Immunoterapia nel Mieloma Multiplo e nel Linfoma di Hodgkin

MILANO
9 Novembre 2017

LINFOMA DI HODGKIN:
RUOLO DEI CHECKPOINT INHIBITORS

Armando Santoro

HUMANITAS
CANCER CENTER

HUMANITAS
UNIVERSITY

CANCER IMMUNOTHERAPY TODAY

TUMORS RESPONSIVE TO ANTI-PD1 OR ANTI-PD-L1 THERAPY

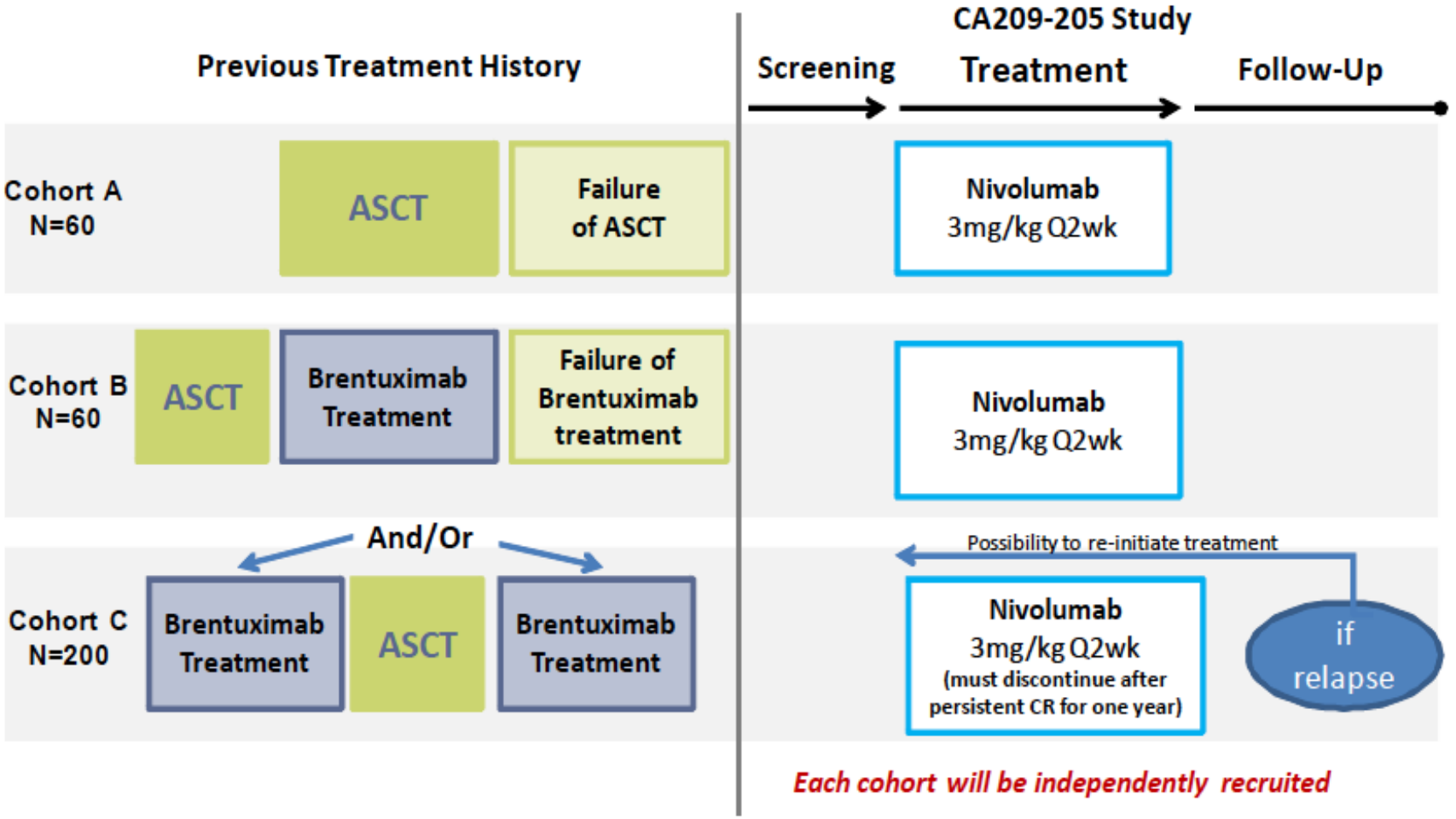
- **MELANOMA**
- **RCC**
- **NSCLC**
- **UROTHELIAL CANCER**
- **HEAD AND NECK CANCER**
- **MERKEL CELL CARCINOMA**
- **MSI**

FDA

EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

CHECKMATE-205 : PHASE 2 STUDY WITH NIVOLUMAB IN R/R HL

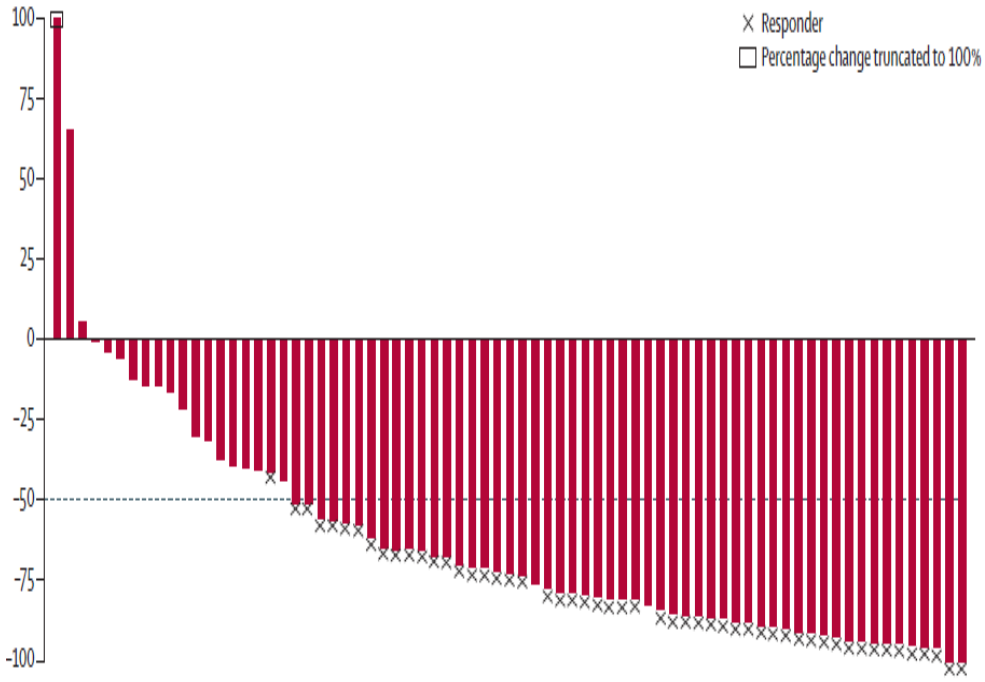
Study Design



CHECKMATE 205: PHASE II STUDY IN cHL- *Cohort B*

Nivolumab for classical Hodgkin's lymphoma after failure of both autologous stem-cell transplantation and brentuximab vedotin: a multicentre, multicohort, single-arm phase 2 trial

Anas Younes, Armando Santoro, Margaret Shipp, Pier Luigi Zinzani, John M Timmerman, Stephen Ansell, Philippe Armand, Michelle Fanale, Voravit Ratanatharathorn, John Kuruvilla, Jonathon B Cohen, Graham Collins, Kerry J Savage, Marek Trneny, Kazunobu Kato, Benedetto Farsaci, Susan M Parker, Scott Rodig, Margaretha G M Roemer, Azra H Ligon, Andreas Engert



COHORT B

NIVO IN

ASCT+BV

(60 PTS)

EFFICACY

OBJECTIVE RESPONSE: 66.3%,

CR 9%,

PR 58%

MEDIAN DOR: 7.8 MS

Lancet Oncol 2016; 17: 1283-94

CHECKMATE 205: PHASE II STUDY IN cHL- *Cohort B*

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COHORT B

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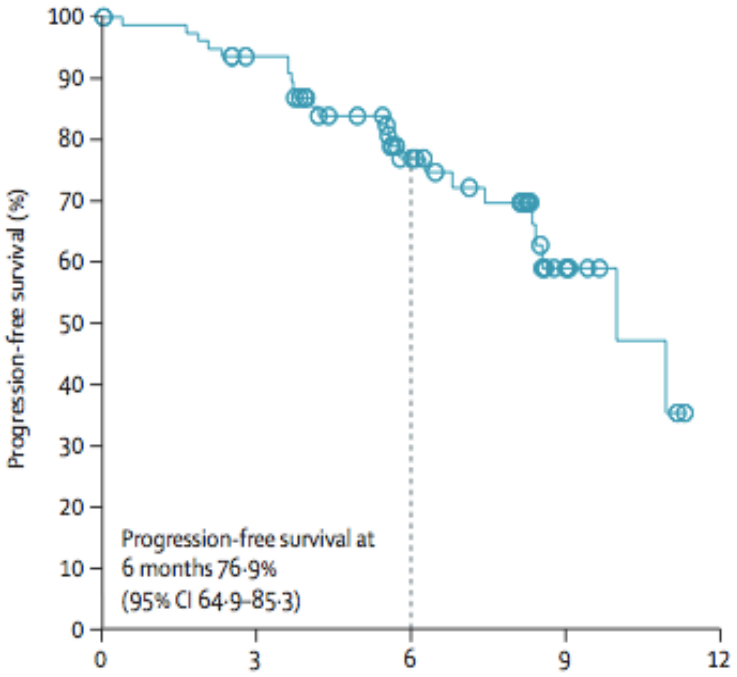
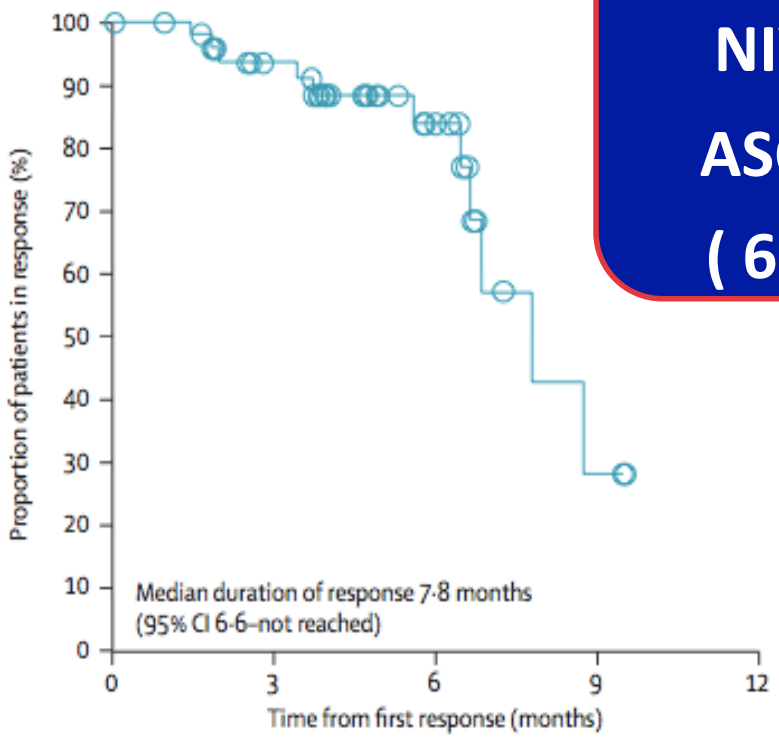




Lancet Oncol 2016; 17: 1283-94

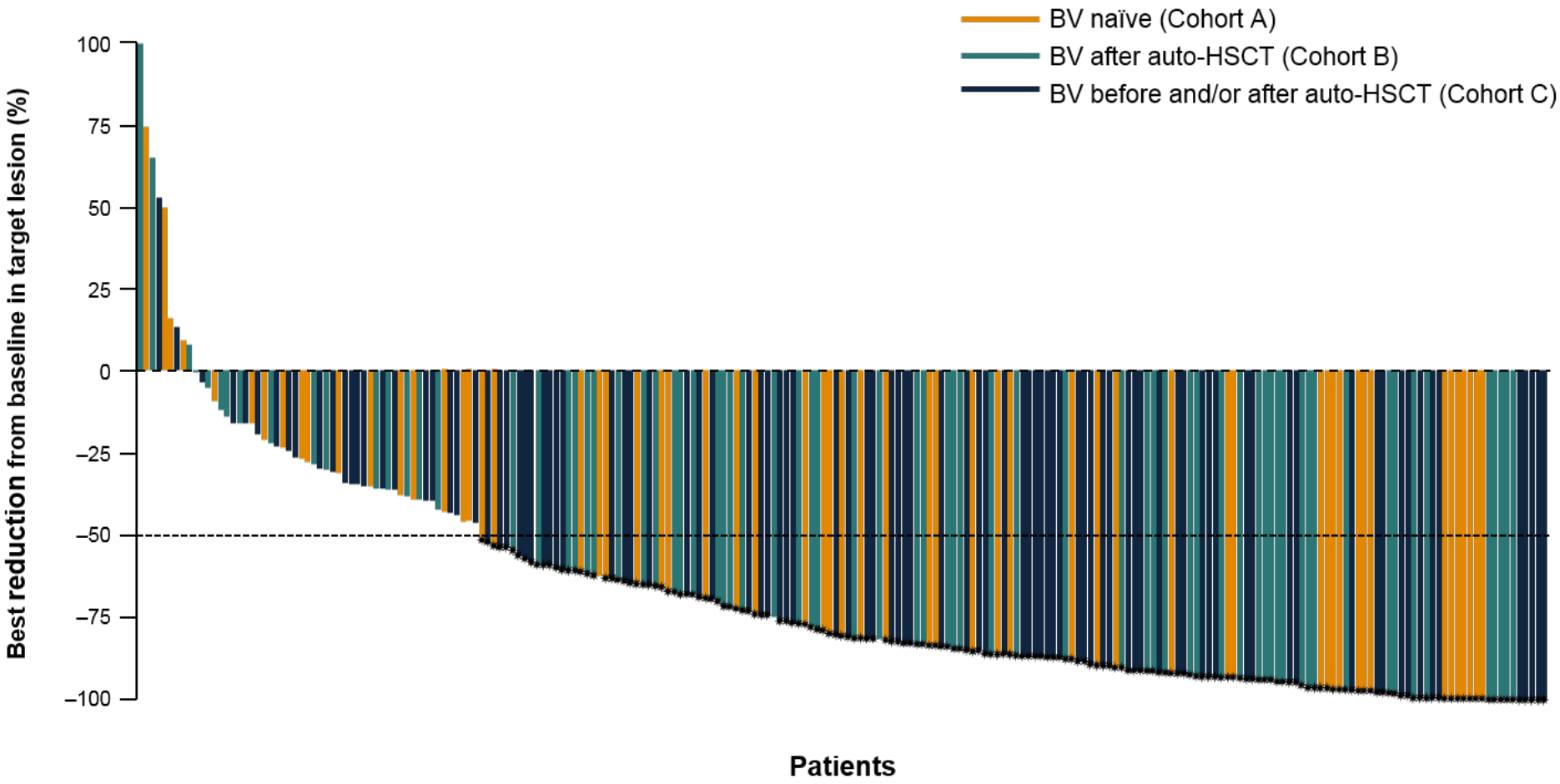
Nivolumab for Relapsed/Refractory Classical Hodgkin Lymphoma After Autologous Transplant: Full Results After Extended Follow-Up of the Phase 2 CheckMate 205 Trial

