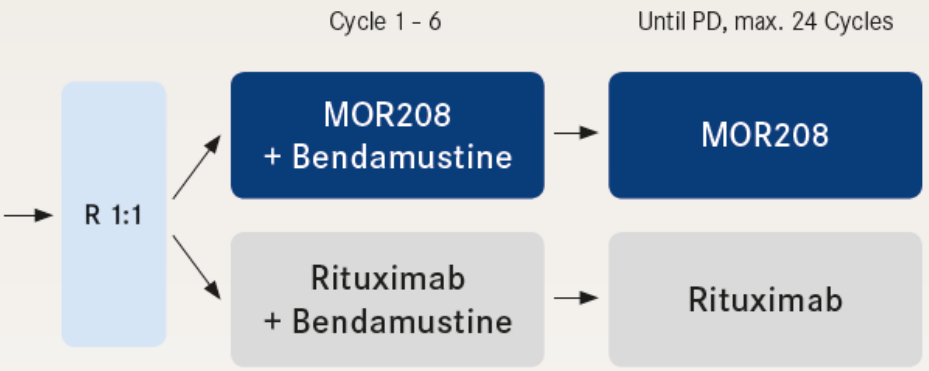
B-MIND

A Phase II/III, Randomised, Multicentre Study of **MOR208 with Bendamustine versus Rituximab with Bendamustine** in Patients with Relapsed or Refractory Diffuse Large B-Cell Lymphoma (R-R DLBCL) Who Are Not Eligible for High-Dose Chemotherapy (HDC) and Autologous Stem-Cell Transplantation (ASCT)

Relapsed/Refractory Diffuse Large B-Cell Lymphoma (R/R DLBCL)

- Patients after failure of ASCT or not eligible for HDC and ASCT
- At least one prior regimen included an anti-CD20 antibody
- 1-3 prior regimen
- ECOG 0 to 2

N=330



We deeply thank the patients, families, clinical researchers, hospitals, and clinics that participate in clinical trials testing the MOR208 drug candidate.

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