haematologica
Journal of the Ferrata Storti Foundation

Bleomycin omission in limited-stage classic Hodgkin lymphoma with negative PET scan after two cycles of ABVD

by Jiayu Yang, Diego Villa, Alina S. Gerrie, R. Petter Tonseth, Don C. Wilson, François Bénard, Graham W. Slack, Christopher P. Venner, Andrea C. Lo, David W. Scott, Laurie H. Sehn and Kerry J. Savage

Received: October 17, 2025.
Accepted: January 23, 2026.

Citation: Jiayu Yang, Diego Villa, Alina S. Gerrie, R. Petter Tonseth, Don C. Wilson, François Bénard, Graham W. Slack, Christopher P. Venner, Andrea C. Lo, David W. Scott, Laurie H. Sehn and Kerry J. Savage. Bleomycin omission in limited-stage classic Hodgkin lymphoma with negative PET scan after two cycles of ABVD.
Haematologica. 2026 Mar 5. doi: 10.3324/haematol.2025.289285 [Epub ahead of print]

Bleomycin omission in limited-stage classic Hodgkin lymphoma with negative PET scan after two cycles of ABVD

Jiayu Yang,[1] Diego Villa,[1,2] Alina S. Gerrie,[1,2] R. Petter Tonseth,[3] Don C. Wilson,[3] François Bénard,[3] Graham W. Slack,[2,4] Christopher P. Venner, [1,2] Andrea C. Lo,[2,5] David W. Scott,[1,2] Laurie H. Sehn,[1,2] Kerry J. Savage[1,2]

[1]Division of Medical Oncology, University of British Columbia, Vancouver, BC, Canada

[2]Centre for Lymphoid Cancer, BC Cancer, Vancouver, BC, Canada

[3]Department of Radiology, University of British Columbia, Vancouver, BC, Canada

[4]Department of Pathology, University of British Columbia, Vancouver, BC, Canada

[5]Department of Radiation Oncology, University of British Columbia, Vancouver, BC, Canada

Authors' contributions: K.J.S. and J.Y. conceived and designed the study; J.Y. and K.J.S. performed statistical analysis; R.P.T., D.C.W., and F.B. conducted the PET imaging review; G.W.S. conducted the pathology review; A.C.L provided radiation oncology review; D.V., A.S.G., C.P.V., D.W.S., and L.H.S. participated in collecting and analyzing clinical data; J.Y. and K.J.S. wrote the manuscript; and all authors edited and approved the final version of the manuscript.

Running title: Bleomycin omission in limited stage cHL

Corresponding author: Kerry J. Savage, MD, FRCPC, ksavage@bccancer.bc.ca

Data Sharing Statement: The original data are available upon request by contacting the corresponding author.

Acknowledgments
The authors are grateful to Dr. Joseph M. Connors and Dr. Randy D. Gascoyne for the development of the Lymphoid Cancer Database.

Conflict of Interest Disclosures
J.Y. reports honoraria from BeiGene and Sanofi. D.V. reports honoraria and advisory boards from AbbVie, Janssen, Kite/Gilead, AstraZeneca, Roche, BeiGene, Bristol Myers Squibb/Celgene, Merck, and Zetagen and research funding (to the institution) from AstraZeneca and Roche. A.S.G. reports honoraria from AbbVie, AstraZeneca, Janssen, and Beigene and research funding (to the institution) from AbbVie, AstraZeneca, Janssen, Roche, and Loxo Oncology. C.P.V reports honoraria from Jansen, AbbVie, Pfizer, Sanofi, Forus, and Amgen. D.W.S. reports consultancy for AbbVie, AstraZeneca, Chugai, GenMab, Incyte, Roche, and Veracyte; research funds from Janssen and Roche/Genentech; and named inventor on a patent describing the use of gene expression to subtype aggressive B-cell lymphomas, one of which is licensed to nanoString

Technologies. L.H.S. reports consulting and honoraria from AbbVie, Acerta, Amgen, Apbiologix, AstraZeneca, Celgene, Chugai, Gilead, Incyte, Janssen, Kite, Karyopharm, Lundbeck, Merck, Morphosys, Roche/Genentech, Sandoz, Seattle Genetics, Servier, Takeda, Teva, TG Therapeutics, and Verastem and research funding from Roche/Genentech and Teva. K.J.S. reports honoraria/consultancy from SeaGen and Roche; research funding from Bristol Myers Squibb; institutional research funding Roche, Merck, Seagenand AstraZeneca; Data Safety Monitoring Committee (DSMC) for Regeneron; and Steering Committee for Corvus. The remaining authors declare no competing financial interests.