Michelle Fanale,[1] Andreas Engert,[2] Anas Younes,[3] Philippe Armand,[4] Stephen Ansell,[5] Pier Luigi Zinzani,[6] John M Timmerman,[7] Graham P Collins,[8] Radhakrishnan Ramchandren,[9] Jonathon B Cohen,[10] Jan Paul De Boer,[11] John Kuruvilla,[12] Kerry J Savage,[13] Marek Trneny,[14] Scott Rodig,[15] Margaret Shipp,[4] Kazunobu Kato,[16] Anne Sumbul,[16] Benedetto Farsaci,[16] Armando Santoro[17]

[1]University of Texas MD Anderson Cancer Center, Houston, TX, USA; [2]University Hospital of Cologne, Cologne, Germany; [3]Memorial Sloan Kettering Cancer Center, New York, NY, USA; [4]Dana-Farber Cancer Institute, Boston, MA, USA; [5]Mayo Clinic, Rochester, MN, USA; [6]Institute of Hematology "L. e A. Seràgnoli", University of Bologna, Bologna, Italy; [7]University of California, Los Angeles, CA, USA; [8]Oxford Cancer and Haematology Centre, Churchill Hospital, Oxford, UK; [9]Barbara Ann Karmanos Cancer Institute, Detroit, MI, USA; [10]Winship Cancer Institute, Emory University, Atlanta, GA, USA; [11]Netherlands Cancer Institute – Antoni van Leeuwenhoek Hospital, Amsterdam, The Netherlands, on behalf of Lunenburg Lymphoma Phase I/II Consortium (LLPC); [12]University of Toronto and Princess Margaret Cancer Centre, Toronto, ON, Canada; [13]British Columbia Cancer Agency, Vancouver, BC, Canada; [14]Charles University in Prague and General University Hospital in Prague, Prague, Czech Republic; [15]Brigham and Women's Hospital, Boston, MA, USA; [16]Bristol-Myers Squibb, Princeton, NJ, USA; [17]Humanitas Cancer Center – Humanitas University, Rozzano–Milan, Italy

Presented at the 14th International Conference on Malignant Lymphoma (ICML); Lugano, Switzerland; June 14–17, 2017

Change in Target Lesion per IRC



>95% of evaluable patients showed a reduction in tumor burden

Asterisks (*) denote responders

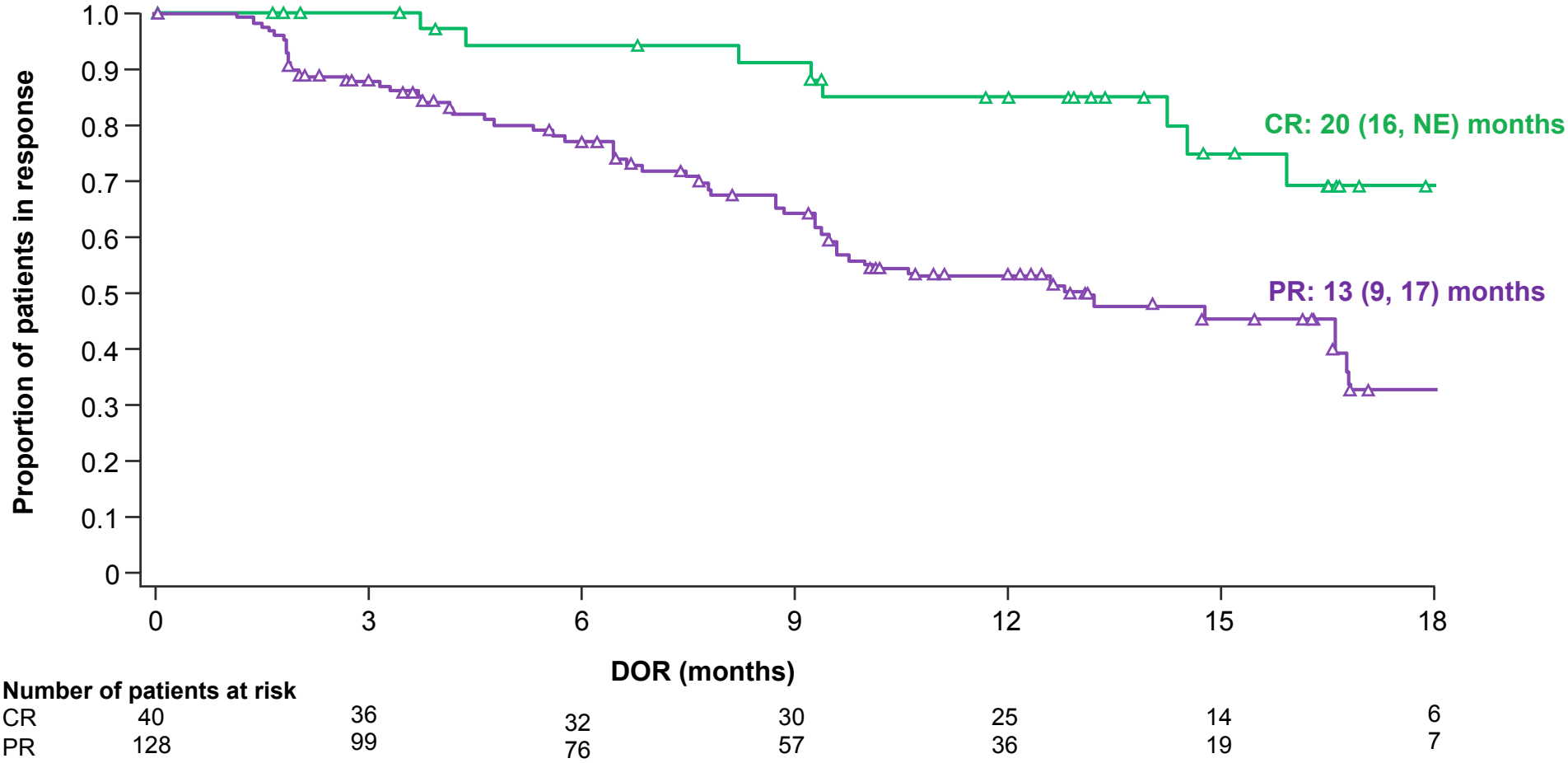
Best Overall Response After Extended Follow-Up

	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.

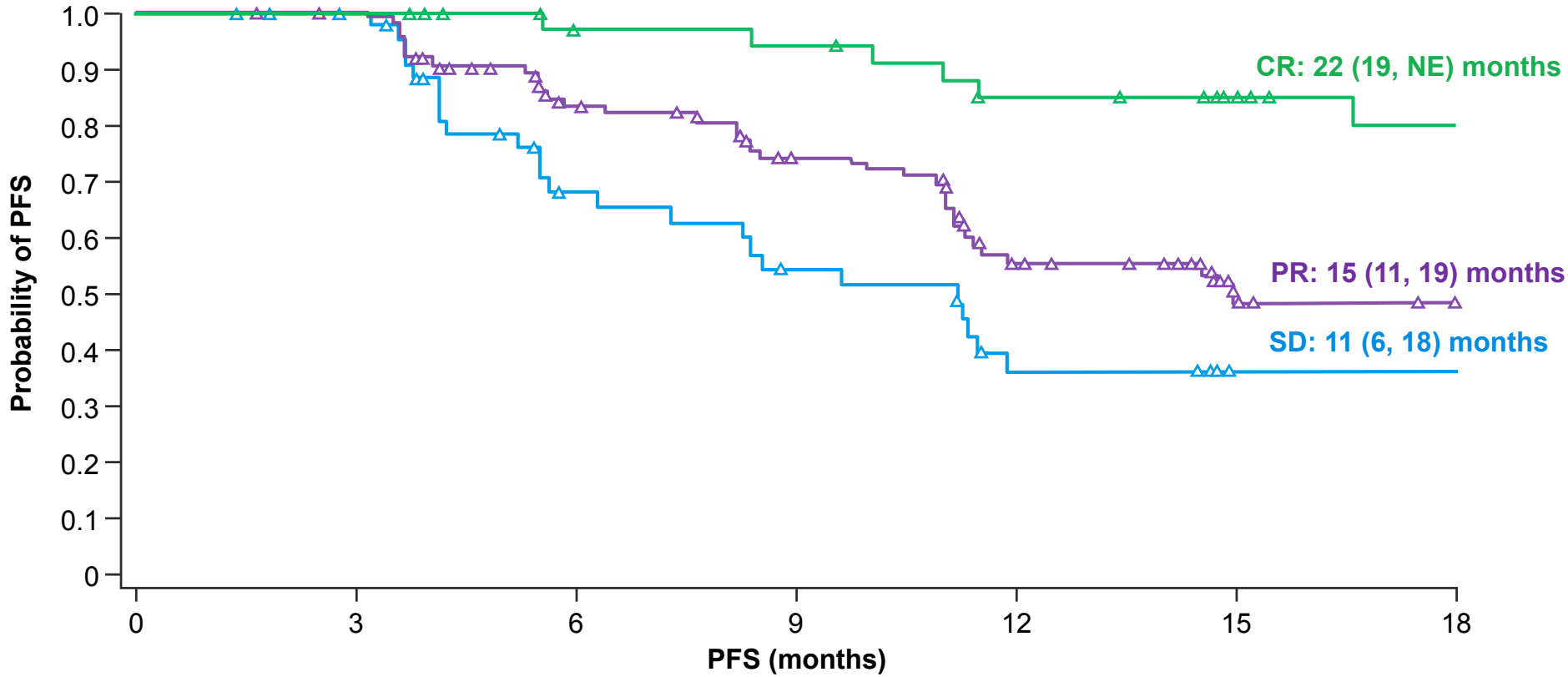
Duration of Response by Best Overall Response



DOR by cohort	Cohort A n = 63	Cohort B n = 80	Cohort C n = 100	Overall N = 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); NE = not evaluable

Progression-Free Survival by Best Overall Response



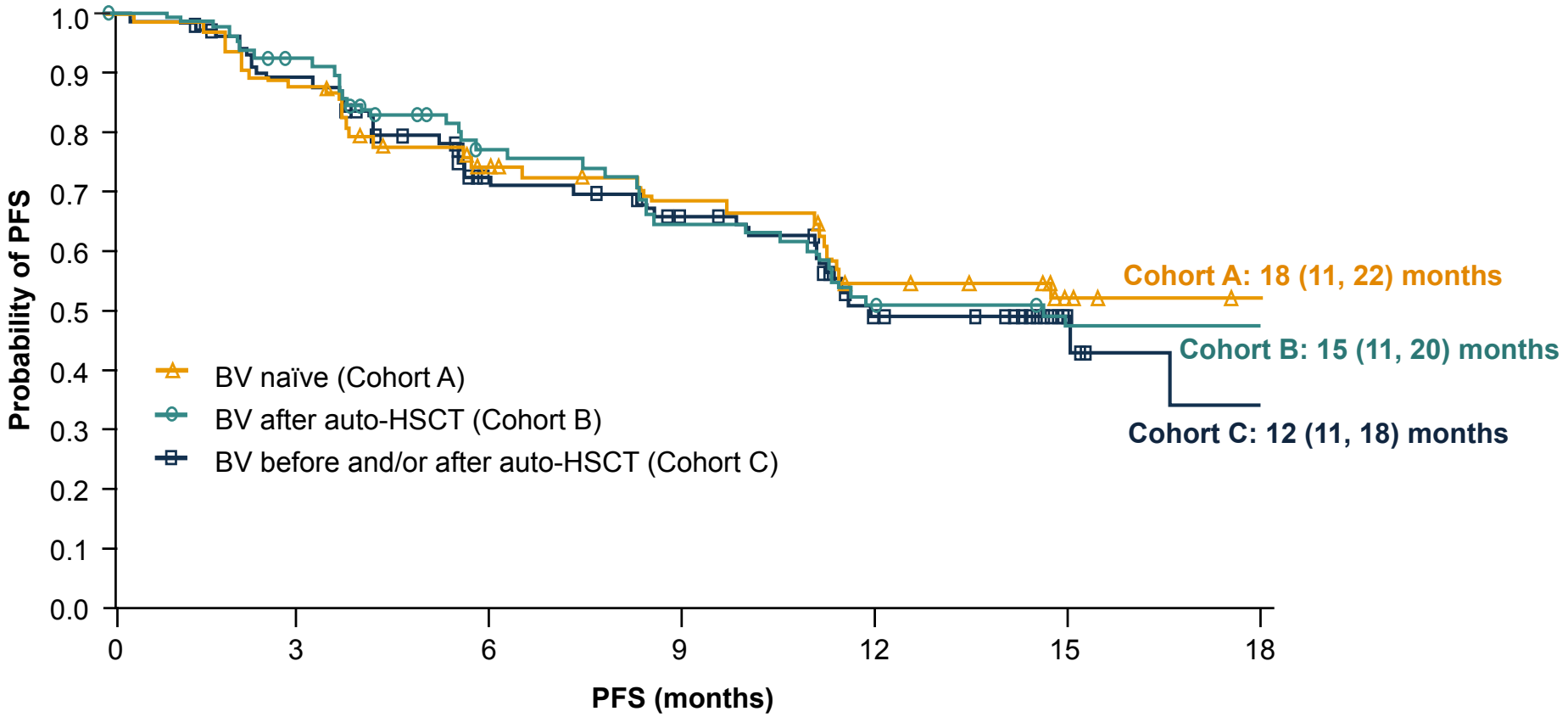
Number of patients at risk

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

- Median PFS for all 243 patients was 15 (11–19) months

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

Progression-Free Survival by Cohort

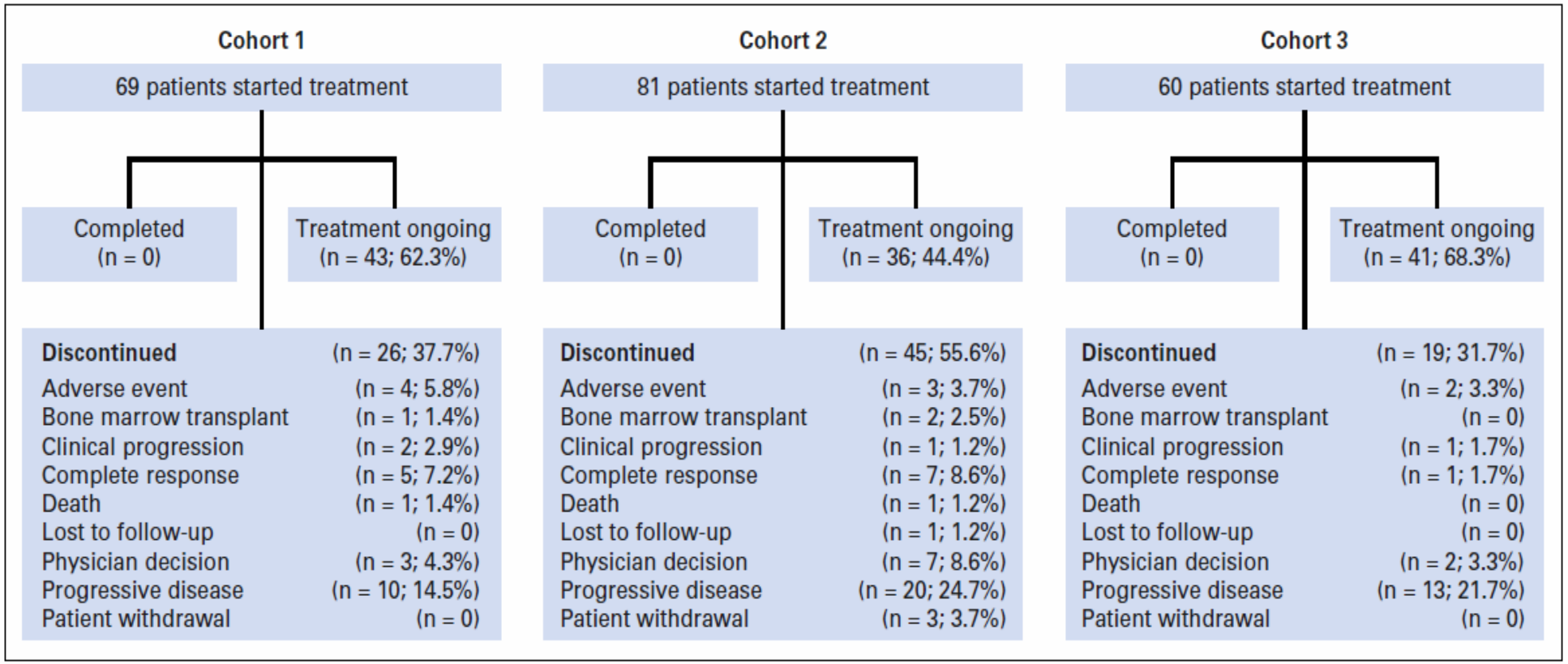


Number of patients at risk

Cohort A	63	56	41	36	26	18	14
Cohort B	80	70	50	42	33	27	27
Cohort C	100	85	56	44	25	8	4

