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MEETING SUMMARY
ASH 2018, SAN DIEGO, USA

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AN UPDATE ON TREATMENT FOR FOLLICULAR LYMPHOMA

DISCLAIMER

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Please note:

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A PHASE II LYSA STUDY OF OBINUTUZUMAB COMBINED WITH LENALIDOMIDE FOR ADVANCED UNTREATED FOLLICULAR B-CELL LYMPHOMA IN NEED OF SYSTEMIC THERAPY

F. Morschhauser et al. Abst #446

A PHASE II STUDY OF OBINUTUZUMAB COMBINED WITH LENALIDOMIDE FOR ADVANCED UNTREATED FL

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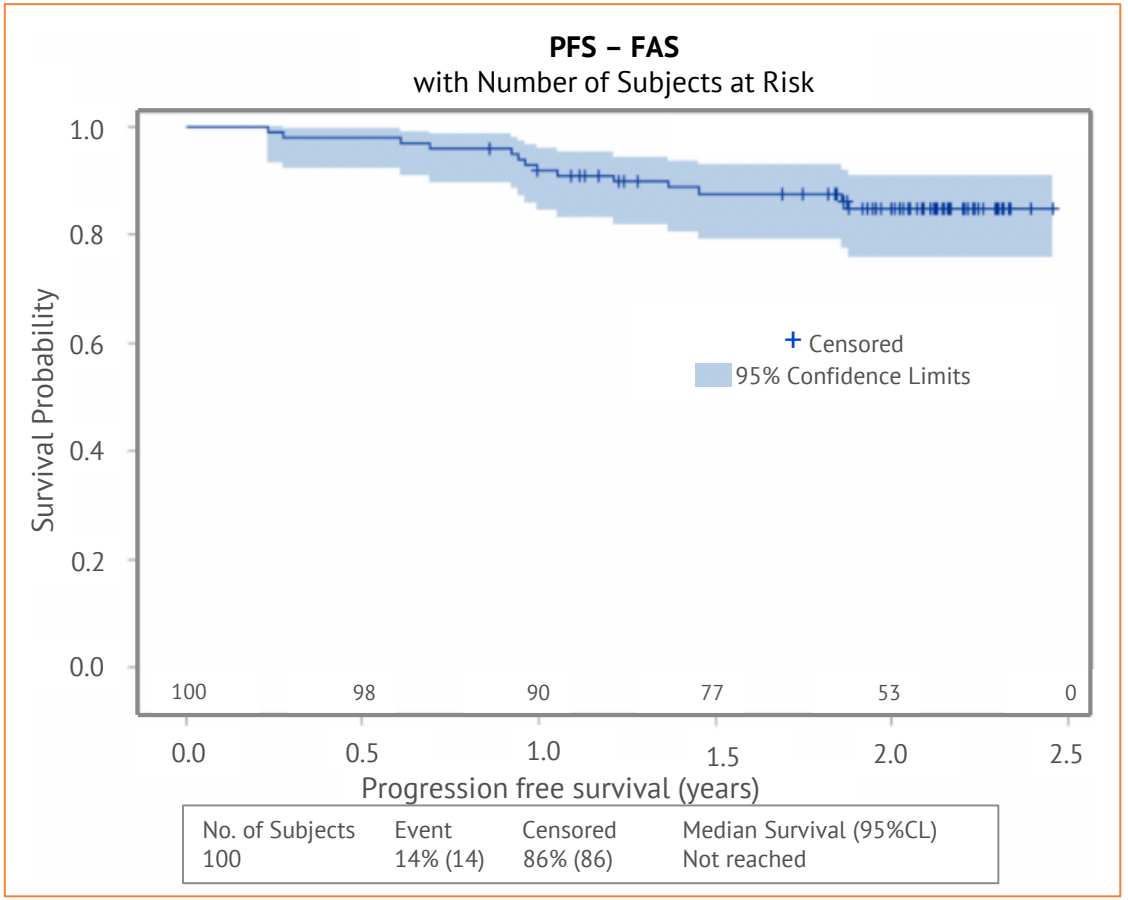
		All pts (N=100)
IWG 1999	ORR, % (95%CI)	91 (83.6–95.8)
	CR/CRu, % (95%CI)	47 (36.9–57.2)
IWG 2007	ORR, % (95%CI)	96 (90.1–98.9)
	CR, % (95%CI)	59 (48.7–68.7)
2-year PFS	% (95%CI)	85.0 (75.9–90.9)
2-year DOR	% (95%CI)	85.5 (76.1–91.3)
2-year OS	% (95%CI)	96.9 (90.5–99.0)



