

Jumping on a Moving Bullet Train:



Emerging Treatments in Hodgkin Lymphoma

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Disclosures

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Research Support	BMS, Curis
Consultancy	AbbVie, Acrotech, Astellas, AZ, BMS, Caribou, CRISPR, Diiachi Sankyo, Fate Therapeutics, Genentech, Genmab, Ipsen, Janssen, Kite, Loxo, Miltenyi, Morphosys, Nurix, Pharmacyclics, Regeneron, Sanofi, Seagen, Takeda
Employment	NONE
Stock/Equity	NONE
Speakers Bureau	NONE



Objectives

- Describe the location, organization, and features of the Reed-Sternberg (R-S) White Death Gang
- Describe the outcomes of the ongoing battle against the Reed-Sternberg White Death Gang
- Describe novel battle techniques against the Reed-Sternberg White Death Gang

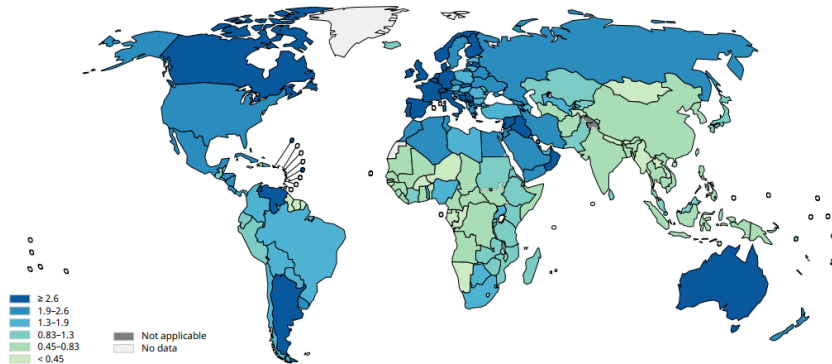


The R-S White Death Gang

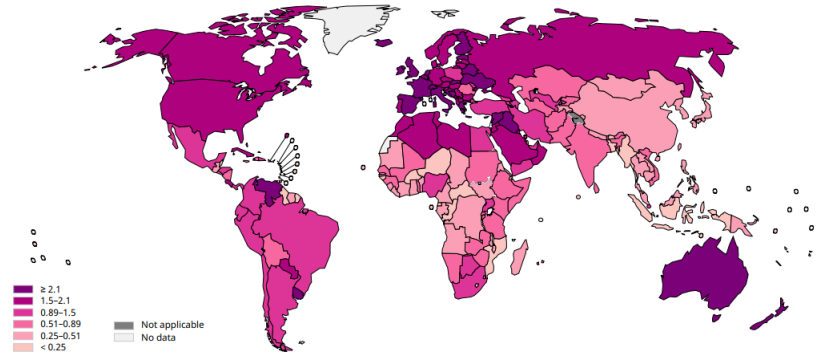


A Global Gang

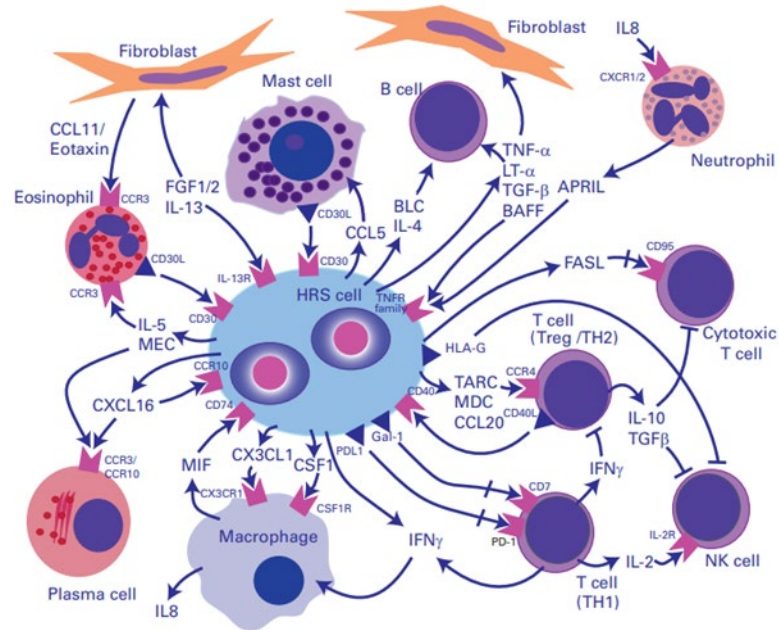
Age standardized (World) incidence rates, hodgkin lymphoma, males, all ages



