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LINFOMI

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Disclosures – Umberto Vitolo

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Consultant	N/A
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Scientific Advisory Board	Janssen, Roche

Outline of discussion

- ✓ Hodgkin
  - ✓ First line
  - ✓ Relapse
- ✓ Non-Hodgkin Lymphoma
  - ✓ MCL
  - ✓ DLBCL
  - ✓ Follicular
  - ✓ Indolent NH

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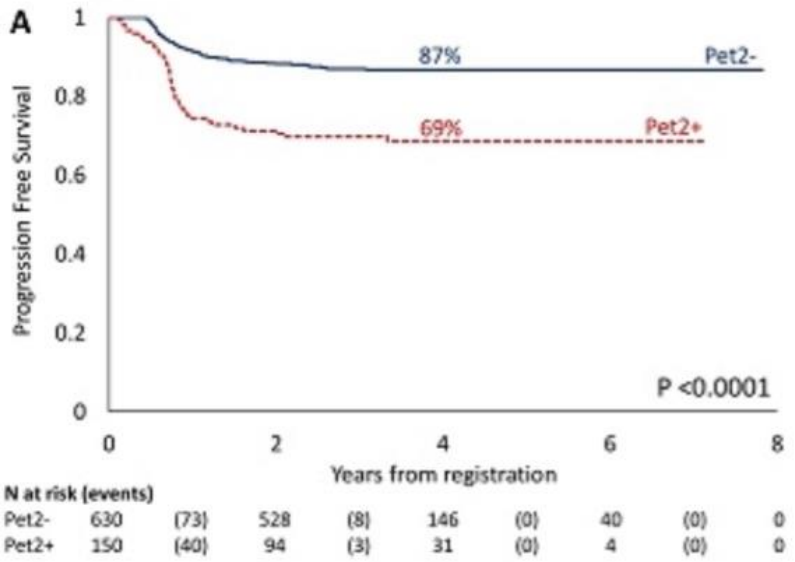
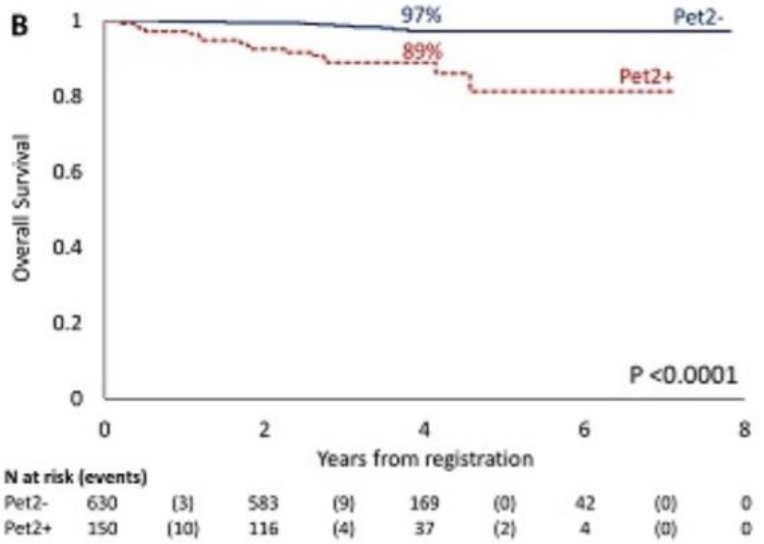
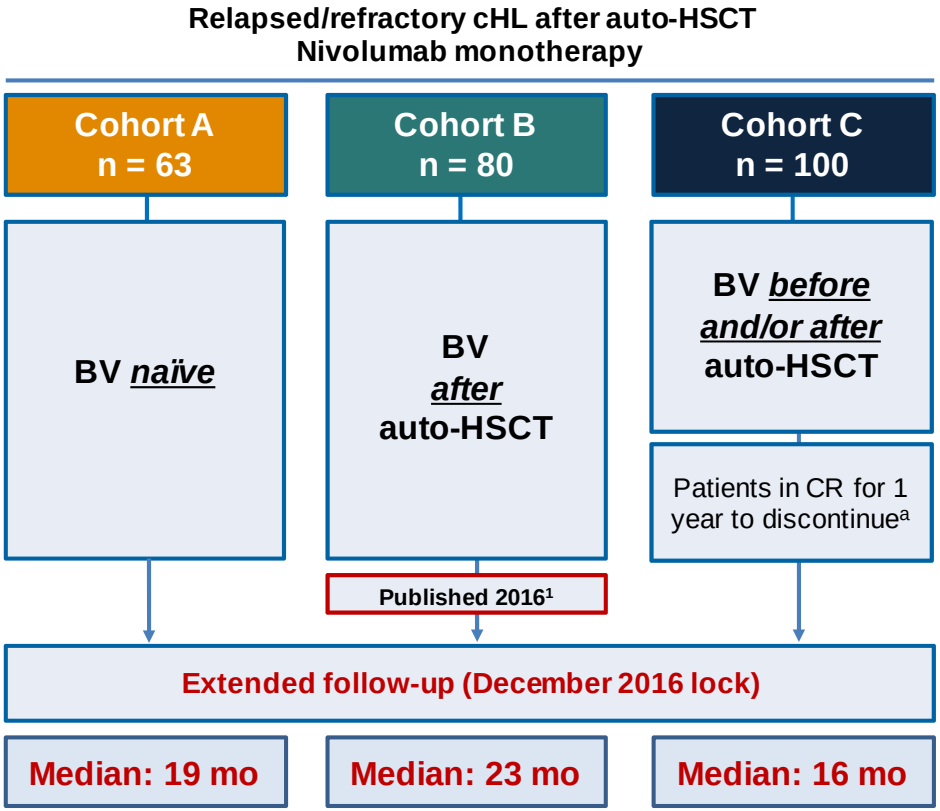
Early chemotherapy intensification with escalated BEACOPP in advanced-stage Hodgkin lymphoma with a positive interim PET-CT after 2 ABVD cycles: long-term results of the GITIL/FIL HD0607 trial





Gallamini A et al, S413.

Nivolumab for Relapsed/Refractory Classical Hodgkin Lymphoma After Autologous Transplant: Full Results After Extended Follow-Up of the Multicohort Multicenter Phase 2 CheckMate 205 Trial



Nivolumab 3 mg/kg IV Q2W
Treatment until disease progression or unacceptable toxicity[a]

Patients could elect to discontinue nivolumab and proceed to allogeneic (allo)-HSCT

Primary endpoint
- ORR by IRC

Additional endpoints
- CR/PR rate
- Duration of CR/PR
- PFS by IRC
- OS
- Safety

Demographics

	BV naïve[a] (Cohort A) n = 63	BV after auto-HSCT (Cohort B) n = 80	BV before and/or after auto-HSCT (Cohort C) n = 100	Overall N = 243
Age, years	33 (18–65)	37 (18–72)	32 (19–69)	34 (18–72)
Male, %	54	64	56	58
ECOG PS, %				
0	62	53	50	54
1	38	48	50	46
Disease stage at study entry, %				
IV	38	68	61	57
Previous lines of therapy	**2 (2–8)**	**4 (3–15)**	**4 (2–9)**	**4 (2–15)**
Prior radiotherapy, %	59	74	69	68
Time from diagnosis to first dose of nivolumab, years	**3.1 (1.0–30.6)**	**6.2 (1.3–25.1)**	**3.5 (1.0–24.9)**	**4.5 (1.0–30.6)**
Time from auto-HSCT to first dose of nivolumab, years	1.0 (0.3–18.2)	3.4 (0.2–19.0)	1.7 (0.2–17.0)	2.0 (0.2–19.0)

[a]All patients received auto-HSCT. Data are median (range) unless otherwise stated. ECOG PS = Eastern Cooperative Oncology Group performance status

Safety Outcomes After Extended Follow-up

Patients with drug-related AEs (≥10%), serious AEs (≥1%), or AEs leading to discontinuation (≥1%)	Overall population N = 243	
	Any grade	Grade 3–4
Drug-related AEs, %		
Fatigue	23	1
Diarrhea	15	1
Infusion-related reaction	14	<1
Rash	12	1
Nausea	10	0
Pruritus	10	0
Drug-related serious AEs, %		
Infusion-related reaction	2	<1
Pneumonitis	1	0
Drug-related AEs leading to discontinuation, %		
Pneumonitis	2	0
Autoimmune hepatitis	1	1

- There were no deaths due to drug-related AEs

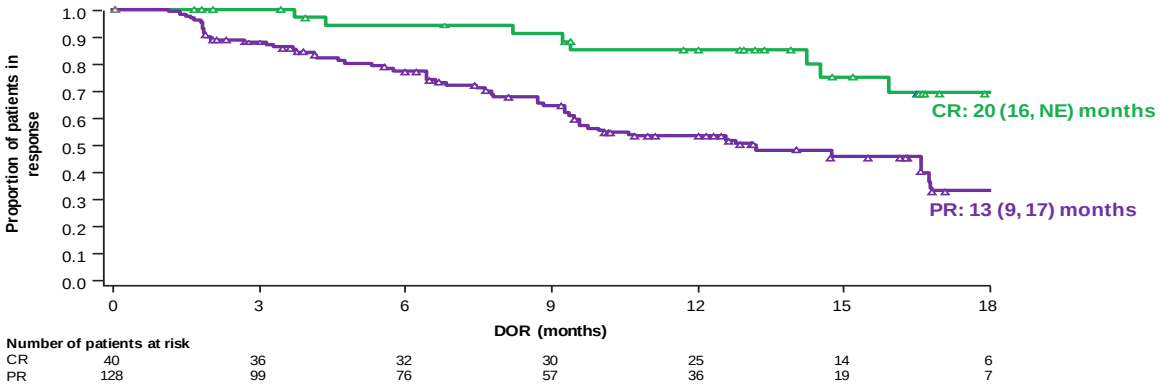
Best Overall Response After Extended Follow-Up

	BV naïve (Cohort A) n = 63	BV after auto-HSCT (Cohort B) n = 80	BV before and/or after auto-HSCT (Cohort C) n = 100	Overall N = 243
Objective response per IRC,[a] % (95% CI)	**65 (52, 77)**	**68 (56, 78)**	**73 (63, 81)**	**69 (63, 75)**
Best overall response per IRC, %				
Complete remission[b]	29	13	12	16
Partial remission	37	55	61	53
Stable disease	24	21	15	19
Progressive disease	11	8	10	9
Unable to determine	0	4	2	2

- Per investigator assessment, 33% of patients achieved CR and 39% achieved PR
- In post-hoc analyses, responses were similar irrespective of BV treatment sequence

