Treatment of relapsed cHL after auto-HSCT

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- 18 years old female presented with extensive LAPs plus B-symptoms (March 2015)
- Cervical LN Biopsy: Classic Hodgkin Lymphoma
- ABVD 3 courses
- Partial response on CT scan
- She received 3 other courses ABVD
- CT scan after treatment shows progressive disease

What is your choice for salvage treatment?

1. Gemcitabine based protocols

2. ICE

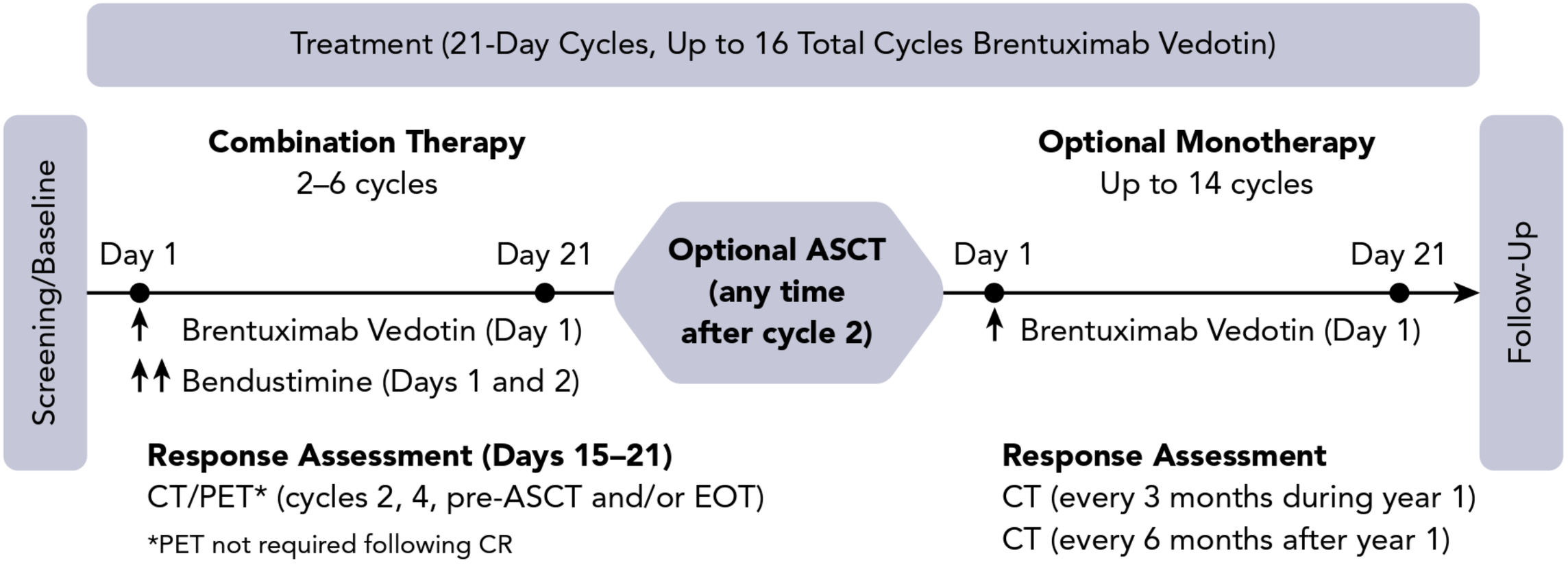
3. DHAP

4. Brentuximab Vedotin +/- chemotherapy

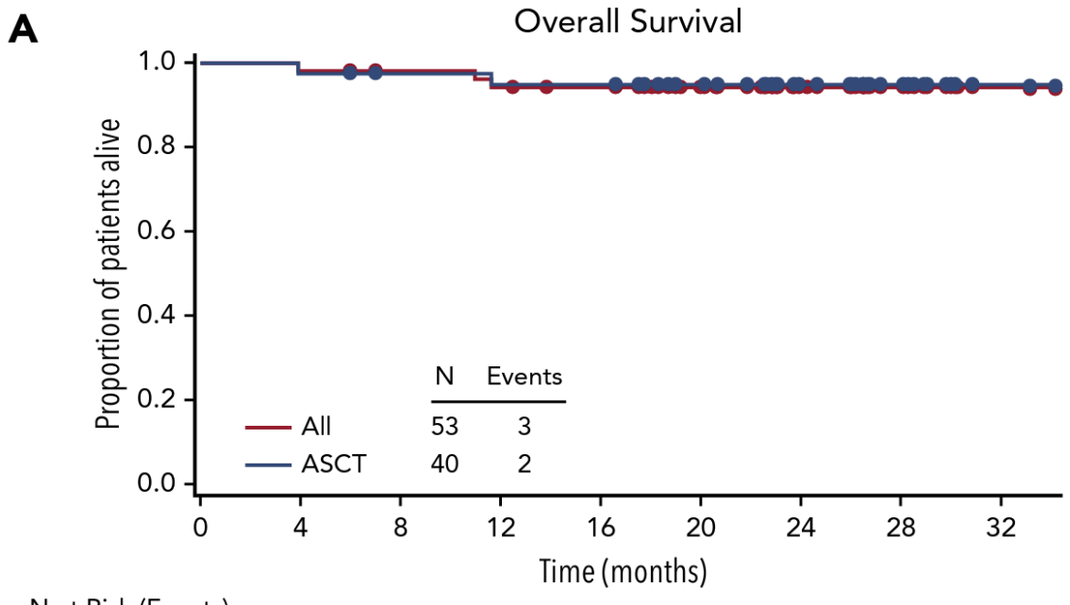
5. Other

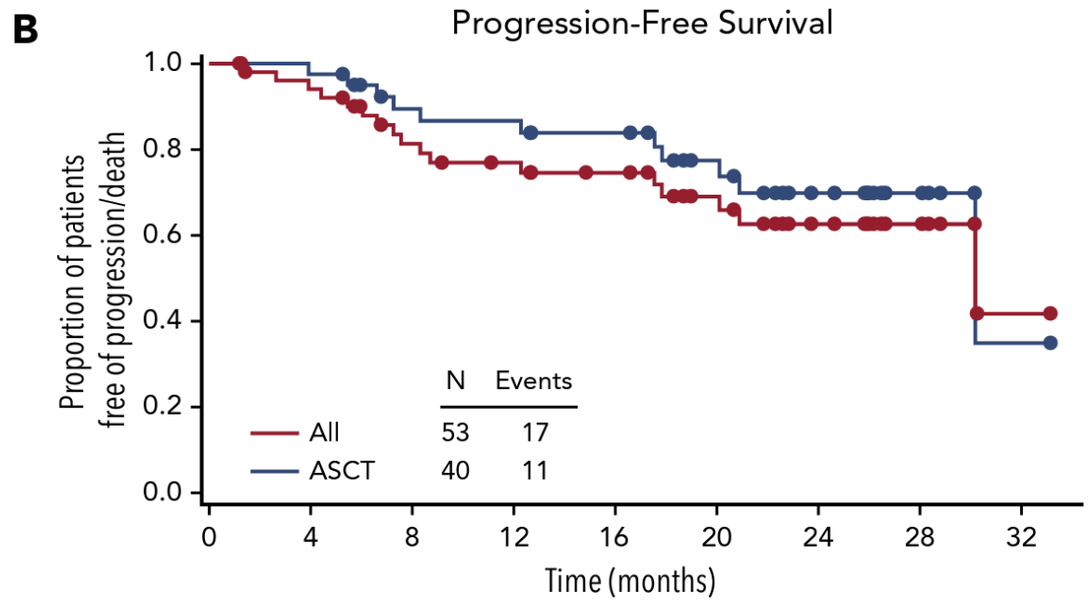
Brentuximab vedotin plus bendamustine: a highly active first salvage regimen for relapsed or refractory Hodgkin lymphoma

Ann S. LaCasce,[1] R. Gregory Bociek,[2] Ahmed Sawas,[3] Paolo Caimi,[4] Edward Agura,[5] Jeffrey Matous,[6] Stephen M. Ansell,[7] Howland E. Crosswell,[8] Miguel Islas-Ohlmayer,[9] Caroline Behler,[10] Eric Cheung,[11] Andres Forero-Torres,[12] Julie Vose,[2] Owen A. O'Connor,[3] Neil Josephson,[13] Yinghui Wang,[13] and Ranjana Advani[14]



Population	Best clinical response, n (%) [95% CI]				
	CR	PR	SD	PD	ORR*
Overall, N = 53	39 (73.6) [59.7, 84.7]	10 (18.9)	3 (5.7)	1 (1.9)	49 (92.5) [81.8, 97.9]
Response to frontline therapy					
Primary refractory, n = 28	18 (64.3) [44.1, 81.4]	6 (21.4)	3 (10.7)	1 (3.6)	24 (85.7) [67.3, 96.0]
Relapsed, n = 25	21 (84.0) [63.9, 95.5]	4 (16.0)	0 (0.0)	0 (0.0)	25 (100) [86.3, 100]
ASCT					
Yes, n = 40	34 (85.0) [70.2, 94.3]	4 (10.0)	2 (5.0)	0 (0.0)	38 (95.0) [83.1, 99.4]
No, n = 13	5 (38.5) [13.9, 68.4]	6 (46.2)	1 (7.7)	1 (7.7)	11 (84.6) [54.6, 98.1]

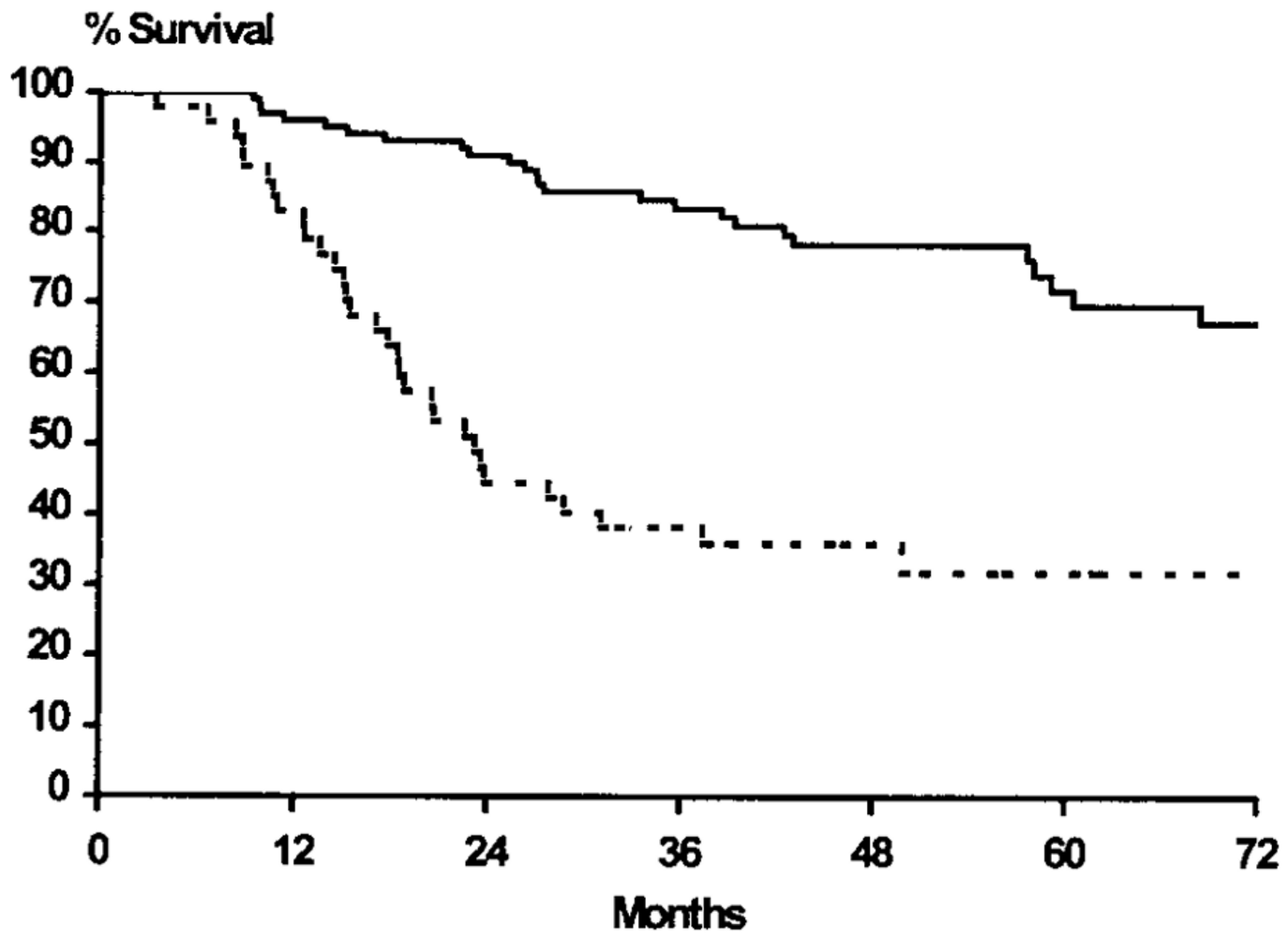




- After 3 courses of GDP: No significant response
- She received 3 courses of ICE: Complete response
- HDCT + Stem cell rescue (Feb 2016)

Intensive Salvage Therapy With High-Dose Chemotherapy for Patients With Advanced Hodgkin's Disease in Relapse or Failure After Initial Chemotherapy: Results of the Groupe d'Études des Lymphomes de l'Adulte H89 Trial

By Christophe Fermé, Nicolas Mounier, Marine Diviné, Pauline Brice, Aspasia Stamatoullas, Oumedaly Reman, Laurent Voillat, Jérôme Jaubert, Pierre Lederlin, Philippe Colin, Françoise Berger, and Gilles Salles



What is your choice in this situation?

