POST-SAN DIEGO 2023
Novità dal Meeting della Società Americana di Ematologia

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Verona
Palazzo della Gran Guardia
15-16-17 Febbraio 2024

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LINFOMA DI HODGKIN

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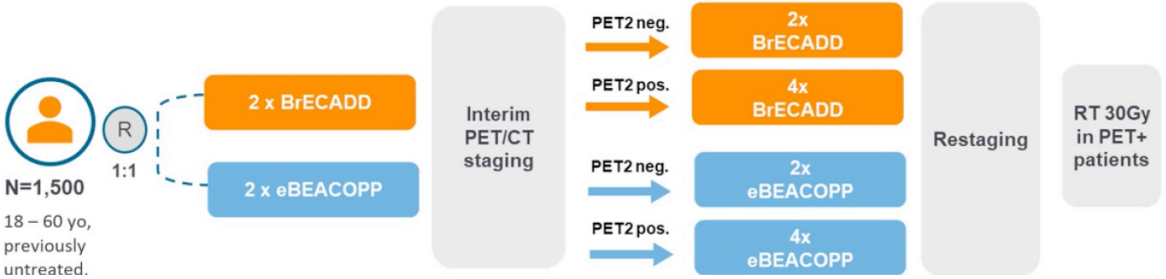
LH: aggiornamenti ASH 2023 sulla TERAPIA DI PRIMA LINEA

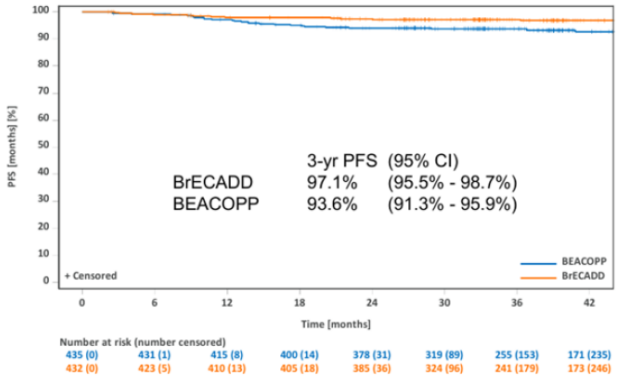
Comprehensive Analysis of Treatment Related Morbidity and Progression-Free Survival in the GHSG Phase III HD21 Trial

Borchmann P[1], Moccia AA[2], Greil R[3], Schneider G[1], Hertzberg[4], Schaub V[5], Hüttmann A[6], Kreil F[7], Dierlamm J[8], Hänel M[9], Nowak U[10], Meissner J[11], Zimmermann A[12], Mathas S[13], Zijlstra JM[14], Fossá A[15], Viardot A[16], Hertenstein B[17], Martin S[18], Giri P[19], Kamper P[20], Molin D[21], Kreissl S[1], Ferdinandus J[1], Fuchs M[1], Rosenwald A[22], Klapper W[23], Eich HT[24], Baues C[25], Hallek M[1], Dietlein M[26], Kobe C[26], Diehl V[1]

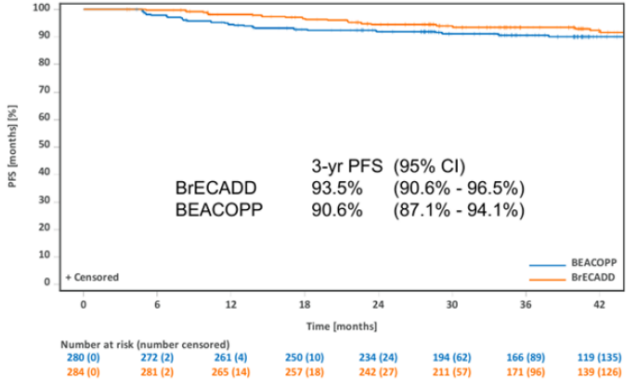


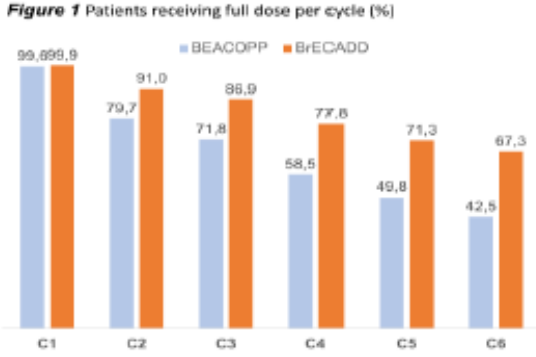
- The highest 3-yr PFS in adv cHL
- Improved tolerability/deliverability
- PET2- : PFS 97% in 12w treatment
- PET2+ : PFS 93.5% (same as beacopp PET2-)

PET2-negative (4 cycles) 59%



PET2-positive (6 cycles) 41%

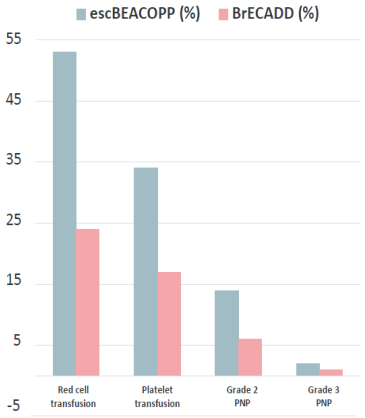




Toxicity, %	escBEACOPP	BrECADD
Red cell transfusion*	53	24
Platelet transfusion*	34	17

	escBEACOPP	BrECADD
Sensory PNP		
All grades	49	38
Grade 2	14	6
Grade 3	2	1

	escBEACOPP	BrECADD
Treatment-related mortality	<1	0

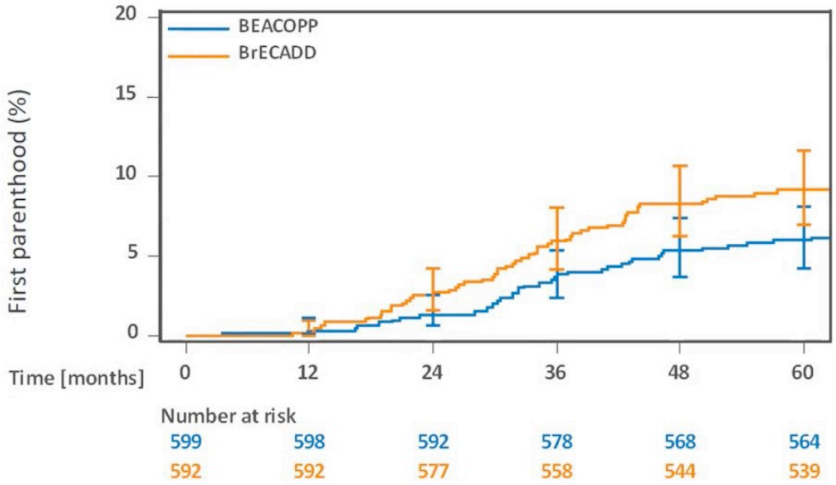


- Tox ematologica inferiore vs. beacopp, ma 24% trasfusioni RBC, 17% plts
- NP < vs. beacopp
- N. nascite osservate > beacopp (nelle femmine dopo 2aa = popolaz. di riferimento)

Pregnancies and childbirth following advanced-stage HL treatment with BrECADD or eBEACOPP in the GHSG randomized phase III HD21 trial

Justin Ferdinandus[1,2*], Gundolf Schneider[1,2*], Alexander Fosså[3*], Alden Moccia[4*], Richard Greil[5], Mark S. Hertzberg[6], Josée M. Zijlstra[7], Peter Kamper[8], Daniel L. Molin[9], Andrea Kerkhoff[10], Sebastian Scheil[11], Yon-Dschun Ko[12], Max S. Topp[13], Joachim Beck[14], Vladan Vucinic[15], Wolfram Jung[16], Roland Schroers[17], Andreas Rank[18], Carla Damaschin[1,2], Anne Sophie Jacob[1,2], Michael Fuchs[1,2], Peter Borchmann[1,2] and Karolin Behringer[1,19*]

Pregnancy rate (%)	Male (n= 704)	Female (n=496)
BEACOPP	2.8	15.9
BrECADD	6.3	16.8



" Notably, childbirth rates in women after the second year of follow-up were comparable to the German population"

Progression-Free Survival (PFS) and Toxicity with Nivolumab-AVD Compared to Brentuximab Vedotin-AVD in Pediatric Advanced Stage (AS) Classic Hodgkin Lymphoma (cHL), Results of SWOG S1826