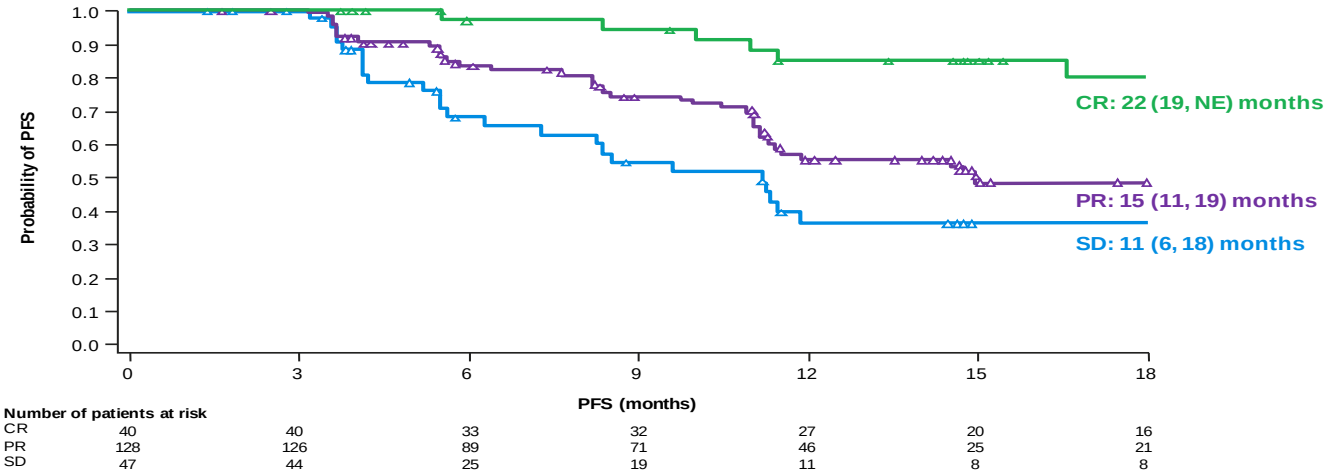
[a]Defined according to 2007 International Working Group criteria. [b]All CRs were confirmed by FDG-PET scan

DOR and PFS by Best Overall Response



DOR (per IRC) by cohort	Cohort A n = 41/63	Cohort B n = 54/80	Cohort C n = 73/100	Overall n = 168/243
Median DOR in all responders, months	20 (13, 20)	16 (8, 20)	15 (9, 17)	17 (13, 20)
Median DOR in CR patients, months	20 (NE, NE)	20 (4, NE)	15 (8, NE)	20 (16, NE)
Median DOR in PR patients, months	17 (9, NE)	11 (7, 18)	13 (9, 17)	13 (9, 17)

All values are medians (95% CI). n = responders/patients. NE = not evaluable



- Median (95% CI) PFS for overall patients (N = 243) was 15 (11, 19) months

All values are medians (95% CI). SD = stable disease

Response According to Refractory Status

	Primary refractory n = 142	Refractory to last line n = 114	Refractory to BV after auto-HSCT n = 70
Objective response, %	**73**	**68**	**69**
Best overall response, %			
Complete remission	18	13	6
Partial remission	55	54	63
Median DOR in patients with PR, months (95% CI)	13 (9, 18)	17 (9, NE)	17 (8, NE)[a]

[a]DOR includes 13 BV-refractory patients who received BV before auto-HSCT

In conclusions, Nivolumab may offer a favorable long-term treatment option for a broad spectrum of patients with cHL progressing after auto-HSCT with:

- ✓ frequent and durable responses, irrespective of depth of response, BV treatment history, and refractoriness to prior therapies; CR rate of 29% in BV-naïve patients; sustained PFS in patients who achieved CR, PR, or SD; acceptable safety profile.

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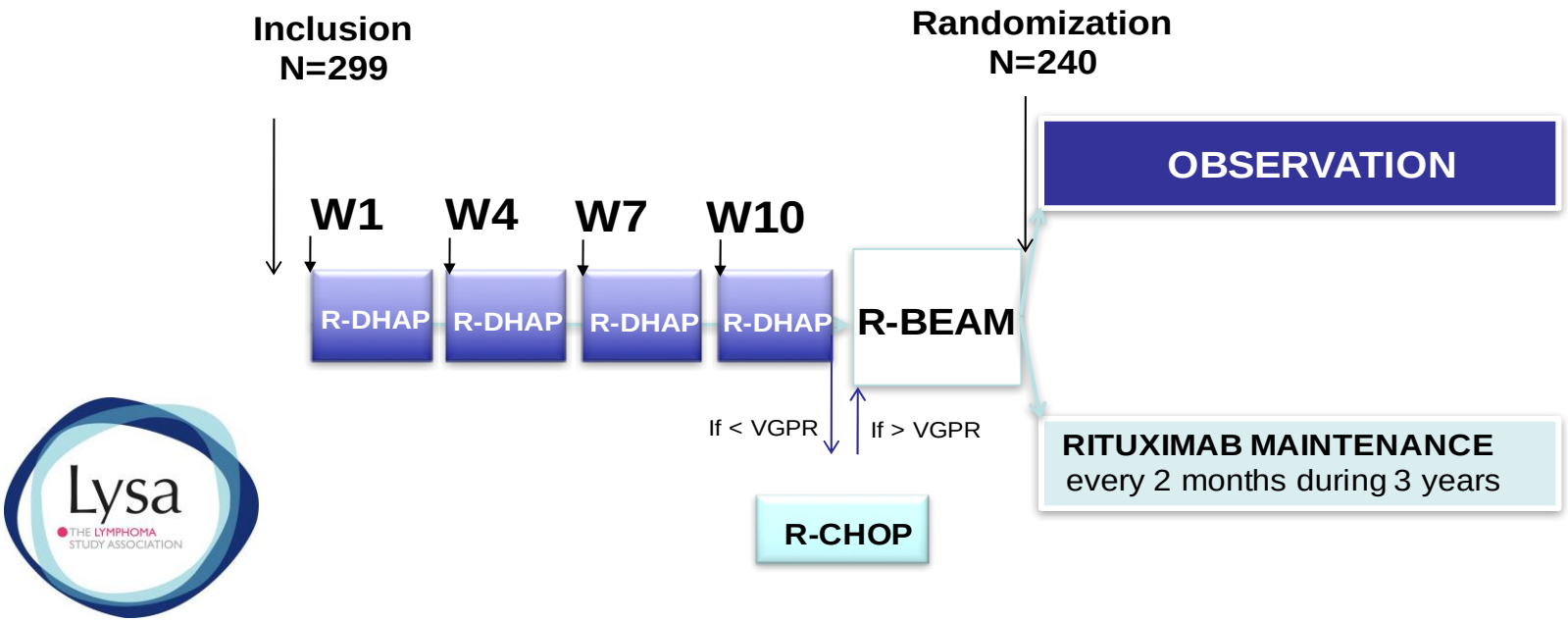
Rituximab maintenance after autologous stem cell transplantation prolongs survival in patients with mantle cell lymphoma (final result of the LyMa trial)



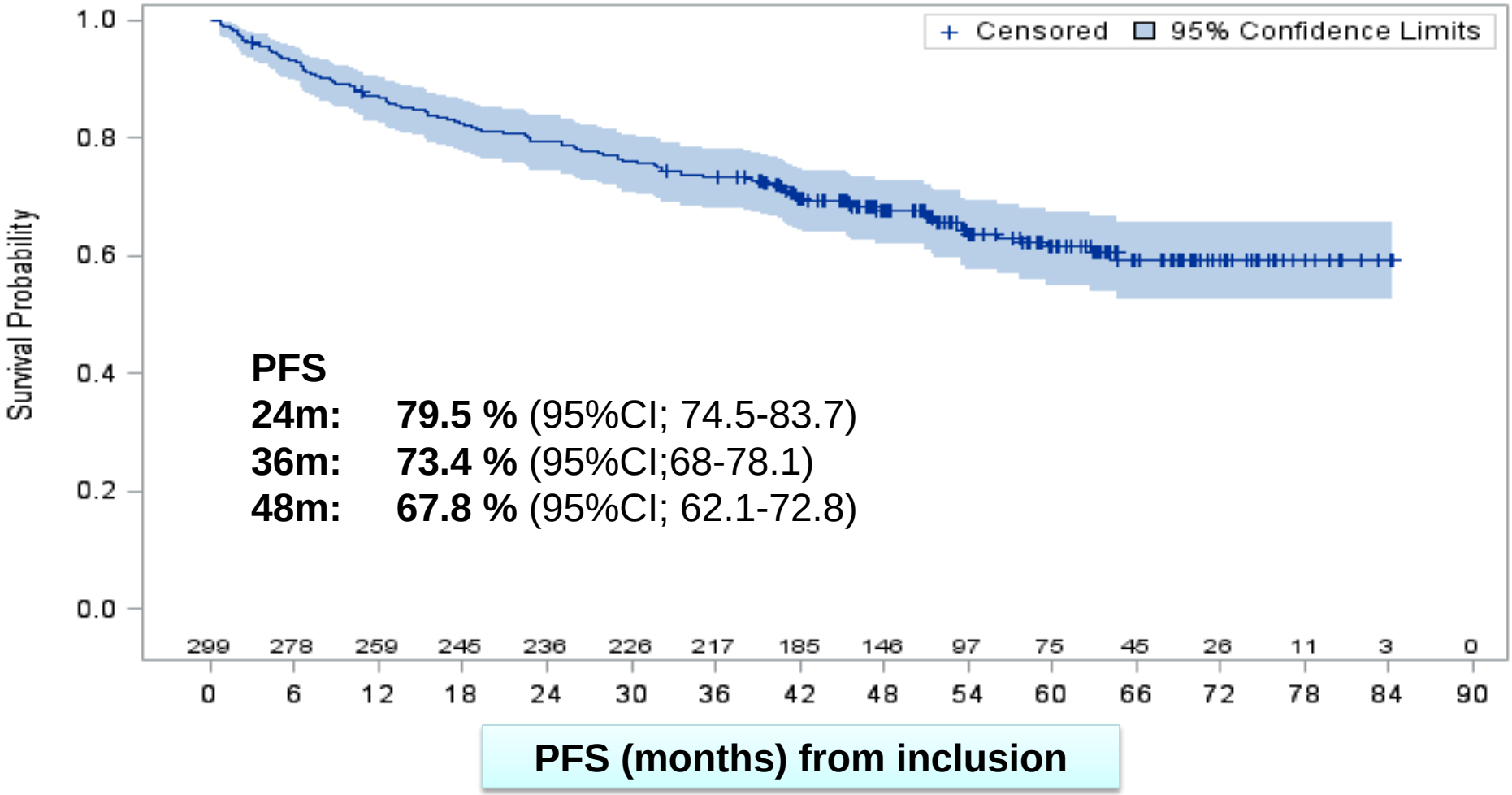
R-DHAP: Rituximab 375mg/m2; aracytine 2g/m2 x2 IV 3 hours injection 12hours interval; dexamethasone 40mg d1-4; Cisplatin 100mg/m2 d1 (or oxaliplatin or carboplatin)

R-BEAM: Rituximab 500mg/m2 d-8; BCNU 300mg/m2 d-7; Etoposide 400mg/m2/d d-6 to -3; aracytine 400mg/m2/d d-6 to d-3; melphalan 140mg/m2 d-2

Le Gouill S et al, S105.

