

Interim FDG-PET in advanced classical Hodgkin lymphoma: will the story continue?

Roma Hematology Conference

Rome, 15 October 2026

Martin Hutchings

Department of Haematology and Phase 1 Unit, Rigshospitalet

Department of Clinical Medicine, University of Copenhagen

Copenhagen, Denmark



UNIVERSITY OF
COPENHAGEN



Disclosures

- **Consultant/advisor:**

- AbbVie, AstraZeneca, Genmab, Johnson&Johnson, Merck, Roche, Takeda

- **Research support (institution):**

- AbbVie, Arvinas, AstraZeneca, BeOne, Bristol Myers-Squibb, Celgene, Lilly, Genentech, Genmab, Immunome, Incyte, Johnson&Johnson, Merck, Pfizer, Roche, Takeda

Background

- ABVD was the global standard for 1st line treatment of advanced HL for 30+ years^{1,2}
 - However, 25-30% of patients either relapse or are refractory to ABVD^{1,2}
- BEACOPPesc gave improved disease control but considerable acute and late toxicity³
- Interim PET was shown >20 ago to hold high prognostic value in advanced HL⁴
- Various PET-response adapted treatment strategies were introduced, adjusting treatment intensity to the individual patient's response⁵
- BV+AVD was compared with ABVD in the 1st line treatment of advanced HL (Echelon-1) and resulted in superior PFS and OS without using interim PET-adaptation⁶
- The more recent HD21 and SWOG1826 studies have redefined the way we treat advanced Hodgkin lymphoma