Front-line therapies in early stage classic Hodgkin lymphoma (cHL) are associated with cure rates of ≥90-95%, with overall survival (OS) approaching 100% given the effectiveness of second-line therapy.[1] Thus, treatment strategies have evolved to minimize long-term treatment-associated morbidity and mortality. The phase 3 NCIC/CCTG HD6 study in early stage cHL evaluated doxorubicin, bleomycin, vinblastine, dacarbazine (ABVD) alone compared to standard therapy incorporating radiation therapy (RT).[2] In the experimental arm, those in a complete response (CR) by CT scan after ABVD x 2 (CT2) received only 2 further cycles (total 4); those with a partial response (PR) received 6 cycles total. Considering both favorable and unfavorable strata, there was a reduced progression free survival (PFS) with RT omission (87% vs. 92%, P=0.05),[2] but improved overall survival (OS) (94% vs. 87%, P=0.04), largely due to the secondary complications from historically used subtotal RT.[3] Importantly, for those in a CR by CT2 after ABVD x 2 and thus received 4 cycles total, the 5-year freedom from progression was 95%, suggesting that a response-adapted approach was feasible.[2] Collectively, subsequent early stage PET-adapted studies suggest an approximate 4-8% risk of relapse with RT omission.[4-6] However, OS is not impacted, and thus PET2-adapted management is widely used.[4-6]

Bleomycin pulmonary toxicity remains a concern with ABVD. As a cumulative toxicity, the UK RATHL study[7] investigated bleomycin omission in patients with advanced stage cHL, with a negative PET scan after ABVD x 2 (PET2-negative Deauville 1-3). PFS was not impacted when bleomycin was omitted in the remaining 4 cycles (AVD), with long term follow-up meeting the pre-defined non-inferiority margin.[8] Importantly, there was a decreased incidence of bleomycin pulmonary toxicity and improved lung function at 5 years.[7, 9] The GHSG HD13 trial evaluated the impact omitting components of ABVD in early stage favorable cHL and did demonstrate a small (3.9%), but statistically significant, increased risk of relapse comparing ABVD and AVD arms, both receiving involved field RT 30 Gy. However, this study was conducted prior to the use of PET scan for response assessment.[10]

Based on the excellent outcomes demonstrated in the HD6 study in those with an interim CT2 CR,[2, 3] a PET2-guided approach was adopted in BC in 2005 for the management of limited stage

cHL, defined as stage I or IIA with non-bulky disease (< 10cm), whereby only those with PET2-positive scan after two cycles of ABVD switched to involved nodal RT,[11] and those with a PET2-negative scan completed therapy with two further cycles of ABVD alone[12] (total 4 cycles). Further, extrapolating from the RATHL study, bleomycin omission was endorsed by our provincial lymphoma tumor group (LYTG) on January 12, 2016, for the remaining 2 cycles (AVD) for limited stage cHL patients with PET2-negative scan. Herein, we evaluated the impact on outcomes of this approach.

Patients aged 17-70 years with limited stage cHL diagnosed between December 2011–June 2022 (follow-up to June 2024) were identified in the BC Cancer Lymphoid Cancer Database, encompassing an era where in addition to response assessment, staging PET scans were also routinely performed. Those planned for curative-intent therapy with ABVD and received at least one cycle were included. Up until 2014, FDG-PET scans were evaluated based on the International Harmonization Project (IHP),[13] and subsequently by the Deauville criteria (for limited stage: D1-2, DX=PET-negative; D3-5=PET-positive),[14] with 'real time' referring to the PET2 interpretation at the time of initial management. Earlier PET scans were re-reviewed and retrospectively assigned a Deauville score as previously described.[12] Patients were recommended to receive ABVD for 2 cycles. If PET2 was positive, patients switched to involved nodal RT; those with a PET2-negative scan were recommended to receive a further 2 cycles of ABVD (December 2011-January 2016, 'ABVD era') or AVD x 2 (January 2016 onward (post LYTG meeting), 'AVD era') for a total of 4 cycles. Bleomycin pulmonary toxicity was determined by the treating physician based on clinical and/or radiographic features, resulting in permanent bleomycin discontinuation.

To evaluate the impact of PET-adapted bleomycin omission in limited stage cHL, 2 analyses were performed: (1) a comparison of outcomes in the ABVD vs. AVD treatment eras, and (2) an as-treated analysis evaluating only patients with a PET2-negative scan, who completed treatment with ABVD or ABVD/AVD alone, including a separate analysis of only those who received ABVD x 4 or ABVD x 2/AVD x 2. PFS, defined as the time from pathologic diagnosis to

relapse, progression, or death from any cause, and OS were calculated. The University of British Columbia/BC Cancer Research Ethics Board approved this study.

A total of 188 patients treated across BC were identified; most had a staging PET scan (n=179, 95.2%). Overall, 17 (9.0%) received RT, primarily for PET2-positive disease as per our management algorithm (14/17, 82%). For all patients, the median follow-up by reverse censoring was 6.2 years (range 1.3-12.4), and the 5-year PFS and OS were 93.8% and 99.3%, respectively. In total, 67 patients were managed in the ABVD era and 121 the AVD era with a median follow-up of 10.2 years (1.3-12.4) and 4.9 years (2.1-8.4) respectively. Baseline clinical features and involved nodal RT use (median dose 35 Gy, range 30-40 Gy) were similar across the eras (Table 1) and RT use was also similar (11.9% vs. 7.4%, P=0.30). Staging PET scans were performed in all patients in the AVD era compared to 86.6% in the ABVD era, (P<0.001); however, this did not impact PFS (P=0.75, results not shown). Considering all 188 patients, the 5-year PFS was 92.3% in the ABVD era compared to 94.9% in the AVD era (P=0.50) (Figure 1); 5-year OS was 98.4% compared to 100%, respectively (P=0.22) (Supplemental Figure 1A). There was only one death due to cHL which occurred during the ABVD era, and two additional deaths during the ABVD era, both due to pancreatic adenocarcinoma. There was one death in the AVD era due to cardiac disease.