CI, confidence interval; CR, complete response; CRu, complete response unconfirmed; DOR, duration of response; FL, follicular lymphoma; IWG, international working group; ORR, overall response rate; OS, overall survival; PFS, progression-free survival

Morschhauser F et al. Presented at ASH 2018 (abstr 446)

CHEMOTHERAPY-FREE COMBINATION OF OBINUTUZUMAB AND IBRUTINIB IN 1ST LINE TREATMENT OF FOLLICULAR LYMPHOMA: THE ALTERNATIVE STUDY BY THE GERMAN LOW-GRADE LYMPHOMA STUDY GROUP (GLSG)

C. Schmidt et al. Abst #448

OBINUTUZUMAB AND IBRUTINIB IN 1ST LINE TREATMENT OF FL

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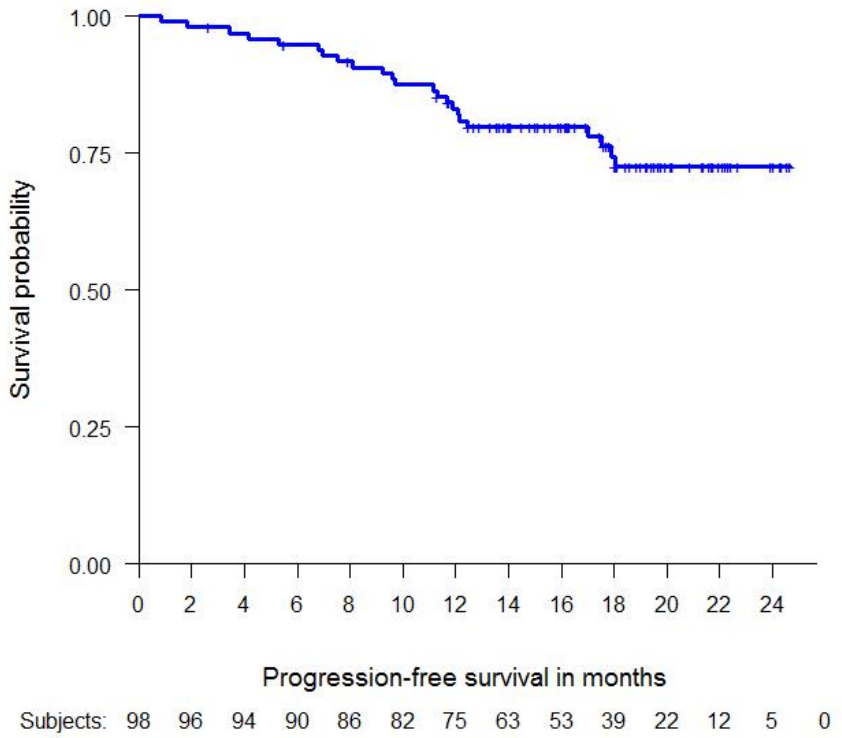
ORR was 90% (87/97)
PR 85% (82/97)
CR 5% (5/97)

Most common AEs:

- diarrhea (30%)
- rash (25%)
- fatigue (23%)
- nasopharyngitis (20%)

