23rd INTERNATIONAL ULTMANN CHICAGO LYMPHOMA SYMPOSIUM

APRIL 10-11, 2026

JW MARRIOTT CHICAGO

#IUCLS2026

This activity is jointly provided by:

THE UNIVERSITY OF CHICAGO MEDICINE & BIOLOGICAL SCIENCES

Bio Ascend™
A Vaniam Group Company

INTERNATIONAL 23rd ULTMANN CHICAGO LYMPHOMA

Updated Strategies in Advanced Stage Classic Hodgkin Lymphoma

Sarah C. Rutherford, MD
Associate Professor of Clinical Medicine
Weill Cornell Medicine
New York, NY

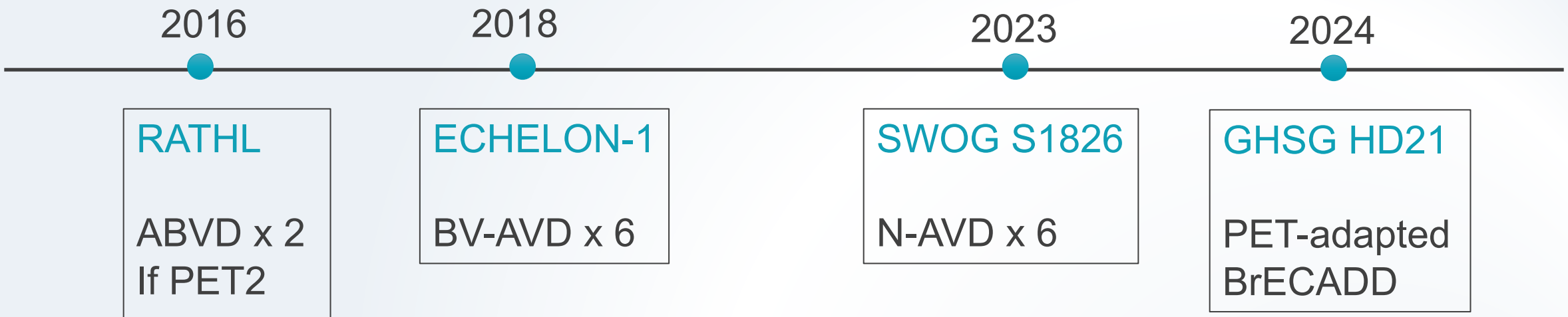
THE UNIVERSITY OF CHICAGO MEDICINE & BIOLOGICAL SCIENCES
Bio Ascend™ A Vaniam Group Company

Disclosures

Consulting: Abbvie, Genmab, Incyte, Ipsen, Kite, Natera, Pfizer

Research Funding: Genentech/Roche, Ipsen, Karyopharm

Evolution in Treatment of Advanced Stage Classic Hodgkin lymphoma (cHL)



Johnson et al NEJM 2016; Connors et al NEJM 2018; Ansell et al NEJM 2022; Herrera et al NEJM 2024Borchmann P et al. Lancet 2024

Updated Strategies in Advanced Stage cHL

1. Consideration of BrECADD

2. Use of CPI-based therapy in the real world

3. Incorporating ctDNA to guide treatment

CPI: checkpoint inhibitor; ctDNA: circulating tumor DNA

Case 1: 32 y/o F w/ Newly Diagnosed cHL and Ulcerative Colitis

UC stable on adalimumab

Presented to PCP w/ 1 year of pruritus, referred to hematology due to labs

Labs: WBC 17, Hgb 13, Plt 537, alk phos 150, LDH 300, ESR 67, EBV PCR neg

PET/CT w/ 14 cm mediastinal mass (SUV 10.7), bone and spleen uptake

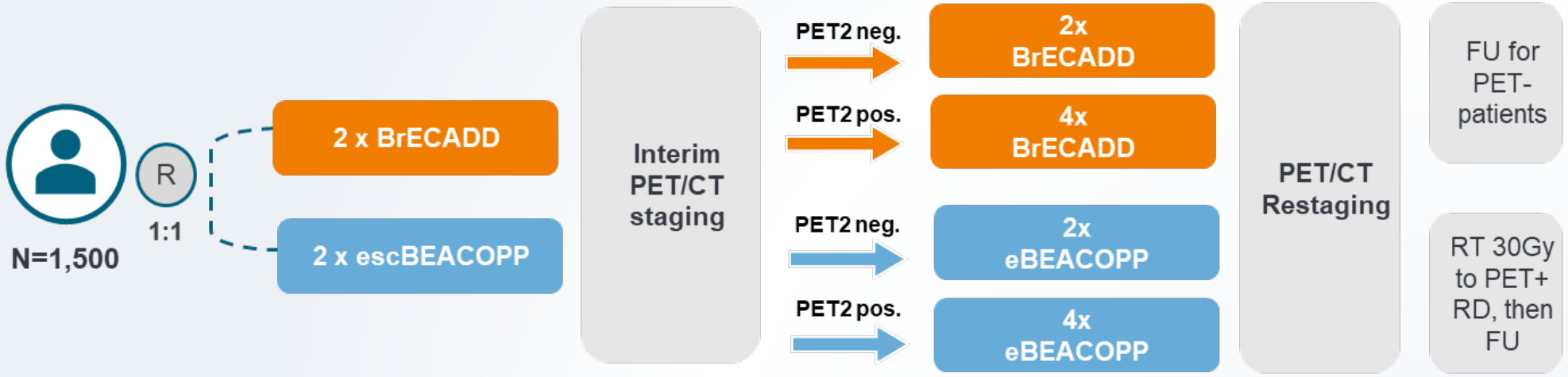
Mediastinal tissue biopsy w/ cHL

Has 2 young children and wants to complete treatment as quickly as possible

BrECADD

GHSG HD21 Study Design and Primary Endpoints

Phase 3 study of BrECADD versus eBEACOPP in adult patients < 60 yo with previously untreated, AS-cHL



Co-primary objectives:

- Demonstrate **superior tolerability** defined by treatment-related morbidity (TRMB) with BrECADD.
- Demonstrate **non-inferior efficacy** of 4-6 x BrECADD compared with 4-6 x BEACOPP determined by PFS (NI margin 6%, HR to be excluded 1.69)

Borchmann P et al. Lancet 2024.

Slides courtesy of Peter Borchmann

GHSG HD21: Treatment Regimens eBEACOPP vs BrECADD

Study Drug	Day	eBEACOPP Dose (mg/m^2)	BrECADD Dose (mg/m^2)
Bleomycin	8	10	–
Etoposide	1–3	200	150
Doxorubicin	1	35	40
Cyclophosphamide	1	1250	1250
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

eBEACOPP and BrECADD cohorts were well balanced

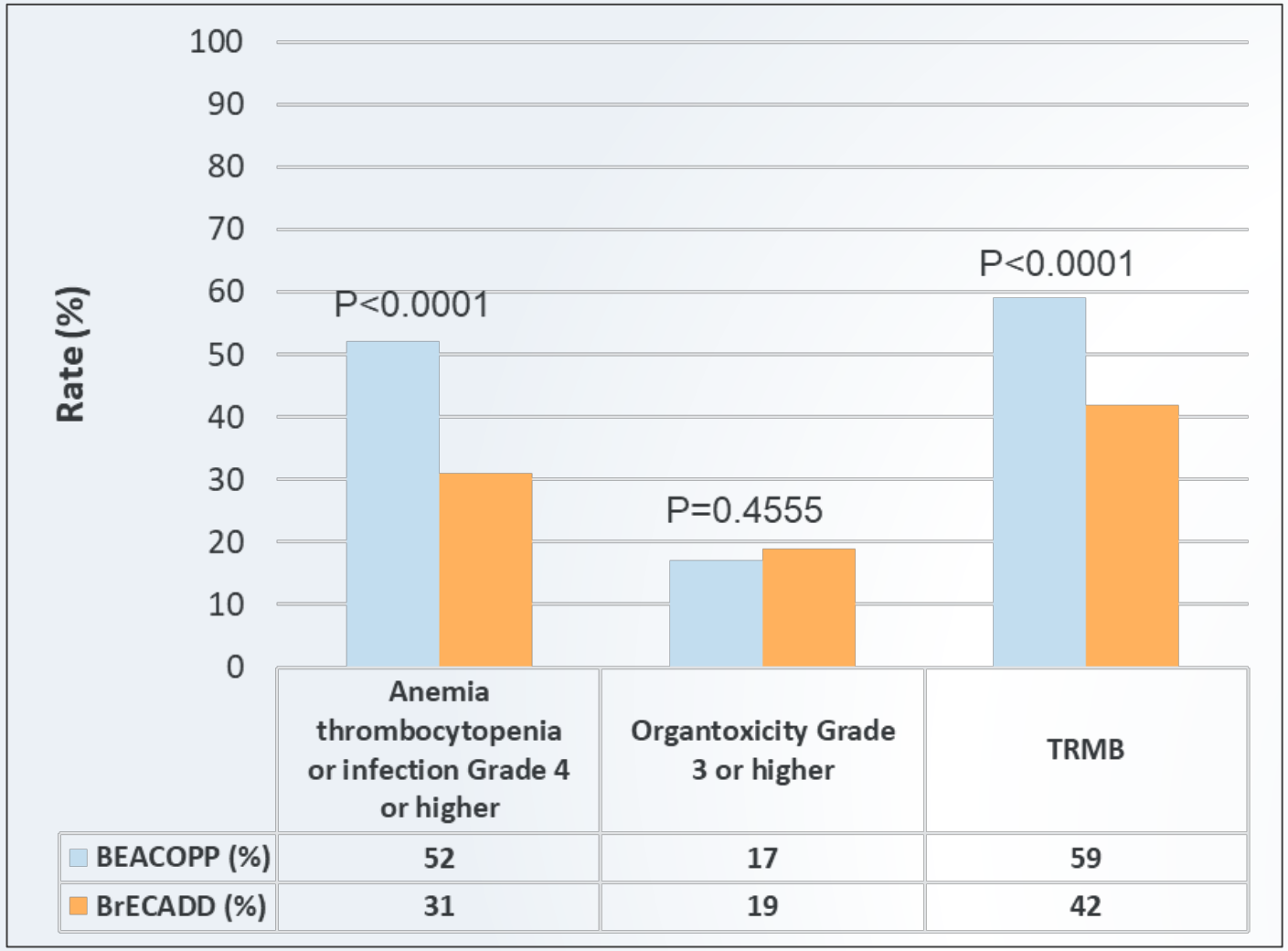
ITT-PFS Stratification factors for randomization	eBEACOPP N=740	BrECADD N=742
	N [%]	NN [%]
Location of recruitment		
Europe	682 **(92)**	684 **(92)**
AU, NZ	58 **(8)**	58 **(8)**
Sex female	326 **(44)**	330 **(44)**
male	414 **(56)**	412 **(56)**
Age < 45	577 **(78)**	587 **(79)**
>= 45	163 **(22)**	155 **(21)**
IPS < 3	399 **(54)**	391 **(53)**
>= 3	341 **(46)**	351 **(47)**

Borchmann P et al. Lancet 2024.

- Median age: 34 y [18-61] vs 34 y [18-61]
- ECOG PS 0: 70% vs 68%
- B-Symptoms: 67% vs 68%
- Stage: IIB 16% and III/IV 84% each
- Histology: 48% vs 53% with nodular sclerosis

Slides courtesy of Peter Borchmann

Treatment-related morbidity (TRMB) was lower on BrECADD arm



	Anemia thrombocytopenia or infection Grade 4 or higher	Organtoxicity Grade 3 or higher	TRMB
BEACOPP (%)	52	17	59
BrECADD (%)	31	19	42

TRMB =

- Anemia, thrombocytopenia or infection grade ≥ 4
- Organ toxicity grade ≥ 3

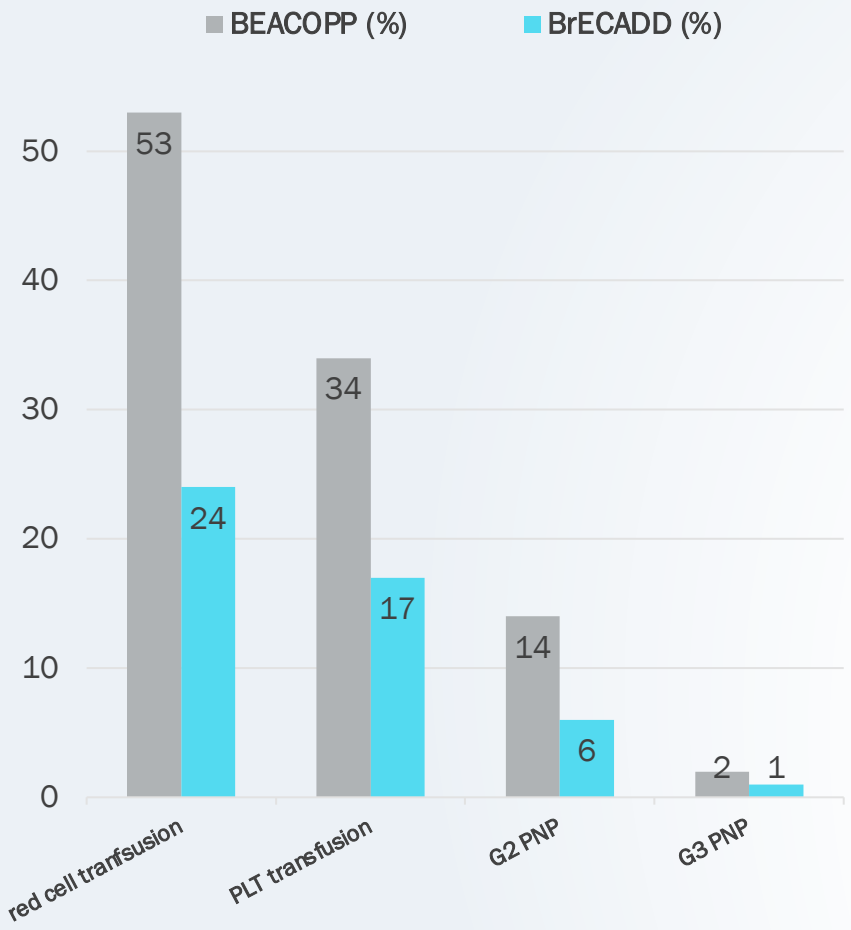
Analysis of TRMB
C-Rel-Risk of BrECADD = **0.70;**
95%-CI = **0.63 – 0.78;** p **< 0.0001**

Borchmann P et al. Lancet 2024.

