Disclosures

Prof. Wojciech Jurczak M.D., Ph.D.,

Advisory Boards:

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MOR208 in R/R B-cell Malignancies

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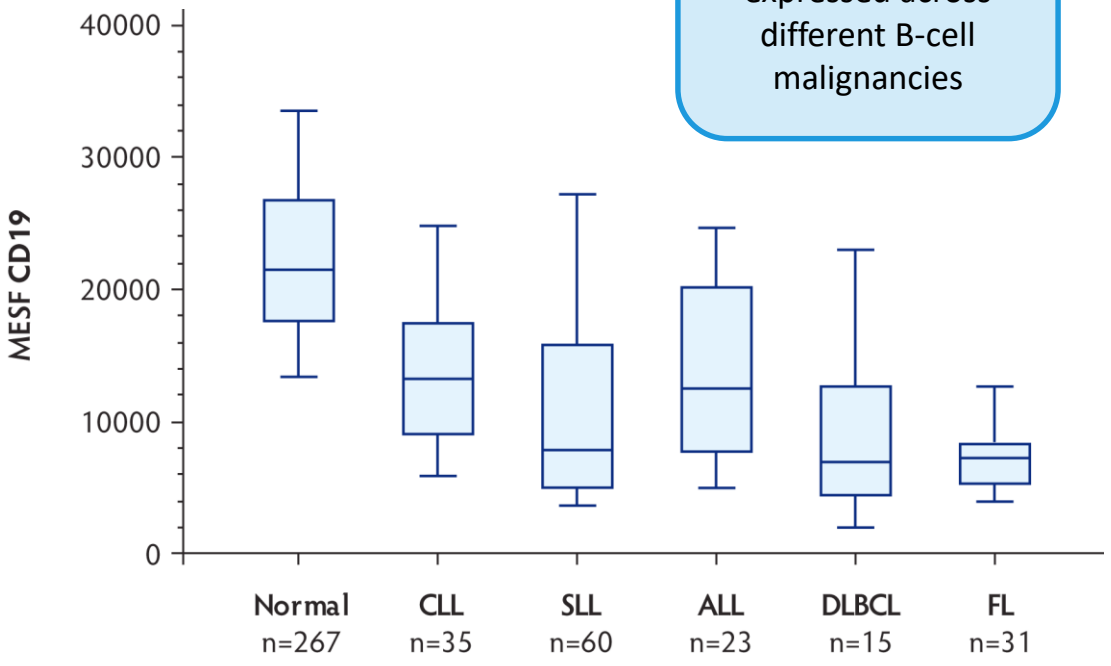
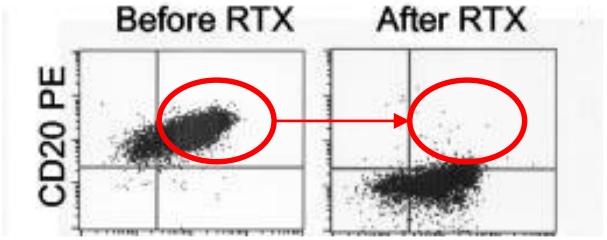
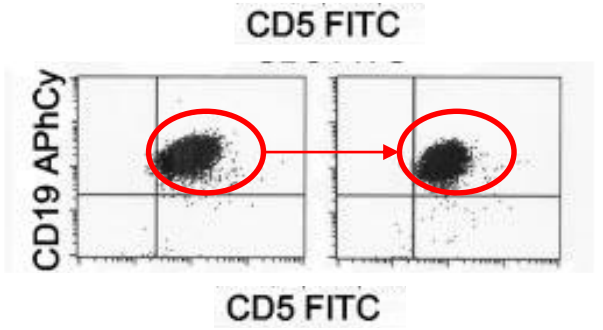
CD19 Expression on B-Cell Tumors

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





Anti-CD20 treatment might lead to loss of target



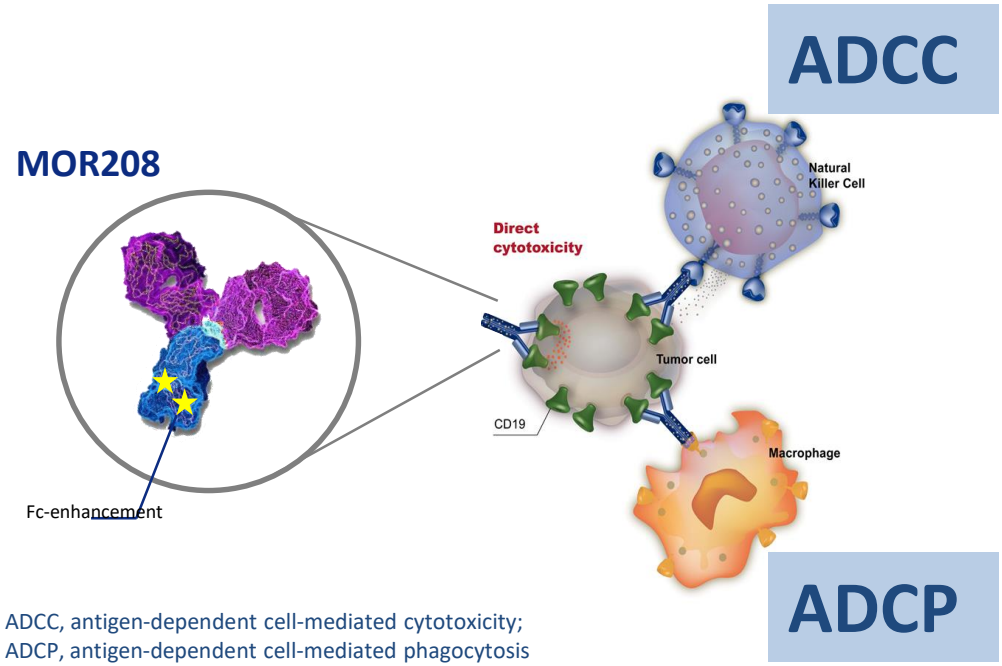
Anti-CD19 expression is preserved after therapy

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

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

MOR208: An Enhanced CD19 Antibody

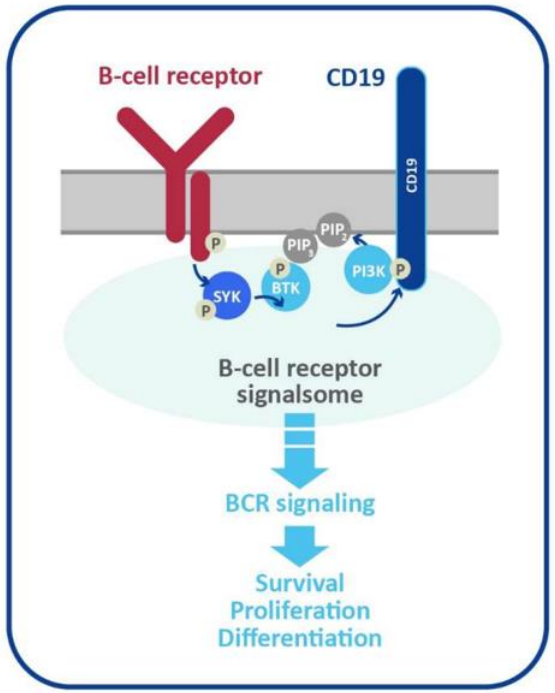
- **MOR208** is an Fc-enhanced monoclonal antibody that targets CD19
- Fc-enhancement of MOR208 leads to a potentiation of **ADCC** and **ADCP**
- MOR208 induces **direct cytotoxicity**



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

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

Direct cytotoxicity



Katz B-Z et al Leukemia & Lymphoma 2014
Fujimoto M, et al. Immunity 2000
Poe JC, et al. J Immunol;2012

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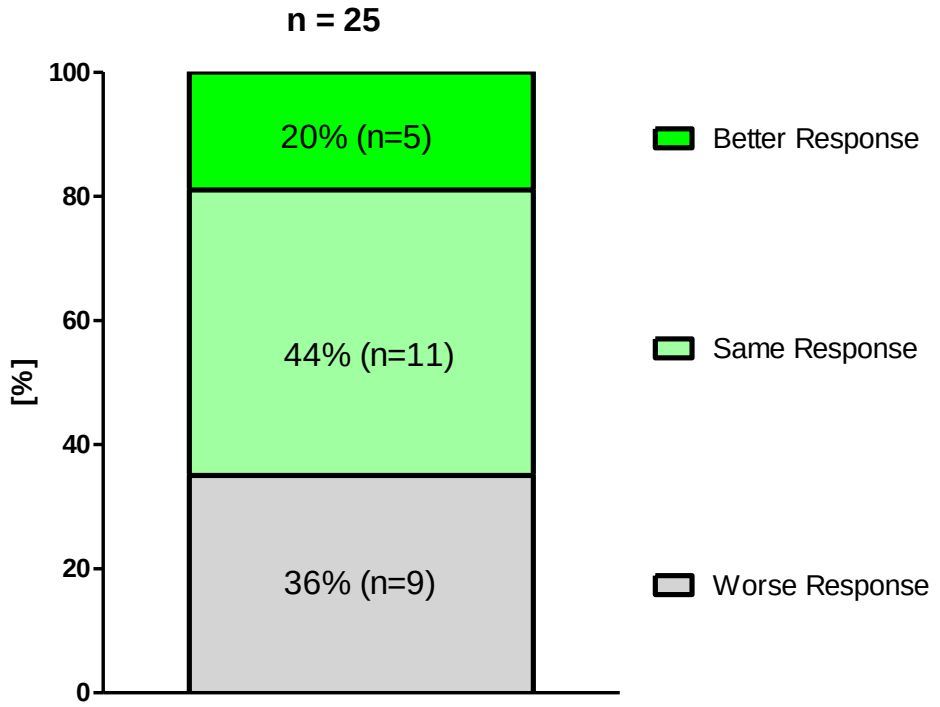
Phase I: MOR208 in in R/R CLL

A typical design of phase I dose escalating study

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 et al., 2014, unpublished post-hoc analysis



