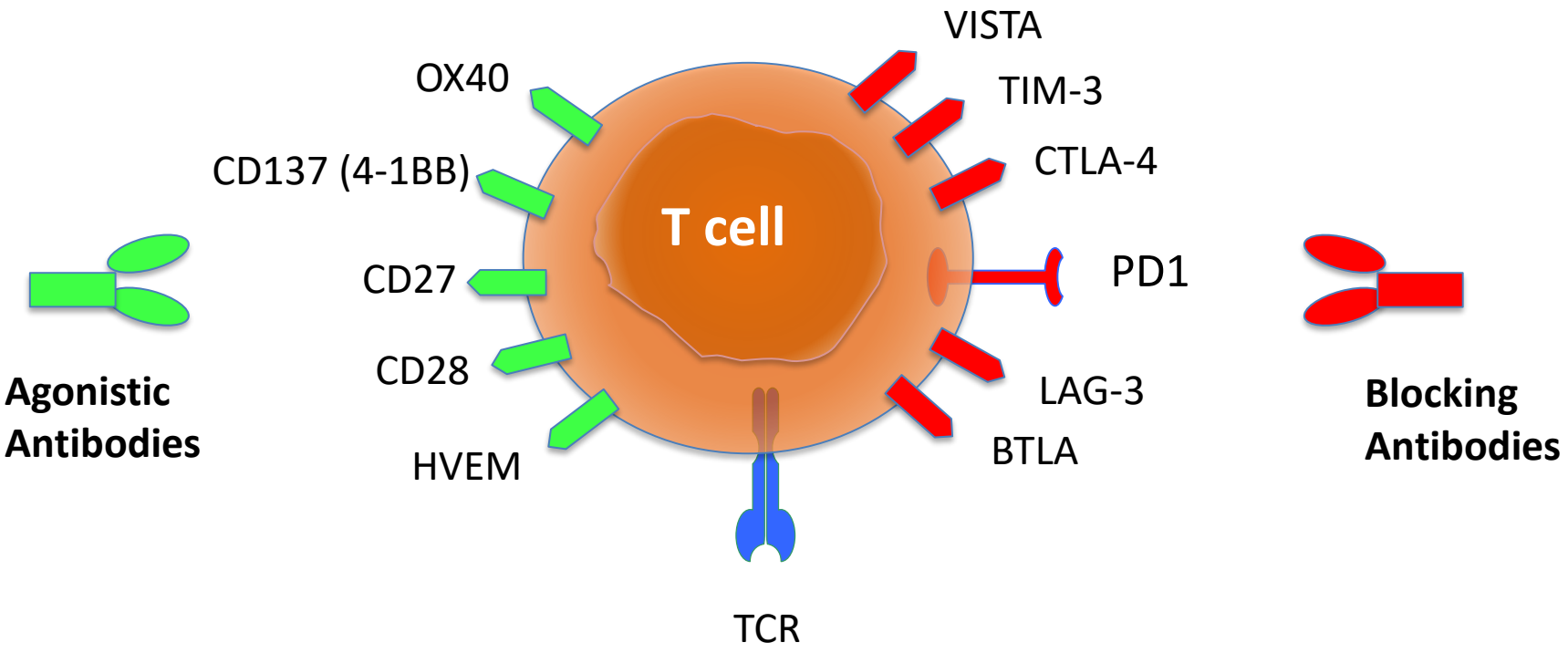
New
Drugs
In Hematology
October 1, 2018

Checkpoint inhibitors

Anas Younes, M.D.
Chief, Lymphoma Service
Memorial Sloan-Kettering Cancer Center

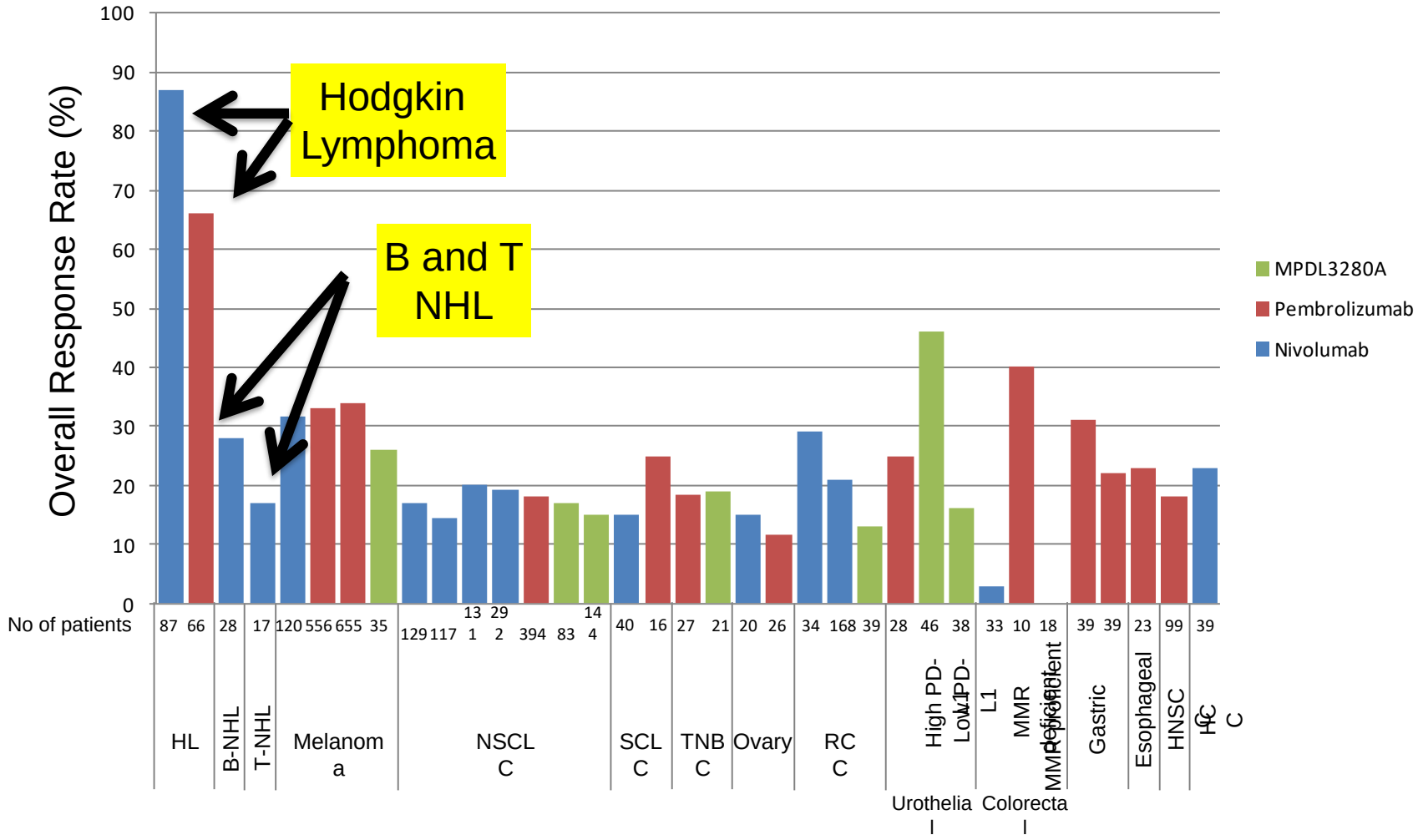
Therapeutic Activation of Autologous T Cells

Immune checkpoint inhibitors



Adapted from Batlevi et al, Nature Rev Clin Oncol 2015

Single agent activity of PD-1/PD-L1 axis blockade in relapsed/refractory Cancer



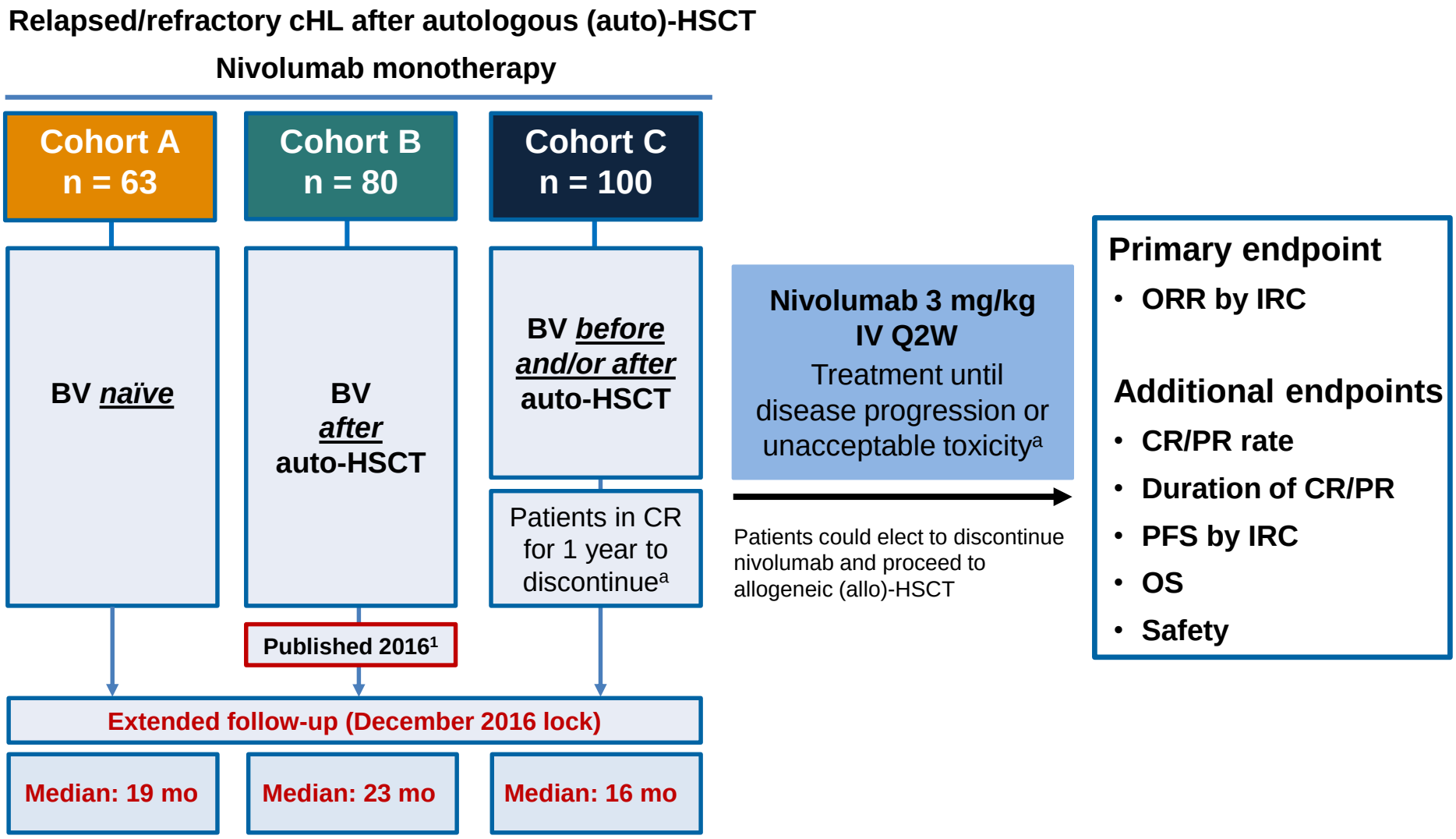
Matsuki E & Younes A, Current Treatment Options in Oncology 2016

Results of PD1 Blocking Antibodies in Relapsed HL

Phase-I Studies

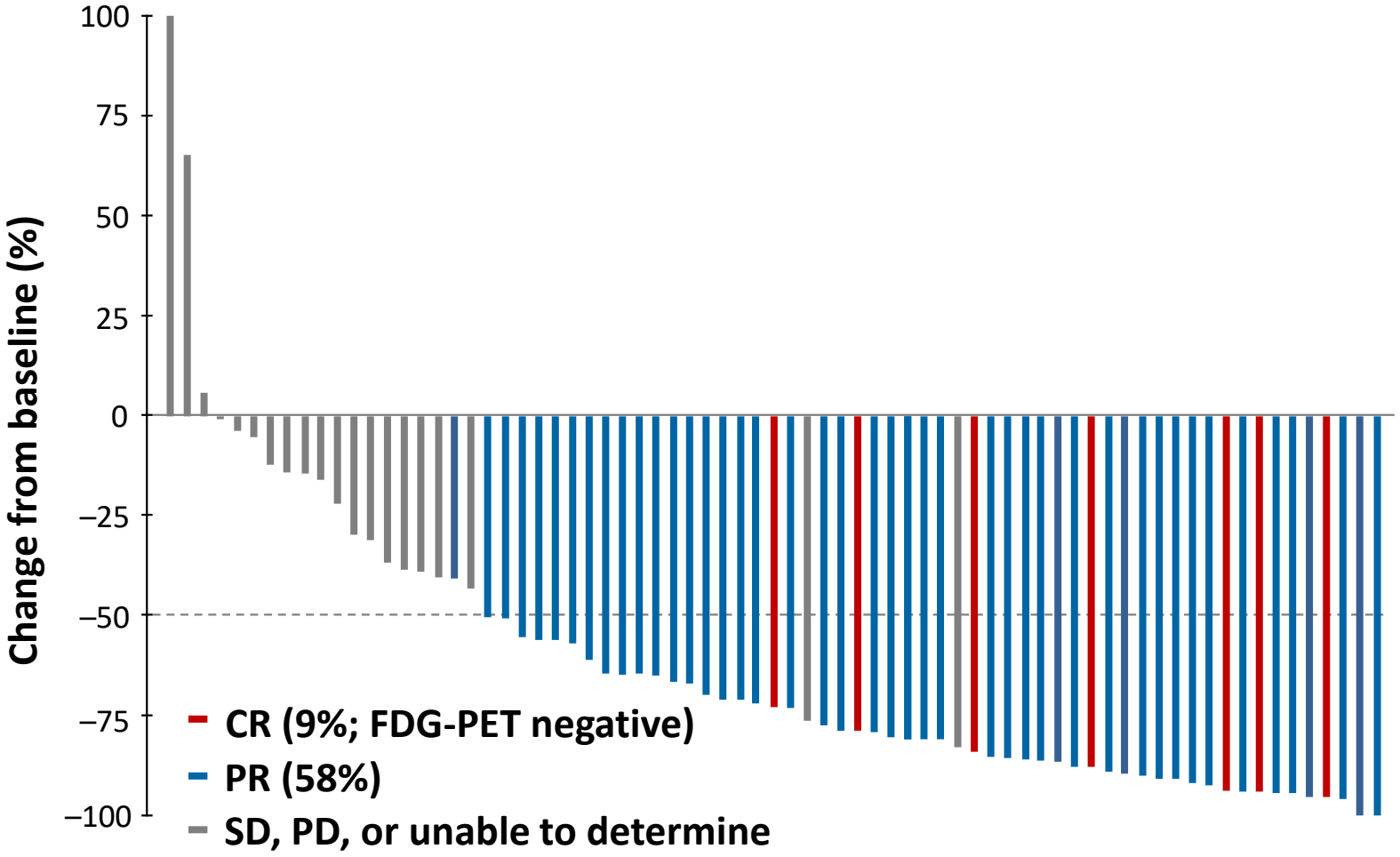
Drug	Dose/Schedule	N	% ORR	% CR	ORR in BV treated HL	1st Author
Pembrolizumab (humanized IgG4)	10 mg/kg IV Q 2wks	29	66%	21%	66% (n=19)	Armand P, JCO 2016
Nivolumab (Fully human IgG4)	3 mg/kg IV Q 2wks	23	87%	17%	70% (n=16)	Ansell S NEJM 2015

Phase 2 CheckMate 205 Study Design



Tumor Burden Change From Baseline (all response-evaluable patients)

- All but 1 responder had a reduction of ≥50% from baseline in tumor burden



Younes A, et al: Lancet Oncology 2016

Nivolumab for Relapsed cHL

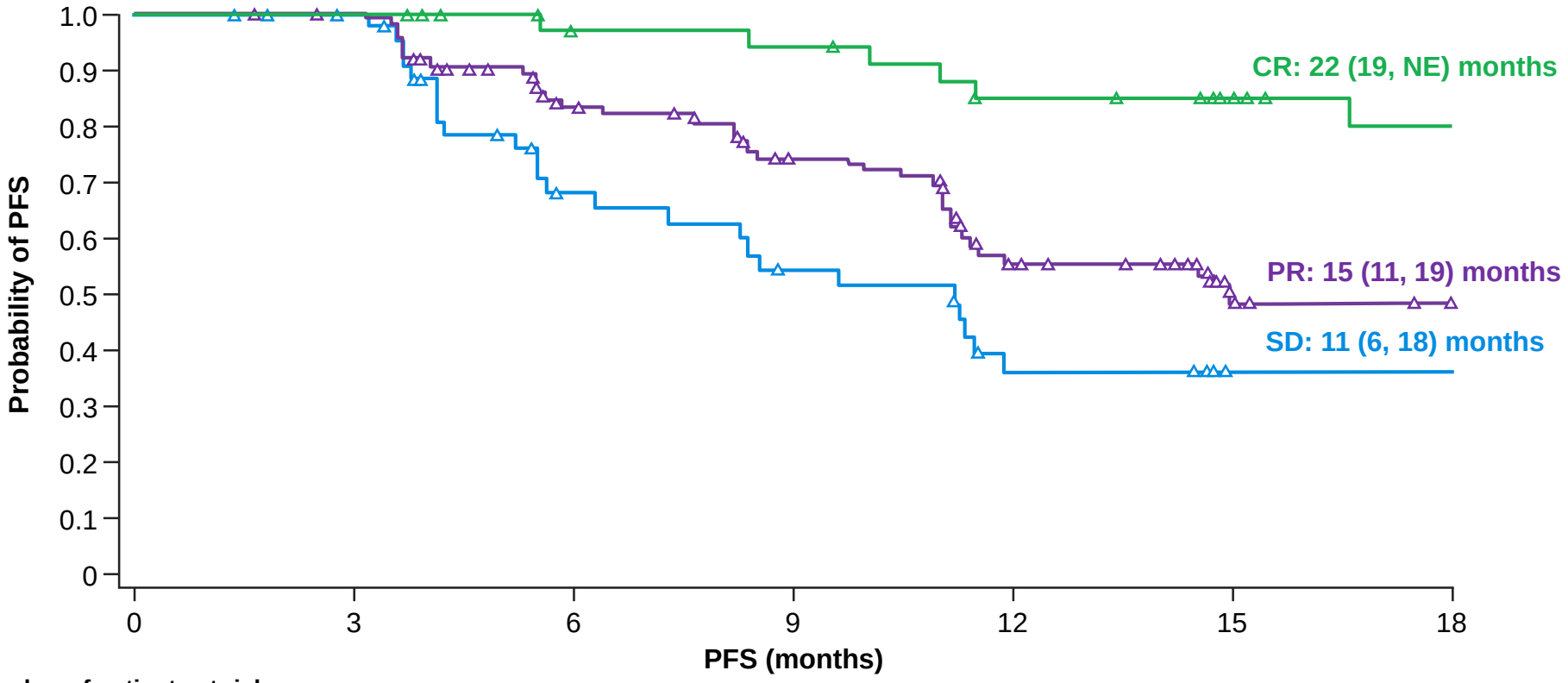
	BV naïve (Cohort A) n = 63	BV after auto-HSCT (Cohort B) n = 80	BV before and/or after auto-HSCT (Cohort C) n = 100	Overall N = 243
Objective response per IRC,[a] % (95% CI)	**65 (52, 77)**	**68 (56, 78)**	**73 (63, 81)**	**69 (63, 75)**
Best overall response per IRC, %				
Complete remission[b]	29	13	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