Recovery of TRMB after 12 months in majority of patients

Slides courtesy of Peter Borchmann

Patients receiving BrECADD required fewer transfusions



Incidence of severe leukopenia, neutropenic fever, and infections

	Leukopenia grade ≥ 3	Neutropenic fever grade ≥ 3	Infection grade ≥ 3
eBEACOPP	691 (94%)	141/677 (21%)	138 (19%)
BrECADD	641 (87%)	193/681 (28%)	150/737 (20%)

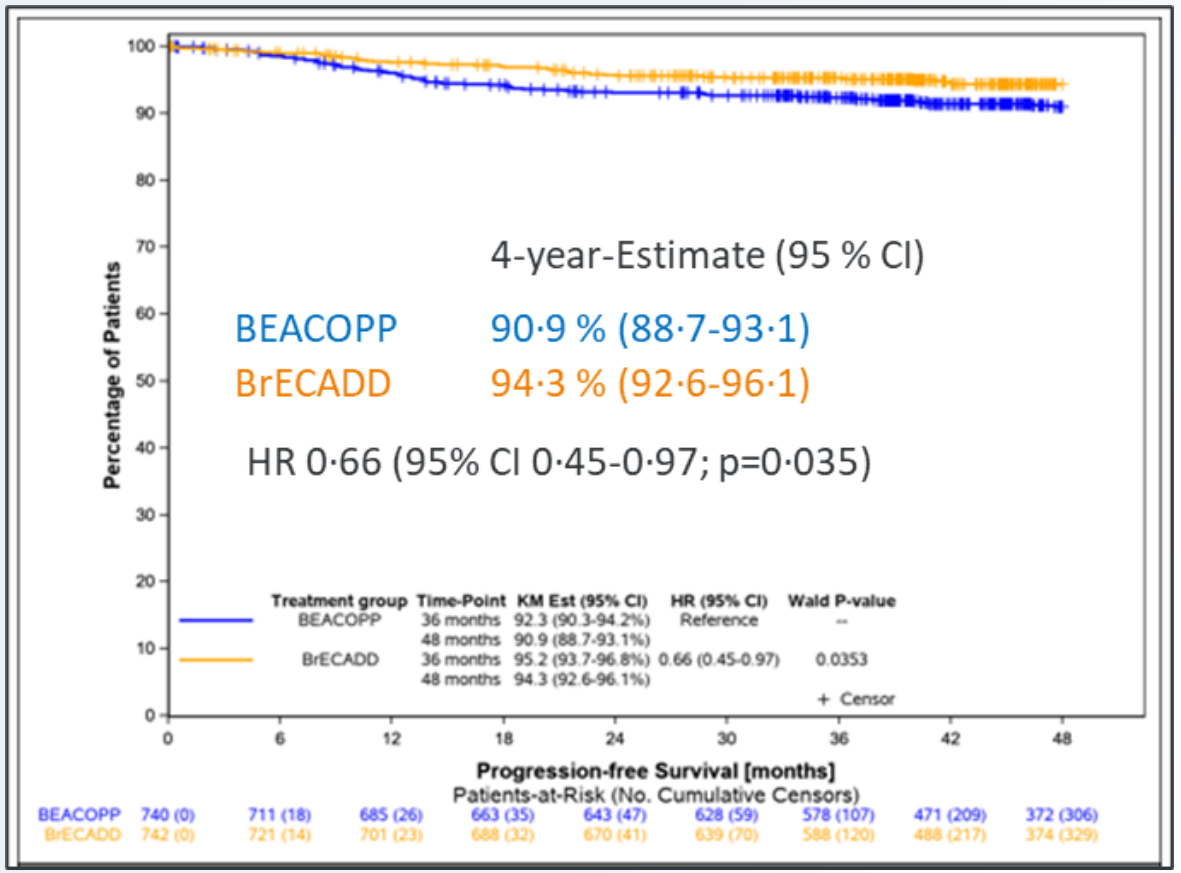
On BreCADD, 24% PRBC and 17% plt transfusions
28% neutropenic fever

Borchmann P et al. Lancet 2024.

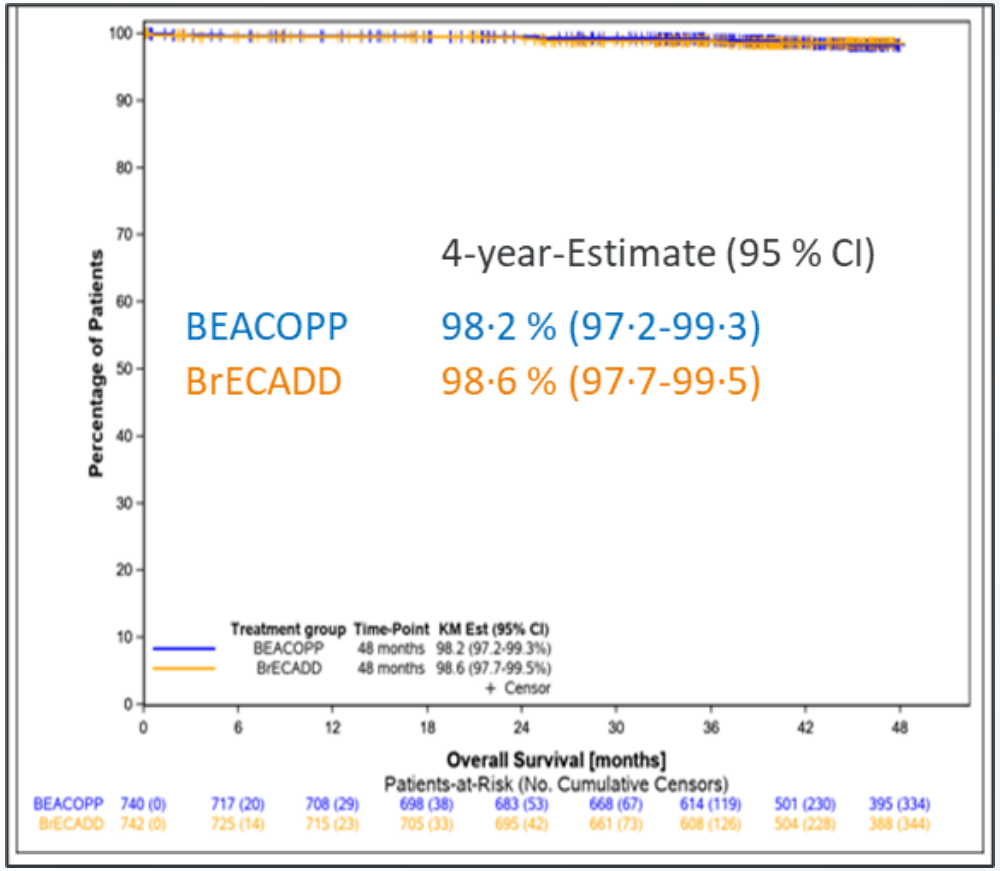
Slides courtesy of Peter Borchmann

BrECADD is non-inferior to eBEACOPP (median follow up 48 m)

Progression-free survival



Overall survival



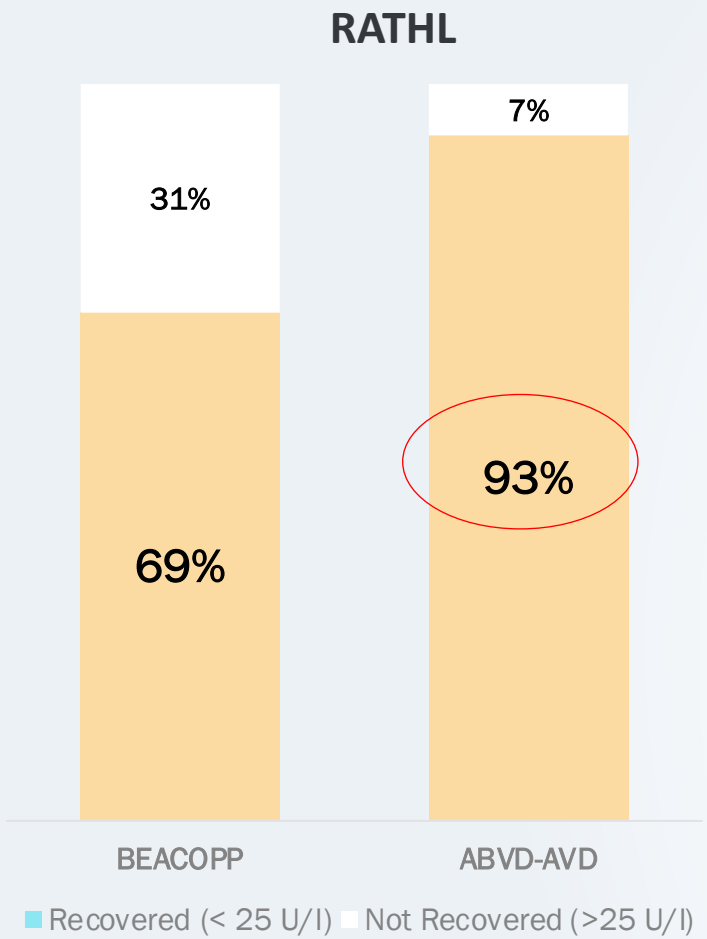
64% of patients on BrECADD received 4 cycles (12 weeks); Cumulative dose doxorubicin = 160 mg/m2

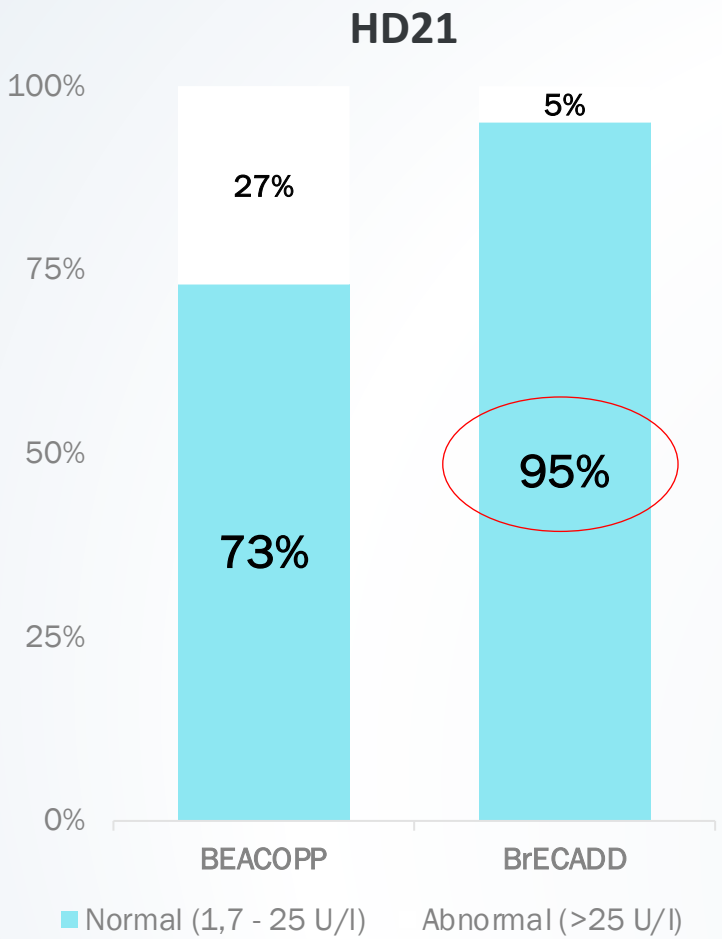
Borchmann P et al. Lancet 2024.

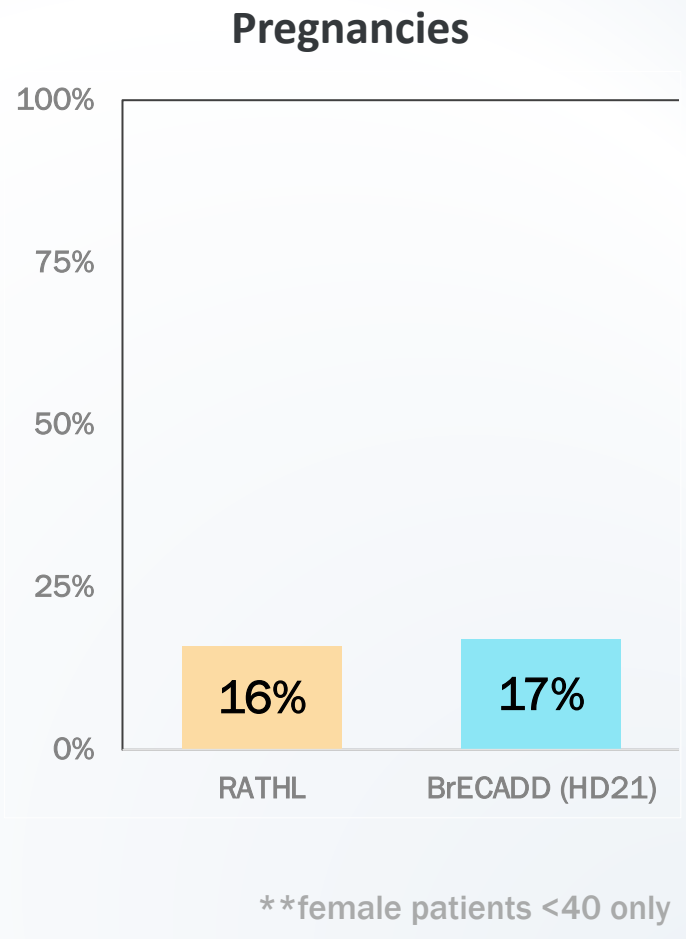
Slides courtesy of Peter Borchmann

Ovarian function recovery and pregnancies after treatment

RATHL vs. HD21 for advanced cHL







**female patients <40 only

Anderson et al., Lancet Oncol 2018; Borchmann P et al. Lancet 2024.