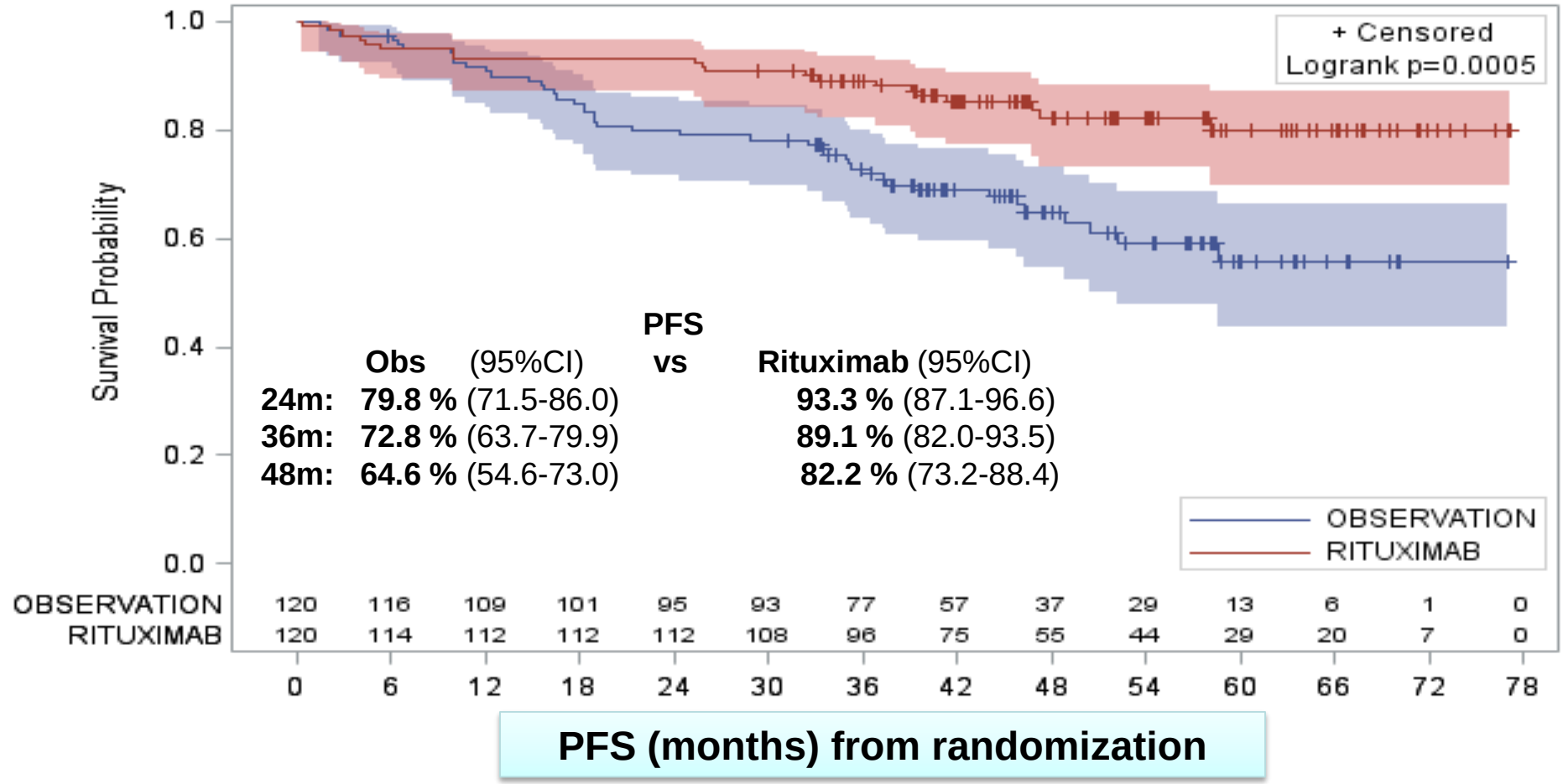
PFS from inclusion

mFU : 54.4m (52.7-59.2)



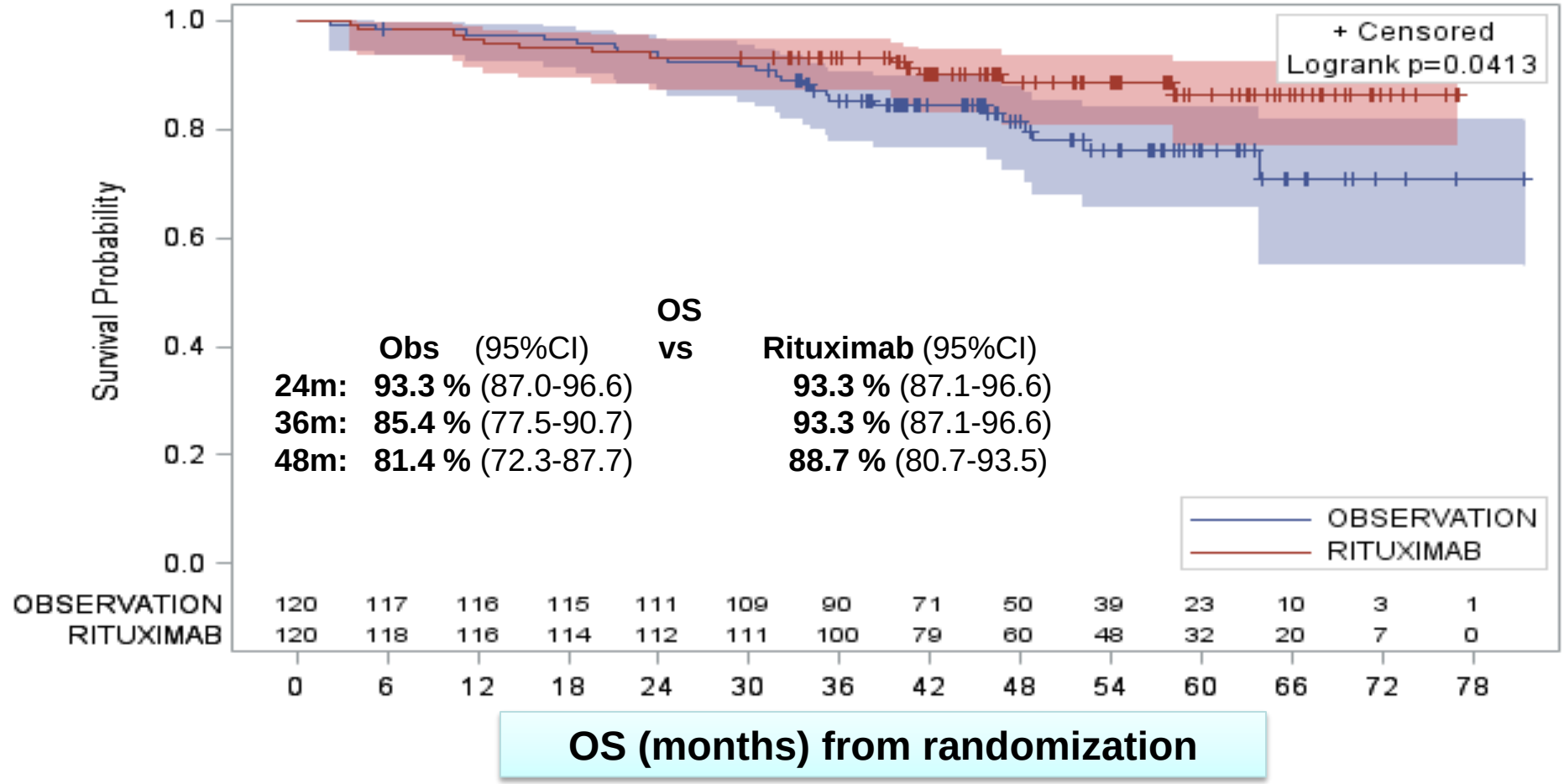
PFS from Randomization

mFU: 50.2m (46.4-54.2)



OS from Randomization

mFU: 50.2m (46.4-54.2)



CONCLUSIONS

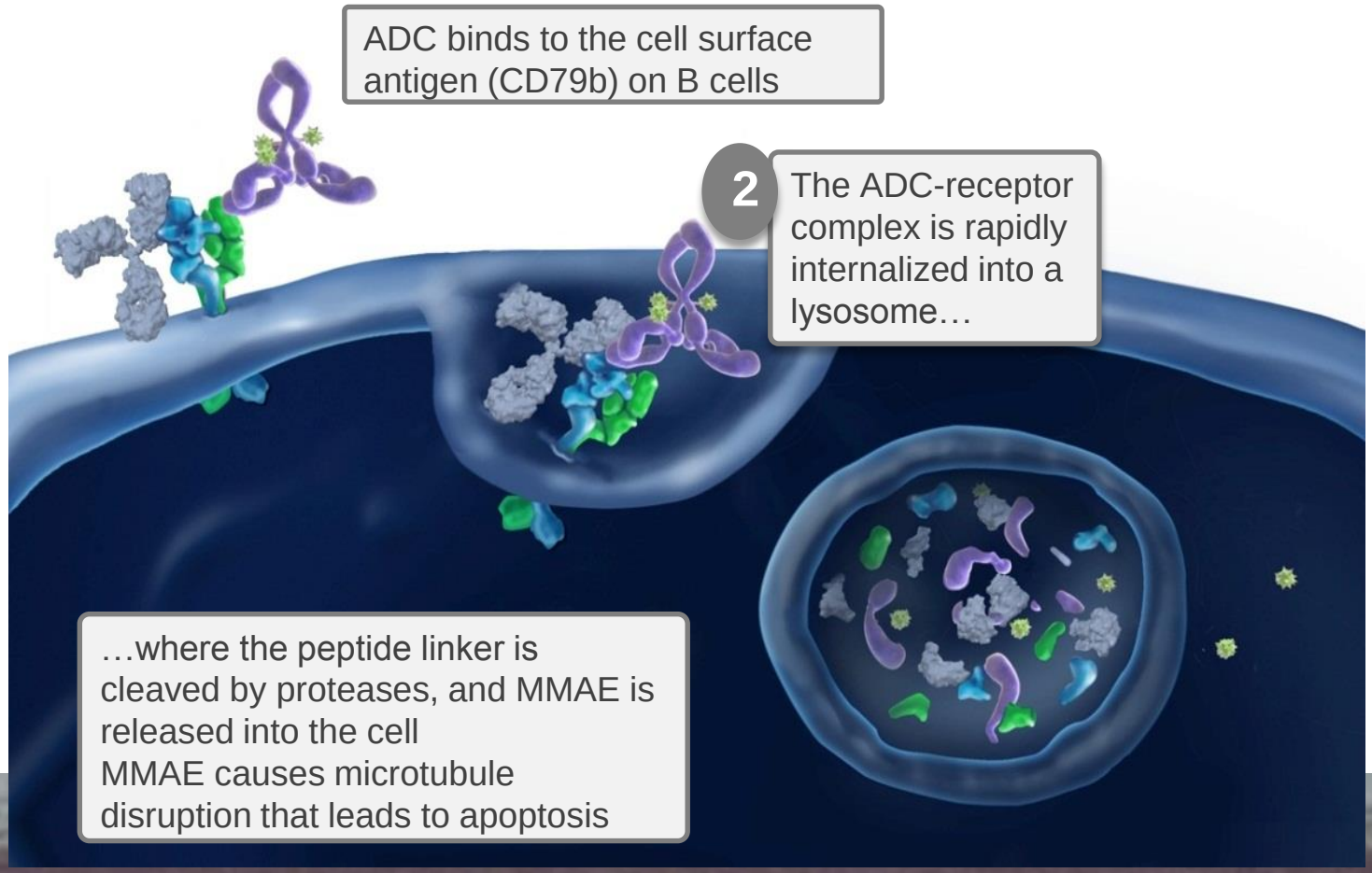
- **The LyMa design (R-DHAP/R-BEAM) provides:**
  - high CR/CRu before and after ASCT (Le Gouill et al. ASH 2013)
  - Longterm disease control (PFS and EFS)
  - Prolonged OS

- **The final analysis demonstrates that Rituximab maintenance after ASCT prolongs:**
  - EFS: 78.9% vs 61.4% at 4 years (HR=0.457; 0.27-0.74; p= 0.0016)
  - PFS: 82.2% vs 64.6 % at 4 years (HR=0.4; 0.23-0.68; p= 0.0007)
  - OS : 88.7% vs 81.4 % at 4 years (HR=0.502; 0.25-0.98; p= 0.0454)

- **Rituximab maintenance (375mg/m2 every 2 months for 3 years) should be recommended to transplanted MCL patients**

- **Ancilary studies:**
  - Genomic (Le Bris et al. ASH 2016 Saturday, abstract 1745)

Pola-R-CHP: Polatuzumab Vedotin Combined with Rituximab, Cyclophosphamide, Doxorubicin, Prednisone for Patients with Previously Untreated Diffuse Large B-Cell Lymphoma



Tilly H et al, S106.