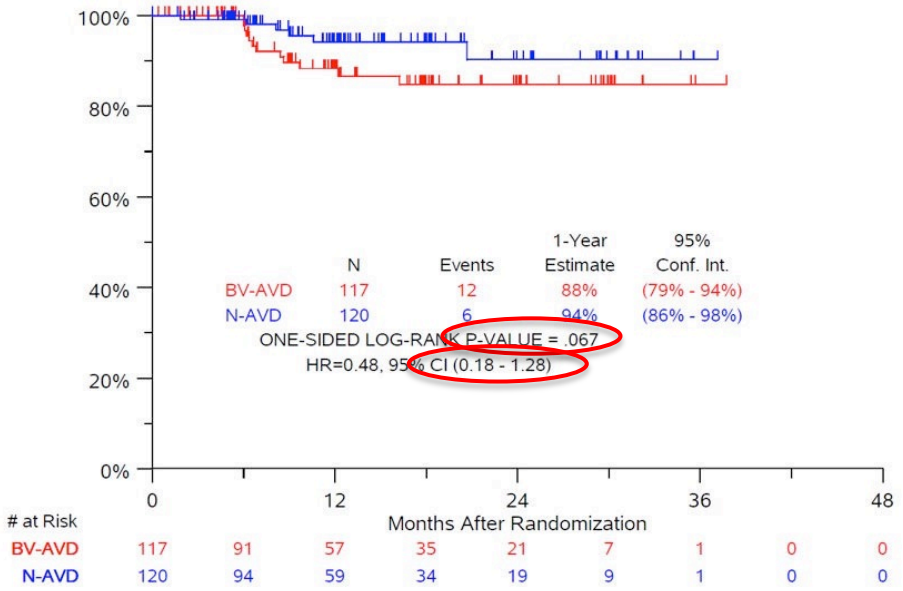
SWOG S1826

Sharon M. Castellino, MD MSc[1,2], Hongli Li, MS[3], Alex F. Herrera, MD[4], Angela Punnett, MD[5], Michael Leblanc[3], Susan K Parsons, MDMRCP[6], David Hodgson, MD[7,8], Frank Keller, MD[9,10], Richard A. Drachtman, MD[11], Adam Lamble, MD[12], Christopher J. Forlenza, MD[13], Andrew Doan, MD[14], Sarah C. Rutherford, MD[15], Andrew M Evens, DO,MBA,MMSc[16,17], Richard F. Little, MDMPH[18], Malcolm A. Smith, MD PhD[19], Joo Y Song, MD[20], Sonali M. Smith[21], Jonathan W. Friedberg, MD MMSc[22], Kara M. Kelly, MD[23]

Disposition	N-AVD (n=120)	Bv-AVD (n=117)
Treatment ongoing	8	16
Completed treatment	102	98
Deaths on treatment	0	0
Discontinued Nivolumab or Bv due to AE	9 (7.5%)	3 (1.8%)
Received radiotherapy	0	2

- N-AVD and BV-AVD are well tolerated and associated with low rates of irAEs in pts ages 12-17y.
- With 12.1 mos median follow-up the PFS benefit observed for N-AVD in pediatric pts mirrors that observed in the overall study.
- RT usage is lower, and cumulative doxorubicin dose is higher than historical pediatric cHL trials.

12 mo PFS

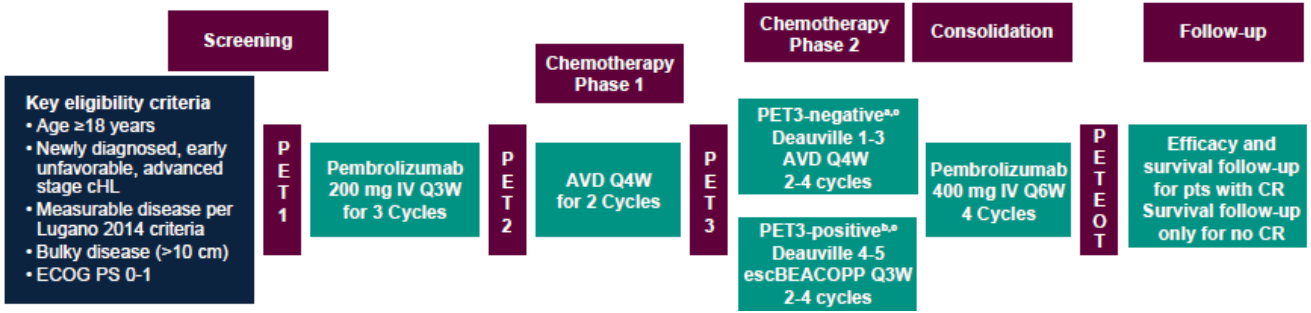


3068

Efficacy and safety of pembrolizumab and chemotherapy in newly diagnosed, early unfavorable or advanced-stage classic Hodgkin lymphoma: The phase 2 KEYNOTE-C11 study

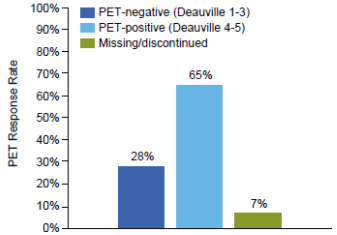
Ranjana H. Advani[1]; Abraham Avigdor[2]; Anna Sureda Balari[3]; David Lavie[4]; Stefan Hohaus[5]; Jan M. Zaucha[6]; Vu Minh Hua[7]; Vittorio R. Zilioli[8]; Raimundo Gazitúa[9]; Muhit Ozcan[10]; Amos Odeleye-Ajakaye[11]; Nishitha Reddy[11]; Patricia Marinello[11]; Jane N. Winter[12]

Figure 1. KEYNOTE-C11 study design



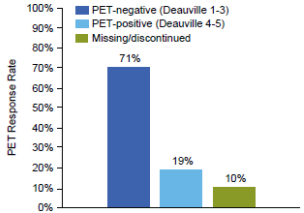
Characteristics, n (%)	All Patients N=146
Median age, years (range)	34.5 (18-78)
≥65 years	19 (13%)
Male	80 (55%)
White	126 (86%)
ECOG 0	110 (75%)
ECOG 1	35 (24%)
Region	
US	21 (14%)
Non-US	125 (86%)
EU	50 (34%)
Non-EU	96 (66%)
Disease stage	
Early unfavorable	62 (42%)
Advanced	84 (58%)
Bulky disease present, yes	39 (27%)
Chemotherapy phase 2 type	
AVD	113 (77%)
BEACOPP	17 (12%)
Not reached	16 (11%)

A. PET2 after pembrolizumab monotherapy



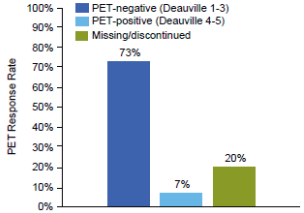
Rate, n (%) PET-negativity at PET2 timepoint	Patients N=146
Negative	41 (28%)
Positive	95 (65%)
Missing and/or discontinued from treatment and study	2 (1%)
Missing, discontinued from treatment and still on study	8 (6%)

B. PET3 after pembrolizumab and AVD chemotherapy



Rate, n (%) PET-negativity at PET3 timepoint	Patients N=146
Negative	103 (71%)
Positive	28 (19%)
Missing and/or discontinued from treatment and study	3 (2%)
Missing, discontinued from treatment and still on study	12 (8%)

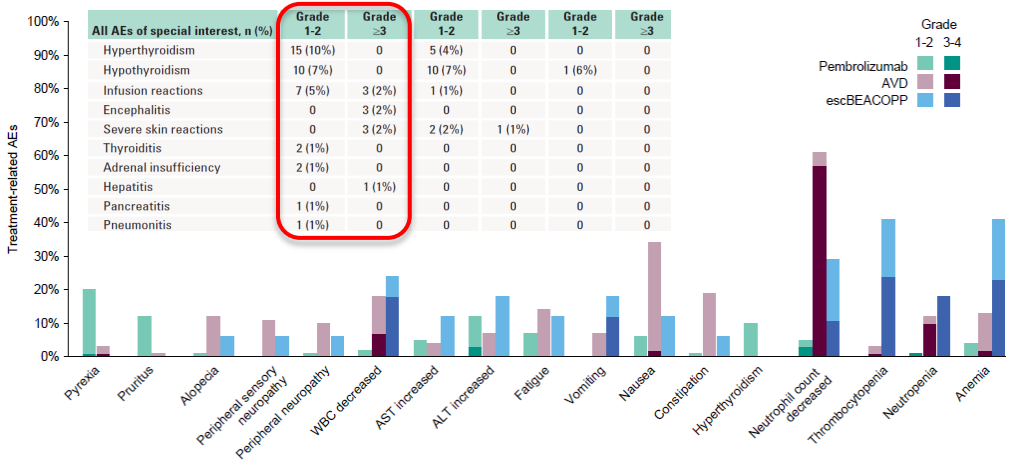
C. PET-negativity at end of treatment



Rate, n (%) PET-negativity at EOT	Patients N=144
Negative	105 (73%)
Positive	10 (7%)
Missing and/or discontinued from treatment and study	4 (3%)
Missing, discontinued from treatment and still on study	25 (17%)

Figure 4. Treatment-related adverse events with incidence ≥10%

All AEs of special interest, n (%)	Grade 1-2	Grade ≥3	Grade 1-2	Grade ≥3	Grade 1-2	Grade ≥3
Hyperthyroidism	15 (10%)	0	5 (4%)	0	0	0
Hypothyroidism	10 (7%)	0	10 (7%)	0	1 (6%)	0
Infusion reactions	7 (5%)	3 (2%)	1 (1%)	0	0	0
Encephalitis	0	3 (2%)	0	0	0	0
Severe skin reactions	0	3 (2%)	2 (2%)	1 (1%)	0	0
Thyroiditis	2 (1%)	0	0	0	0	0
Adrenal insufficiency	2 (1%)	0	0	0	0	0
Hepatitis	0	1 (1%)	0	0	0	0
Pancreatitis	1 (1%)	0	0	0	0	0
Pneumonitis	1 (1%)	0	0	0	0	0



Manageable safety prophyle

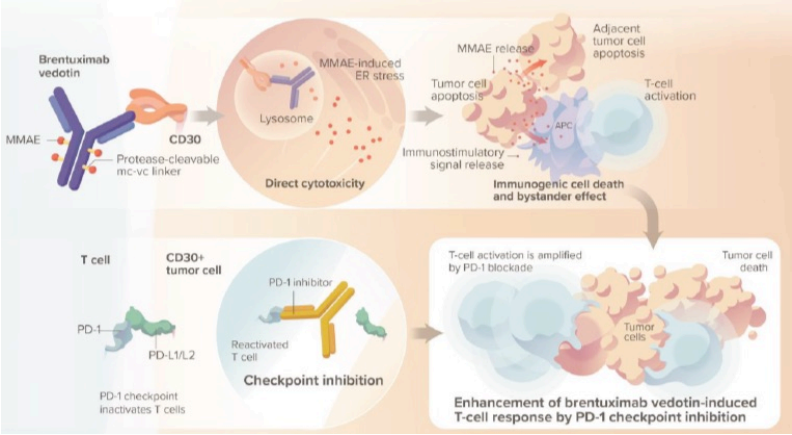
- Rare but serious immune toxicities (robust immune response in untreated pts)

High rate of PET+ may reflect immune flare

Longer follow up needed

Brentuximab Vedotin, Nivolumab, Doxorubicin, and Dacarbazine (AN+AD) for Early-Stage Classical Hodgkin Lymphoma (SGN35-027 Part C)

Abramson J.S. et al.