Grade 3-4 neutropenia and thrombopenia were seen in 8% and 4%

PFS



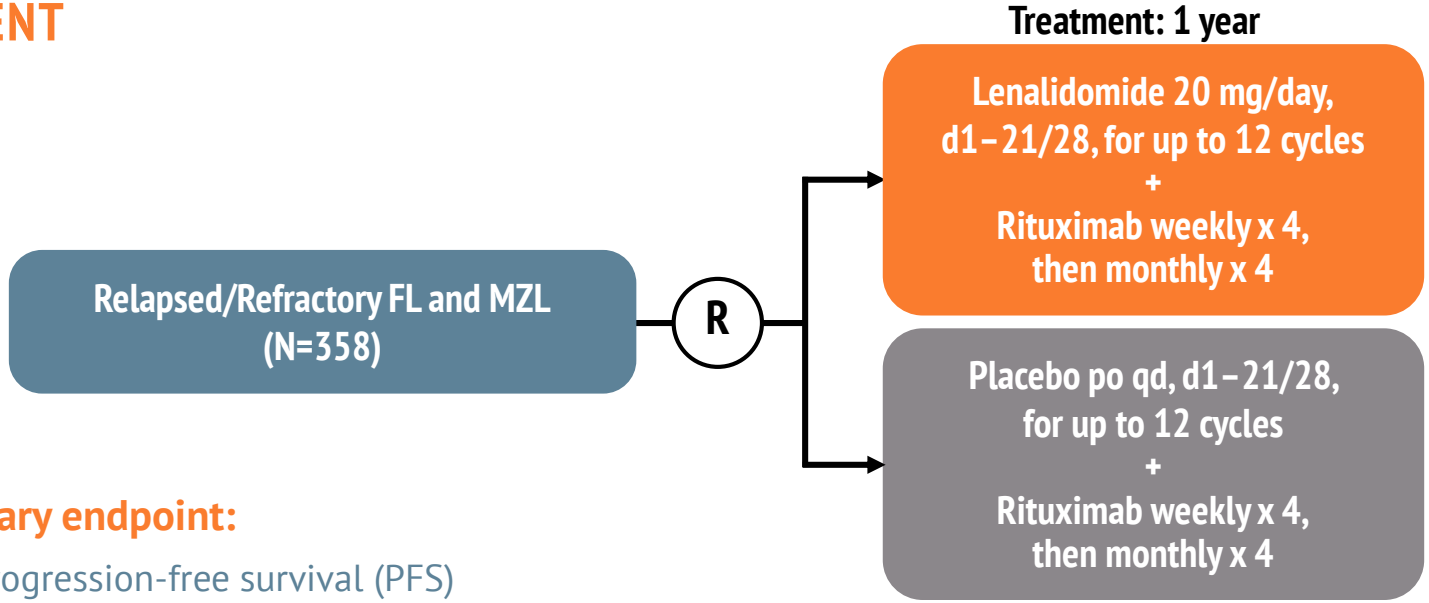
AE, adverse event; CR, complete response; ORR, overall response rate; PFS, progression-free survival; PR, partial response
Schmidt C et al. Presented at ASH 2018 (abstr 448)

AUGMENT: A PHASE III RANDOMIZED STUDY OF LENALIDOMIDE PLUS RITUXIMAB (R^2) VERSUS RITUXIMAB/PLACEBO IN PATIENTS WITH RELAPSED/REFRACTORY INDOLENT NHL

J.P. Leonard et al. Abst #445

LENALIDOMIDE PLUS RITUXIMAB IN R/R FL

AUGMENT



- **Primary endpoint:**
  - Progression-free survival (PFS)
    - 90% power, 60% improvement in PFS (median 17.6 vs 11 months)
    - HR = 0.625
    - Final analysis at 193 events, IRC-assessed
- **Secondary endpoints:**
  - ORR, CR, DOR, safety

Stratification factors:

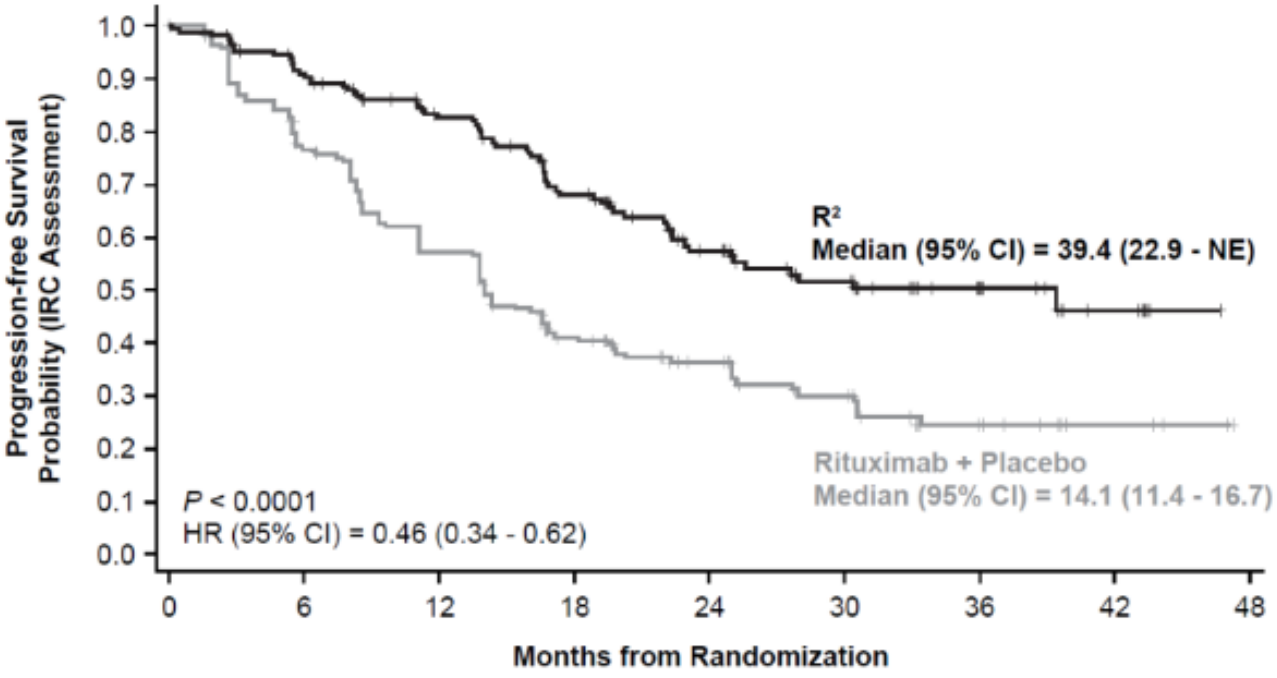
- Previous Rituximab treatment (yes/no)
- Time since last lymphoma therapy (≤2 yrs/>2 yrs)
- FL/MZL

CR, complete response; DOR, duration of response; FL, follicular lymphoma; HR, hazard ratio; IRC independent review committee; MZL, marginal zone lymphoma; ORR, overall response rate; PFS, progression-free survival; R/R, relapsed/refractory

Leonard J.P et al. Presented at ASH 2018 (abstr 445)

LENALIDOMIDE PLUS RITUXIMAB IN R/R FL

PRIMARY ENDPOINT: PFS PER IRC ASSESSMENT



Number of Patients at Risk									
R²	178	148	124	91	59	39	20	7	0
Rituximab + Placebo	180	132	92	58	40	26	10	4	0

CI, confidence interval; FL, follicular lymphoma; HR, hazard ratio; IRC independent review committee; NE, not evaluable; PFS, progression-free survival; R/R, relapsed/refractory

Leonard J.P et al. Presented at ASH 2018 (abstr 445)

OUTCOMES FOR PATIENTS WITH HIGH-RISK RELAPSED OR REFRACTORY INDOLENT B-CELL LYMPHOMA TREATED WITH COPANLISIB IN THE CHRONOS-1 STUDY

A. Santoro et al. Abst #395

COPANLISIB IN R/R FL

CHRONOS-1

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iNHL progressed after ⩾2 lines of treatment