Slides courtesy of Peter Borchmann

Case 1: 32 y/o F w/ Newly Diagnosed cHL and Ulcerative Colitis

Underwent treatment with BrECADD x 2 cycles

Experienced fatigue and grade 3 cytopenias, no need for transfusions

PET/CT after 2 cycles with CR

Completing 2 additional cycles of BrECADD

Case 2: 23 y/o M w/ Newly Diagnosed cHL and LV EF 17%

23 y/o M admitted to ICU with fevers, chills, night sweats

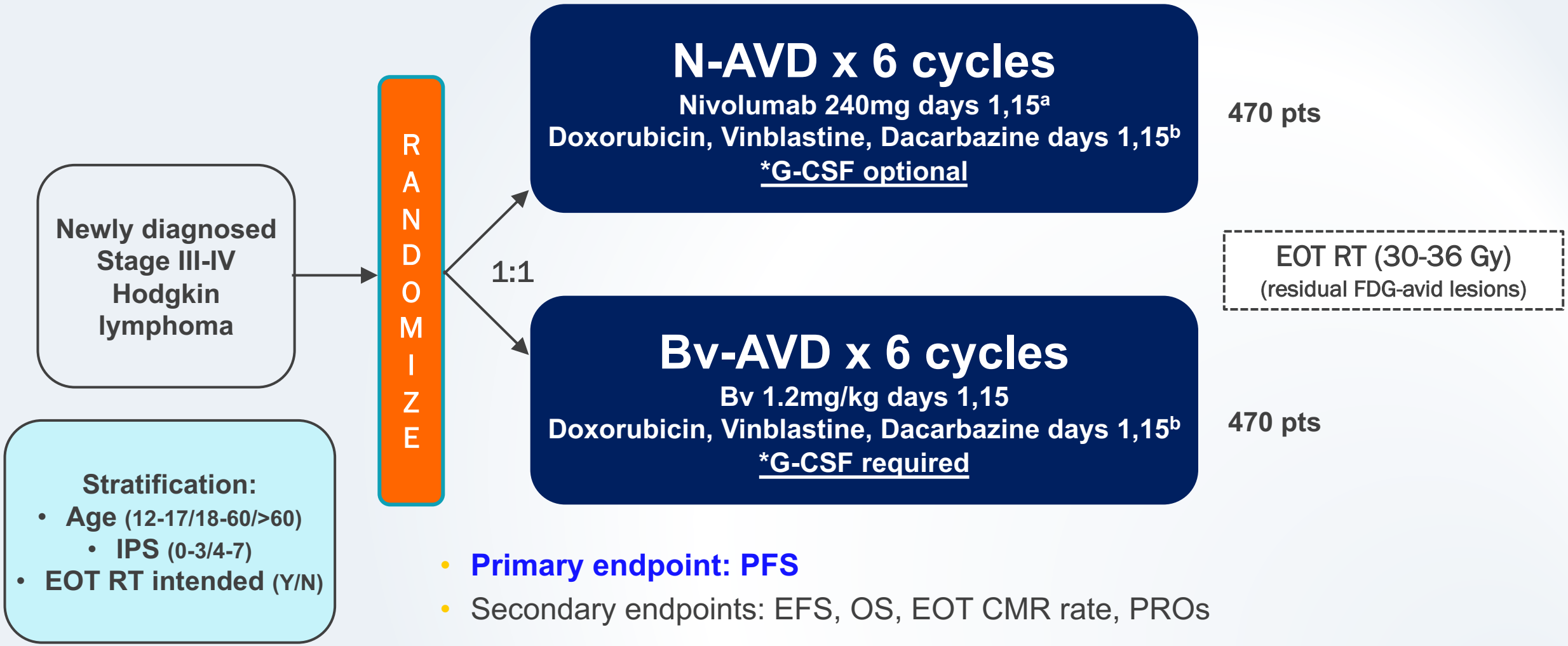
Labs: WBC 2, Hgb 10, Plt 80, bili 5, LDH 350, ESR 52, EBV VL >400,000 copy/mL

BM biopsy w/ classic Hodgkin lymphoma

TTE w/ diffuse hypokinesis (LV EF 17%)

N-AVD

S1826 Study Design



- **Primary endpoint: PFS**
- Secondary endpoints: EFS, OS, EOT CMR rate, PROs

Herrera A et al. NEJM 2024.

[a] Nivolumab 3mg/kg for ages ≤ 17, max 240mg
[b] Conventional doses of AVD: Stephens DM et al Blood 2019, Ansell SM et al NEJM 2022

S1826 was well balanced b/t arms and inclusive of high-risk pts

Baseline characteristics	N-AVD n=487 N (%)	Bv-AVD n=483 N (%)
Age, median (range)	27 (12-83)	26 (12-81)
12-17 years	118 (24%)	118 (24%)
18-60 years	321 (66%)	318 (66%)
≥ 61 years	48 (10%)	47 (10%)
Female Sex	216 (44%)	210 (43%)
Race		
White	372 (76%)	361 (75%)
Black	58 (12%)	56 (12%)
Asian	11 (2%)	17 (4%)
Other/Unknown	46 (9%)	49 (10%)
Hispanic	66 (14%)	58 (12%)

Baseline characteristics	N-AVD n=487 N (%)	Bv-AVD n=483 N (%)
Stage		
III	185 (38%)	168 (35%)
IV	302 (62%)	315 (65%)
B symptoms present	288 (59%)	273 (57%)
IPS Score		
0-3	332 (68%)	328 (68%)
4-7	155 (32%)	155 (32%)
Bulky disease > 10cm	156 (32%)	127 (26%)
HIV+	11 (2%)	5 (1%)

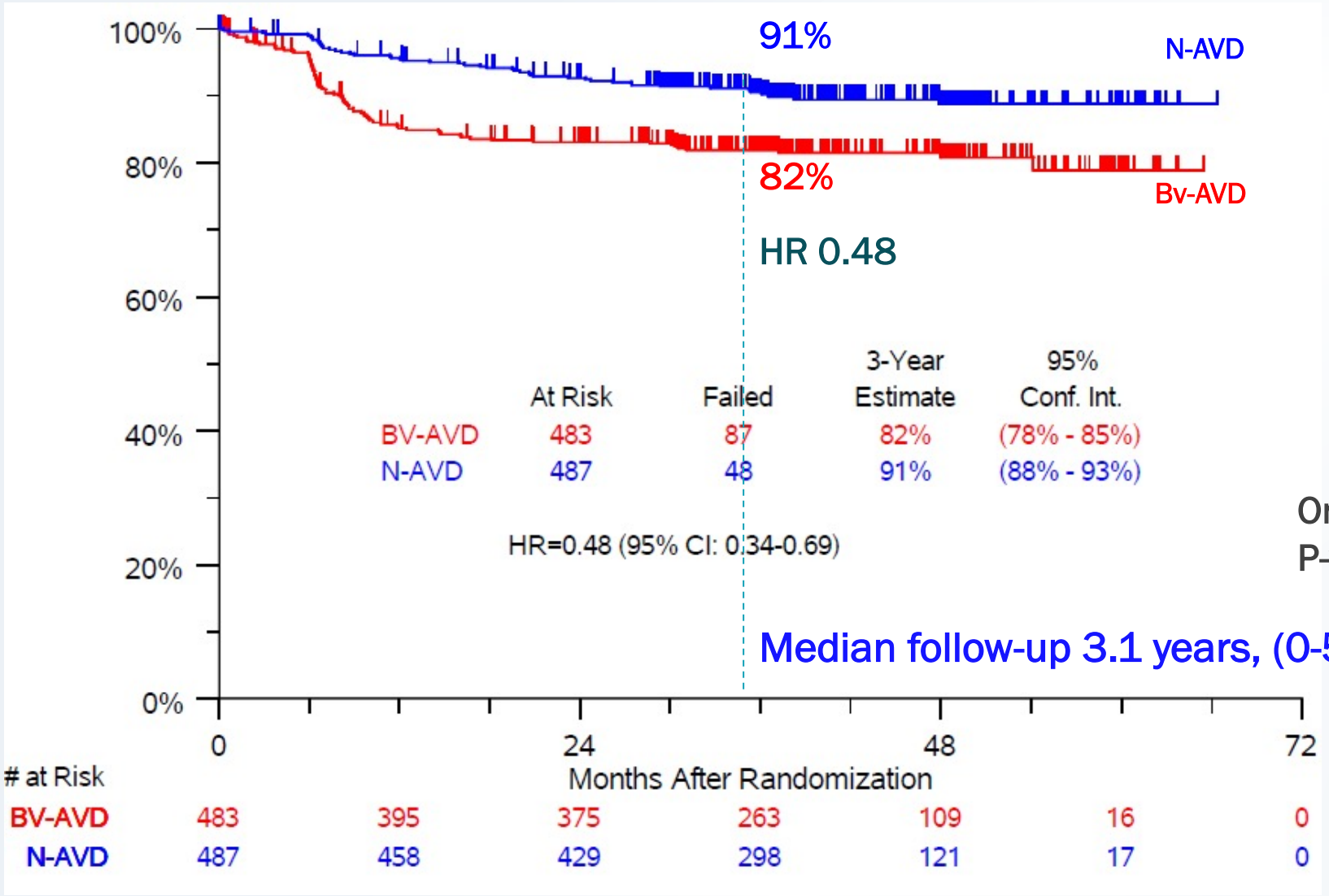
Herrera A et al. NEJM 2024.

N-AVD was better tolerated than BV-AVD

	Received G-CSF	Gr ≥ 3 neutropenia	Febrile neutropenia	Gr ≥ 3 infections, infestations	Sepsis	Bone pain
N-AVD (n = 482)	56%	48%	6%	5%	2%	8%
BV-AVD (n = 476)	97%	26%	7%	7%	3%	20%
	Peripheral sensory Neuropathy All Gr/Gr 2+	Peripheral motor neuropathy All Gr/Gr 2+	Thyroid dysfunction	ALT increased	Pneumonitis	Colitis
N-AVD (n = 482)	29%/8%	4%/1%	10%	33%	2%	1%
BV-AVD (n = 476)	56%/32%	7%/5%	1%	42%	3%	1%

Herrera, AF et al. N Eng J Med. 2024.