Fanale, M et al: ICML 2017

Nivolumab for Relapsed cHL

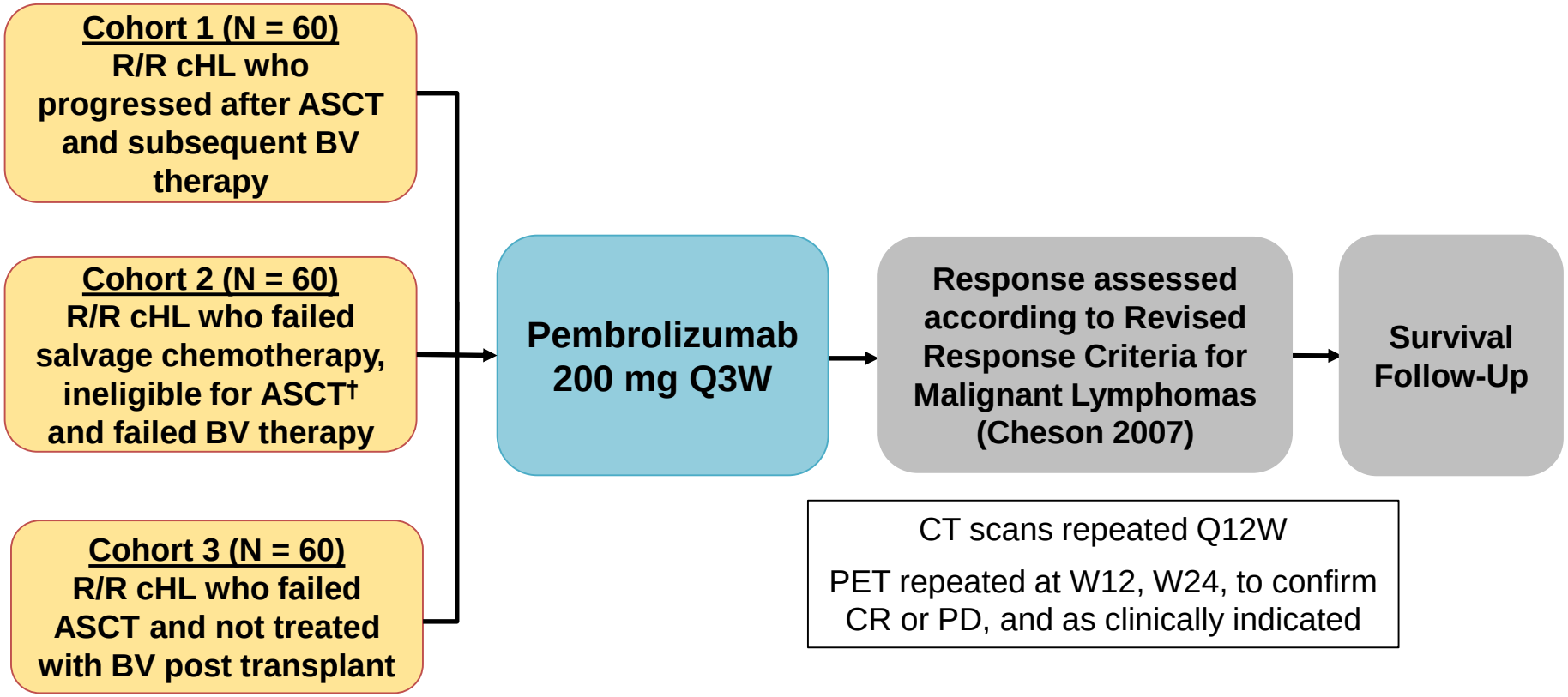
Progression-Free Survival by Best Overall Response



Number of patients at risk

CR	40	40	33	32	27	20	16
PR	128	126	89	71	46	25	21
SD	47	44	25	19	11	8	8

Pembrolizumab : KEYNOTE-087 Study Design



- **Primary end point:** ORR (central review)
- **Secondary end points:** ORR (investigator review), PFS, OS
- Prespecified interim analysis, based on investigator-assessed response, performed after 30 patients in all 3 cohorts reached first response assessment

†Unable to achieve a CR or PR to salvage chemotherapy

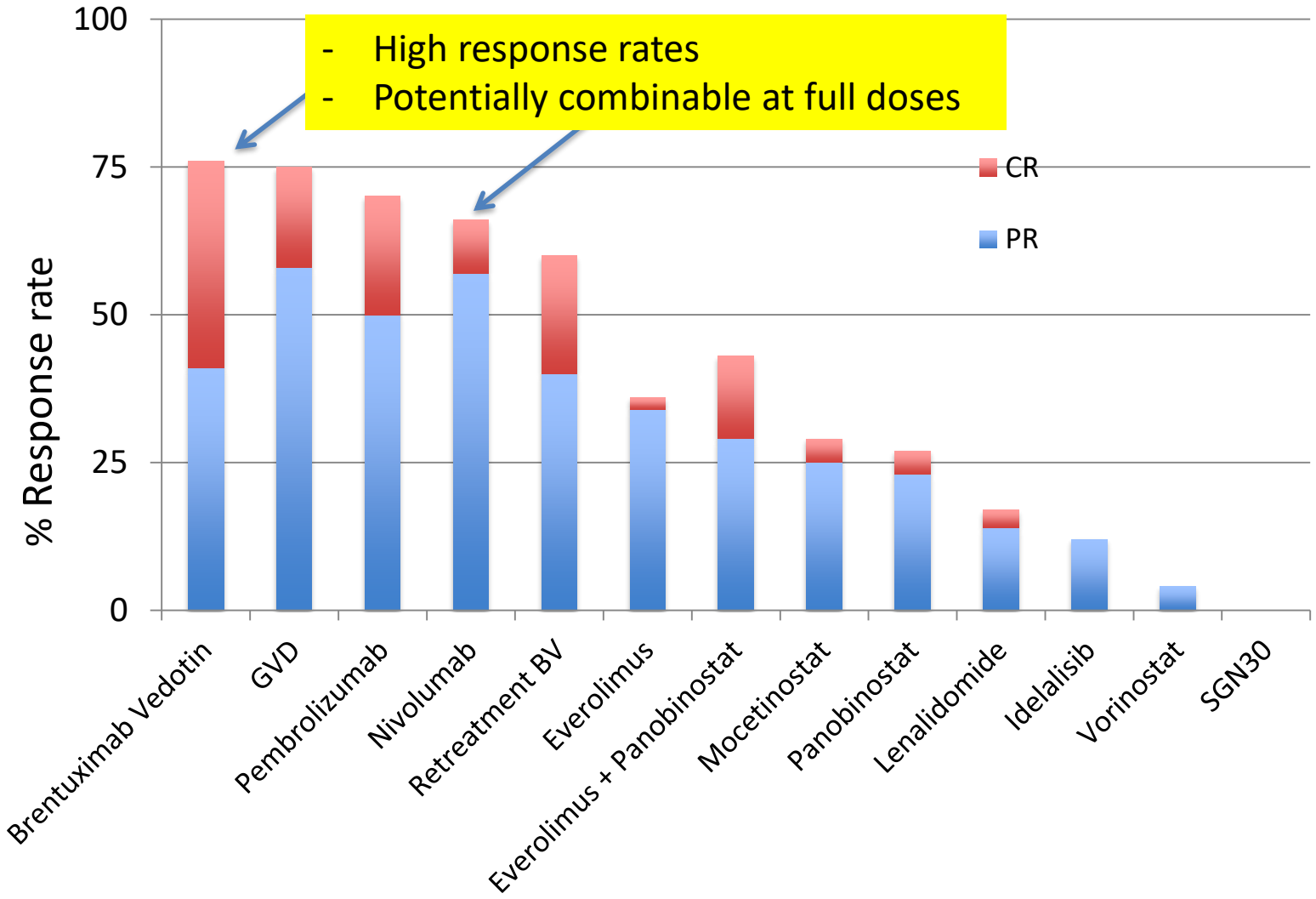
Pembrolizumab for Relapsed/Refractory cHL

KEYNOTE-087: Study Design

	Cohort 1 Post ASCT and BV N=69		Cohort 2 Post chemo and BV but no eligible for ASCT N = 81		Cohort 3 Post ASCT but no BV N = 60	
	n (%)	95% CI†	n (%)	95% CI†	n (%)	95% CI†
ORR	**50 (72.5)**	**60.4-82.5**	**53 (65.4)**	**54.0-75.7**	**40 (66.7)**	**53.3-78.3**
Complete remission*	15 (21.7)	12.7-33.3	18 (22.2)	13.7-32.8	13 (21.7)	12.1-34.2
Partial remission	35 (50.7)	38.4-63.0	35 (43.2)	32.2-54.7	27 (45.0)	32.1-58.4
Stable disease	13 (18.8)	10.4-30.1	9 (11.1)	5.2-20.0	13 (21.7)	12.1- 34.2
Progressive disease	3 (4.3)	0.9-12.2	17 (21.0)	12.7-31.5	7 (11.7)	4.8-22.6
Unable to determine	3 (4.3)	0.9-12.2	2 (2.5)	0.3-8.6	0 (0)	–

Moskowitz C, et al ASH 2016

Single agent activity of novel agents in relapsed cHL



Updated from Betlevi and Younes, Hematology Am Soc Hematol Educ Program. 2013
Smith, K et al : Hodgkin Lymphoma, Hoffan Textbook of Hematology 2015 (In Press)

1105 Preliminary Results from a Phase 1/2 Study of Brentuximab Vedotin in Combination with Nivolumab in Patients with Relapsed or Refractory Hodgkin Lymphoma

Alex F Herrera, MD[1], Nancy L Bartlett, MD[2], Radhakrishnan Ramchandren, MD[3*], Julie M Vose, MD[4], Alison J Moskowitz, MD[5], Tatyana A Feldman, MD[6], Ann S LaCasce, MD[7], Stephen M Ansell, MD, PhD[8*], Craig H. Moskowitz, MD[5], Keenan Fenton[9*], Kazunobu Kato, MD[10], Abraham Fong, MD, PhD[9] and Ranjana H Advani, MD[11]

Nivolumab + Brentuximab Salavage Therapy for HL

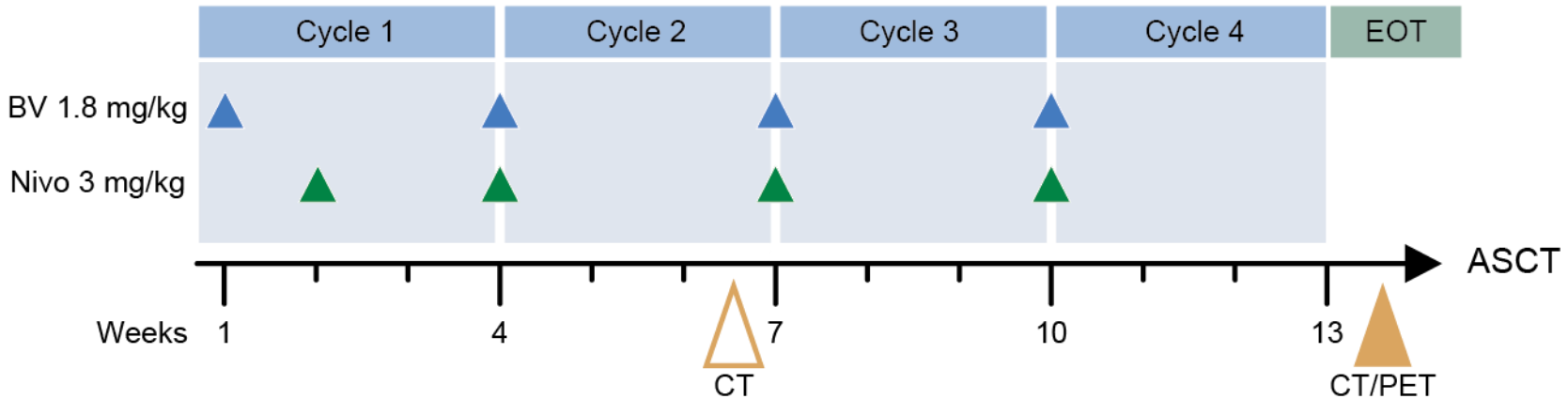
Brentuximab Vedotin 1.8mg/kg

Nivolumab 240 mg

Q 3wks x 4

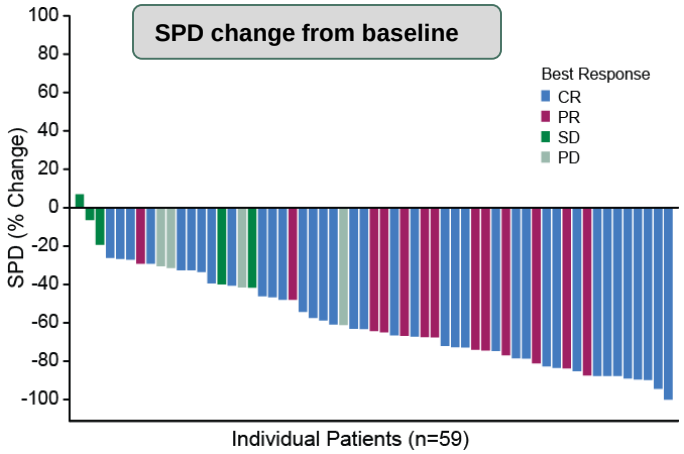
→ Restage

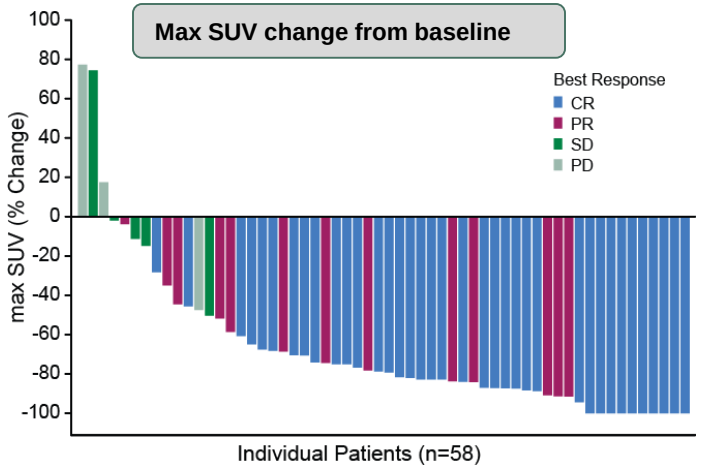
- PR/CR → Stem cell collection => BEAM ASCT
- < PR → Chemo salvage → Stem cell collection => BEAM ASCT



Tumor Response (N=59)

85% objective response rate with 63% complete responses



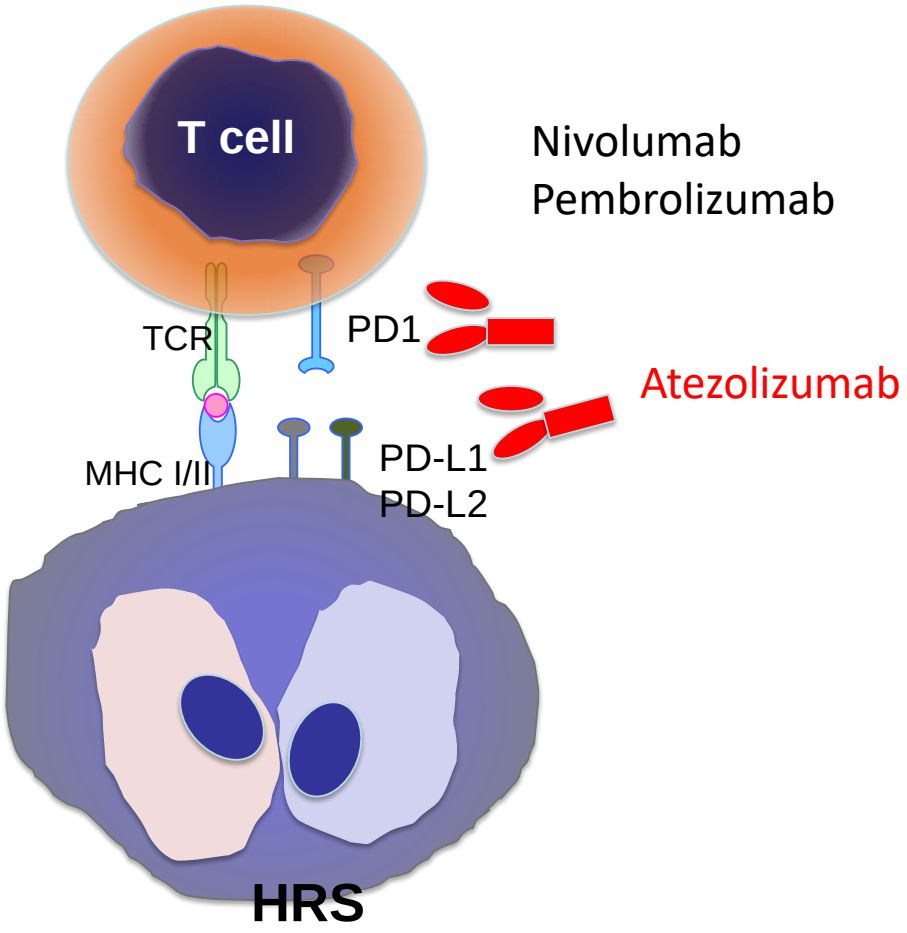


	N = 59 n (%)
Complete response (CR)	**37 (63)**
Deauville ≤ 2	29 (49)
Deauville 3	7 (12)
Deauville 5[a]	1 (2)
Partial response (PR)	**13 (22)**
Deauville 4	7 (12)
Deauville 5	6 (10)
No metabolic response (SD)	**5 (8)**
Deauville 5	5 (8)
Progressive disease (PD)	**3 (5)**
Deauville 5	2 (3)
Missing	1 (2)
Clinical Progression (CP)	**1 (2)**

a. 1 pt had uptake in lymph node, but no evidence of disease was found on biopsy

SPD, sum of the product of the diameters; SUV, standard uptake value

Is there a role of targeting PDL-1 in HL?