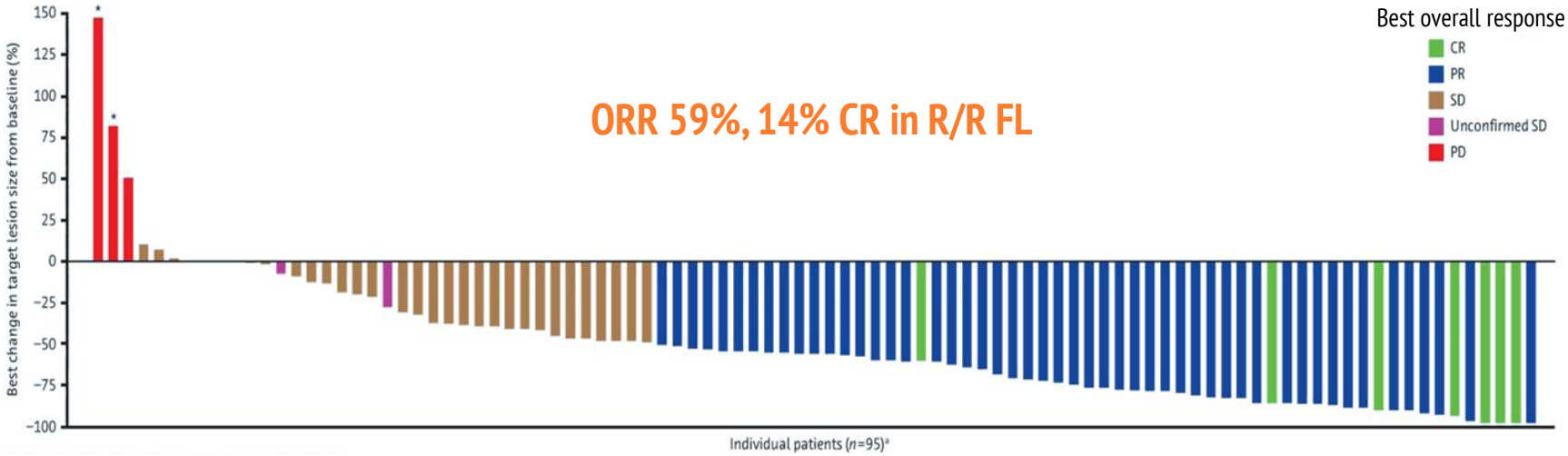
Phase IIB study

Single-arm study (N=142)

Copanlisib 60 mg IV
Days 1, 8, 15 of a 28 day cycle

Therapy maintained until progression or unacceptable toxicity

Copanlisib is approved for patients with relapsed FL who have failed at least 2 prior lines of therapy



ORR 59%, 14% CR in R/R FL

*Patient was assessed as having SD by independent review
[a]1 patient classed by the investigator as having FL, but who was reclassified by independent assessment as having diffuse large B-cell lymphoma, is not shown in the plot (change in lesions: increase of 250%)

CLL, chronic lymphocytic leukaemia; CR, complete response; FL, follicular lymphoma; iNHL, indolent non-hodgkin lymphoma; IV, intravenous; ORR, overall response rate; PD, progressive disease; PR, partial response; R/R, relapsed/refractory; SD, stable disease

Dreyling M, et al. J Clin Oncol 35, 2017 (suppl; abstr 7535)

TOXICITY PROFILE OF COPANLISIB

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Incidence of TEAEs occurring in ⩾ 10% of patients N (%)	Any grade (N=104)	Grade 3 (N=104)	Grade 4 (N=104)
Hyperglycemia	50 (48.1)	33 (31.7)	9 (8.7)
Diarrhea	36 (34.6)	6 (5.8)	0
Hypertension	31 (29.8)	24 (23.1)	0
Decreased neutrophil count	31 (29.8)	6 (5.8)	19 (18.3)
Fatigue	29 (27.9)	0	0
Fever	28 (26.9)	5 (4.8)	0
Decrease platelet count	26 (25.0)	7 (6.7)	1 (1.0)
Lung infection	24 (23.1)	15 (14.4)	3 (2.9)
Oral muscocitis	24 (23.1)	4 (3.8)	0
Nausea	23 (22.1)	0	0
Upper respiratory tract infection	20 (19.2)	3 (2.9)	0
Cough	17 (16.3)	0	0
Anemia	16 (15.4)	5 (4.8)	0
Constipation	14 (13.5)	0	0
Vomiting	14 (13.5)	0	0
Bronchial infection	13 (12.5)	1 (1.0)	0
Headache	13 (12.5)	1 (1.0)	0
Musculo-papular rash	11 (10.6)	1 (1.0)	0
Dyspnea	11 (10.6)	4 (3.8)	0
Flu-like symptoms	11 (10.6)	1 (1.0)	0
Anorexia	11 (10.6)	0	0
Skin infection	11 (10.6)	0	0

TEAEs, Treatment emergent adverse events
Dreyling M, et al. J Clin Oncol 35, 2017 (suppl; abstr 7535)