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

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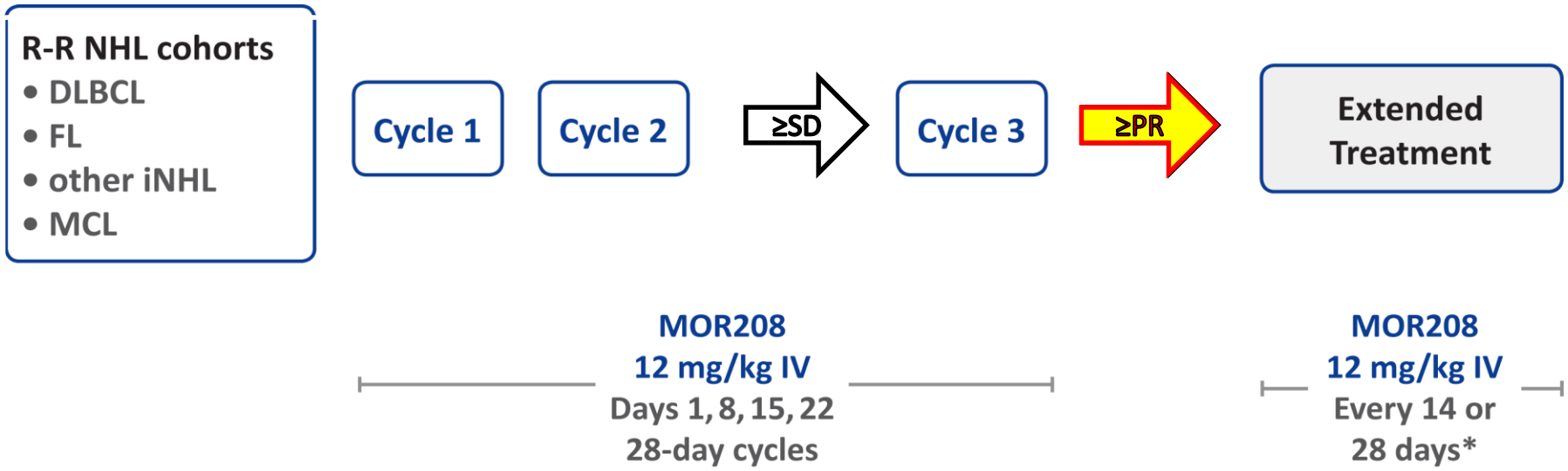
Phase II a: MOR208 in R-R NHL – study design

Multicentre study with 2-stage design (NCT01685008)



Primary objective

- **ORR**

Secondary objective

- DoR & PFS
- Safety and tolerability
- Pharmacokinetics and pharmacodynamics

Excluding Patients with SD from further therpy
Leeds to underestimation of MOR-208 efficeacy
- Especially in iNHL

Jurczak et al., Ann.Oncol 2018

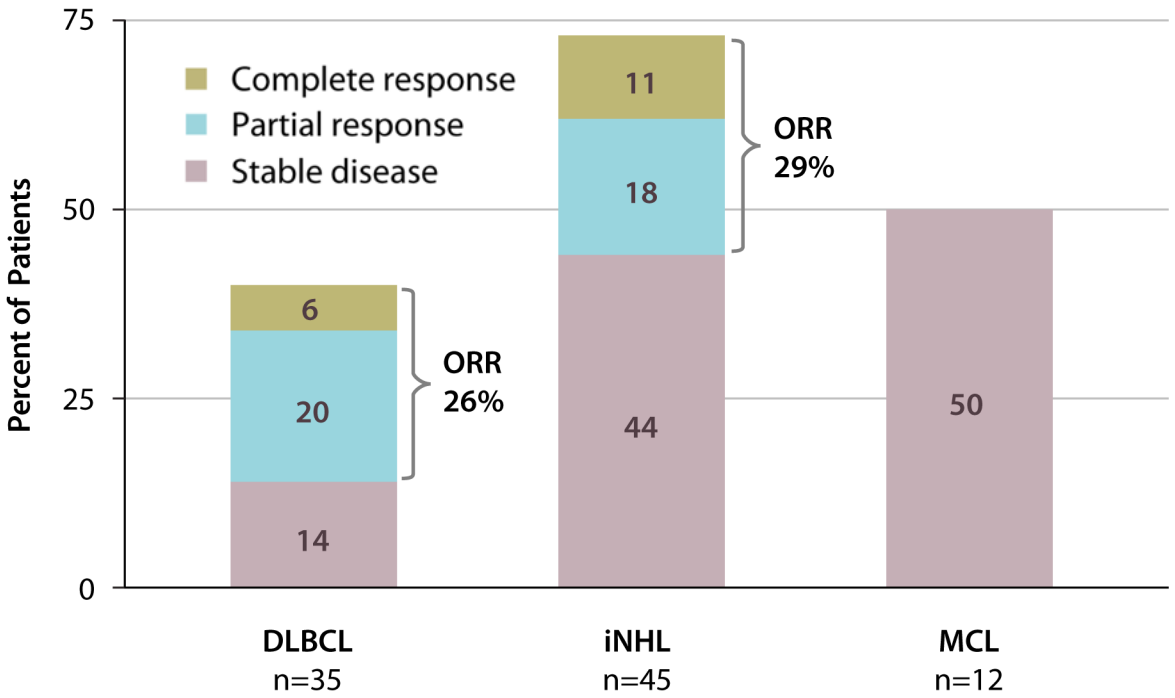
Phase II a: MOR208 in R-R NHL – Baseline Characteristics

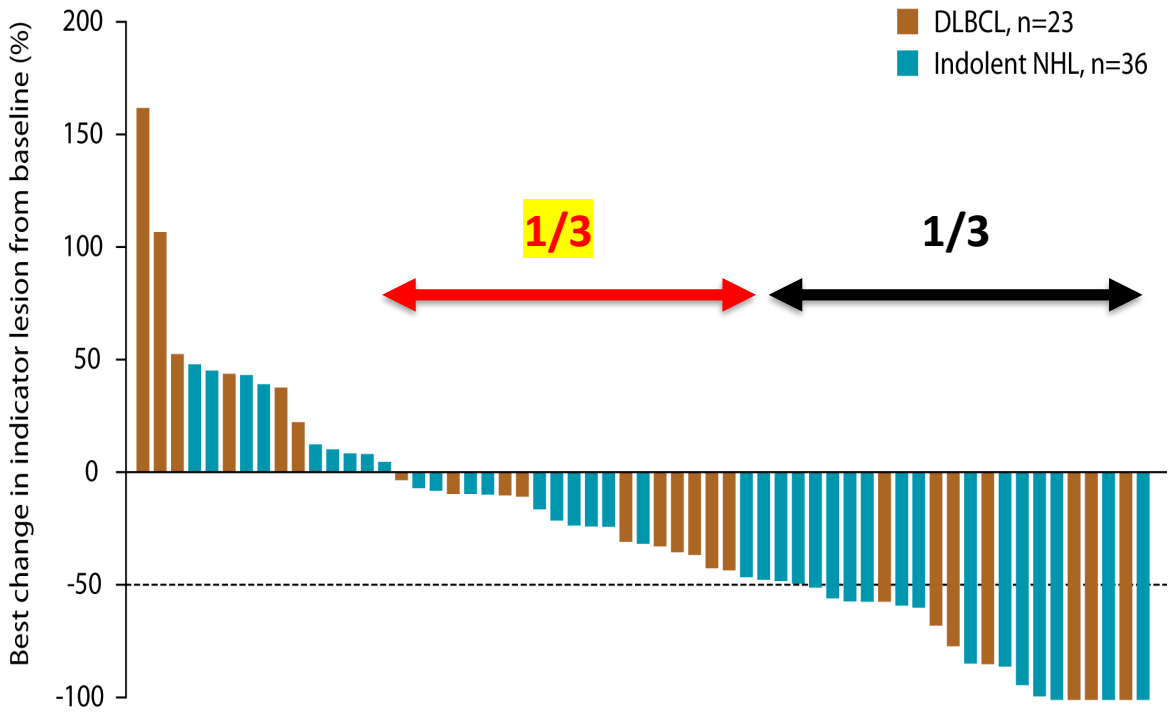
Characteristic, n (%)		DLBCL n=35	iNHL* n=45	MCL n=12	Total n=92
Age, years	Median	71	66	64.5	66.5
Sex	Male	24 (69)	21 (47)	11 (92)	56 (61)
Ann Arbor stage	I-II	4 (11)	5 (11)	1 (8)	10 (11)
	III-IV	30 (86)	40 (89)	11 (92)	81 (88)
	Missing	1 (3)	0	0	1 (1)
ECOG PS	0-1	34 (97)	43 (96)	11 (92)	88 (96)
	2	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