Adapted from Stathis & Younes: Ann Oncology 2015
And Younes A & Ansell S : Seminars in Hematology, 2016, 186–189

Blockade of the PD-1 checkpoint with anti–PD-L1 avelumab is sufficient for clinical activity in relapsed/refractory classical Hodgkin lymphoma (cHL)

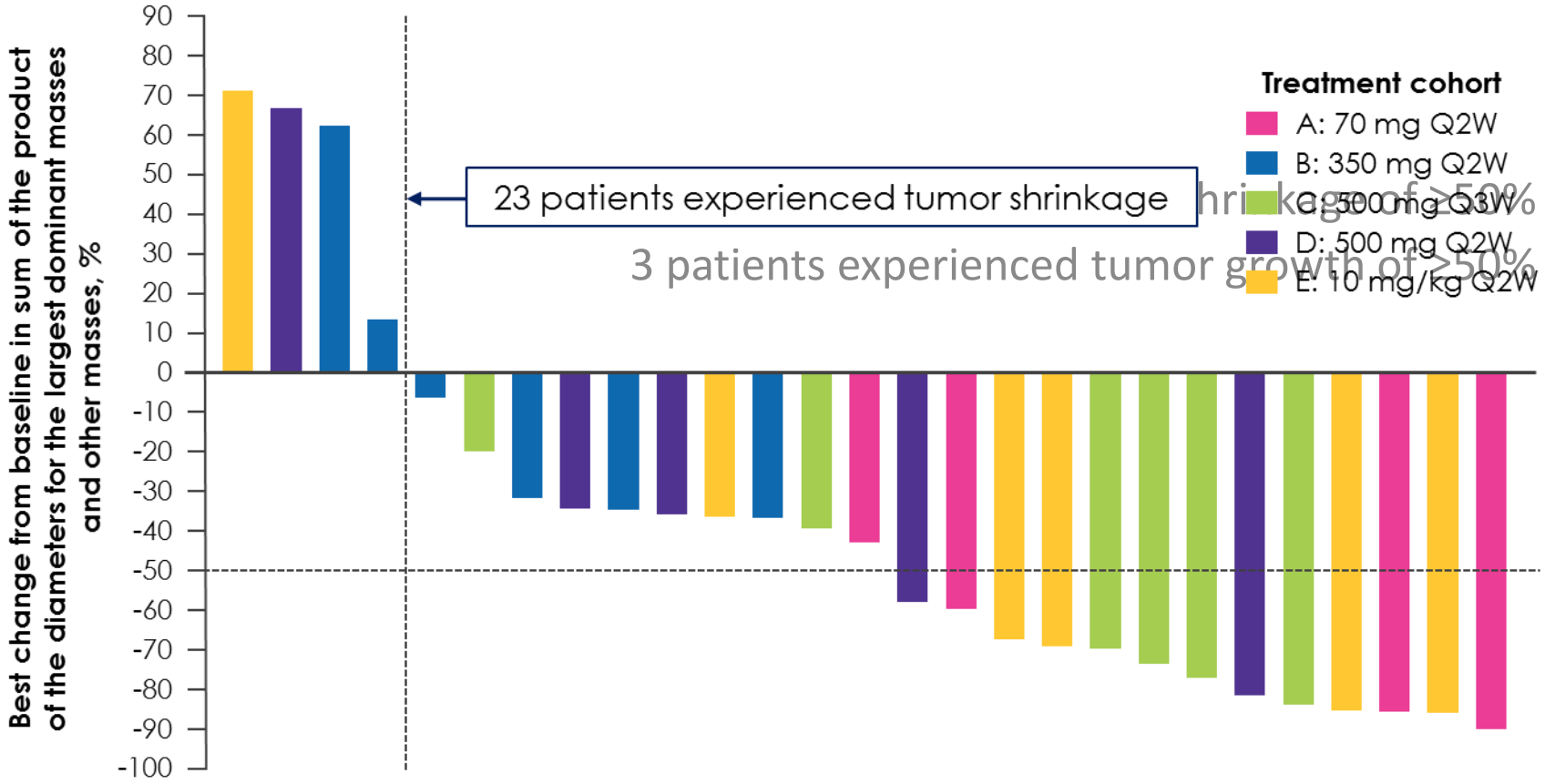
Robert Chen[1], Adam Gibb[2], Graham P. Collins[3], Rakesh Popat[4], Dima El-Sharkawi[4], Cathy Burton[5], David Lewis[6], Fiona Miall[7], Alison Forgie[8], Anna Compagnoni[9], Giovanna Andreola[9], Satjit Brar[10], Aron Thall[10], Adrian Woolfson[11], and John Radford[2]

[1]City of Hope Medical Center, Duarte, California, USA; [2]The Christie NHS Foundation Trust, Manchester, United Kingdom; [3]Churchill Hospital, Cancer and Haematology Centre, Oxford, United Kingdom; [4]University College London Hospitals NHS Foundation Trust, London, United Kingdom; [5]St. James's University Hospital, Leeds, United Kingdom; [6]Plymouth Hospital NHS Trust, Plymouth, United Kingdom; [7]University Hospitals of Leicester NHS Trust, Leicester, United Kingdom; [8]Pfizer Oncology Research and Development, San Francisco, California, USA; [9]Pfizer Oncology, Milano, Italy; [10]Pfizer Oncology, La Jolla, California, USA; [11]Pfizer Oncology, New York, New York, USA

Oral Presentation at the 14th International Conference on Malignant Lymphoma; June 14-17, 2017; Lugano, Switzerland

Abstract No. 055

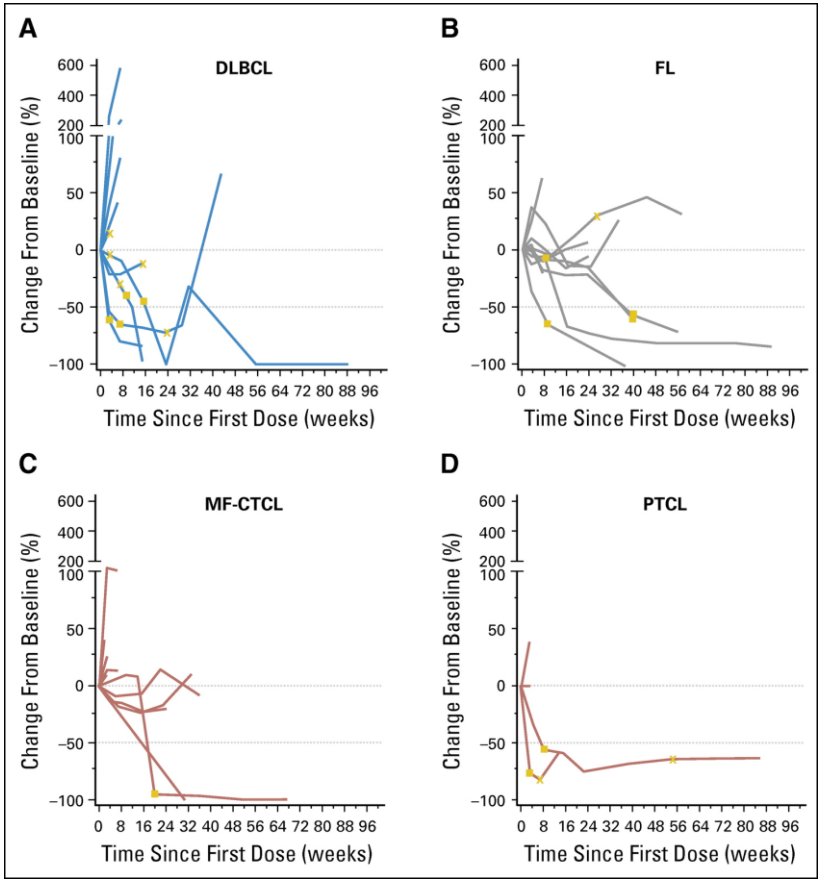
Best percent change in tumor burden from baseline (n=27*)



* Only patients with baseline and ≥1 post-baseline largest dominant mass or other mass based on investigator assessment per Response Criteria for Malignant Lymphoma are included.

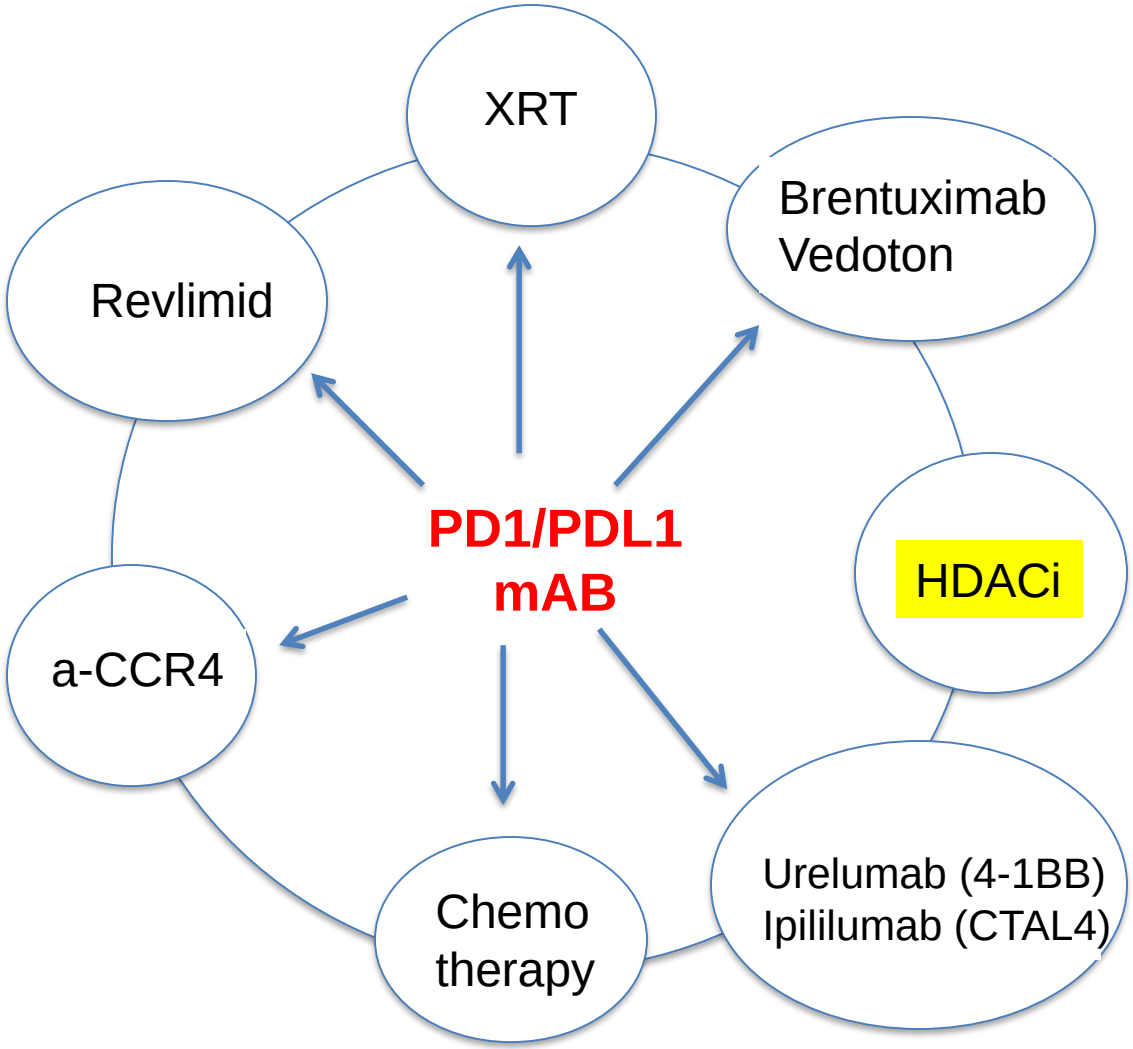
Nivolumab in Patients With Relapsed or Refractory Hematologic Malignancy:

Preliminary Results of a Phase Ib Study



Lesokhin A, et al: JCO 2016

Development of Anti-PD1/PDL1-Based Therapy

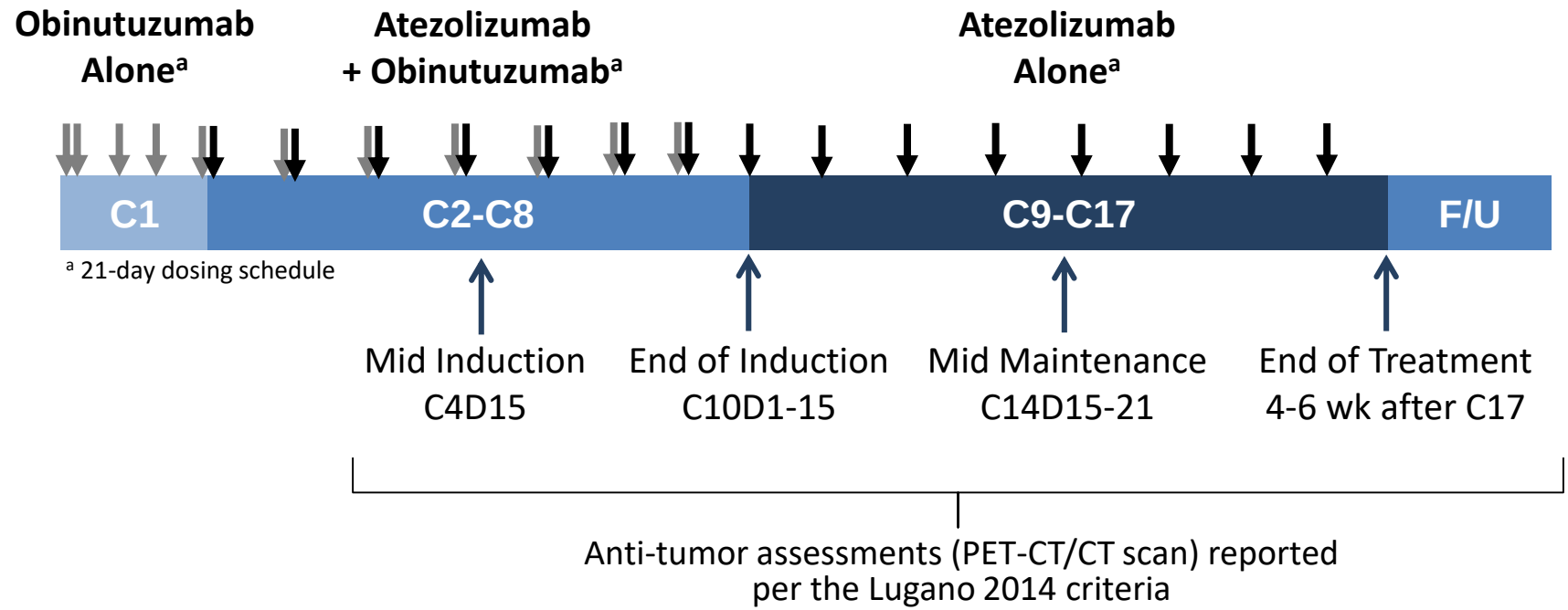


A Phase Ib Study Evaluating the Safety and Clinical Activity of Atezolizumab Combined With Obinutuzumab in Patients With Relapsed or Refractory Non-Hodgkin Lymphoma

M. Lia Palomba,[1] Brian G. Till,[2] Steven I. Park,[3] Franck Morschhauser,[4] Guillaume Cartron,[5] Reinhard Marks,[6] Elicia Penuel,[7] Surya Chitra,[7] Melissa Kuhn,[7] Leslie Popplewell[8]

[1]Lymphoma Service, Memorial Sloan Kettering Cancer Center, New York, NY, USA; [2]Seattle Cancer Care Alliance, Fred Hutchinson Cancer Research Center, Seattle, WA, USA; [3]Lineberger Comprehensive Cancer Center, University of North Carolina, Chapel Hill, NC, USA; [4]Department of Clinical Hematology, Lille University Hospital Center, Lille Cedex, France; [5]Department of Clinical Hematology, University Hospital Center of Montpellier, Montpellier, France; [6]Department of Hematology, Oncology and Stem Cell Transplantation, Universitätsklinikum Freiburg, Freiburg, Germany; [7]Product Development Oncology, Genentech, Inc., South San Francisco, CA, USA; [8]Hematology and Hematopoietic Cell Transplantation, City of Hope, Duarte, CA, USA

Phase I Study of Atezolizumab + Obinutuzumab in NHL (FL or DLBCL)