Age standardized (World) incidence rates, hodgkin lymphoma, females, all ages



Organized Gang



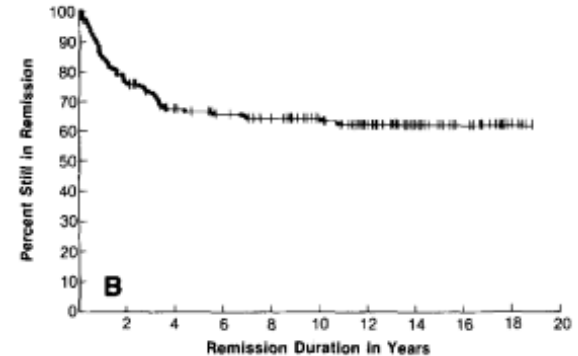
R-S Assassins



The OG



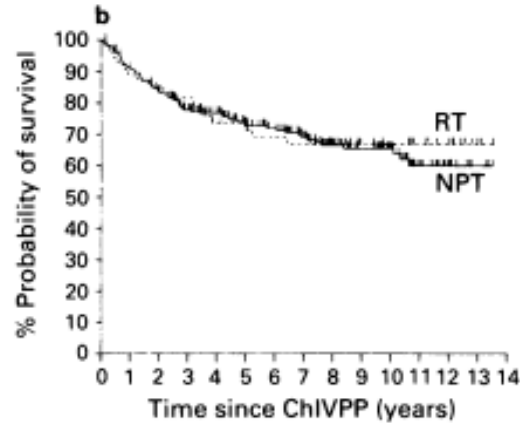
	Last Analysis (%)	Updated 198 (%)	188 (%)
No. of evaluable patients	198	198	188
No. of CRs	159 (80)	160 (81)	157 (84)
No. of induction failures	39 (20)	38 (19)	31 (16)
No. of relapses	52 (33)	57 (36)	56 (34)
No. continuously free of disease	107 (54)	103 (52)	101 (54)
No. of deaths	98 (49)	106 (54)	98 (52)
With Hodgkin's disease	75	76	68
Free of disease	23	30	30
No. alive	100 (51)	92 (46)	90 (48)
With Hodgkin's disease		2	2
Free of disease		90	88



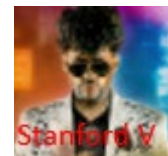
The Alternative



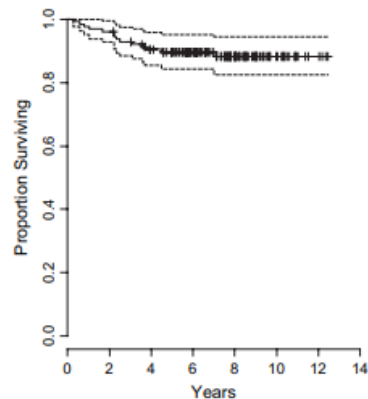
	No. patients	No. CR (%)	Remaining in remission		Survival	
			5 years %	10 years %	5 years %	10 years %
Total	229	194 (85%)	74.4	71.3	73.1	65.2



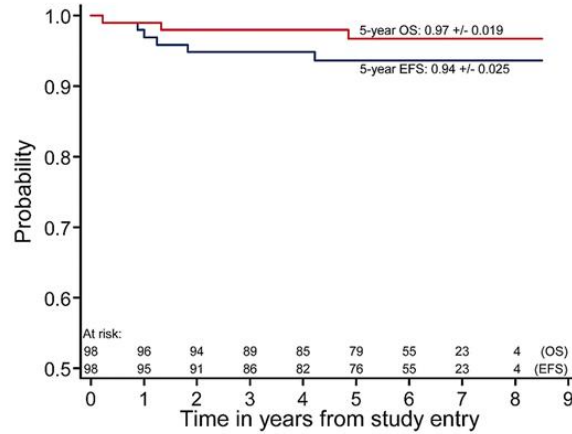
The 5th HL Regimen



Outcomes	Stanford [14]	Aversa [22]	Nebraska [23]	MSKCC	Italian Stanford arm [16]
5-year OS	96	95	84	90	82 ^a
5-year PFS	89	86	74	81 ^b	73
5-year FFS	NR ^c	NR ^c	NR	78	53 ^a
RT guidelines					
% Irradiated	90	90	74	88	66
Definition of bulky (cm)	≥5	≥5	≥5	≥5	≥6
RT to macroscopic splenic disease	Yes	Yes	Yes	Yes	Unclear ^d
Median chemoradiotherapy interval, weeks	2–4	2–4	3–4	4	6
RT to patients with more than two involved sites	Yes	Yes	Yes	Yes	No
RT to patients with postchemotherapy CR	Yes	Yes	Not all ^e	Yes	No ^f



The Option



Race	
White	67 (66)
Hispanic	12 (12)
Black	9 (9)
Other	7 (7)
Not reported	3 (3)