Jurczak et al., Ann.Oncol 2018

Phase II a: MOR208 in R-R NHL – Best Overall Response Rate





Jurczak et al., Ann.Oncol 2018

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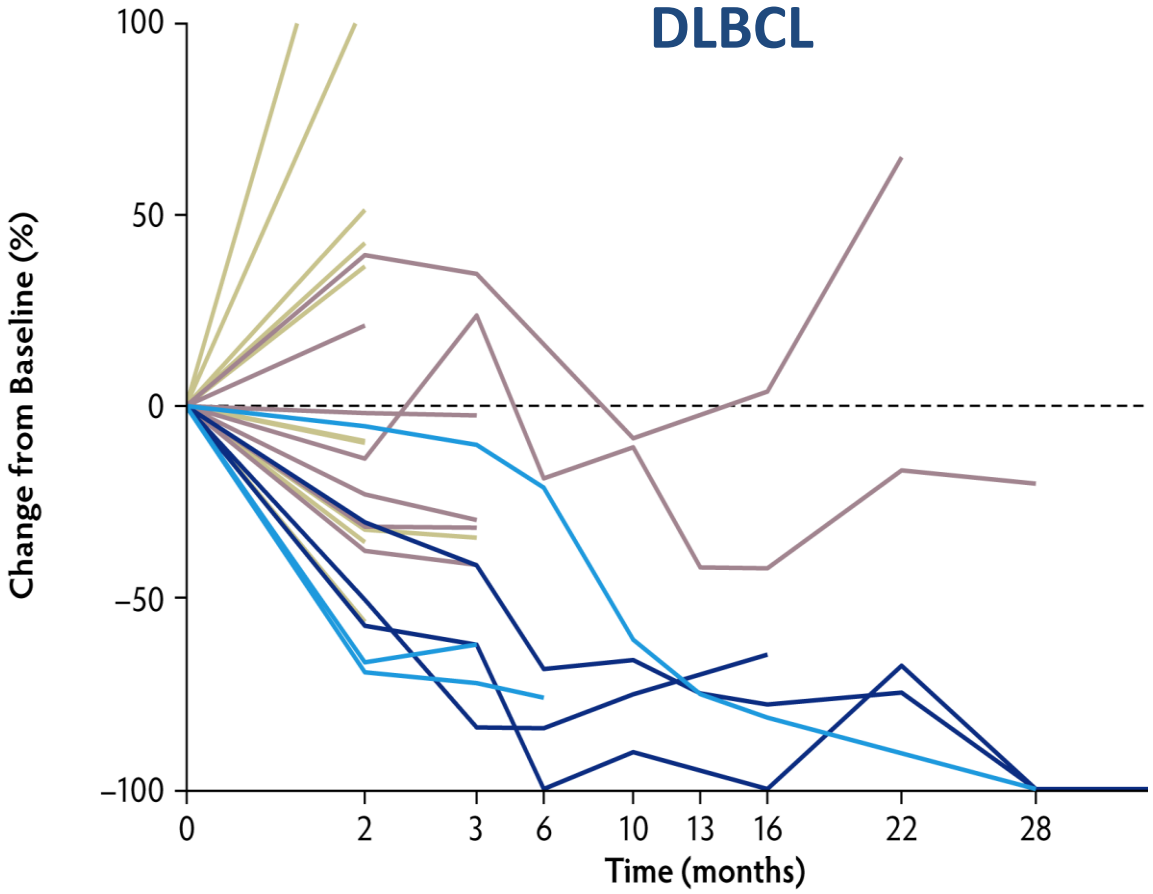
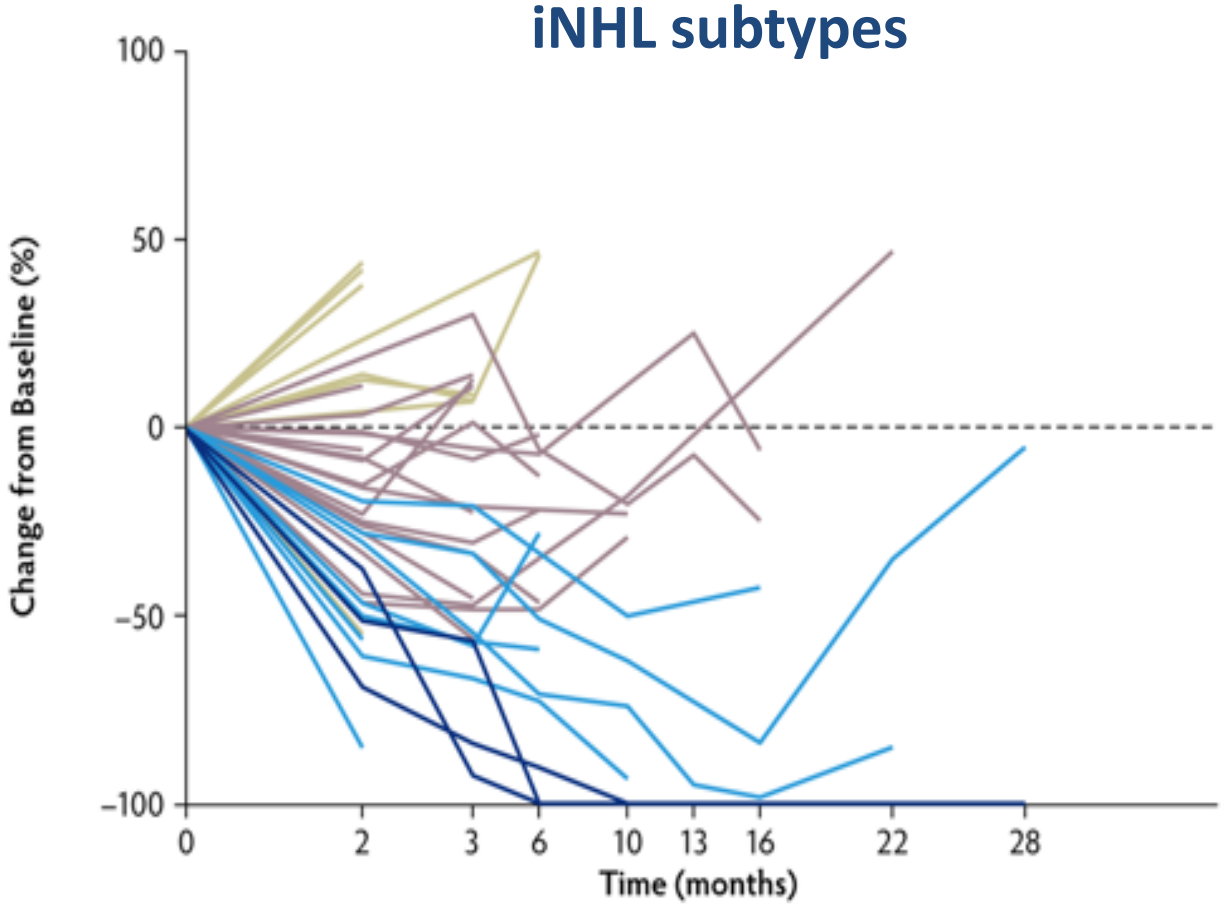
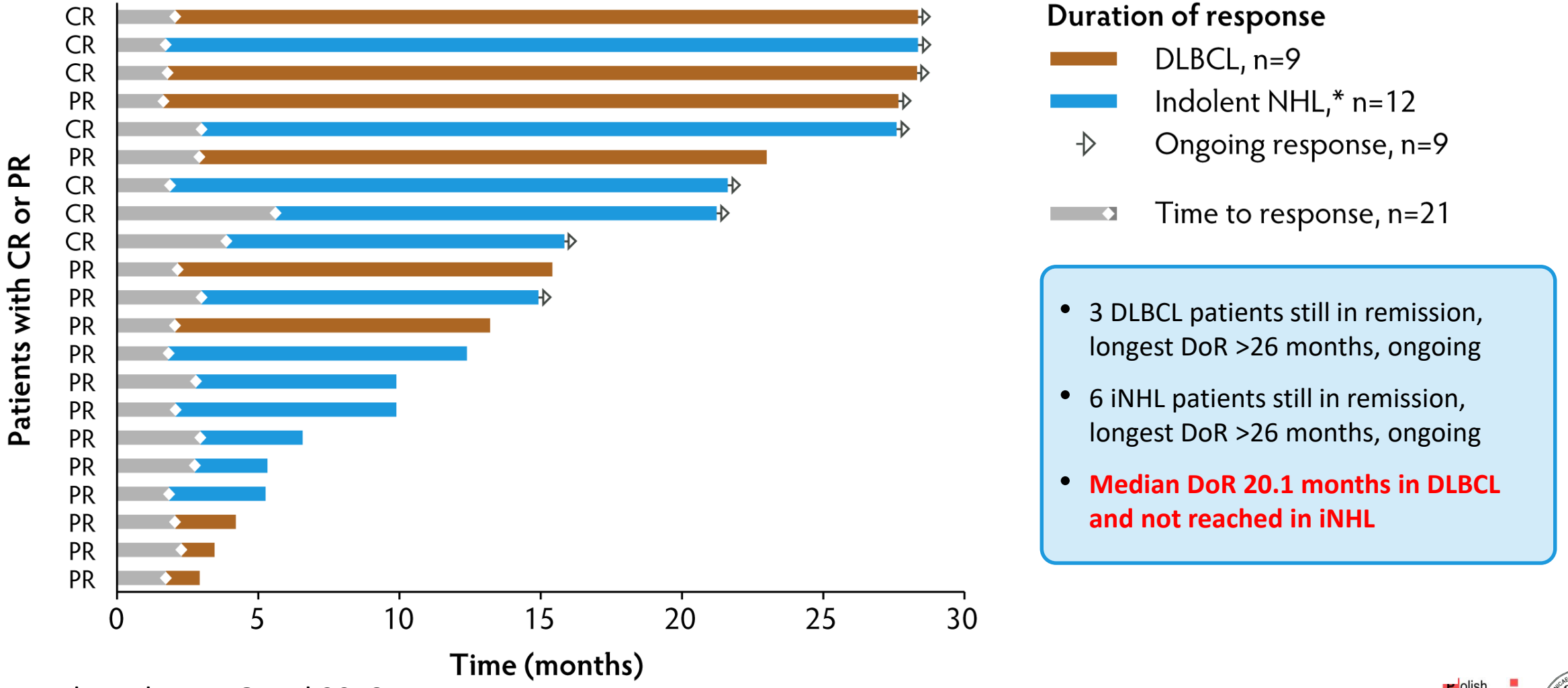
Phase II a: MOR208 in R-R NHL – Tumor shrinkage spiderplots





Jurczak et al., Ann.Oncol 2018

Phase II a: MOR208 in R-R NHL –Duration of Response

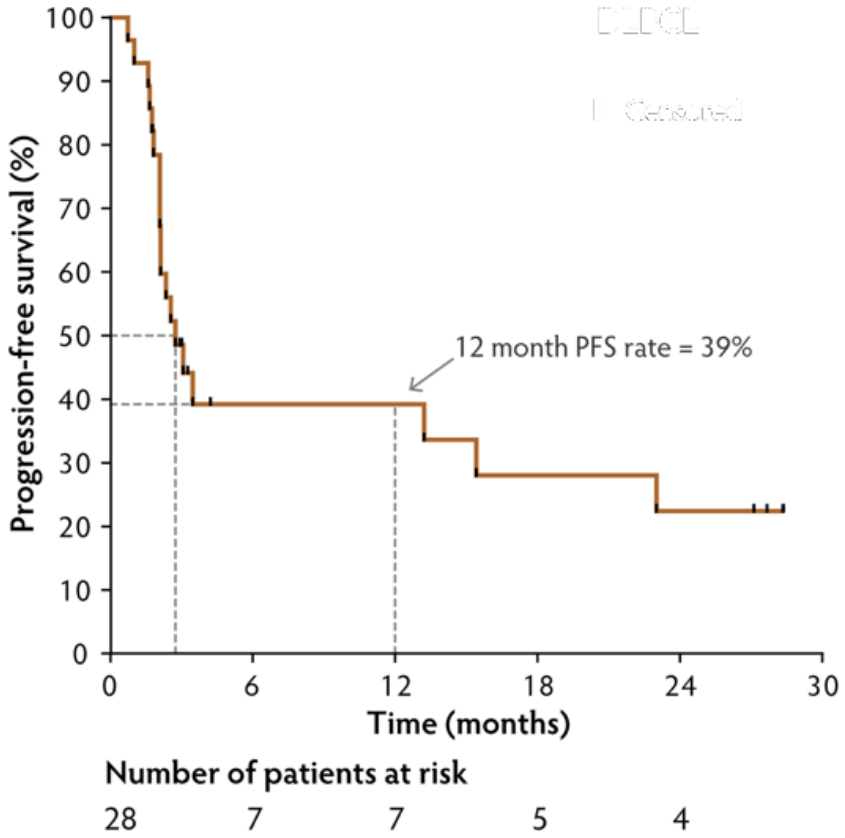


- 3 DLBCL patients still in remission, longest DoR >26 months, ongoing
- 6 iNHL patients still in remission, longest DoR >26 months, ongoing
- **Median DoR 20.1 months in DLBCL and not reached in iNHL**