PFS benefit of N-AVD sustained with 3y follow-up

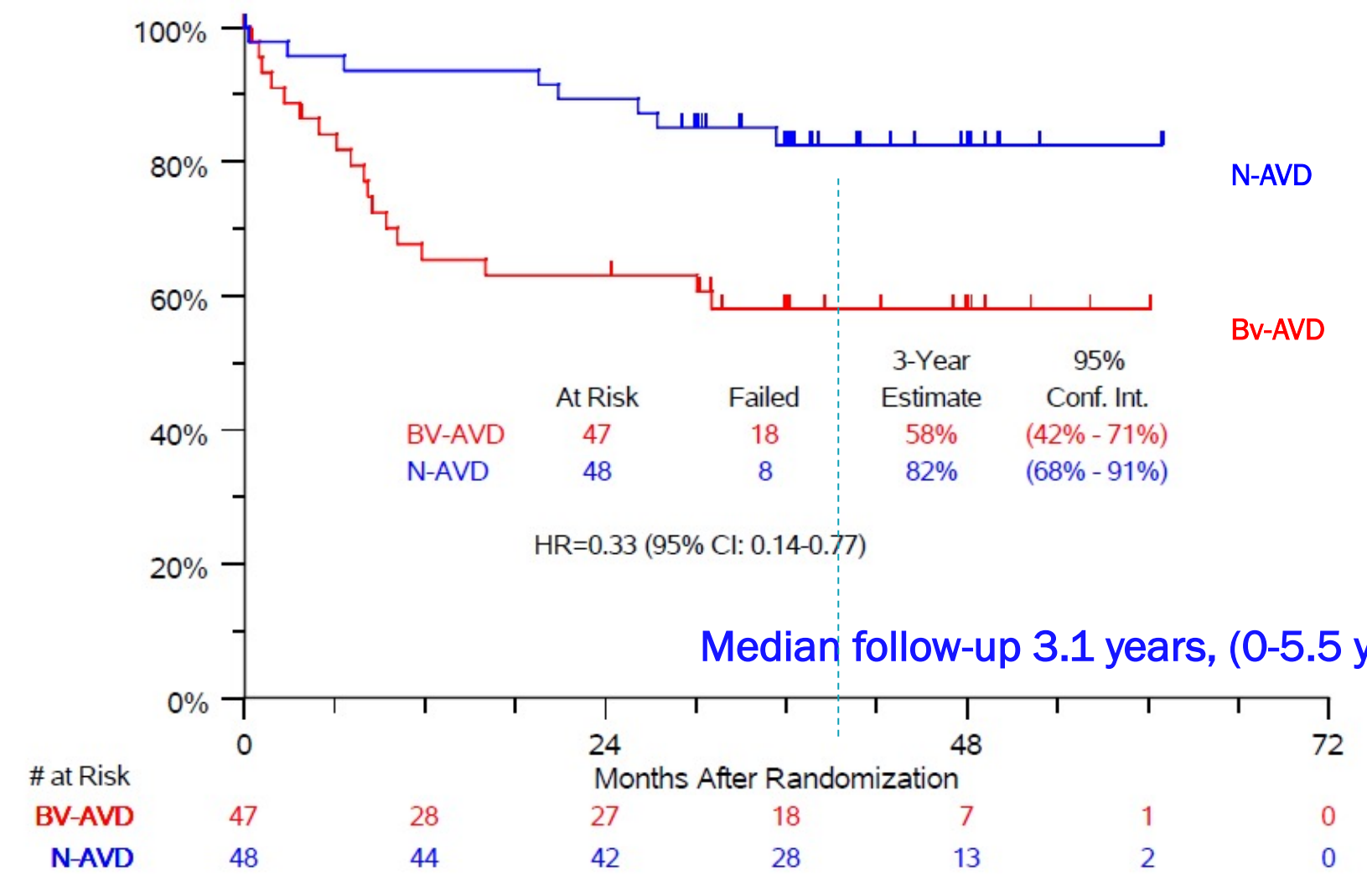


3-year PFS
N-AVD 91%
BV-AVD 82%

One-sided Stratified Log-rank
P-value < .0001

Herrera A et al. NEJM 2024; ASH 2025

N-AVD markedly improved PFS in older adults

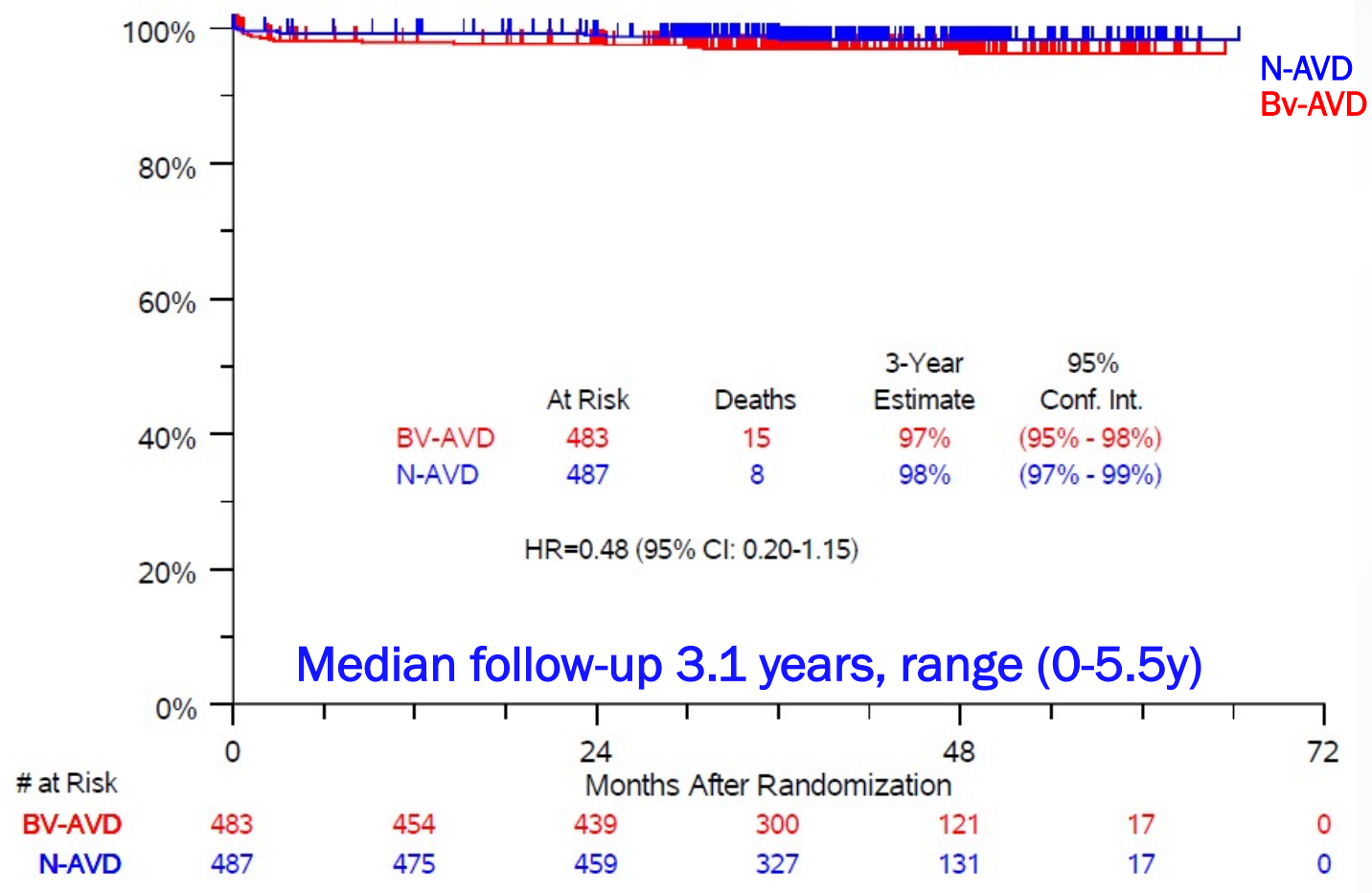


3-year PFS
N-AVD 82%
BV-AVD 58%

One-sided Stratified Log-rank P-value = .003

Herrera A et al. NEJM 2024; ASH 2025

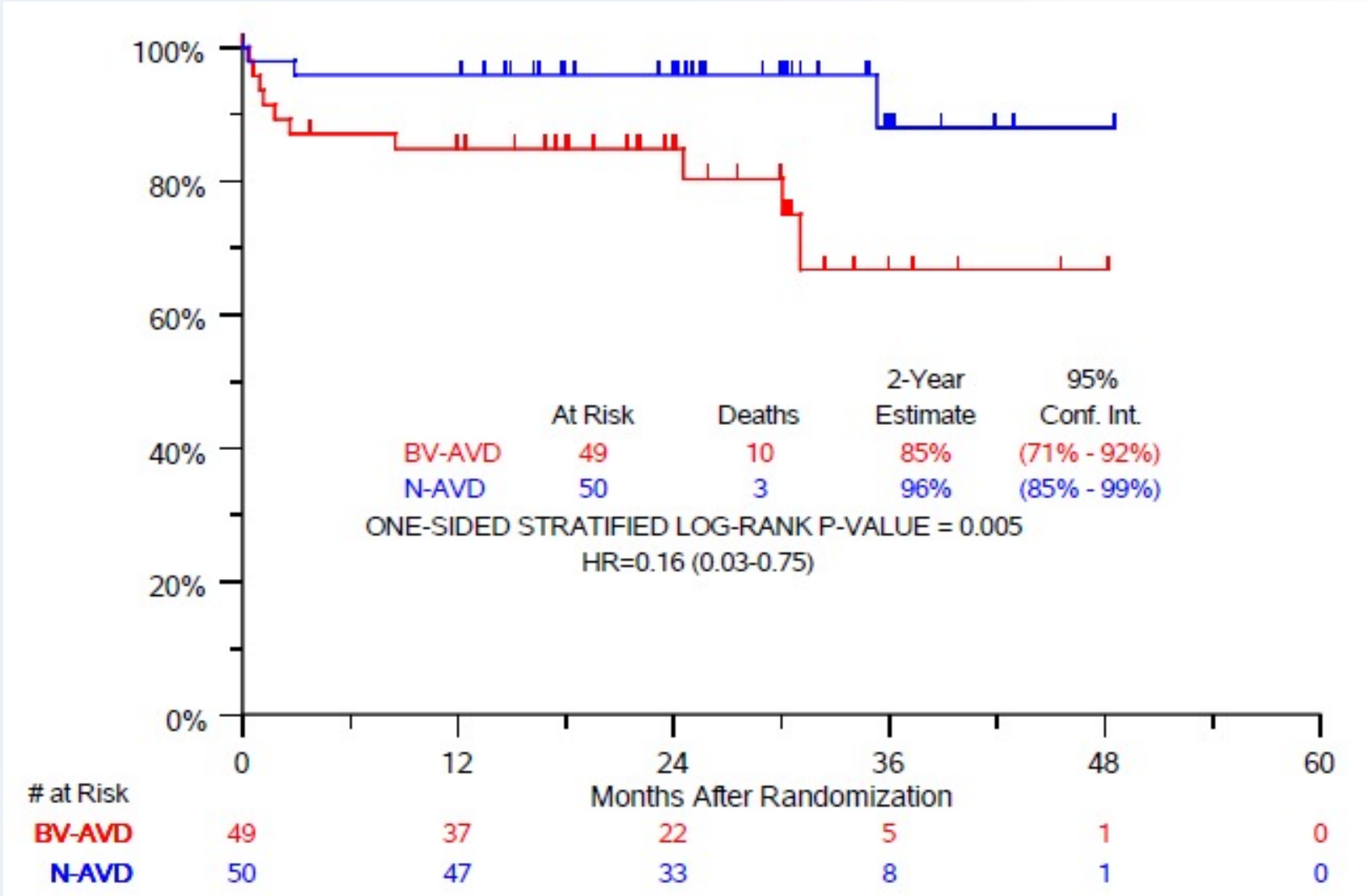
Overall survival similar between arms



Cause of Death	N-AVD N=487	BV-AVD N=483
Infection/Sepsis	5	6
Lymphoma	1	2
Medical issues other than cancer	2	4
New primary cancer	0	1
Unknown	0	2
Total	**8**	**15**

Herrera A et al. NEJM 2024; ASH 2025

N-AVD improved OS over BV-AVD in older adults



2-year OS

N-AVD 96%

BV-AVD 85%

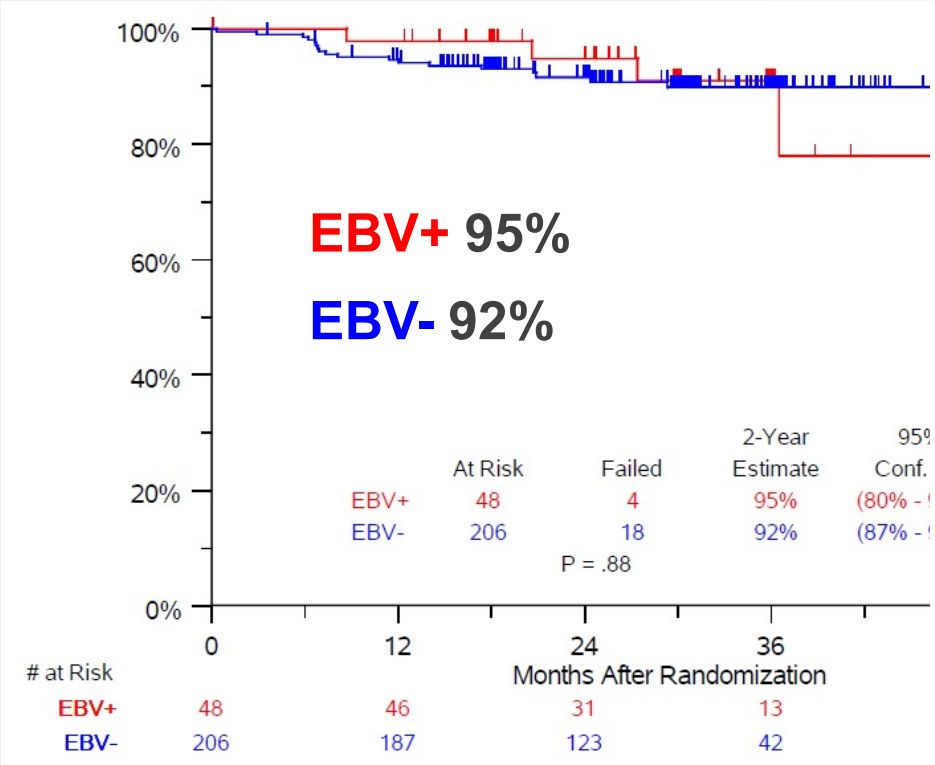
Median follow-up 2.1y

p-value = 0.005
HR=0.16,
95% CI (0.03-0.75)

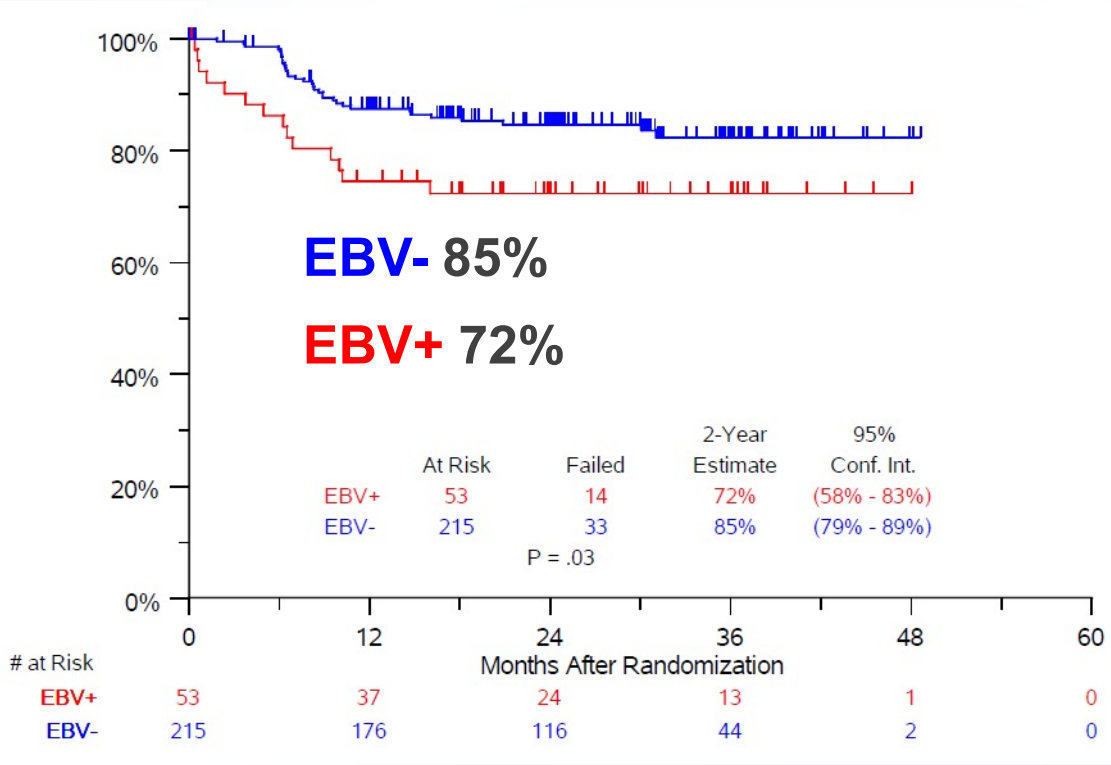
Rutherford et al. JCO 2025.