All values are medians (95% CI)

KEYNOTE-087 : PHASE 2 STUDY WITH PEMBROLIZUMAB IN R/R HL



Cohort 1

ASCT and subsequent BV

Cohort 2

Salvage chemotherapy and BV (ineligible for ASCT)

Cohort 3

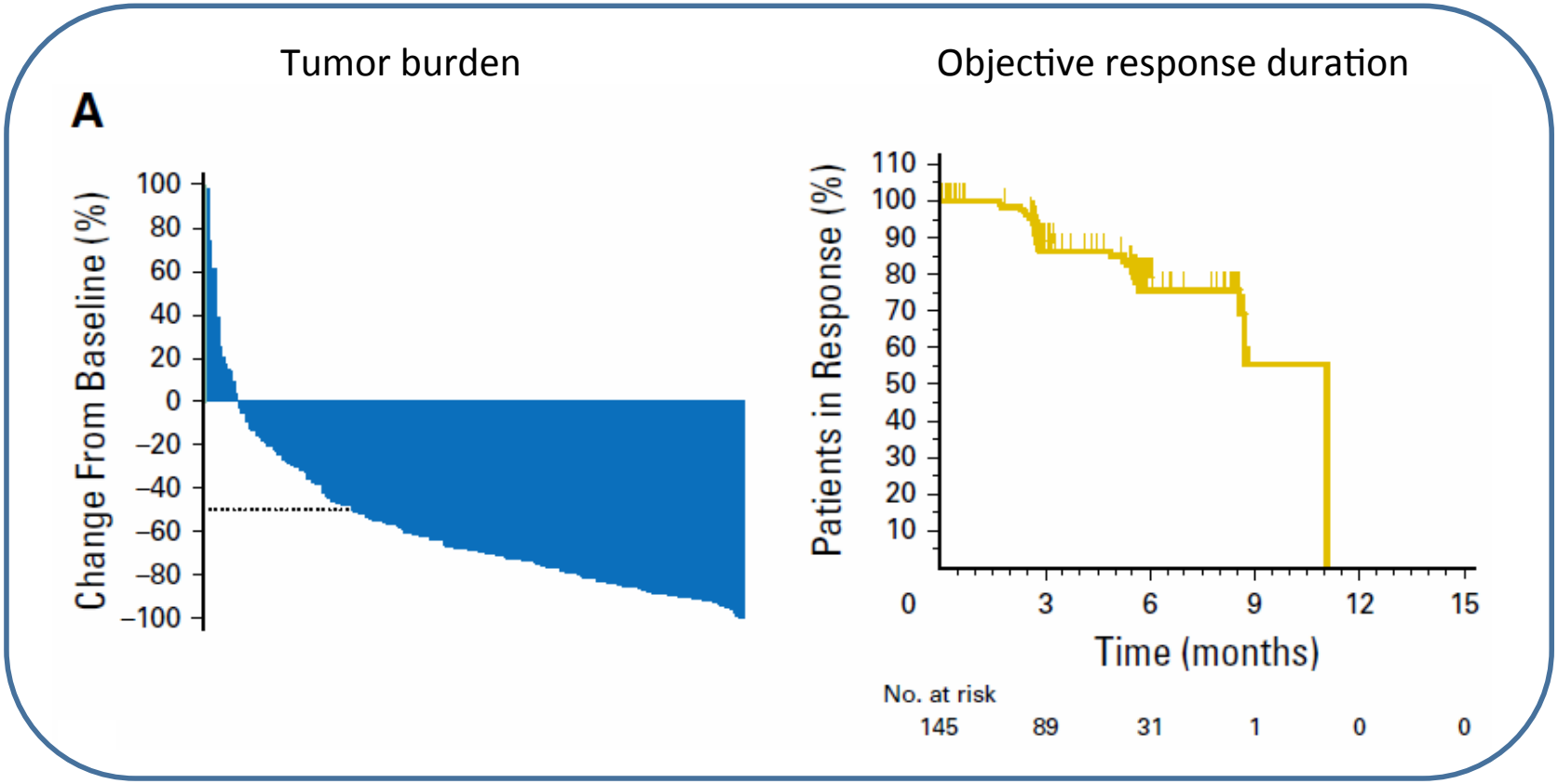
ASCT but not BV

Chen et al., Journal of Clinical Oncology 25 April 2017

KEYNOTE-087 : PHASE 2 STUDY WITH PEMBROLIZUMAB IN R/R HL

Decrease from baseline in tumor burden (left) and Kaplan-Meier estimates of objective response duration (right) on the basis of central review in patients with response.

All cohorts



Chen et al., Journal of Clinical Oncology 25 April 2017

RUOLO DEL TRAPIANTO

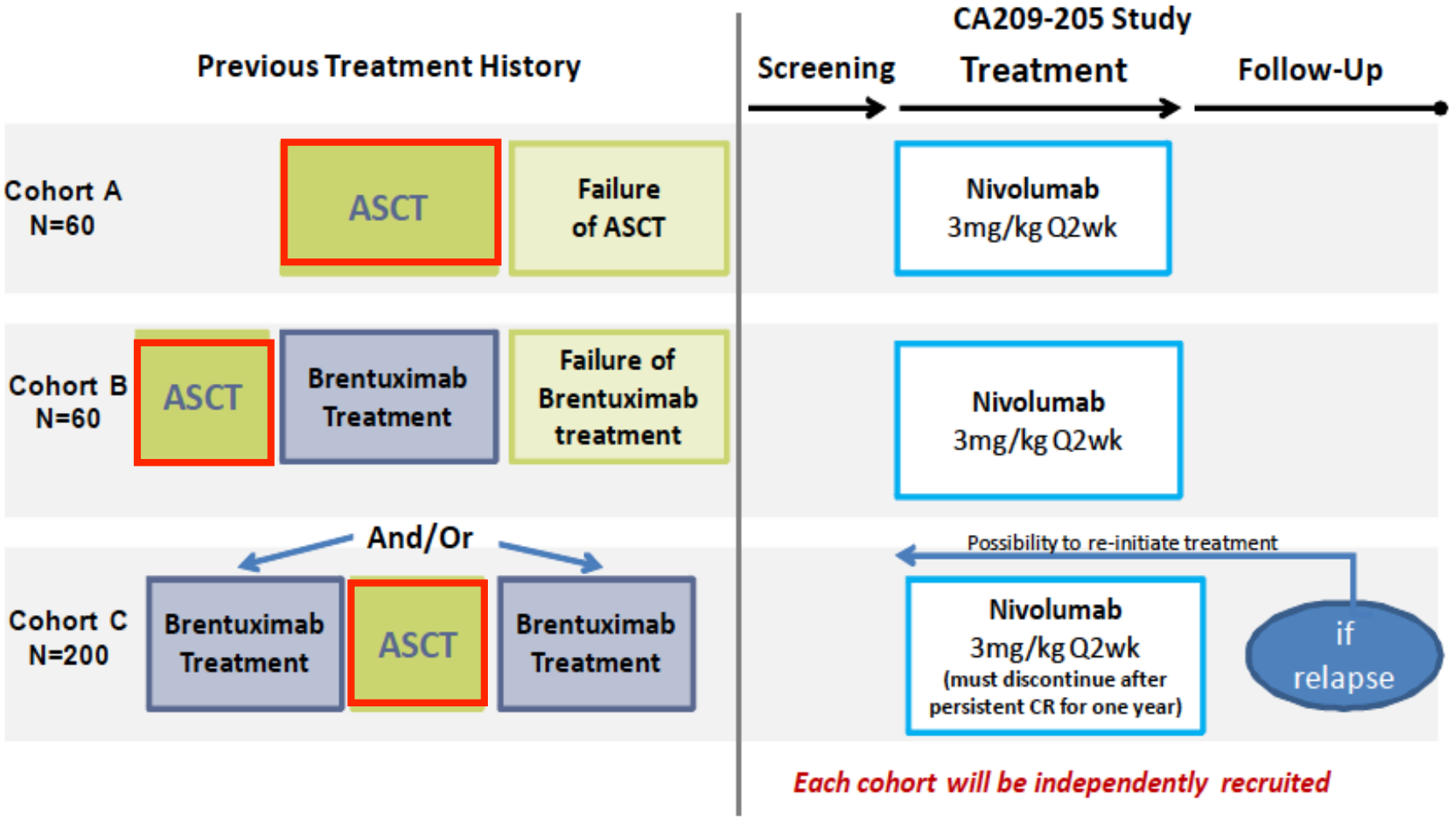
CONSOLIDARE LA RISPOSTA CON IL TRAPIANTO ?

AUTOLOGO?

ALLOGENICO?

CHECKMATE-205 : PHASE 2 STUDY WITH NIVOLUMAB IN R/R HL

Study Design



NIVOLUMAB IN HODGKIN'S LYMPHOMA

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News

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FDA Approves Nivolumab for Hodgkin Lymphoma

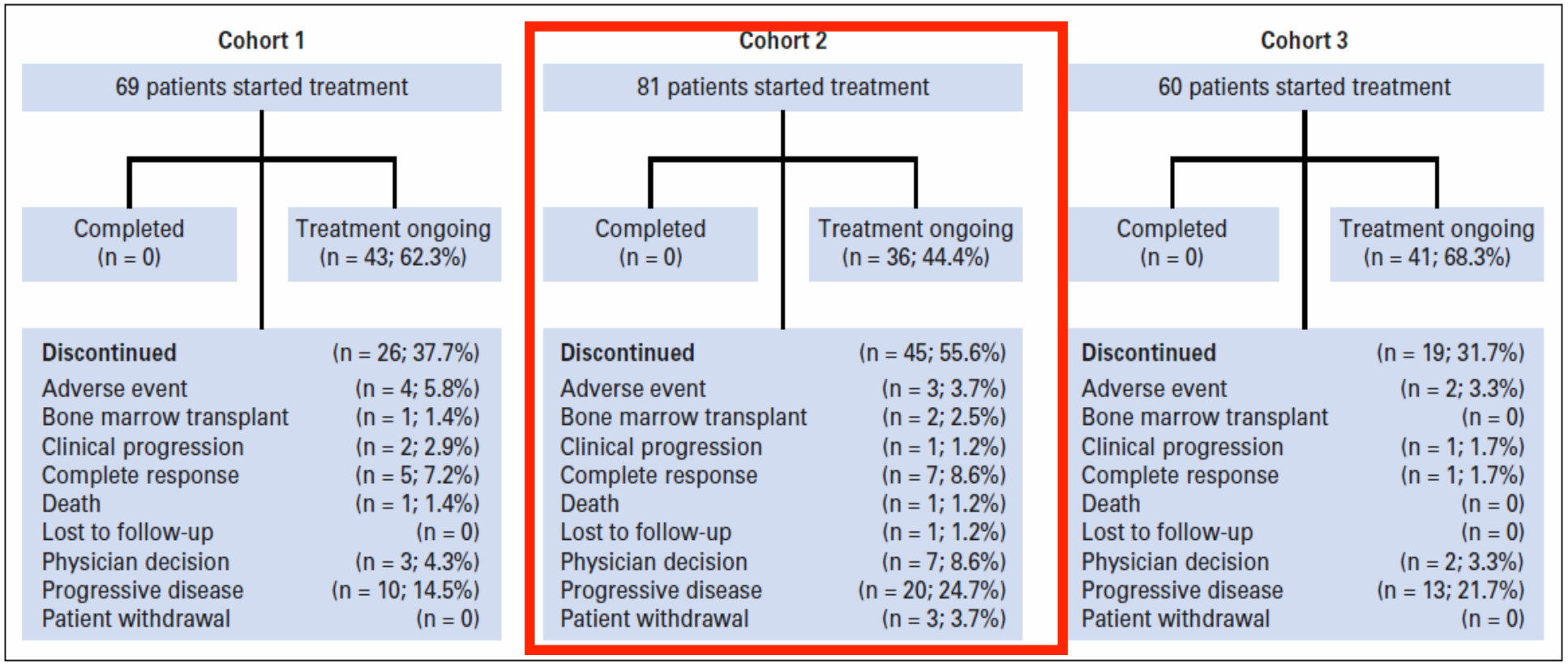
The FDA granted nivolumab (Opdivo) ac
(cHL) that has relapsed or progressed af
posttransplantation brentuximab vedotin

The approval was based on an objective
(Trial 8 and Trial 9) of nivolumab in patie
approved for a hematologic malignancy.