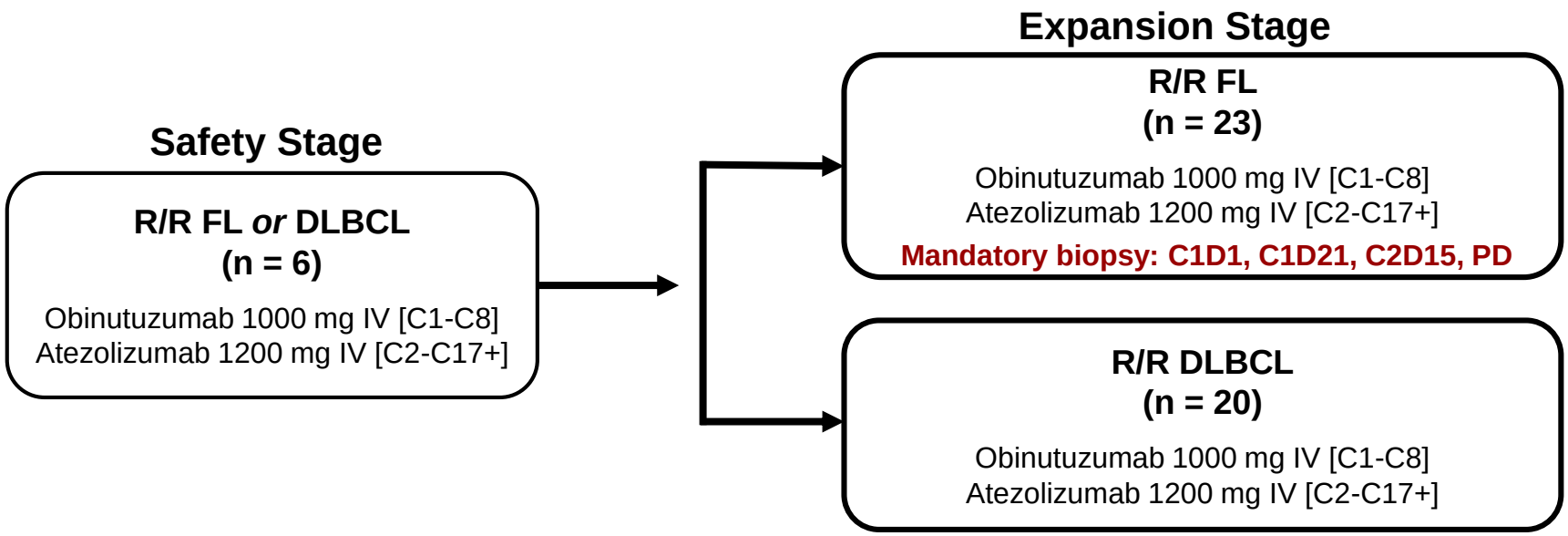


Obinutuzumab 1000 mg IV q3w

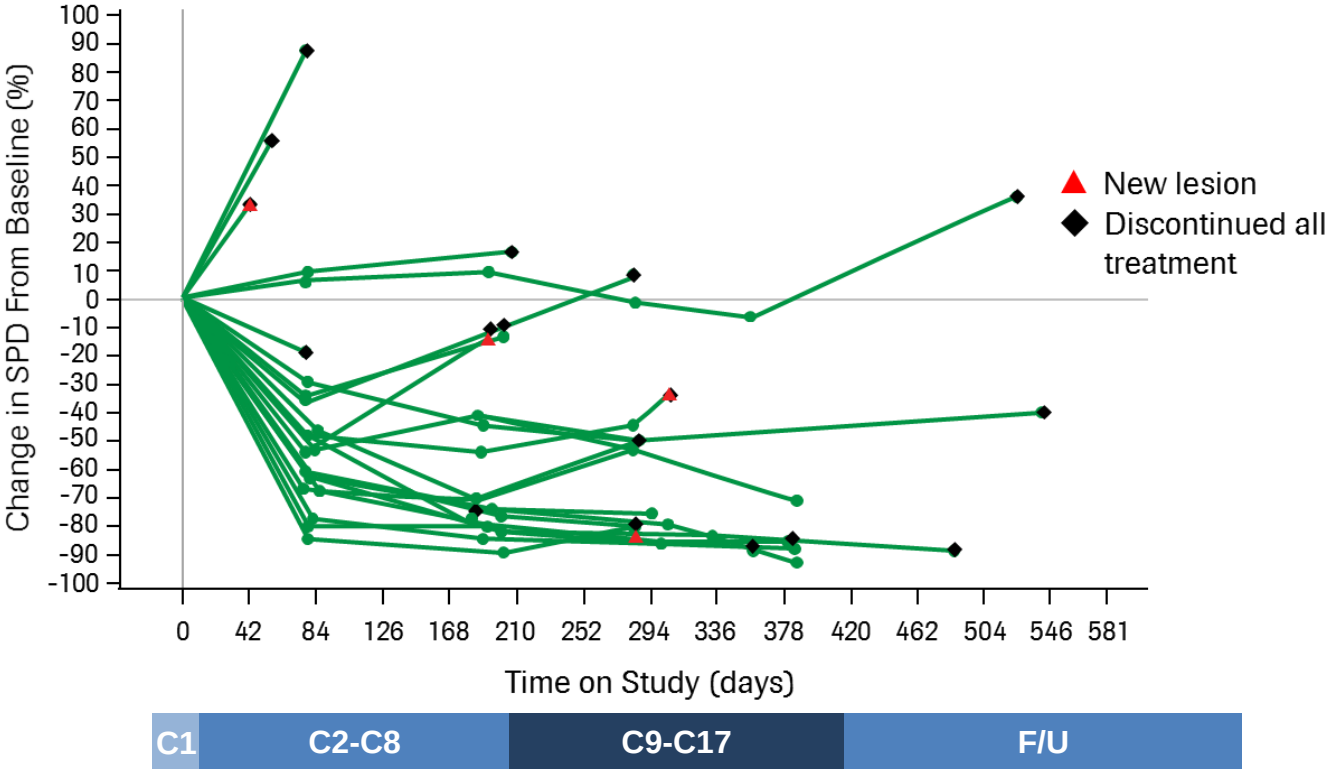
Atezolizumab 1200 mg IV q3w

Palomba et al. Atezolizumab + Obinutuzumab in NHL, ICML 2017. http://tago.ca/1BGT

Phase I Study of Atezolizumab + Obinutuzumab in NHL (FL or DLBCL)



Change in Tumor Burden in R/R FL

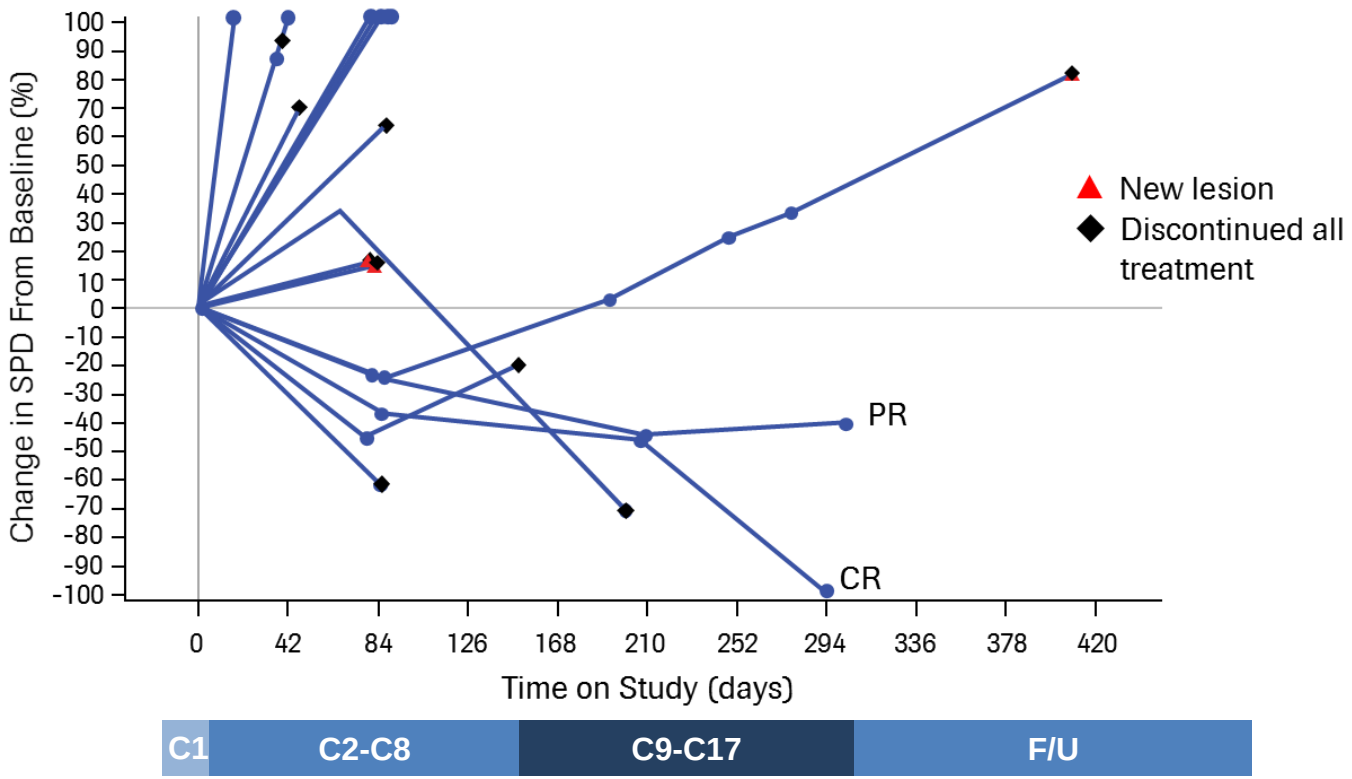


- **14/23 patients (61%)** with FL achieved a response[a] (PET-CT) at or prior to the End of Induction response assessment, as measured by the investigator
- Among the 14 responders, median duration of response was 15.0 months, with 10 patients still in response at data cutoff

Palomba et al. Atezolizumab + Obinutuzumab in NHL, ICML 2017. http://tago.ca/1BGT

SPD, sum of the product of the diameters. [a] Per the Lugano 2014 response criteria.

Change in Tumor Burden in R/R DLBCL



- Four patients with DLBCL achieved a response[a] (PET-CT) at or prior to the End of Induction response assessment, as measured by the investigator
- Among the 4 responders, median duration of response was 4.9 months, with 1 patient still in response at data cutoff

SPD, sum of the product of the diameters. [a] Per the Lugano 2014 response criteria.

Palomba et al. Atezolizumab + Obinutuzumab in NHL, ICML 2017. http://tago.ca/1BGT

Pembrolizumab in Combination with Rituximab in Patients with Relapsed Follicular Lymphoma:

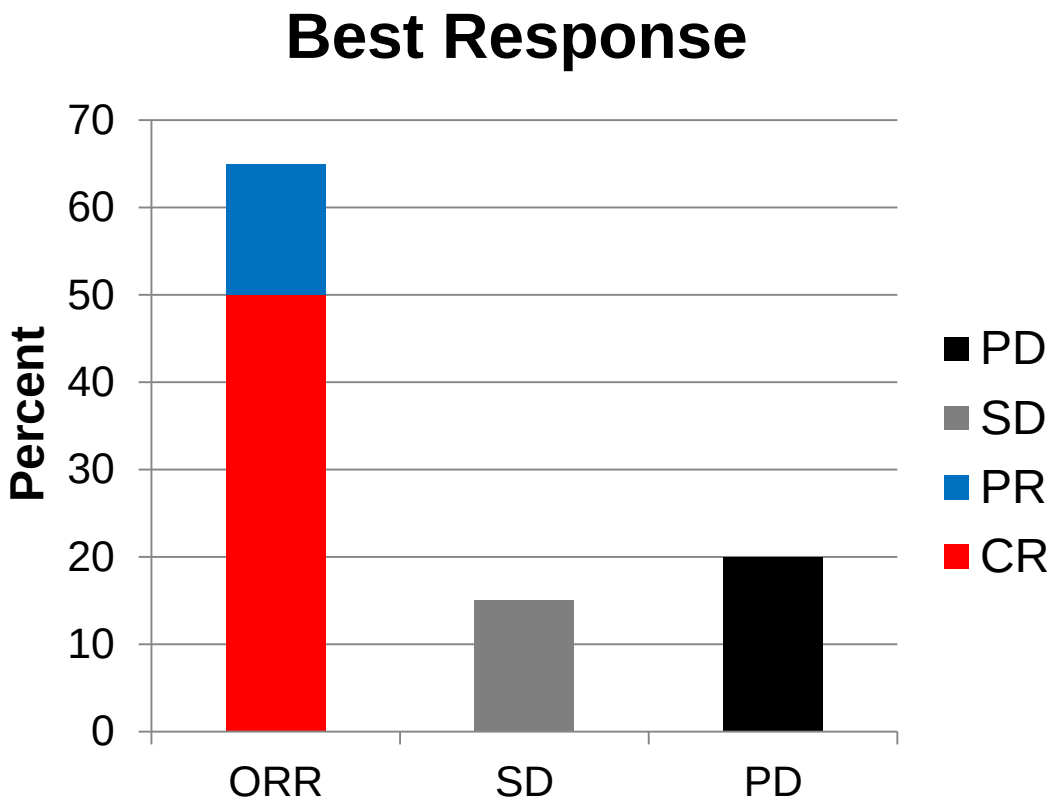
Loretta J. Nastoupil, Jason Westin, Nathan Fowler, Michelle Fanale, Felipe Samaniego, Yasohiro Oki, Chizobam Obi, JingJing Cao, Xiaoyun Cheng, Man Chun John Ma, Zhiqiang Wang, Fuliang Chu, Lei Feng, Shouhao Zhou, R. Eric Davis, and Sattva S. Neelapu

THE UNIVERSITY OF TEXAS
MD Anderson Cancer Center
Making Cancer History®

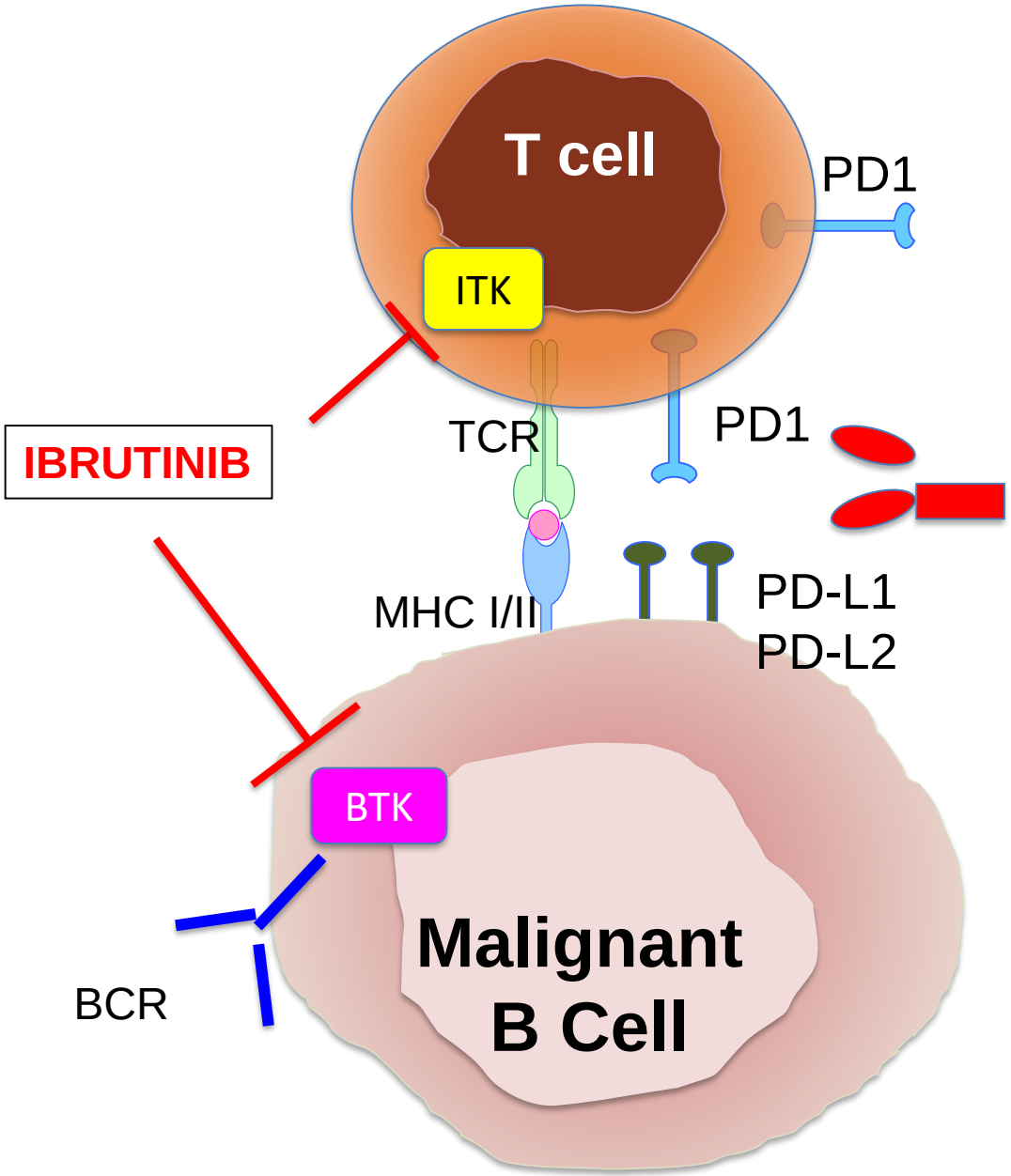
Pembrolizumab + Rituximab in Relapsed FL

- 20 evaluable for response
- **ORR was 65%**

  (CR N=10/PR N=3)
- **CR rate was 50%**
- 3 patients with stable disease and 4 with progressive disease as best response