High PFS experienced by pts on N-AVD regardless of EBV status

2-Year PFS by EBV Status in N-AVD



2-year PFS by EBV Status in BV-AVD



Pts with EBV+ cHL have inferior PFS with BV-AVD compared to pts who are EBV-

Ahmed et al. iSHL 2025.

Case 2: 23 y/o M w/ Newly Diagnosed cHL and LV EF 17%

23 y/o M admitted to ICU with fevers, chills, night sweats

Labs: WBC 2, Hgb 10, Plt 80, bili 5, LDH 350, ESR 52, EBV VL >400,000 copy/mL

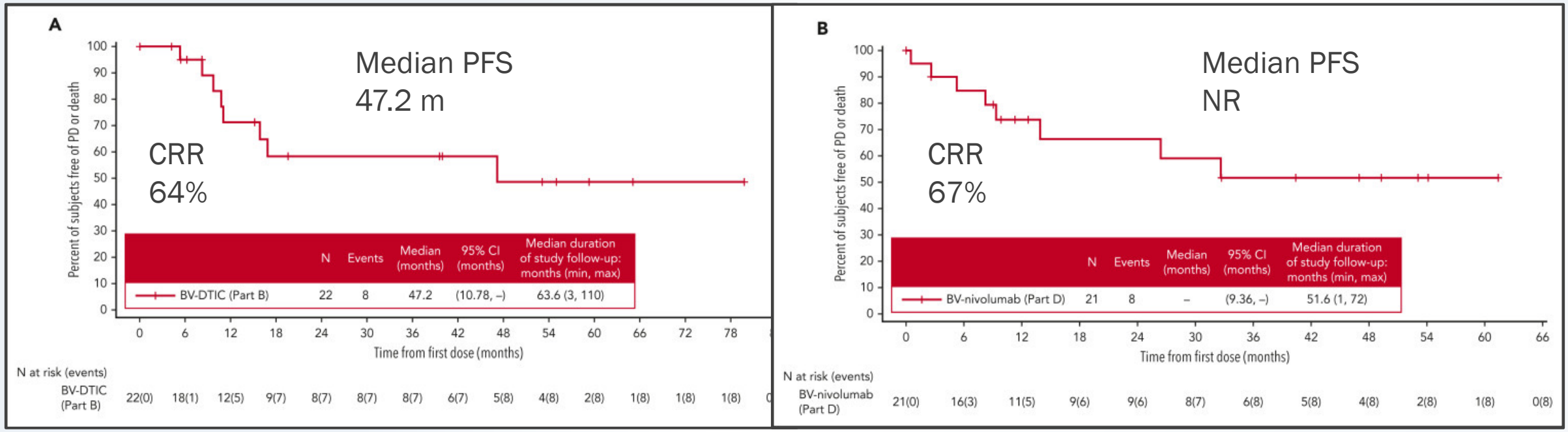
BM biopsy w/ classic Hodgkin lymphoma

TTE w/ diffuse hypokinesis (LV EF 17%)

BV-dacarbazine and BV-nivolumab are not curative regimens

BV-DTIC

BV-N



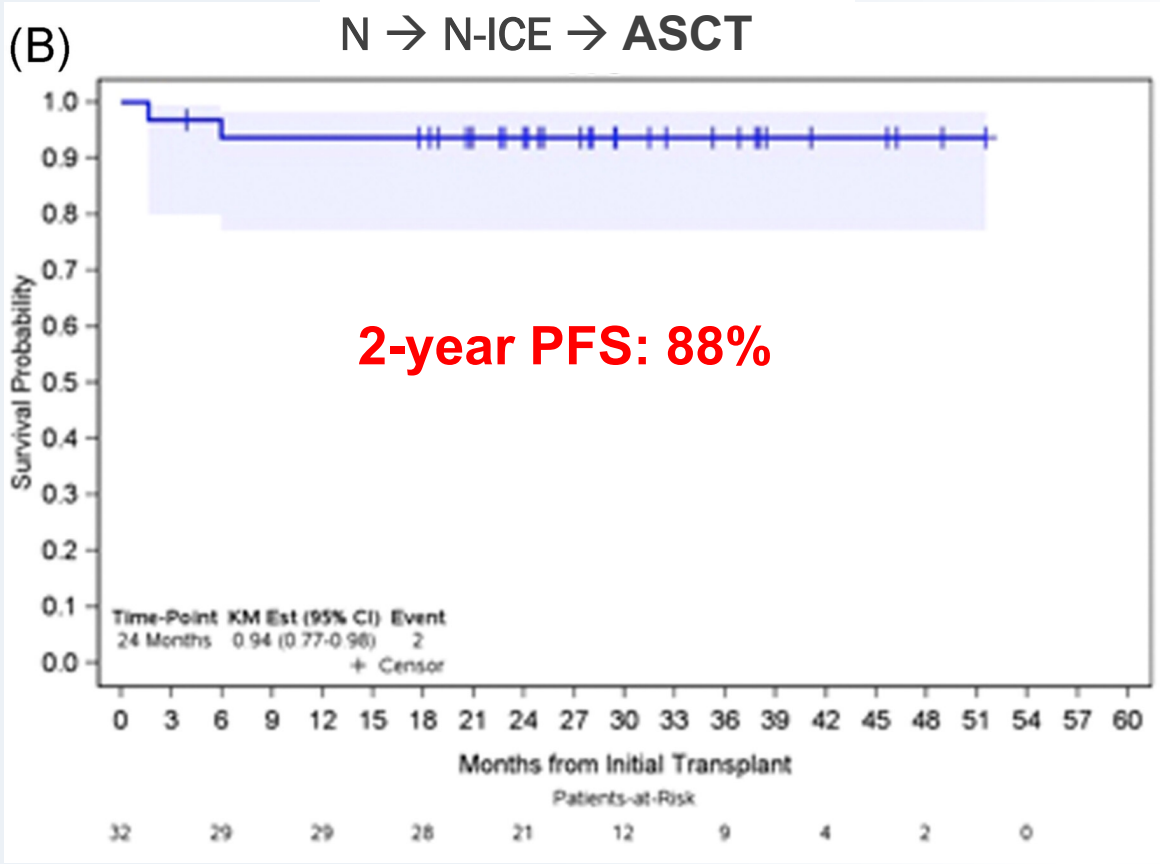
Median f/u 63.6 m

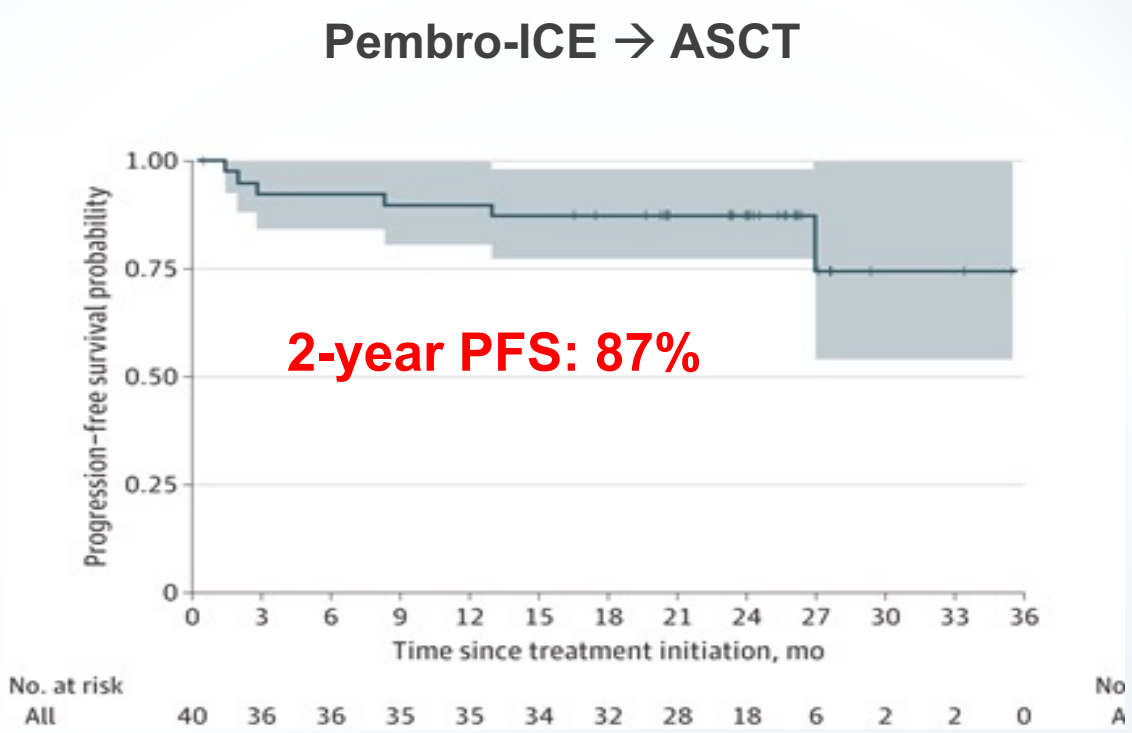
Median f/u 51.6 m

Nearly 20% of patients on both arms received subsequent BV-AVD based therapy

Freidberg et al, Blood 2024.

Consider 2nd line regimen (N-ICE or Pembro-ICE)





Mei M et al Hemasphere 2025, Bryan L et al. JAMA Oncol 2023

Case 1: 23 y/o M w/ Newly Diagnosed cHL and LV EF 17%

23 y/o M admitted with fevers, chills, night sweats, BM biopsy w/ cHL, TTE w/ diffuse hypokinesis (LV EF 17%)