1. Canellos GP, et al. N Engl J Med 1992;327:1478–84

2. Gordon LI, et al. J Clin Oncol 2013;31:684–91

3. Kreissl S, et al. Lancet Haematol 2021;8:e398–409

4. Hutchings M, et al. Blood 2006;107:52–9.

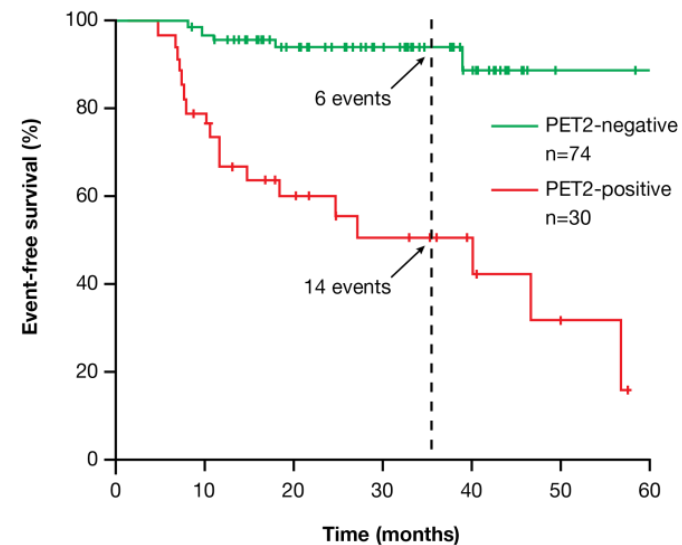
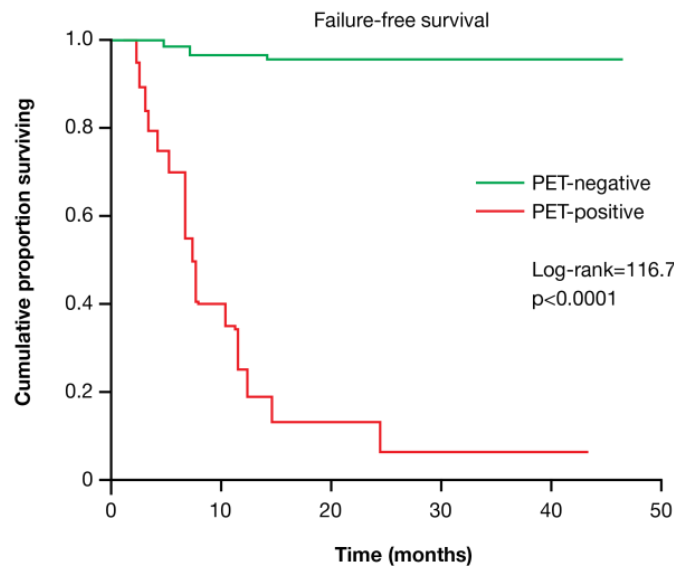
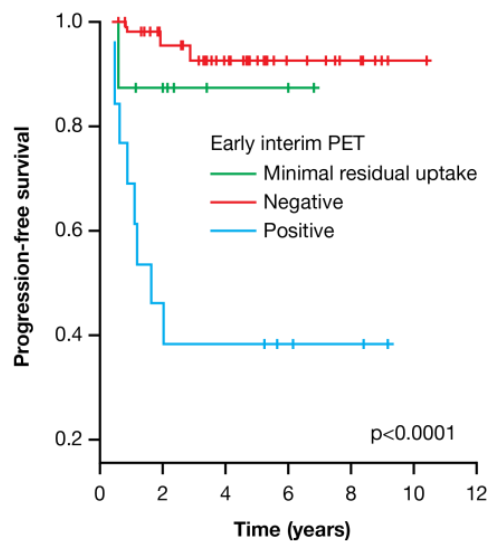
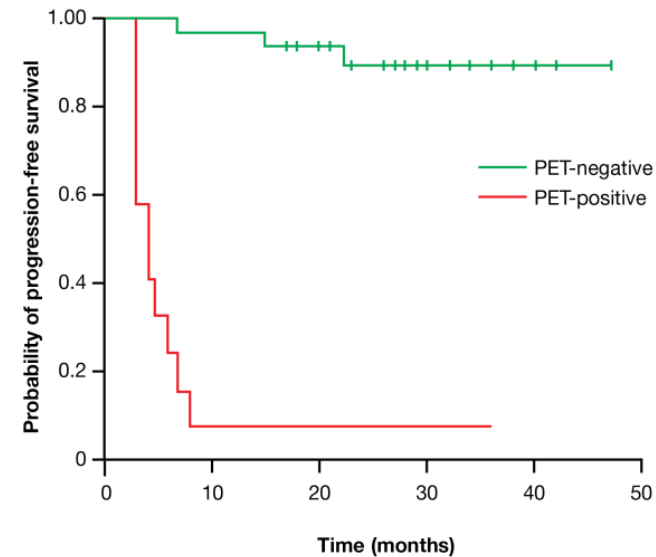
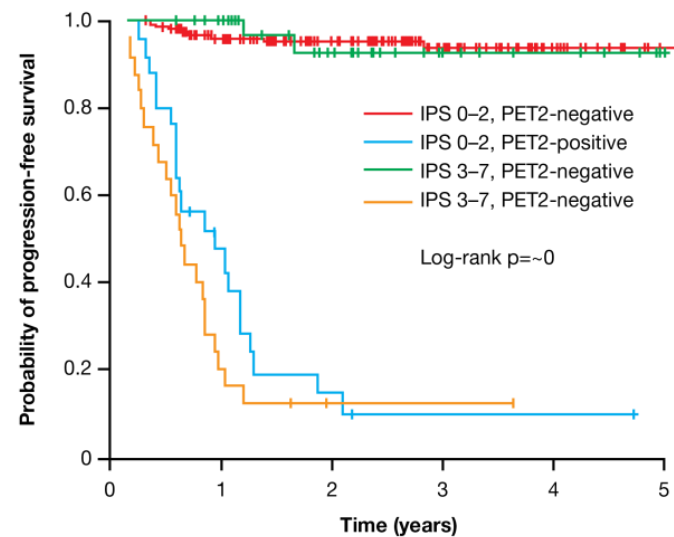
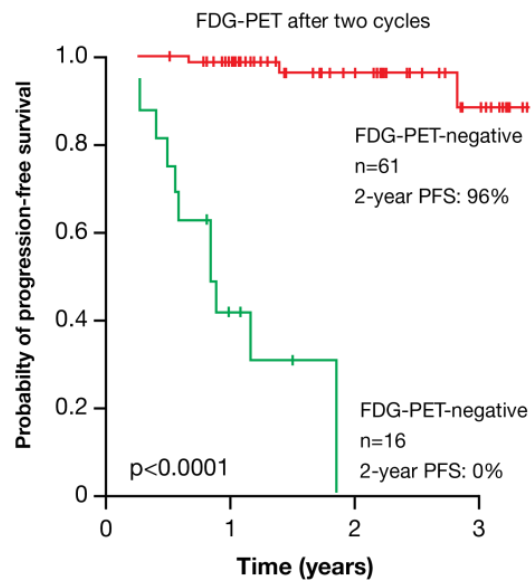
5. Hutchings M. Hematology 2012;2012:322-7.