1. Active surveillance

2. Post HSCT Brentuximab Vedotin consolidation

3. Post HSCT PD-1 inhibitor

Biol Blood Marrow Transplant 19 (2013) 1740–1744

Simplified Validated Prognostic Model for Progression-Free Survival after Autologous Transplantation for Hodgkin Lymphoma*

Theresa Hahn [1], Philip L. McCarthy [1], Jeanette Carreras [2], Mei-Jie Zhang [2], Hillard M. Lazarus [3], Ginna G. Laport [4], Silvia Montoto [5], Parameswaran N. Hari [2,*]

Multivariate Model for the Risk of Treatment Failure (1-PFS or the Risk of Relapse or Death)

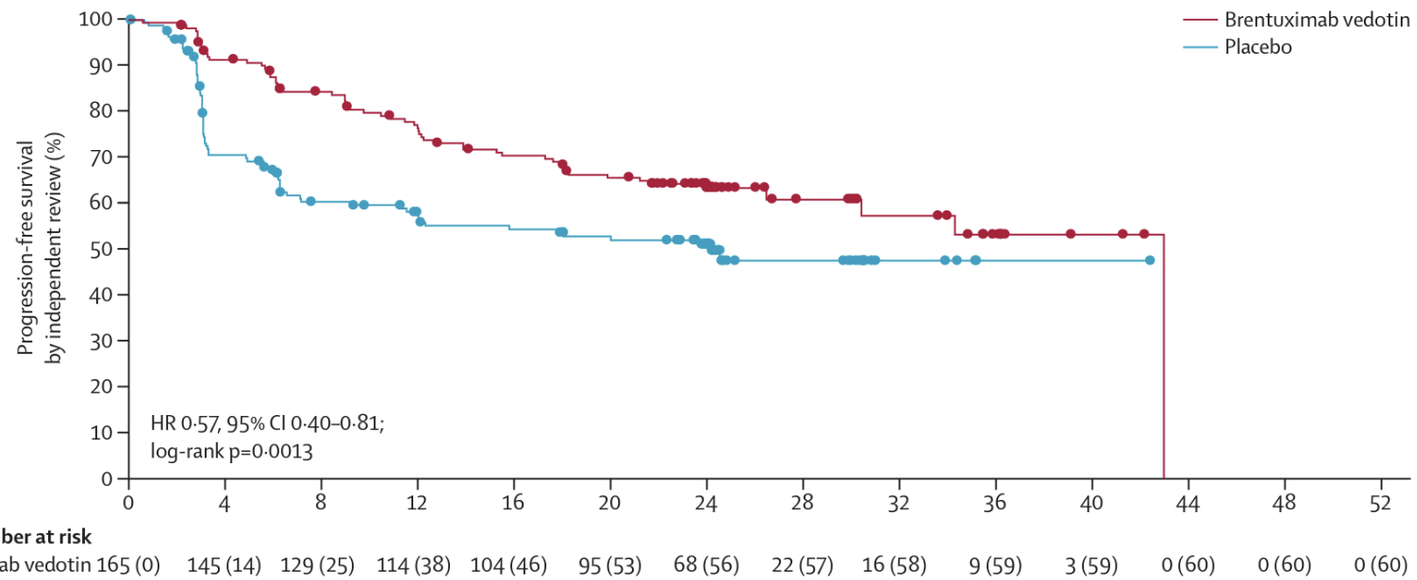
Variable	RR of Treatment Failure (95% Confidence Interval)	*P*	Score
Number of prior chemotherapy regimens: 3-5 vs. 1-2	1.80 (1.31-2.47)	.0003	2
Extranodal involvement before AHCT: yes vs. no	1.77 (1.24-2.53)	.0018	2
Karnofsky score before AHCT: <90 vs. 90-100	1.47 (1.04-2.07)	.0275	1
Chemotherapy-sensitivity pre-AHCT: resistant vs. sensitive	1.45 (1.01-2.07)	.0440	1

P values of additional risk factors considered in the model are as follows: HL histology ($P = .6295$), B symptoms at diagnosis ($P = .1516$), relapse/primary induction failure at AHCT ($P = .2025$), elevated lactate dehydrogenase at AHCT ($P = .1319$), ≥5 cm mass at AHCT ($P = .9553$), age >40 ($P = .2700$), and <12 months from diagnosis to transplant ($P = .2433$).

low-risk group (score 0)
intermediate-risk group (score 1 to 3)
high-risk group (score 4 to 6).

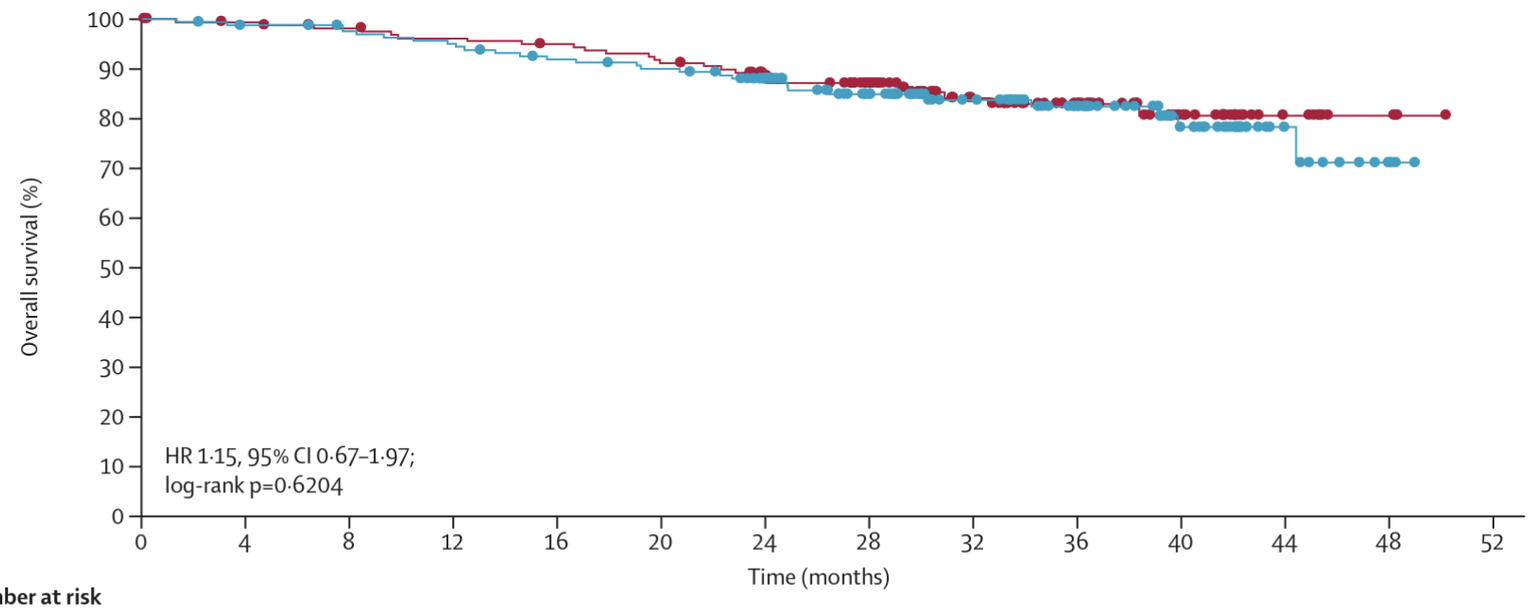
Brentuximab vedotin as consolidation therapy after autologous stem-cell transplantation in patients with Hodgkin's lymphoma at risk of relapse or progression (AETHERA): a randomised, double-blind, placebo-controlled, phase 3 trial

Craig H Moskowitz, Auayporn Nademanee, Tamas Masszi, Edward Agura, Jerzy Holowiecki, Muneer H Abidi, Andy I Chen, Patrick Stiff, Alessandro M Gianni, Angelo Carella, Dzhelil Osmanov, Veronika Bachanova, John Sweetenham, Anna Sureda, Dirk Huebner, Eric L Sievers, Andy Chi, Emily K Larsen, Naomi N Hunder, Jan Walewski, for the AETHERA Study Group



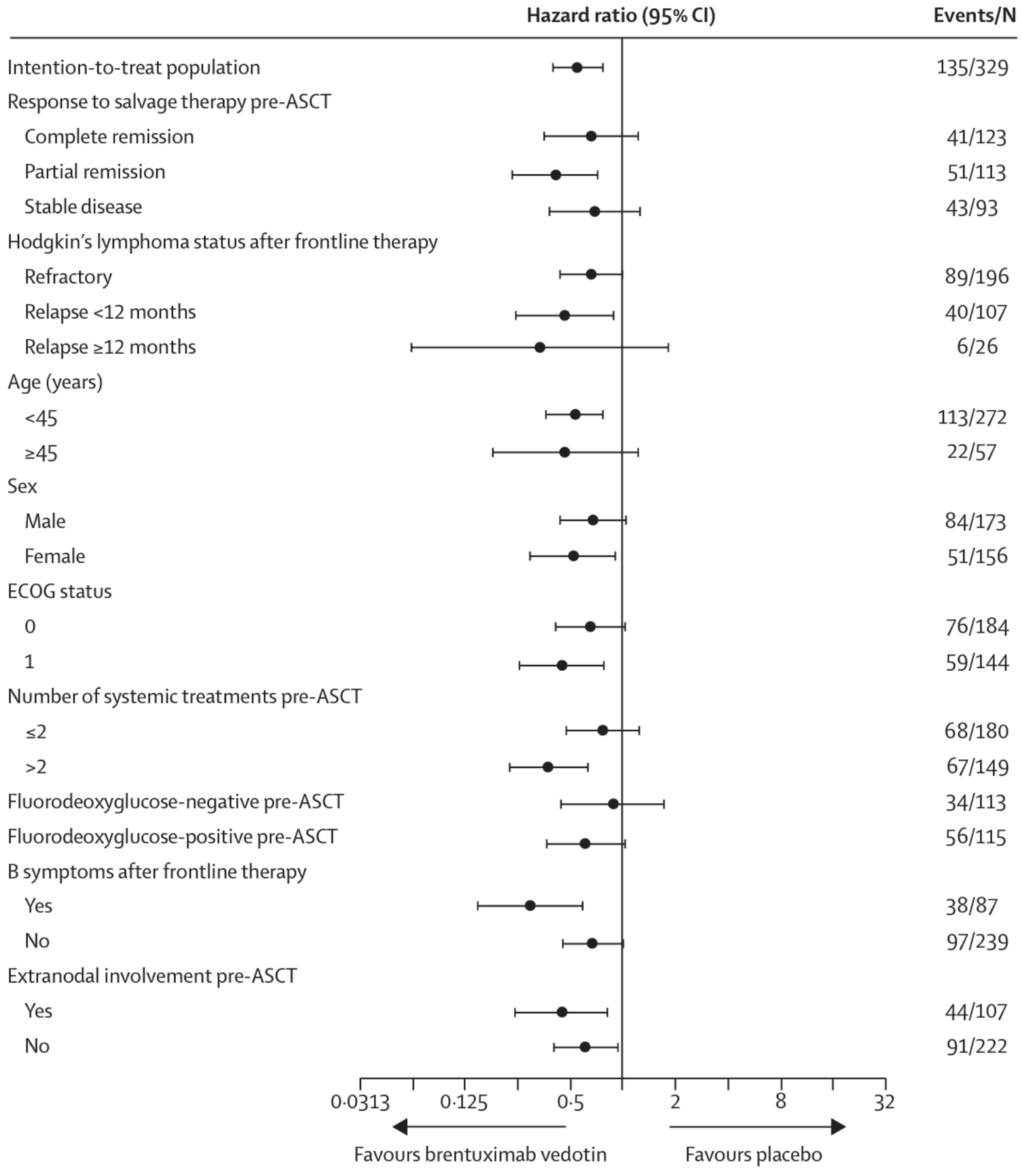
Number at risk

Brentuximab vedotin 165 (0)	145 (14)	129 (25)	114 (38)	104 (46)	95 (53)	68 (56)	22 (57)	16 (58)	9 (59)	3 (59)	0 (60)	0 (60)	0 (60)
Placebo 164 (0)	108 (46)	85 (61)	75 (66)	71 (69)	65 (72)	44 (73)	17 (75)	5 (75)	1 (75)	1 (75)	0 (75)	0 (75)	0 (75)