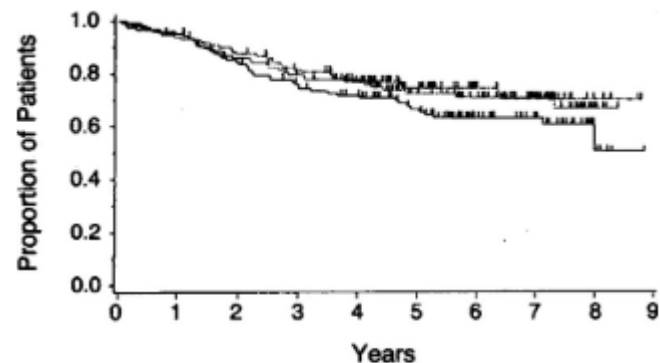


The Queen



TYPE OF RESPONSE	MOPP	ABVD	MOPP-ABVD
No. of patients	123	115	123
	<i>no. (% of group)</i>		
Complete response	83 (67)*	94 (82)*	102 (83)*
Partial response	29 (24)	15 (13)	12 (10)
Improvement	4 (3)	3 (3)	7 (6)
No response or progression	5 (4)	2 (2)	0 (0)
No evaluation	2 (2)	1 (1)	2 (2)

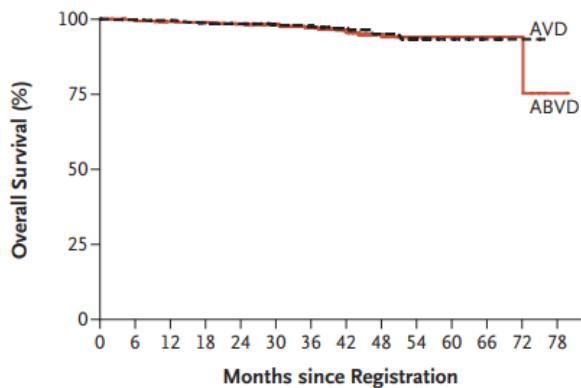
*P = 0.006 for MOPP as compared with ABVD and MOPP-ABVD.



Regimen	No. of Patients	No. (%) of Treatment Failures	Median Survival
— MOPP	123	44 (36)	None
- - - ABVD	115	32 (28)	None
- · - · MOPP-ABVD	123	31 (25)	None
All	361	107 (30)	—

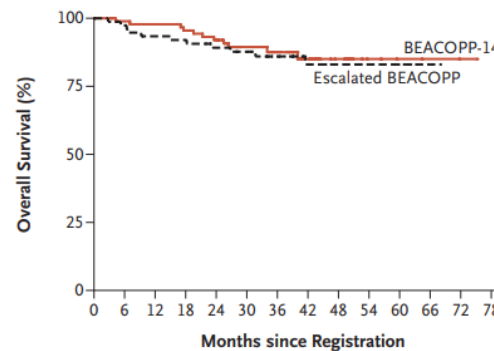


The Queen



No. at Risk

ABVD	470	464	459	456	441	385	298	197	119	79	33	16	5	1
AVD	465	457	450	438	421	371	298	209	126	72	29	16	3	0

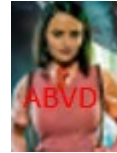


No. at Risk

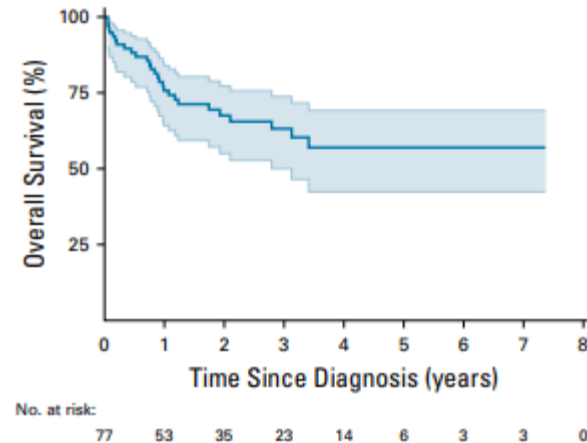
BEACOPP-14	94	89	85	85	80	58	47	36	18	7	4	3	2	1
Escalated BEACOPP	78	73	68	66	63	56	45	34	22	17	10	4	1	0



The Queen in Africa



Demographic and pathologic (N = 85)	
Age, years	
Median (IQR)	16.8 (11.0-30.5)
Mean (range)	22.3 (4.1-66.9)
Sex	
Male	49 (58)
Female	36 (42)
Country	
Rwanda	74 (87)
Burundi	5 (6)
Democratic Republic of Congo	4 (5)
Other	2 (2)
HIV status	
Positive	10 (12)
Negative by laboratory result (n = 61) or self-report (n = 14)	75 (88)
Histologic subtype (n = 74)	
Classic HL, nodular sclerosis	39 (53)
Classic HL, mixed cellularity	27 (36)
Classic HL, lymphocyte depleted	5 (7)
Classic HL, lymphocyte rich	2 (3)
Nodular lymphocyte predominant	1 (1)
EBV status (available in n = 21)	
Positive	14 (67)
Negative	7 (33)