6. Ansell SM, et al. N Engl J Med 2022;387:310–20

7. Borchmann P, et al. Lancet 2024; 404(10450): 341-352.

8. Herrera AF, et al. N Engl J Med 2024; 391: 1379-1389.

Prognostic value of early interim PET
PET-response adapted treatment of HL

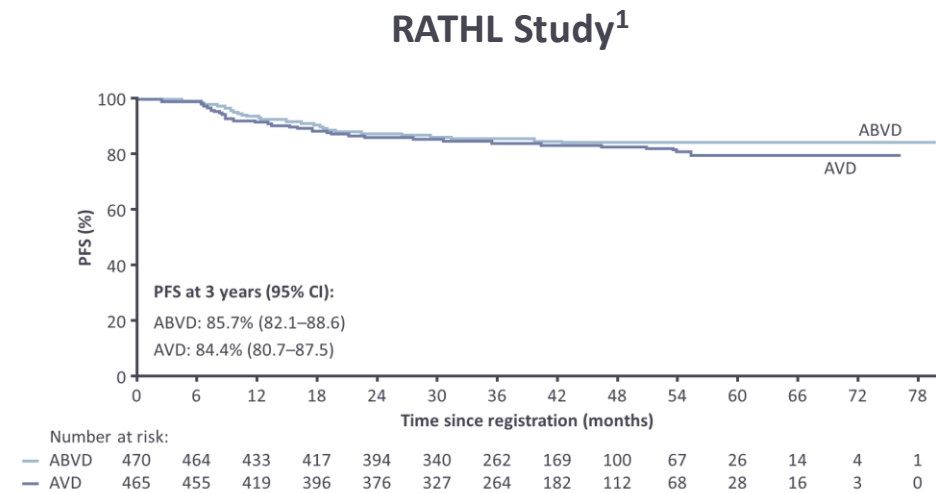


1. Hutchings M, *et al.* Blood 2006;107:52–9.
2. Hutchings M, *et al.* Ann Oncol 2005;16:1160–8.

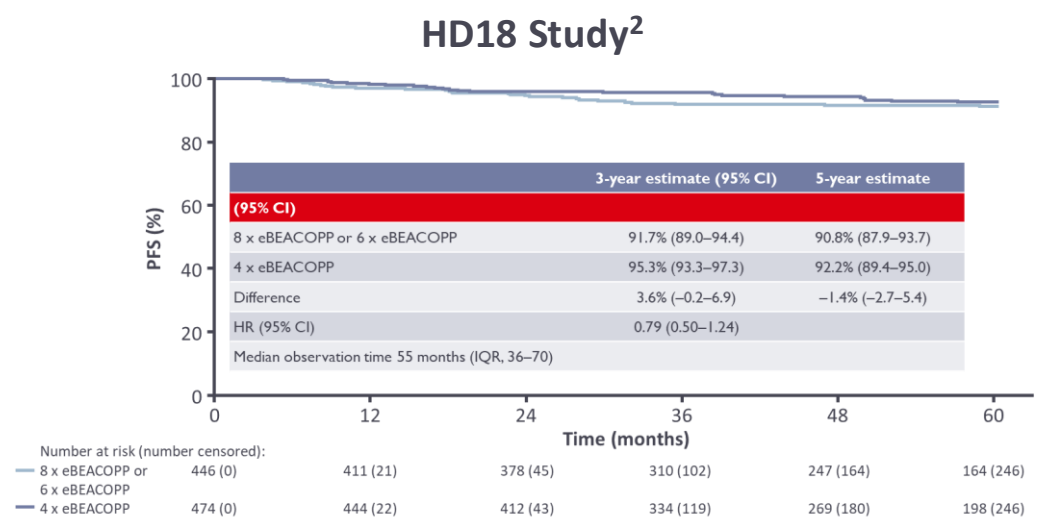
3. Gallamini A, *et al.* J Clin Oncol 2007;25:3746–52.
4. Gallamini A, *et al.* Haematologica 2006;91:475–81.