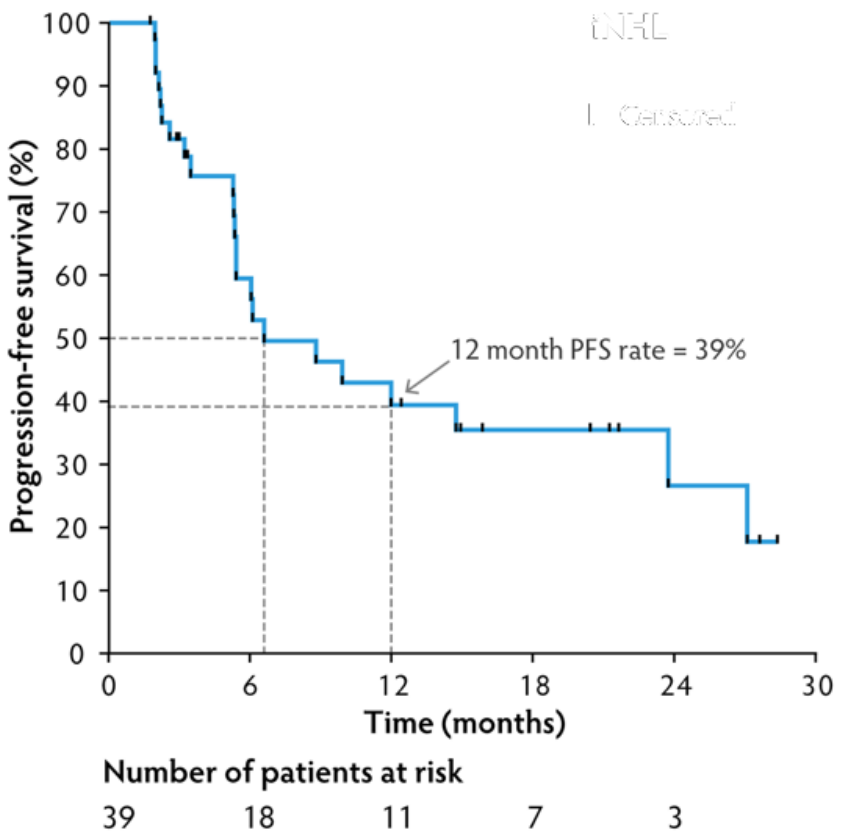
Jurczak et al., Ann.Oncol 2018

Phase II a: MOR208 in R-R NHL – PFS

DLBCL

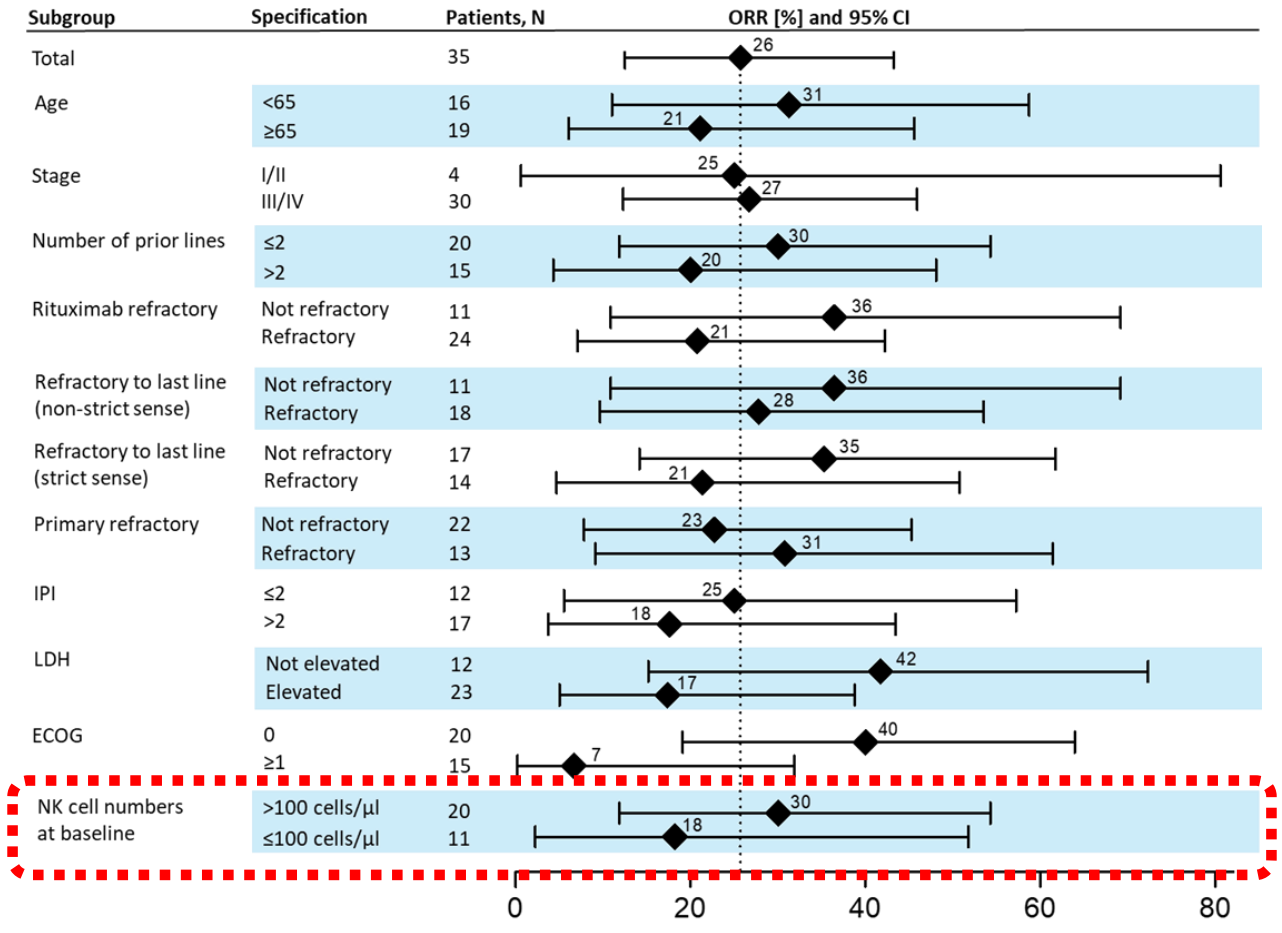


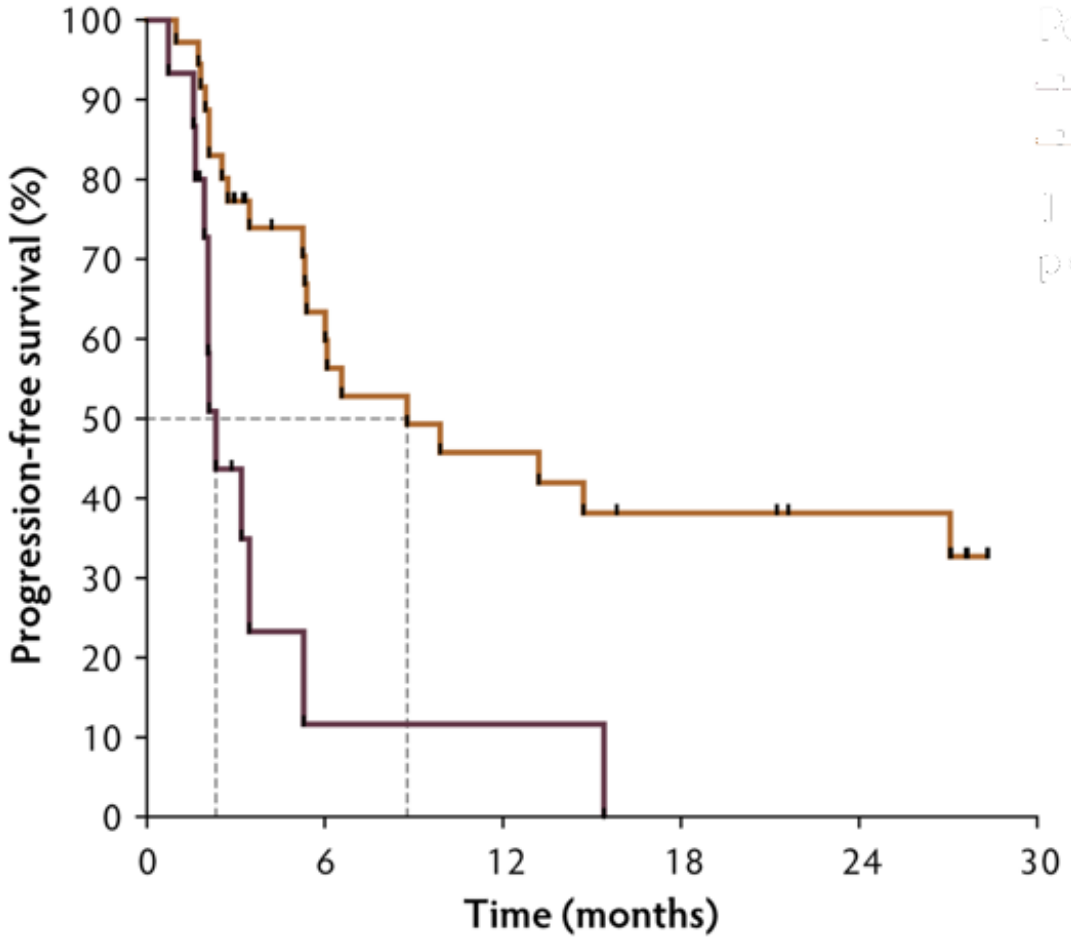
iNHL subtypes



Jurczak et al., Ann.Oncol 2018

Phase II a: MOR208 in R-R NHL – Subgroup Analysis





Jurczak et al., Ann.Oncol 2018

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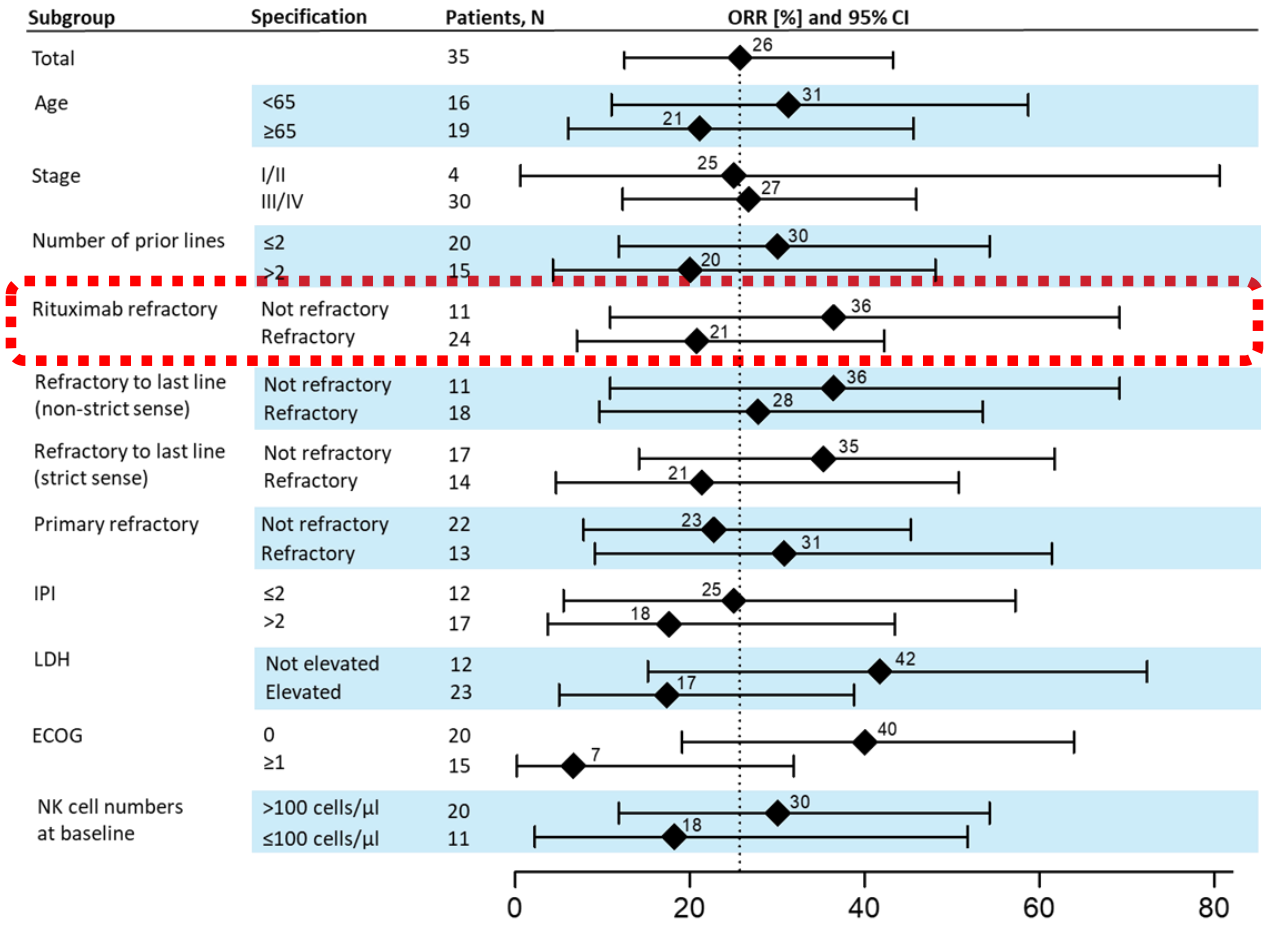
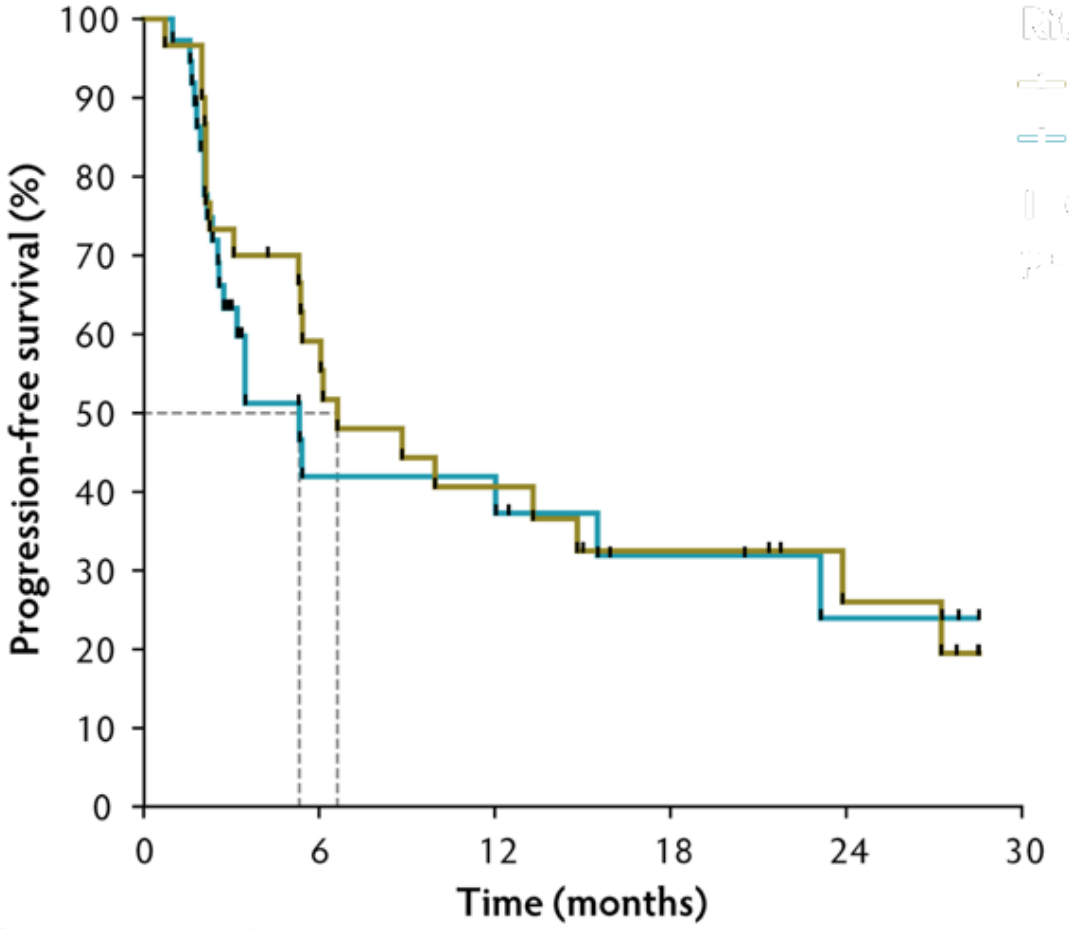
Phase II a: MOR208 in R-R NHL – Subgroup Analysis





Jurczak et al., Ann.Oncol 2018

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Phase II a: MOR208 in R-R NHL – AE 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, 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)