Number at risk

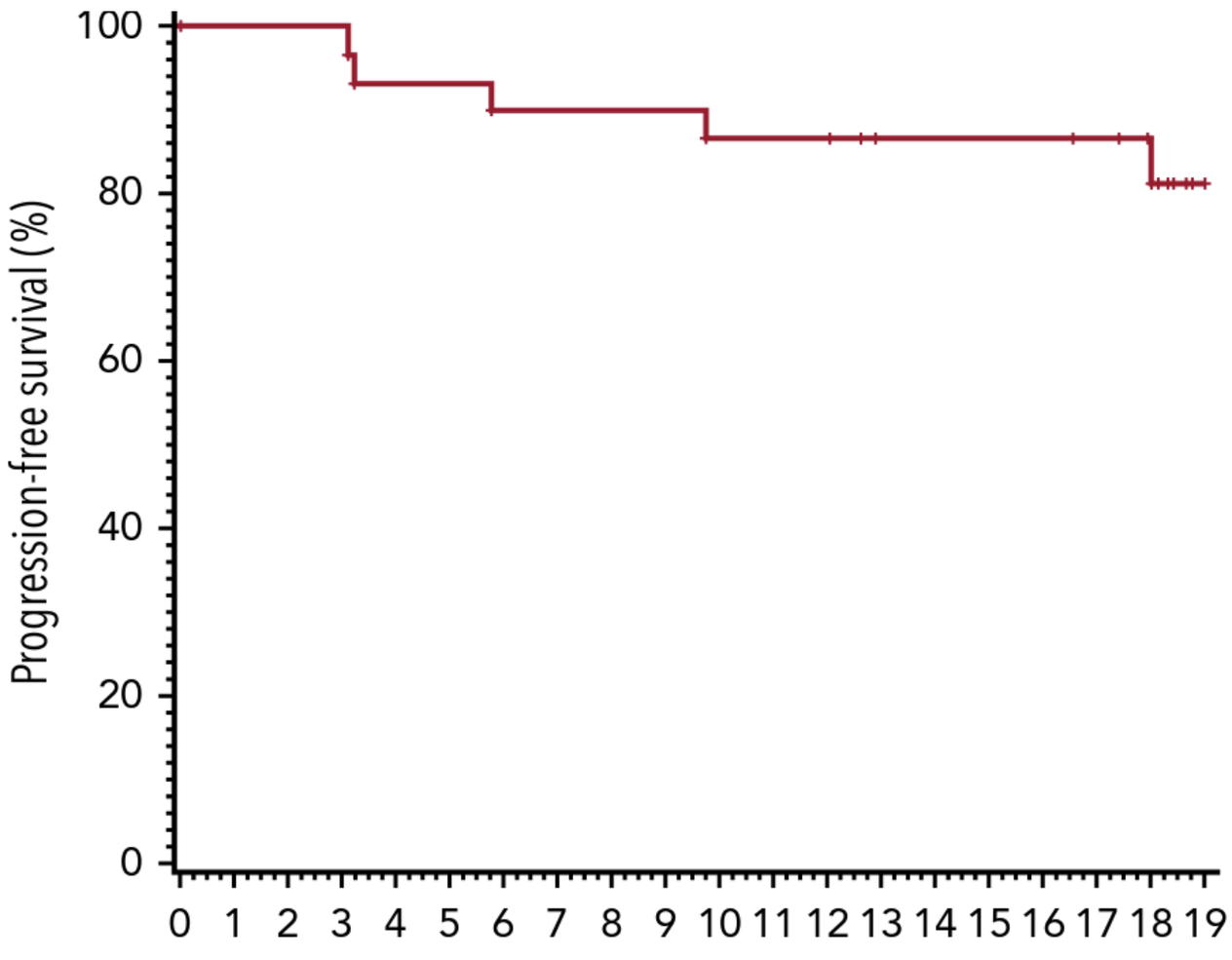
Brentuximab vedotin 165 (0)	160 (2)	156 (4)	152 (8)	145 (13)	141 (16)	125 (19)	97 (23)	72 (24)	57 (25)	35 (27)	12 (27)	4 (28)	0 (28)
Placebo 164 (0)	160 (1)	156 (3)	152 (6)	149 (8)	143 (14)	131 (18)	104 (20)	70 (23)	52 (24)	29 (25)	10 (25)	4 (25)	0 (25)


Hazard ratio (95% CI)
Events/N
Intention-to-treat population 135/329
Response to salvage therapy pre-ASCT
Complete remission 41/123
Partial remission 51/113
Stable disease 43/93
Hodgkin's lymphoma status after frontline therapy
Refractory 89/196
Relapse <12 months 40/107
Relapse ≥12 months 6/26
Age (years)
<45 113/272
≥45 22/57
Sex
Male 84/173
Female 51/156
ECOG status
0 76/184
1 59/144
Number of systemic treatments pre-ASCT
≤2 68/180
>2 67/149
Fluorodeoxyglucose-negative pre-ASCT 34/113
Fluorodeoxyglucose-positive pre-ASCT 56/115
B symptoms after frontline therapy
Yes 38/87
No 97/239
Extranodal involvement pre-ASCT
Yes 44/107
No 91/222
0·0313
0·125
0·5
2
8
32
Favours brentuximab vedotin
Favours placebo

CLINICAL TRIALS AND OBSERVATIONS

PD-1 blockade with pembrolizumab for classical Hodgkin lymphoma after autologous stem cell transplantation

Philippe Armand,[1] Yi-Bin Chen,[2] Robert A. Redd,[3] Robin M. Joyce,[4] Jad Bsat,[1] Erin Jeter,[1] Reid W. Merryman,[1] Kimberly C. Coleman,[1] Parastoo B. Dahi,[5] Yago Nieto,[6] Ann S. LaCasce,[1] David C. Fisher,[1] Samuel Y. Ng,[1] Oreofe O. Odejide,[1] Arnold S. Freedman,[1] Austin I. Kim,[1] Jennifer L. Crombie,[1] Caron A. Jacobson,[1] Eric D. Jacobsen,[1] Jeffrey L. Wong,[1] Sanjay S. Patel,[7] Jerome Ritz,[1] Scott J. Rodig,[7] Margaret A. Shipp,[1] and Alex F. Herrera[8]



- Inguinal LAP (Feb 2017)
- Bx : cHL
- CT scan: multiple sites LAPs
- GVD for 3 courses : progressive disease (Stage IV)

What is your recommendation?

1. Brentuximab Vedotin

2. Nivolumab

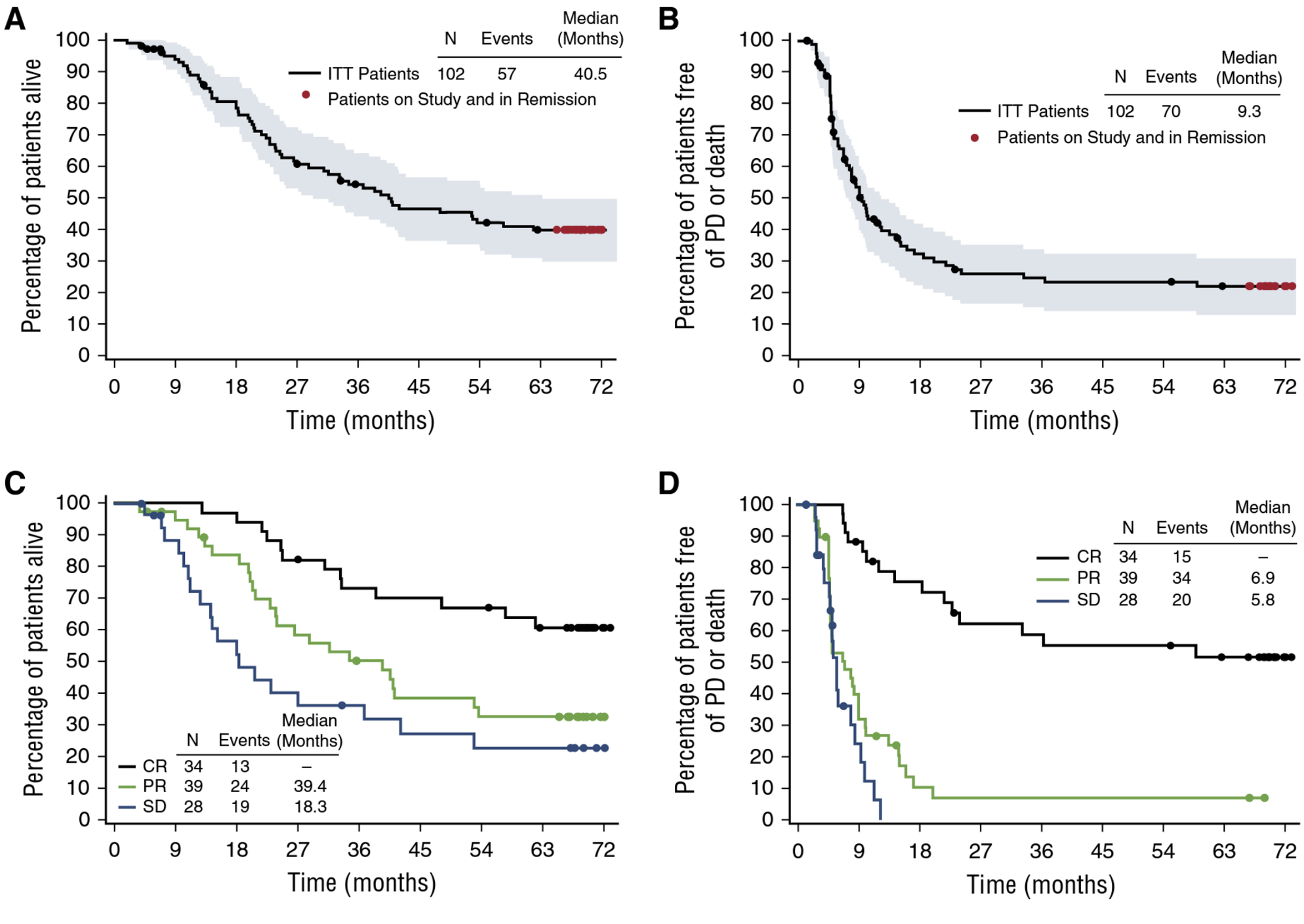
3. Pembrolizumab

- She received 4 times Brentuximab Vedotin: No response
- Treatment with Opdivo started (Jan 2018)
- Very good partial response (hyper-metabolic lesions in liver, T8 and L2, inguinal LAP)
- She has a full matched sibling donor (her sister)

Immunotherapy vs. Allo-HSCT

Five-year survival and durability results of brentuximab vedotin in patients with relapsed or refractory Hodgkin lymphoma

Robert Chen,[1,*] Ajay K. Gopal,[2,*] Scott E. Smith,[3] Stephen M. Ansell,[4] Joseph D. Rosenblatt,[5] Kerry J. Savage,[6] Joseph M. Connors,[6] Andreas Engert,[7] Emily K. Larsen,[8] Dirk Huebner,[9] Abraham Fong,[8] and Anas Younes[10]