5. Kostakoglu L, *et al.* Cancer 2006;107:2678–87.
6. Cerci JJ, *et al.* J Nucl Med 2010;51:1337–43.

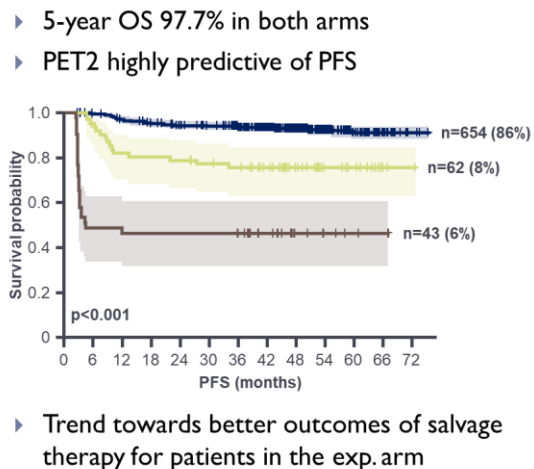
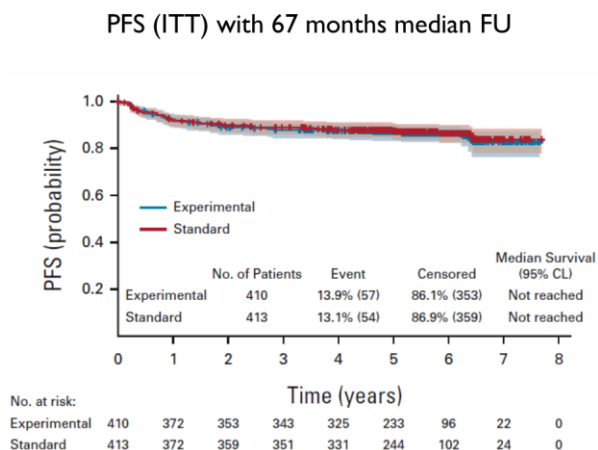
PET-adapted treatment strategies for advanced stage HL



In PET-negative patients, omission of bleomycin reduced pulmonary toxicity without significantly lowering efficacy



In PET2-negative patients, eBEACOPP may be reduced to 4 cycles without loss of tumour control



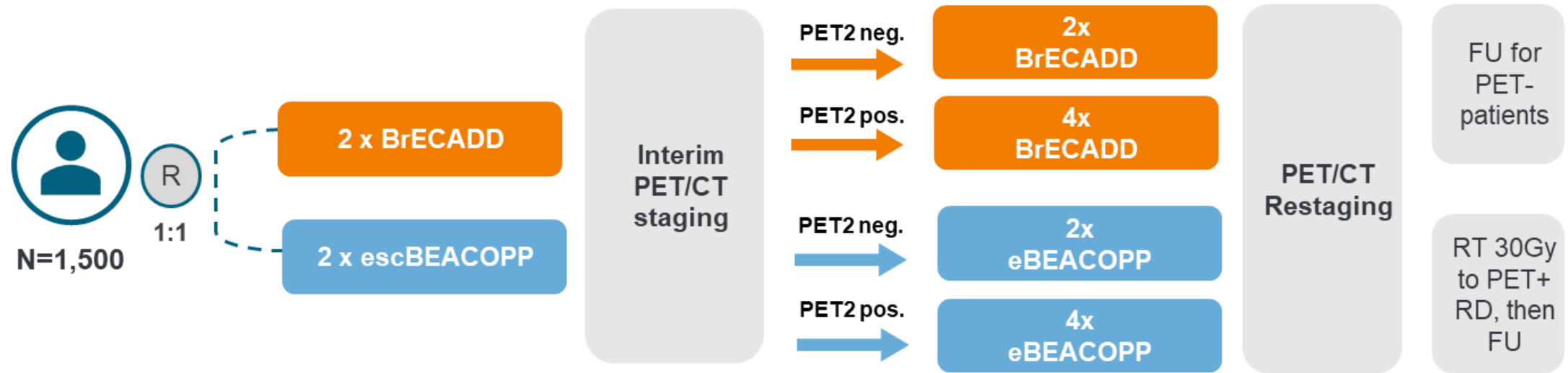
AHL 2011 Study^{3,4}

No loss of efficacy if patients PET-negative after 2x BEACOPPesc move to 4x ABVD instead of continued BEACOPPesc

- Johnson P, et al. N Engl J Med 2016;374:2419–29
- Borchmann P, et al. Lancet 2018;390:2790–802.
- Casasnovas RO, et al. Lancet Oncol 2019;20(2):202-15.
- Casasnovas RO, et al. J Clin Oncol 2022;40(10):1091-1101.