OUTCOMES FOR PATIENTS WITH HIGH-RISK R/R iNHL TREATED WITH COPANLISIB IN THE CHRONOS-1 STUDY

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RESPONSE EVALUATION BY INDEPENDENT ASSESSMENT

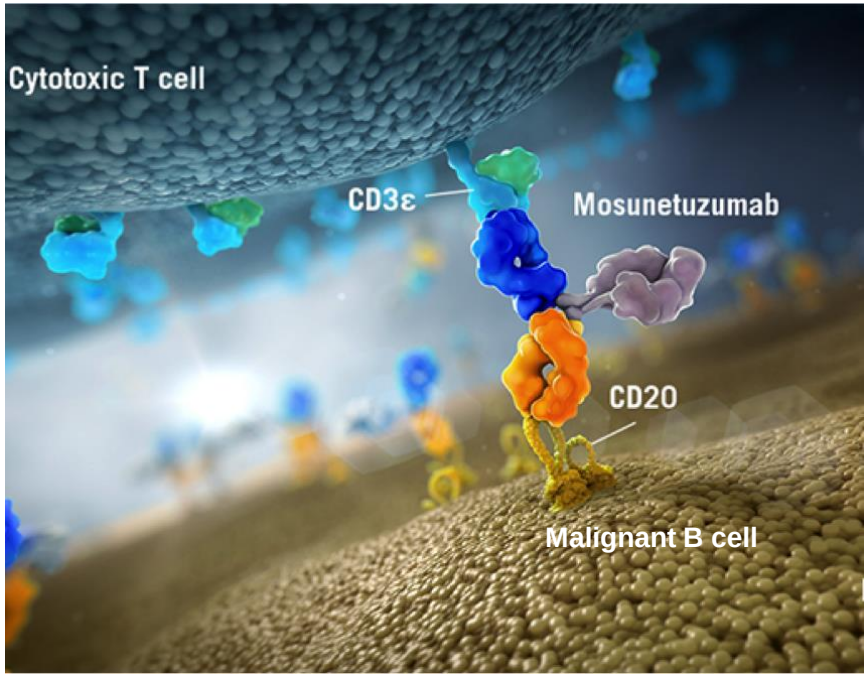
	All (n=140)		Follicular lymphoma (n=102)	
	POD <24 (n=93) N (%)	POD ≥24 (n=47) N (%)	POD <24 (n=68) N (%)	POD ≥24 (n=34) N (%)
Complete response (CR)	16 (17.2)	8 (17.0)	15 (22.1)	6 (17.6)
Partial response (PR)	38 (40.9)	24 (51.1)	26 (38.2)	14 (41.2)
Objective response (ORR)	54 (58.1)	32 (68.1)	41 (60.3)	20 (58.8)
Stable disease (SD)	26 (28.0)	12 (25.5)	21 (30.9)	11 (32.4)
Progressive disease (PD)	1 (1.1)	2 (4.3)	0	2 (5.9)
Unconfirmed early SD	1 (1.1)	0	1 (1.5)	0
NA/NE	11 (11.8)	1 (2.1)	5 (7.4)	1 (2.9)

iNHL, indolent non-hodgkin lymphoma; NA, not available; NE, not evaluable; R/R, relapsed/refractory; SD, stable disease
Santoro A et al. Presented at ASH 2018 (abstr 395)

MOSUNETUZUMAB, A FULL-LENGTH BISPECIFIC CD20/CD3 ANTIBODY, DISPLAYS CLINICAL ACTIVITY IN RELAPSED/REFRACTORY B-CELL NHL: INTERIM SAFETY AND EFFICACY RESULTS FROM A PHASE I STUDY