Pola-R-CHP Administration and Patient Baseline Chracteristics

Drug	Route	Dose	Days
Rituximab	IV	375 mg/m^2	1
Cyclophosphamide	IV	750 mg/m^2	1
Doxorubicin	IV	50 mg/m^2	1
Vincristine	-	-	-
Prednisone	PO	100 mg/day	1–5
Polatuzumab vedotin	**IV**	**1.8 mg/kg**	**2** (cycle 1 and cycle 2) **1** (subsequent cycles)

- 6–8 cycles at 21-day intervals
- Response evaluation (CT and PET) after 4 cycles and end of treatment

Characteristics	N = 45
Median age, yr (range)	**69** (45–80)
Sex Male, n (%) Female, n (%)	 22 (49) 23 (51)
ECOG PS, n (%) 0–1 2	 30 (67) 15 (33)
Stage III/IV disease, n (%)	**37 (82)**
International Prognosis Index (IPI), n (%) 0–1 2 3 4–5	 1 (2) 9 (20) **18 (40)** **17 (38)**
Available cell of origin, n = 34 Activated B-cell, n (%) Germinal center B-cell, n (%) Unclassified, n (%)	 12 (35) 17 (50) 5 (15)

CT and PET assessed by investigator. Cheson BD et al. J Clin Oncol 2007;25:579-86

Adverse Events

	Pola-R-CHP N = 45 n (%)	R-CHOP-21 BO21005/GOYA[1] N = 703 (%)
Grade 3–5 adverse events	**26 (58)**	**(65)**
Neutropenia	12 (27)	(38)
Febrile neutropenia	5 (11)	(15)
Infections and infestations	5 (11)	(15)
Thrombocytopenia	2 (4)	(1)
Grade 5 adverse events	**1 (2)***	**(4)**
Serious adverse events	**17 (38)**	**(38)**
Infections and infestations	5 (11)	NA
Febrile neutropenia	3 (7)	NA
Pulmonary embolism	2 (4)	NA

	Pola-R-CHP N = 45 n (%)	R-CHOP-21 BO21005/GOYA N = 703 (%)
Peripheral neuropathy		
Grade 1	12 (27)	(26)
Grade 2	4 (9)	(7)
Grade 3	2 (4)	(1)

	Pola-R-CHP N = 45 n (%)
AE leading to pola dose reduction	6 (13)
AE leading to discontinuation of chemotherapy	3 (7)

* Gr 5 due to atrial fibrillation with cardiac failure

[1]Vitolo U, et al. Blood 2016:128:470

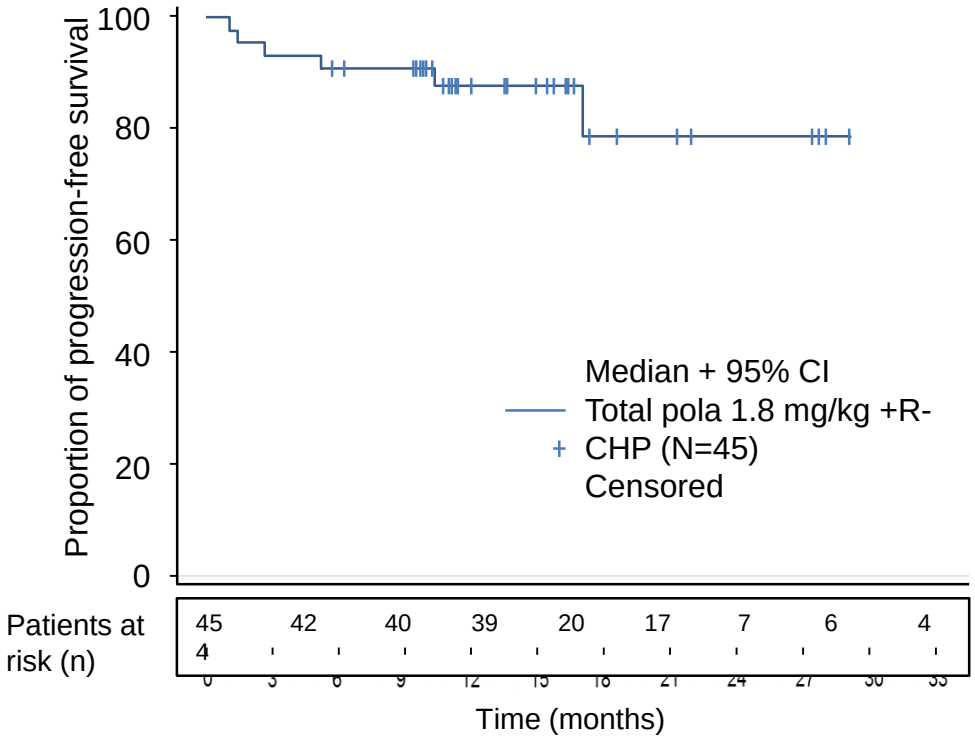
PET Response at End of Treatment

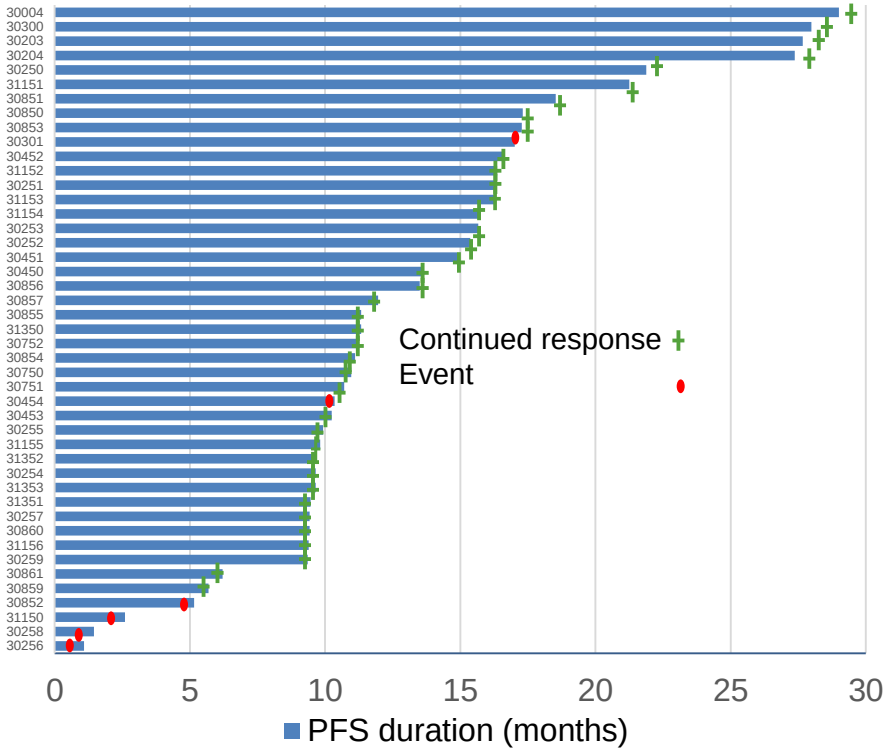
	Pola-R-CHP N = 45 n (%)	90% CI	IPI 0–2 n = 10	IPI 3–5 n = 35
Overall response rate	**41 (91)**	[81, 97]	**10 (100)**	**31 (89)**
Complete response	**35 (78)**	[65, 87]	**10 (100)**	**25 (71)**
Partial response	**6 (13)**	[6, 25]	-	**6 (17)**
Progressive disease	**3 (7)**	[2, 16]	-	1 (3)
Unevaluable/missing	**1 (2)**	[0, 10]	-	3 (9)

PET as assessed by investigator. Cheson BD et al. J Clin Oncol 2007;25:579-86

Progression-Free Survival

- Median study duration = 14.9 months

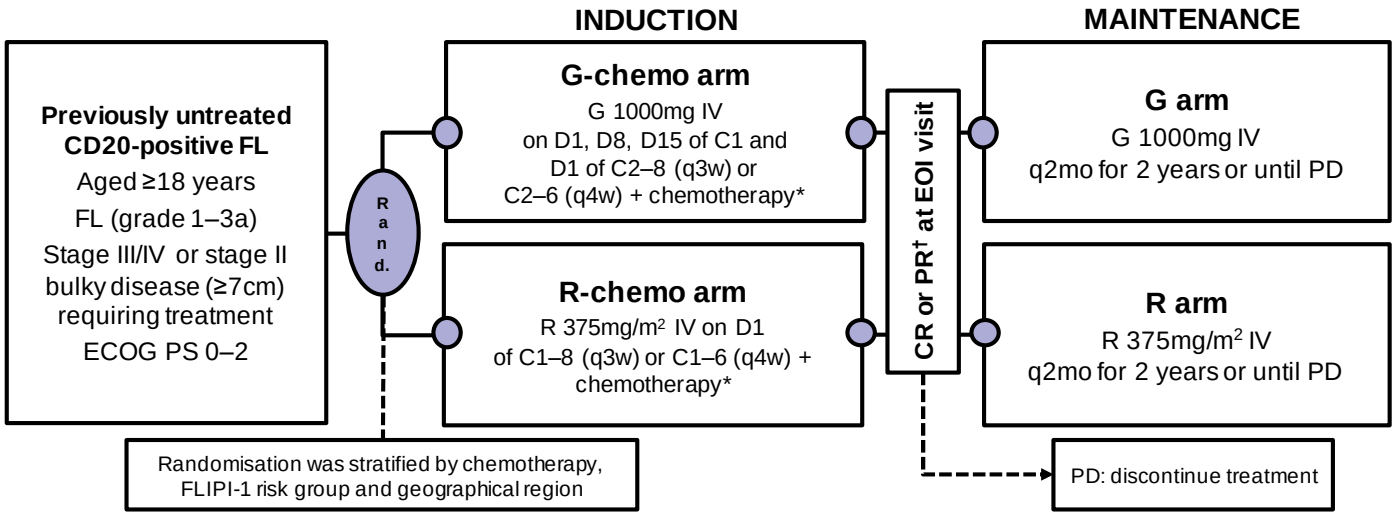




Data Cut-Off: April 14, 2017

Immunochemotherapy with obinutuzumab or rituximab in previously untreated follicular lymphoma (FL) in the randomised Phase III GALLIUM study: analysis by chemotherapy regimen

International, open-label, randomised Phase III study in 1L pts (NCT01332968)



Primary endpoint

- PFS (INV-assessed)

Secondary endpoints

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

*CHOP q3w × 6 cycles, CVP q3w × 8 cycles, bendamustine q4w × 6 cycles; chemo regimen chosen by site prior to initiation and received by all FL pts at site;
†patients with SD at EOI entered observation for up to 2 years or until PD if earlier