HD21: BEACOPPesc vs. BRECADD

GHSB HD21: Open-label, randomised phase 3 study of BrECADD versus eBEACOPP in patients 18-60 yo with previously untreated advanced cHL



Co-primary objectives:

- Demonstrate **superior tolerability** defined by treatment-related morbidity 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)

GHSB HD21: Analysis of treatment-related morbidity (TRMB) endpoint

Median follow-up 48 months)

A significant, clinically meaningful reduction in acute and severe TRMB (combined primary endpoint) with BrECADD vs. BEACOPP

- 59% 42%; relative risk 0.72; 95% CI 0.65, 0.79; p<0.0001

TRMB benefit was observed for all subgroups including age, sex, IPS

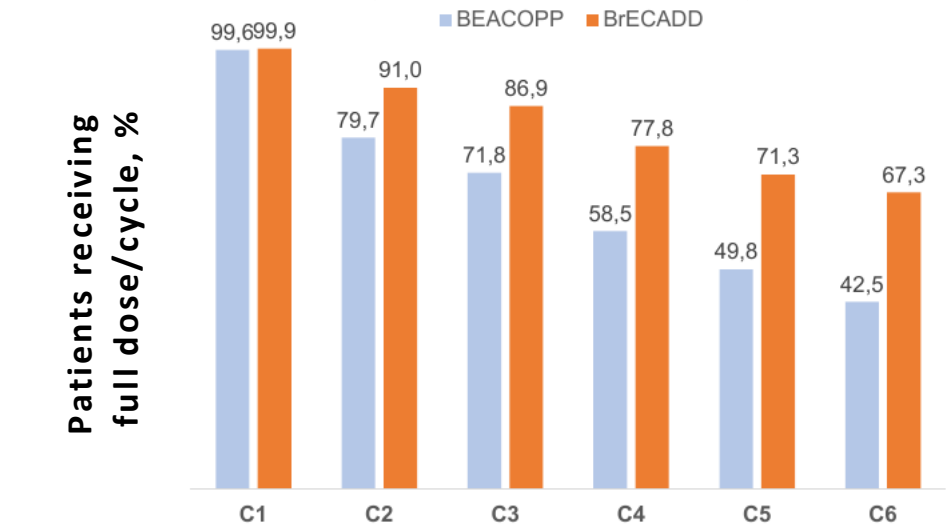
The reduction in acute TRMB with BrECADD vs BEACOPP was accompanied by a reduction of:¹

- RBC transfusion frequency: **24%** vs 52%
- Platelet transfusion frequency **17%** vs 34%
- Peripheral sensory neuropathy:
 - All grades: **39%** vs 49%
 - Grade 2: **6%** vs 14%
 - Grade 3: **1%** vs 2%

Persistence of TRMB at 12 months follow-up

TRMB, n (%)	BrECADD (n=677)	BEACOPP (n=657)
Anemia, thrombopenia, or infection of CTCAE Grade 4	1 (<1)	0 (0)
Organ toxicity of CTCAE Grade 3/4	6 (1)	2 (<1)
Total TRMB	7 (1)	2 (<1)