Patient Population

Previously untreated advanced (Parts A and B) or **early stage (Part C) cHL**

Treatment Arms

Part A: Brentuximab vedotin + AVD | up to 6 cycles

Part B: Brentuximab vedotin with nivolumab + AD | up to 6 cycles

Part C: Brentuximab vedotin with nivolumab + AD | 4 cycles

Primary Endpoint

Part A: Rate of febrile neutropenia

Parts B and C: CR rate at EOT

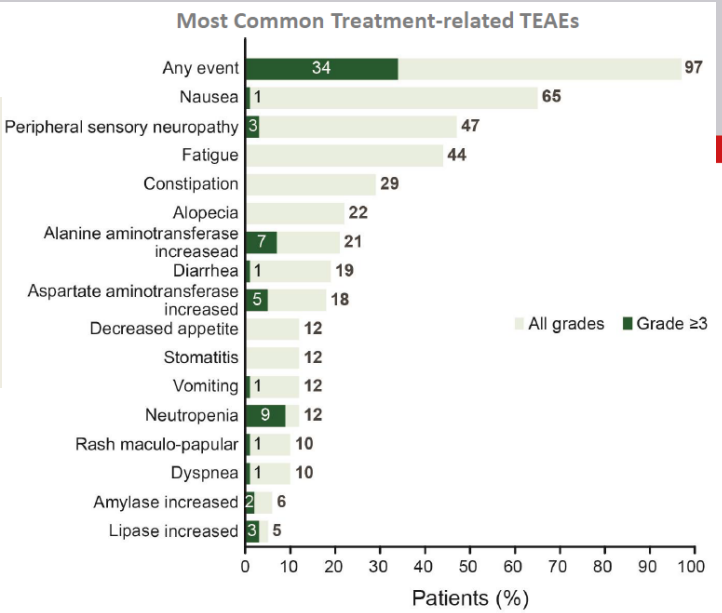
Key Secondary Endpoint

Part A: PFS

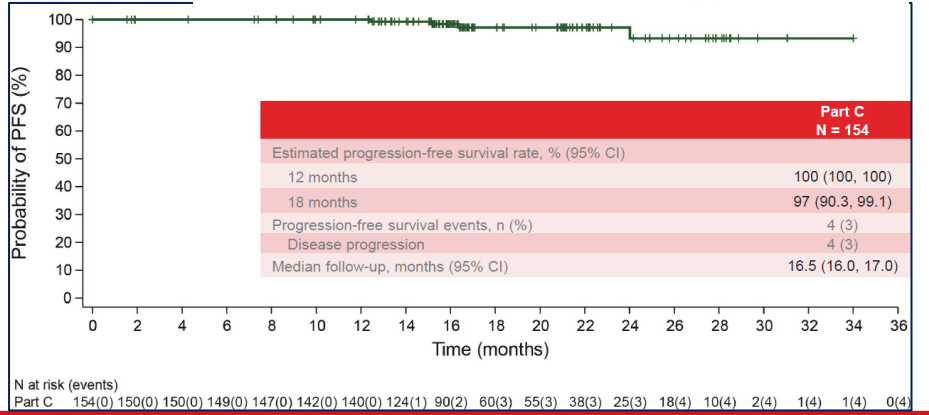
Parts B and C: ORR, DOR, DOCR, PFS

Patient Demographics and Disease Characteristics	Part C N = 154
Age, median years (range)	31 (18, 77)
Sex, Female, n (%)	84 (55)
Race, White, n (%)	129 (84)
Disease stage at initial diagnosis, n (%)	
I	17 (11)
II	137 (89)
Extranodal disease present, n (%)	15 (10)
B symptoms present at initial diagnosis, n (%)	35 (23)

- AN + AD was well tolerated
- No cases of febrile neutropenia
- Peripheral neuropathy was primarily low grade
- ImAEs were primarily low-grade
- ctDNA changes might have predictive value



Overall Response at EOT per Investigator, n (%)	All treated patients N = 154
Objective response rate (complete + **partial response**)	147 (95)
95% CI	(90.9, 98.2)
Complete response	140 (91)
95% CI	(85.2, 94.9)
Partial response	7 (5)
Stable disease	0
Progressive disease	0
Indeterminate response[b]	3 (2)
Not evaluable[c]	4 (3)



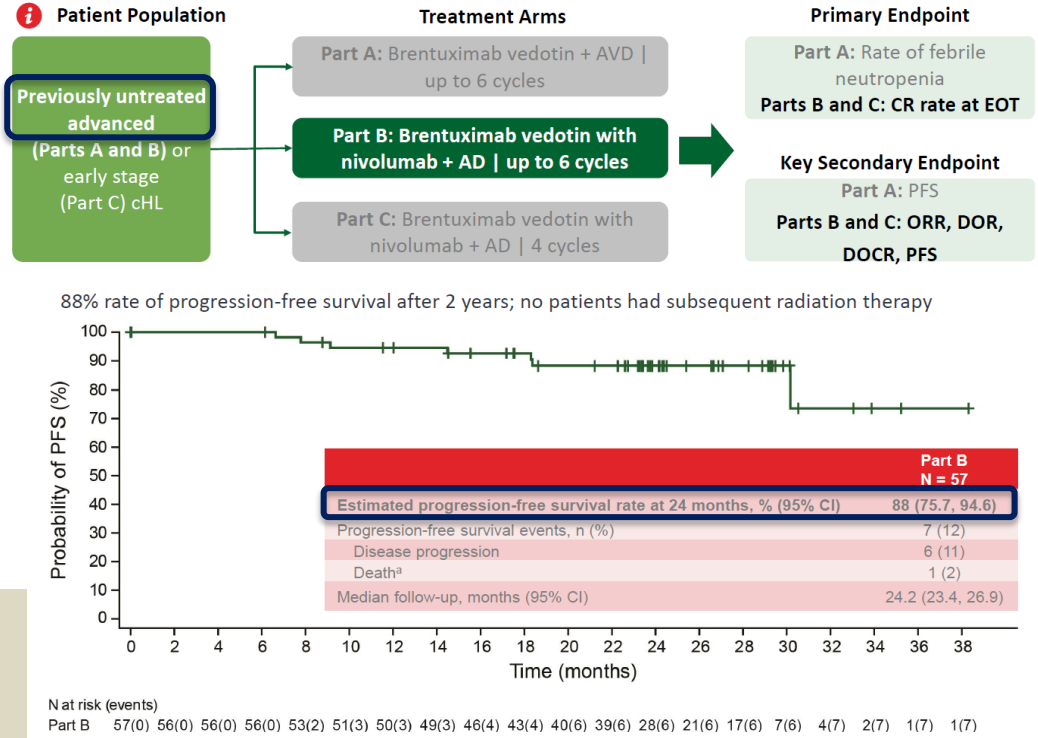
AN + AD shows promising efficacy and tolerability in patients with 1L early stage cHL

Brentuximab Vedotin, Nivolumab, Doxorubicin, and Dacarbazine for Advanced-Stage Classical Hodgkin Lymphoma: Updated Efficacy and Safety Results from the Single-Arm Phase 2 Study (SGN35-027 Part B)

Lee H. J. et al.
Abstract #608

Overall Response at EOT per Investigator, n (%)	All treated patients N = 57
Objective response rate (complete + partial response)	53 (93)
95% CI	(83.0, 98.1)
Complete response	50 (88)
95% CI	(76.3, 94.9)
Partial response	3 (5)
Stable disease	0
Progressive disease	2 (4)
Indeterminate response[b]	1 (2)
Not evaluable[c]	1 (2)

- 88% of patients remained progression-free after 2 years with a median follow-up of 24.2 months
- AN+AD was well tolerated
- No cases of febrile neutropenia
- Peripheral neuropathy was primarily low grade.
- ImAEs were primarily low-grade



AN + AD shows promising efficacy and tolerability warranting further exploration for the treatment of patients with 1L advanced cHL

Bleomycin Affects Lung Function for at Least 5 Years after Treatment for Hodgkin Lymphoma - Data from the International, Randomised Phase 3 RATHL Trial