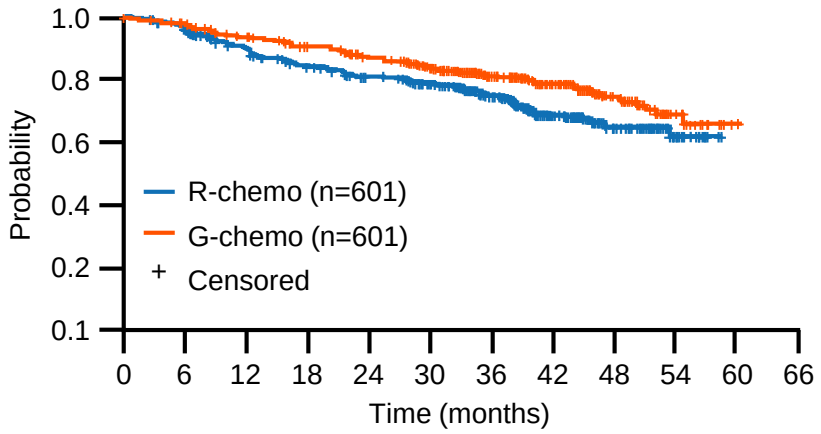
Baseline characteristics*

n (%)	*R-chemo, n=601*	*G-chemo, n=601*
Median age, years (range)	58.0 (23–85)	60.0 (26–88)
Male	280 (46.6)	283 (47.1)
Ann Arbor stage at diagnosis		
I	8 (1.3)†	10 (1.7)‡
II	44 (7.4)†	41 (6.9)‡
III	208 (34.8)†	209 (34.9)‡
IV	337 (56.4)†	338 (56.5)‡
FLIPI risk group		
Low (0–1)	125 (20.8)	127 (21.1)
Intermediate (2)	223 (37.1)	225 (37.4)
High (≥3)	**253 (42.1)**	**249 (41.4)**
Bone marrow involvement	295 (49.3)‡	318 (53.7)§
Extranodal involvement	396 (65.9)	392 (65.2)
Bulky disease (≥7cm)	**271 (45.2)¶**	**255 (42.5)¶**
Median time from diagnosis to randomisation, months (range)	**1.4 (0–168.1)‡**	**1.5 (0.1–121.6)‡**

*ITT population; †n=597; ‡n= 598; §n=592; ¶n=600

PFS after 41.1 months median follow-up*

INV-assessed PFS

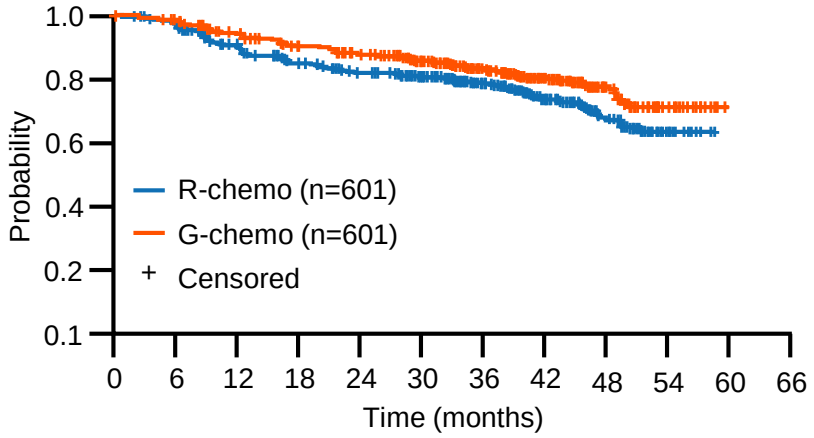


No. of patients at risk

G-chemo	601	561	505	464	438	396	267	149	77	18	
R-chemo	601	569	535	505	478	420	291	176	85	25	1

	R-chemo, n=601	G-chemo, n=601
3-yr PFS, % (95% CI)	75.0 (71.0, 78.5)	81.5 (77.9, 84.6)
HR (95% CI), p-value†	0.68 (0.54, 0.87), p=0.0016	

IRC-assessed PFS



No. of patients at risk

G-chemo	601	563	502	463	438	394	271	151	73	16
R-chemo	601	571	532	497	476	414	287	179	79	22

	R-chemo, n=601	G-chemo, n=601
3-yr PFS, % (95% CI)	78.9 (75.2, 82.1)	83.4 (79.9, 86.3)
HR (95% CI), p-value†	0.72 (0.56, 0.93), p=0.0118	

*ITT population; †stratified analysis; stratification factors = FLIPI, chemotherapy regimen

Selected grade 3–5 AEs of particular interest (frequency >2%)*

n (%) of pts reporting ≥1 one event	*R-chemo, n=597*	*G-chemo, n=595*
Neutropenia	236 (39.5)	**278 (46.7)**
Infections†	98 (16.4)	**121 (20.3)**
Infusion-related reactions‡	40 (6.7)	**74 (12.4)**
Thrombocytopenia	16 (2.7)	**36 (6.1)**
Second malignancies (SMQ)§	21 (3.5)	29 (4.9)
Cardiac events	17 (2.8)	23 (3.9)

*AEPIs occurring in >2% of patients in safety population, in either treatment arm
†System Organ Class 'Infections and Infestations'
‡Related to study treatment and occurring during or in the 24 hours after infusion
§Standardised MedDRA query, i.e. malignant or unspecified tumours occurring >6 mo after study drug intake

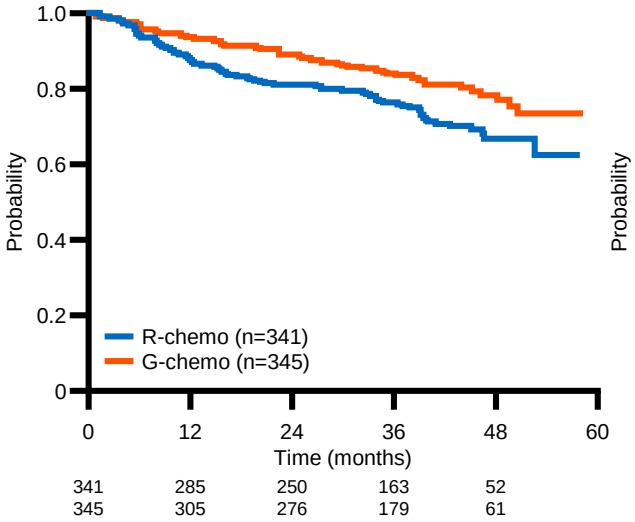
Baseline characteristics by chemo*

n (%)	*Benda, n=686*	*CHOP, n=399*	*CVP, n=117*
Median age, years (range)	59 (23–88)	58 (31–85)	59 (32–85)
Age ≥80 years	**23 (3.4)**	3 (0.8)	**4 (3.4)**
Male	332 (48.4)	177 (44.4)	54 (46.2)
Charlson Comorbidity Index score ≥1†	**163 (23.8)**	69 (17.3)	22 (18.8)
ECOG PS 2	24 (3.5)	8 (2.0)	6 (5.1)
FLIPI high risk (≥3)	274 (39.9)	**187 (46.9)**	41 (35.0)
Bulky disease (≥7cm)	274 (39.9)	**206 (51.6)**	46 (39.3)

*ITT population; †scored retrospectively based on conditions reported on medical history page of CRF

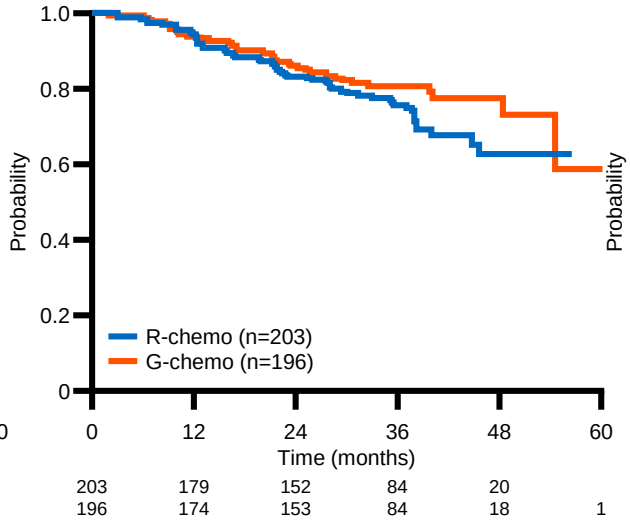
INV-assessed PFS by chemo*

Benda



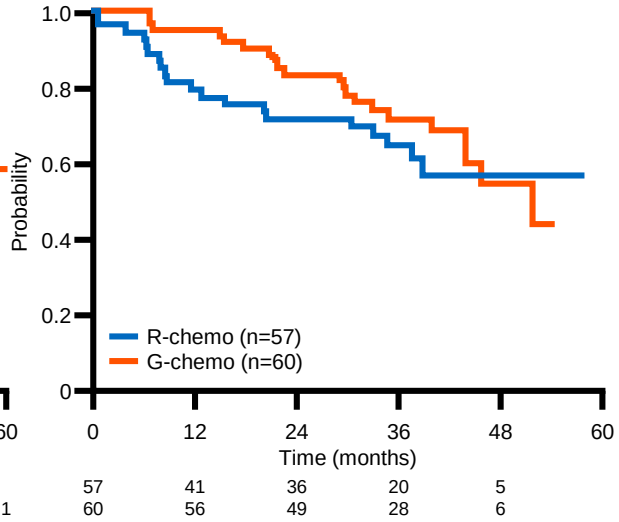
HR (95% CI)†	0.63 (0.46, 0.88)
3-yr PFS	84.1% G-B vs 76.4% R-B

CHOP



HR (95% CI)†	0.72 (0.48, 1.10)
3-yr PFS	80.6% G-CHOP vs 75.6% R-CHOP

CVP

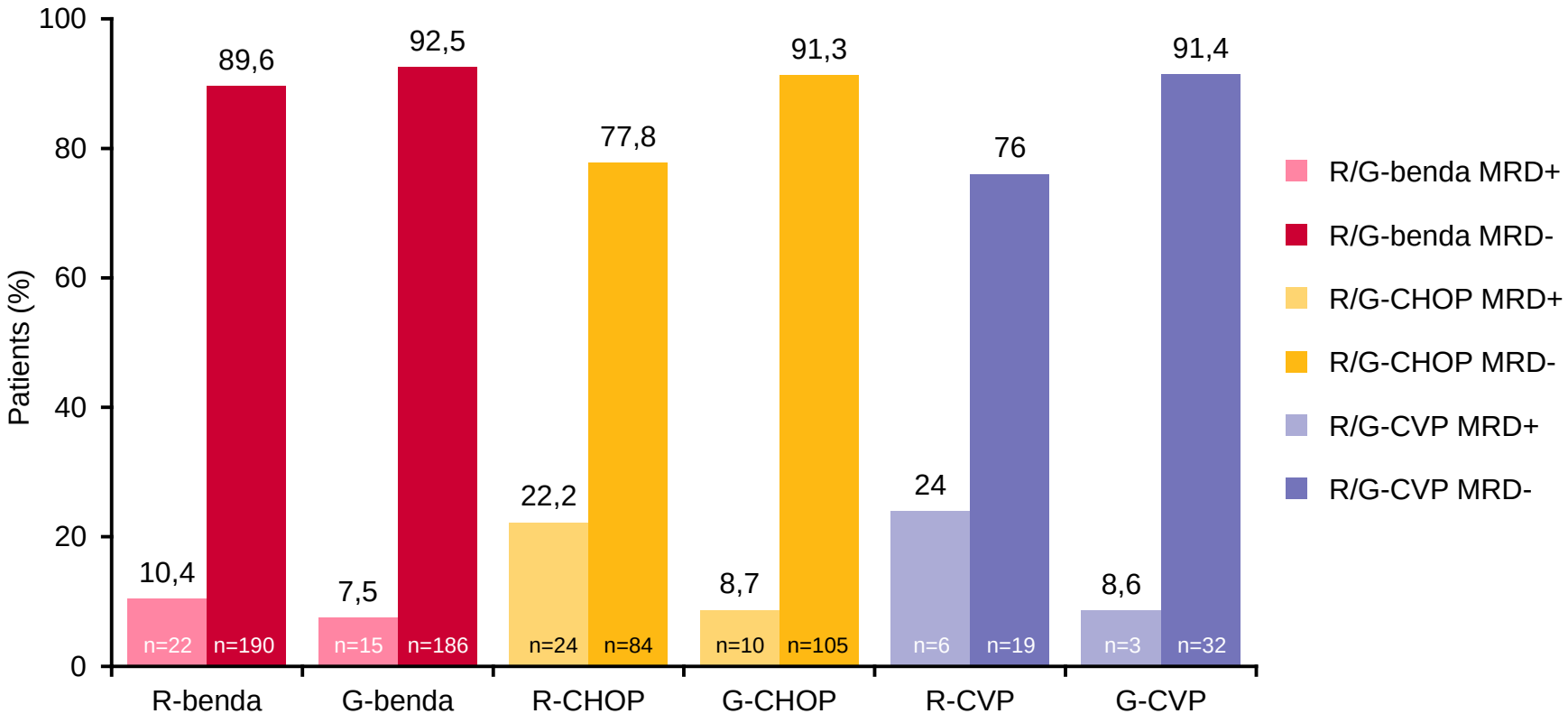


HR (95% CI)†	0.79 (0.42, 1.47)
3-yr PFS	71.3% G-CVP vs 64.2% R-CVP

- By chemo analysis not powered to demonstrate statistically significant differences between treatment arms