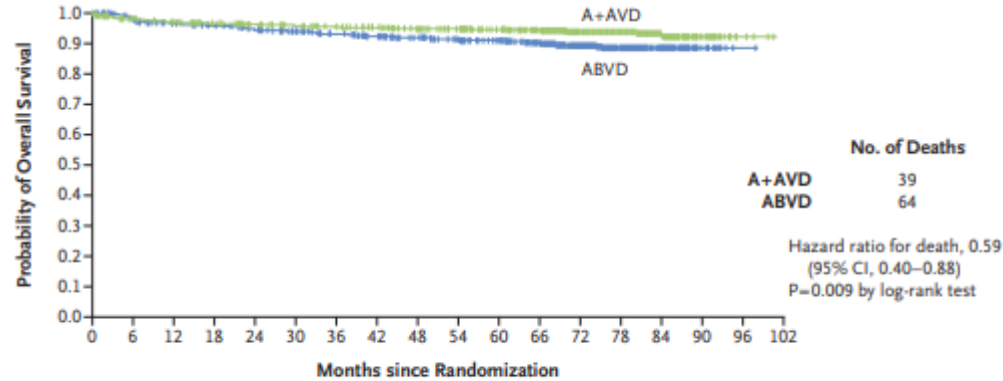


Hodgkin Assassins

Year	Regimen
2003	ABVD vs. MOPP/ABV
2003	ABVD vs. ABVD/ASCT
2004	ABVD vs. COPP/ABV/IEMP vs. COPP/ABVD
2005	ABVD vs. Stanford V vs. MOPPEBCAD
2005	ABVD vs. ChIVPP/EVA vs. alternating EVA, ChIVPP
2006	ABVD vs. MOPP/ABV vs. ABVPP
2009	ABVD vs. Stanford V
2010	ABVD vs. BEACOPP std x 4 RT
2011	ABVD vs. Stanford V vs. MOPPEBCAD
2011	ABVD vs. BEACOPP esc x 4 vs. BEACOPP std x 4
2012	ABVD vs. BEACOPP esc 6 vs. 8
2013	ABVD vs. Stanford V vs. BEACOPP-14
2014	ABVD vs. BEACOPP 4/4
2016	ABVD vs. BEACOPP 4/2 vs. COPP/EBV/CAD
2016	ABVD vs. BEACOPP 4 esc/4 std
2016	ABVD vs. AVD (PET2 negative)



The King



No. at Risk

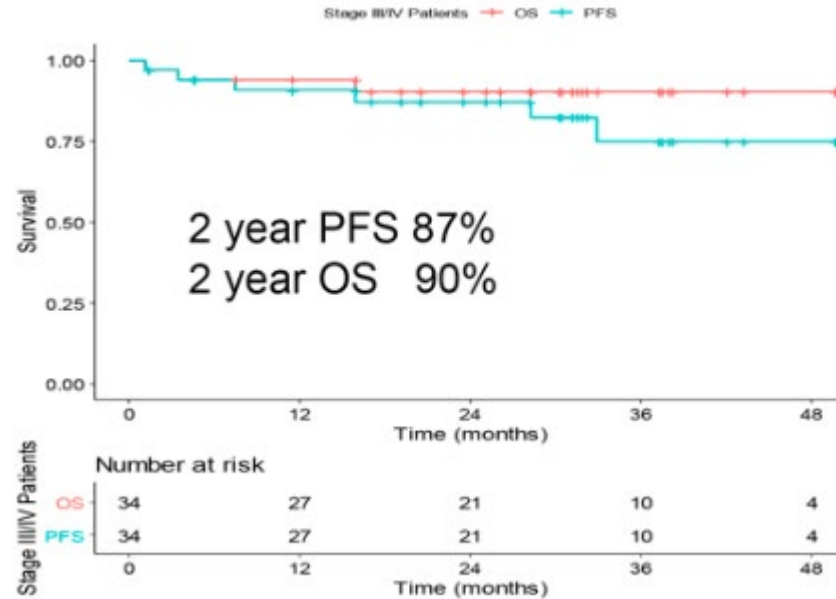
A+AVD	664	638	626	612	598	584	572	557	538	517	494	461	350	209	97	27	4	0
ABVD	670	634	614	604	587	567	545	527	505	479	454	411	308	191	84	11	1	0

Race — n (%)

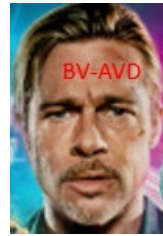
White	560 (84)	554 (83)	1114 (84)
Asian	56 (8)	57 (9)	113 (8)
Korean	23 (3)	22 (3)	45 (3)
Japanese	10 (2)	12 (2)	22 (2)
Asian Indian	8 (1)	9 (1)	17 (1)
Chinese	9 (1)	7 (1)	16 (1)
Other	3 (<1)	4 (1)	7 (1)
Black or African American	20 (3)	25 (4)	45 (3)
Other	18 (3)	17 (3)	35 (3)
Not reported	10 (2)	17 (3)	27 (2)