In total, 186 patients had a PET2 scan as planned (Supplemental Figure 2), with 87.6% (n=163) 'real time' PET2-negative and 12.4% (n=23) PET2-positive. Review of earlier PET scans to assign a Deauville score did not alter PET2 response status: PET2-negative (87.6%) D1 n=41, D2 n=87, DX n=35; PET2-positive (12.4%) D3 n=13, D4 n=9, D5 n=1. 5-year PFS was 95.0% and 83.5% for patients with a PET2-negative and PET2-positive scan, respectively (P=0.02); 5-year OS estimates were 99.3% and 100%, respectively (P=0.17). All but four patients with a PET2-negative scan completed treatment with further chemotherapy; two patients switched to RT and two patients refused further therapy (Supplemental Figure 2). Thus, 159 patients continued chemotherapy alone (Supplementary Figure 2/3). In total, there were eight recurrences in the PET2-negative cases, two patients of which had refused further chemotherapy after 2 cycles of

ABVD, and the remaining six relapses were all at the original disease site. Of the 23 PET2-positive cases (one case with a PET scan after cycle 3A), 14 (60.9%) switched to RT as planned. Of these 14 patients, one had relapsed disease outside of the RT field, and one died of pancreatic cancer. The remaining nine PET2-positive cases completed treatment with ABVD (n=4, one of whom received 6 cycles) or a combination of ABVD/AVD (n=1) or AVD alone (n=4) (physician discretion n=8; patient refusal of RT n=1) (Supplemental Figure 2); two relapsed, one exclusively in sites that would have been included in a RT field, and one also relapsed in distant sites.

There were some management variations in each era, most commonly due to physician decision or toxicity (Supplemental Figure 2). In the ABVD era, 2 patients with PET2 D3 (i.e.. PET2-positive) received a further ABVD x 2; and 13 with a PET2-negative scan did not complete two full cycles of ABVD, most commonly due to bleomycin pulmonary toxicity (n=11). The remainder of the treatment variations (n=27) occurred in the AVD era; the most common reasons were failure to omit bleomycin despite a PET2-negative scan (n=19) and failure to switch to RT with D3 (n=5) (Supplemental Figure 2).

Of the 159 patients with a PET2-negative scan who completed treatment with further chemotherapy alone; 62/159 received a ABVD x 2 and 97/159 received AVD x 2 (n=84) as per protocol during the AVD era or, during the ABVD era received < 2 subsequent cycles of ABVD (n=13) most commonly due to bleomycin toxicity (Supplemental Figure 3). In this 'as treated' analysis focusing only on PET2-negative cases, baseline clinical features were similar (results not shown). The 5-year PFS was 96.7% (ABVD4) and 95.7% (ABVD/AVD), respectively (P=0.36) , and the 5-year OS 98.3% and 100% (P=0.75) (results not shown). Considering only patients who received a full 4 cycles of chemotherapy (n=146) (ABVD x 4 n=62 vs ABVD x 2/AVD x 2 n=84) (Supplemental Figure 3), the results are similar: 5 year PFS 96.7% vs 95.0% respectively (P=0.60) (Figure 2); 5 year OS 98.3% vs 100% respectively (P=0.32) (Supplemental Figure 1B).

In total, 16/188 patients (8.5%) had bleomycin pulmonary toxicity. The majority of patients with bleomycin toxicity were female (11/16, 68.8%); median age was 47 years (17-65) and four patients (25.0%) were 60 years of age or older, representing 18.2% of patients in the latter age group. Overall, 15 patients had clinical symptoms, and one had toxicity detected on PET2 scan; 12/16 patients had radiographic findings and seven had abnormal pulmonary function tests. Corticosteroids were used in nine patients (56.3%), and bleomycin was permanently discontinued in all patients. In total, 12/67 (17.9%) patients had bleomycin toxicity in the ABVD era, nine of which occurred during cycle 3 or 4, compared with only 4/121 (3.3%) in the AVD era ($P<0.001$), all of which occurred during cycle 2.

We extrapolated the results of the RATHL study and introduced a similar management approach for limited stage cHL, a lower risk group than advanced stage. We confirm that outcomes are preserved in both an era-to-era comparison and considering only those with a PET2-negative scan treated with chemotherapy alone, thus supporting the adoption of this strategy more widely. Notably, bleomycin-associated pulmonary toxicity was lower in the AVD era, but across the study, rare pulmonary toxicity did occur during ABVD cycle 2, thus supporting ongoing studies investigating the omission of bleomycin altogether.