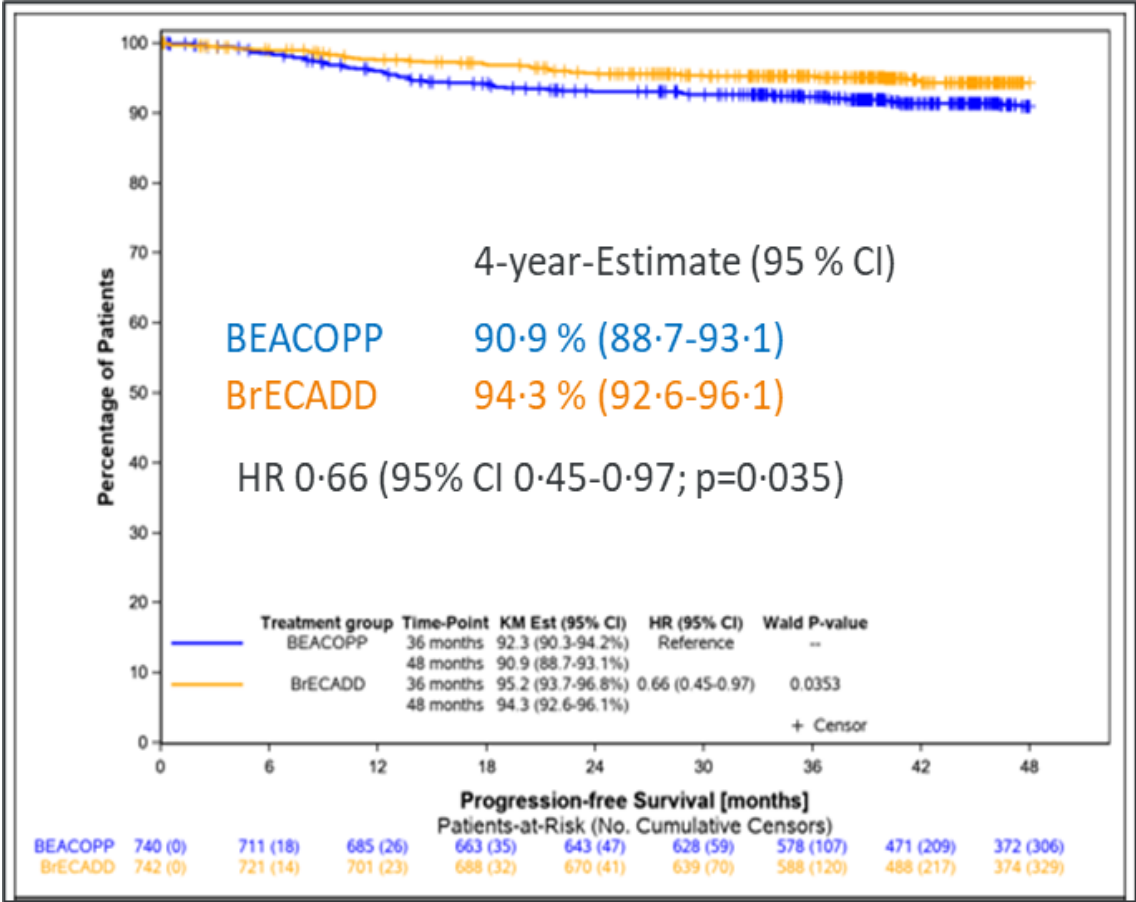
Treatment intensity (median follow-up 40 months)



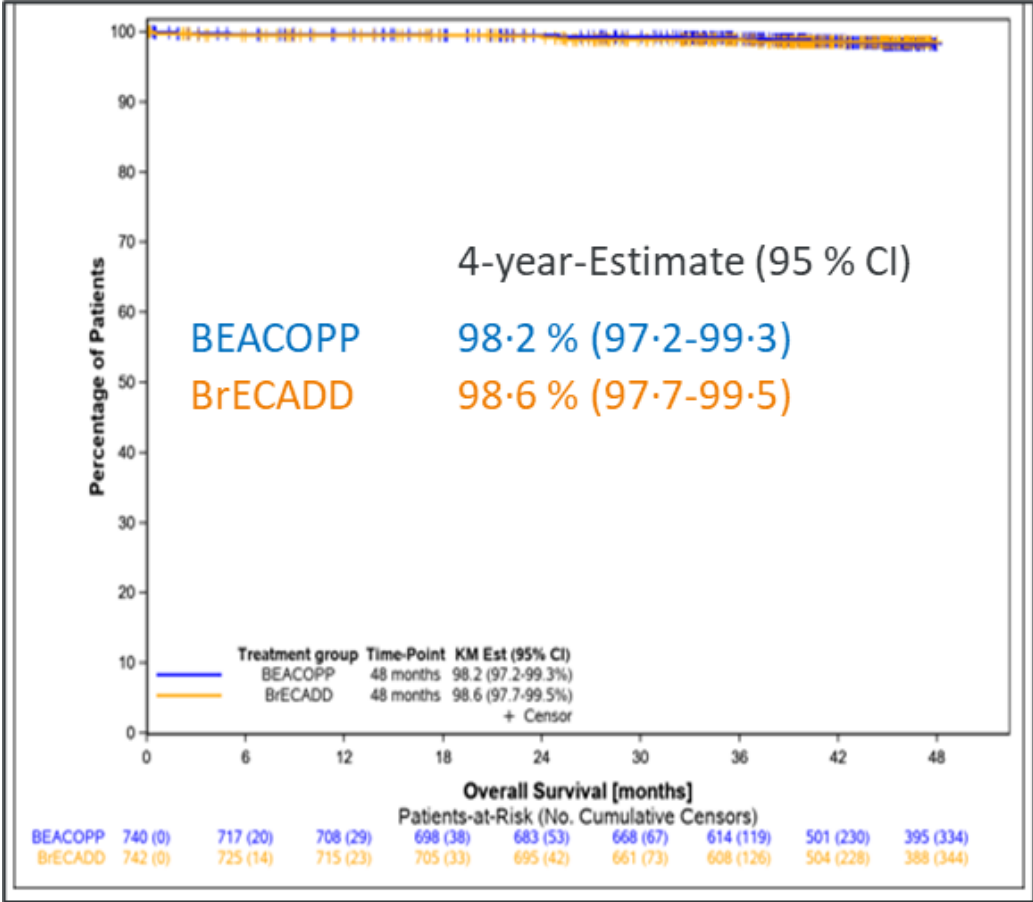
GHSB HD21: Analysis of efficacy endpoint