There were no treatment-related deaths

Jurczak et al., Ann.Oncol 2018

MOR208 Single Agent in R/R NHL

MOR208

Showed encouraging single-agent activity in R-R DLBCL and R-R iNHL for further development:

- **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)
- Efficacious in patients with **rituximab-refractory disease**

MOR208

Is able to induce **long-lasting responses** in DLBCL and iNHL

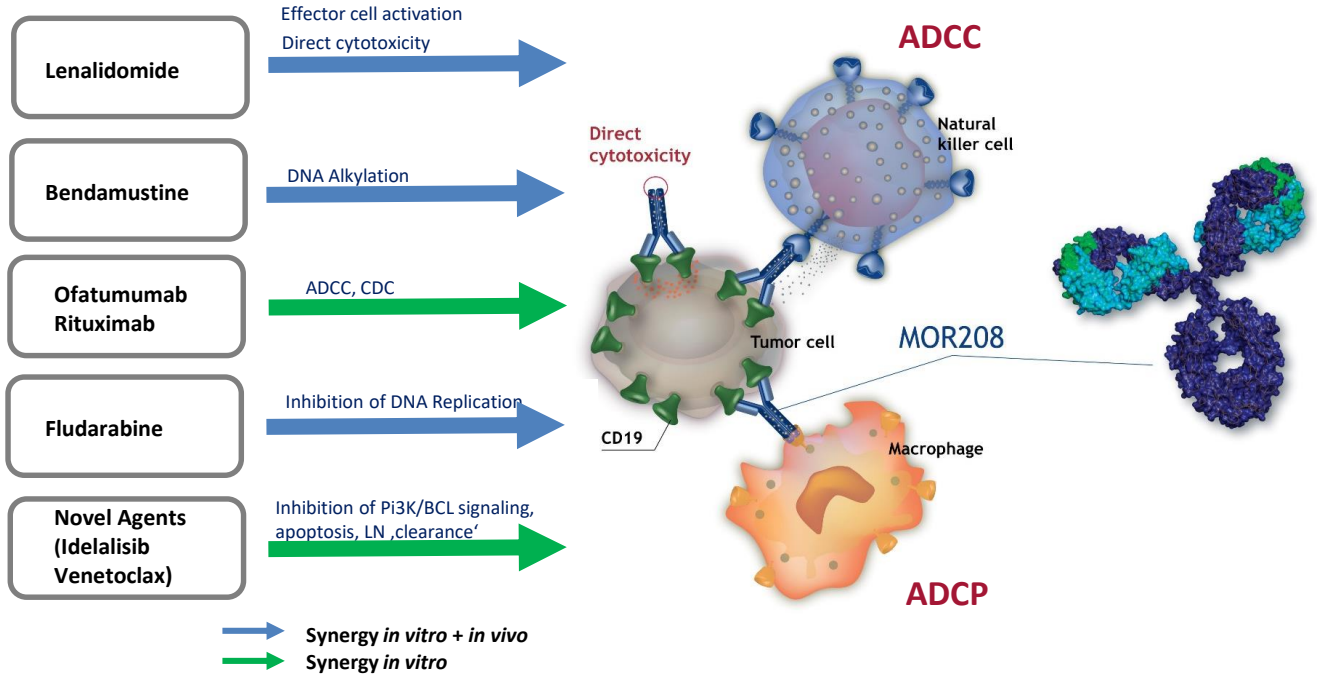
- **12 month PFS rate: 39%** in DLBCL and iNHL
- Longest responses: five iNHL and one DLBCL patient are on treatment for more than 4 years