CR after 2 cycles of Nivo-DICE

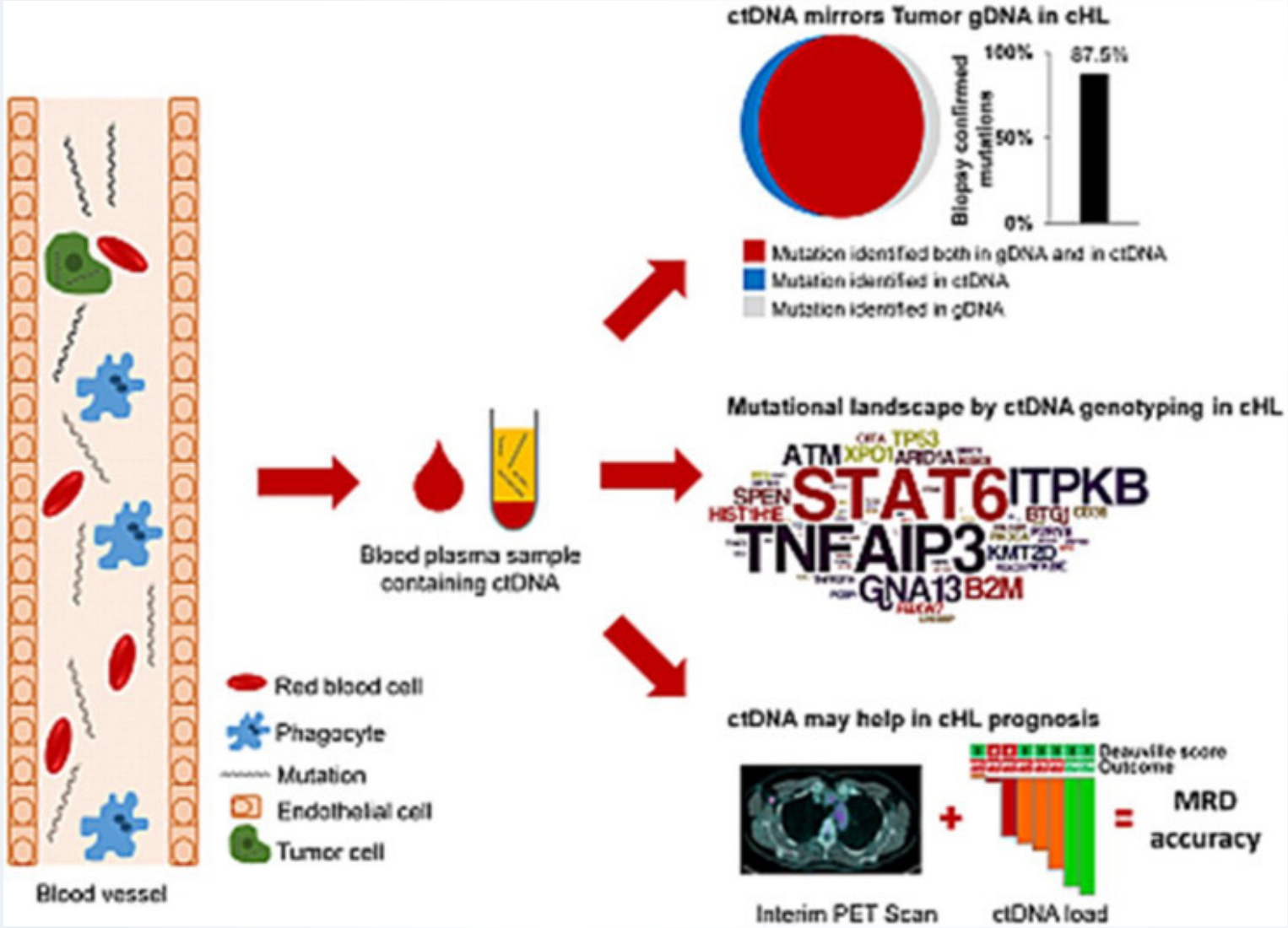
Repeat TTE with LV EF 60%

Completed 4 cycles of N-AVD

Remains in CR 1 yr after completing treatment, normal ejection fraction

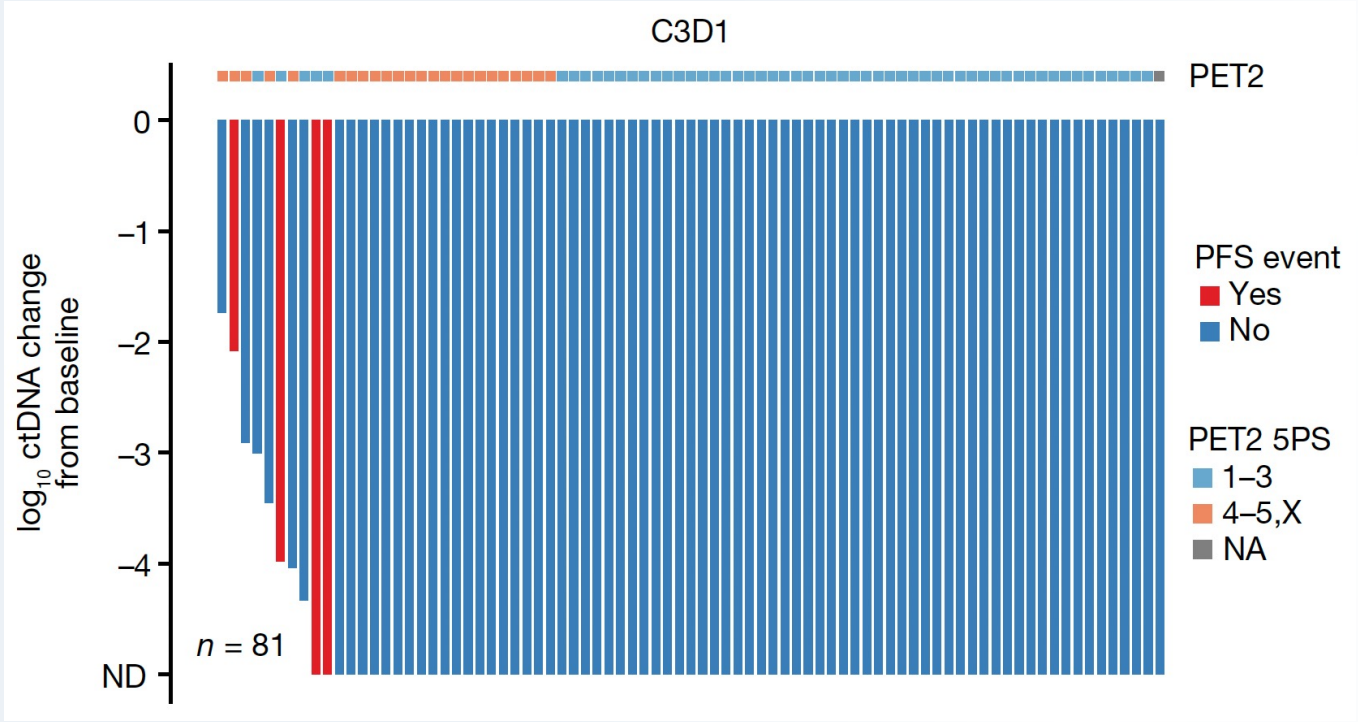
ctDNA in cHL

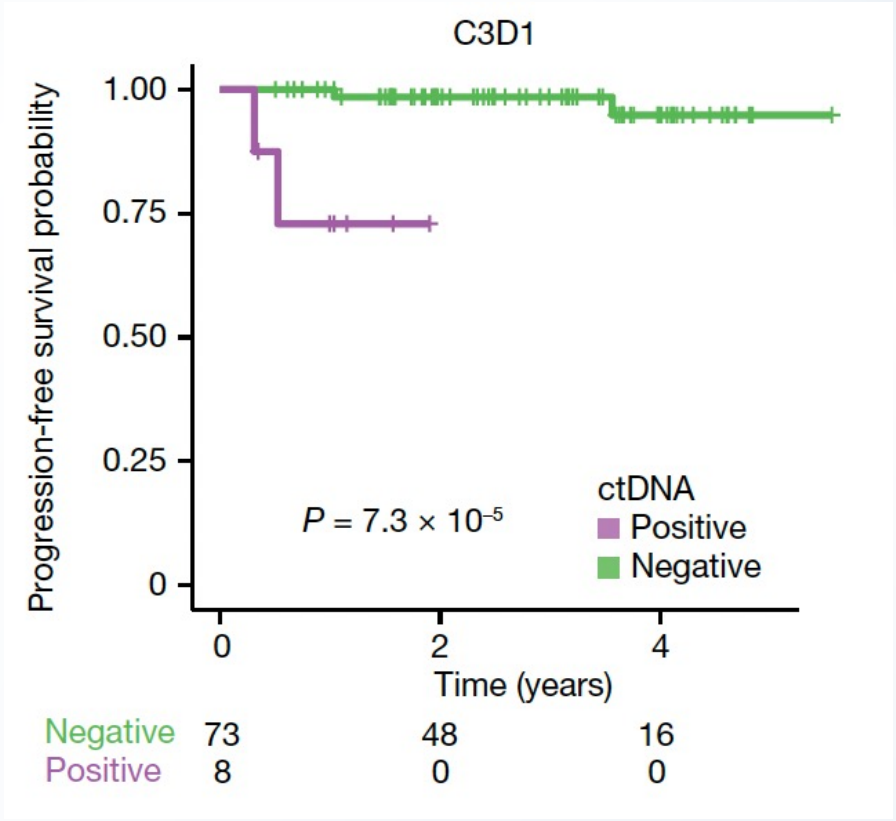
In 2018, ctDNA was reported to mirror tumor DNA in cHL



Spina et al Blood 2018

Retrospective analysis showed improved PFS when C3D1 ctDNA-



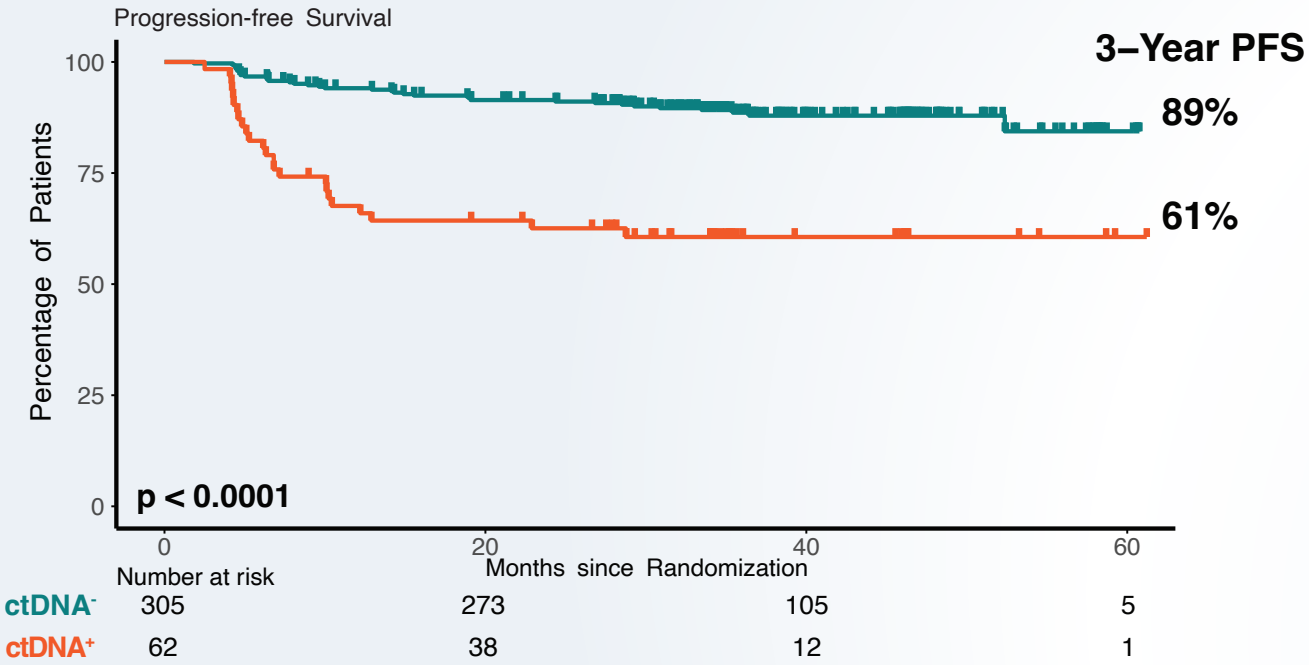


BV-AVD (46%), ABVD (23%), pembro-AVD (23%); stage: advanced (30%), early (70%)

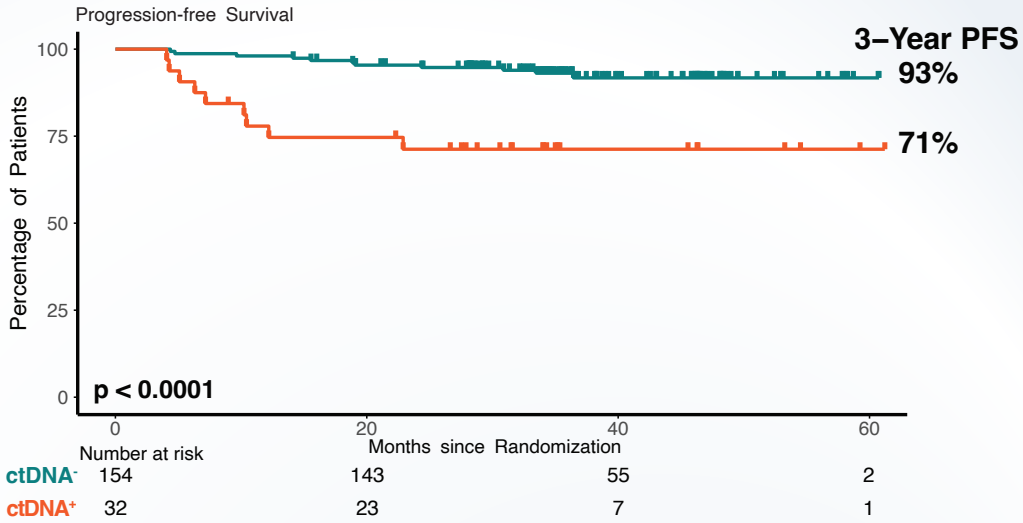
Alig et al. Nature 2024.