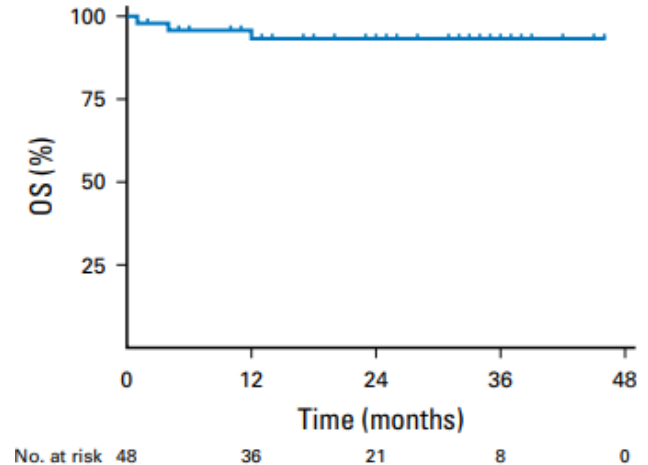
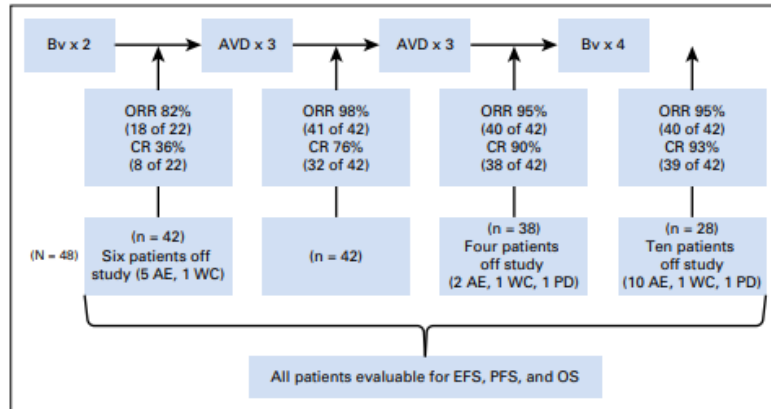
The King in HIV+ cHL

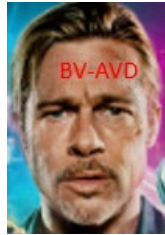


The King

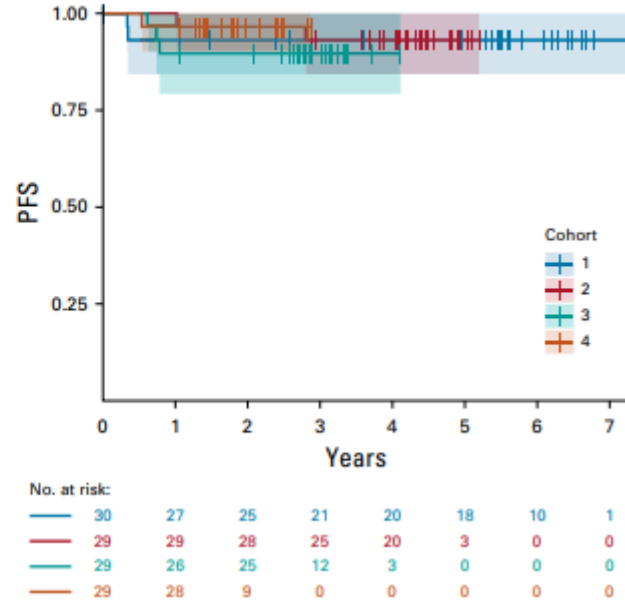
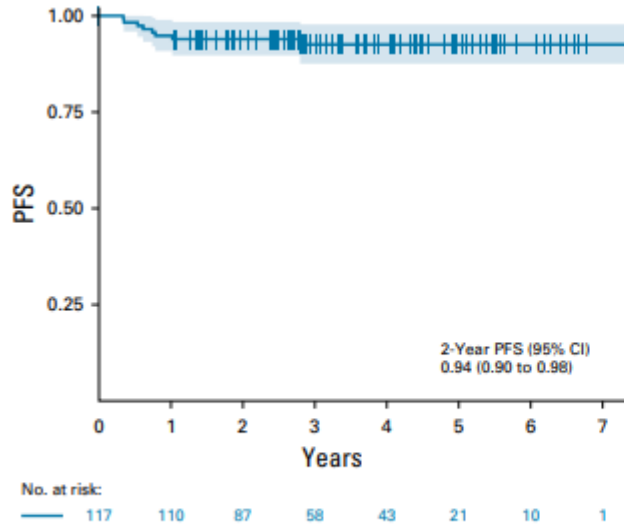