Phillips E et al.
Abstract #612

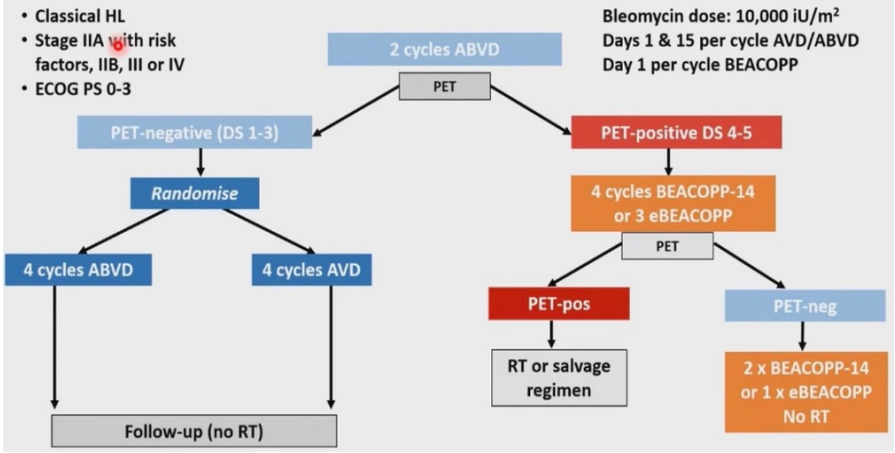
	All (N=1201)	ABVD (N=469)	AVD (N=464)	BEACOPP (N=172)
Age (years), median (IQR)	**33 (25 - 46)**	32 (24 - 44)	32.5 (24 – 45)	32.5 (24 - 46)
DLCO (% predicted), median (IQR)	**82 (73-93)**	82 (73.9 – 93.9)	83 (73.3 – 93)	79 (70.5 – 90)
DLCO <75% predicted, N (%)	**327 (29.4)**	121 (27.3)	129 (29.1)	59 (38.1)

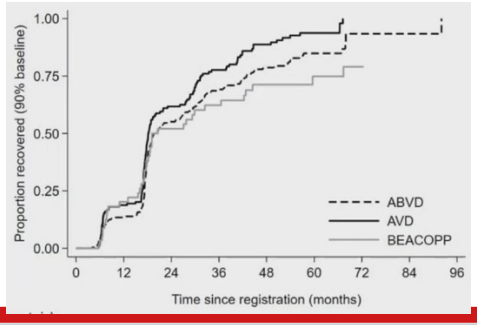
	ABVD (N=469)	AVD (N=464)	BEACOPP (N=172)
Bleomycin doses: median (IQR)	12 (12-12)	4 (4-4)	8 (8-10)
Cycles with G-CSF: median (IQR)	0 (0-3)	0 (0-4)	5 (4-6)
G-CSF use (% pts)	40.7%	39.7%	98.3%
Grade ≥3 respiratory AE: N (%)	17 (3.6)	7 (1.5)	10 (5.8)
	p=0.041		
Grade 5 respiratory AEs: N (%)	1 (0.2)	0	0
Mean change in DLCO (95% CI)	-11.6 (-13.1 to -10.0)	-3.8 (-5.4 to 2.2)	-9.5 (-12.5 to -6.4)
	Difference* 7.1 (5.1 to 9.0), p <0.001		
DLCO <90% baseline	247/413 (59.8%)	167/411 (40.6%)	63/121 (52.1%)
	p<0.001		

RATHL Trial Design

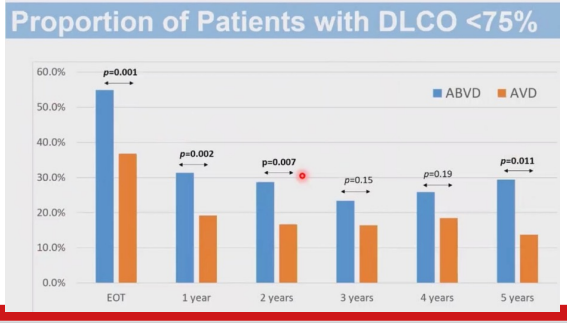
- Classical HL
- Stage IIA with risk factors, IIB, III or IV
- ECOG PS 0-3

Bleomycin dose: 10,000 iU/m²
Days 1 & 15 per cycle AVD/ABVD
Day 1 per cycle BEACOPP





Proportion of Patients with DLCO <75%



- Population-wide reduction in diffusion capacity in the ABVD arm that was only partially reversible and persisted at 5 years
- This may have clinical consequences in later years for pts cured of HL
- These data strongly support efforts to minimise bleomycin use in HL

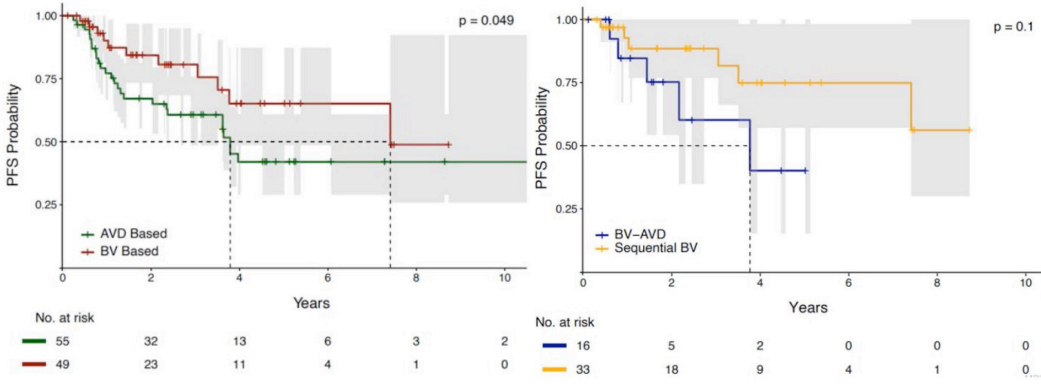
Brentuximab Vedotin-Based Regimens for Older Patients with Newly Diagnosed Classical Hodgkin Lymphoma-Real World Experience

Luttwak E. et al.
Abstract #3059

Baseline characteristics	BV based regimens n= 55 (%)
Male, n (%)	37(67)
Age, years (median, range)	70(60-88.5)
ECOG*, n (%)	
0-1	40(83)
2	8(17)
EBV*, n (%)	24(50)
Stage IV at diagnosis, n (%)	35(71)
B symptoms*, n (%)	34(65)
Albumin* <4gr/dl, n (%)	30(66)
IPS*, 4-7 n (%)	23(56)

Baseline characteristics	BV based regimens n= 55 (%)
Histology, n (%)	
Nodular sclerosis	29(53)
Mixed cellularity	6(11)
Lymphocyte rich	4(7)
Classical, unspecified	16(29)
CIRS-G score, median(range)	5(0-11)
Regimens	
BV-AVD	15(27)
Sequential BV	35(64)

For a historical cohort, we reviewed older pts consecutively diagnosed with cHL between 01/2014-03/2018, representing the pre-brentuximab era. Matching 1:1 (the BV cohort to the historical cohort) by age, sex and ECOG was performed.

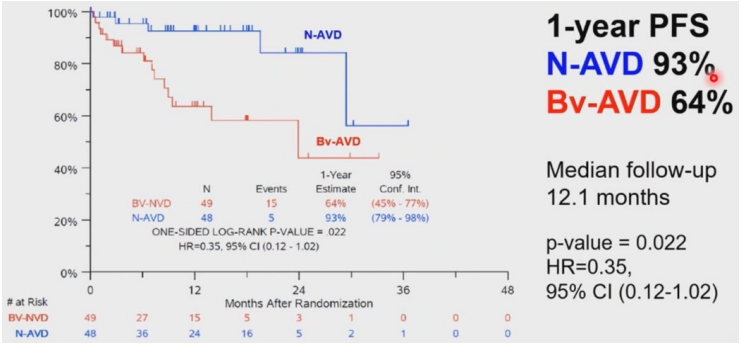


- Pts treated with BV-based regimens had significantly better PFS compared to the historical cohort
- Sequential BV-AVD was well-tolerated and safe with outcomes that are favorable and comparable to results from the phase II study by Evens et al (JCO 2018)

Nivolumab-AVD Is Better Tolerated and Improves Progression-Free Survival Compared to Bv-AVD in Older Patients (Aged ≥60 Years) with Advanced Stage Hodgkin Lymphoma Enrolled on SWOG S1826

Sarah C. Rutherford, MD[1], Hongli Li, MS[2], Alex F. Herrera, MD[3], Michael Leblanc[2], Sairah Ahmed, MD[4], Kelly L. Davison, MD PhD[5], Carla Casulo, MD[6], Nancy L. Bartlett, MD[7], Joseph M Tuscano, MD[8], Brian Hess, MD[9], Pallawi Torka, MD[10], Pankaj Kumar, MD[11], Ryan W Jacobs, MD[12], Joo Y Song, MD[13], Sharon M. Castellino, MD MSc[14], Brad S. Kahl, MD[15], John P. Leonard[1], Sonali M. Smith[16], Jonathan W. Friedberg, MD MMSc[6], Andrew M Evens, DO,MBA,MMSc[17]

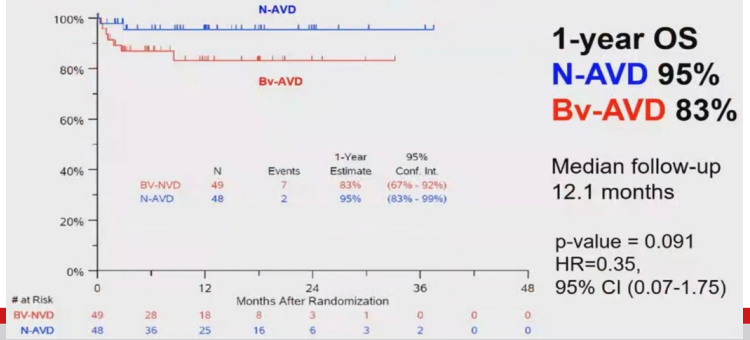
SWOG S1826



1-year PFS
N-AVD 93%
Bv-AVD 64%

Median follow-up 12.1 months

p-value = 0.022
HR=0.35,
95% CI (0.12-1.02)



1-year OS
N-AVD 95%
Bv-AVD 83%

Median follow-up 12.1 months

p-value = 0.091
HR=0.35,
95% CI (0.07-1.75)

Disposition	N-AVD N = 48, N (%)	Bv-AVD N = 49, N (%)
Treatment ongoing	1 (2%)	2 (4%)
Completed treatment	42 (88%)	31 (63%)
Discontinued all treatment early	**5 (10%)**	**16 (33%)**
Adverse event	2 (4%)	7 (14%)
Refusal unrelated to AE	1 (2%)	2 (4%)
Progression/relapse	0 (0%)	1 (2%)
Death on treatment	**1 (2%)**	**5 (10%)**
Other – not protocol specified	1 (2%)	1 (2%)
Received protocol radiotherapy	0 (0%)	0 (0%)

- N-AVD improved PFS and EFS, and was better tolerated than Bv-AVD in pts aged 60 with AS HL.
- More pts discontinued Bv-AVD than N-AVD, primarily due to toxicity.