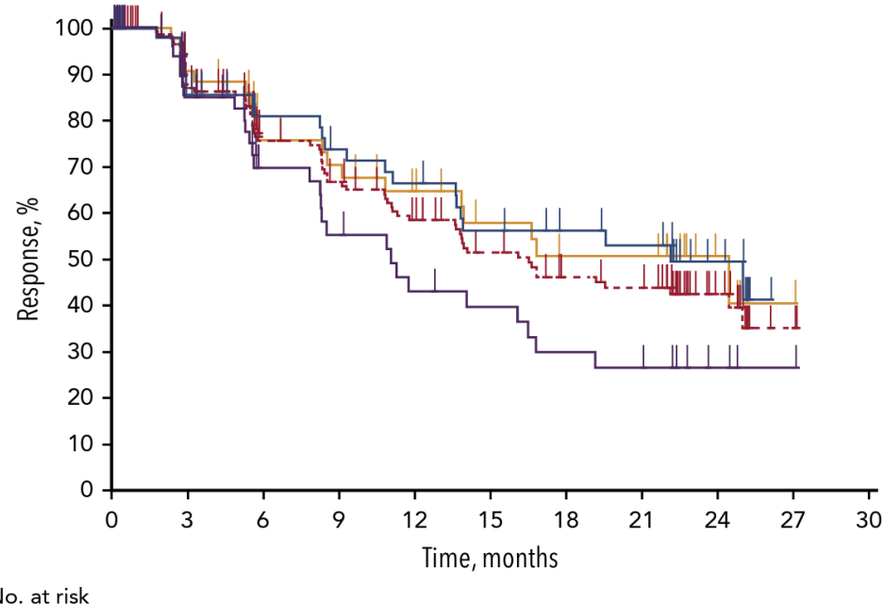


Pembrolizumab in relapsed or refractory Hodgkin lymphoma: 2-year follow-up of KEYNOTE-087

Robert Chen,[1,*] Pier Luigi Zinzani,[2,*] Hun Ju Lee,[3] Philippe Armand,[4] Nathalie A. Johnson,[5] Pauline Brice,[6] John Radford,[7] Vincent Ribrag,[8] Daniel Molin,[9] Theodoros P. Vassilakopoulos,[10] Akihiro Tomita,[11] Bastian von Tresckow,[12] Margaret A. Shipp,[4] Jianxin Lin,[13] Eunhee Kim,[13] Akash Nahar,[13] Arun Balakumaran,[13] and Craig H. Moskowitz[14]

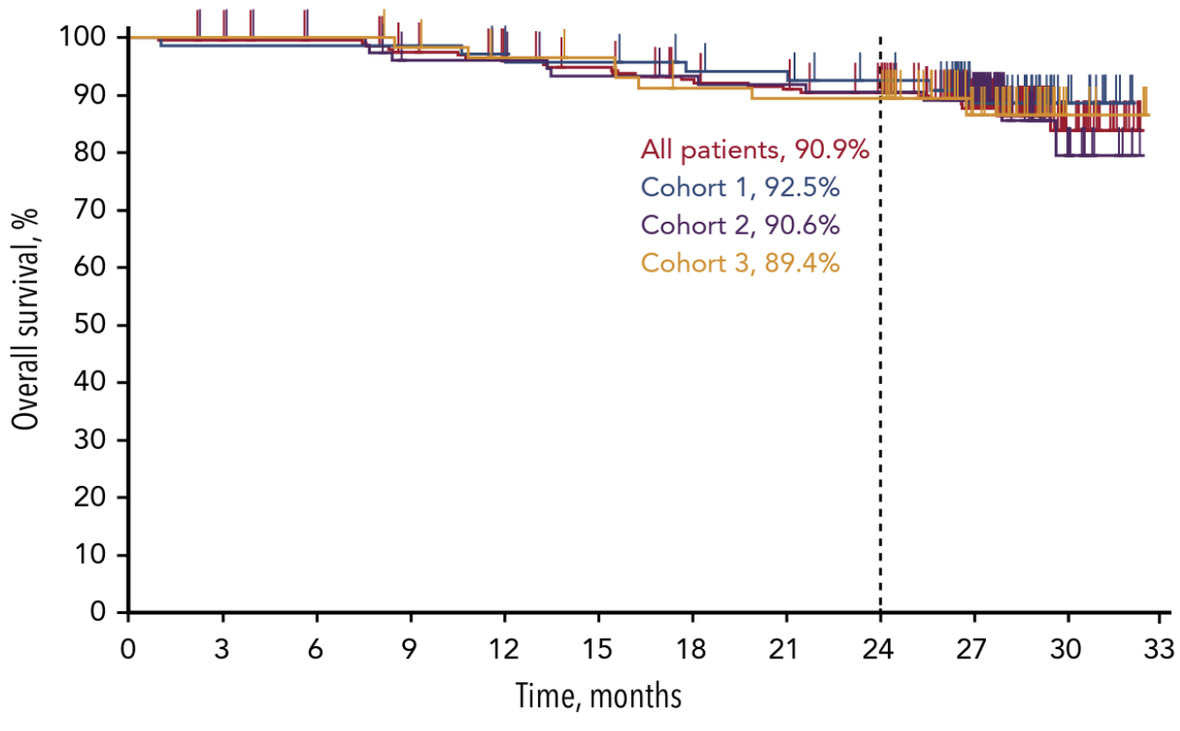
	Cohort 1 (n = 69): after ASCT/BV		Cohort 2 (n = 81): ineligible for ASCT and treatment failure with BV therapy		Cohort 3 (n = 60): no BV after ASCT		All patients (N = 210)	
	n (%)	95% CI*	n (%)	95% CI*	n (%)	95% CI*	n (%)	95% CI*
ORR	53 (76.8)	65.1-86.1	54 (66.7)	55.3-76.8	44 (73.3)	60.3-83.9	151 (71.9)	65.3-77.9
CR†	18 (26.1)	16.3-38.1	21 (25.9)	16.8-36.9	19 (31.7)	20.3-45.0	58 (27.6)	21.7-34.2
PR	35 (50.7)	38.4-63.0	33 (40.7)	29.9-52.2	25 (41.7)	29.1-55.1	93 (44.3)	37.5-51.3
SD	9 (13.0)	6.1-23.3	7 (8.6)	3.5-17.0	7 (11.7)	4.8-22.6	23 (11.0)	7.1-16.0
PD	5 (7.2)	2.4-16.1	18 (22.2)	13.7-32.8	9 (15.0)	7.1-26.6	32 (15.2)	10.7-20.8
No assessment	2 (2.9)	0.4-10.1	2 (2.5)	0.3-8.6	0 (0)	—	4 (1.9)	0.5-4.8

	Responders, n	TTR, median (range), mo	DOR,* median (range), mo	DOR* ≥24 mo, %
All responders	151	2.8 (2.1-16.5)	16.5 (0.0+ to 27.0+)	42.5
Cohort 1	53	2.7 (2.1-12.9)	22.1 (0.0+ to 26.0+)	49.6
Cohort 2	54	2.8 (2.2-11.0)	11.1 (0.0+ to 27.0+)	26.4
Cohort 3	44	2.8 (2.6-16.5)	24.4 (0.0+ to 27.0+)	50.7



No. at risk

151	117	87	75	61	50	41	37	16	1	0
53	41	34	30	27	22	19	17	8	0	0
54	37	24	19	14	12	9	7	3	1	0
44	39	29	26	20	16	13	13	5	0	0



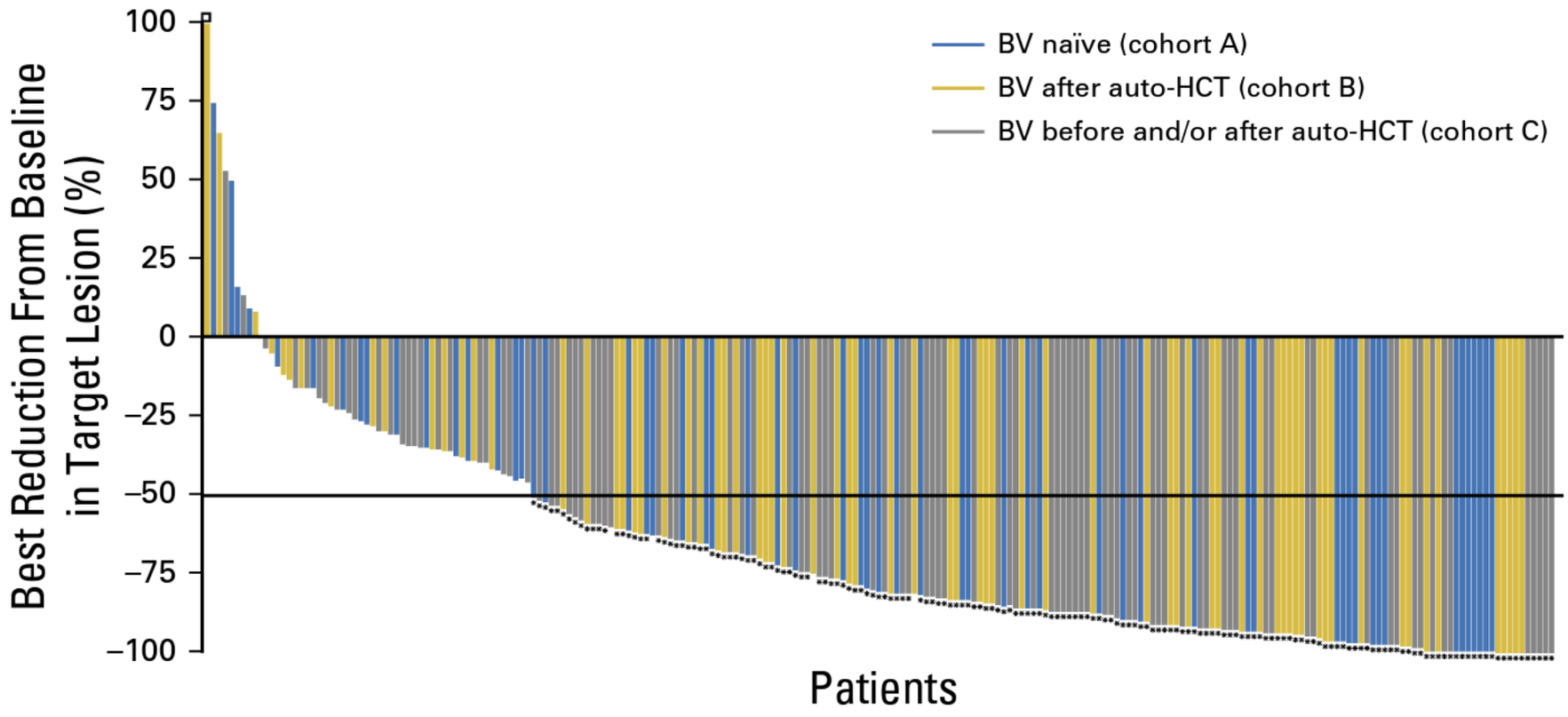
No. at risk

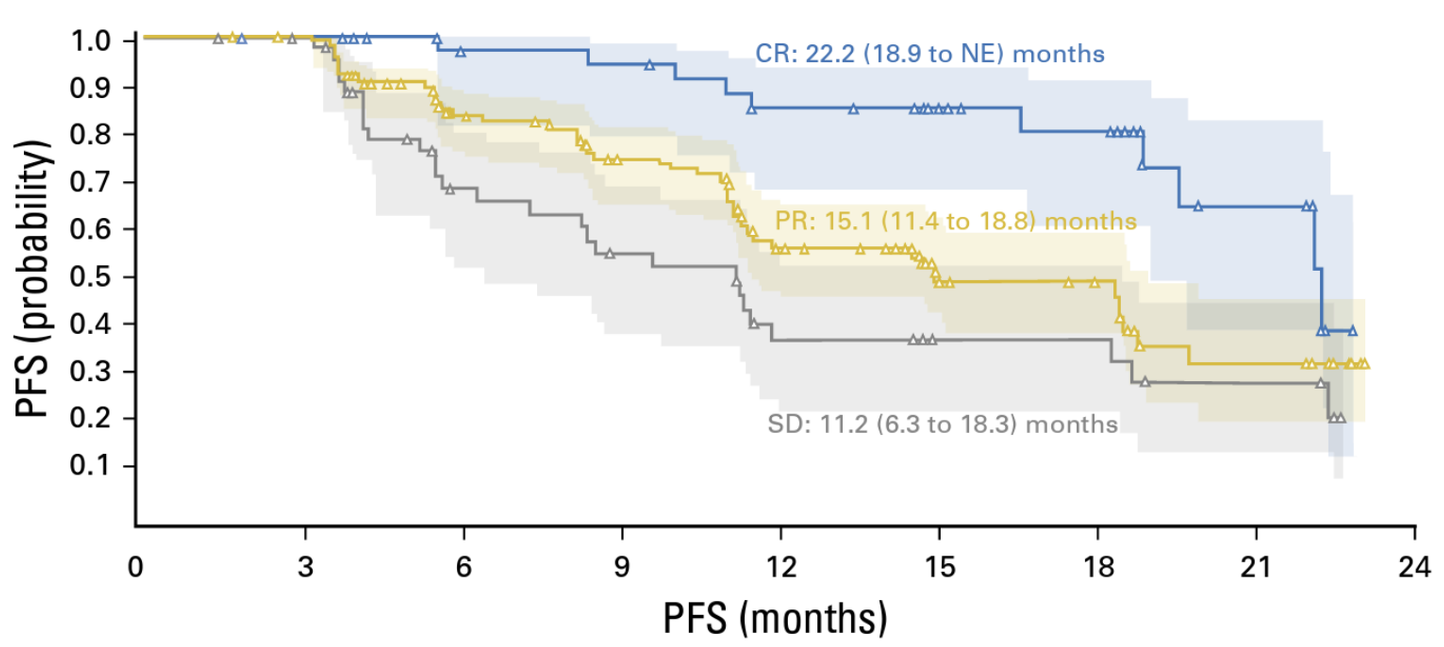
210	207	205	198	190	186	178	175	170	115	26	0
69	68	68	68	64	64	61	60	56	40	11	0
81	79	77	72	71	68	67	66	65	47	10	0
60	60	60	58	55	54	50	49	49	28	5	0