Although not the focus of the current study, patients with a PET2-negative scan had a more favourable PFS, but not OS compared with those with a PET2-positive scan. Like the RAPID and H10 trials,[4, 6] we apply a conservative definition of PET2-negative (D1-2, DX) as RT is omitted. This difference in comparison to the RATHL study (PET2-negative D1-3) did lead to some variability in response interpretation by the treating physician. Regardless, for all patients with a PET2-negative scan, the 5-year PFS was 95% with chemotherapy alone.

There are some study limitations, including the retrospective nature and some non-adherence to our management policy, most commonly due to differences in PET2 CR definition in limited and advanced stage. However, strengths of our study include provincially implemented treatment guidelines, broad capture of patients in BC through our provincial database, in

addition to both centralized PET reporting and hematopathology review. In summary, our data support that bleomycin can be safely omitted from subsequent treatment in limited stage patients with a negative PET scan following ABVD x 2 without compromising cure and may reduce overall bleomycin-related toxicity.

References

1. Ansell SM. Hodgkin lymphoma: 2018 update on diagnosis, risk-stratification, and management. Am J Hematol. 2018;93(5):704-715.

2. Meyer RM, Gospodarowicz MK, Connors JM, et al. Randomized comparison of ABVD chemotherapy with a strategy that includes radiation therapy in patients with limited-stage Hodgkin's lymphoma: National Cancer Institute of Canada Clinical Trials Group and the Eastern Cooperative Oncology Group. J Clin Oncol. 2005;23(21):4634-4642.

3. Meyer RM, Gospodarowicz MK, Connors JM, et al. ABVD alone versus radiation-based therapy in limited-stage Hodgkin's lymphoma. N Engl J Med. 2012;366(5):399-408.

4. André MPE, Girinsky T, Federico M, et al. Early Positron Emission Tomography Response-Adapted Treatment in Stage I and II Hodgkin Lymphoma: Final Results of the Randomized EORTC/LYSA/FIL H10 Trial. J Clin Oncol. 2017;35(16):1786-1794.

5. Fuchs M, Goergen H, Kobe C, et al. Positron Emission Tomography-Guided Treatment in Early-Stage Favorable Hodgkin Lymphoma: Final Results of the International, Randomized Phase III HD16 Trial by the German Hodgkin Study Group. J Clin Oncol. 2019;37(31):2835-2845.

6. Radford J, Illidge T, Counsell N, et al. Results of a trial of PET-directed therapy for early-stage Hodgkin's lymphoma. N Engl J Med. 2015;372(17):1598-1607.

7. Johnson P, Federico M, Kirkwood A, et al. Adapted Treatment Guided by Interim PET-CT Scan in Advanced Hodgkin's Lymphoma. N Engl J Med. 2016;374(25):2419-2429.

8. Luminari S, Fossa A, Trotman J, et al. Long-Term Follow-Up of the Response-Adjusted Therapy for Advanced Hodgkin Lymphoma Trial. J Clin Oncol. 2024;42(1):13-18.

9. Phillips EH, Kirkwood AA, Hague C, et al. Bleomycin Affects Lung Function for at Least 5 Years after Treatment for Hodgkin Lymphoma - Data from the International, Randomised Phase 3 RathI Trial. Blood. 2023;142(Supplement 1):612.

10. Behringer K, Goergen H, Hitz F, et al. Omission of dacarbazine or bleomycin, or both, from the ABVD regimen in treatment of early-stage favourable Hodgkin's lymphoma (GHSG HD13): an open-label, randomised, non-inferiority trial. Lancet. 2015;385(9976):1418-1427.

11. Campbell BA, Voss N, Pickles T, et al. Involved-nodal radiation therapy as a component of combination therapy for limited-stage Hodgkin's lymphoma: a question of field size. J Clin Oncol. 2008;26(32):5170-5174.

12. Villa D, Sehn LH, Aquino-Parsons C, et al. Interim PET-directed therapy in limited-stage Hodgkin lymphoma initially treated with ABVD. Haematologica. 2018;103(12):e590-e593.

13. Cheson BD, Pfistner B, Juweid ME, et al. Revised response criteria for malignant lymphoma. J Clin Oncol. 2007;25(5):579-586.

14. Barrington SF, Mikhaeel NG, Kostakoglu L, et al. Role of imaging in the staging and response assessment of lymphoma: consensus of the International Conference on Malignant Lymphomas Imaging Working Group. J Clin Oncol. 2014;32(27):3048-3058.