Trials 8 and 9 both included patients with cHL after failure of autologous HSCT and post
status. Nivolumab was administered at 3 mg/kg IV over 60 minutes every 2 weeks until

OncLive.com

KEYNOTE-087 : PHASE 2 STUDY WITH *PEMBROLIZUMAB* IN R/R HL



Cohort 1	Cohort 2	Cohort 3
69 patients started treatment	81 patients started treatment	60 patients started treatment
Completed (n = 0)	Completed (n = 0)	Completed (n = 0)
Treatment ongoing (n = 43; 62.3%)	Treatment ongoing (n = 36; 44.4%)	Treatment ongoing (n = 41; 68.3%)
Discontinued (n = 26; 37.7%)	**Discontinued** (n = 45; 55.6%)	**Discontinued** (n = 19; 31.7%)
Adverse event (n = 4; 5.8%)	Adverse event (n = 3; 3.7%)	Adverse event (n = 2; 3.3%)
Bone marrow transplant (n = 1; 1.4%)	Bone marrow transplant (n = 2; 2.5%)	Bone marrow transplant (n = 0)
Clinical progression (n = 2; 2.9%)	Clinical progression (n = 1; 1.2%)	Clinical progression (n = 1; 1.7%)
Complete response (n = 5; 7.2%)	Complete response (n = 7; 8.6%)	Complete response (n = 1; 1.7%)
Death (n = 1; 1.4%)	Death (n = 1; 1.2%)	Death (n = 0)
Lost to follow-up (n = 0)	Lost to follow-up (n = 1; 1.2%)	Lost to follow-up (n = 0)
Physician decision (n = 3; 4.3%)	Physician decision (n = 7; 8.6%)	Physician decision (n = 2; 3.3%)
Progressive disease (n = 10; 14.5%)	Progressive disease (n = 20; 24.7%)	Progressive disease (n = 13; 21.7%)
Patient withdrawal (n = 0)	Patient withdrawal (n = 3; 3.7%)	Patient withdrawal (n = 0)

Cohort 1

ASCT and subsequent BV

Cohort 2

Salvage chemotherapy and BV (ineligible for ASCT)

Cohort 3

ASCT but not BV

Chen et al., Journal of Clinical Oncology 25 April 2017

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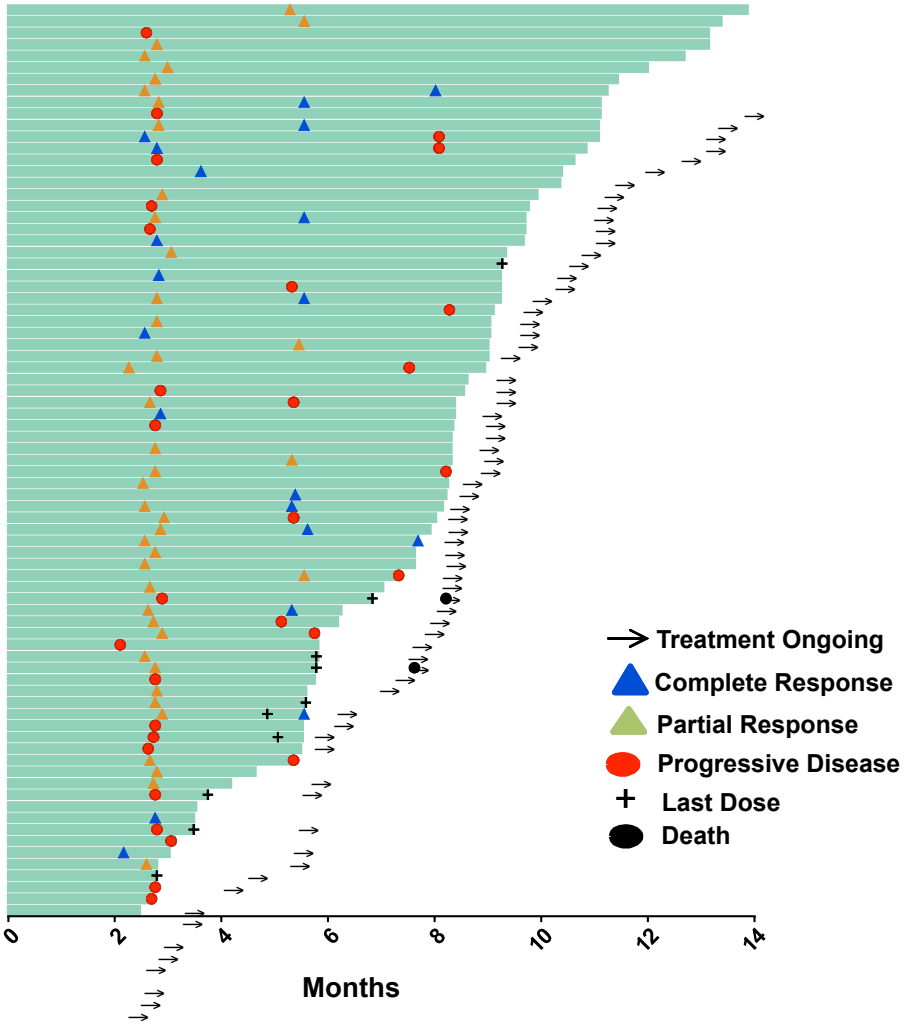
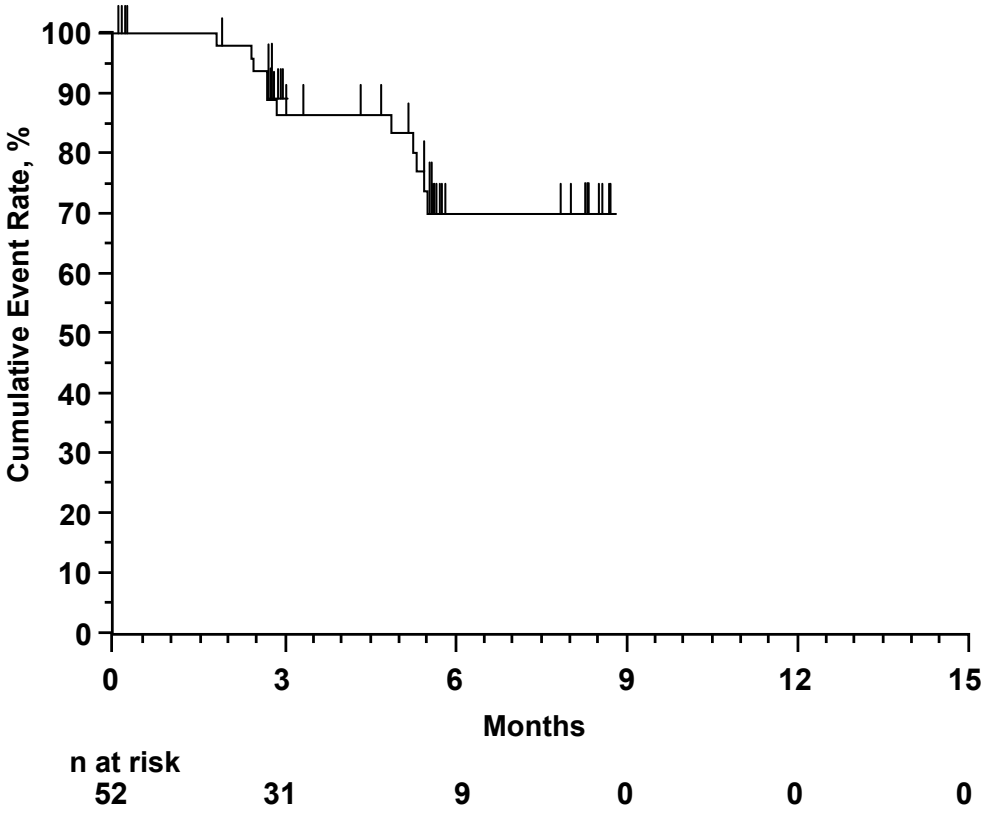


COHORT B
INELIGIBLE TO ASCT



- **Median number of treatment cycles**
  - 12 (range 1, 21)

- **Median (range) time to response**
  - 2.8 (2.2-5.6) months
- **Response duration ≥6 months:** 70%

Clinical Evaluation of PD-1 Blockade Relapsed/Refractory cHL

Disease	Study	Response rate (# pts)	PFS
cHL	Nivolumab pilot[1]	87% (20/23)	PFS 48% at median FU 9 mos
	Nivolumab registration trial		
	Cohort B (S/P ASCT/BV)[2]	68% (54/80)	PFS 62% at median FU 9 mos
	FDA approval 5/ 2016		
	Pembrolizumab pilot[3]	58% (18/31)	PFS ≥ 12 mos - 70%
	Pembrolizumab registration trial[4]		
	Cohort 1 (S/P ASCT/BV)	74% (51/69)	PFS ≥ 6 mos - 82%
	Cohort 2 (ASCT ineligible)	64% (52/81)	PFS ≥ 6 mos - 70%
	Cohort 3 (s/p ASCT, no BV)	70% (42/60)	PFS ≥ 6 mos - 76%
	FDA approval 3/ 2017		

[1]Ansell *et al.,N. Engl. J. Med.* 2015; 372(4):311-9 and ASH 2016
[2]Younes *et al., Lancet Oncol.* 2016; 17(9):1283-1294 and Timmerman ASH 2016
[3]Armand *et al., J. Clin. Oncol.* Jun 27, 2016 Epub ahead of print
[4]Moskowitz *et al., J. Clin. Oncol.* Apr 25, 2017 Epub ahead of print

RUOLO DEL TRAPIANTO: PD-1 In POST-ALLO

ALLOGENICO → PD-1 In

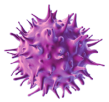
IPILIMUMAB AFTER ALLOTRANSPLANT IN HL

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Ipilimumab for Patients with Relapse after Allogeneic Transplantation

Outcome of treatment	
Patients who received maximum administered dose (10 mg/kg)	22
Complete response	5
Partial response	2
Stable disease	6
Progression of disease	9



Davids MS et al, NEJM 2016

Regular Article *September 18th, 2017* Charles Herbaux *et al.* blood

CLINICAL TRIALS AND OBSERVATIONS

Efficacy and tolerability of nivolumab after allogeneic transplantation for relapsed Hodgkin lymphoma

This study retrospectively assessed the efficacy and toxicity of **nivolumab** (PD-1 pathway blocking monoclonal antibody) as a single agent in 20 HL patients relapsing after allo-HCT

Key Points:

- PD-1 blockade with nivolumab provides durable disease control after allo-HCT
- PD-1 blockade with nivolumab after allo-HCT is associated with 30% acute GVHD

Regular Article blood

TRANSPLANTATION BLOOD, 13 JULY 2017 • VOLUME 130, NUMBER 2 *Bradley M. Haverkos et al.*

PD-1 blockade for relapsed lymphoma post–allogeneic hematopoietic cell transplant: high response rate but frequent GVHD

Key Points

- Checkpoint blockade via anti–PD-1 mAbs was associated with a high overall response rate in relapsed HL allo-HCT patients.
- Checkpoint blockade via anti–PD-1 mAbs after allo- HCT can be complicated by rapid onset of severe and treatment-refractory GVHD.

RUOLO DEL TRAPIANTO: ALLO POST-PD1 IN

ALLOGENICO?

CHECKMATE-205 : PHASE 2 STUDY WITH NIVOLUMAB IN R/R HL

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COHORT B

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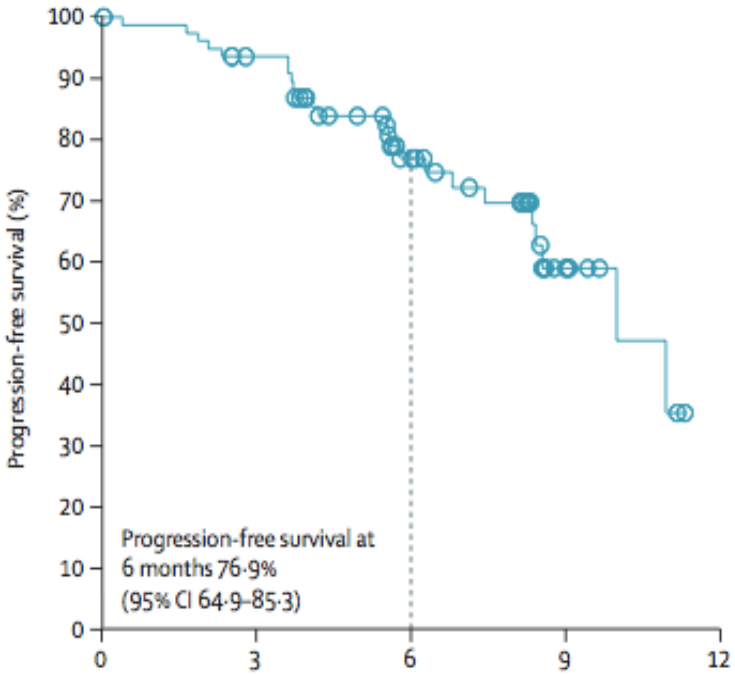
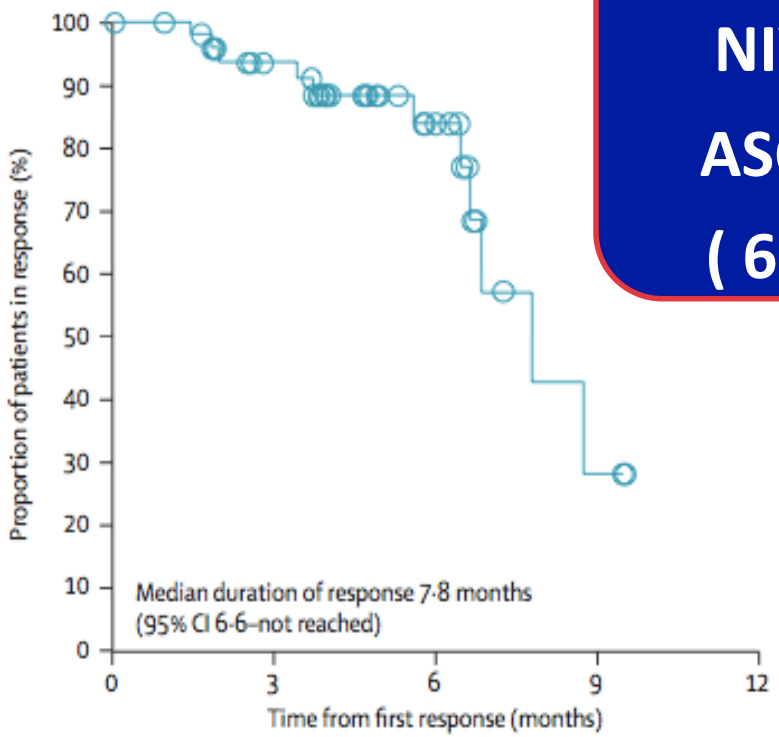
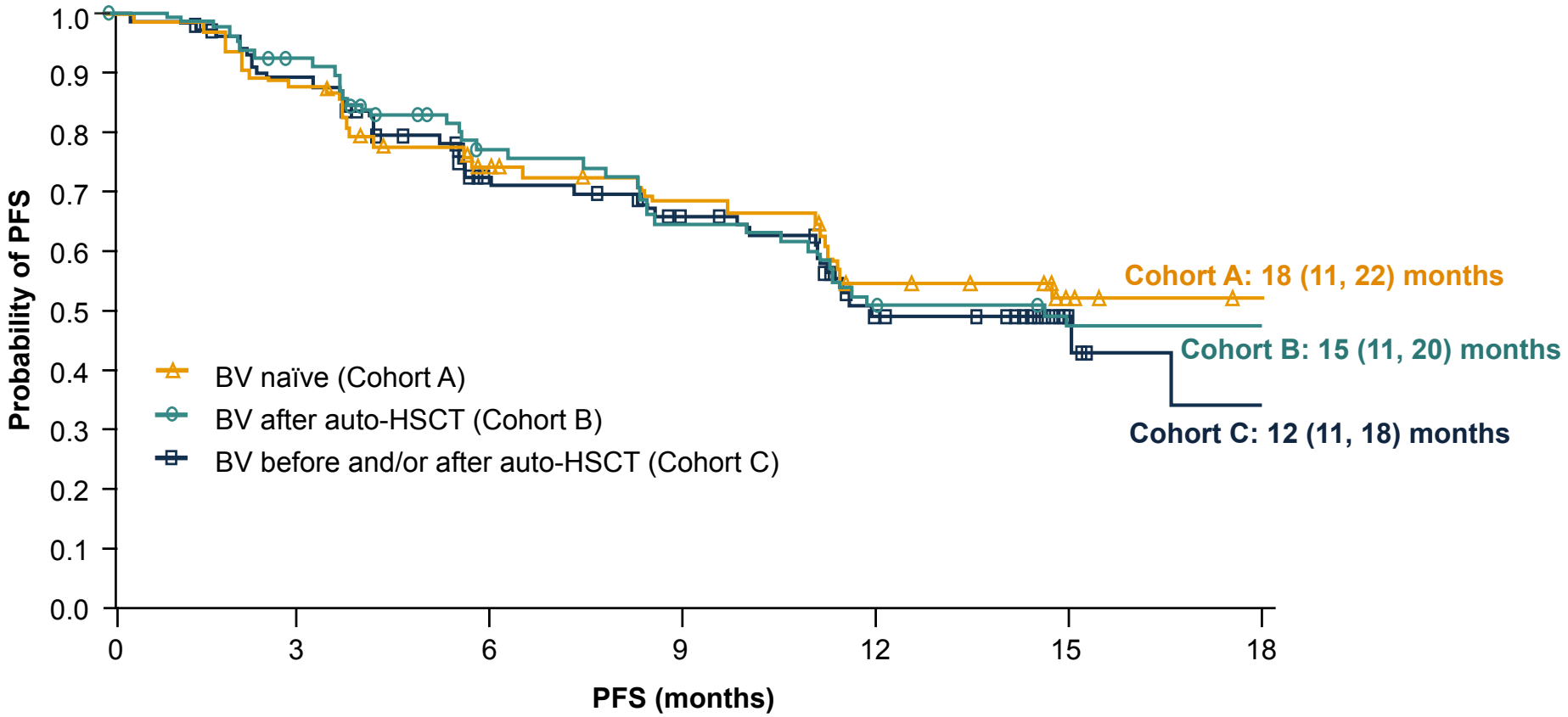




Lancet Oncol 2016; 17: 1283-94

Progression-Free Survival by Cohort



Number of patients at risk

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M. Fanale et al ICML 2017

All values are medians (95% CI)

KEYNOTE-087 : PHASE 2 STUDY WITH PEMBROLIZUMAB IN R/R HL

Decrease from baseline in tumor burden (left) and Kaplan-Meier estimates of objective response duration (right) on the basis of central review in patients with response.