In S1826, C3D1 ctDNA- status was associated with improved PFS

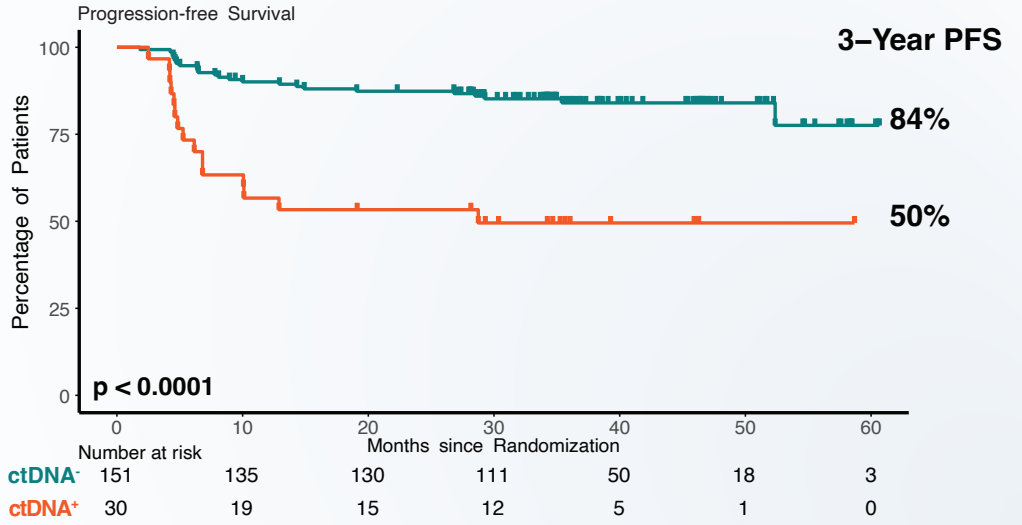
C3D1 ctDNA positivity/negativity (All)



C3D1 ctDNA positivity/negativity (N-AVD)

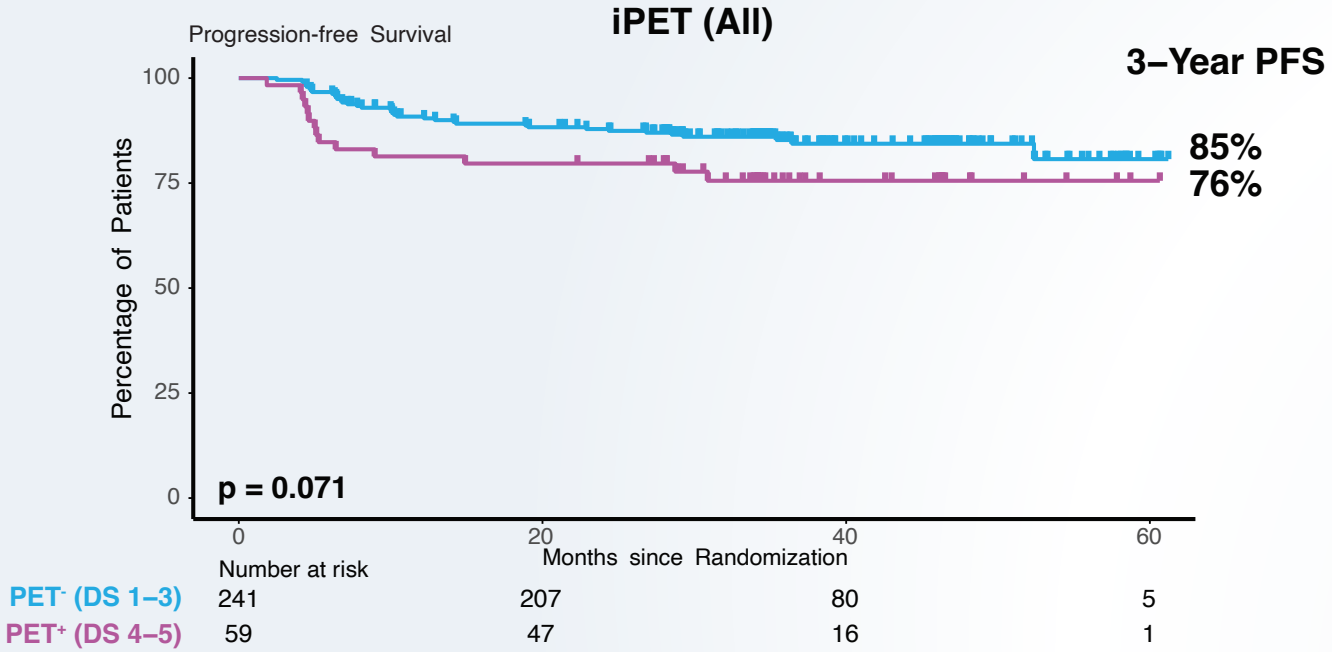


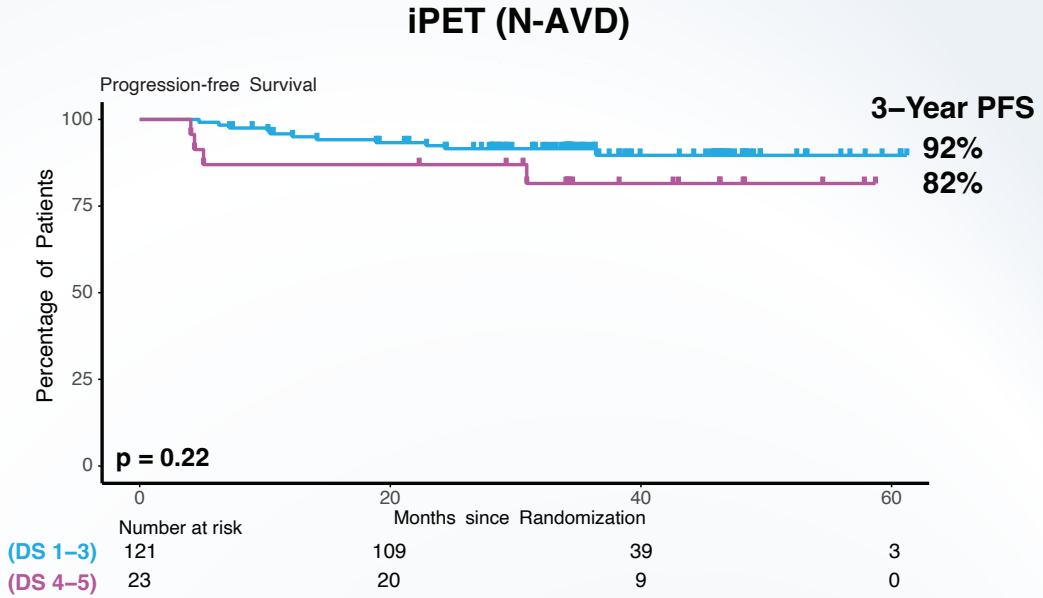
C3D1 ctDNA positivity/negativity (BV-AVD)

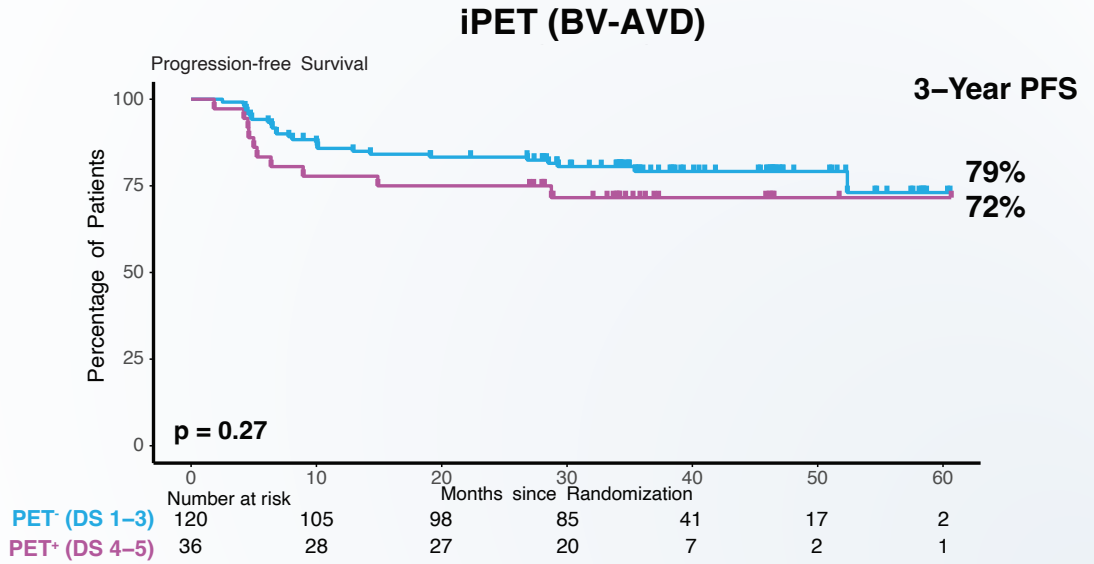


Paczkowska et al. ASH 2025.

In S1826, interim PET prior to C3D1 was not associated with PFS



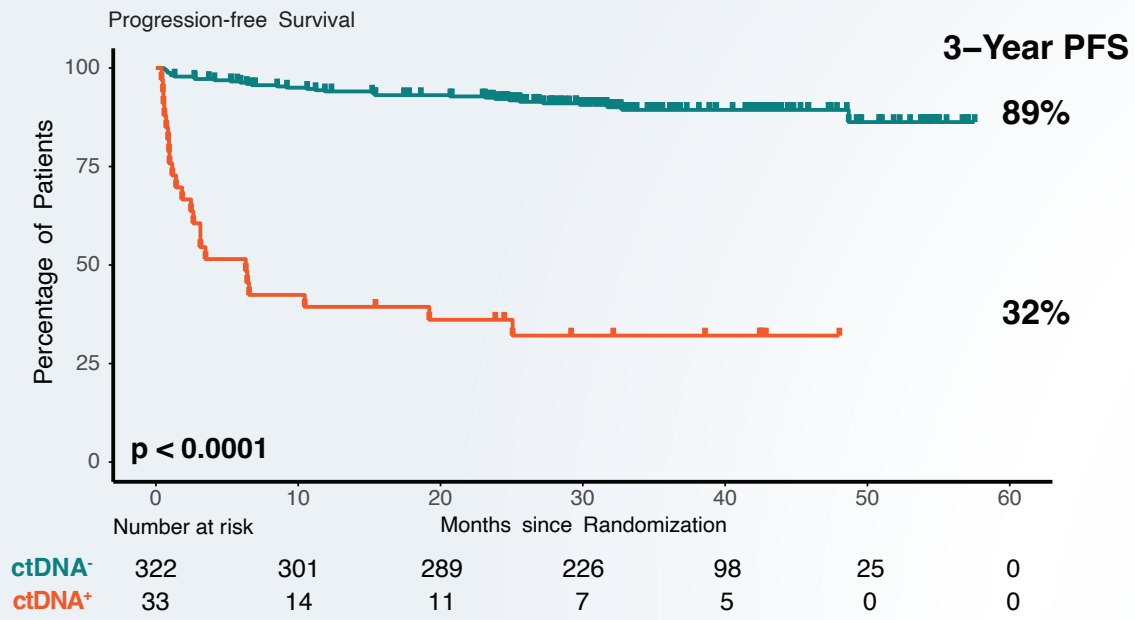




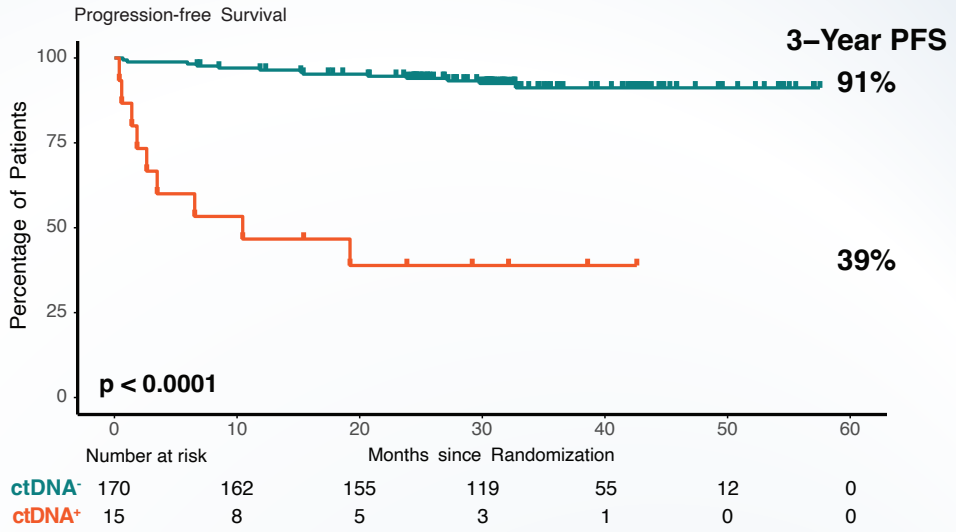
Paczkowska et al. ASH 2025; Bartlett et al. ASH 2025

In S1826, EOT ctDNA- was associated w/ markedly improved PFS

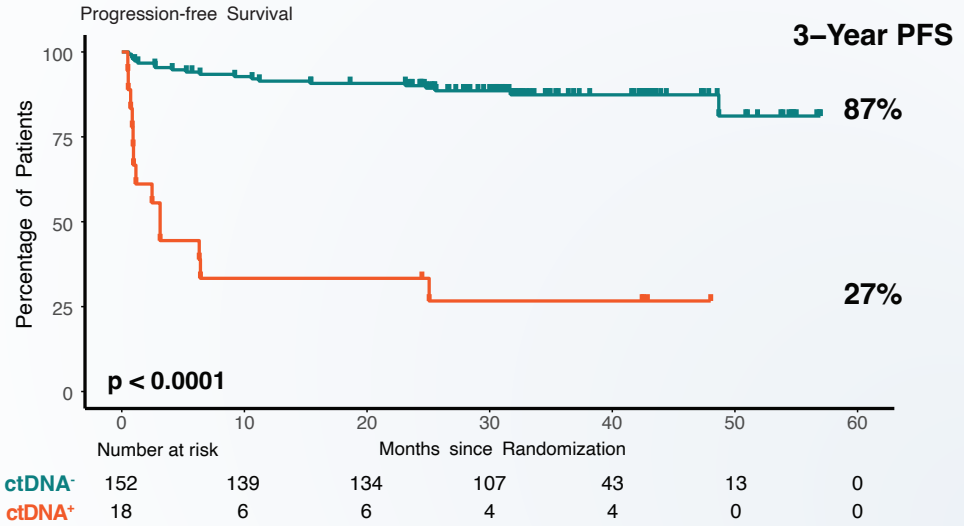
EOT ctDNA positivity/negativity (All)



EOT ctDNA positivity/negativity (N-AVD)



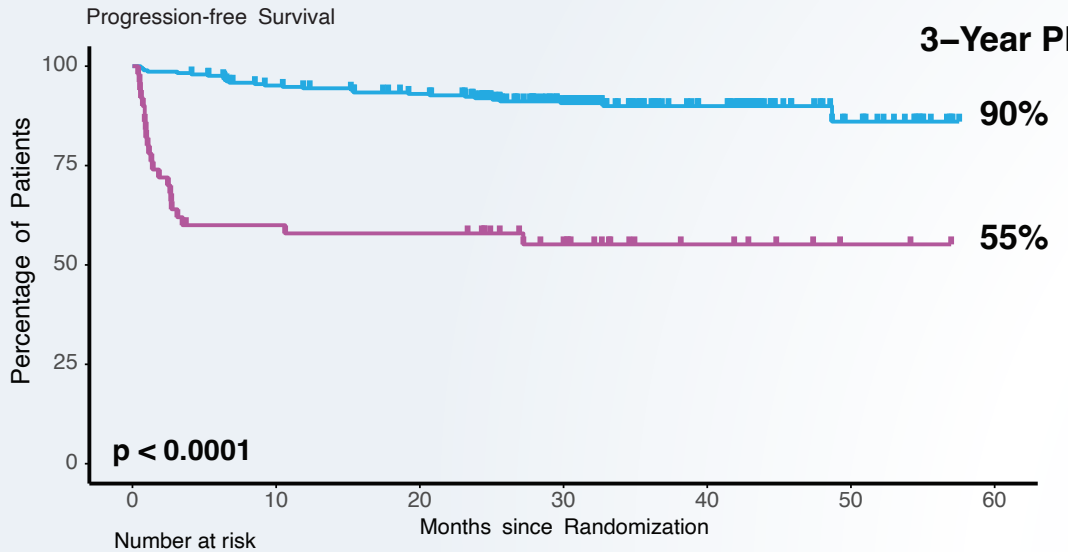
EOT ctDNA positivity/negativity (BV-AVD)



Paczkowska et al. ASH 2025.