Nivolumab for Relapsed/Refractory Classic Hodgkin Lymphoma After Failure of Autologous Hematopoietic Cell Transplantation: Extended Follow-Up of the Multicohort Single-Arm Phase II CheckMate 205 Trial

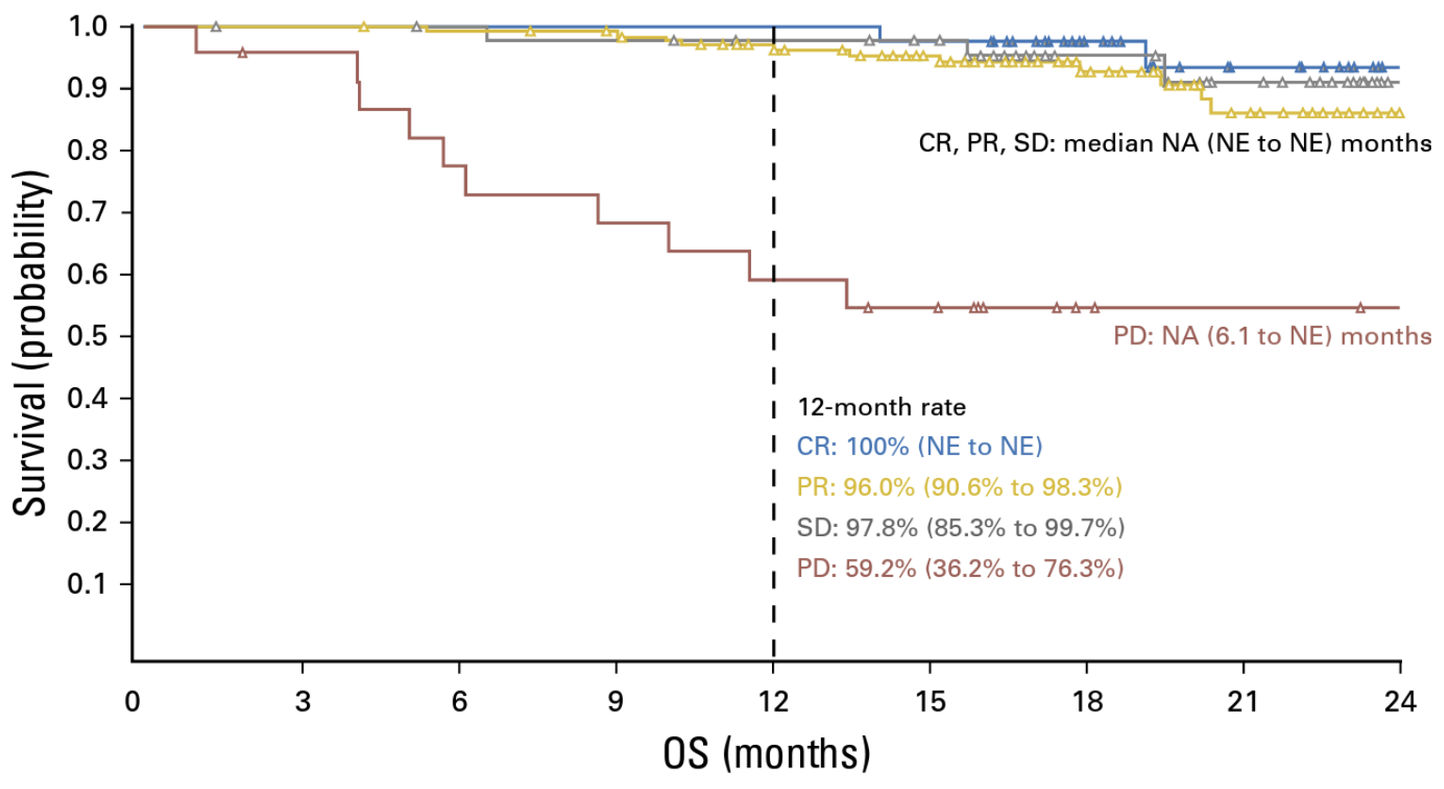
Philippe Armand, Andreas Engert, Anas Younes, Michelle Fanale, Armando Santoro, Pier Luigi Zinzani, John M. Timmerman, Graham P. Collins, Radhakrishnan Ramchandren, Jonathon B. Cohen, Jan Paul De Boer, John Kuruvilla, Kerry J. Savage, Marek Trneny, Margaret A. Shipp, Kazunobu Kato, Anne Sumbul, Benedetto Farsaci, and Stephen M. Ansell

Response	Protocol-Specified Analysis by Cohort			All patients (N = 243)
	BV Naïve: Cohort A (n = 63)	BV After Auto-HCT: Cohort B (n = 80)	BV Before and/or After Auto-HCT: Cohort C (n = 100)	
ORR, % (95% CI)	65 (52-77)	68 (56-78)	73 (63-81)	69 (63-75)
Best overall response				
Complete remission	18 (29)	10 (13)	12 (12)	40 (16)
Partial remission	23 (37)	44 (55)	61 (61)	128 (53)
Stable disease	15 (24)	17 (21)	15 (15)	47 (19)
Progressive disease	7 (11)	6 (8)	10 (10)	23 (9)
Unable to determine	0	3 (4)	2 (2)	5 (2)





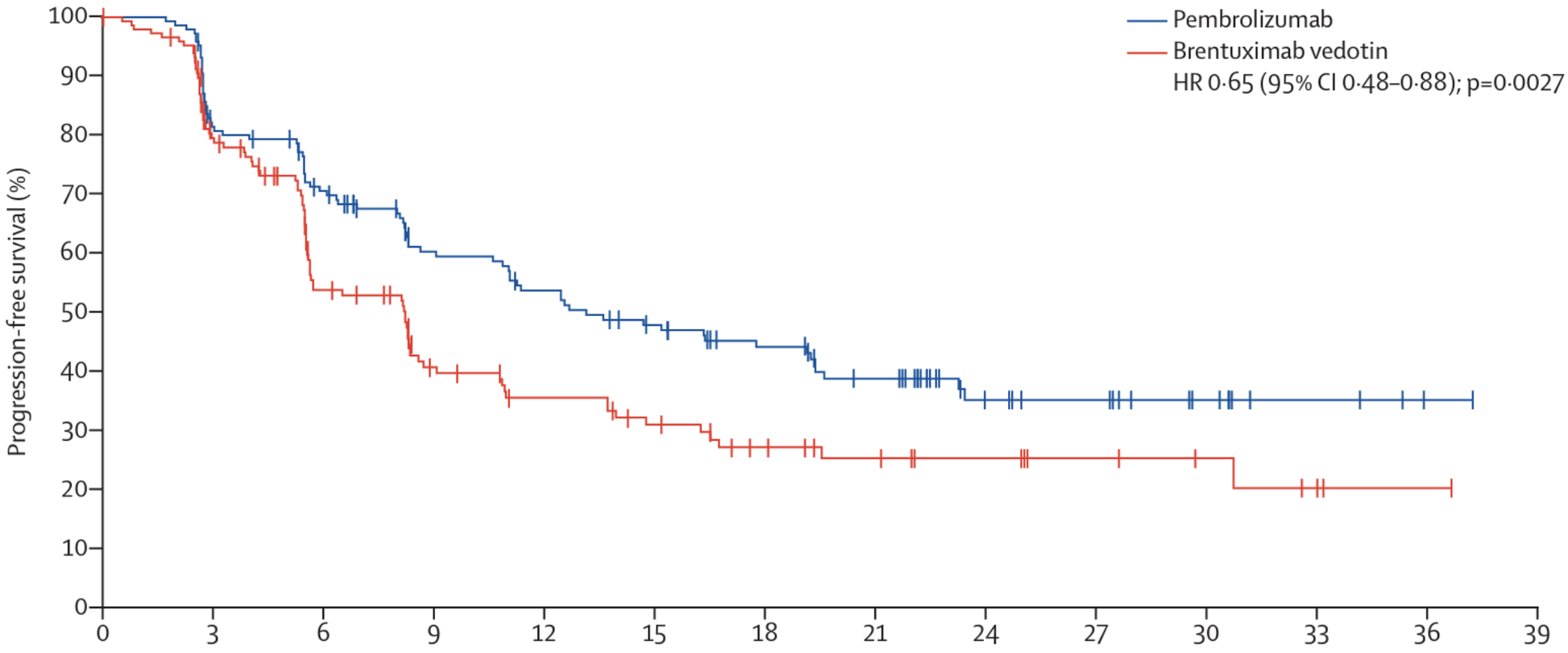
No. at risk:									
CR	40	40	33	32	27	20	16	7	0
PR	128	126	89	71	46	25	21	8	0
SD	47	44	25	19	11	8	8	5	0



No. at risk:									
CR	40	40	40	40	40	39	26	16	7
PR	128	128	126	123	113	97	59	34	10
SD	47	46	45	44	42	39	25	16	3
PD	23	21	17	15	13	11	5	4	3