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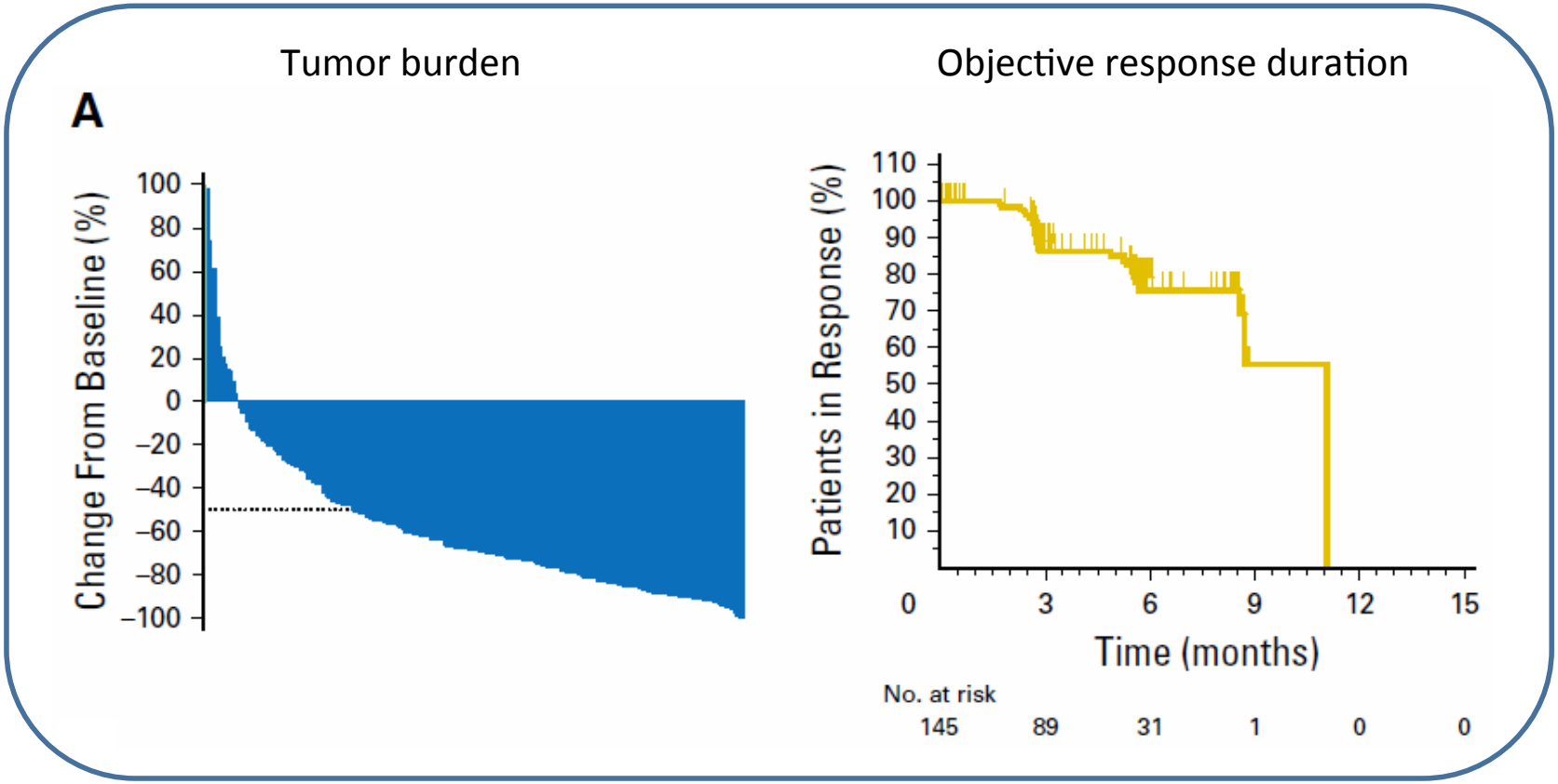
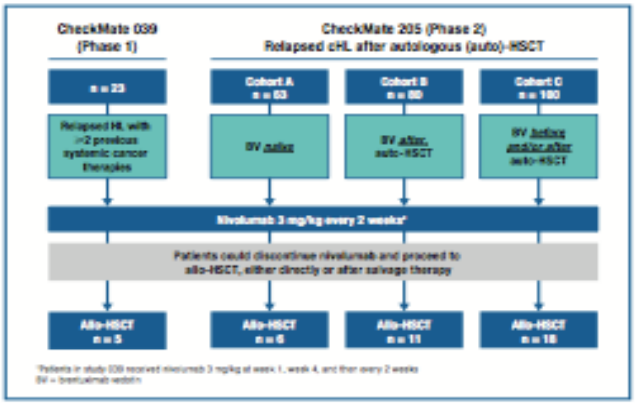


Chen et al., Journal of Clinical Oncology 25 April 2017

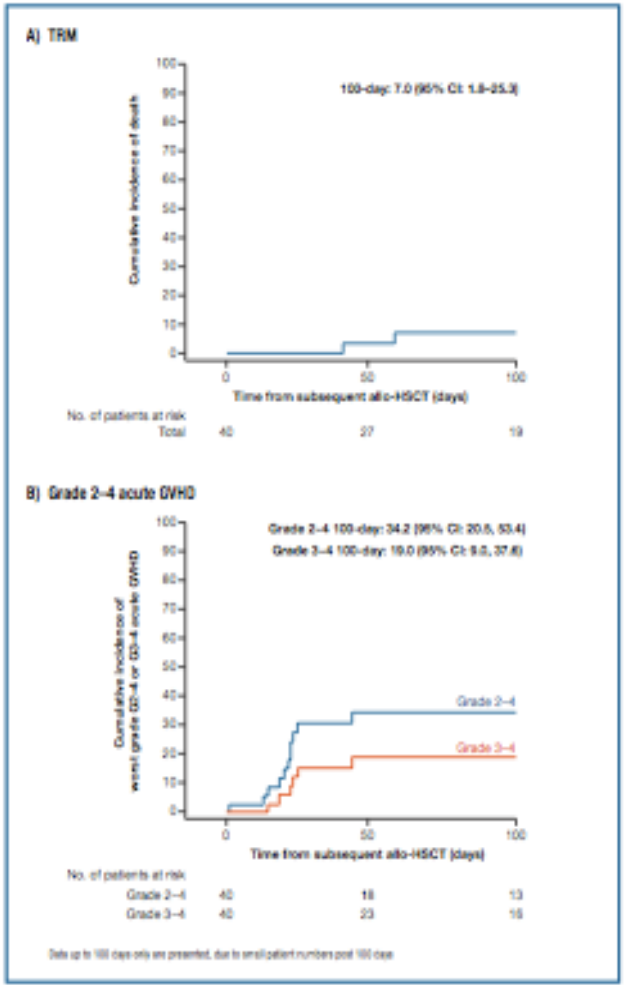
Outcomes of Allogeneic Hematopoietic Stem Cell Transplantation After Treatment With Nivolumab for Relapsed/Refractory Hodgkin Lymphoma

Philippe Armand,[1] Pier Luigi Zinzani,[2] Graham P Collins,[3] Jonathon B Cohen,[4] Ahmad Halwani,[5] Carmelo Carlo-Stella,[6] Michael Millenson,[7] Mariano Provencio,[8] Eva Domingo Domenech,[9] Lisa Giulino-Roth,[10] Luca Castagna,[6] Kazunobu Kato,[11] Mihaela Popa McKiver,[11] Anne Sumbul,[11] Lili Zhu,[11] Armando Santoro[6]



Conclusions

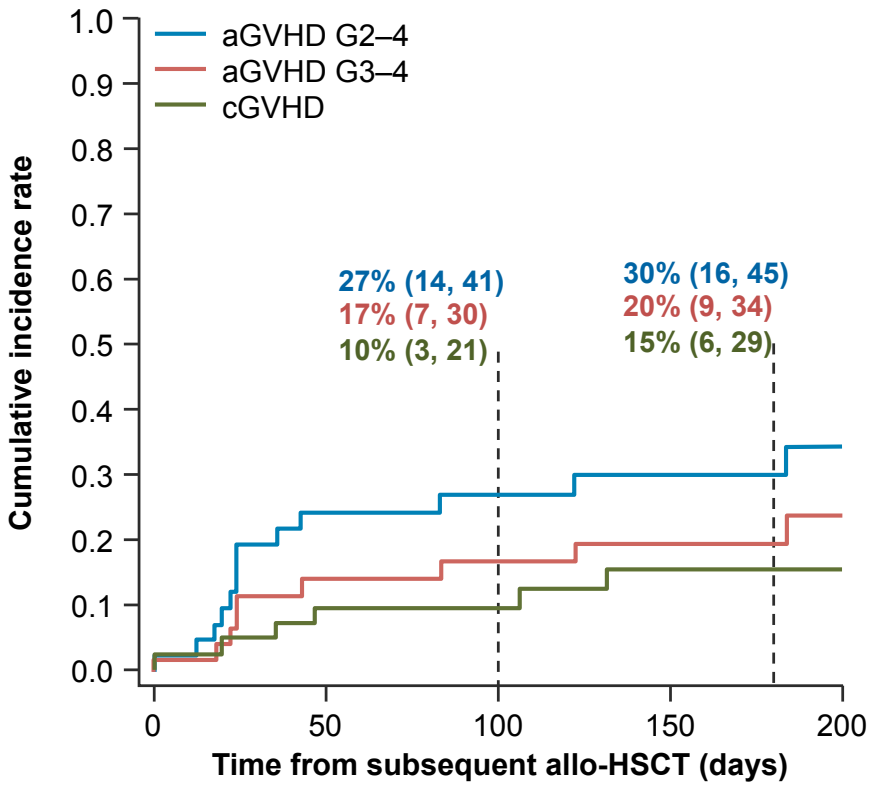
- After limited follow-up the incidence of severe (G4) acute GVHD was 19% in this cohort, and included fatalities
- Overall incidence of TRM and GVHD are within the range of published data for patients with cHL undergoing allo-HSCT
  - Rate of G3–4 GVHD in this study may have been overestimated due to imputation of 2 GVHD cases with unknown grade as G4
- To date, these data suggest that treatment with nivolumab is not a strict contraindication to subsequent allo-HSCT; however, caution about early or severe GVHD seems warranted
- Additional follow-up and experience using allo-HSCT after nivolumab will provide clarity on the patient demographics, clinical factors, and treatment timings that may influence outcomes



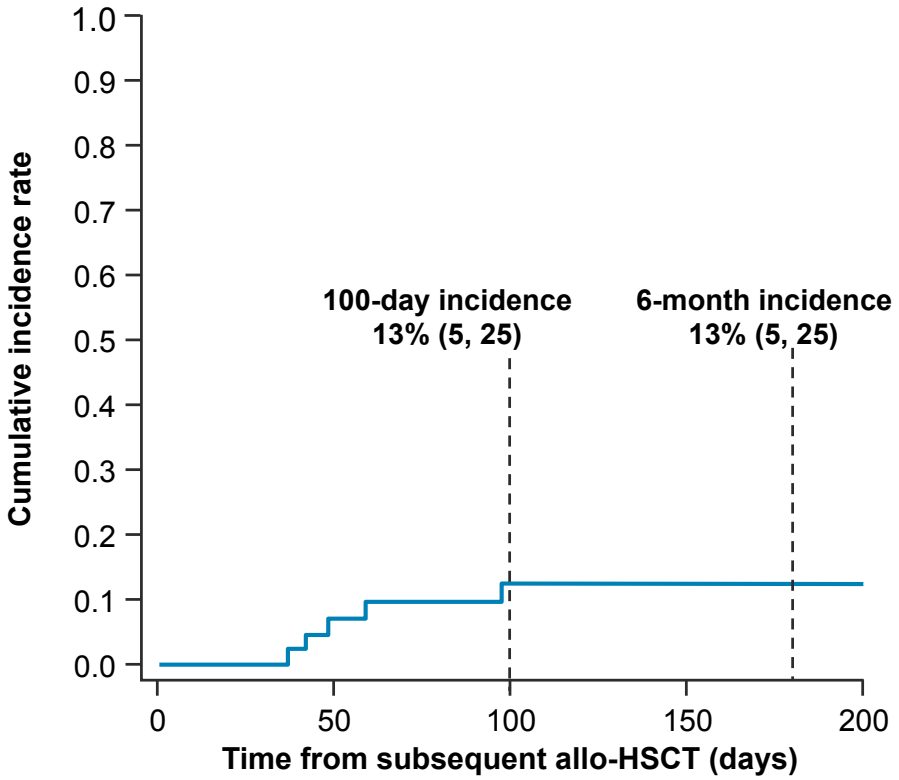
ASH 2016

Outcomes After Allogeneic HSCT

Graft versus host disease



Transplant-related mortality



- Median post-transplant follow-up for 44 patients who received allo-HSCT after nivolumab was 5.5 months (019.0)
- Median time from last dose of nivolumab to allo-HSCT was 1.6 months (0.5–13.5)
- Historical 100-day incidence of aGVHD and TRM was 26–60% and 6–28%, respectively[1-5]

Unknown aGVHD onset dates imputed to allo-HSCT date and GVHD of unknown grade imputed to G4. Death was considered a competing risk to aGVHD (2/44 competing events) and cGVHD (6/44 competing events). Post-transplant progression was considered a competing risk to TRM (3/44 competing events). Data are % (95% CI). aGVHD = acute graft versus host disease; cGVHD = chronic GVHD; G = grade; TRM = transplant-related mortality

1. Sureda A, et al. *J Clin Oncol* 2008;26:455–462; 2. Devetten MP, et al. *Biol Blood Marrow Transplant* 2009;15:109–117; 3. Robinson SP, et al. *Haematologica* 2009;94:230–238; 4. Marcais A, et al. *Haematologica* 2013;98:1467–1475; 5. Anderlini P, et al. *Biol Blood Marrow Transplant* 2016;22:1333–1337