*ITT population; †analysis stratified by FLIPI (as well as chemotherapy regimen)

MRD response at end of induction



AEs by chemo*

n (%) of pts reporting ≥1 event	*R-benda, n=338*	*G-benda, n=338*	*R-CHOP, n=203*	*G-CHOP, n=193*	*R-CVP, n=56*	*G-CVP, n=61*
Any AE	331 (97.9)	338 (100)	201 (99.0)	191 (99.0)	56 (100)	61 (100)
Grade 3–5 AE	228 (67.5)	233 (68.9)	**151 (74.4)**	**171 (88.6)**	30 (53.6)	42 (68.9)
SAE	**160 (47.3)**	**176 (52.1)**	67 (33.0)	76 (39.4)	19 (33.9)	26 (42.6)
Grade 5 (fatal) AE†	**16 (4.7)**	**20 (5.9)**	4 (2.0)	3 (1.6)	1 (1.8)	1 (1.6)
AE leading to treatment discontinuation	48 (14.2)	52 (15.4)	31 (15.3)	32 (16.6)	9 (16.1)	11 (18.0)

- Grade 3–5 AEs most frequent with CHOP (neutropenia, leukopenia, febrile neutropenia, IRRs); SAEs and fatal AEs most frequent with benda
- Frequency of grade 5 AEs similar to R-CHOP arms in SABRINA (5.7%, i.v.; 3.6%, s.c.)

*Safety population, i.e. all randomised FL pts who received at least one dose of study drug; †includes 6 pts with fatal AEs that occurred after start of new anti-cancer therapy (G-benda, 4; R-benda, 2)

Selected grade 3–5 AEs of particular interest by chemo*

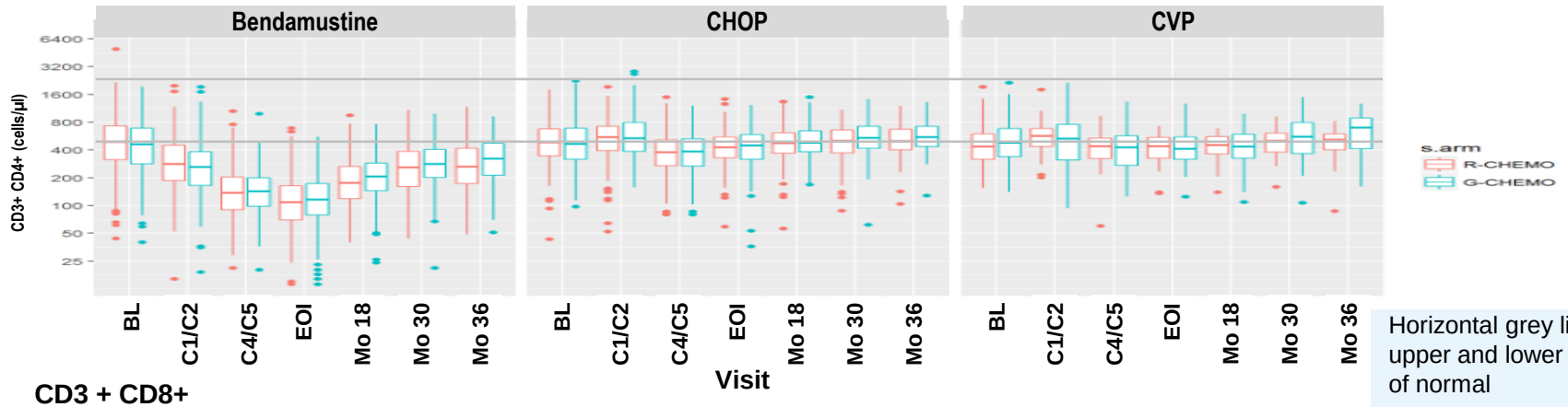
n (%) of pts reporting ≥1 event	*R-benda, n=338*	*G-benda, n=338*	*R-CHOP, n=203*	*G-CHOP, n=193*	*R-CVP, n=56*	*G-CVP, n=61*
Cardiac events	12 (3.6)	13 (3.8)	5 (2.5)	6 (3.1)	0 (0.0)	4 (6.6)
Neutropenia	107 (31.7)	107 (31.7)	**115 (56.7)**	**142 (73.6)**	14 (25.0)	29 (47.5)
Febrile neutropenia	13 (3.8)	18 (5.3)	**14 (6.9)**	**22 (11.4)**	2 (3.6)	2 (3.3)
Second malignancies†	**12 (3.6)**	**21 (6.2)**	7 (3.4)	7 (3.6)	2 (3.6)	1 (1.6)
Other solid tumours	9 (2.7)	11 (3.3)	7 (3.4)	4 (2.1)	2 (3.6)	0
Hematological tumours‡	0	3 (0.9)	0	3 (1.6)	0	0
Non-melanoma skin cancer	**3 (0.9)**	**7 (2.1)**	0	0	0	1 (1.6)
Infections	**66 (19.5)**	**89 (26.3)**	25 (12.3)	23 (11.9)	7 (12.5)	8 (13.1)
Opportunistic infections§	6 (1.8)	10 (3.0)	2 (1.0)	5 (2.6)	0	0

- Frequency of grade 3–5 second malignancy and infections similar in G and R arms for CHOP and CVP groups but not for benda
- Comparisons confounded by imbalances in baseline patient and disease characteristics between chemo groups

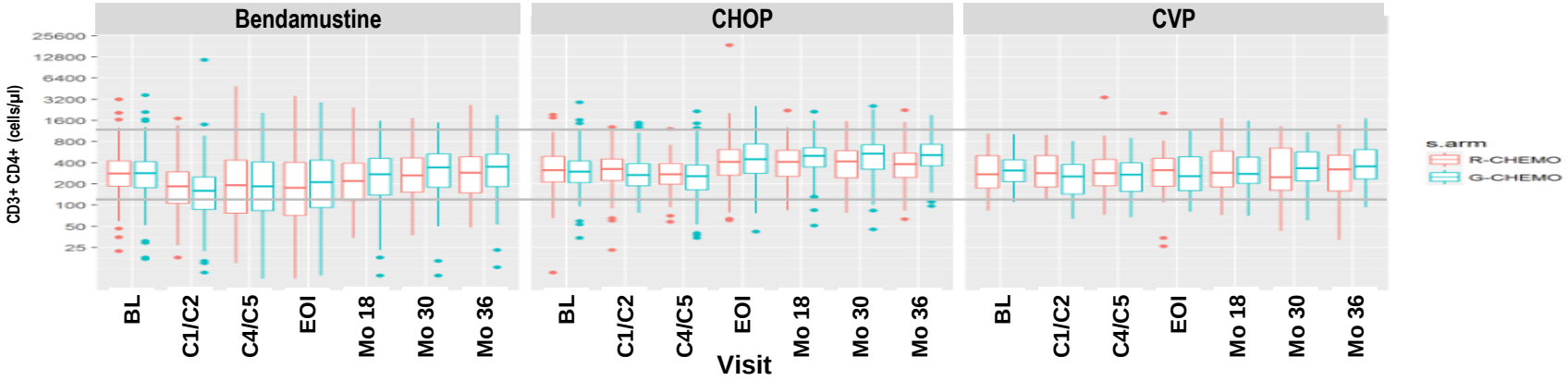
*Safety population; †standardised MedDRA query = malignant or unspecified tumours occurring >6 months after first study drug intake; ‡Hodgkin disease (n=3), AML (n=2), and ALL (n=1); §including fungal infections, cytomegalovirus, herpes zoster and pneumocystis jirovecii pneumonia

T-cell counts over time

CD3 + CD4+



CD3 + CD8+



Horizontal grey lines = upper and lower limit of normal

Low T-cell count at baseline	*R-benda, n=341*	*G-benda, n=345*	*R-CHOP, n=203*	*G-CHOP, n=196*	*R-CVP, n=57*	*G-CVP, n=60*
CD3+/CD4+ cell count of ≤200/mm^3	36 (12.5%)	36 (11.4%)	12 (7.2%)	9 (5.1%)	2 (4.4%)	4 (7.4%)

Grade 3–5 infections by chemo and by phase

n (%) of pts reporting ≥1 event	*R-benda, n=338*	*G-benda, n=338*	*R-CHOP, n=203*	*G-CHOP, n=193*	*R-CVP, n=56*	*G-CVP, n=61*
All study periods	66 (19.5)	89 (26.3)	25 (12.3)	23 (11.9)	7 (12.5)	8 (13.1)
Induction	26 (7.7)	27 (8.0)	13 (6.4)	14 (7.3)	4 (7.1)	3 (4.9)
Maintenance	**39 (13.0)**	**51 (16.7)**	11 (5.9)	7 (3.9)	1 (2.5)	5 (8.8)
Observation	12 (3.8)	28 (8.8)	6 (3.1)	3 (1.6)	3 (5.7)	1 (1.7)
N (%) of pts receiving G-CSF prophylaxis	48 (14.2)	54 (16.0)	108 (53.2)	112 (58.0)	13 (23.2)	10 (16.4)

- Comparisons confounded by imbalances in baseline patient and disease characteristics between chemo groups

*Safety population

Conclusions

Overall analysis

- Outcomes of updated analysis highly consistent with primary analysis
  - clinically meaningful improvement in PFS in G-chemo arm
  - higher rates of grade 3–5 and SAEs in G-chemo group
    - imbalance mainly driven by cytopenias, infections and IRRs
    - similar incidence of AEs leading to discontinuation

By chemo analysis

- Confounded by imbalances in baseline characteristics
  - no randomised comparison between chemo backbones
- Beneficial effect of G evident with all chemo backbones
  - study not designed to show significant differences between G and R within backbones
- Evidence of prolonged T-cell depletion in B arms
  - caution when treating pts with B

Prognostic value of PET-CT after first-line immunochemotherapy for follicular lymphoma in the Phase III GALLIUM Study

Based on early data[1–4] we hypothesised that

- Patients achieving PET negativity have a significant PFS and OS advantage
- If obinutuzumab-chemo is more effective than rituximab-chemo a higher percentage of patients should achieve PET negativity

Baseline and EOI PET imaging

Mandatory for first 170 pts where PET scanner available, and optional for remaining patients

EOI response assessments

By investigator and IRC* with and without PET according to IHP 2007[5,6]

By IRC using 5PS[7] and Lugano 2014 criteria[8]