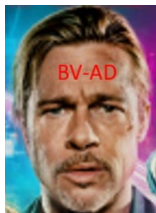
in Elderly cHL





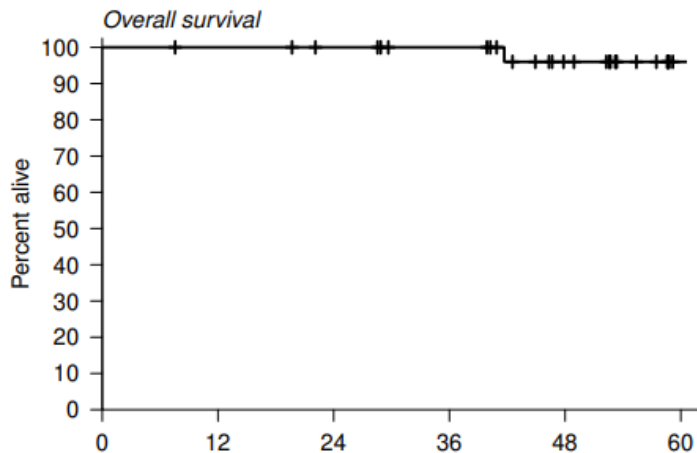
The King in Early Unfavorable cHL





The King

in Nonbulky limited stage

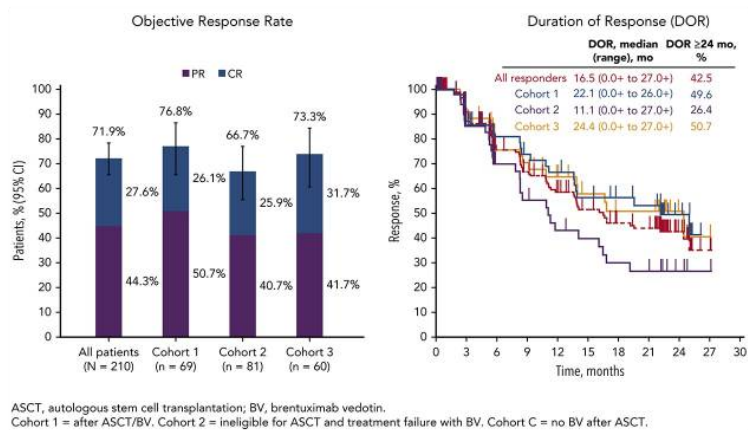


What to Do When the R-S White Death Gang Strikes Back

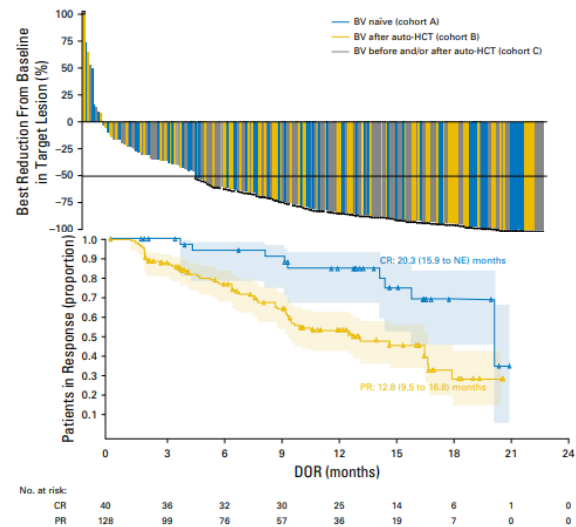


Pembro & Nivo

Pembrolizumab (Pembro) KEYNOTE-087

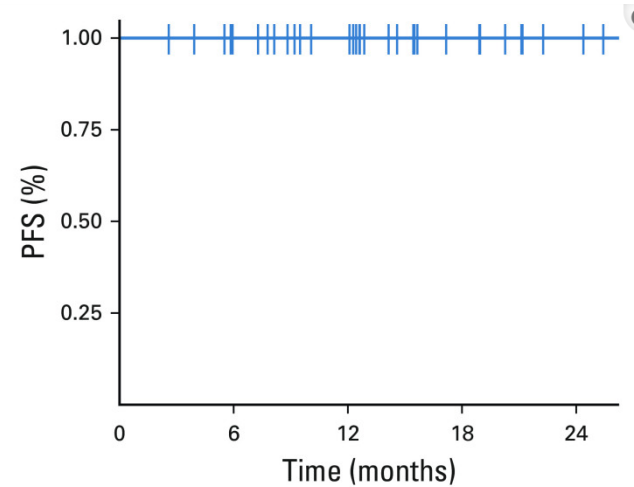
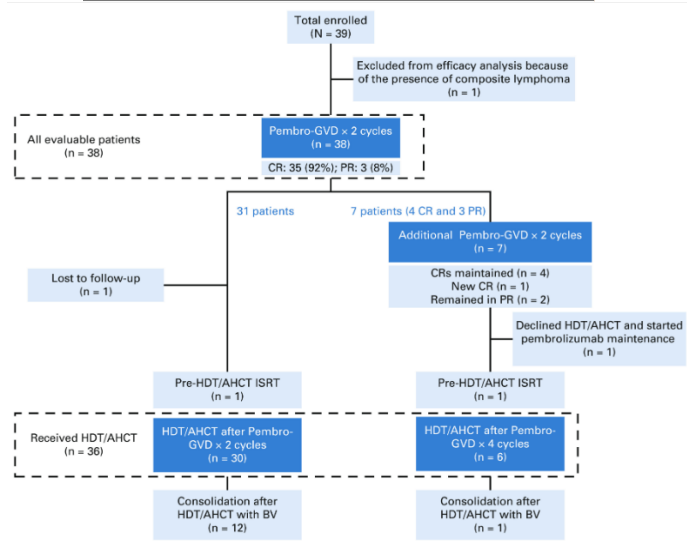