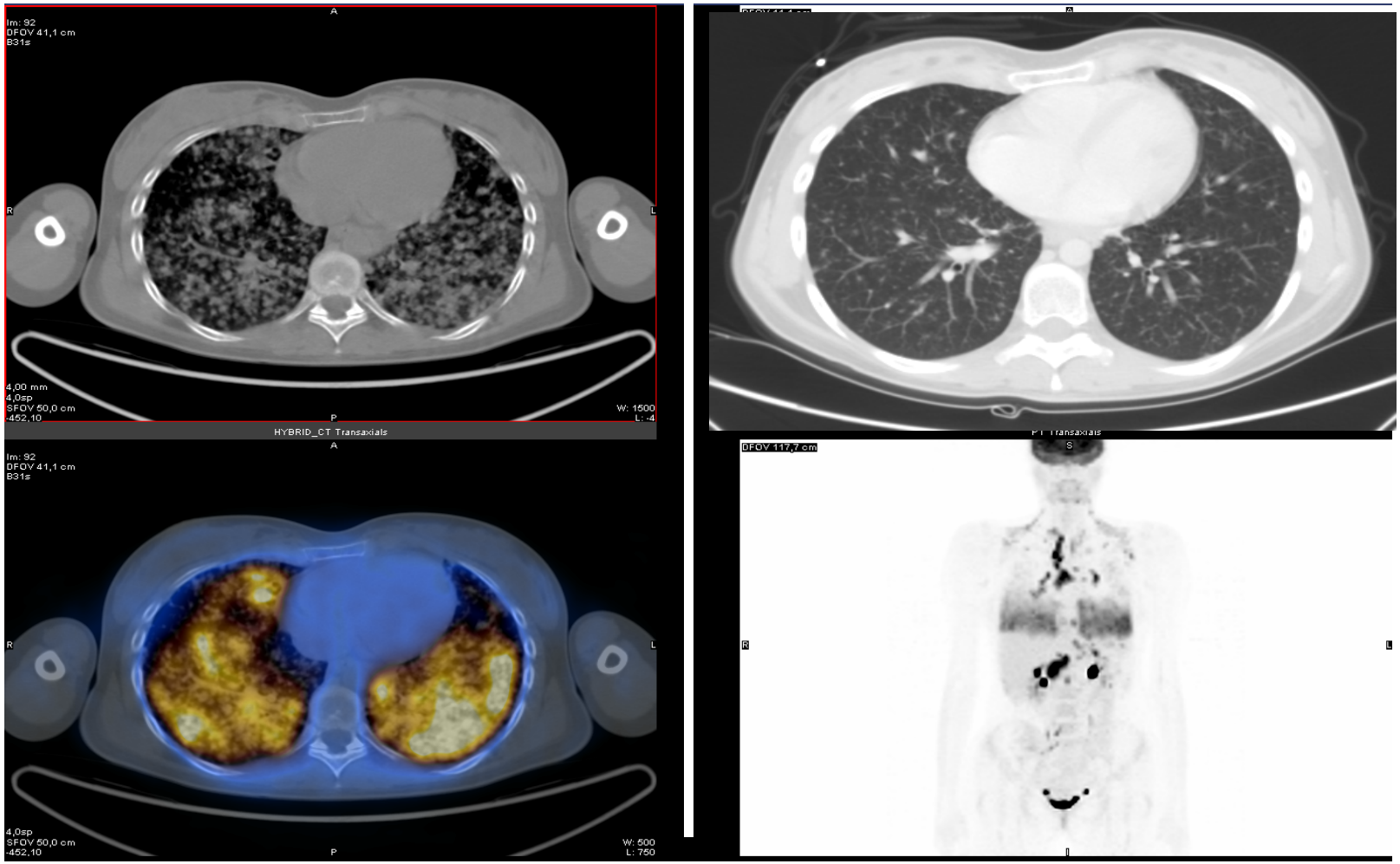
RUOLO DEL TRAPIANTO: ALLO POST-PD1 IN

ALLOGENICO?

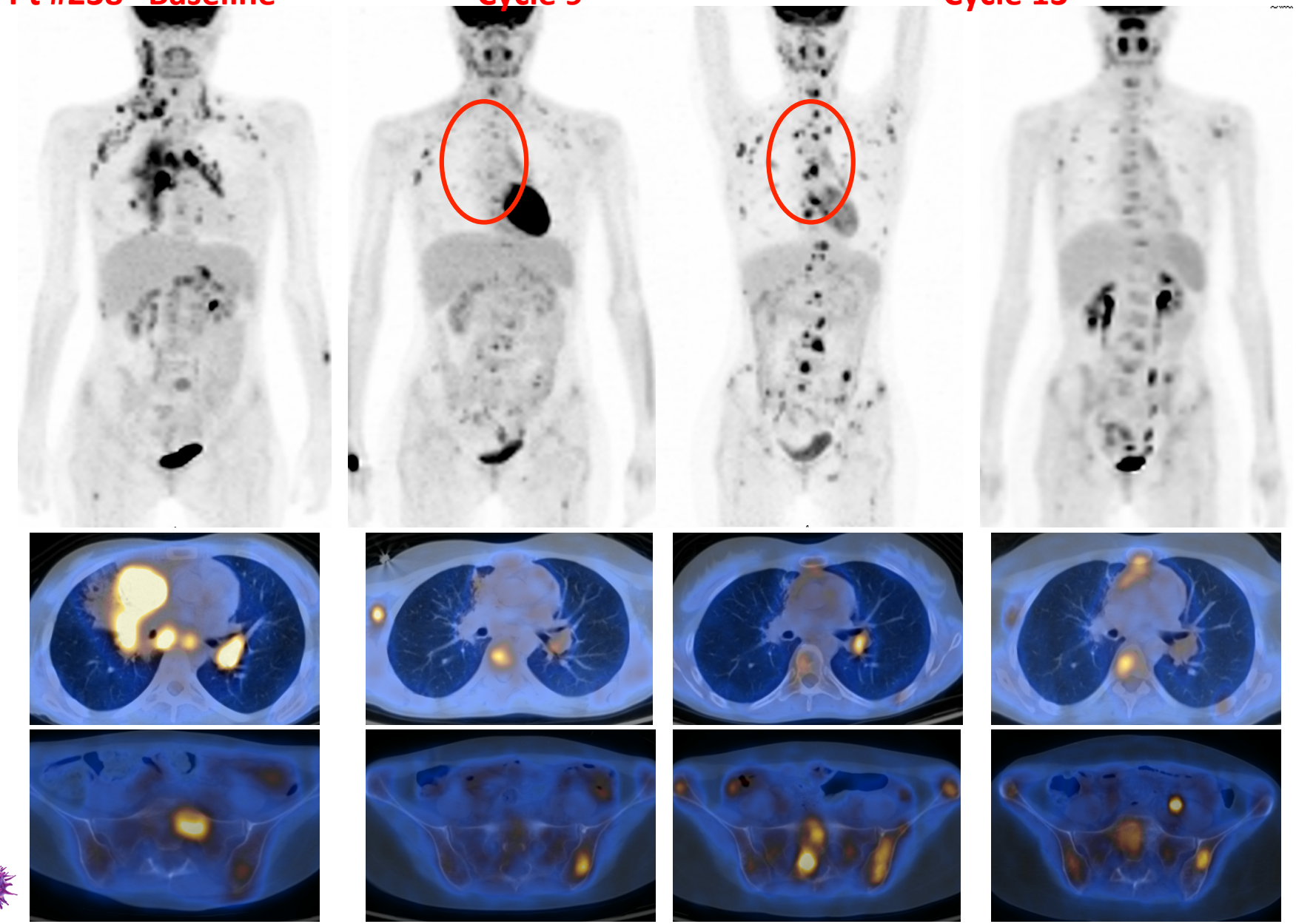
CHECKPOINT INHIBITORS: *RESPONSE EVALUATION*

Pt #270 - Baseline

Cycle 3



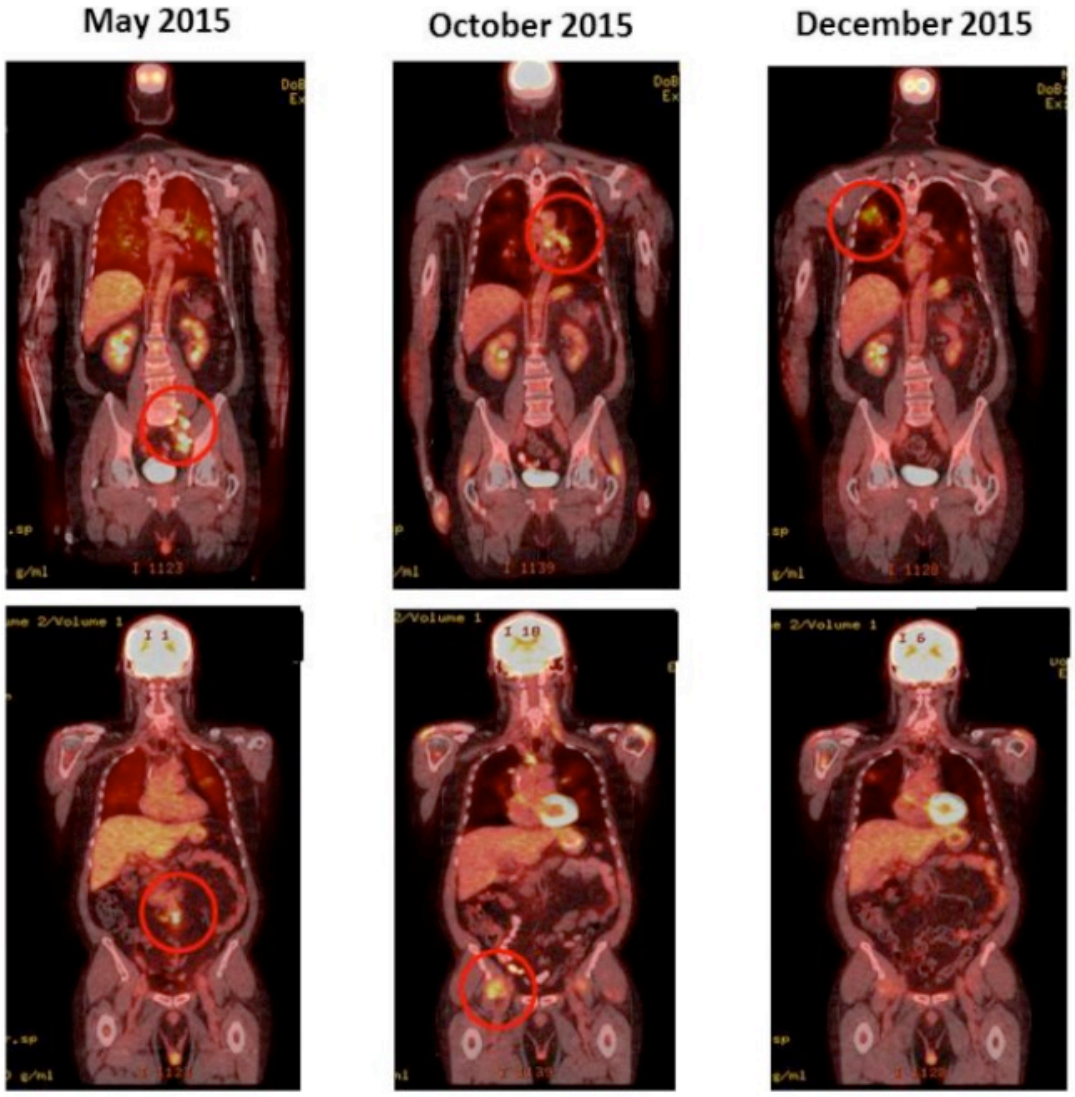
CHECKPOINT INHIBITORS: *RESPONSE EVALUATION*



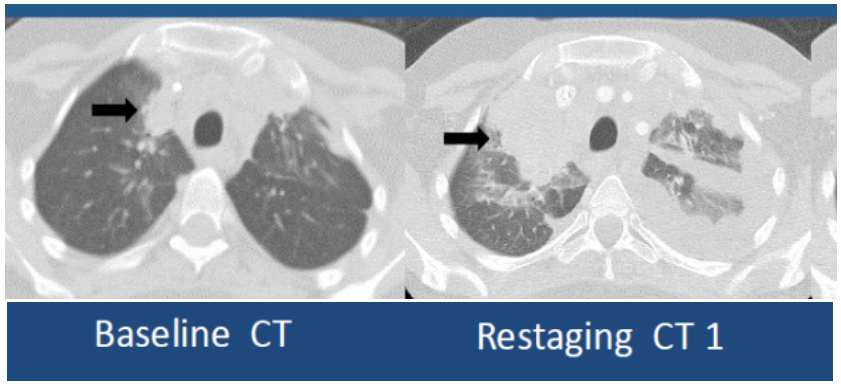
blood®
Prepublished online August 29, 2016;
doi:10.1182/blood-2016-05-718528

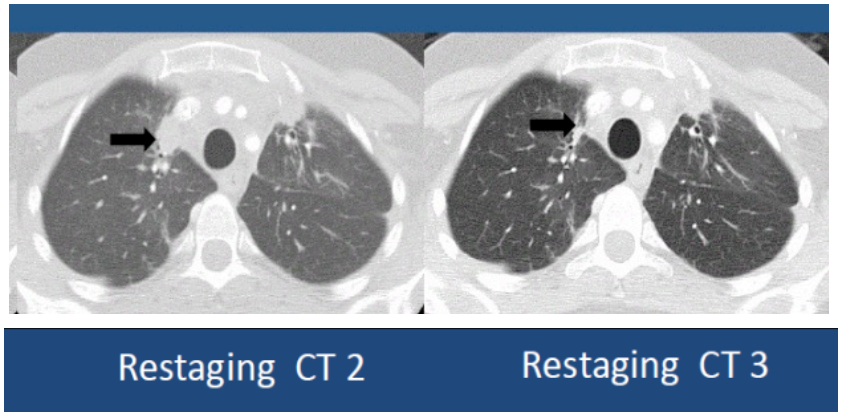
Refinement of the Lugano classification response criteria for lymphoma in the era of immunomodulatory therapy

Bruce D. Cheson, Stephen Ansell, Larry Schwartz, Leo I. Gordon, Ranjana Advani, Heather A. Jacene, Axel Hoos, Sally F. Barrington and Philippe Armand



Lymphoma **R**esponse to **I**mmunomodulatory therapy **C**riteria (**LyRIC**)



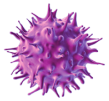


CHECKPOINT INHIBITORS: *RESPONSE EVALUATION*

LYmphoma
Response to
Immunomodulatory therapy
Criteria

→ **INDETERMINATE RESPONSE CATEGORY**

IR	Definition
IR1	*Increase in overall tumor burden (SD)≥50% of up to 6 measurable lesions in the first 12 ws of therapy without clinical deterioration*
IR2	*Appearance of new lesions, or growth of one or more existing lesions ≥50% at any time during treatment, occuring in the context of lack of overall progression of overall tumor burden*
IR3	*Increase in FDG uptake of one or more lesions without a concomitant increase in lesion size or number*



Cheson B et al, Blood 2016

CHECKPOINT INHIBITORS: *TREATMENT DURATION*

NO ALLO-TRANSPLANT

2 YEARS?

ALLO- TRANSPLANT

8 COURSES?

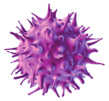
CHECKPOINT INHIBITORS: SAFETY

	All-cause adverse events (n=80)			Drug-related adverse events (n=80)		
	Grade 1–2	Grade 3	Grade 4	Grade 1–2	Grade 3	Grade 4
(Continued from previous page)						
Cardiac failure	0	1 (1%)	0	0	0	0
Left ventricular dysfunction	0	1 (1%)	0	0	0	0
Pericardial effusion	0	0	1 (1%)	0	0	0
Autoimmune hepatitis	0	1 (1%)	0	0	1 (1%)	0

Data are n (%). Adverse events in this table include grade 1–2 events reported in ≥10% of patients, and all grade 3–4 events. One patient died as a result of multi-organ failure that was unrelated to treatment.