EOI response assessed by IRC

Assessment criteria, n (%)	*R-chemo, n=298*	*G-chemo, n=297*	*p-value*
CT response[1]*	82 (27.5)	96 (32.3)	0.28
PET response			
IHP 2007[1]	178 (59.7)	212 (71.4)	0.006
Lugano 2014[2,3]†	217 (72.8)	232 (78.1)	0.18

- >2.5-fold increase in CR/CMR rate with PET vs CT assessment

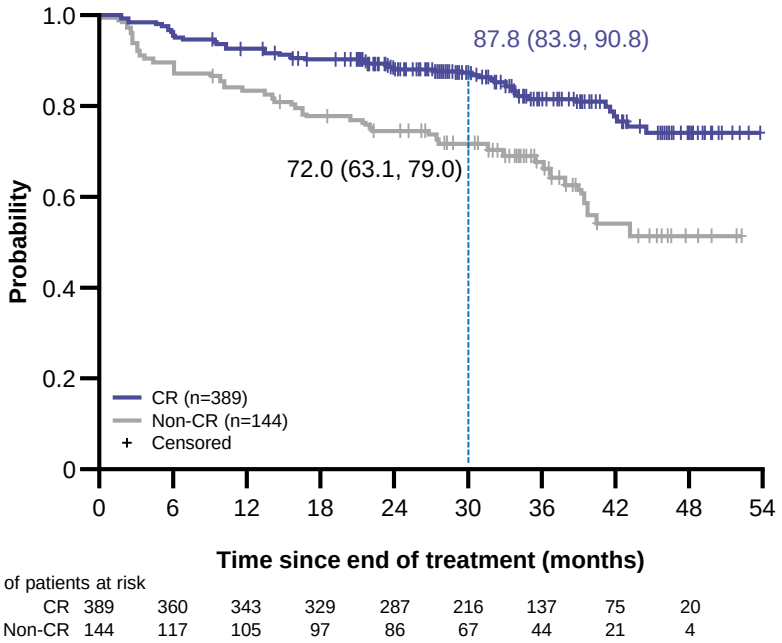
*PET population only; †For PET response required at least a PR by CT
‡Patients with missing scans were included
CMR, complete metabolic response

1. Cheson BD, et al. JCO 2007;25:579–86
2. Barrington SF, et al. JCO 2014;32:3048–58
3. Cheson BD, et al. JCO 2014;32:3059–68

Landmark (from EOI) PFS analysis: by PET criteria

PFS for non-CR/CMR vs CR/CMR status according to IRC*

IHP 2007 criteria (N=533)[1]

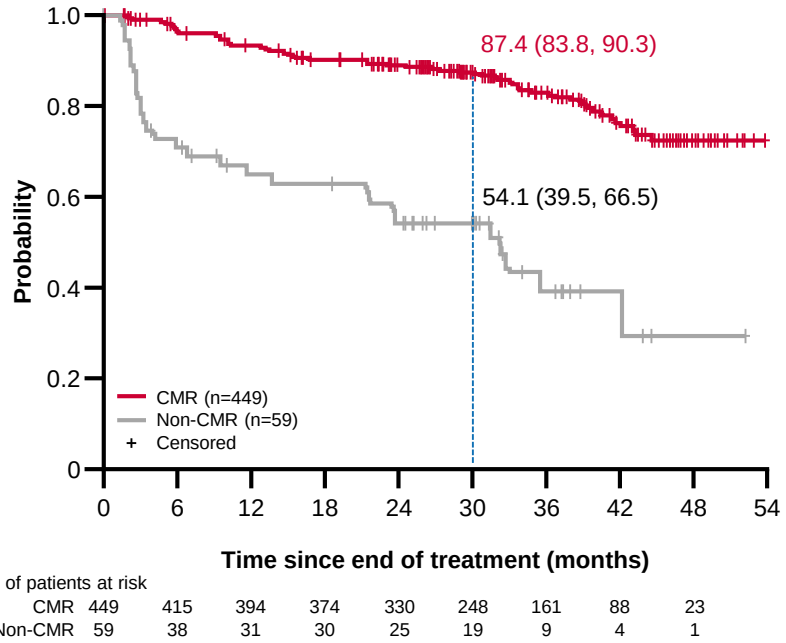


No. of patients at risk

CR	389	360	343	329	287	216	137	75	20
Non-CR	144	117	105	97	86	67	44	21	4

HR 0.37 (95% CI 0.25, 0.56); p<0.0001

Lugano 2014 criteria (N=508)[2,3]



No. of patients at risk

CMR	449	415	394	374	330	248	161	88	23
Non-CMR	59	38	31	30	25	19	9	4	1

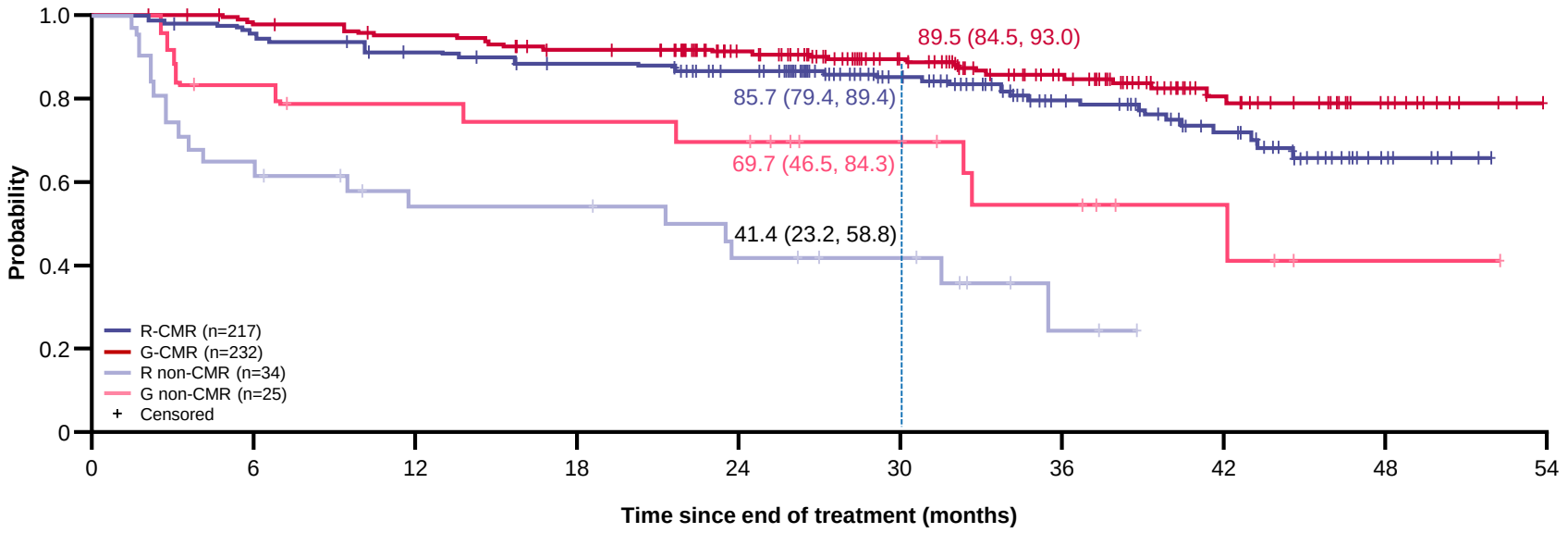
HR 0.21 (95% CI 0.13, 0.34); p<0.0001

*Patients who died or progressed (CT-based PD assessment or started next anti-lymphoma treatment) before or at EOI were excluded

1. Cheson BD, et al. JCO 2007;25:579–86
2. Barrington SF, et al. JCO 2014;32:3048–58
3. Cheson BD, et al. JCO 2014;32:3059–68

Landmark (from EOI) PFS analysis: by antibody arm

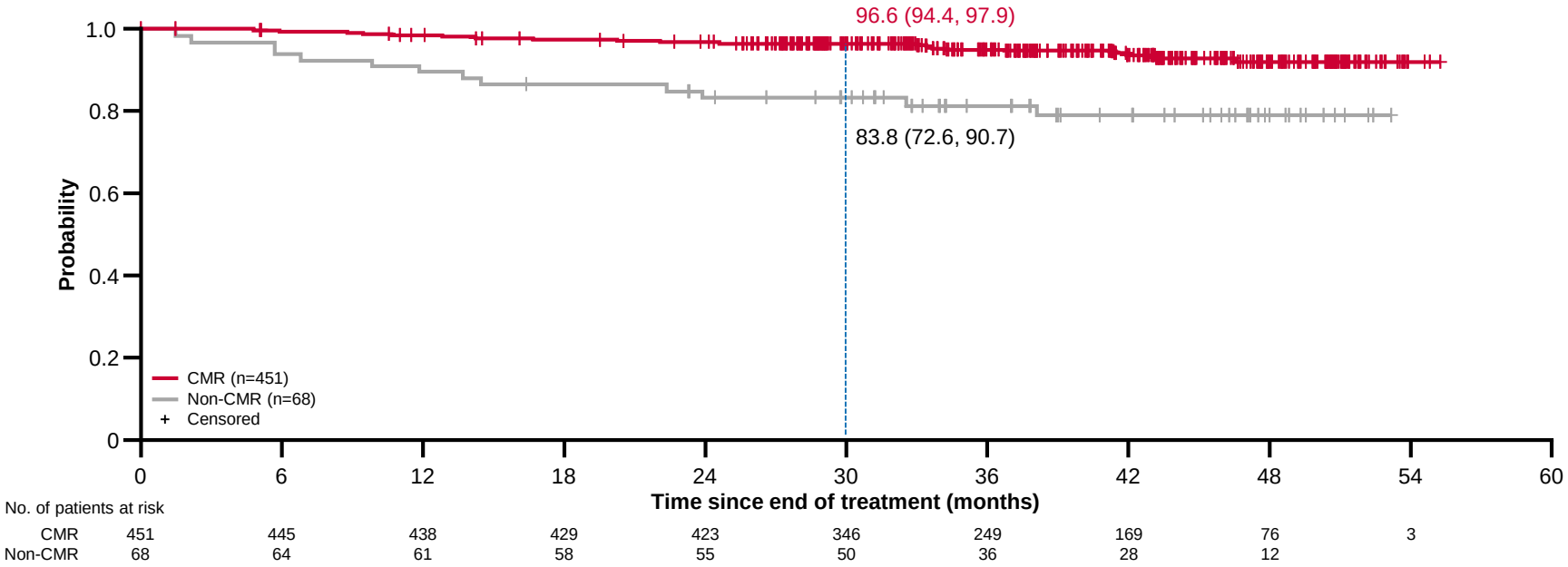
PFS for non-CMR vs CMR status using Lugano 2014 criteria (N=508)



	R-CMR, n=217	*G-CMR, n=232*	*R non-CMR, n=34*	*G non-CMR, n=25*
2.5-year PFS from EOI, % (95% CI)	85.7 (79.4, 89.4)	89.5 (84.5, 93.0)	41.4 (23.2, 58.8)	69.7 (46.5, 84.3)
HR (95% CI)		**0.7 (0.4, 1.0); p=0.06**		**0.5 (0.2, 1.2); p=0.10**