Nivolumab (Nivo) CHECKMATE-205

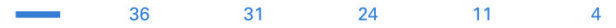


Pembro + GVD

Race	
White	29 (74)
African American or Black	3 (8)
Asian	2 (5)
Unknown or not reported	5 (13)

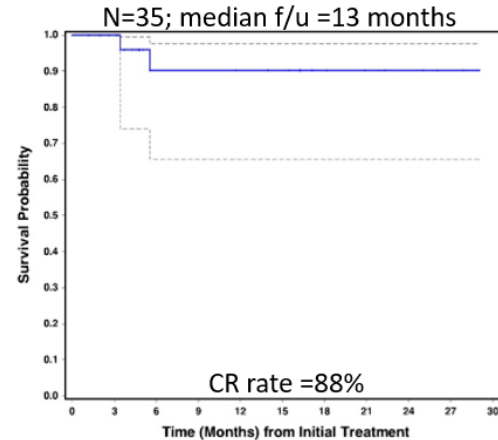


No. at risk:



Nivo + ICE

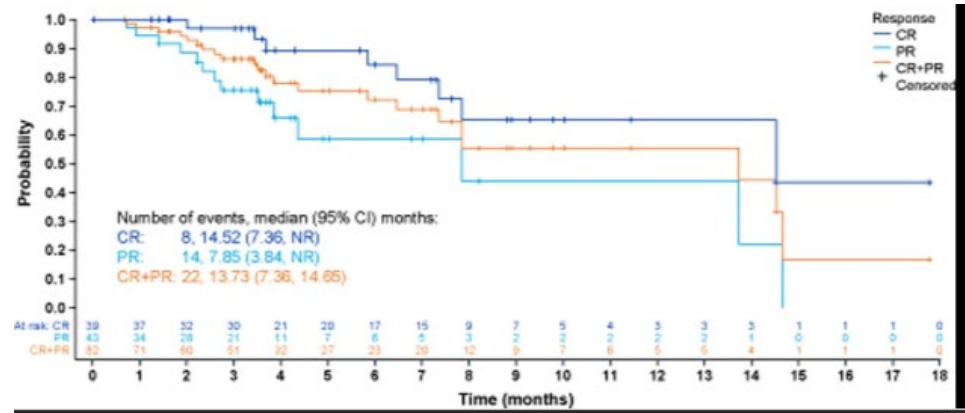
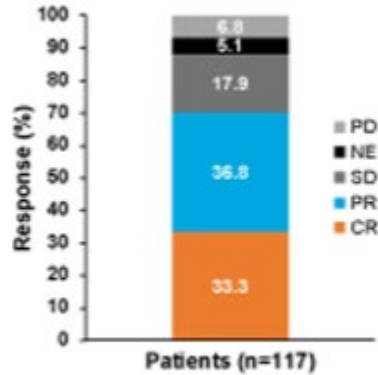
Variable	N (%)
Male gender	21 (60)
Age	30 (19-70)
Stage at Baseline	
I-II	19 (55)
III-IV	16 (45)
B Symptom at Baseline	
No	29 (83)
Yes	6 (17)
Extranodal Disease at Baseline	10 (29)
Primary refractory	23 (66)
Frontline regimen	
ABVD	29 (83)
BV+AVD	6 (17)
Stage at diagnosis	
I-II	17 (49)
III-IV	18 (51)
Prior radiation	5 (14)
Prior brentuximab vedotin	6 (17)