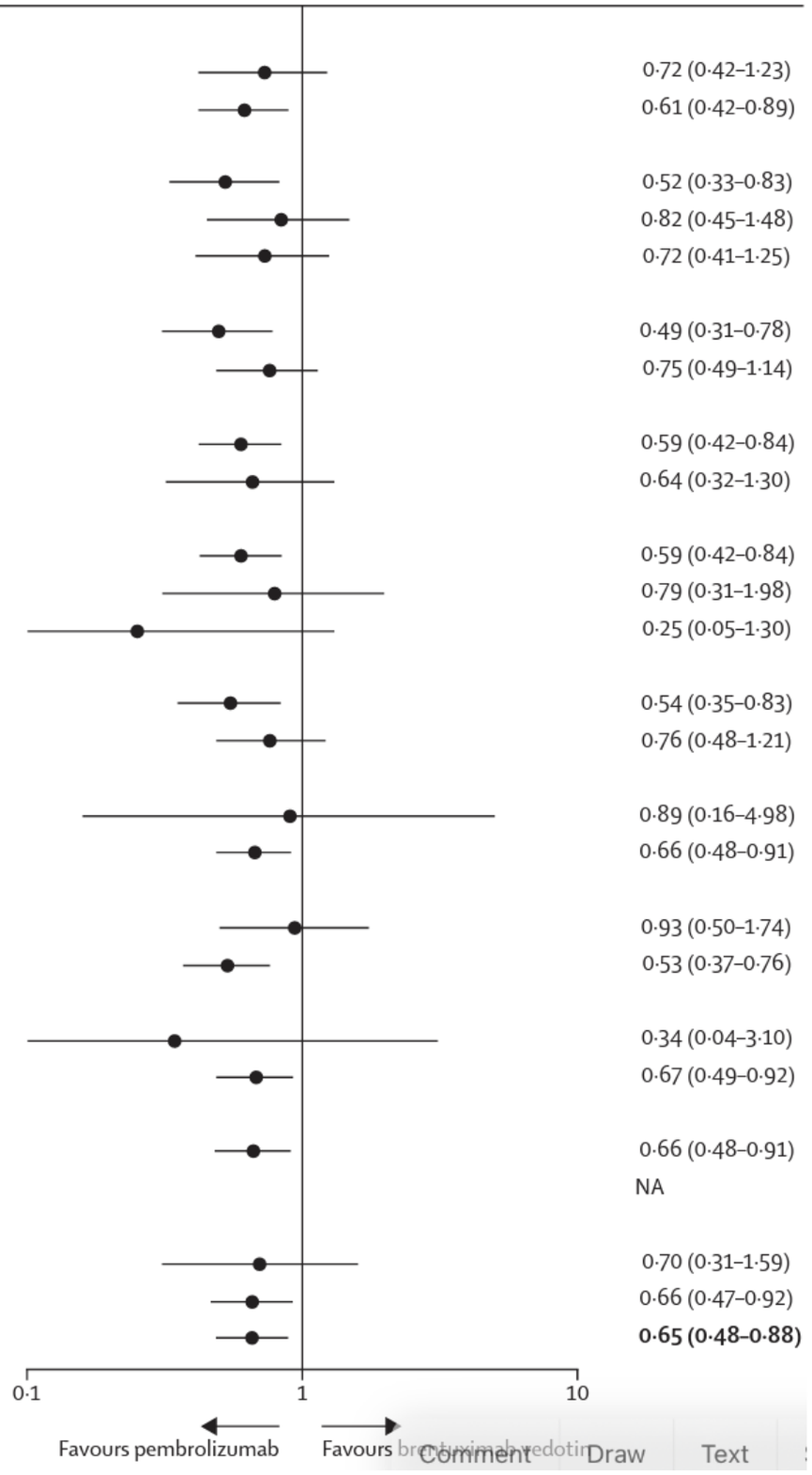
Pembrolizumab versus brentuximab vedotin in relapsed or refractory classical Hodgkin lymphoma (KEYNOTE-204): an interim analysis of a multicentre, randomised, open-label, phase 3 study

*John Kuruvilla, Radhakrishnan Ramchandren, Armando Santoro, Ewa Paszkiewicz-Kozik, Robin Gasiorowski, Nathalie A Johnson, Laura Maria Fogliatto, Iara Goncalves, Jose S R de Oliveira, Valeria Buccheri, Guilherme F Perini, Neta Goldschmidt, Iryna Kriachok, Michael Dickinson, Mieczyslaw Komarnicki, Andrew McDonald, Muhit Ozcan, Naohiro Sekiguchi, Ying Zhu, Akash Nahar, Patricia Marinello, Pier Luigi Zinzani, on behalf of the KEYNOTE-204 investigators**



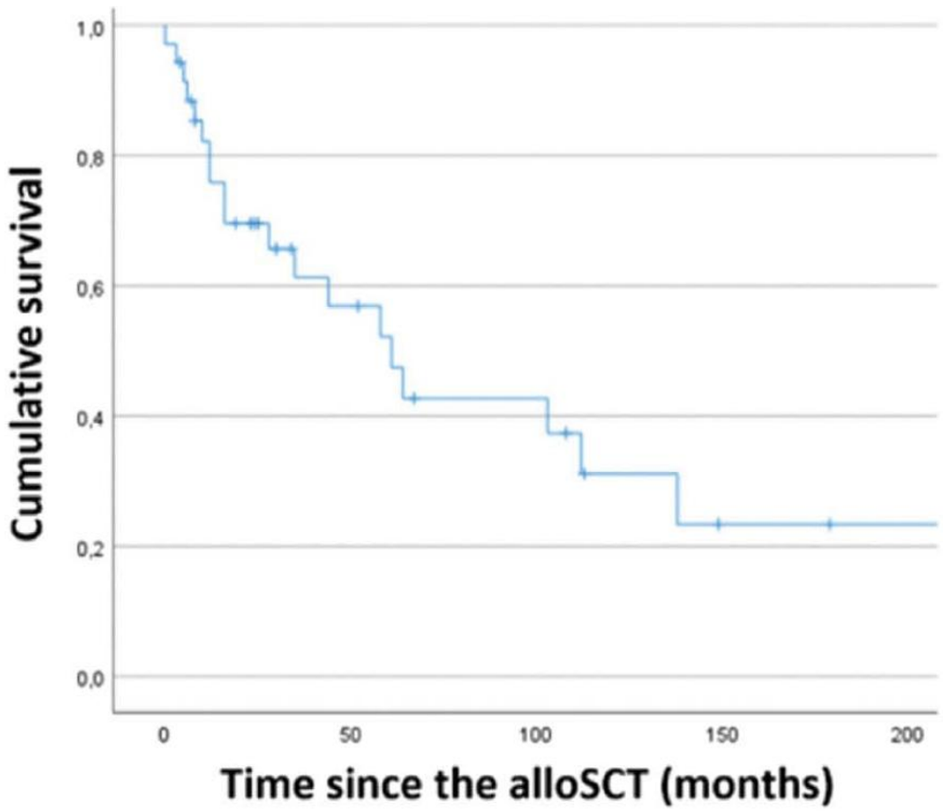
Number at risk (number censored)													
Pembrolizumab	151 (0)	116 (9)	96 (13)	74 (22)	65 (23)	55 (26)	44 (33)	35 (37)	18 (52)	15 (55)	9 (61)	4 (66)	1 (69)	0 (70)
Brentuximab vedotin	153 (0)	103 (22)	63 (30)	41 (38)	32 (42)	26 (44)	19 (48)	14 (52)	10 (56)	7 (59)	5 (61)	2 (63)	1 (64)	0 (65)

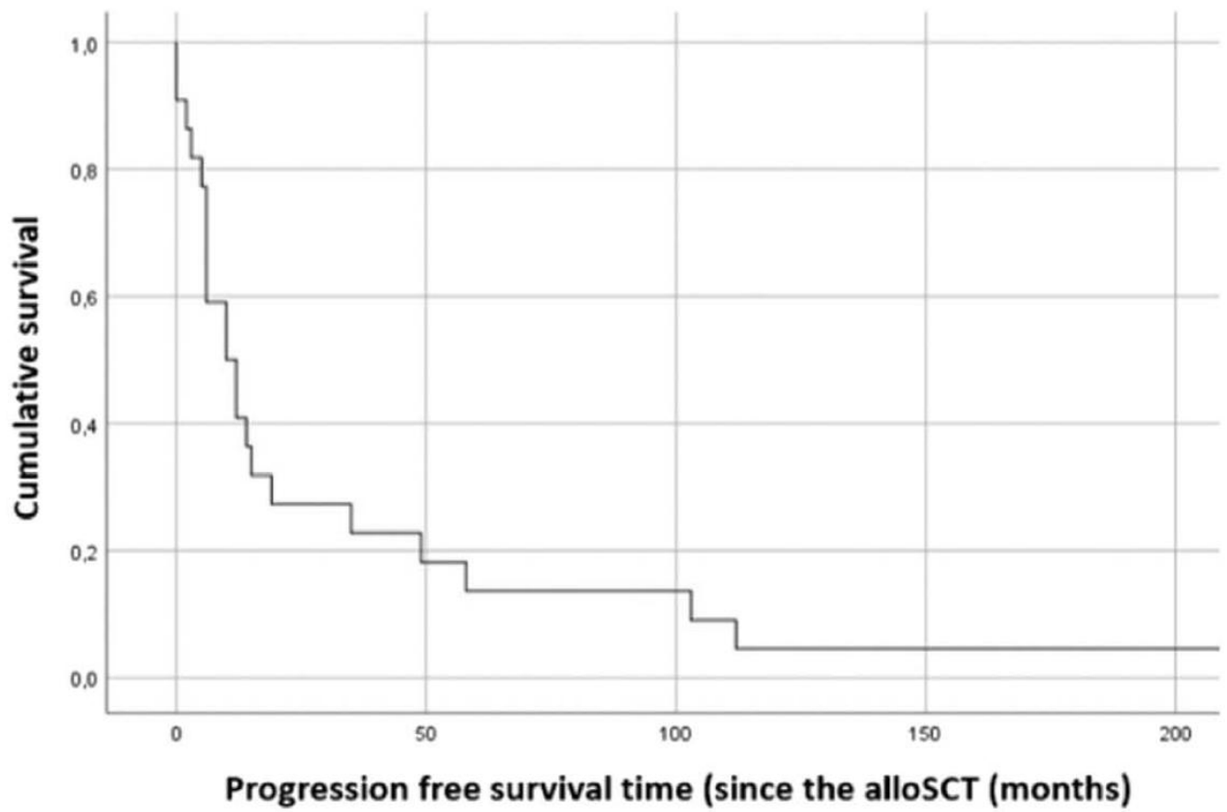
	Pembrolizumab group		Brentuximab vedotin group		HR (95% CI)
	n/N	Median progression-free survival (95% CI)	n/N	Median progression-free survival (95% CI)	
Previous autologous stem-cell transplantation					
Yes	30/56	14·7 (8·3–NR)	27/56	10·8 (5·8–19·6)	0·72 (0·42–1·23)
No	51/95	12·5 (8·3–19·4)	61/97	5·7 (5·5–8·3)	0·61 (0·42–0·89)
Disease status after front-line therapy					
Primary refractory	34/61	12·5 (8·2–23.4)	38/62	5·5 (3·1–8·2)	0·52 (0·33–0·83)
Relapsed <12 months	22/42	16·4 (8·3–NR)	24/42	11·0 (8·2–16·6)	0·82 (0·45–1·48)
Relapsed ≥12 months	25/48	13·6 (7·0–NR)	26/49	8.3 (5·6–14·0)	0·72 (0·41–1·25)
Sex					
Female	38/67	15·2 (11·1–19·6)	43/63	5·7 (5·6–8·8)	0·49 (0·31–0·78)
Male	43/84	11·4 (8·2–NR)	45/90	8·4 (5·8–14·0)	0·75 (0·49–1·14)
Age, years					
<65	60/124	19·3 (11·3–NR)	72/131	8·3 (5·7–11·0)	0·59 (0·42–0·84)
≥65	21/27	8·2 (3·0–11·4)	16/22	5·5 (3·9–8·3)	0·64 (0·32–1·30)
Age, years					
<65	60/124	19·3 (11·3–NR)	72/131	8·3 (5·7–11·0)	0·59 (0·42–0·84)
≥65 to <75	16/18	8·0 (2·8–11·4)	10/16	5·7 (3·9–8·4)	0·79 (0·31–1·98)
≥75 to <85	5/9	8·3 (2·8–NR)	6/6	3·5 (0·9–14·8)	0·25 (0·05–1·30)
ECOG performance status					
0	40/86	19·4 (13·6–NR)	51/100	8·4 (5·8–11·0)	0·54 (0·35–0·83)
1	40/64	8·2 (5·6–12·5)	37/53	5·6 (4·3–8·3)	0·76 (0·48–1·21)
Patient in USA					
Yes	3/11	NR (2·8–NR)	6/13	8·6 (2·9–NR)	0·89 (0·16–4·98)
No	78/140	13·2 (9·1–19·4)	82/140	8·2 (5·6–8·4)	0·66 (0·48–0·91)
Patient in EU					
Yes	24/49	16·4 (6·4–NR)	19/46	8·3 (5·6–NR)	0·93 (0·50–1·74)
No	57/102	13·2 (9·1–19·4)	67/107	8·2 (5·6–9·1)	0·53 (0·37–0·76)
Previous use of brentuximab vedotin					
Yes	1/5	NR (2·9–NR)	6/10	5·6 (2·6–8·4)	0·34 (0·04–3·10)
No	80/146	12·7 (9·1–19·3)	82/143	8·3 (5·7–10·8)	0·67 (0·49–0·92)
PD-L1 status					
≥1%	78/142	12·7 (9·1–19·3)	77/133	8·3 (5·7–9·1)	0·66 (0·48–0·91)
<1%	NA	NA	1/3	NR (5·8–NR)	NA
Number of previous lines of therapy					
1	13/27	16·4 (8·3–NR)	13/28	8·4 (5·4–NR)	0·70 (0·31–1·59)
≥2	68/124	12·6 (8·7–19·4)	75/125	8·2 (5·6–8·8)	0·66 (0·47–0·92)
Overall	**81/151**	**13·2 (10·9–19·4)**	**88/153**	**8·3 (5·7–8·8)**	**0·65 (0·48–0·88)**