***Table 3*: Adverse events**

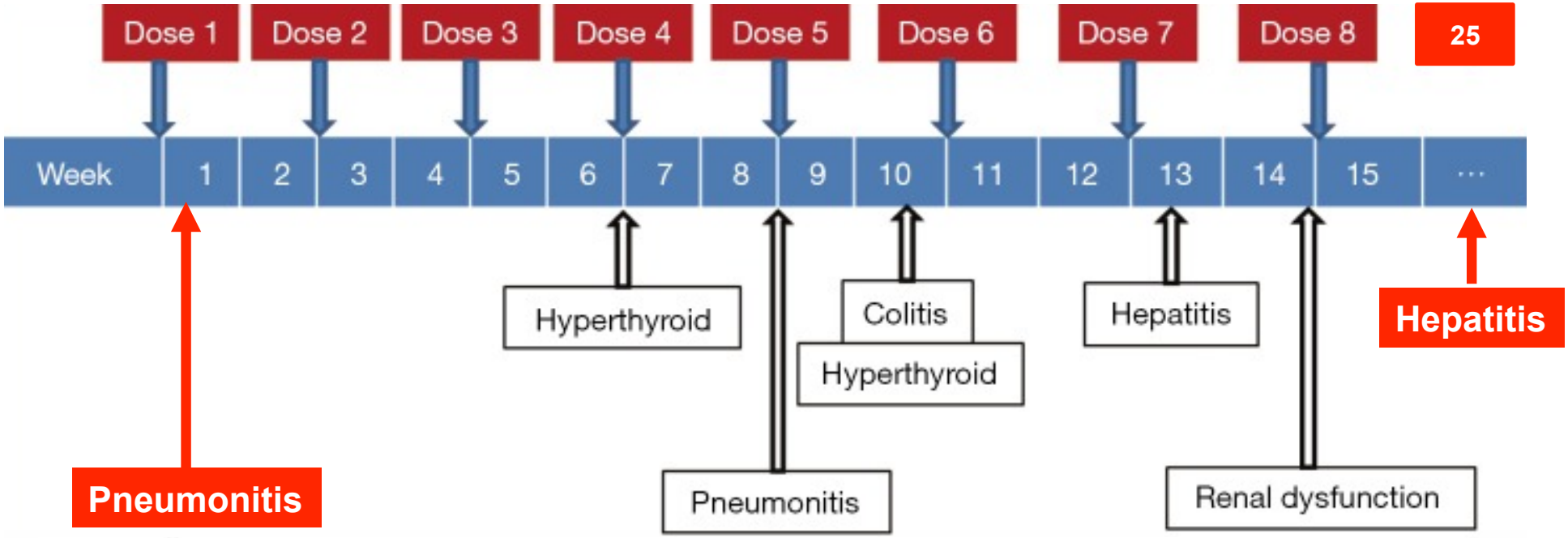
-MORE COMMON AE: FATIGUE (25%), IRR (20%), RASH (16%)
-MORE COMMON SAES ≥GR3: NEUTROPENIA (5%), INCREASED LIPASE LEVEL (5%)
-MOST COMMON SAE ANY GRADE: FEVER

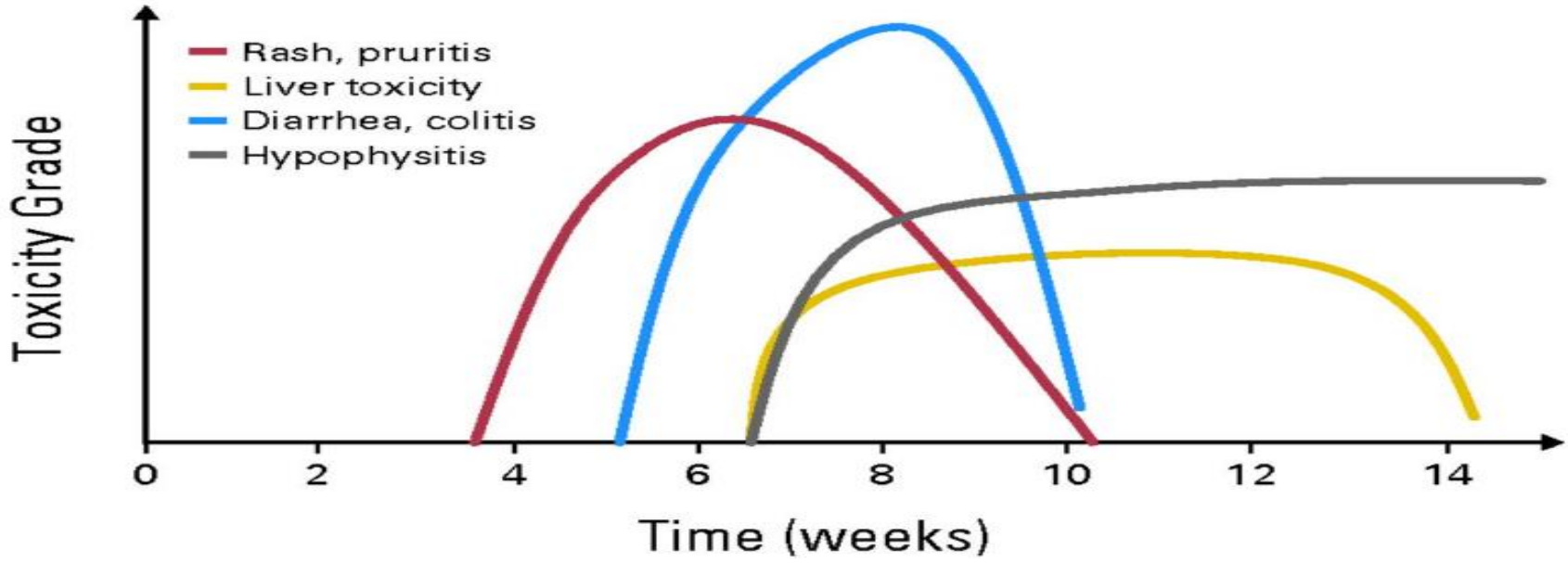


Younes A et al Lancet Oncol 2016

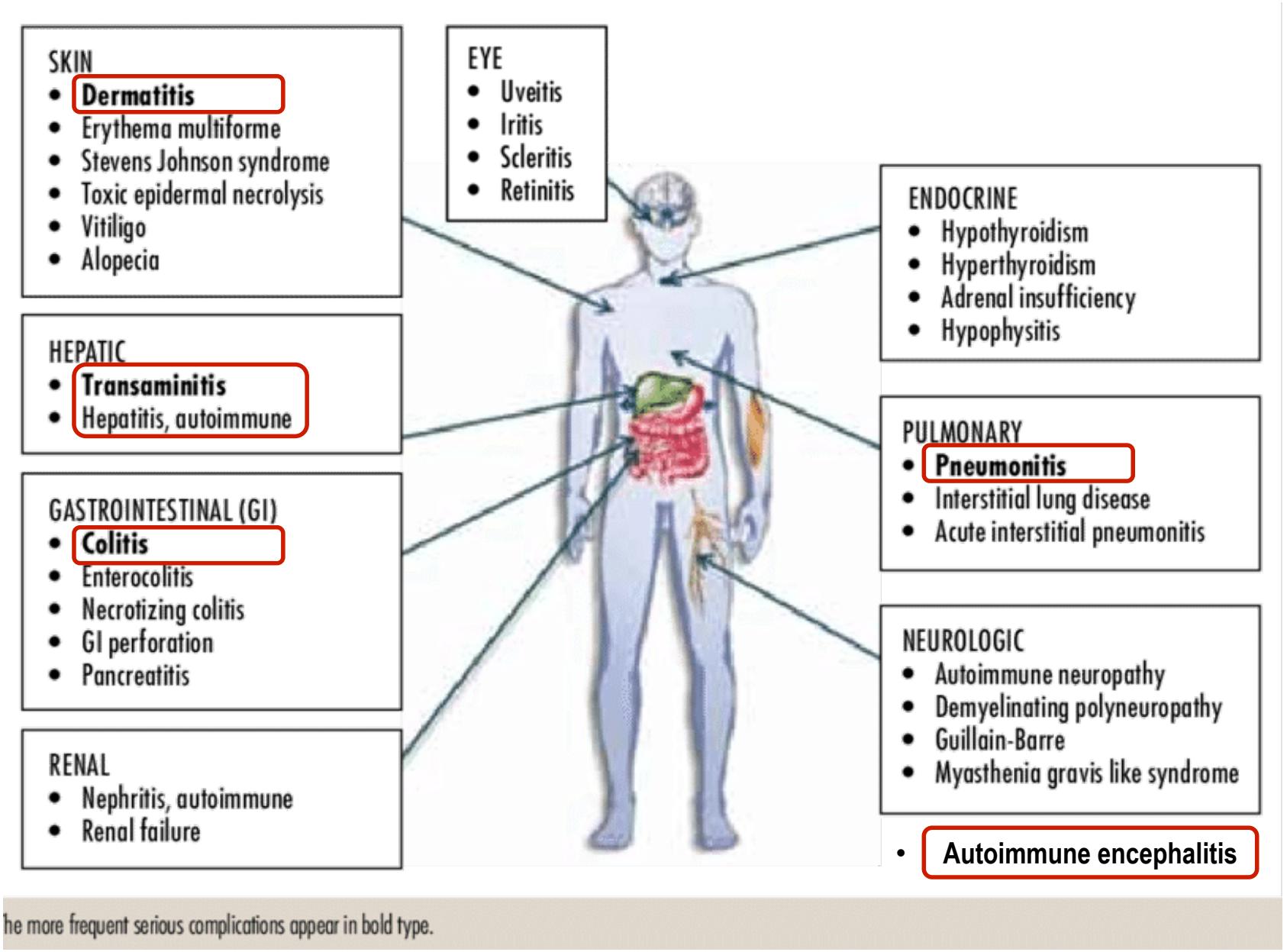
PD1-blockade: safety profiles

- **Nivolumab: Median time for appearance of immune-related adverse events**





PD1-blockade and Hodgkin Lymphoma: Safety Issues



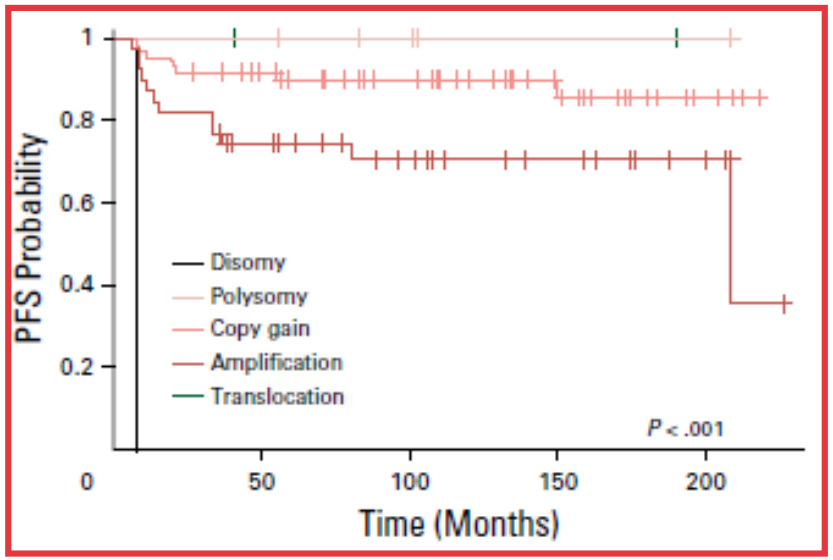
I-O Therapies Have Unique Safety Profiles[1-5]

GENERAL RULES: MANAGEMENT OF NIVOLUMAB-RELATED SELECT AES

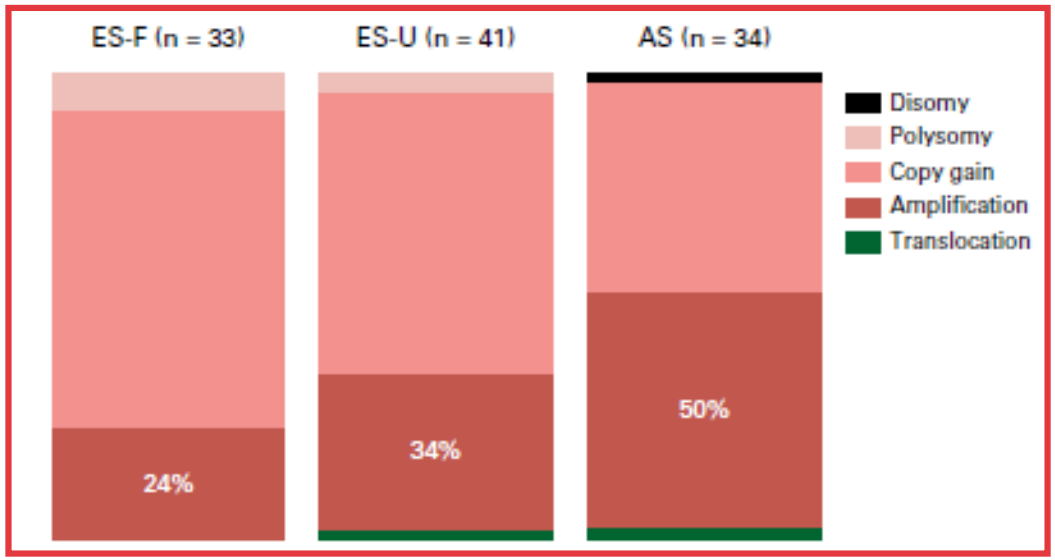
Grade	Management	Continue the study drug?
Low	Delay the dose	Resume Nivolumab when AEs resolve to grade ≤ 1 or baseline
Moderate ~ High	Administer Corticosteroids ± Immunosuppressants (anti-TNF, mycophenolate, etc)	Discontinue Nivolumab permanently (Delay in some situations)

CHECKPOINT INHIBITORS: *BIOMARKERS*

PFS by 9p24.1 alterations



Frequency of 9p24.1 alterations by stage



- **PD-L1/PD-L2 alterations** are a defining feature of cHL **(97%)**
- **Amplification of 9p24.1** are more common in **advanced stage** pts and correlate with **shorter PFS**
- Near-uniform alterations of PD-L1/PD-L2 loci explain the remarkable **activity of PD-1 blockade** in cHL