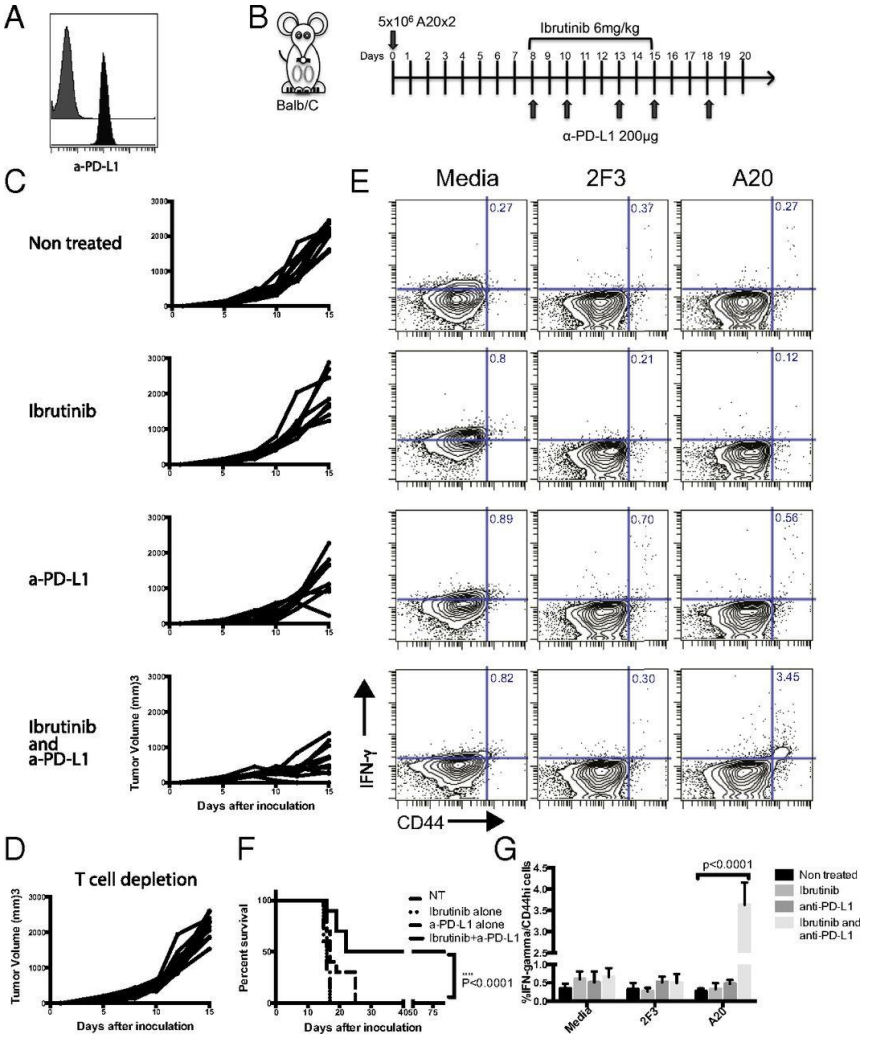


Rationale for combining Ibrutinib with PD1/PDL1 antibodies



Ibrutinib in combination with anti–PD-L1 induces an antitumor immune response

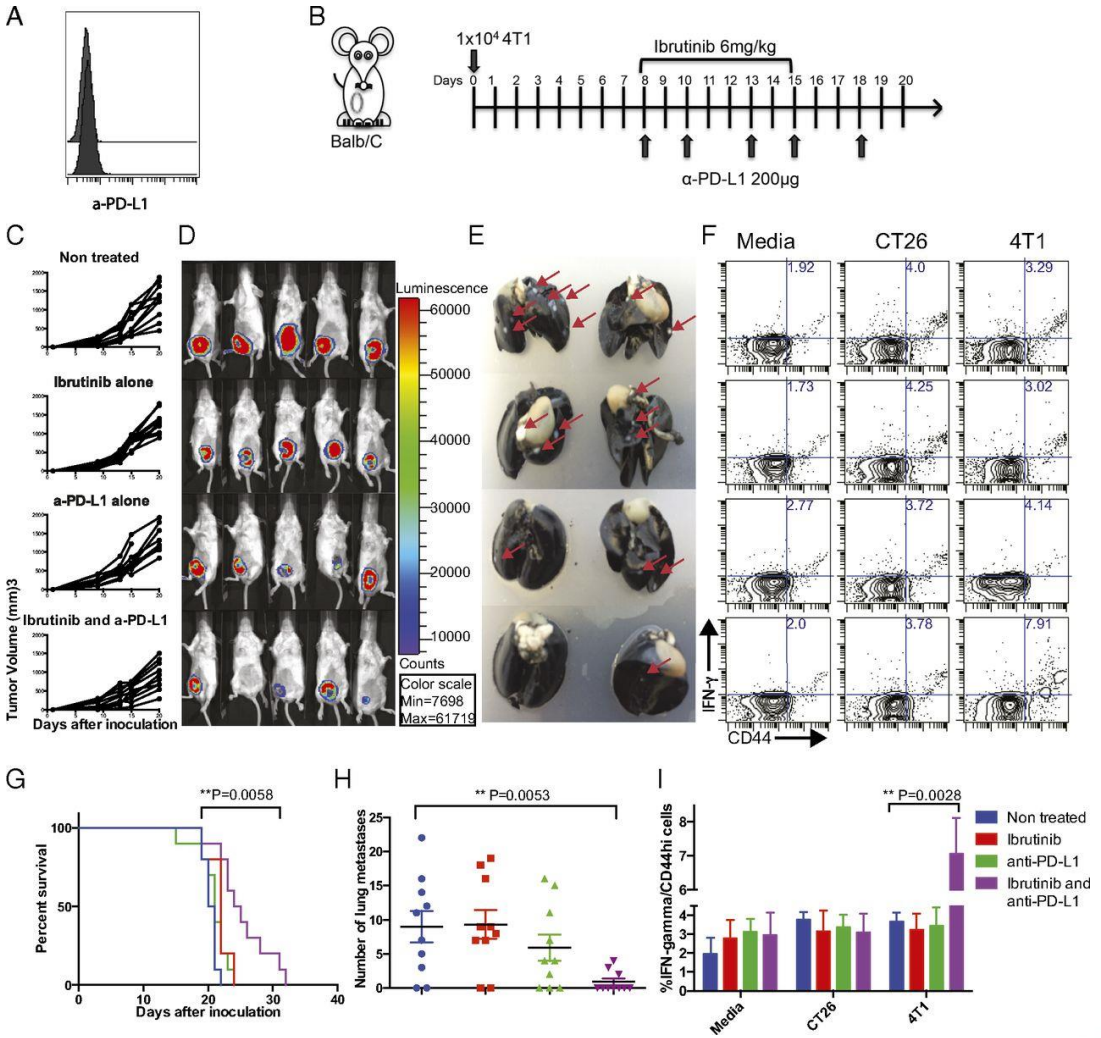
A20 mouse B cell lymphoma model



Idit Sagiv-Barfi et al. PNAS 2015;112:E966-E972

PNAS

The combination of ibrutinib with anti–PD-L1 reduces tumor burden in 4T1 (Mouse Tripple Negative Breast Carcinoma) tumor-bearing mice.



Idit Sagiv-Barfi et al. PNAS 2015;112:E966-E972

PNAS

PCI32765-LYM-1002: Study Design

Nivolumab + Ibrutinib in relapsed B-cell malignancies

Part A n=18
(Dose Optimization)

A-1
I: 420 mg , po, qd
N: 3mg/kg , i.v., q14d

A-2
I: 560 mg, p.o., qd
N: 3 mg/kg, i.v., q14d

Part B (n=30 in each cohort)
(Expansion Cohort: Two-stage design)

B 1: I: 420 mg/qd PO + N: 3 mg/kg/q14d

B1: CLL (del 17p or del 11q)

B 2 and B 3: I: 560 mg/qd PO + N: 3 mg/kg/q14d

B2: Follicular Lymphoma

B3: DLBCL

Safety and Efficacy of the Combination of Ibrutinib and Nivolumab in Patients With Relapsed Non-Hodgkin Lymphoma or Chronic Lymphocytic Leukemia

Anas Younes,[1] Joshua Brody,[2] Cecilia Carpio,[3] Armando López-Guillermo,[4] Dina Ben-Yehuda,[5] Burhan Ferhanoglu,[6] Arnon Nagler,[7] Muhit Ozcan,[8] Irit Avivi,[9] Francesc Bosch,[3] Maria Dolores Caballero Barrigon,[10] Daniela Buglio,[11] Michael Streit,[12] John Alvarez,[12] Rob Ceulemans,[13] Behzad Kharabi Masouleh,[13] Sriram Balasubramanian,[12] Michael Schaffer,[12] Shean-Sheng Wang,[14] Nele Fourneau,[13] Wojciech Jurczak[15]

[1]Memorial Sloan Kettering Cancer Center, New York, NY, USA; [2]Icahn School of Medicine at Mount Sinai, New York, NY, USA; [3]University Hospital Vall d'Hebron, Barcelona, Spain; [4]University of Barcelona, Barcelona, Spain; [5]Hadassah-Hebrew University Medical Center, Jerusalem, Israel; [6]Koc University, Istanbul, Turkey; [7]Chaim Sheba Medical Center, Tel-Hashomer, Israel; [8]Ankara University School of Medicine, Ankara, Turkey; [9]Tel Aviv Medical Center, Tel Aviv, Israel; [10]Hospital Clínico Universitario de Salamanca, Salamanca, Spain; [11]Bristol-Myers Squibb, Lawrenceville, NJ, USA; [12]Janssen R&D, Spring House, PA, USA; [13]Janssen R&D, Beerse, Belgium; [14]Janssen R&D, Raritan, NJ, USA; [15]Jagiellonian University, Krakow, Poland

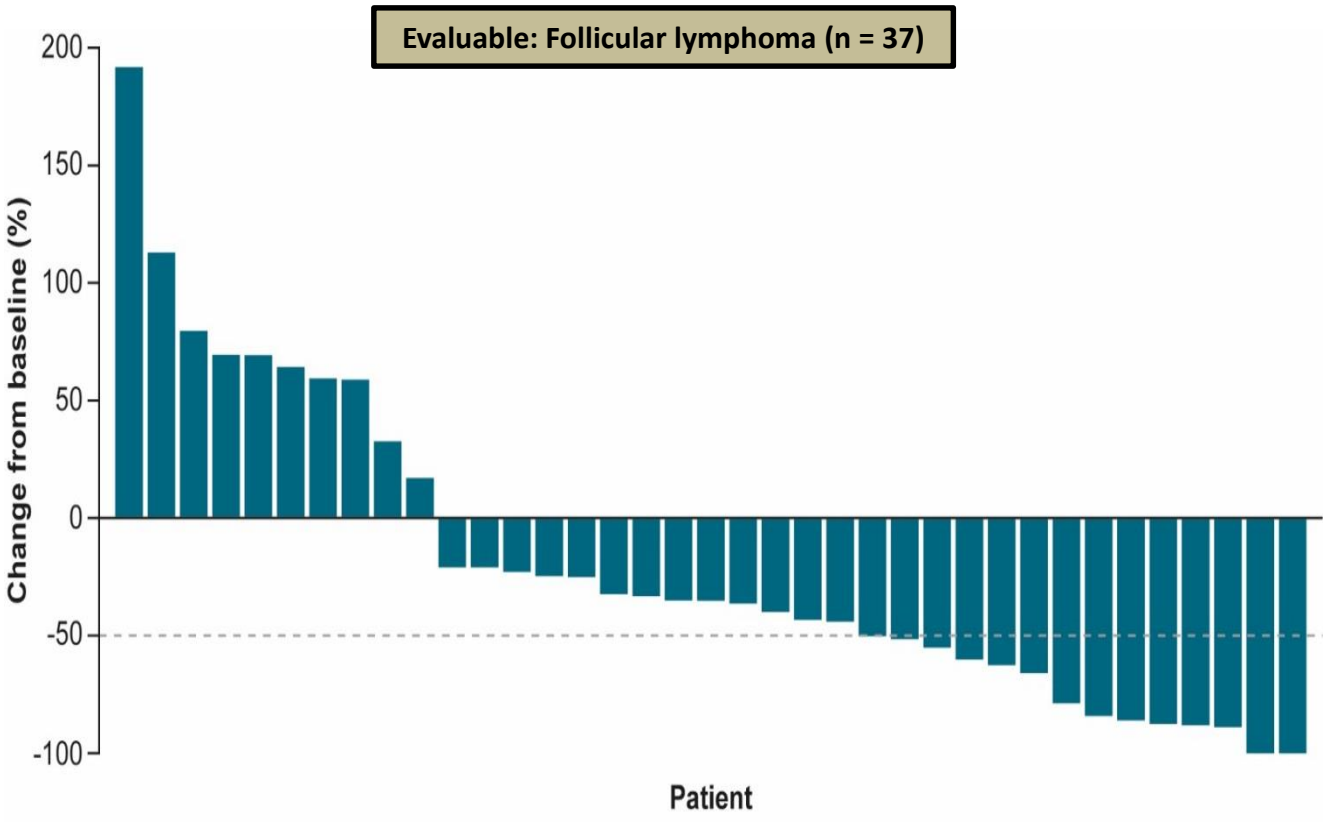
Demographics and Characteristics

	CLL/SLL (n = 36)	FL (n = 40)	DLBCL (n = 45)	Richter (n = 20)	Total (N = 141)
Age, years					
Median (range)	65 (41-79)	63 (42-83)	64 (20-89)	68 (41-83)	65 (20-89)
Sex, n (%)					
Male	27 (75)	23 (58)	29 (64)	8 (40)	87 (62)
Female	9 (25)	17 (42)	16 (36)	12 (60)	54 (38)
ECOG, n (%)					
0	17 (47)	30 (75)	19 (42)	4 (20)	70 (50)
1	18 (50)	8 (20)	21 (47)	13 (65)	60 (43)
2	1 (3)	2 (5)	5 (11)	3 (15)	11 (8)
Prior lines of therapy, n					
Median (range)	2.0 (1-6)	3.0 (2-12)	3.0 (1-9)	2.0 (1-5)	3.0 (1-12)
Bulky disease (≥ 5 cm), n (%)	26 (72)	15 (38)	17 (38)	10 (50)	68 (48)

59th ASH Annual Meeting 2017, LYM1002 Study, Younes A, et al. Abstract #833. Funded by Janssen Research & Development, LLC.

Efficacy: Follicular Lymphoma

Maximum Decrease in Target Lesions

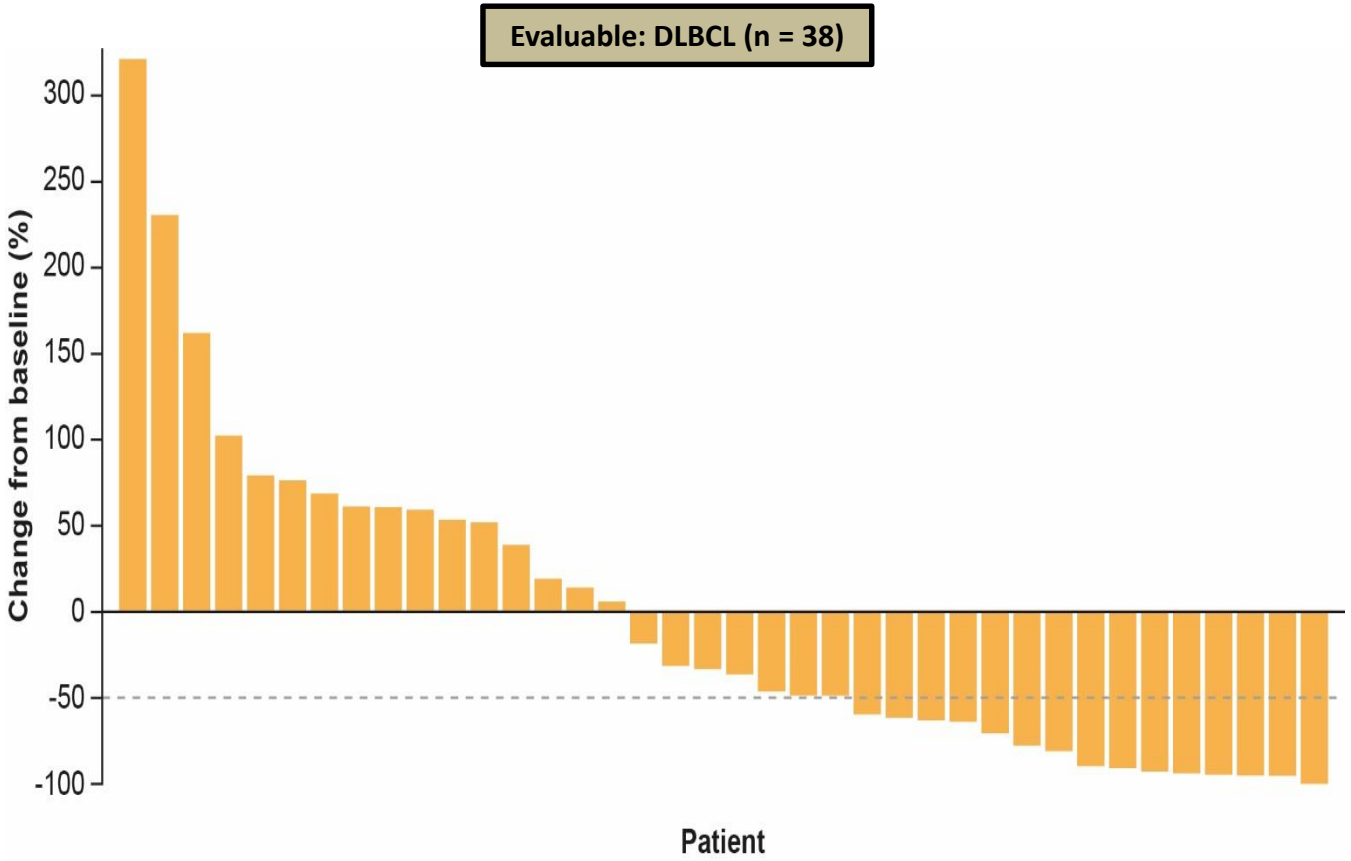


n (%)	FL (n = 40)
ORR,[a,b]	13 (32)
CR	4 (10)
PR	9 (22)
SD	13 (32)
PD	11 (28)
Missing	3 (8)

[a]ORR includes CR and PR.
[b]Lugano classification.

Efficacy: Diffuse Large B-Cell Lymphoma

Maximum Decrease in Target Lesions

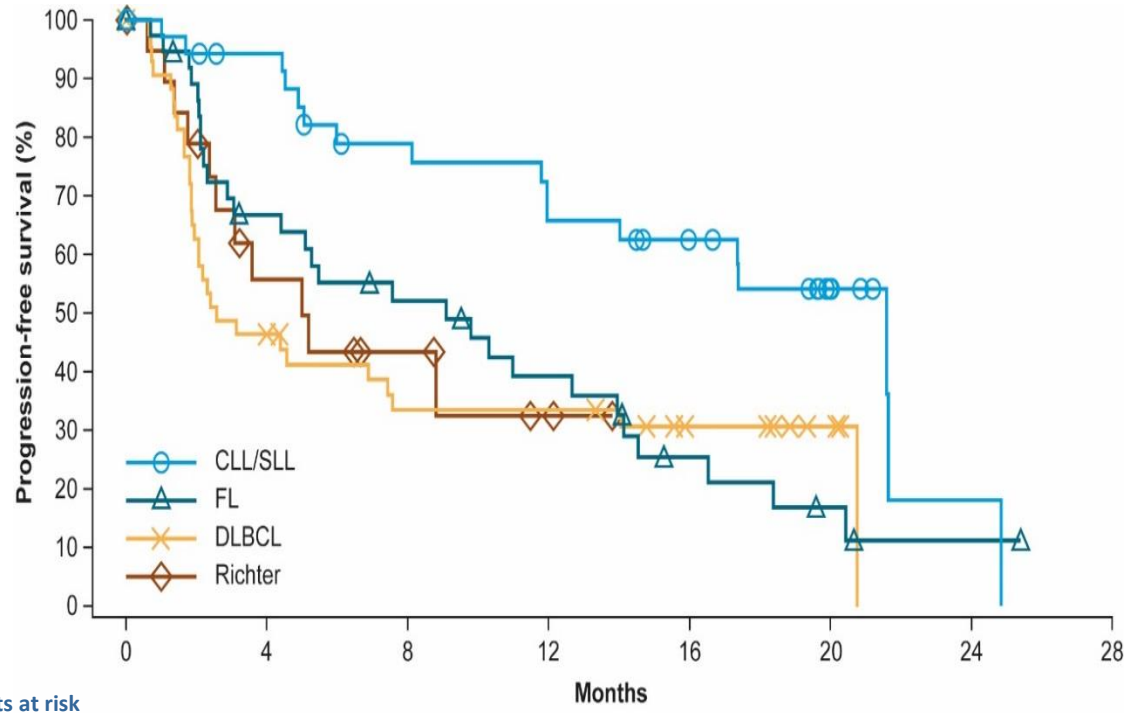


n (%)	DLBCL (n = 45)
ORR,[a,b]	16 (36)
CR	7 (16)
PR	9 (20)
SD	6 (13)
PD[c]	19 (42)
Missing	4 (9)

[a]ORR includes CR and PR.
[b]Lugano classification.
[c]Data not available for 3 patients (PD based on clinical progression).