In S1826, PET at EOT was associated with PFS (but less marked than ctDNA- status)

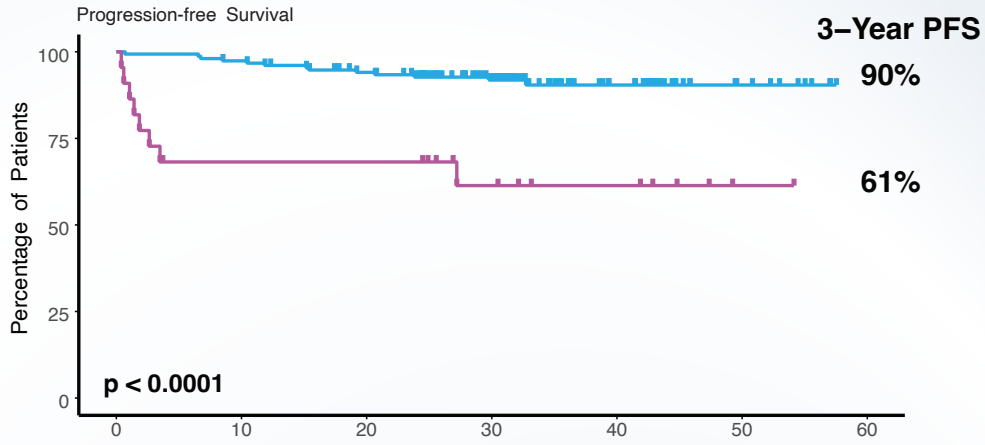
EOT PET (All)



Number at risk

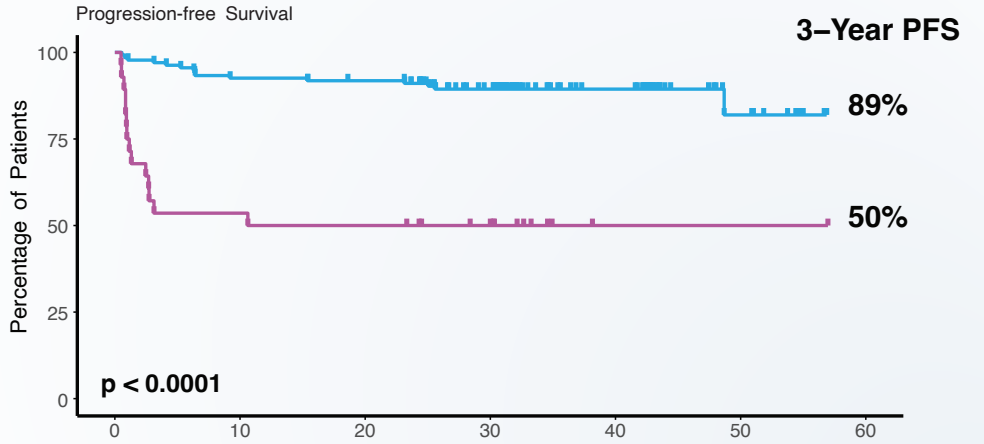
PET⁻ (DS 1–3)	289	272	259	206	91	20	0
PET⁺ (DS 4–5)	50	29	28	19	7	2	0

EOT PET (N-AVD)



PET⁻ (DS 1–3)	154	148	138	108	47	9	0
PET⁺ (DS 4–5)	22	14	14	9	6	1	0

EOT PET (BV-AVD)



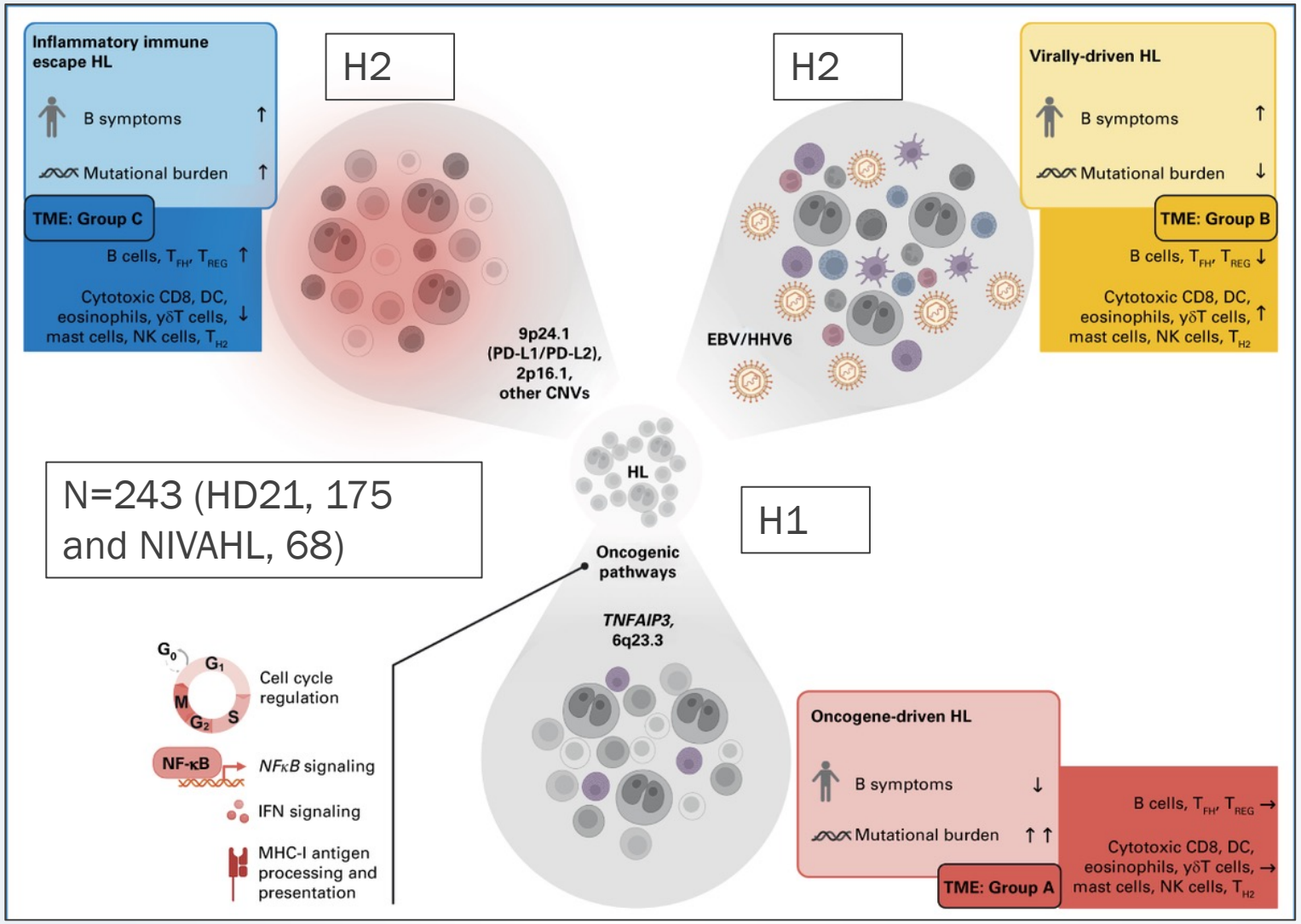
PET⁻ (DS 1–3)	135	124	121	98	44	11	0
PET⁺ (DS 4–5)	28	15	14	10	1	1	0

Paczkowska et al. ASH 2025; Bartlett et al. ASH 2025.

Biologic classification of cHL using ctDNA may enable tailored treatment in future

Inflammatory Immune Escape

45%



Virally-driven

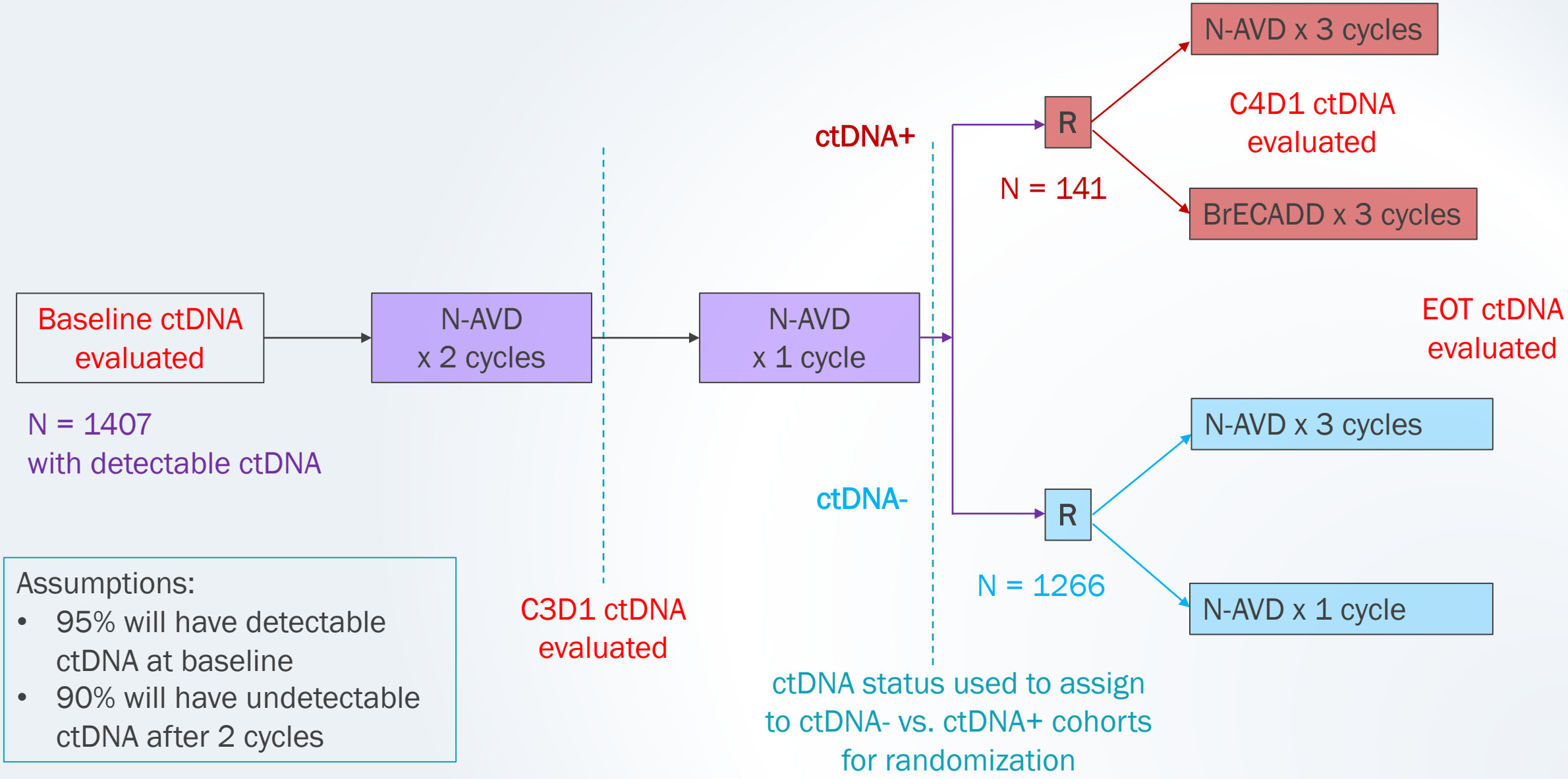
23%

Oncogene-driven

32%

Heger et al. JCO 2024; Alig et al Nature 2024.

Proposed NCTN Advanced Stage Hodgkin Lymphoma Trial



Assumptions:

- 95% will have detectable ctDNA at baseline
- 90% will have undetectable ctDNA after 2 cycles

Conclusions

There is a potential role for BrECADD in pts w/ contraindication to CPI or who desire quicker treatment/are at increased risk of cardiotoxicity.

N-AVDx6 remains standard of care in US for frontline advanced stage cHL based on S1826 3-year data; real world scenarios may require alternate strategies.

Use of ctDNA to guide treatment escalation or de-escalation is promising and will be assessed in forthcoming NCTN clinical trial.

23rd INTERNATIONAL ULTMANN CHICAGO LYMPHOMA

Questions?

sar2014@med.cornell.edu

THE UNIVERSITY OF CHICAGO MEDICINE & BIOLOGICAL SCIENCES

Bio Ascend™ A Vaniam Group Company