Roemer MGM et al, JCO 2016

CHECKMATE 205: BIOMARKERS - *Cohort B-C*

Figure 4. PFS according to 9p24.1 genetic alterations

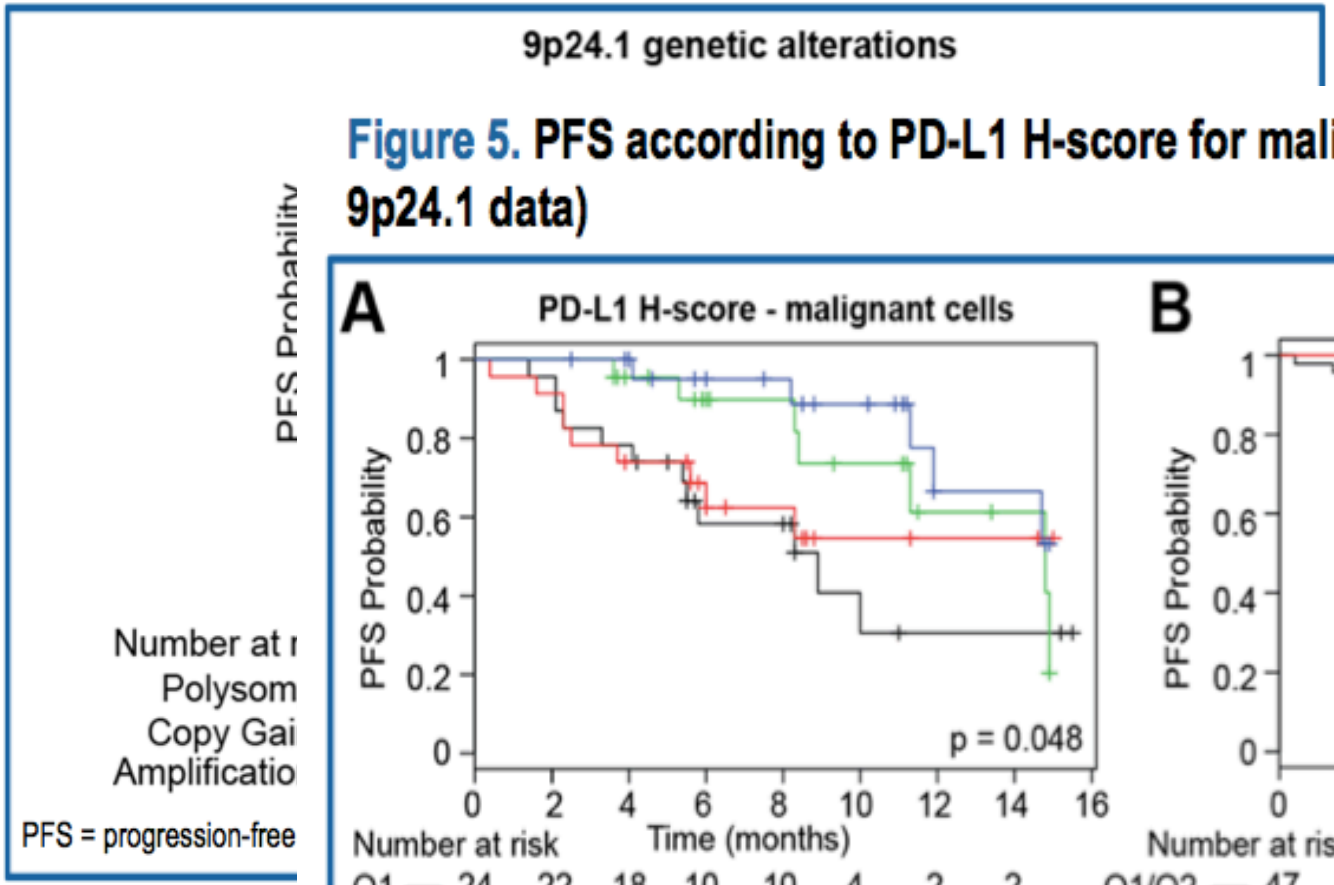


Figure 5. PFS according to PD-L1 H-score for malignant cells (in cases with 9p24.1 data)

NIVOLUMAB IN HODGKIN'S LYMPHOMA

PD-1 INHIBITOR
REPRESENTS
A REAL ACHIEVEMENT
IN HL PATIENT CARE

WHAT THE NEXT STEP?

THE NEXT SCENARIOS IN HL TREATMENT

Interim Results From a Phase 1/2 Study of Brentuximab Vedotin in Combination With Nivolumab in Patients with Relapsed or Refractory Hodgkin Lymphoma

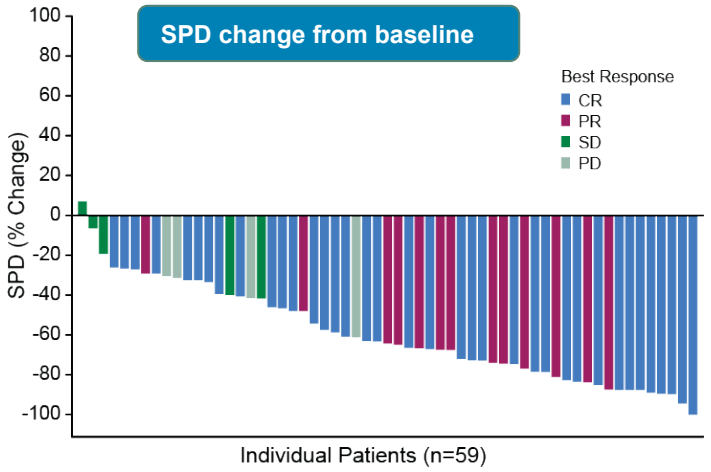
Alex F. Herrera[1], Alison J. Moskowitz[2], Nancy L. Bartlett[3], Julie M. Vose[4], Radhakrishnan Ramchandren[5], Tatyana A. Feldman[6], Ann S. LaCasce[7], Stephen M. Ansell[8], Craig H. Moskowitz[2], Keenan Fenton[9], Carol Anne Ogden[9], David Taft[9], Qu Zhang[9], Kazunobu Kato[10], Mary Campbell[9], Ranjana H. Advani[11]

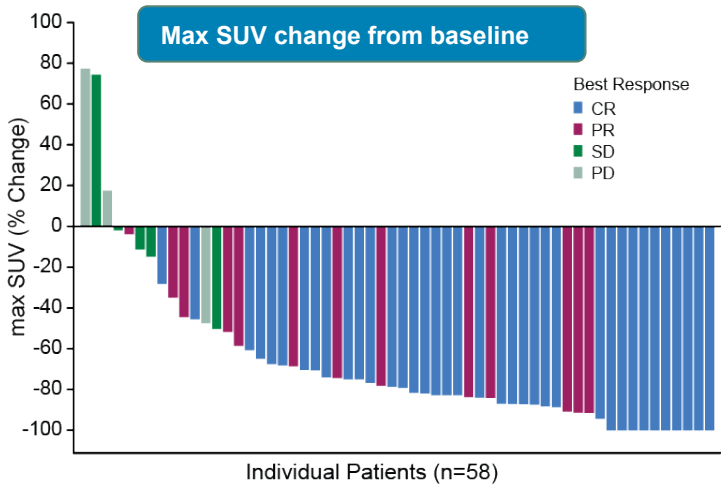
[1]City of Hope National Medical Center, Duarte, CA, USA; [2]Memorial Sloan Kettering Cancer Center, New York, NY, USA; [3]Washington University School of Medicine, St. Louis, MO, USA; [4]University of Nebraska Medical Center, Omaha, NE, USA; [5]Karmanos Cancer Institute, Detroit, MI, USA; [6]Hackensack University Medical Center, Hackensack, NJ, USA; [7]Dana Farber Cancer Institute, Boston, MA, USA; [8]Mayo Clinic, Rochester, MN, USA; [9]Seattle Genetics, Inc., Bothell, WA, USA; [10]Bristol-Myers Squibb, Princeton, NJ, USA; [11]Stanford University Medical Center, Palo Alto, CA, USA

Presented at the 14th International Conference on Malignant Lymphoma (ICML); Lugano, Switzerland; June 14–17, 2017

Tumor Response

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

THE NEXT SCENARIOS IN HL TREATMENT

PD-1/PD-L1
+
CHT

PD-1/PD-L1
+
BV

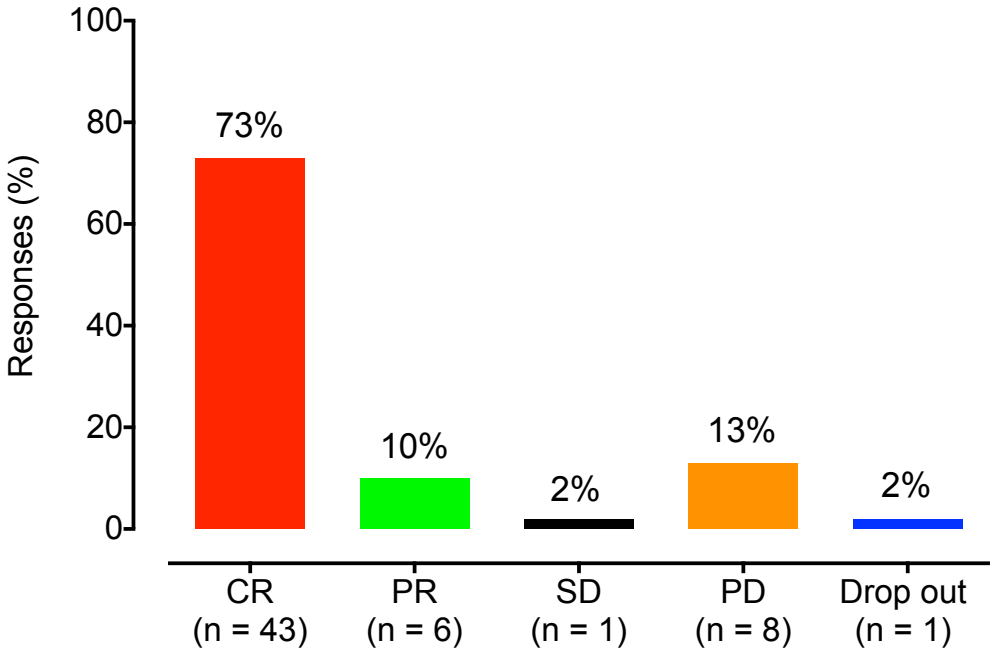
PD-1/PD-L1
+
other IO-T

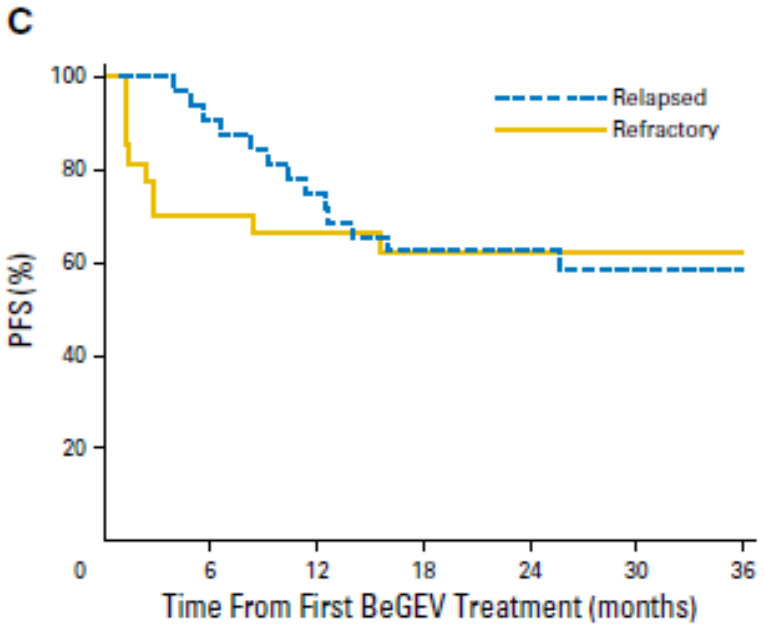
PD-1/PD-L1
+
NEW TARGETED TH

BeGEV

Bendamustine in Combination With Gemcitabine and Vinorelbine Is an Effective Regimen As Induction Chemotherapy Before Autologous Stem-Cell Transplantation for Relapsed or Refractory Hodgkin Lymphoma: Final Results of a Multicenter Phase II Study

Bendamustine 90 mg/mq d 2-3, Gemcitabine 800 mg/mq d 1-4, Vinorebine 20 mg/mq d 1





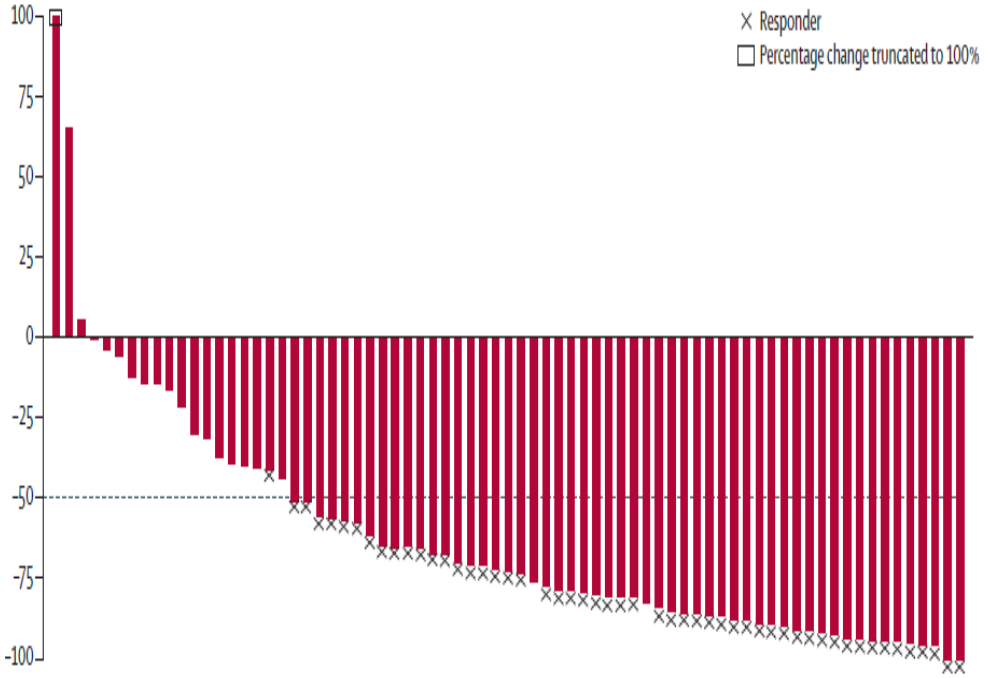
Median CD34+ cells/kg 8.8 x 10^6

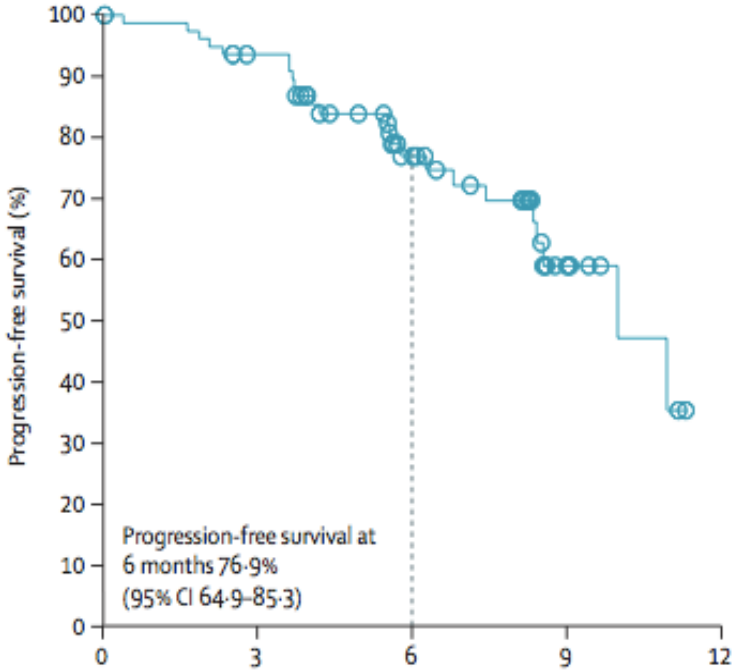
Santoro A et al, JCO 2016

WHY NOT ?

Bendamustine in Combination With Gemcitabine and Vinorelbine Is an Effective Regimen As Induction Chemotherapy Before Autologous Stem-Cell Transplantation for Relapsed or Refractory Hodgkin Lymphoma: Final Results of a Multicenter Phase II Study

Bendamustine 90 mg/mq d 2-3, Gemcitabine 800 mg/mq d 1-4, Vinorebine 20 mg/mq d 1





Lancet Oncol 2016; 17: 1283–94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