Nivolumab + Ibrutinib

Progression-Free Survival

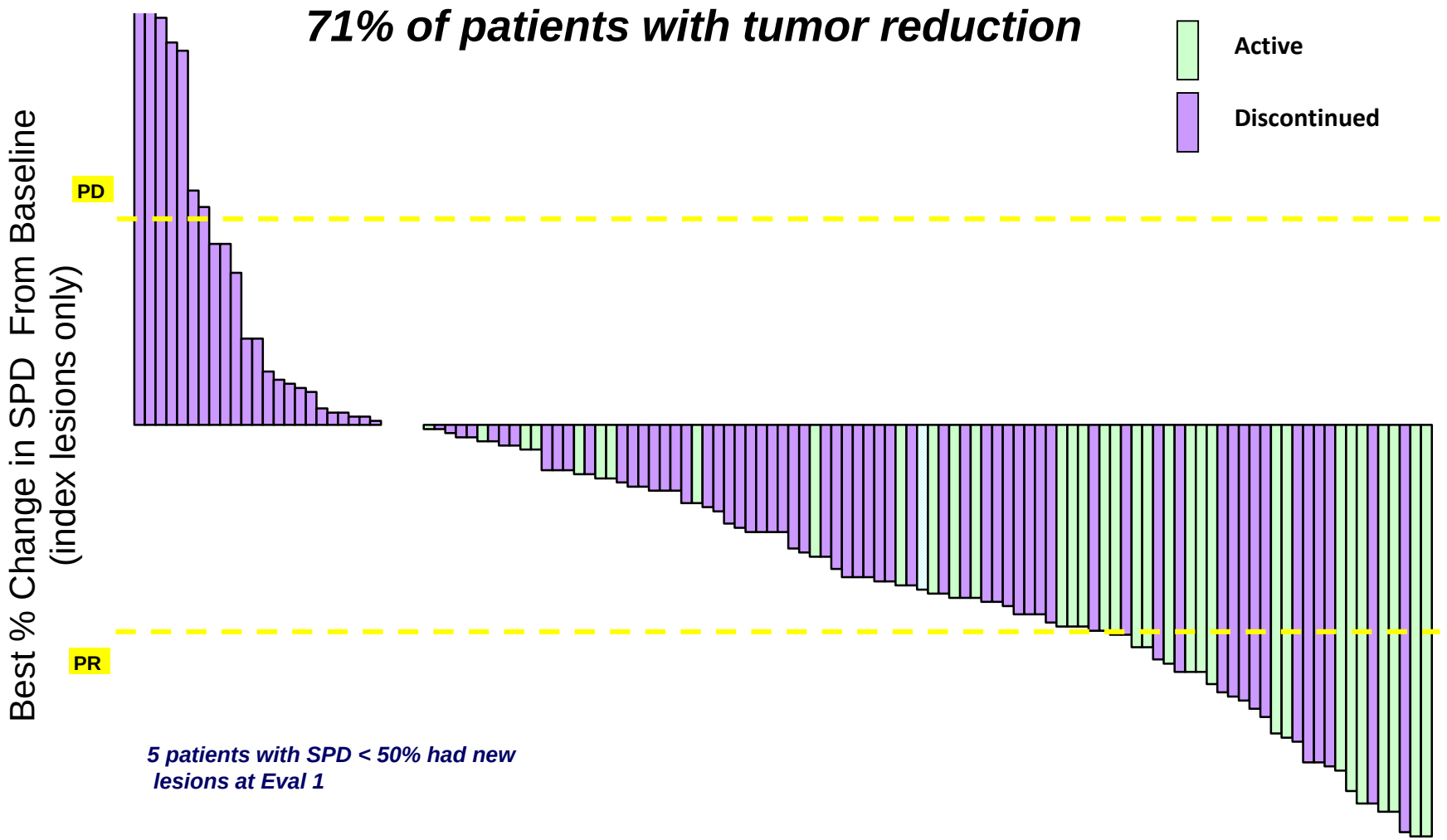


Patients at risk

CLL/SLL	36	31	24	20	16	8	1	0
FL	40	23	17	12	6	3	1	0
DLBCL	45	20	13	13	8	3	0	0
Richter	20	9	5	2	0	0	0	0

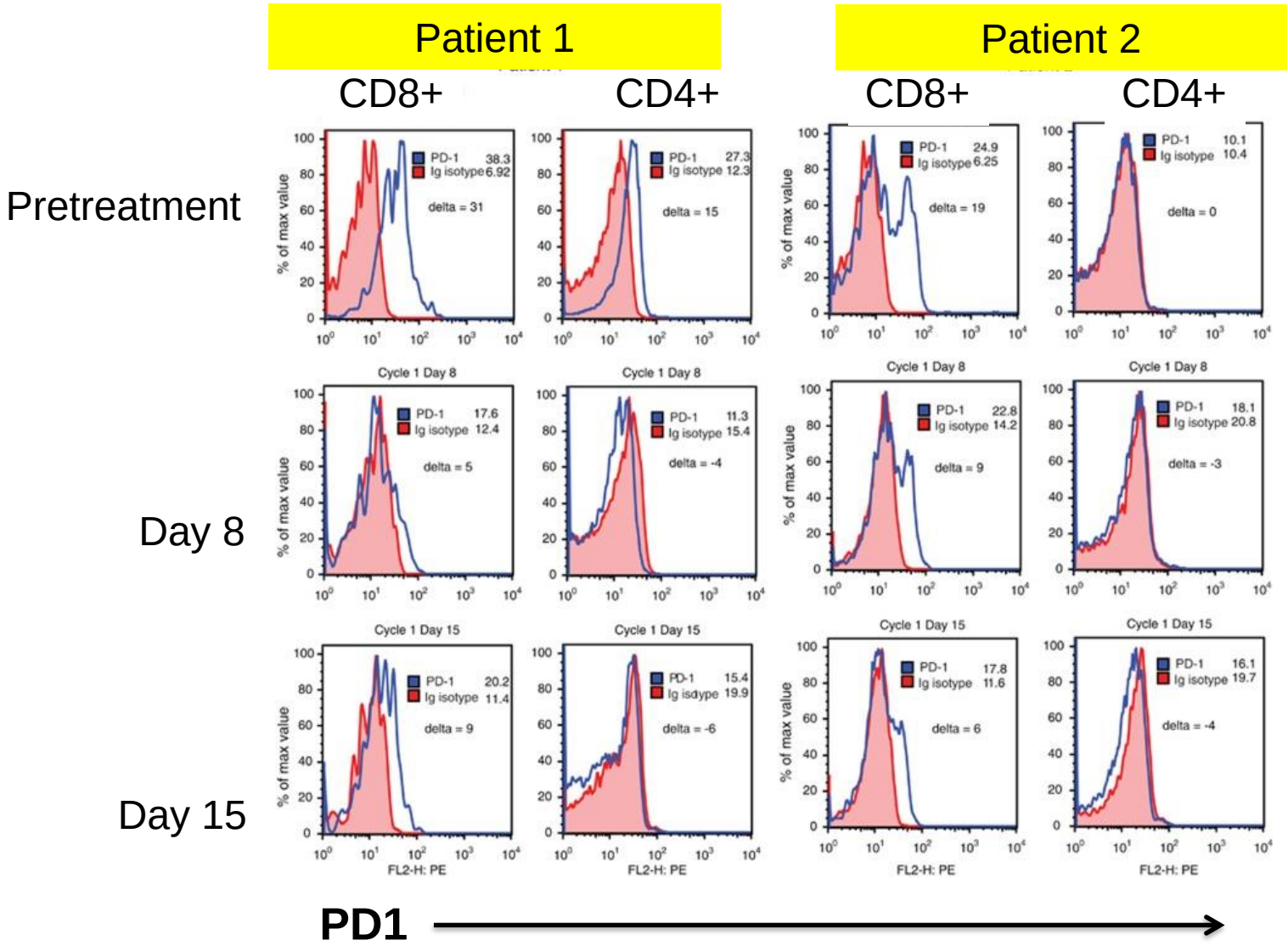
	CLL/SLL (n = 36)	FL (n = 40)	DLBCL (n = 45)	Richter (n = 20)
Median PFS, months (95% CI)	NE	9 (3-14)	3 (2-8)	5 (2-NE)
Median follow-up, months (95% CI)	20 (16-20)	20 (14-25)	18 (15-19)	9 (6-12)

Panobinostat Phase II Study in Relapsed HL



Younes A,,Soreda A,, et al. JCO 2012

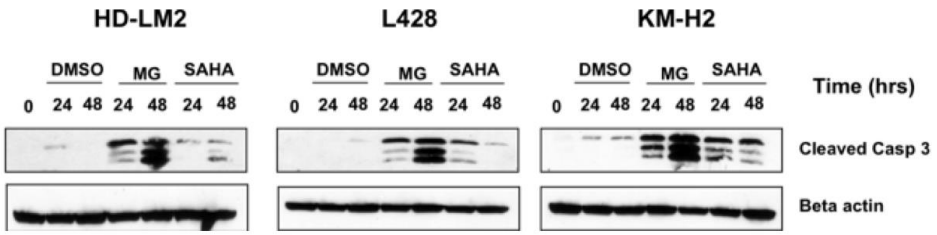
Panobinostat Downregulates PD-1 on T cells of Patients with Relapsed HL in Vivo

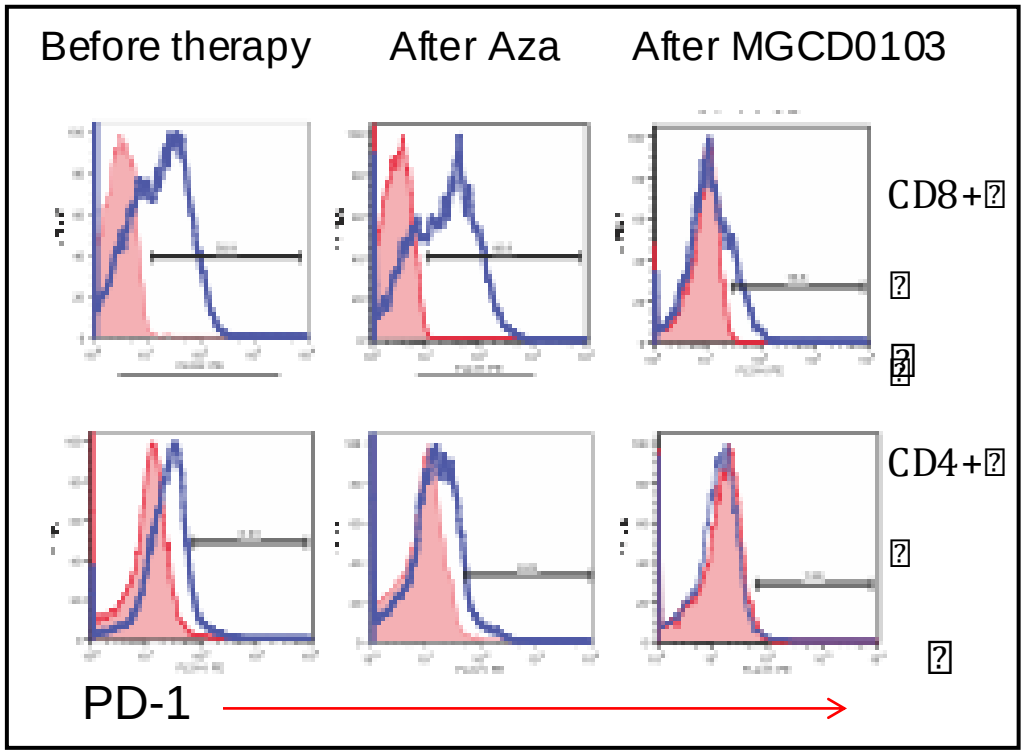


Oki Y and Younes A - Blood Cancer J. 2014 Aug; 4(8): e236.

HDAC Inhibitors in HL:

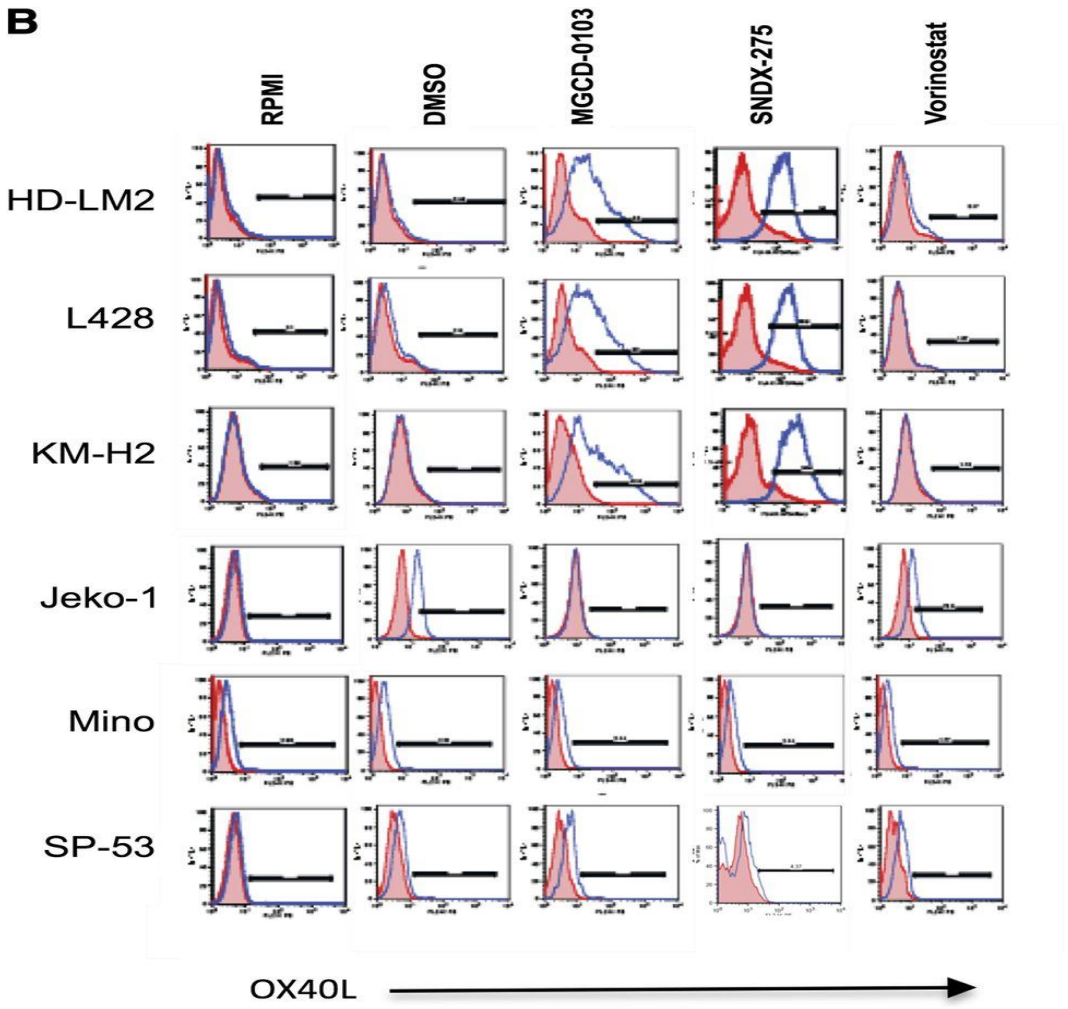
Regulation of Cell Survival and Immunity