Brentuximab Vedotin in Frontline Therapy of Hodgkin Lymphoma in Patients with Significant Comorbidities Ineligible for Standard Chemotherapy (SGN35-015 Part E)

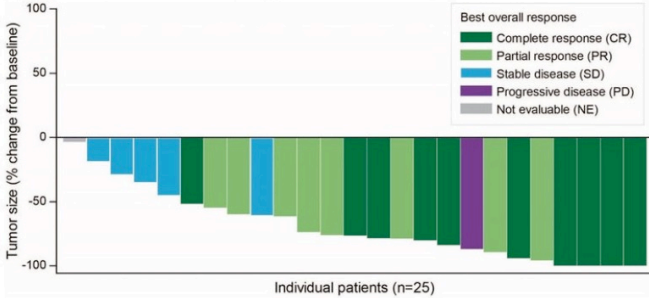
Yasenchak C. et al.
Abstract #4435

Category/variable	Per BICR (N=30)
Best clinical response[a], n (%)	
Complete response (CR)	10 (33)
95% CI[b]	17.3, 52.8
Partial response (PR)	8 (27)
Stable disease (SD)	5 (17)
Progressive disease (PD)	1 (3)
Not evaluable (NE)	1 (3)
No post-baseline response assessment[c]	5 (17)
Objective response rate (CR + PR), n (%)	18 (60)
95% CI[c]	40.6, 77.3
Disease control rate (CR + PR + SD), n (%)	23 (77)
95% CI[c]	57.7, 90.1

30 pts with cHL received BV
median age was 76 years (54-93).

median DOR was 7.4 months
median PFS was 8.7 months
median follow-up of 14.6 months

Figure 1 Maximum SPD Percentage Reduction from Baseline by BICR



In patients with cHL who are unfit for initial conventional chemotherapy because of comorbidities, BV monotherapy as frontline treatment appears effective and has an acceptable safety profile

LH in fase avanzata

PD-1 Blockade before Autologous Stem Cell Transplantation Improves Outcomes in Relapsed/Refractory Classic Hodgkin Lymphoma: Results from a Multicenter Cohort

Sanjal H. Desai, MBBS[1,2], Reid W. Merryman, MD[3], Harsh Shah, DO[4], Levi D. Pederson, MS[2], Susan M. Geyer, PhD[2], Nivetha Ganesan[5], Tiffany Chang, MS[5], Tamer Othman, MD[6], Ayo S Falade, MDMBA[3], Gunjan L. Shah[5], Urshila Durani, MD MPH[7], Kelsey Baron, MD[8], Shin Yeu Ong, MD FRCPath[9], Steve M Ansell[7], Philippe Armand, MD PhD[10], Siddharth Iyengar, MD[11], Ivana Micallef, MD[2], Alison Moskowitz, MD[5], Alex F. Herrera, MD[12], Robert Stuver, MD[5], Matthew Genyeh Mei, MD[12]

Retrospective study comparing post-transplant outcomes of R/R cHL patients who received PD1-based regimen and other novel and conventional regimen.

981 pts of R/R cHL were identified

- 195 (20%) patients received a PD-1 agent with or without BV at any point before ASCT ***(PD-1 group)***
- 312 (32%) patients received BV at any point before ASCT without PD-1 ***(BV group)***
- 474 (48%) patients received no novel agent before ASCT ***(chemo group)***

Receipt of PD-1 based salvage therapy at any point before ASCT is associated with significantly improved PFS compared to either BV or chemotherapy-based salvage treatments

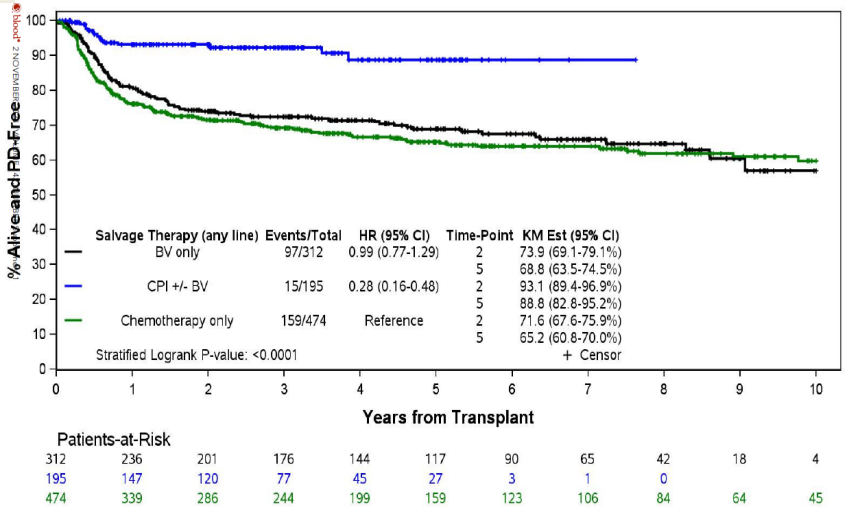


Fig 1: PFS by type of salvage therapy

Impact of Peri-Transplant Radiation on Outcomes in Patients with Relapsed/Refractory Classical Hodgkin Lymphoma Undergoing Autologous Stem Cell Transplant

Kelsey Baron, MD[1], Esther Drill, DrPH[2], Nivetha Ganesan[3], Reid W. Merryman, MD[4], Matthew G. Mei, MD[5],

Characteristics by PTRT	No PTRT, N = 719	PTRT, N = 239	P-value
Median age at diagnosis	32 (24,46)	30 (24,38)	0.018
Ann Arbor Stage at relapse			<0.001
I-II	265 (47%)	141 (73%)	
III-IV	300 (53%)	52 (27%)	
Unknown	154	46	
Bulky disease (>5cm) at relapse	116 (22%)	51 (30%)	0.048
Unknown	200	68	
Primary refractory disease	221 (40%)	117 (56%)	<0.001
Unknown	173	31	
Lines of salvage therapy prior to ASCT			<0.001
>1 line	206 (29%)	96 (40%)	
1 line	513 (71%)	143 (60%)	
Final PET/CT response before ASCT			0.007
CR	520 (73%)	153 (64%)	
<CR	190 (27%)	86 (36%)	
Unknown	9	0	
Extra-nodal disease at relapse	269 (42%)	39 (19%)	<0.001
Unknown	72	32	
B symptoms at relapse	148 (24%)	34 (17%)	0.035
Unknown	95	35	
Salvage regimen at any point			<0.001
Chemotherapy only	333 (46%)	124 (52%)	
BV only (+/- chemotherapy)	220 (31%)	88 (37%)	
CPI (+/- BV or +/- chemotherapy)	166 (23%)	27 (11%)	
BV maintenance	220 (31%)	47 (20%)	0.001

Figure 1. Kaplan Meier Curve of PFS

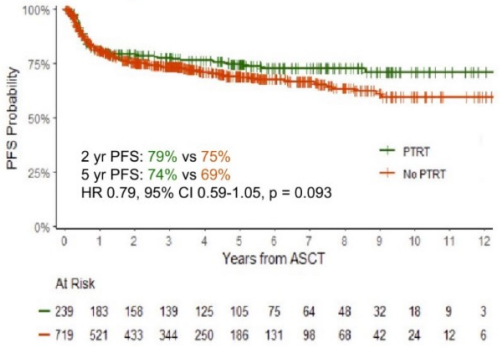
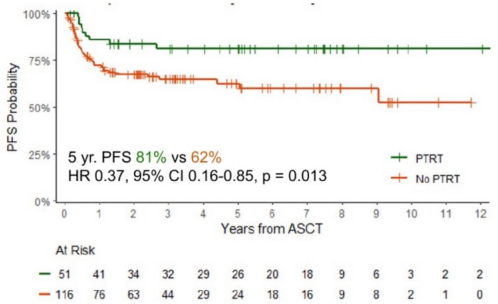


Figure 2. PFS in patients with bulky disease by PTRT



No significant difference in PFS regardless of receipt of PTRT.