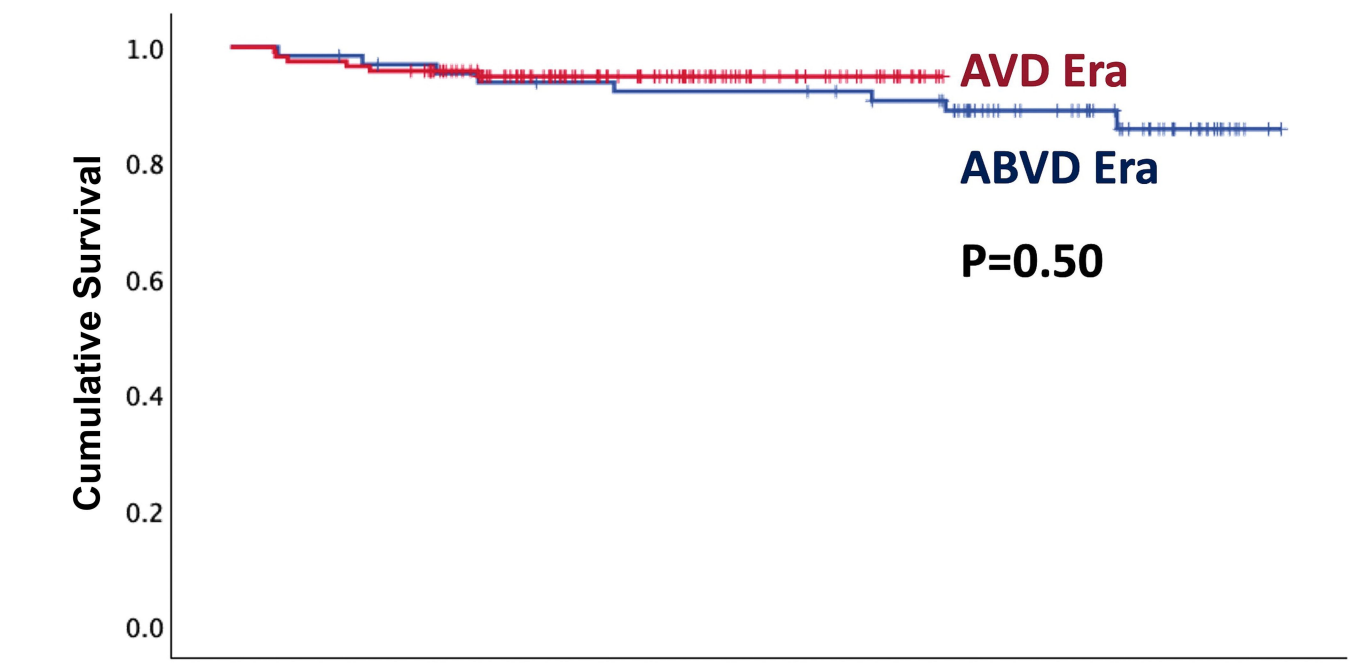
	All patients n=188	ABVD era n=67	AVD era n=121	P-value
Male (%)	90 (47.9)	34 (50.7)	56 (46.3)	0.56
Median age in years (range)	34 (17-68)	32 (17-67)	35 (18-68)	-
Age ≥60 years (%)	22 (11.7)	8 (11.9)	14(11.6)	0.94
Stage IIA (%)	154 (81.9)	57 (85.1)	97(80.2)	0.40
Extranodal involvement (%)	7 (3.7)	4 (6.0)	3 (2.5)	0.23
Median size of largest mass in cm (range)	4 (1-9)	4 (1-9)	4 (1-9)	-
Mass size (%) **<5 cm** **5-7 cm** **>7-9 cm**	 120 (63.8) 45 (12.2) 179(95.2)	 43 (64.2) 13 (19.4) 11 (16.4)	 77 (63.6) 32 (26.4) 12 (9.9)	0.30
Hemoglobin < 105 g/dL (%)	2 (1.1)	1(1.5)	1 (.8)	0.67
Staging PET scan (%)	179 (95.2)	58 (86.6)	121 (100)	<0.001
Involved nodal radiation therapy (%)	17 (9.0)	8 (11.9)	9 (7.4)	0.30

Table 1. Baseline characteristics, use of staging PET scan and receipt of radiotherapy in all patients with limited stage classic Hodgkin lymphoma, with comparison of those managed in the ABVD and AVD era