MOR208

- **Well tolerated**, also in long-term treatment

Jurczak et al., Ann.Oncol 2018

MOR 208 - Synergy with all tested B cell therapies

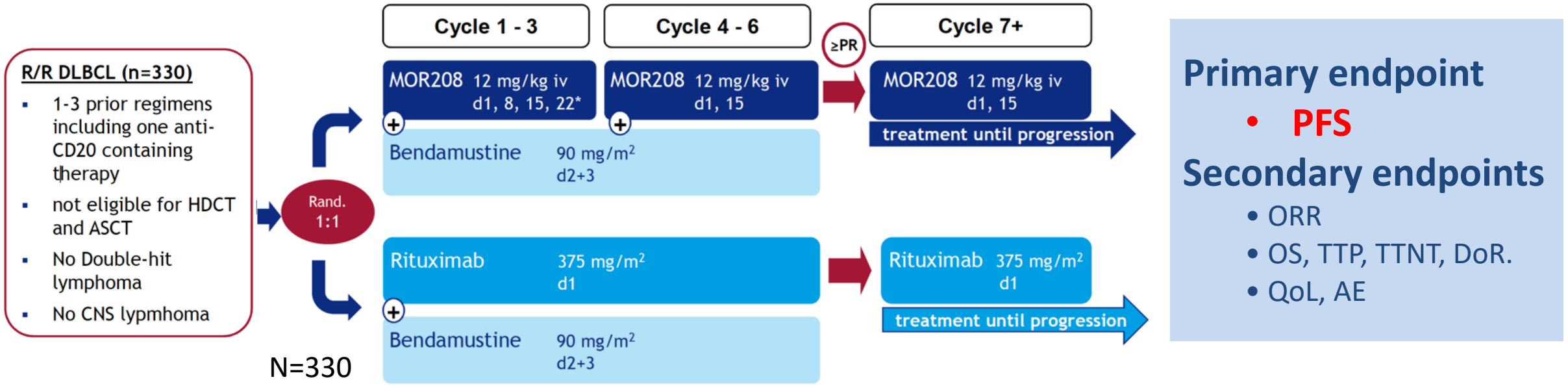


L-MIND II phase trial in R/R DLBCL

B-MIND III pase trial in R/R DLBCL

COSMOS phase II study in R/R CLL

B-MIND, phase III trial: BR vs B-MOR208



Primary endpoint

- **PFS**

Secondary endpoints

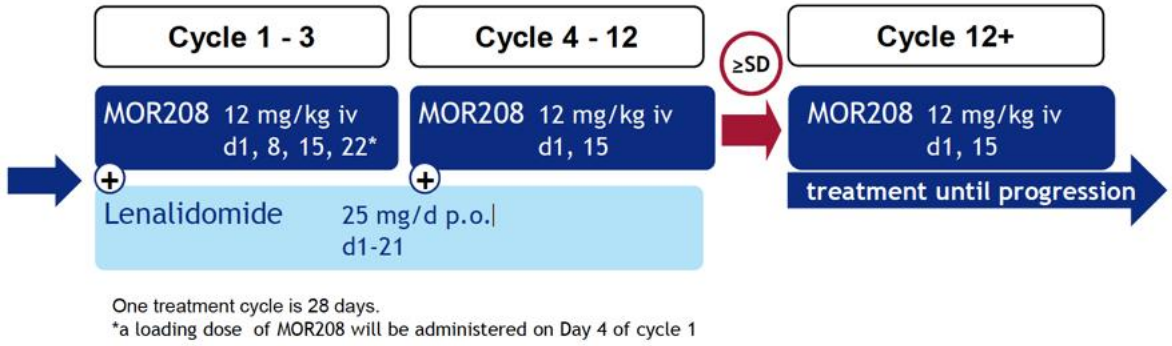
- ORR
- OS, TTP, TTNT, DoR.
- QoL, AE

Nowakowski et al., ASH 2017

L-MIND, phase II trial: MOR 208 + LEN

R/R DLBCL

- 1-3 prior regimens
- not eligible for HDCT and ASCT
- N=81



One treatment cycle is 28 days.
*a loading dose of MOR208 will be administered on Day 4 of cycle 1

- Response assessment after cycles 2, 4, 6, 9 and 12, thereafter every 3 cycles.
- Safety data from the first six patients were evaluated in a safety run-in to determine the starting dose of lenalidomide (len) for the remainder of study

Primary endpoint - ORR

Secondary endpoints

- DoR
- PFS,OS,
- safety, AE,
- AE (Exploratory and biomarker-based analyses)

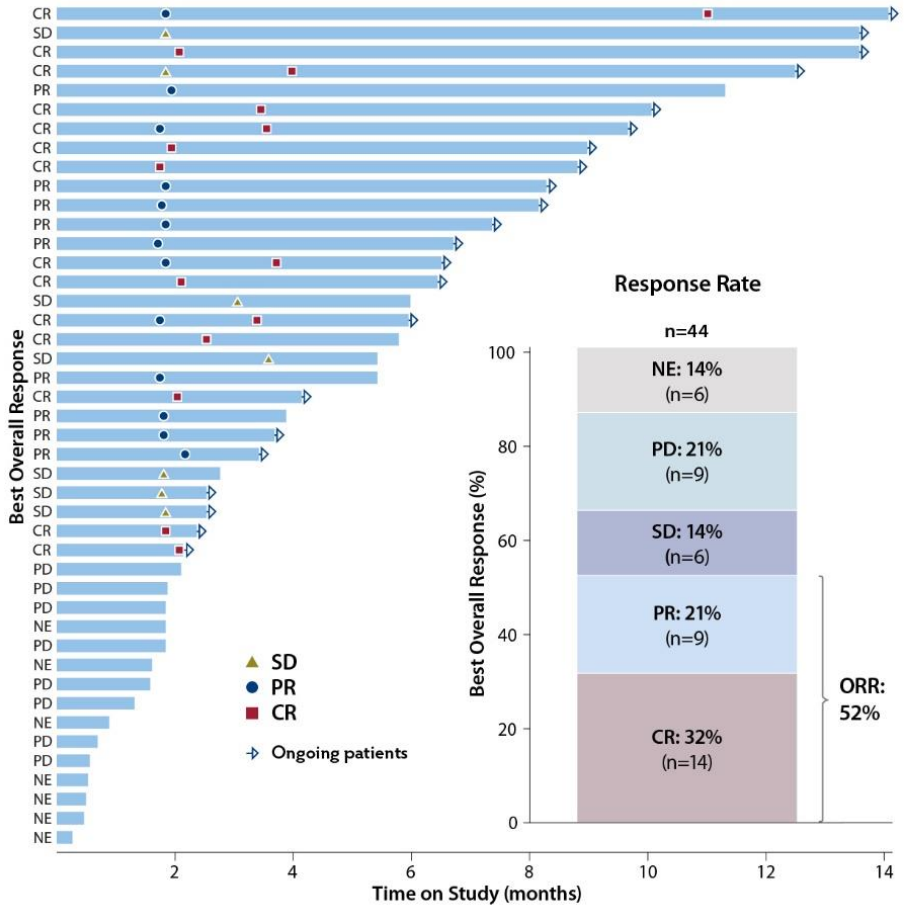
Salles et al., ASH 2017

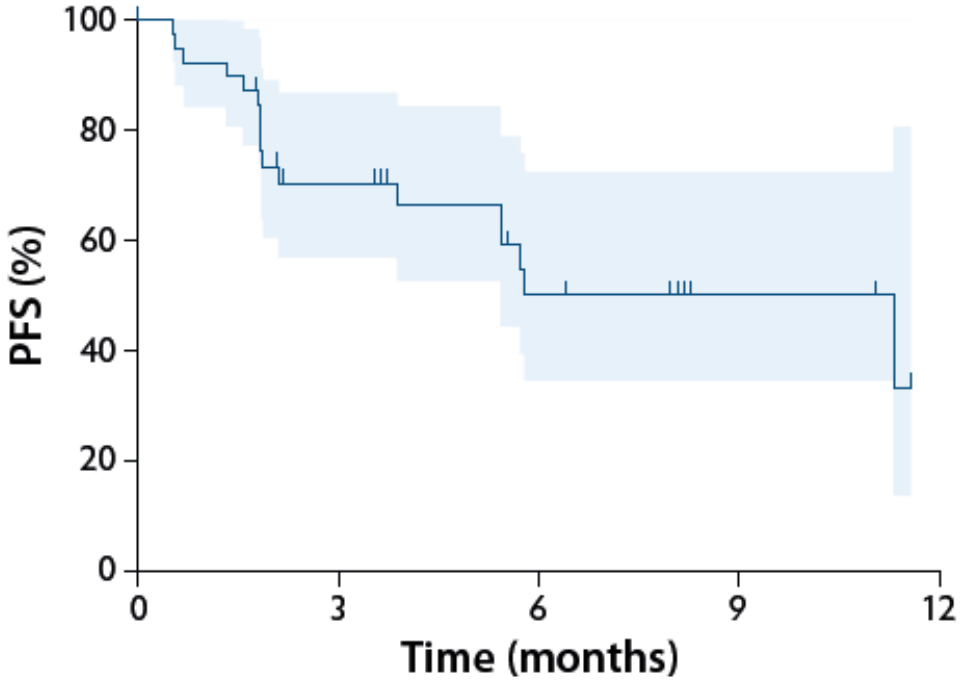
L-MIND, phase II trial: Lenalidomide + MOR 208

Characteristic		n (%) N=51
Age, years	Median (range)	73 (47-82)
Sex	Female/Male	27/24
Ann-Arbor	III-IV	30 (59)
ECOG-PS	0-1	47 (92)
	2	3 (6)
IPI	Low (0-1)	8 (16)
	Low-Intermediate (2)	13 (25)
	High-Intermediate (3)	9 (18)
	High (4-5)	15 (29)
Prior therapies	1	26 (51)
	≥2	24 (47)
LDH level	Elevated	28 (55)
Refractory to rituximab	Yes	18 (35)
Refractory to last prior line	Yes	21 (41)
Prior ASCT	Yes	2 (4)