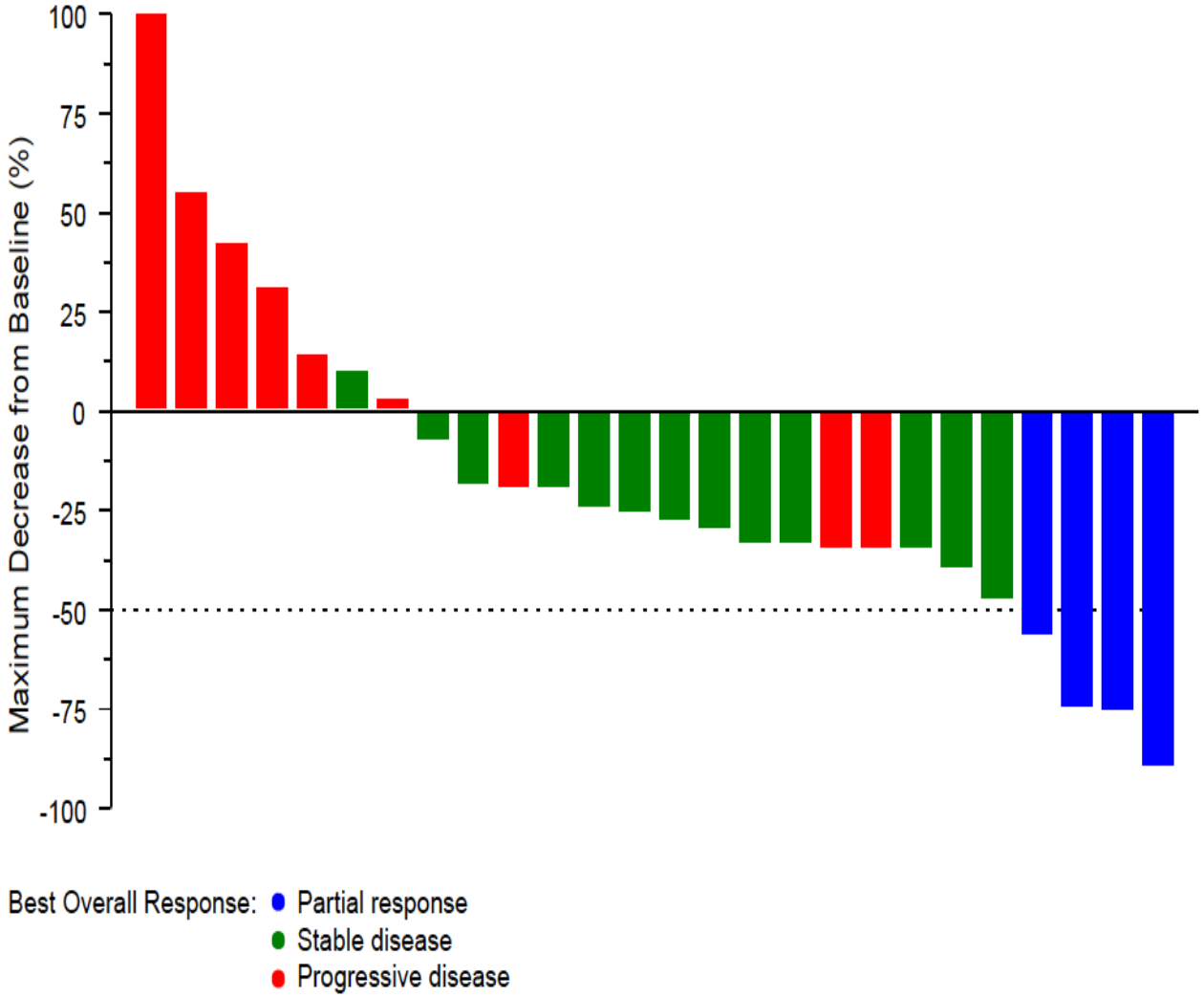
HDACi Upregulate OX40L on HRS Cells

Inhibition of T-reg function



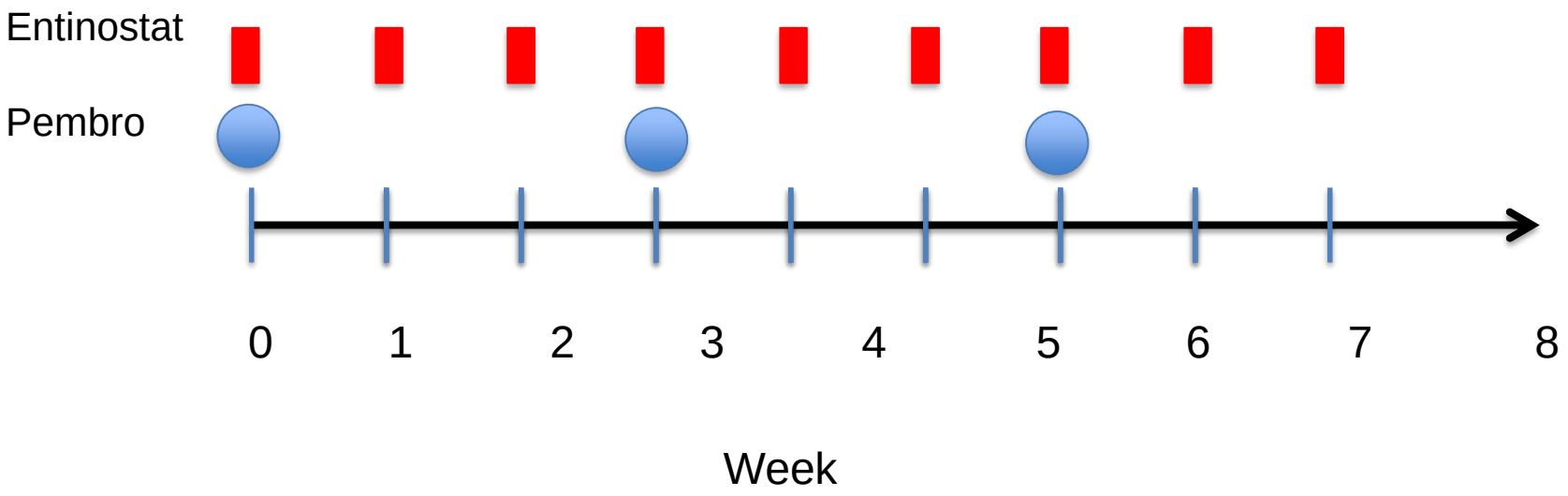
Buglio D, et al BLOOD 2011

Entinostat in Relapsed HL

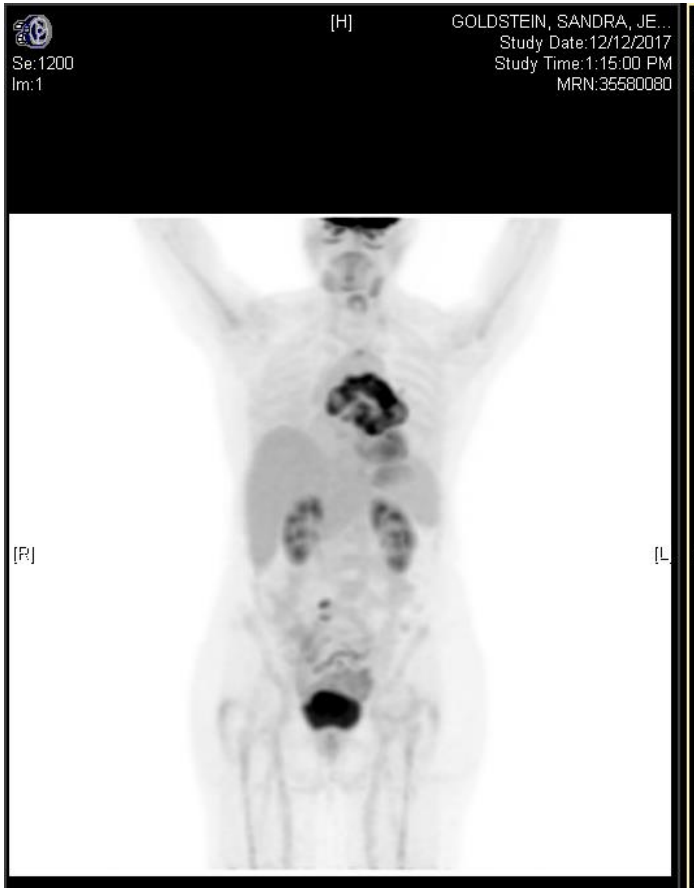
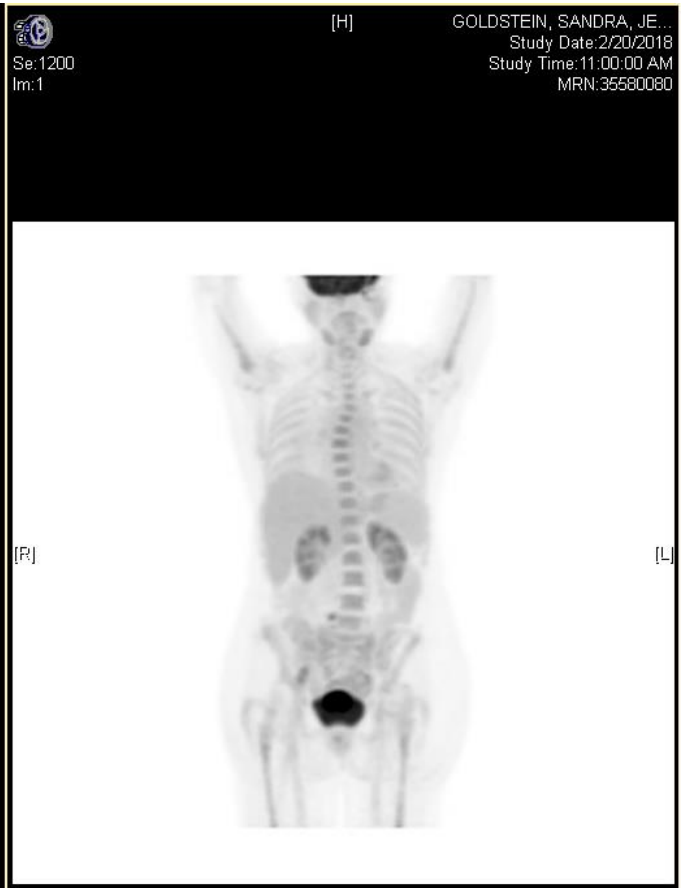


Batlevi et al, Haematologica 2017

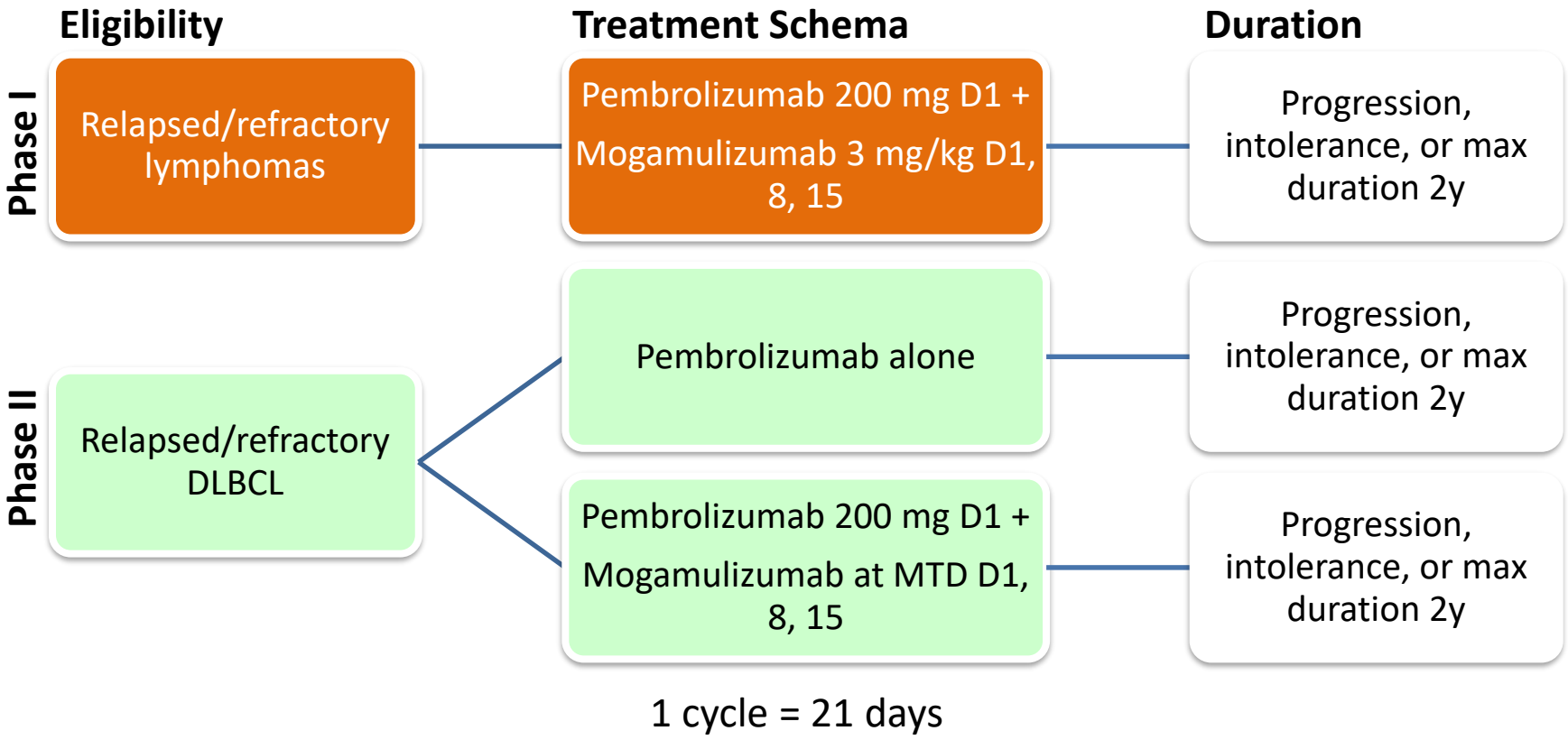
Phase I/II Study of Entinostat (HDACi) + Pembrolizumab (anti-PD1)



Phase I/II Study of Entinostat (HDACi) + Pembrolizumab (anti-PD1)

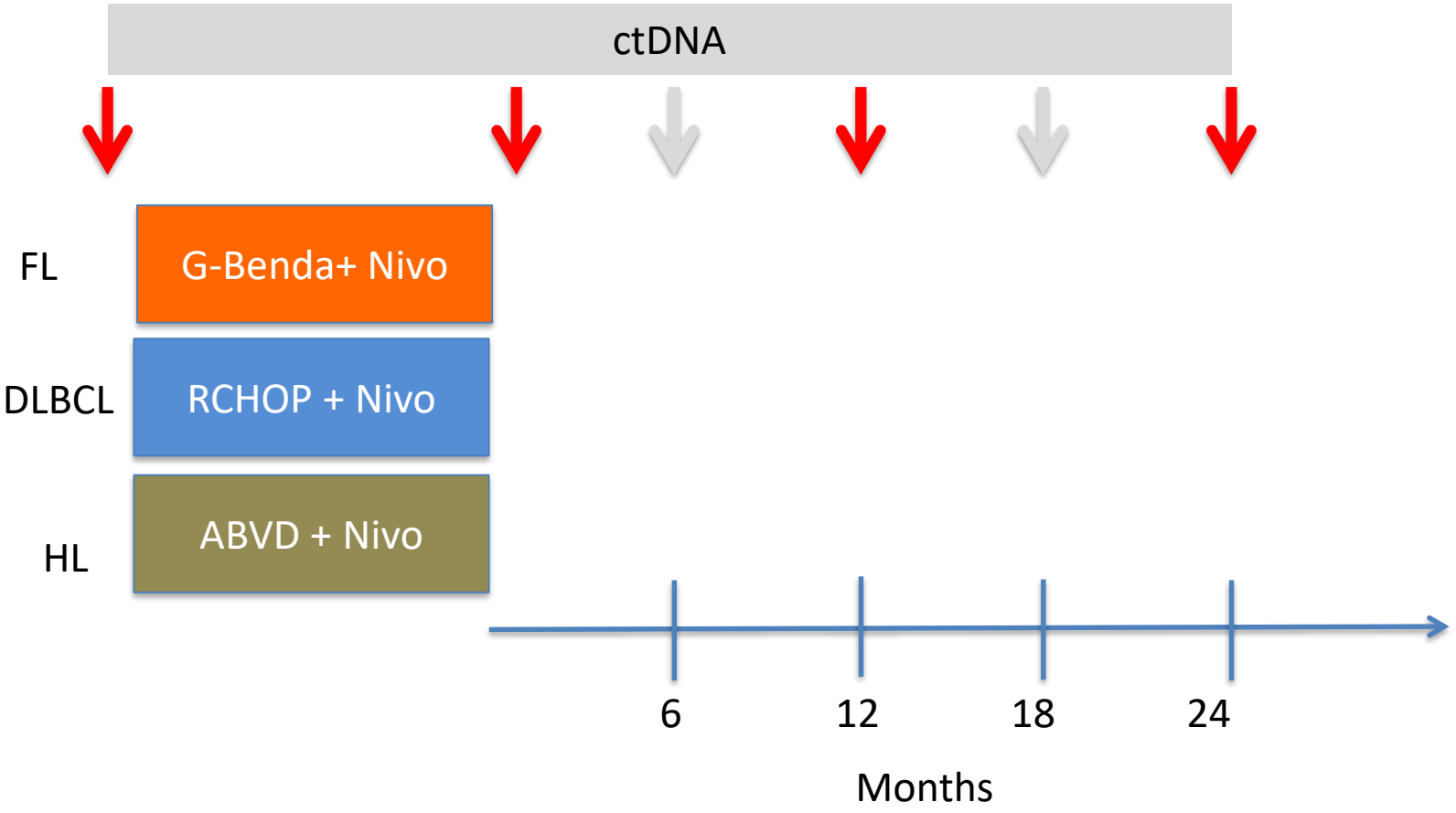
	Screening	Post C3
Sandra Goldstein		

A phase I/II of mogamulizumab (anti CCR4 antibody) and pembrolizumab in relapsed/refractory DLBCL

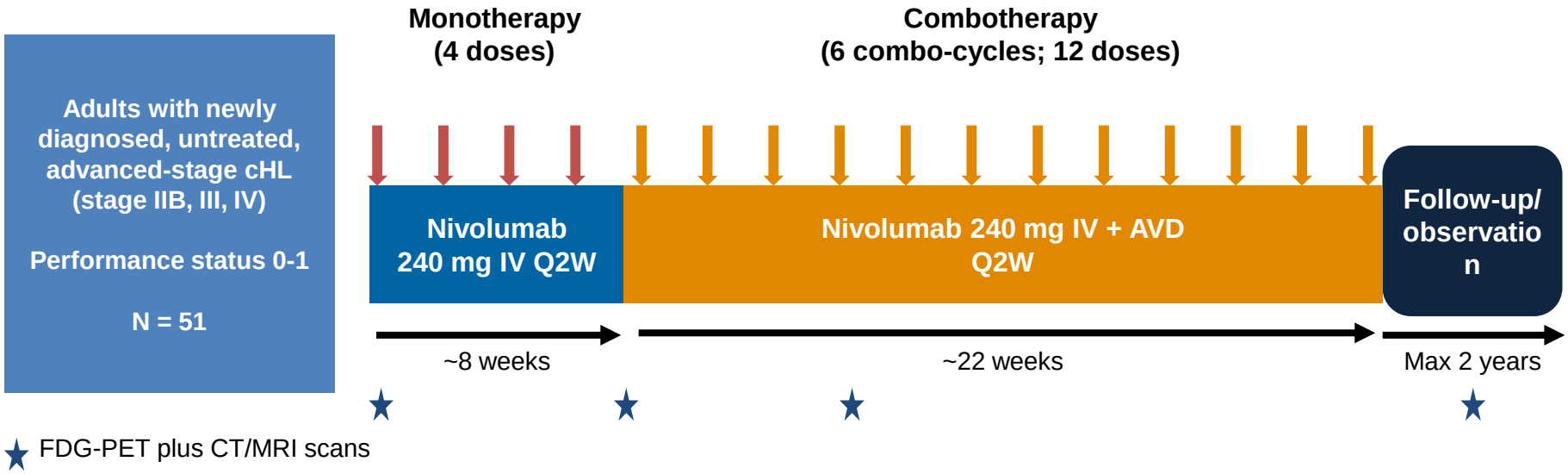


1 cycle = 21 days

Evaluating ctDNA in Curable Lymphomas (HL and DLBCL)



Phase 2 CheckMate 205 Study Design: Nivolumab in Newly Diagnosed cHL[1]



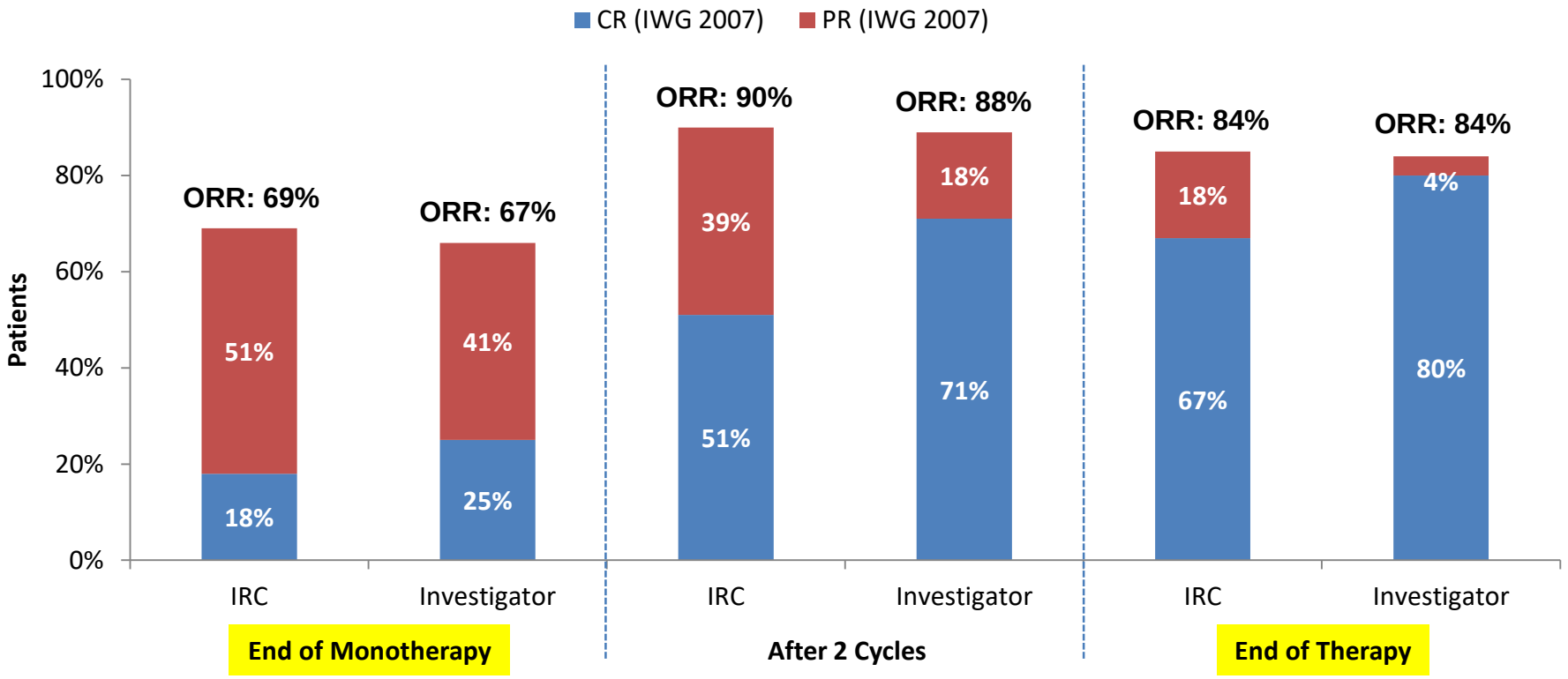
Primary Endpoint
- Safety and tolerability (Grade 3-5 TRAEs)

Additional Endpoints
- Discontinuation rate
- CR and ORR by IRC
- CR and ORR by investigator
- mPFS
- OS

Responses were assessed using the IWG 2007 criteria.
At database lock (October 2017), median duration of follow-up was 11.1 months.
Bleomycin excluded due to potential overlapping pulmonary toxicity.