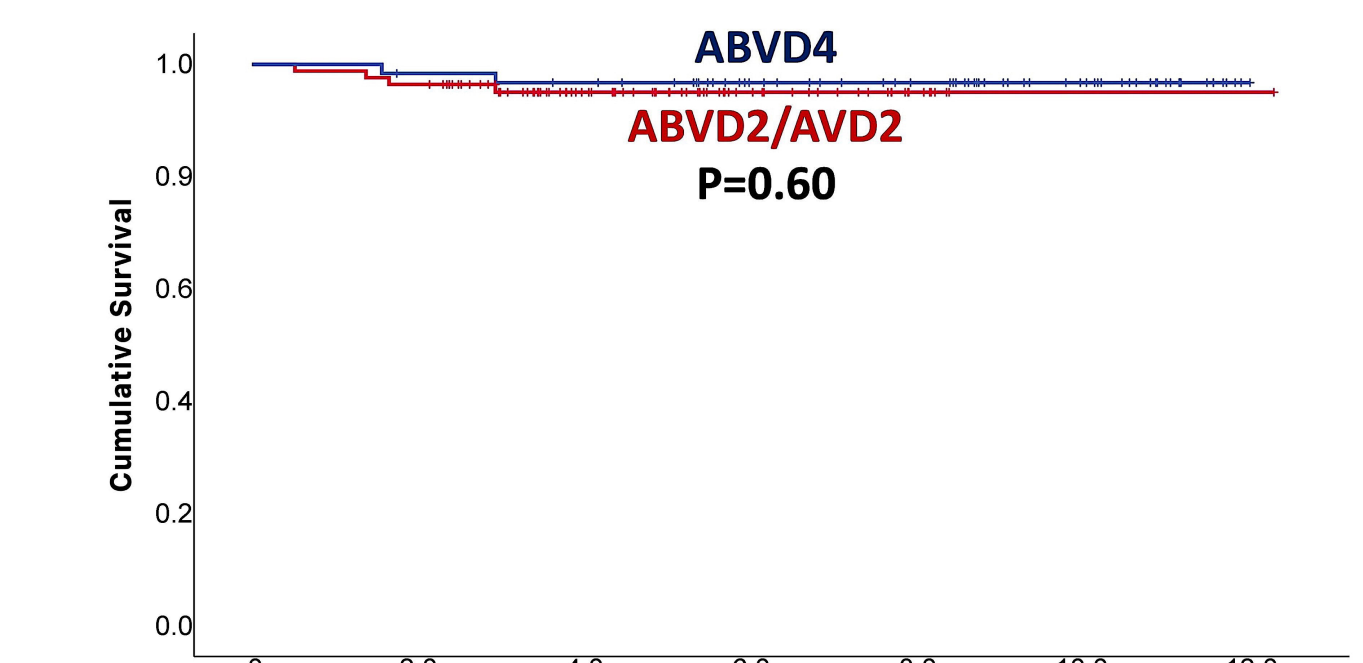
Figure Legends

Figure 1. Progression free survival of limited stage classic Hodgkin lymphoma patients managed in the ABVD era vs. AVD era.

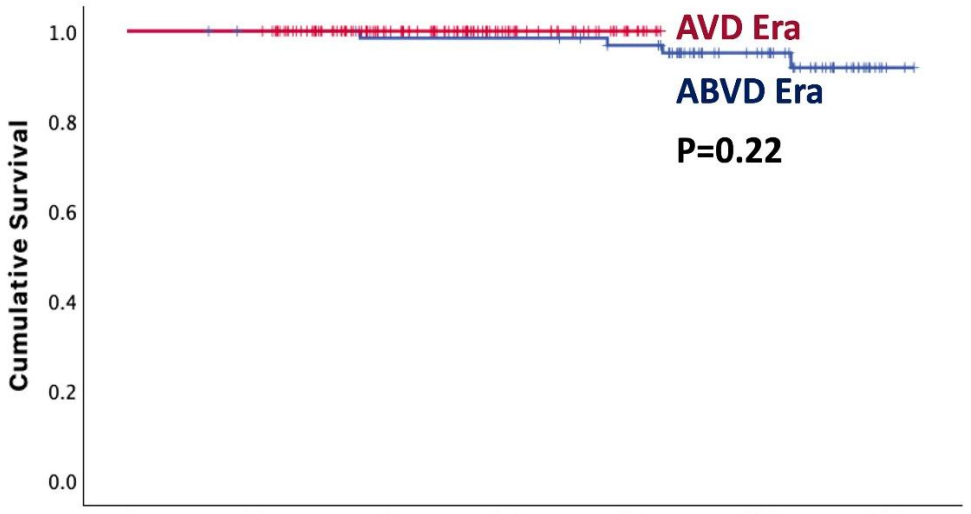
Figure 2. Progression-free survival of limited stage classic Hodgkin lymphoma patients with a PET2-negative scan (Deauville DX, D1-2) following 2 cycles of ABVD treated with ABVD x 4 vs. ABVD x 2/AVD x 2.