Salles et al., ASH 2017

L-MIND, phase II trial: MOR 208 + LEN

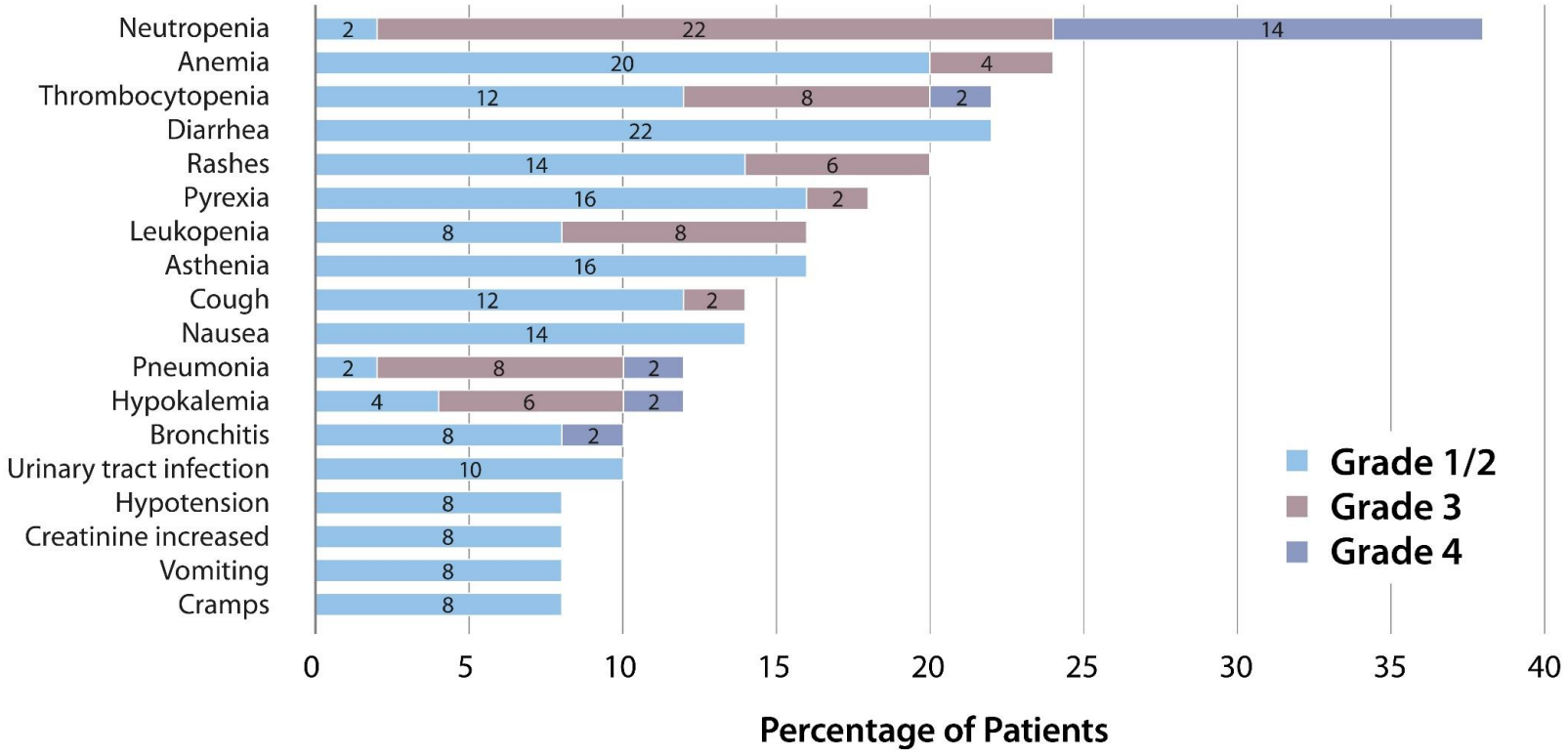




- median time to response 1.8 months, median time to CR 2.3 months
- **median PFS – not reached**
- **PFS at 12 months – 50.4%**
- 19 out of 23 responders (13 out of 14 CRs) ongoing

Salles et al., ASH 2017

L-MIND, phase II trial: MOR 208 + LEN



- No infusion-related reactions were reported for MOR208
- Treatment-related **SAE occurred in eight (16%)** patients (pneumonia, febrile neutropenia, agranulocytosis, bronchitis, tumor flare, pyrexia, asthenia, pulmonary embolism, arthritis)
- As of now no unexpected toxicities were observed compared to the known toxicity profiles of LEN and MOR208 monotherapy
- **A LEN dose reduction was required in 23 (45%)** of 51 patients

Salles et al., ASH 2017

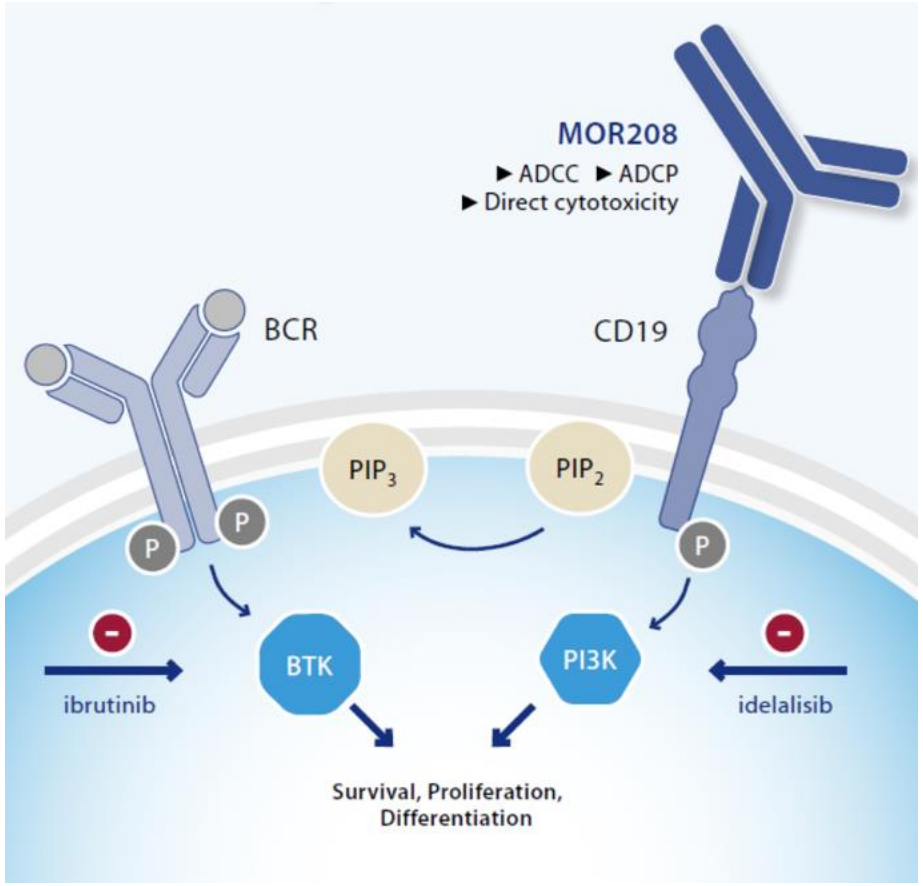
MOR 208 + LEN Promising PFS Compared to Existing and Upcoming Therapies in NTE-R/R DLBCL

	MOR208C201 Jurczak et al, ASH 2016	Witzig et al., 2011	Czuczman et al.,2017	Wang et al., 2013	Morschauser et al, ASH 2016	L-MIND, Data cut-off December 12, 2018
Regimen	**MOR208**	**LEN** (in aNHL)	**LEN**	**R + LEN**	**Obinutuzumab + LEN**	**MOR208 + LEN**
Baseline Characteristics						
Evaluable patient population	R/R DLBCL N=35	R/R DLBCL N=108	R/R DLBCL N=51	R/R DLBCL N=32	R/R DLBCL N=71	R/R DLBCL N=68
Age, median	71	66 (overall)	69	65	70	72
Prior lines, median	2	3 (overall)	2	3	2	2
Refractory, (%)	46%*	44% (overall)	unknown	unknown	70%	40%
Outcome						
Objective response rate	26%	28%	27%	28%	45%	49%
Complete response rate	6%	7%	10%	22%	16%	31%
Median PFS, months	2.7	2.7	3.1	2.8	4.1	Not reached 12 mo PFS rate 50.4%
Median overall survival, months	-	-	7.1	10.2	-	NR* at med FU

MOR 208 + LEN Promising PFS Compared to Existing and Upcoming Therapies in NTE-R/R DLBCL

	L-MIND Cut-Off Dec.12, 2018	Dang et al., BJH 2017*	Sehn et al., ASH 2017	Pettengel et al., The Lancet, 2012	SCHOLAR-1 Crump et al., Blood, 2017**	ZUMA-1 Locke And Neelapu et al.,ASH, 2017
Regimen	MOR208 + LEN	R + bendamustine	polatuzumab + R + bendamustine	pixantrone	Salvage chemotherapies and radiation	axi-cel
Phase	2	3	2	3	Retrospective study	2
Evaluable patient population	R/R DLBCL n=68	R/R DLBCL n=137	R/R DLBCL n=40	R/R DLBCL n=104	Refractory DLBCL n=635	Refractory DLBCL n=108
Best ORR	49%	49%	70%	37%	26%	82%
Best CR	31%	18%	58%	11.4%	8%	58%
Median PFS, months	Not reached 12 mo PFS rate 50.4%	3.7	6.7	5	n/a	5.9
Median overall survival, months	NR*** at med FU	9.5	11.8	7.5	6.6	NR

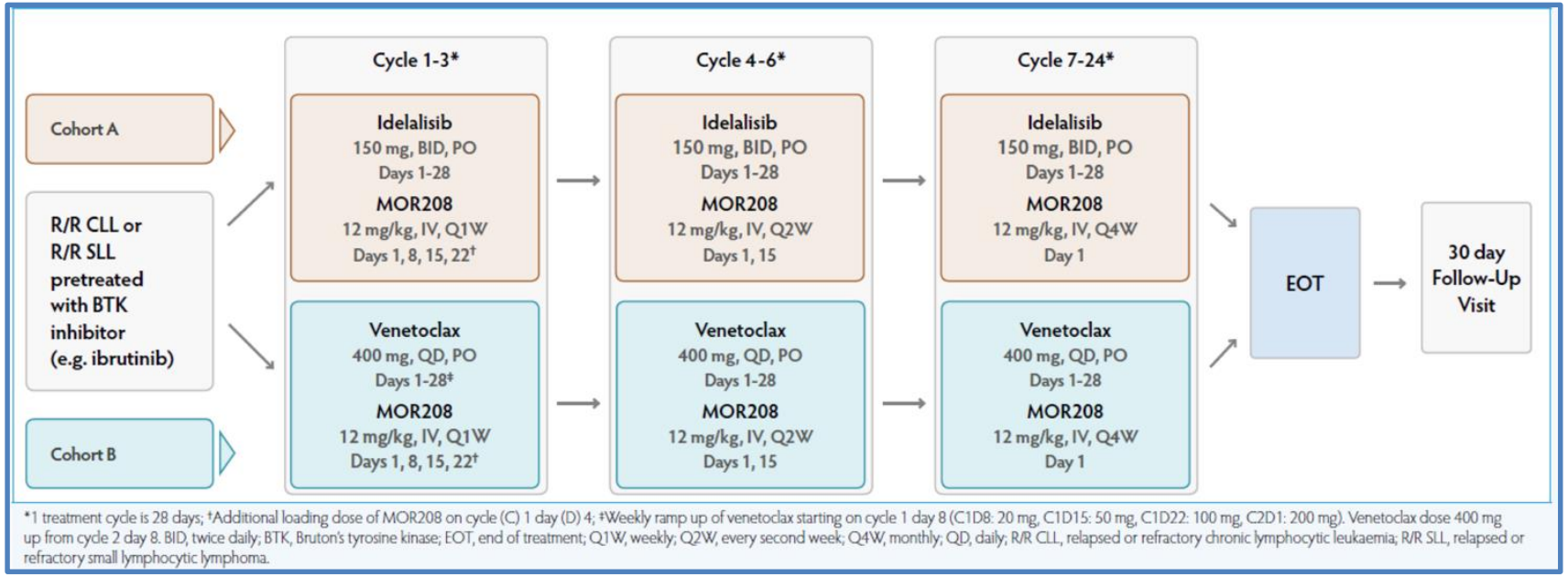
Two-cohort, phase II study in R/R CLL (COSMOS)