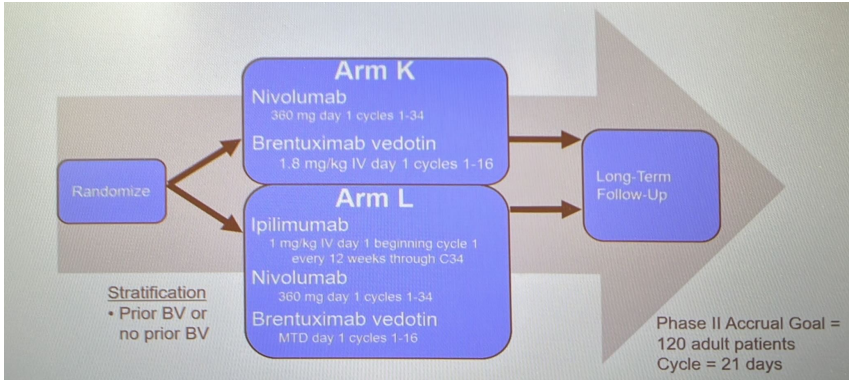
After adjusting for known clinically relevant factors, receipt of PTRT was signficantly associated with PFS and was particularly beneficial for patients with bulky disease or B-sx at relapse

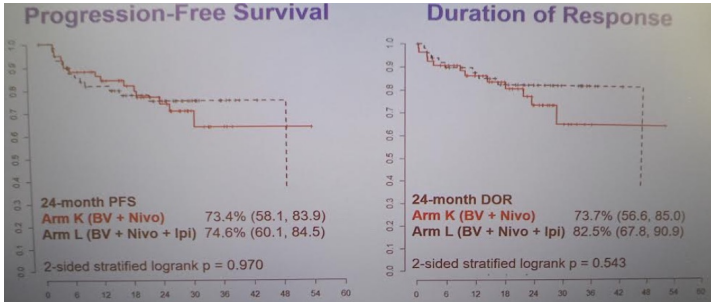
Results from an Intergroup Randomized Phase II Study of the Combinations of Ipilimumab, Nivolumab and Brentuximab Vedotin in Patients with Relapsed/Refractory Classic Hodgkin Lymphoma: A Trial of the ECOG-ACRIN Research Group (E4412)

Catherine S Diefenbach, MD[1], Opeyemi Jegede[2], Stephen M Ansell, MD PhD[3], Christian Steidl, MD PhD[4], Yasodha Natkunam, MD PhD[5,6], David W. Scott, PhDMD,FRACP,FRCPA[7], Neha Mehta-Shah, MD[8], Jennifer E Amengual, MD[9], Christopher J. Forlenza, MD[10], Peter D. Cole, MD[11], Nancy L. Bartlett, MD[12], Kevin A. David, MD[13], Ranjana H. Advani, MD[14], Richard F. Ambinder, MD[15], Sachdev Thomas, MD[16], Sami Ibrahimi, MD[17], Brad S. Kahl, MD[18]

	Arm K (BV + Nivo)	Arm L (BV+ Nivo + Ipi)
Complete Response	37 (60.7%)	38 (66.7%)*
Partial Response	17 (27.9%)	12 (21.1%)
Stable Disease	2 (3.3%)	-
Progressive Disease	1 (1.6%)	4 (7.0%)
*Unevaluable/ Indeterminate	4 (6.6%)	3 (5.3%)
Total	61	57

Anti-PD1
Anti-CD30
+/-
anti-CTLA-4





- Non significant 6.7% improvement in CR for the triplet
- Safety comparable except for rash
- At 24 mo median PFS and DOR not reached

IMM01 Plus Tislelizumab in Prior Anti-PD-1 Failed Classic Hodgkin Lymphoma: An Open Label, Multicenter, Phase 2 Study (IMM01-04) Evaluating Safety As Well As Preliminary Anti-Tumor Activity

Keshu Zhou, MD[1], Yuqin Song, MD[2], Tienan Yi[3], Shuling Hou[4], Xingchen Liu[5], Ningjing Lin[6], Tingting Du[6], Xing Zhao[3], Xiaobo Wu[4], Xiwen Zhao[7], Wei Meng[7], Wencheng Xu[7], Qiying Lu[7], Wenzhi Tian[7], Jun Zhu, MD[8]

CD47 is an innate CPI that binds SIRP alpha producing immune surveillance evasion and phagocytosis suppression
IMM01, a recombinant SIRPa-Fc fusion protein, can activate macrophages to enhance anti-tumor activity by blocking CD47-SIRPa interaction
IMM01 plus tislelizumab has the potential to augment both innate and adaptive anti-tumor immune responses.

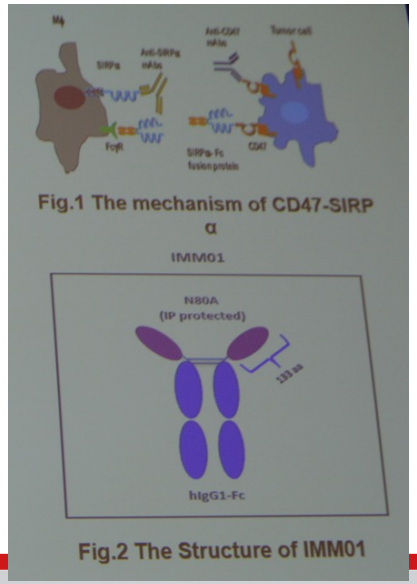


Fig.1 The mechanism of CD47-SIRP α

Fig.2 The Structure of IMM01

- IMM01 (Timdartacept) + tislelizumab showed good antitumor efficacy in anti-PD1 failed pts
- ORR 65.2%, CR 17.4%, DCR 100%
- The combination was well tolerated

Timdarpacept combined with tislelizumab showed high response in anti-PD-1 failed cHL patients

- Of 23 efficacy-evaluable patients, median follow-up time was 5.32 months.
- Best overall response was 65.2%, with 4 CR, 11 PR, 8 SD.
- Median time to response (TTR) was 1.6 months.
- mDoR, mPFS, and mOS were not reached.

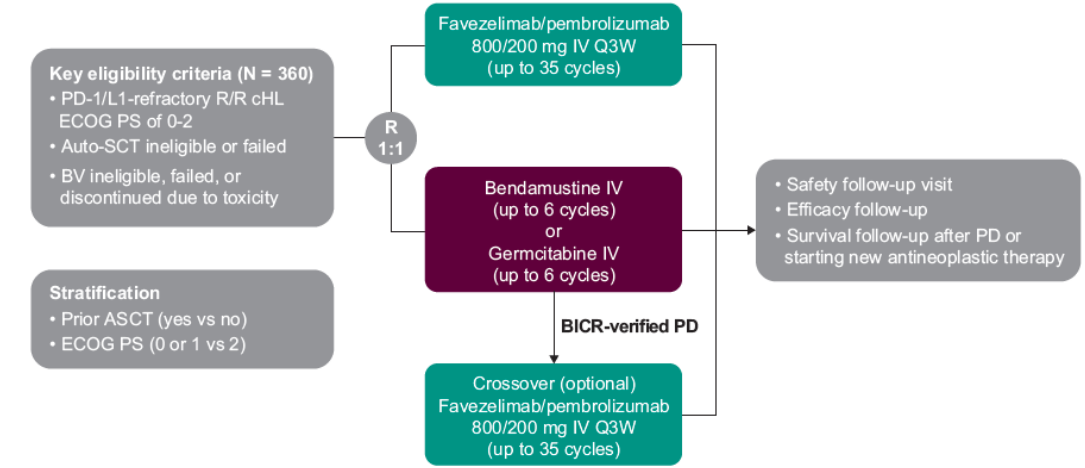
Best Response	Efficacy Evaluable (N=23)
CR, n (%)	4 (17.4)
PR, n (%)	11 (47.8)
SD, n (%)	8 (34.8)
PD, n (%)	0
ORR, n (%)	15 (65.2)
DCR, n (%)	23 (100)

Cut off date: Nov 20, 2023

Open-Label, Randomized, Phase 3 Study of Coformulated Favezelimab and Pembrolizumab Versus Chemotherapy in Patients With Relapsed or Refractory Classical Hodgkin Lymphoma Refractory to Anti-PD-1 Therapy: KEYFORM-008

- There is an unmet need for effective therapies for anti–PD-1–resistant cHL
- Upregulation of lymphocyte-activation gene 3 (LAG-3) expression in cHL is proposed to contribute to anti–PD-1 resistance1
- The anti–LAG-3 antibody favezelimab plus the anti–PD-1 therapy pembrolizumab has shown promising antitumor activity and manageable safety in patients with R/R cHL after anti–PD-1 therapy2

Study design



TISLELIZUMAB, AN ANTI–PD-1 ANTIBODY, IN PATIENTS WITH RELAPSED/REFRACTORY CLASSICAL HODGKIN LYMPHOMA IN TIRHOL BGB-A317-210: A PROSPECTIVE MULTICENTER LYSA PHASE 2 STUDY CONDUCTED IN WESTERN COUNTRIES

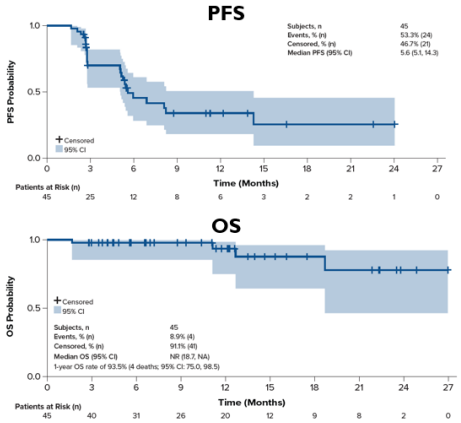
Ghesquières H, et al. Poster Presentation at ASH 2023; poster number 1717.