Number at Risk							
ABVD Era	67	63	60	59	55	34	2
AVD Era	121	116	72	33	8	0	0

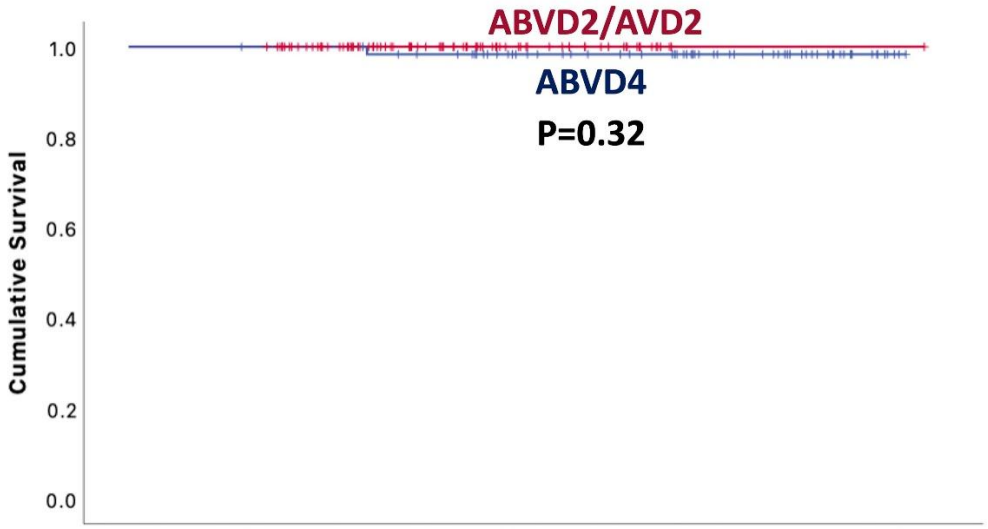


Number at Risk							
ABVD4	62	60	58	46	38	23	0
ABVD2/AVD2	84	81	48	23	7	0	0



Number at Risk							
ABVD Era	67	65	63	63	59	36	2
AVD Era	121	121	77	35	8	0	0

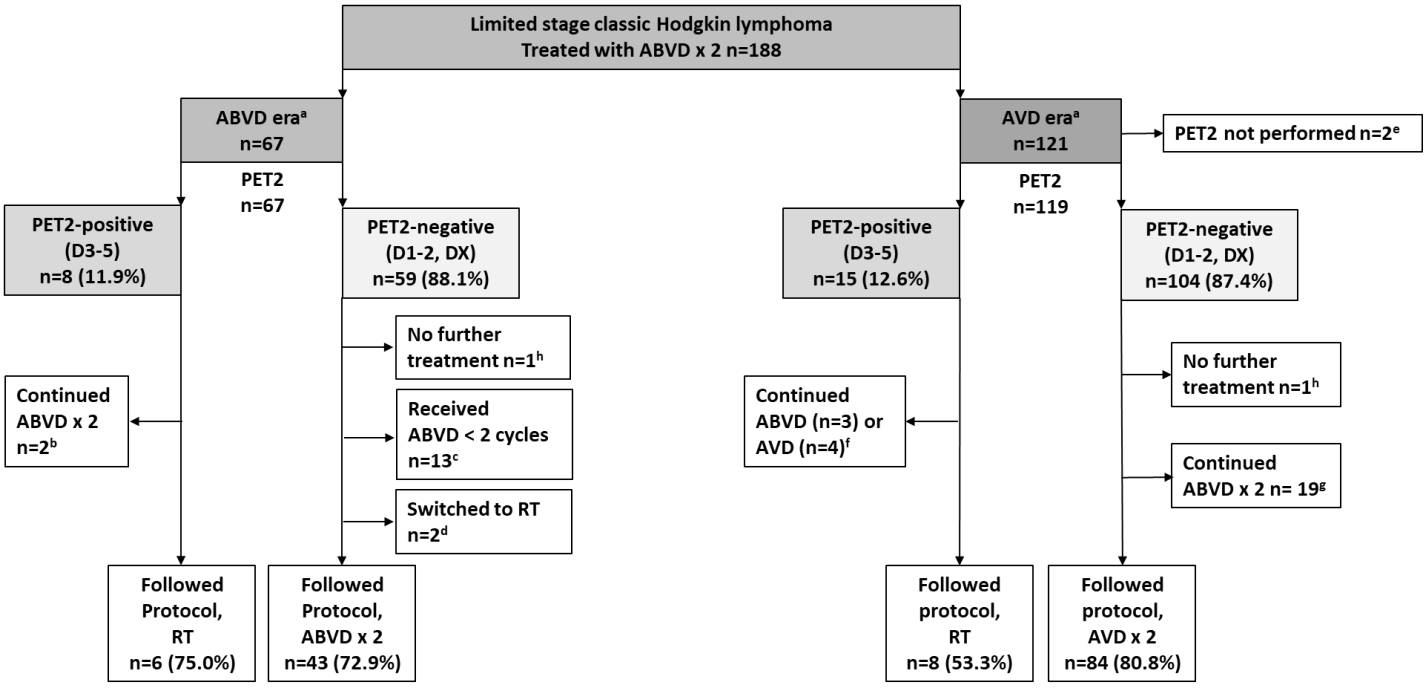
A.



Number at Risk							
ABVD4	62	61	59	47	39	24	0
ABVD2/AVD2	84	83	52	25	7	0	0

B.

Supplemental Figure 1. Overall survival for limited stage classic Hodgkin lymphoma patients (A) All patients (n=188): ABVD era vs. AVD era (B) PET2-negative scan (n=146) following 2 cycles of ABVD treated with subsequent ABVD x 2 vs. AVD x 2


Limited stage classic Hodgkin lymphoma
Treated with ABVD x 2 n=188
ABVD era[a]
n=67
AVD era[a]
n=121
PET2 not performed n=2[e]
PET2
n=67
PET2
n=119
PET2-positive
(D3-5)
n=8 (11.9%)
PET2-negative
(D1-2, DX)
n=59 (88.1%)
PET2-positive
(D3-5)
n=15 (12.6%)
PET2-negative
(D1-2, DX)
n=104 (87.4%)
No further
treatment n=1[h]
Continued
ABVD x 2
n=2[b]
Received
ABVD < 2 cycles
n=13[c]
Switched to RT
n=2[d]
Continued
ABVD (n=3) or
AVD (n=4)[f]
No further
treatment n=1[h]
Continued
ABVD x 2 n= 19[g]
Followed
Protocol,
RT
n=6 (75.0%)
Followed
Protocol,
ABVD x 2
n=43 (72.9%)
Followed
protocol,
RT
n=8 (53.3%)
Followed
protocol,
AVD x 2
n=84 (80.8%)

Supplemental Figure 2. CONSORT diagram outlining treatment received for all limited stage classic Hodgkin lymphoma patients diagnosed December 2011 to June 2022 by treatment era. ABVD era 2011-Jan 2016; AVD era Jan 2016-2022.