- CD19 enhances BCR signaling and tumor cell proliferation and is a common adaptor used by multiple intracellular docking molecules for PI3K signaling
- MOR208 showed synergistic potential in combination with IDE during in vitro experiments
- Therefore, it is hypothesized that the combination of anti-CD19 MOR208 and idelalisib **may be beneficial to overcome ibrutinib resistance in a clinical setting**

Jurczak et al, EHA 2018

Two-cohort, phase II study in R/R CLL (COSMOS)



*1 treatment cycle is 28 days; †Additional loading dose of MOR208 on cycle (C) 1 day (D) 4; ‡Weekly ramp up of venetoclax starting on cycle 1 day 8 (C1D8: 20 mg, C1D15: 50 mg, C1D22: 100 mg, C2D1: 200 mg). Venetoclax dose 400 mg up from cycle 2 day 8. BID, twice daily; BTK, Bruton's tyrosine kinase; EOT, end of treatment; Q1W, weekly; Q2W, every second week; Q4W, monthly; QD, daily; R/R CLL, relapsed or refractory chronic lymphocytic leukaemia; R/R SLL, relapsed or refractory small lymphocytic lymphoma.

Primary endpoint - AE

Secondary endpoints

- ORR
- Anti-MOR208 Ab form.
- Pharmacokinetics

Exploratory endpoints

- Analysis of biomarkers

Jurczak et al, EHA 2018

MOR208 + Idelalisib, phase II study in R/R CLL (COSMOS)

- Median time from CLL diagnosis to first study dose of MOR208+IDE was **7.2 years** (range: 3.7 to 23.7 years)
- Pts were heavily pre-treated with a **median of 5 prior lines of therapy** (range: 2-9)
- **9 pts (82%) discontinued prior ibrutinib treatment due to PD** and 2 pts (18%) due to toxicity. Median time from last BTKi intake to first study
- Dose of MOR208+IDE was 30 days (range: 5 to 236 days)

Characteristic	Specification	n (%), N=11 patients
Del17p* or TP53 mutation*	No lesion	1 (9.1)
	Deletion and/or mutation	7 (63.6)
	Unknown	3 (27.3)
IGVH status*	No mutation	7 (63.6)
	Mutation	1 (9.1)
	Unknown	3 (27.3)
BTK status*	No mutation	0 (0)
	Mutation	5 (45.5)
	Unknown	6 (54.4)
PLCγ status*	No mutation	0 (0)
	Mutation	3 (27.3)
	Unknown	8 (72.7)
Prior treatment	Ibrutinib	11 (100)
	FCR (CIT)	8 (72.7)
	CT/CIT other than FCR	9 (81.8)
	Anti-CD20 mAb	11 (100)
	Rituximab	10 (90.9)
	Ofatumumab	1 (9.1)
	Allogeneic SCT	1 (9.1)
	Autologous SCT	2 (18.2)
	Venetoclax	1 (9.1)
	Alemtuzumab	2 (18.2)

Jurczak et al, EHA 2018

MOR208 + Idelalisib, phase II study in R/R CLL (COSMOS)

Preferred Term	n (%), N=11			
	TEAEs (≥2 pts)		SAEs (any)	
	All Grades	Grade ≥3	All Grades	Grade ≥3
Hematological				
Neutropenia	5 (45)	4 (36)	0	0
Anaemia	5 (45)	3 (27)	1 (9)	1 (9)
Thrombocytopenia	2 (18)	2 (18)	1 (9)	1 (9)
Pancytopenia	n.a	n.a	1 (9)	0
Non-Hematological				
Dyspnea	5 (45)	1 (9)	0	0
Pyrexia	5 (45)	0	0	0
Infusion related reaction	4 (36)	0	0	0
Cough	3 (27)	0	0	0
Amylase increased	2 (18)	2 (18)	0	0
ALT increased	2 (18)	1 (9)	0	0
Bronchitis	2 (18)	1 (9)	1 (9)	1 (9)
Hypertension	2 (18)	1 (9)	0	0
Cytomegalovirus infection	2 (18)	0	0	0

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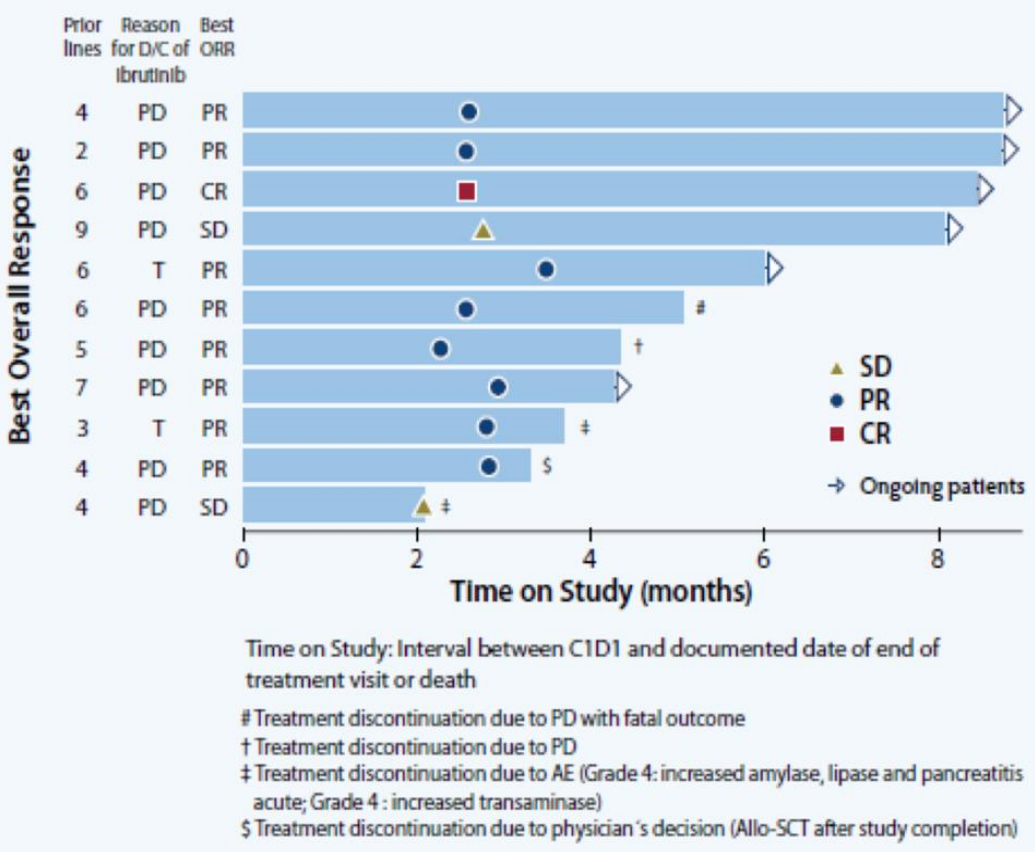
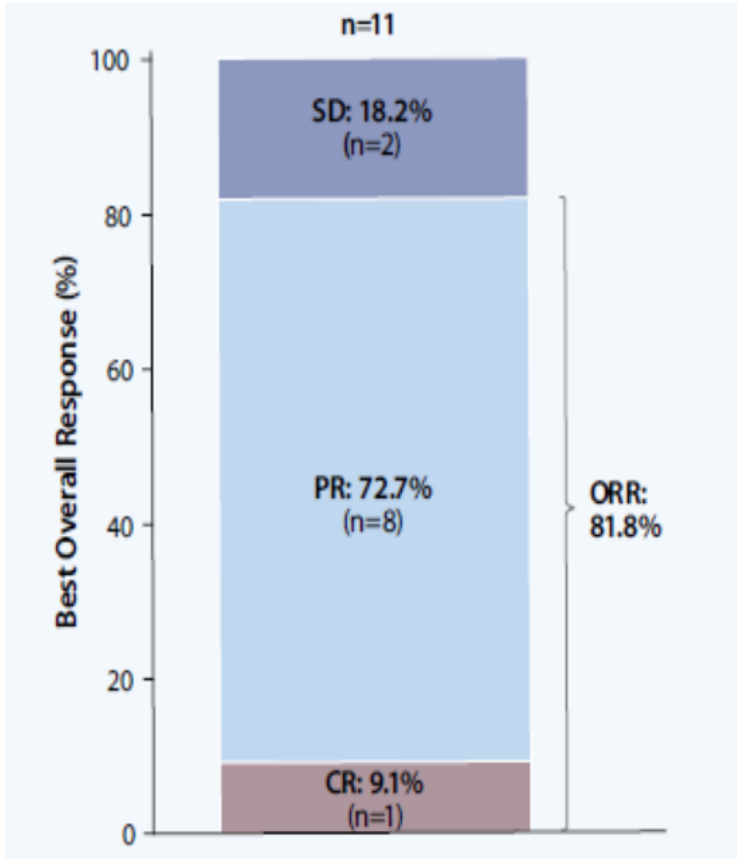
MOR208 + Idelalisib, phase II study in R/R CLL (COSMOS)





- The median observation time at cut off was **4.2 months**
- Investigator assessed **ORR was 82% including 1 CR (9%)** confirmed by bone marrow biopsy and 8 PR (73%)
- Two pts had PD, one of them resulted in fatal cardiorespiratory failure.
- Treatment of 6 pts is ongoing

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MOR208 - Summary

MOR208 Monotherapy in R/R NHL

- **ORR: 26%** in DLBCL and 29% in iNHL, **12 month PFS rate: 39%** in DLBCL and iNHL
- Target lesion shrinkage also observed in patients with stable disease
- Efficacious in patients with **rituximab-refractory** disease
- **Longe responses**: five iNHL and one DLBCL patient are on treatment for more than 4 years
- **Well tolerated**, also in long-term treatment

MOR208 – LEN in R/R DLBCL

- **ORR: 48,5%, 31% CR** in R/R DLBCL
- Median follow-up: 8,3 months, **12 months PFS rate – 50.4%**
- Particularly effective in patients with normal NK cell counts
- **Well tolerated**, also in long-term treatment

MOR208 = Idelalisib in R/R CLL

- **ORR: 81.8%, 9.8% CR** in R/R CLL
- **Well tolerated**, short follow-up

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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