Allogeneic stem cell transplant in relapsed/ refractory Hodgkin lymphoma: A 21 years' experience

Maria Eduarda Couto[a,*], Carlos Pinho Vaz[a], Rosa Branca[a], Luís Leite[a], Gil Brás[a], Susana Roncon[b], Antonio Campos Junior[b]





Allogeneic Stem Cell Transplantation for Relapsed and Refractory Hodgkin Lymphoma: Real World Experience of a Single Center

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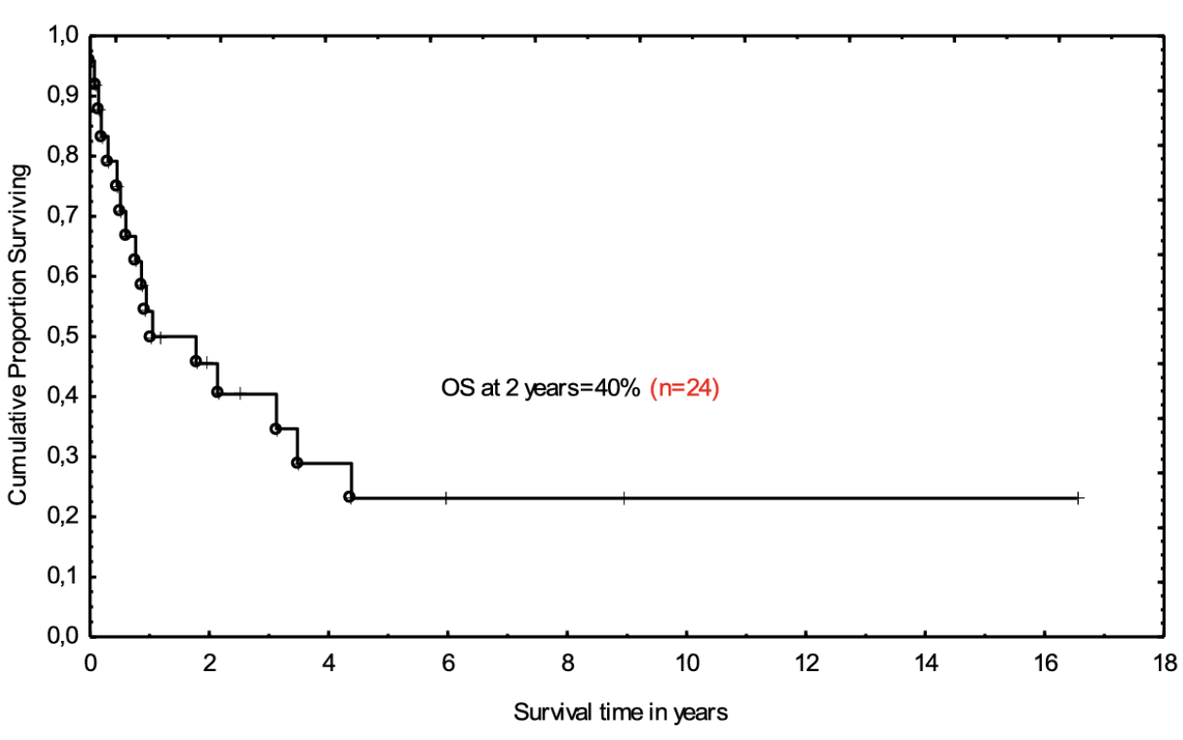
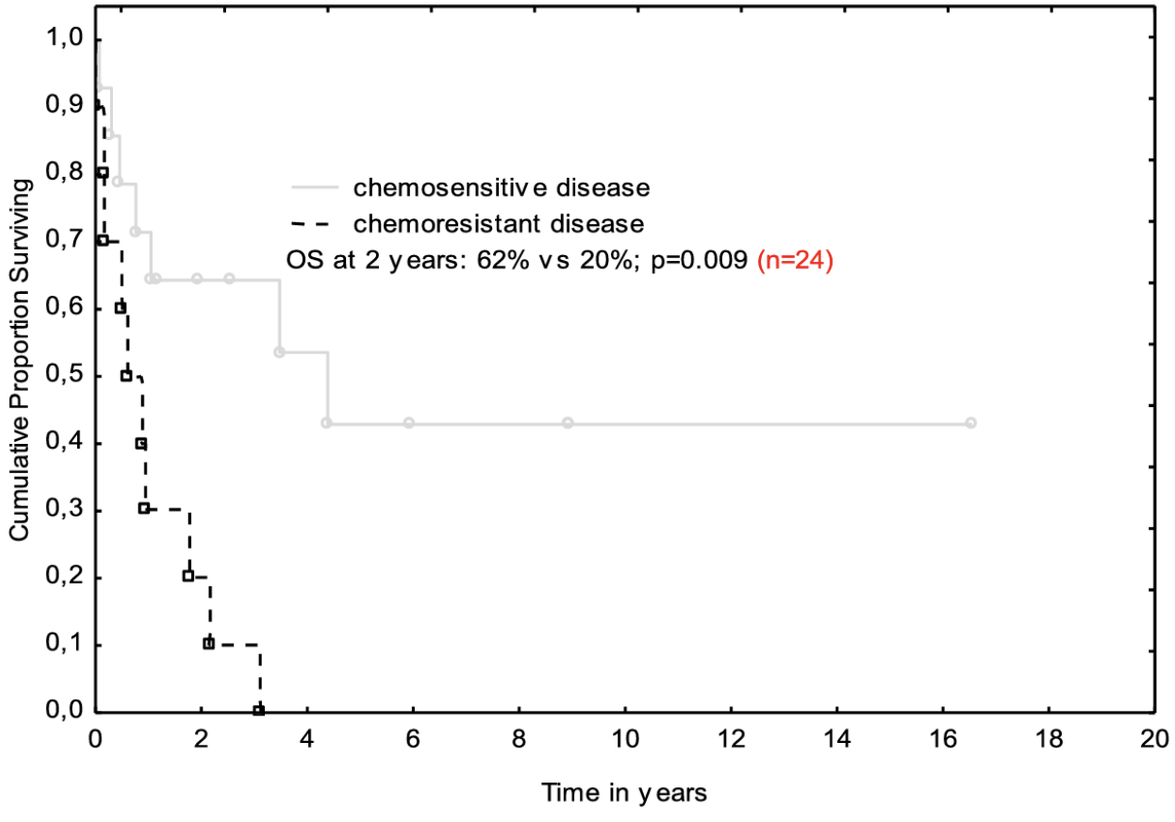
OS after allotransplantation for R/R HL depending on disease status at transplant





Review

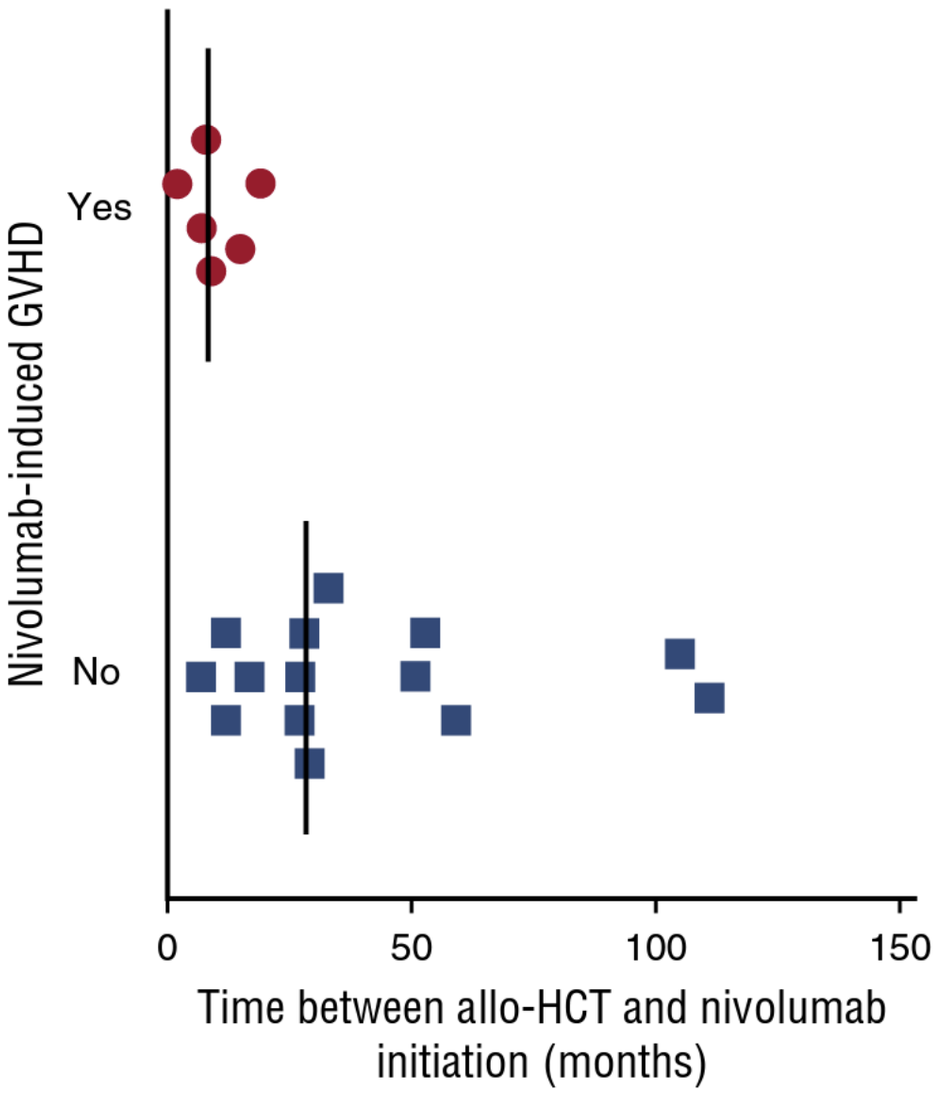
Reappraising the Role of Allogeneic Hematopoietic Stem Cell Transplantation in Relapsed and Refractory Hodgkin's Lymphoma: Recent Advances and Outcomes

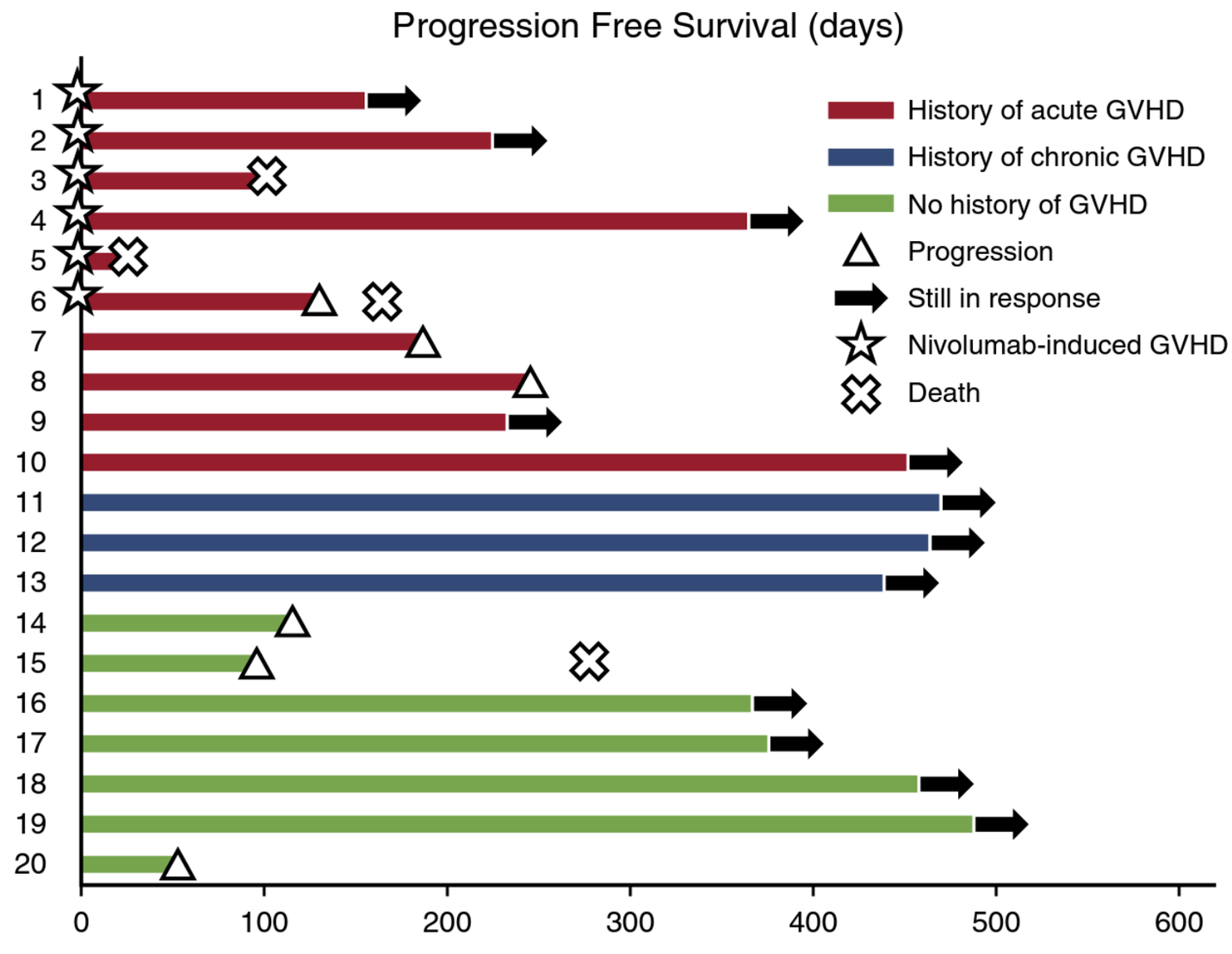
Taha Al-Juhaishi [1,*], Azra Borogovac [1], Sami Ibrahimi [1], Matthew Wieduwilt [1] and Sairah Ahmed [2]