What to Do When the White Death Strikes Back AGAIN



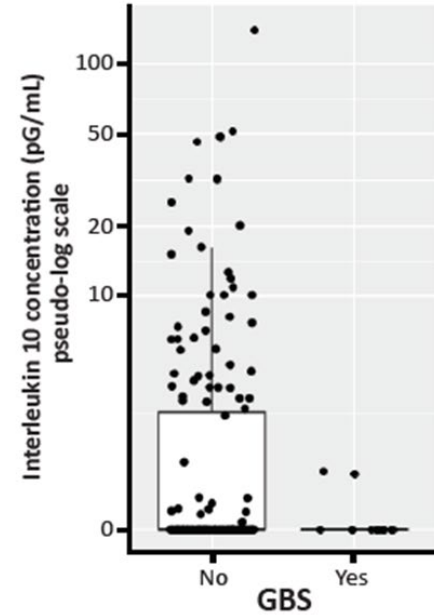
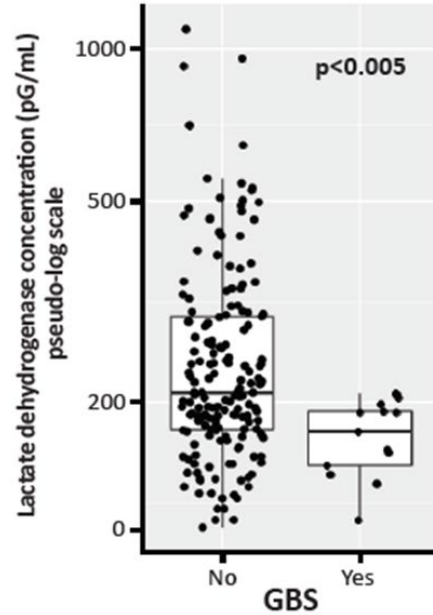
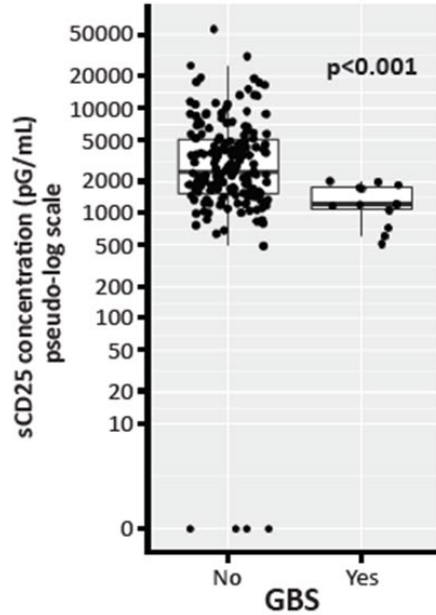
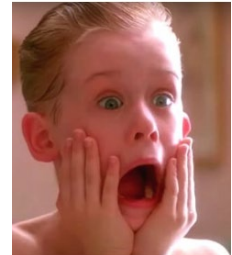
Camidanlumab Teserine (Cami-T)



CR, complete response; NE, not evaluable; PD, progressive disease; PR, partial response; SD, stable disease



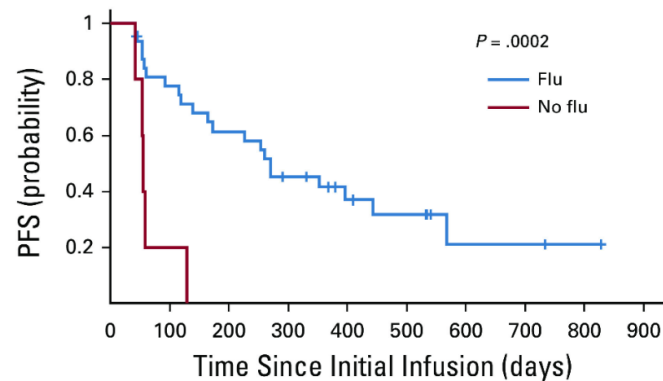
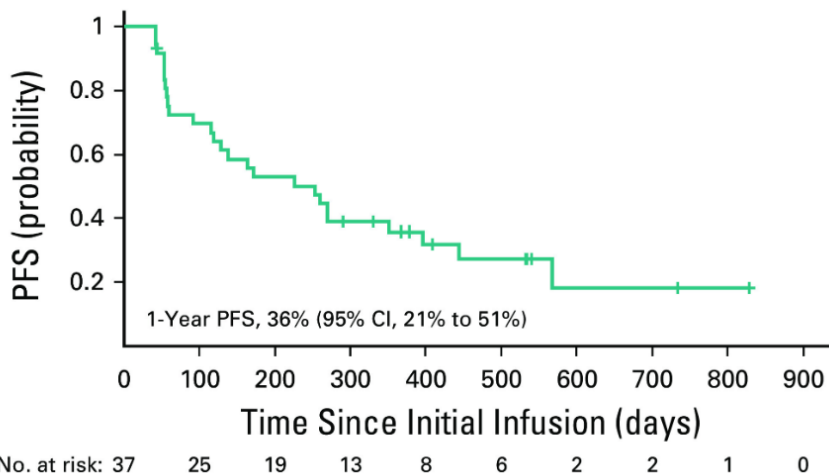
Cami T



CAR-T



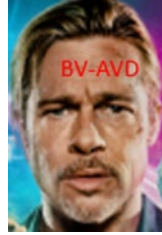
CD30 CAR-T



No. at risk:		0	100	200	300	400	500	600	700	800	900
Flu	32	24	19	13	8	6	2	2	1	0	0
No flu	5	1	0	0	0	0	0	0	0	0	0



New King



VS



FULLY ACCRUED!!!!
Phase 3: Nivo+AVD or BV+AVD
Newly diagnosed
stage III-IV Hodgkin lymphoma
1:1 randomization
Experimental: Nivo+AVD x 6 cycles
Control: BV+AVD x 6 cycles
Primary endpoint: PFS
Secondary endpoints: EFS, OS, CR