1. Ramchandren R et al. *Blood*. 2017;130:Abstract 651.

Response per IRC and Investigator: ITT Population[1]



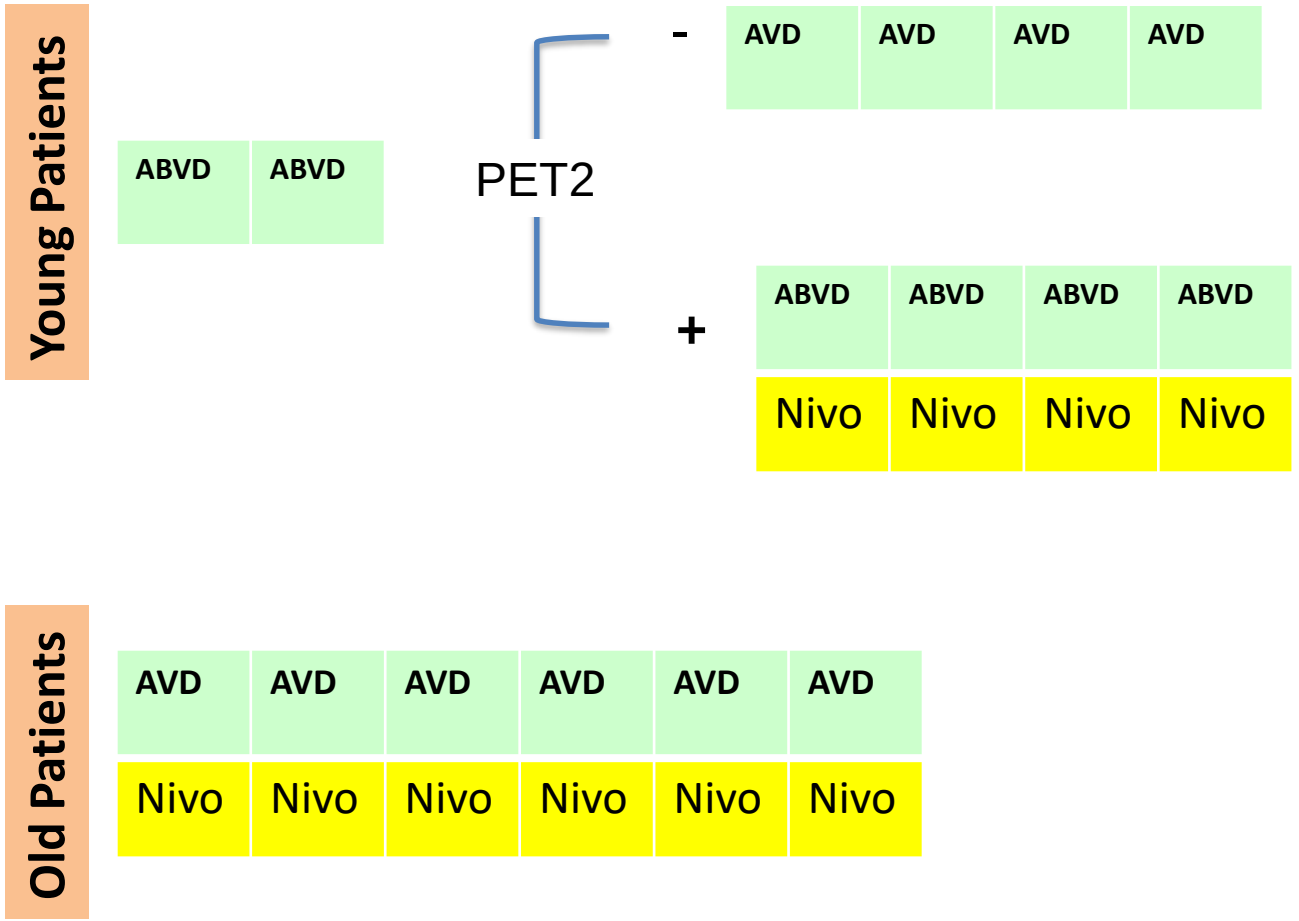
- **At end of therapy, ORR per investigator for the ITT population was 84%, with 80% of patients achieving CR**
- **Five patients were nonevaluable at end of therapy[a]**

[a] No evaluable scan in at least one on-study time point.
Biopsies were not required for patients to be considered to have progressive disease.
Values may not add together due to rounding.

1. Ramchandren R et al. *Blood*. 2017;130:Abstract 651.

MSKCC Phase I/II ABVD + Nivolumab in Advanced Stage HL

PI: A. Moskowitz



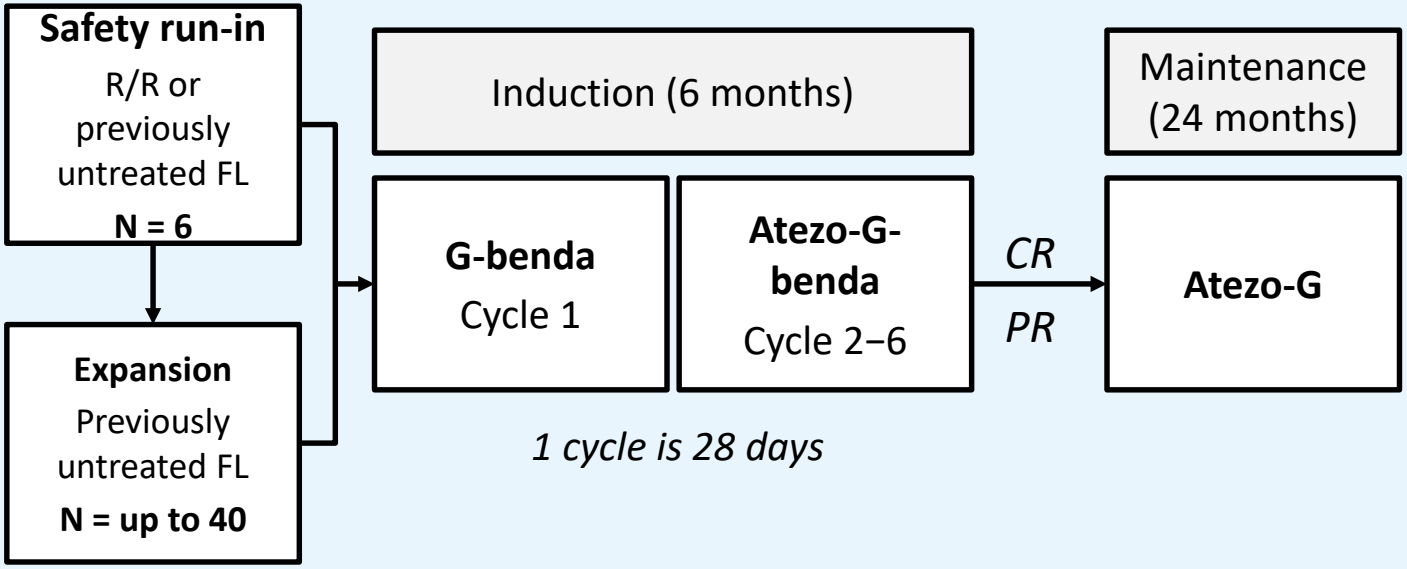
Safety and efficacy of atezolizumab in combination with obinutuzumab and bendamustine in patients with previously untreated follicular lymphoma (FL): primary analysis

Anas Younes,[1] John M Burke,[2] Catherine Diefenbach,[3] Silvia Ferrari,[4] Cyrus Khan,[5] Jeff Sharman,[6] Monica Tani,[7] Chaitra Ujjani,[8] Umberto Vitolo,[9] Sam Yuen,[10] Melissa Kuhn,[11] Mikkel Z Oestergaard,[12] Kirsten Mundt,[12] Günter Fingerle-Rowson,[12] Surya Chitra,[12] Gila Sellam,[12] Rodica Morariu-Zamfir,[12] Michael Gilbertson[13]

[1]Memorial Sloan Kettering Cancer Center, New York City, NY, USA; [2]US Oncology Research, The Woodlands, TX, USA; [3]NYU Langone Medical Center, New York City, NY, USA; [4]Azienda Ospedaliera Papa Giovanni XXIII, Bergamo, Italy; [5]Allegheny Health Network Cancer Institute, Pittsburgh, PA, USA; [6]Willamette Valley Cancer Institute, Eugene, OR, USA; [7]Ospedale Santa Maria delle Croci, Ravenna, Italy; [8]Georgetown University Medical Center, Washington, DC, USA; [9]Azienda Ospedaliera Universitaria Città della Salute e della Scienza di Torino, Turin, Italy; [10]Calvary Mater Newcastle Hospital, Newcastle, NSW, Australia; [11]Genentech Inc, South San Francisco, CA, USA; [12]F. Hoffmann-La Roche Ltd, Basel, Switzerland; [13]Monash Health, Melbourne, VIC, Australia

Atezolizumab +obinutuzumab + bendamustine in previously untreated FL

Open-label, single-arm Phase Ib/II study in FL patients (NCT02596971)



Primary endpoints

- CR at EOI by PET-CT (IRC, modified Lugano 2014[1])
- Safety profile

Secondary endpoints

- CR at EOI (INV, modified Lugano 2014[1])
- CR at EOI (IRC and INV, Cheson 2007[2])
- ORR at EOI (IRC and INV, modified Lugano 2014[1] and Cheson 2007[2])
- DoR and PFS by INV
- Molecular response

1. Cheson D, et al. J Clin Oncol 2014;32:3059–68
2. Cheson D, et al. J Clin Oncol 2007;5:579–86

End-of-induction (EOI) response rates in 1L FL (N=40)

n (%)	Modified Lugano 2014[1]		Cheson 2007[2]	
	IRC	INV	IRC	INV
ORR	**34 (85)**	**38 (95)**	**36 (90)**	**38 (95)**
CR	**30 (75)**	**34 (85)**	**30 (75)**	**32 (80)**
PR	4 (10)	4 (10)	6 (15)	6 (15)
SD	4 (10)	0	2 (5)	0
PD	0	0	0	0
Not evaluable*	2 (5)	2 (5)	2 (5)	2 (5)

Modified Lugano 2014

- The designation of a PR requires PR criteria by PET and CR or PR by CT scan
- If BM involvement at baseline, CR must be confirmed with a negative BM at EOI

1. Cheson D, et al. J Clin Oncol 2014;32:3059–68
2. Cheson D, et al. J Clin Oncol 2007;5:579–86

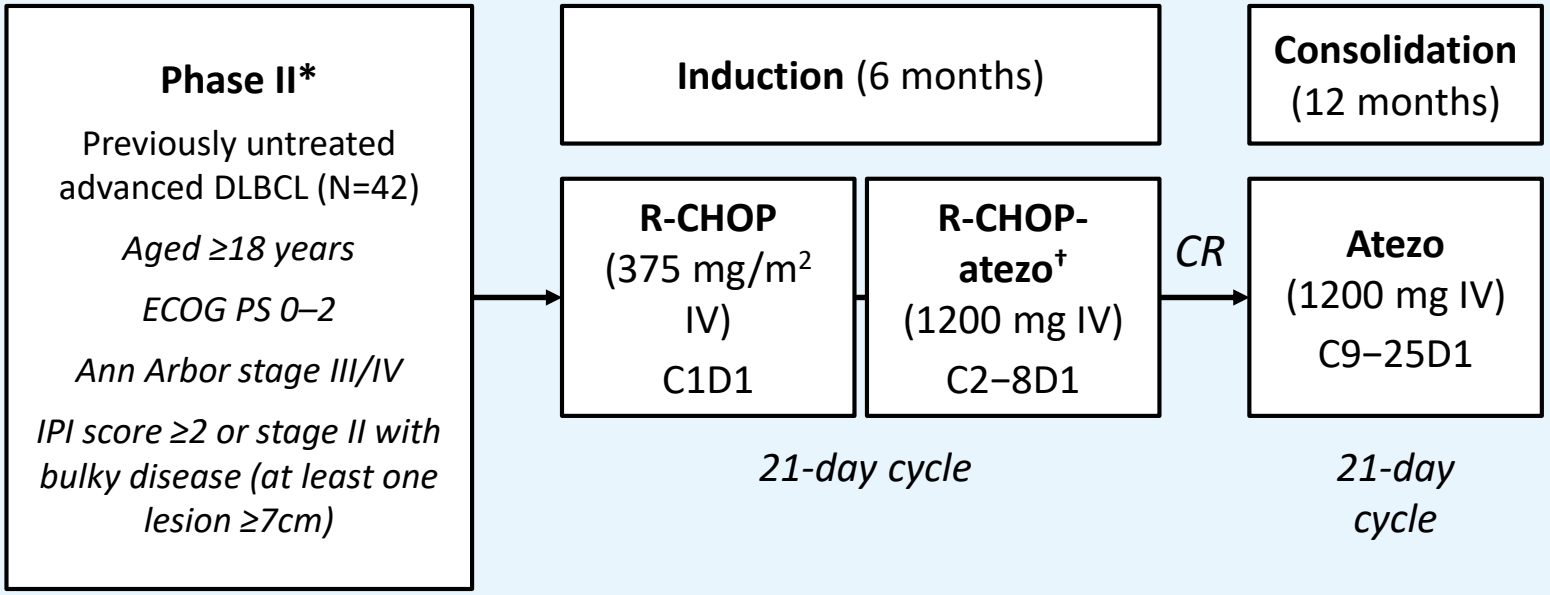
Atezolizumab plus R-CHOP shows encouraging activity and acceptable toxicity in previously untreated patients with diffuse large B-cell lymphoma (DLBCL): an interim analysis of a phase I/II study

Anas Younes,[1] John M Burke,[2] Catherine Diefenbach,[3] Silvia Ferrari,[4] Uwe Hahn,[5] Eliza Hawkes,[6] Cyrus Khan,[7] Izidore S Lossos,[8] Gerardo Musuraka,[9] Monica Tani,[10] Chaitra Ujjani,[11] Umberto Vitolo,[12] Sam Yuen,[13] Surya Chitra,[14] Kartik Krishnan,[14] Mikkel Z Oestergaard,[15] Michael Wenger,[15] Gila Sellam,[15] Rodica Morariu-Zamfir,[15] Jeff Sharman[2,16]

[1]Memorial Sloan Kettering Cancer Center, New York City, NY, USA; [2]US Oncology Research, The Woodlands, TX, USA; [3]Perlmutter Cancer Center at NYU Langone Health, New York City, NY, USA; [4]Azienda Ospedaliera Papa Giovanni XXIII, Bergamo, Italy; [5]The Queen Elizabeth Hospital, Adelaide, SA, Australia; [6]Olivia Newton-John Cancer Centre, Austin Hospital, Melbourne, VIC, Australia; [7]Allegheny Health Network Cancer Institute, Pittsburgh, PA, USA; [8]Sylvester Comprehensive Cancer Center, University of Miami, Miami, FL, USA; [9]Istituto Scientifico Romagnolo Per Lo Studio e La Cura Dei Tumori, Meldola, Italy; [10]Ospedale Santa Maria delle Croci, Ravenna, Italy; [11]The Seattle Cancer Care Alliance, Seattle, WA, USA; [12]Azienda Ospedaliera Universitaria Città della Salute e della Scienza di Torino, Turin, Italy; [13]Calvary Mater Newcastle Hospital, Newcastle, NSW, Australia; [14]Genentech Inc, South San Francisco, CA, USA; [15]F. Hoffmann-La Roche Ltd, Basel, Switzerland; [16]Willamette Valley Cancer Institute, Eugene, OR, USA

Study design

Open-label, single-arm Phase Ib/II study in DLBCL pts (NCT02596971)



*Phase II preceded by safety run-in phase (atezo-G-benda/G-CHOP in FL [n=12])

†R for C1–8, atezo for C2–8 on D1, and 6 or 8 cycles of CHOP (D1: cyclophosphamide 750 mg/m^2 IV, doxorubicin 50 mg/m^2 IV, vincristine 1.4 mg/m^2 [max. 2 mg] IV; D1–5: prednisone 40 mg/m^2 PO) as determined by the investigator

End-of-induction response rates
Interim analysis efficacy-evaluable population (N=15)

	Modified Lugano 2014[1]		*Cheson 2007[2]*	
N (%)	*IRC*	*INV*	*IRC*	*INV*
ORR	**13 (87)**	**13 (87)**	**13 (87)**	**13 (87)**
CR	**13 (87)**	**13 (87)**	**11 (73)**	**11 (73)**
PR	–	–	2 (13)	2 (13)
PD	2 (13)	2 (13)	2 (13)	2 (13)

Modified Lugano 2014

- Designation of PR requires PR by PET, and CR/PR by CT
- If BM involvement at baseline, CR must be confirmed by negative BM at end of induction

1. Cheson D, et al. J Clin Oncol 2014;32:3059–68
2. Cheson D, et al. J Clin Oncol 2007;5:579–86

Conclusions

- Antibodies targeting PD1 demonstrated significant clinical activity in HL and PMBL leading to regulatory approval
- Anti PD1/PDL1 antibodies have modest single agent activity in the majority of NHL subtypes => Combination strategies
- The role of immune checkpoint inhibitors in eradicating MRD/ctDNA in HL and NHL is being investigated