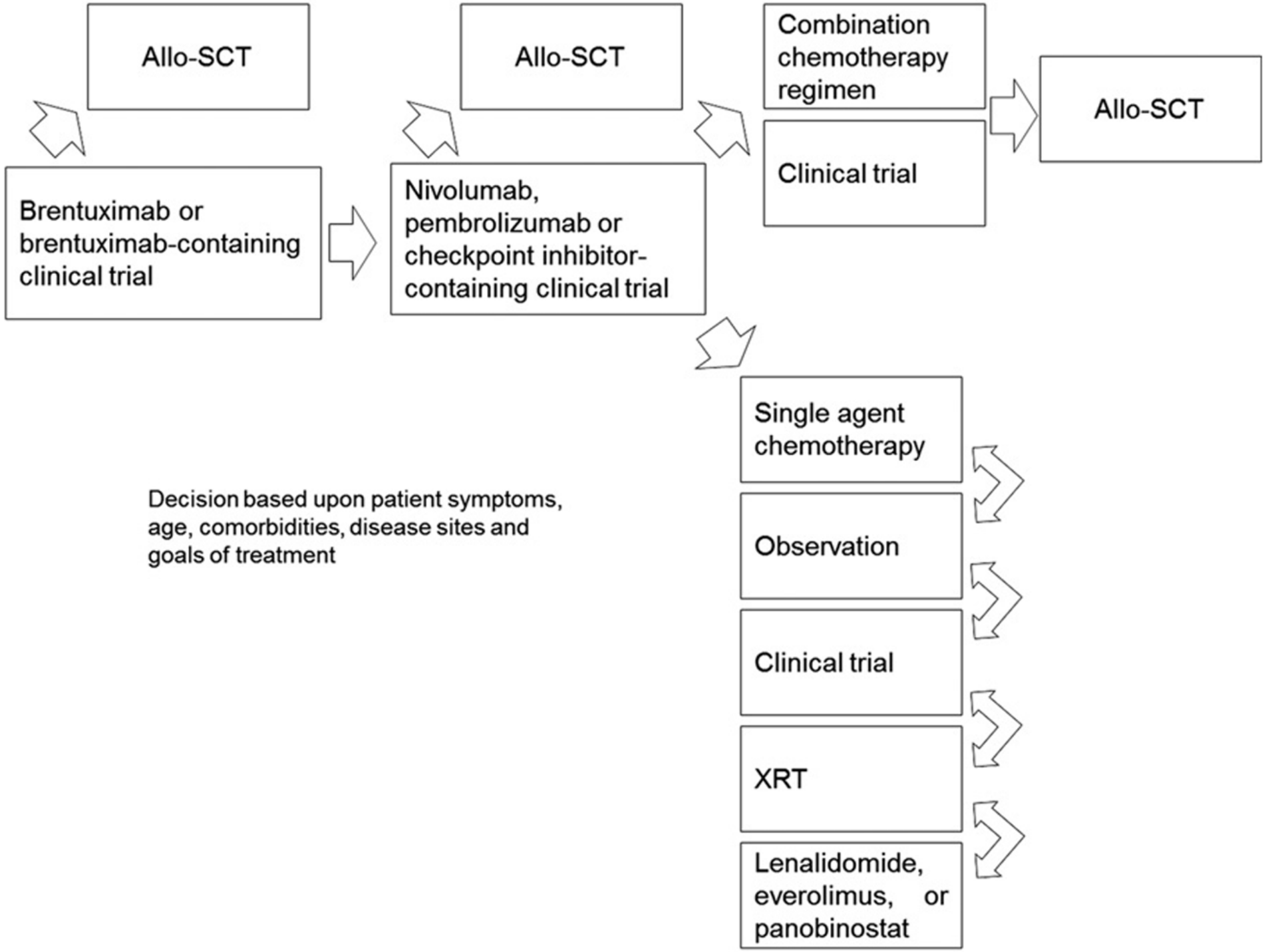
Study	Type	Number of Patients	Prior AHSCT	Donor Type	Conditioning	PFS	OS
Sureda et al. [34]	Retrospective registry (EBMT)	168	52%	MSD for more than 70%, rest are MUD	MAC 47%, RIC 53%	20% MAC and 18% RIC at 5 years	22% MAC and 28% RIC at 5 years
Anderlini et al. [35]	Single center prospective	58	83%	MSD 43%, 57% MUD	RIC 100% (fludarabine and Melphalan)	32% at 2 years	64% at 2 years
Robinson et al. [36]	Retrospective registry (EBMT)	285	80%	MSD 60%, MUD 33%	RIC 100% Fludarabine based (79.5%), low dose TBI (16%)	25% at 3 years	29% at 3 years
Devetten et al. [37]	Retrospective registry (CIBMTR)	143	89%	Unrelated 100% (matched in 77%)	RIC/NMA 100% Melphalan based 34%	20% at 2 years	37% at 2 years
Marcais et al. [38]	Multicenter retrospective in France	191	92%	MSD 60%, MUD 40%	RIC 100% Fludarabine and busulfan in 36%	39% at 3 years	63% at 3 years
Kako et al. [39]	Retrospective registry (Japanese society for HSCT)	122	67%	MSD 39% MUD 17%	MAC 30% RIC 62%	31%	66% at 3 years
Sarina et al. [40]	Retrospective multicenter in Italy	104	100%	MSD 55% MUD 32%	RIC 100% (Fludarabine based in 100%)	31% at 2 years	57% at 2 years

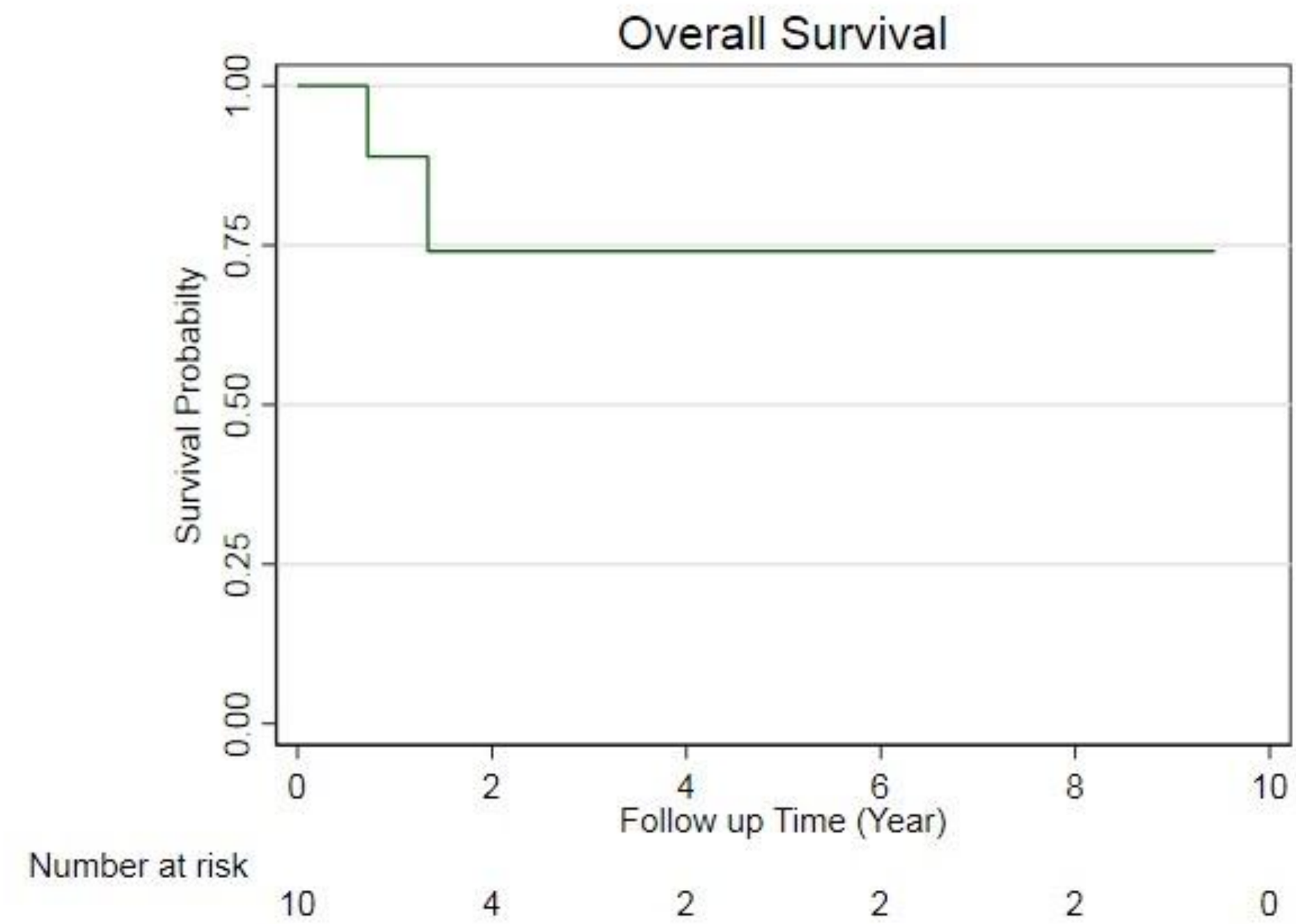
Efficacy and tolerability of nivolumab after allogeneic transplantation for relapsed Hodgkin lymphoma

Charles Herbaux,[1] Jordan Gauthier,[1] Pauline Brice,[2] Elodie Drumez,[3] Loic Ysebaert,[4] Hélène Doyen,[5] Luc Fornecker,[6] Krimo Bouabdallah,[7] Guillaume Manson,[8] Hervé Ghesquières,[9] Reza Tabrizi,[10] Eric Hermet,[11] Julien Lazarovici,[12] Anne Thiebaut-Bertrand,[13] Adrien Chauchet,[14] Hélène Demarquette,[1] Eileen Boyle,[1] Roch Houot,[8] Ibrahim Yakoub-Agha,[1,15]






Allo-SCT
Allo-SCT
Combination chemotherapy regimen
Allo-SCT
Brentuximab or brentuximab-containing clinical trial
Nivolumab, pembrolizumab or checkpoint inhibitor-containing clinical trial
Clinical trial
Single agent chemotherapy
Observation
Clinical trial
XRT
Lenalidomide, everolimus, or panobinostat
Decision based upon patient symptoms, age, comorbidities, disease sites and goals of treatment


Overall Survival
Survival Probabilty
1.00
0.75
0.50
0.25
0.00
0
2
4
6
8
10
Follow up Time (Year)
Number at risk
10
4
2
2
2
0

- She refused allo-HSCT
- After 3 years treatment with Opdivo she presented with dysphasia and back pain
- Hyper-metabolic lesions in pharynx and T8
- Radiotherapy was done
- Pembrolizumab (ZakArya) started (April 2021)
- Near complete response in las PET-CT scan


Research Institute for
Oncology/Hematology
Stem Cell Transplantation
Emergency Department