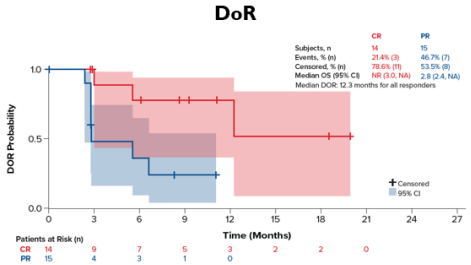
TIRHOL

Inclusion Criteria

- Histologically confirmed cHL
- Patients must have relapsed or refractory cHL
- ECOG PS of 0 or 1
- Measurable disease defined as ≥1 F-fluorodeoxyglucose-avid lesion
- **Cohort 1** included patients who previously underwent ASCT
- **Cohort 2** included patients who were ineligible for ASCT
- Prior therapy with brentuximab vedotin was required in initial design

	N=45
Best response according to Lugano classification, n (%)	
Complete remission	14 (31.1)
Partial remission	15 (33.3)
Stable disease	2 (4.4)
Progressive disease	13 (28.9)
Not evaluated	1 (2.2)
ORR according to Lugano classification, n (%)	29 (64.4)
90% CI for ORR rate	51.1–76.3

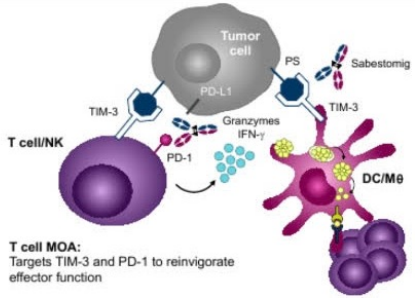




Discontinuation (n=9) or interruption (n=2) Immune-related AEs: 15 (33%) pts
ORR was similar in cohort 1 (n=9/14, 64.3%) and cohort 2 (n=20/31, 64.5%)
Tislelizumab is a promising treatment option in cHL

Safety and Preliminary Efficacy of Sabestomig (AZD7789), an Anti-PD-1 and Anti-TIM-3 Bispecific Antibody, in Patients with Relapsed or Refractory Classical Hodgkin Lymphoma Previously Treated with Anti-PD-(L)1 Therapy

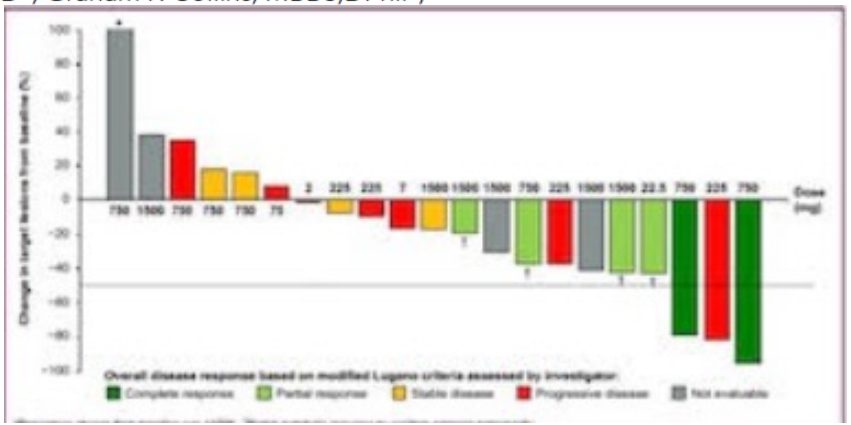
Matthew G. Mei, MD[1], Gaetano Corazzelli[2], Frank Morschhauser[3], Elizabeth Phillips, MD[4], Graham P. Collins, MBBS,DPhil[5],



- Sabestomig binds to PD-1 and a unique TIM-3 epitope compared to other anti-TIM-3 molecules to unlock distinct biology.
- Two MOAs:
  - T cells: Targets PD-1 and TIM-3 to reinvigorate T cell function and improve antitumor immune response[9]
  - Myeloid/dendritic cells: Targets TIM-3 to increase tumor cell phagocytosis and antigen presentation[9]

T cell MOA:
Targets TIM-3 and PD-1 to reinvigorate effector function

Myeloid/DC MOA:
Targets TIM-3 to increase phagocytosis, tumor antigen presentation, and antitumor T cell expansion



Safety, n (%)	N=32	
	Treatment-emergent	Possibly related to sabestomig
Any AE	26 (81.3)	20 (62.5)
Grade ≥3 AE	3 (9.4)	1 (3.1)**
AE with outcome of death	1 (3.1)*	0
AE leading to discontinuation of sabestomig	1 (3.1)	0
Serious AE	7 (21.9)	4 (12.5)†
AESI	10 (31.3)	8 (25.0)‡
Grade ≥3 AESI	0	0
Immune-mediated AE	3 (9.4)§	3 (9.4)§

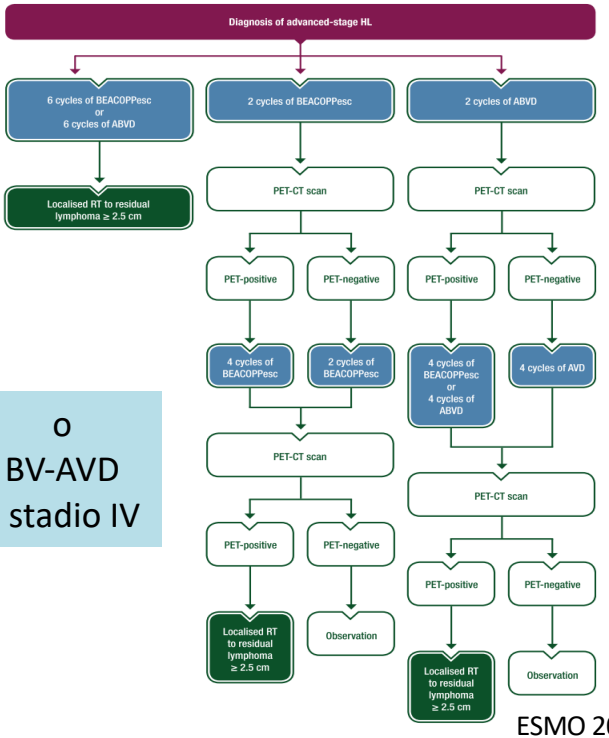
- Sabestomig was well tolerated with a manageable safety profile
- Objective responses in 5/13 patients, including those who were anti-PD-1 refractory

CONSIDERAZIONI CONCLUSIVE

Drug	Day	escBEACOPP[1] Dose (mg/m²)	BrECADD Dose (mg/m²)
Bleomycin	8	10	-
Etoposide	1–3	200	*150*
Doxorubicin	1	35	*40*
Cyclophosphamide	1	1,250	*1,250*
Vincristine	8	1.4	-
Brentuximab vedotin	1	-	*1.8 mg/kg*
Procarbazine	1–7	100	-
Prednisone	1–14	40	-
Dacarbazine	2–3	-	*250*
Dexamethasone	1–4	-	*40*

Nuove prospettive in prima linea:

oggi



ESMO 2018

o
BV-AVD
x stadio IV

Domani?

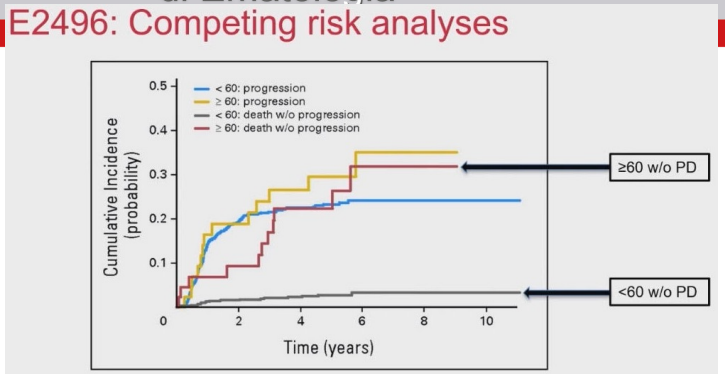
- ❑ **BRECADD**
  - Tossicità <eBEACOPP ma >ABVD
  - 3yPFS 95%
  - Nei PET2neg (59%) durata 12 sett, 3yPFS >97%
- ❑ **BV+CHEMO**
  - Maggiore PFS e OS vs. ABVD
- ❑ **CPI+CHEMO**
  - Maggiore efficacia vs. BV+chemo, ma FU 12mo
  - Rari ma seri episodi di tossicità immunomediata
- ❑ **BV+CPI+CHEMO**
  - Risultati promettenti sia early che advanced

CONSIDERAZIONI CONCLUSIVE

LH nel paziente anziano 1

1) Valutazione geriatrica multifunzionale: **FIT** **UNFIT** **FRAIL**

anziano FIT:



- Gli insuccessi sono prevalentemente legati a decessi in assenza di progressione
- L'introduzione di BV ha migliorato la prognosi rispetto all'era pre-BV
- Schema sequenziale BV-AVD-BV (Evens 2018): migliori rispetto al contemporaneo
- N-AVD (SWOG S1826) particolarmente efficace nell'anziano?
  (vantaggio significativo in PFS rispetto a BV-AVD contemporaneo, breve Follow-up)