L.E. Budde et al. Abst #399

MOSUNETUZUMAB: A BISPECIFIC ANTIBODY TARGETING CD3 AND CD20



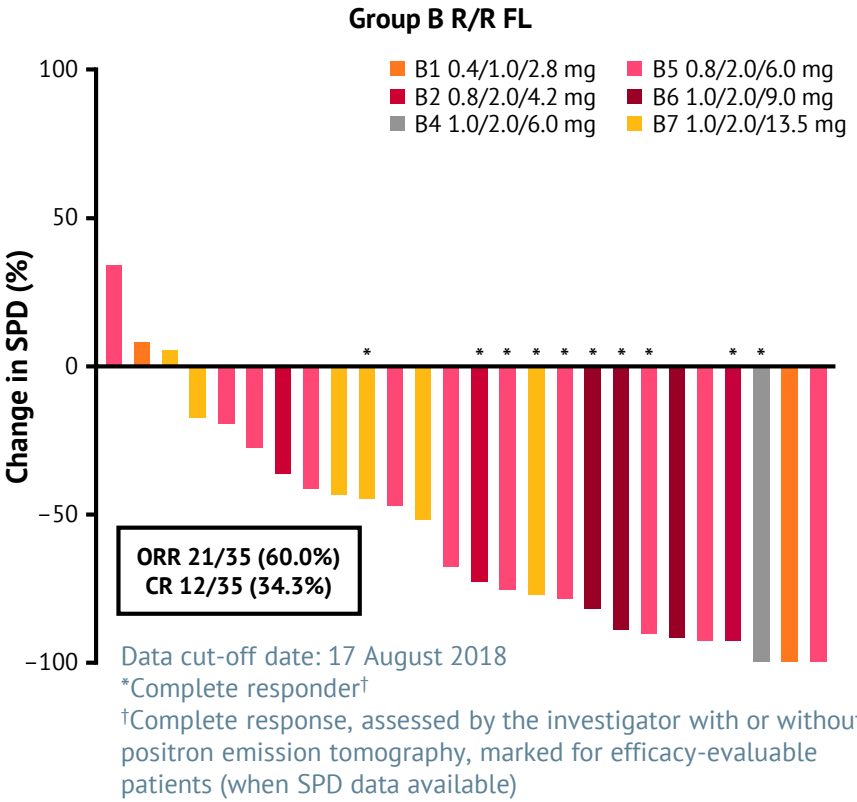
- **Mechanism of action**
  - Redirects T-cells to engage and eliminate malignant B-cells
  - Conditional agonist: T-cell activation dependent on B-cell engagement
  - Amino-acid substitution (N297G) to inactivate ADCC and avoid destruction of engaged T cells
- **Full-length humanized IgG1 antibody**
  - Longer half-life than fragment-based drug formats
  - PK properties enable QW to Q3W dosing
  - Does not require *ex-vivo* T-cell manipulation
  - Off the shelf, readily available treatment

ADCC, antibody-dependent cell-mediated cytotoxicity; IgG Immunoglobulin G; PK, Pharmacokinetic; QW, once weekly; Q3, every 3 weeks

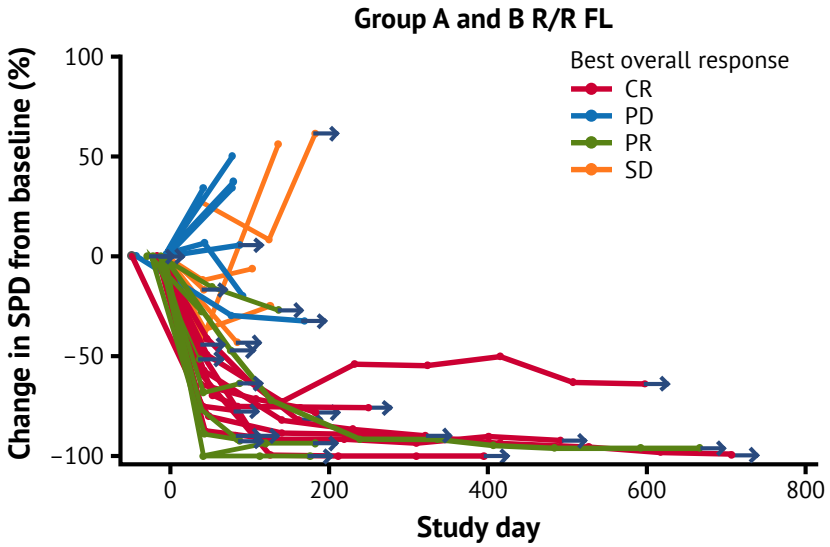
Mosunetuzumab investigator brochure

EFFICACY OF MOSUNETUZUMAB IN R/R FL

EARLY EVIDENCE OF DURABLE CR; NO RELAPSES OBSERVED TO DATE



Data cut-off date: 17 August 2018
*Complete responder†
†Complete response, assessed by the investigator with or without positron emission tomography, marked for efficacy-evaluable patients (when SPD data available)



- Median duration of CR: not reached
- Median duration of follow-up for CR: 330 days (range 54–788 days)

CR, complete response; FL, follicular lymphoma; ORR, overall response rate; PD, Progressive disease; PR, Partial response; R/R, relapsed/refractory; SD, Stable disease; SPD, sum of the products of the greatest diameters

Budde L.E. et al. Presented at ASH 2018 (abstr 399)

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