Landmark (from EOI) OS analysis

OS for non-CMR vs CMR status using Lugano 2014 criteria (N=519)*



HR 0.22 (95% CI 0.11, 0.45); p<0.0001

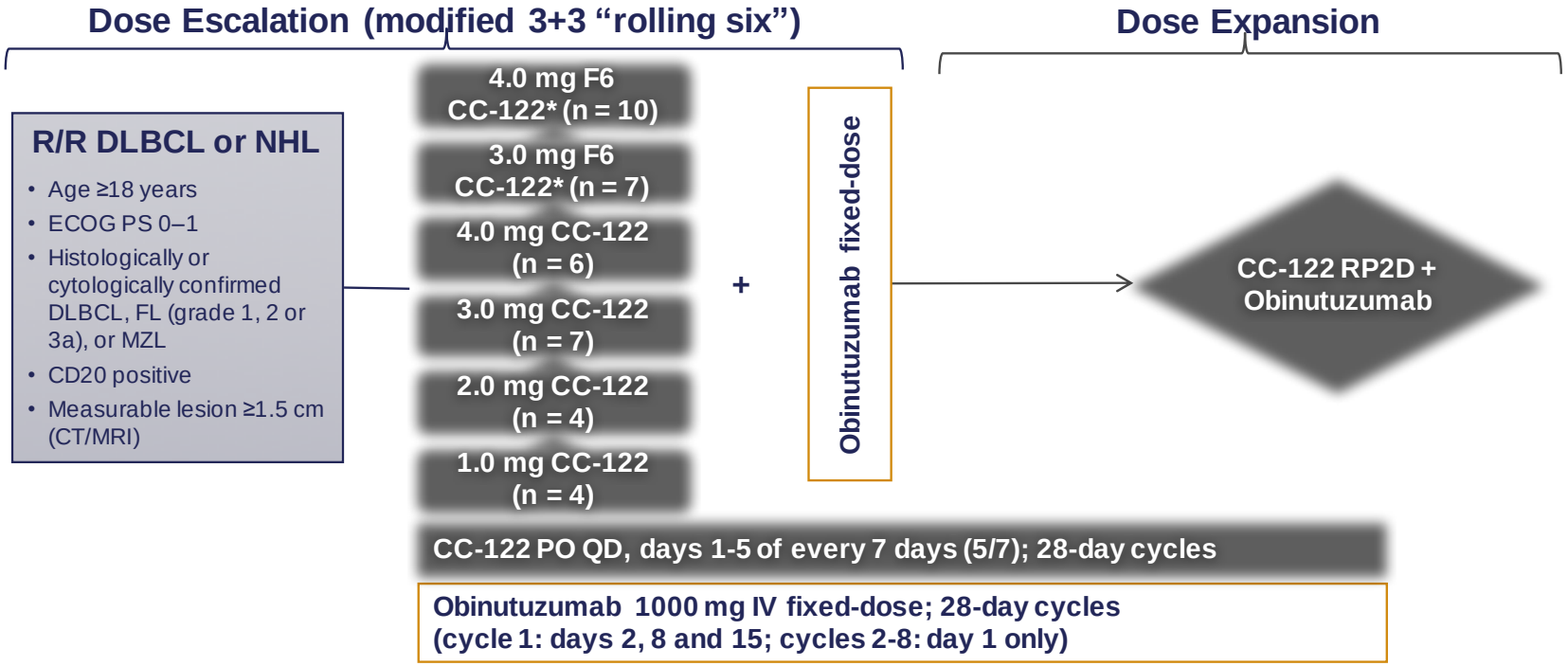
*Patients who died or started a new anti-lymphoma treatment before EOI were excluded

Conclusions from GALLIUM: Large prospective analysis in 1L FL patients

- The 77% of pts who achieve PET-CMR have a superior PFS and OS
- There is a higher PET-CR rate with G-chemo vs R-chemo with IHP 2007 criteria; and a trend favouring G-chemo with Lugano 2014 criteria
- Validates PET as the gold standard imaging modality for response assessment
- Timely to evaluate PET as a potential surrogate for PFS and OS, and a platform for response-adapted therapy

CC-122 In Combination With Obinutuzumab (GA101): Phase IB Study in Relapsed or Refractory Patients With DLBCL, FL, or MZL

- Multicenter, open-label, phase IB dose-escalation and expansion study of CC-122 + obinutuzumab in patients with R/R DLBCL and NHL (FL and MZL; EUDRACT 2014-003333-26; NCT02417285)



F6, formulated capsule; RP2D, recommended phase II dose.
*An alternate dosing schedule with a formulated CC-122 capsule was examined in the 5th and 6th cohorts to assess safety.

Primary endpoints: examine safety and tolerability of CC-122 when co-administered with obinutuzumab; identify NTD, MTD, and RP2D of CC-122 when co-administered with obinutuzumab.

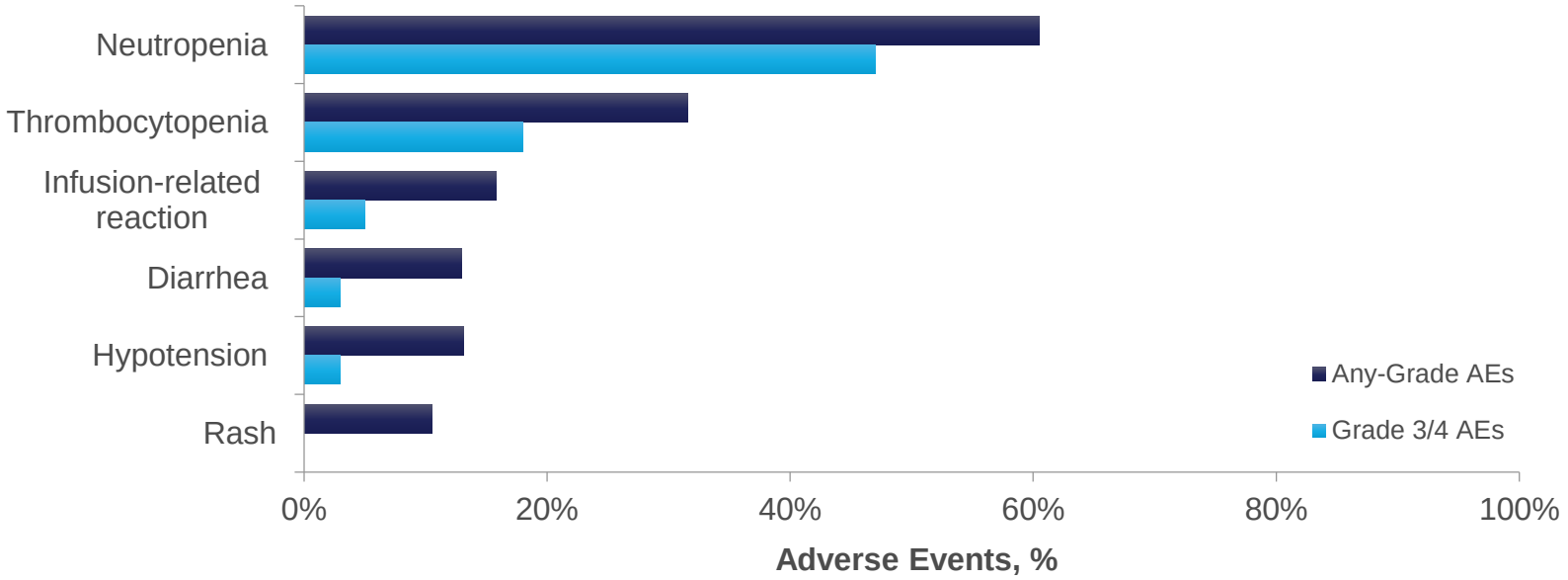
Michot JM et al, S467.

CC-122-NHL-001: BASELINE PATIENT CHARACTERISTICS FOR DOSE ESCALATION PHASE

Characteristics, n (%)		All Patients
		(N = 38)
Median age, years (range)		**60 (26-81)**
Age >65 years		13 (34)
Male		**26 (68)**
ECOG PS	0	22 (58)
	1	16 (42)
NHL type	Diffuse large B-cell lymphoma (DLBCL)	19 (50)
	Follicular lymphoma (FL)	18 (47)
	Marginal zone lymphoma (MZL)	1 (3)
Ann Arbor stage III/IV		28 (74)
IPI*	Low/intermediate (0-2)	10 (26)
	Intermediate/high risk (3-5)	9 (24)
FLIPI*	Low/Intermediate (0-2)	4 (11)
	Intermediate/high risk (3-5)	7 (18)
Positive bone marrow involvement		**8 (21)**
Median number of prior therapies (range)		**4 (1-12)**
Prior SCT		**14 (37)**

*8 patients had unknown IPI scores. IPI and FLIPI were calculated as percentage of the total population.
ECOG PS, Eastern Cooperative Oncology Group performance status; (FL)IPI, (Follicular Lymphoma) International Prognostic Index; SCT, stem cell transplantation.

CC-122-NHL-001: SAFETY WITH CC-122 + OBINUTUZUMAB (N = 38)



- Most common grade 3/4 AEs (>10%) were hematologic AEs
  - 2 patients (5%) had grade 4 febrile neutropenia
  - 2 patients have discontinued treatment due to AEs
- 2 patients had a DLT
  - 1 patient had grade 4 neutropenia (3.0 mg CC-122 + obinutuzumab)
  - 1 patient had grade 5 tumor flare reaction (4.0 mg F6 CC-122 + obinutuzumab)

Data cut-off 15May2017. DLT, dose-limiting toxicity.

CC-122-NHL-001: EFFICACY BY NHL TYPE

Outcomes by Histology, n (%)	All Patients* (N = 38)	DLBCL (n = 19)	FL/MZL (n = 19)
ORR	25 (66)	9 (47)	16 (84)
CR	12 (32)	3 (16)	9 (47)
PR	13 (34)	6 (32)	7 (37)
SD	4 (11)	3 (16)	1 (5)
PD	6 (16)	4 (21)	2 (11)
Not evaluable/missing	3 (8)	3 (16)	0

- ORR was 66% overall, including 12 patients (32%) with a CR
- Median time to best response was 57 days (95% CI, 56-114)
- 23 of 30 (77%, including 40% CR) patients responded to CC-122 doses ≥ 3.0 mg + obinutuzumab
- To date, patients receiving CC-122 at a dose of 3.0 mg and higher have shown the best and more durable responses to CC-122 + obinutuzumab (n = 30)

Data cut-off 15May2017.
*Includes 19 DLBCL, 18 FL, and 1 MZL patients.

CC-122-NHL-001: CONCLUSIONS

- First phase IB study of CC-122 + obinutuzumab to show clinically-meaningful activity in heavily pretreated patients with R/R DLBCL and iNHL (FL++)
- CC-122 + obinutuzumab is well-tolerated, with a safety profile consistent with either therapy alone
  - Most common grade 3/4 AEs are myelosuppression, and are manageable
- CC-122 at doses ≥3.0 mg combined with obinutuzumab showed increased ORR and longer duration of responses in DLBCL and FL
  - Responding patients had durable responses
- Dose escalation (Part A) has completed and the study is enrolling in dose expansion (Part B) with a RP2D of 3 mg F6 CC-122 + obinutuzumab in R/R FL patients

Take home messages

- **Hodgkin**
  - ABVD is the standard first line treatment; PET2 is able to identify early failures and shifting treatment at this point improves the outcome of PET2 positve patients
  - Immuno-checkpoint inhibitors represent an effective new salvage tool for relapsed/refractory patients either BV exposed or not

- **Non-Hodgkin Lymphoma**
  - Rituximab maintenance after ASCT in MCL may improve the outcome of these patients
  - Obinutuzomab reduce the risk of /relapse/progression in first line FL inducing a better quality of response (MRD and/or PET negativity)
  - The continuous monitoring of safety is important during treatment also with old drugs
  - Chemo-free regimens represent an option in relapsed/refractory patients