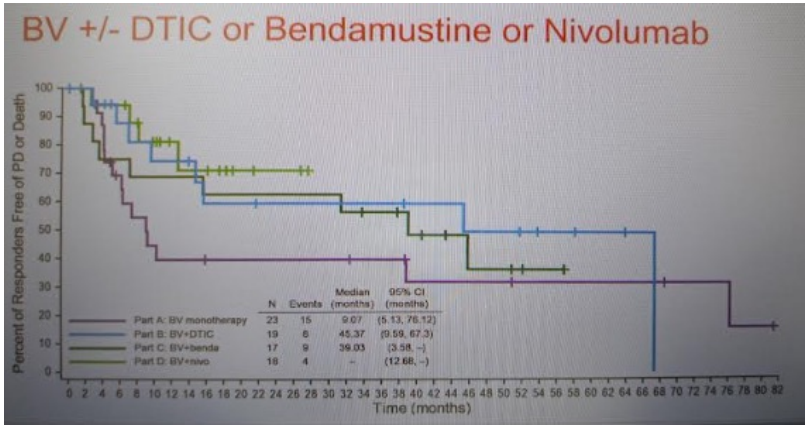
CONSIDERAZIONI CONCLUSIVE

LH nel paziente anziano 2

anziano UNFIT/FRAIL:

"Unfit" Older HL: BV +/- DTIC or Bendamustine or Nivo

Efficacy Evaluable Set	Part A BV mono N=25	Part B BV+DTIC N=19	Part C BV+benda N=17	Part D BV+nivo N=19
ORR, n (%)	23 (92)	19 (100)	17 (100)	18 (95)
Best overall response				
Complete response	18 (72)	13 (68)	15 (88)	15 (79)
Partial response	5 (20)	6 (32)	2 (12)	3 (16)
Stable disease	2 (8)	0	0	1 (5)
Progressive disease	0	0	0	0
Duration of response, n	23	19	17	18
Median (min, max)	9.1 (2.8, 81.4+)	45.4 (0.0+, 67.3)	39.0 (0.0+, 56.8+)	NR (1.4+, 27.5+)



- BV single agent: elevato tasso di risposta ma di breve durata
- BV + DTIC: risposte di più lunga durata
- BV + NIVO: risultati promettenti ma breve Follow-up

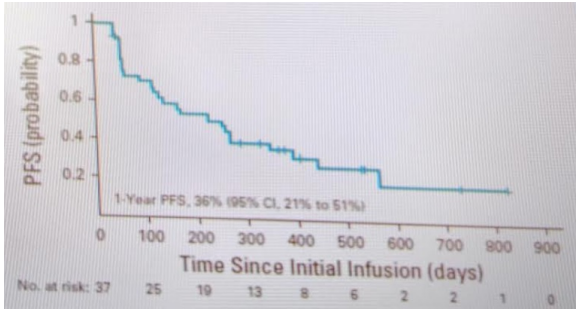
CONSIDERAZIONI CONCLUSIVE

R/R - Approcci futuri

- Ruolo CPI pre-ASCT
- Ruolo RT peritrapianto nelle forme bulky

- Combinazioni di diversi CPI
  (timdartacept-tisle, favelizumab-pembro)
- Combinazioni CPI-BV-chemo
  (AN AD, IPI-NIVO-BV)
- MoAb bispecifici?
  (Anti PD1-Anti TIM3)
- CAR-T

  Methods to improve CAR-t (combination with CPI, enhance trafficking: CD30/CCR4 coexpression, product enrichment with memory T cells..)



Ramos JCO 2020

Novità dal Meeting della Società Americana di Ematologia

Verona, 15-16-17 Febbraio 2024

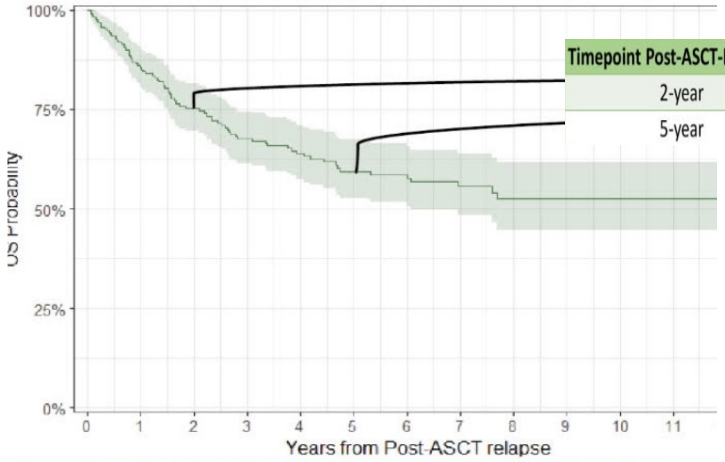
Outcomes for Patients with Classical Hodgkin Lymphoma Who Relapse after Autologous Stem Cell Transplant in the Era of Novel Therapies

Robert Stuver, MD[1], Esther Drill, DrPH[2], Nivetha Ganesan[1], Kelsey Baron, MD[3], Ellie Casper[1], Tiffany Chang, MS[1],

Table 2. Univariable Cox Regression on Post-ASCT-Relapse OS.

Characteristic	N, Event N	HR (95% CI)	p-value
Age at transplant, y	215, 82	1.05 (1.04-1.07)	**<0.001**
Age at post-ASCT-relapse, y	215, 82	1.05 (1.04-1.07)	**<0.001**
Time to relapse, m	215, 82	0.98 (0.95-1.00)	**0.043**
≤ 6 months			**0.007**
≤ 6 months		–	
> 6 months		0.55 (0.35-0.85)	
≤ 12 months			**0.024**
≤ 12 months		–	
> 12 months		0.53 (0.29-0.96)	
First regimen for post-ASCT-relapse[1]	126, 45		**0.030**
Chemotherapy only		–	
BV only		0.43 (0.20-0.95)	
Anti-PD1 +/- BV		0.44 (0.18-1.08)	
Other		1.24 (0.50-3.07)	
Relapse era	215, 82		0.083
Pre-BV approval (pre-7/31/11)		–	
Post-BV approval (8/1/11-4/30/16)		0.70 (0.39-1.24)	
Post-anti-PD1 approval (post-5/1/16)		0.45 (0.23-0.91)	

Figure 1. Post-ASCT-Relapse Overall Survival Probability.

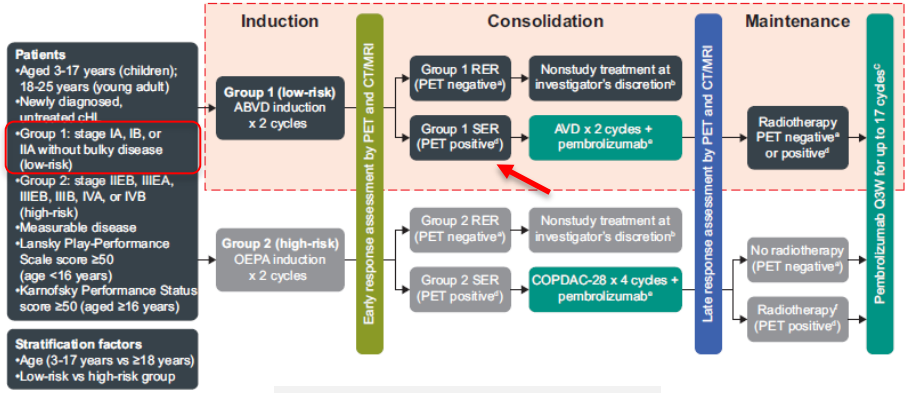


Timepoint Post-ASCT-Relapse	Post-ASCT-Relapse OS (95% CI)
2-year	75% (70%-81%)
5-year	59% (53%-67%)

Receipt of a novel agent (compared to chemotherapy alone) as the first salvage regimen for post-ASCT relapse was associated with improved post-ASCT OS (BV: HR 0.43, 95% CI 0.20-0.96; anti-PD-1: HR 0.44, 95% CI 0.18-1.08).

Pembrolizumab in Children and Young Adults With Low-Risk Classical Hodgkin Lymphoma With Slow Early Response to Front-Line Chemotherapy: Early Results From the Phase 2 KEYNOTE-667 Study

Figure 1. KEYNOTE-667 study design



SER (PET+) = 9/76

Table 2. Response by BICR per Cheson 2007 IWG criteria

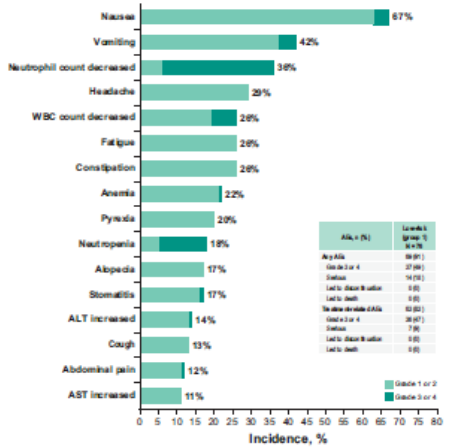
	Low-risk SER (group 1) n = 9
ORR, n (%) [95% CI]	9 (100) [66-100]
BOR, n (%)	
CR	7 (78)
PR	2 (22)
SD	0 (0)
PD	0 (0)

BOR, best overall response; PD, progressive disease; PR, partial response; SD, stable disease.

Table 3. Summary of late response assessment in patients who had SER to ABVD induction

	Low-risk SER (group 1) n = 9
Late response assessment by BICR	9 (100)
PET negative[a]	5 (56)
PET positive[b]	4 (44)
Late response assessment by investigator	9 (100)
PET negative[a]	6 (67)
PET positive[b]	3 (33)

Figure 2. Summary of AEs with ≥10% incidence in all patients during ABVD induction (N = 76)



- Only 9 patients
- AEs manageable with ABVD induction and P-AVD
- OR 100%
- CR 78% (7/9)