D=Deauville. RT=radiotherapy

[a] Did not receive full ABVD x 2 pre-PET2 (n=2): ABVD x 1 then AVD (patient decision n=1, ABVD era); ABVD x 1.5 then AVD (suspected bleomycin toxicity not confirmed n=*1, AVD era see also [f]); one case each had a PET scan after cycle 3 (ABVD era) or after cycle 1 (AVD era) due to scheduling (both PET-negative and included with PET2-negative analyses)

[b]ABVD era PET2-positive (PET2 D3) ABVD continued (MD choice n=2)

[c]ABVD era PET2-negative received ABVD < 2 cycles (n=13): AVD x 1 (bleomycin hypersensitivity post cycle 2B and then poor tolerance n=1); ABVD x 1 (patient decision n=1); ABVD/AVD x total 2 cycles (bleomycin pulmonary toxicity n=11)

[d]ABVD era PET2-negative switched to RT (n=2)(poor tolerance n=1; bleomycin toxicity n=1)

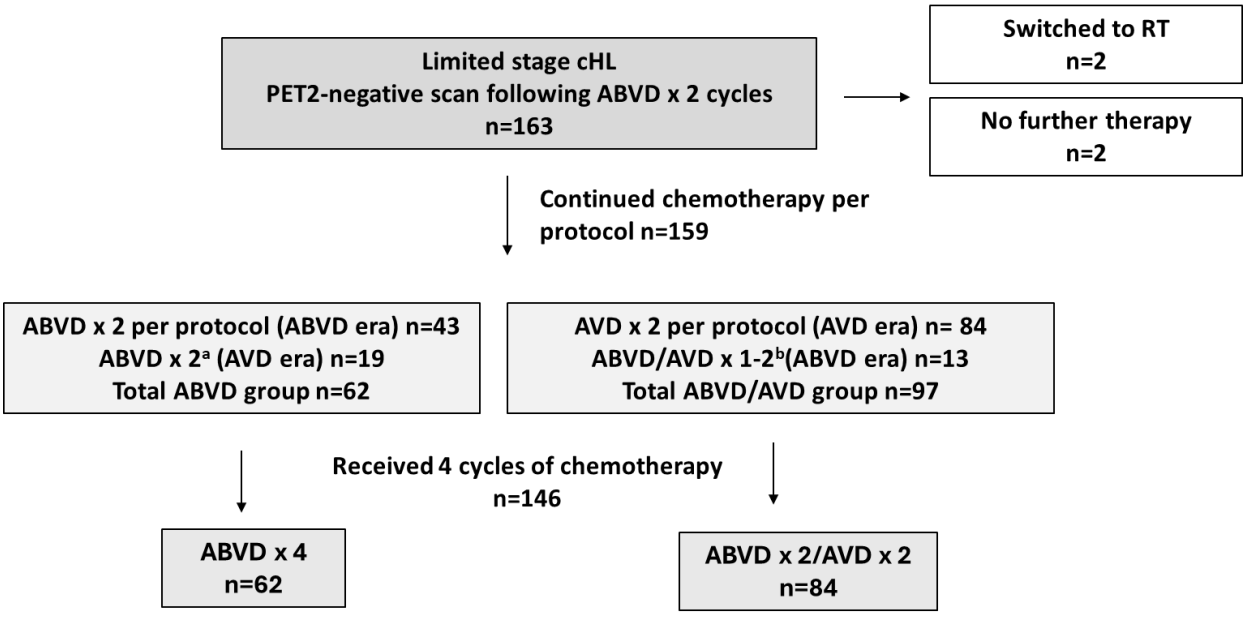
[e]AVD era PET2 not performed (patient decision n=2): Treatment received - ABVD x 2 + RT n=1; ABVD x 4 n=1

[f]AVD era PET2-positive continued ABVD or AVD (n=7): PET2 D4 ABVD x 2 or 4 (MD choice 1 patient each), PET2 D3 AVD x 2 (MD choice n=4); ABVD x 1.5 →?bleomycin toxcity AVD cycle 2B normal PFTs → PET2 D3 → ABVD cycle 3A → AVD cycle 3B/4 (MD choice n=1*)

[g]AVD era PET2-negative continued ABVD x 2 (MD choice n=19)

[h]Following ABVD x 2, PET2-negative, no further treatment (patient decision n=2 (1 in each era))

*Same patient



Supplemental Figure 3. CONSORT diagram of limited stage classic Hodgkin lymphoma PET2-negative cases

Note: Analyses are in patients who received subsequent chemotherapy alone; 1 case each had PET scan after cycle 3 or cycle 1 and are included in PET2-negative analysis.

[a]ABVD continued in AVD era by MD choice

[b]Received < 2 cycles of ABVD due to bleomycin toxicity or MD choice (see Supplemental Figure 2[c])