BrECADD is superior to BEACOPPesc (median FU 48 months)

Progression-free survival

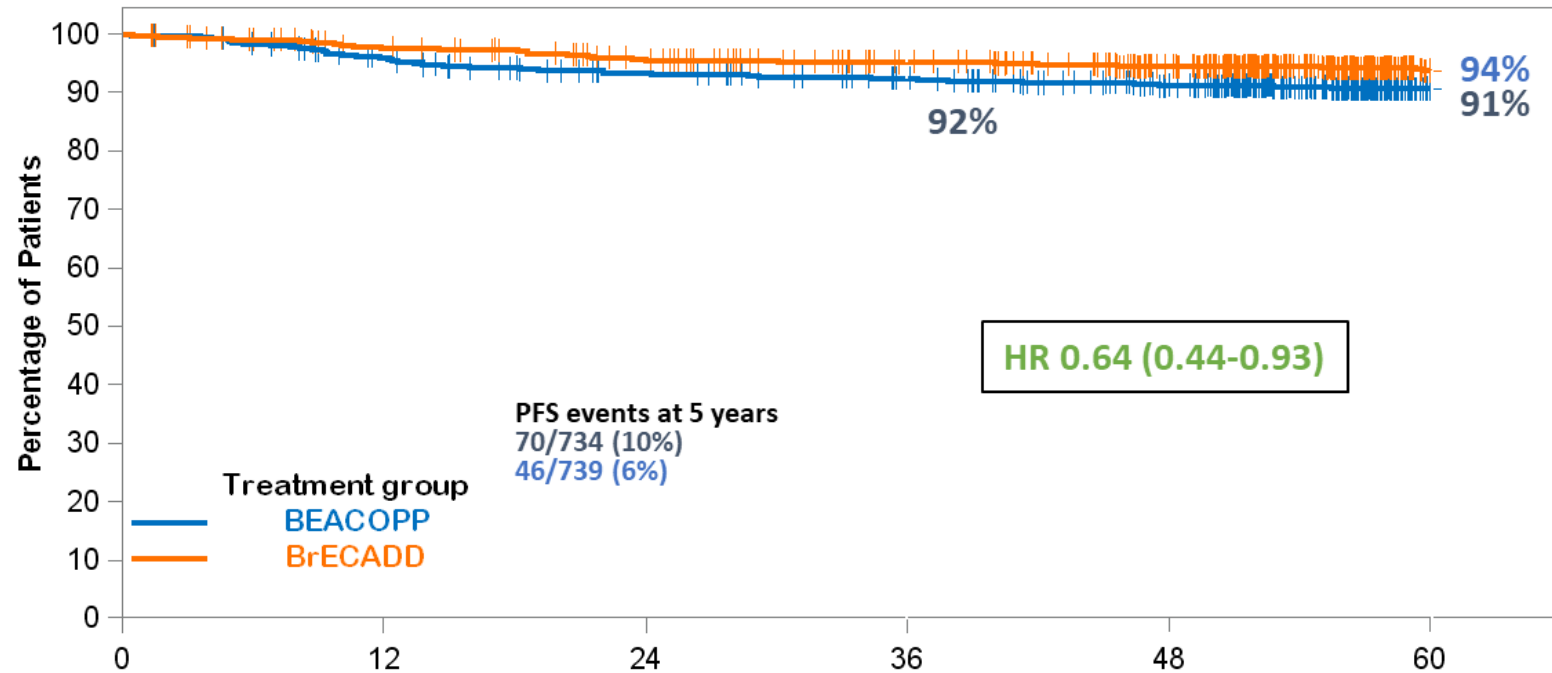


Overall survival



GHSB HD21: 5-year update presented at ASH 2025

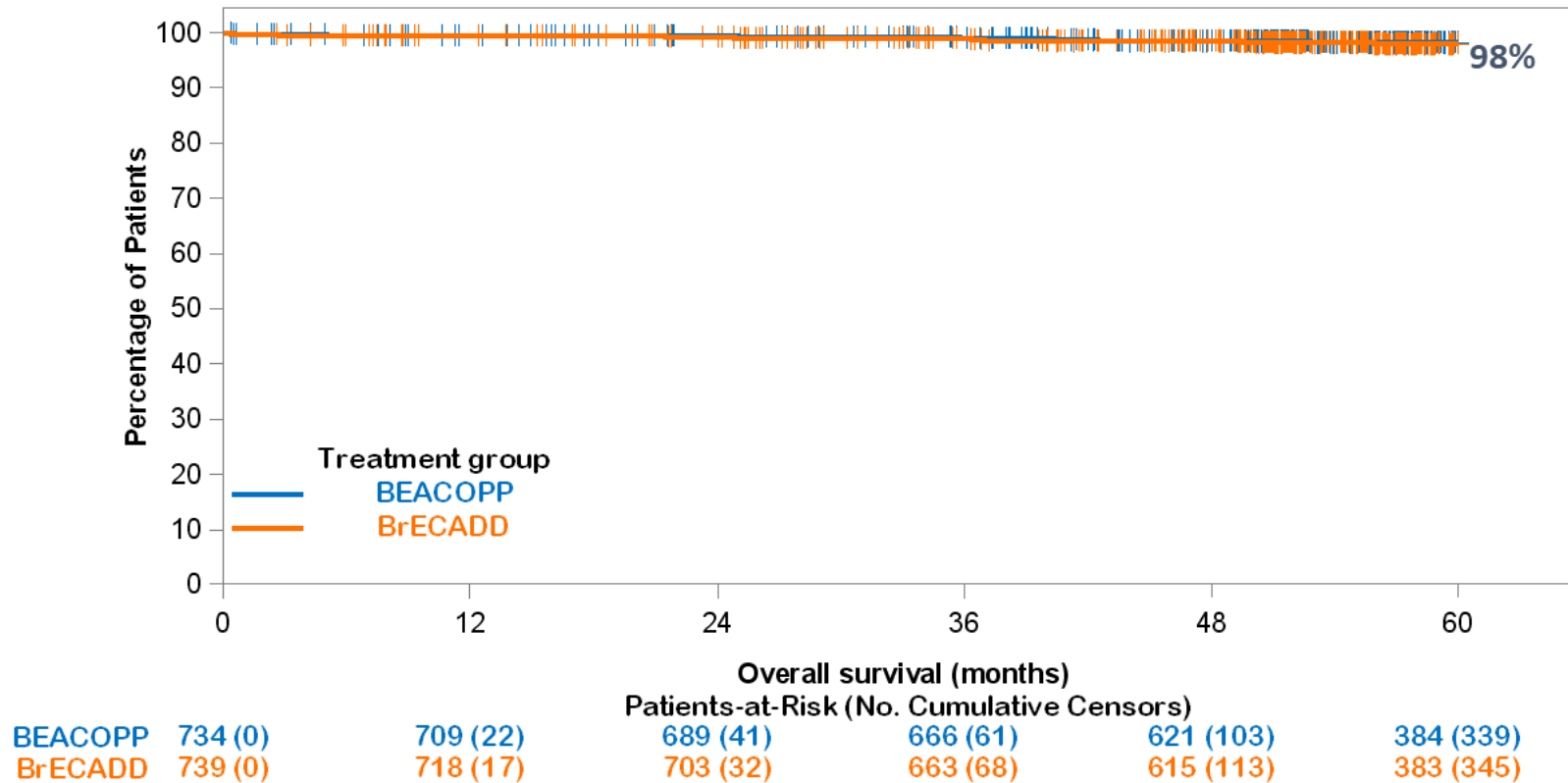
Progression-free survival in the ITT population



Only one PFS-event since publication in BrECADD arm (vs. 4 in eBEACOPP)

GHSB HD21: 5-year update presented at ASH 2025

Overall survival in the ITT population



GHSB HD21: 5-year update presented at ASH 2025

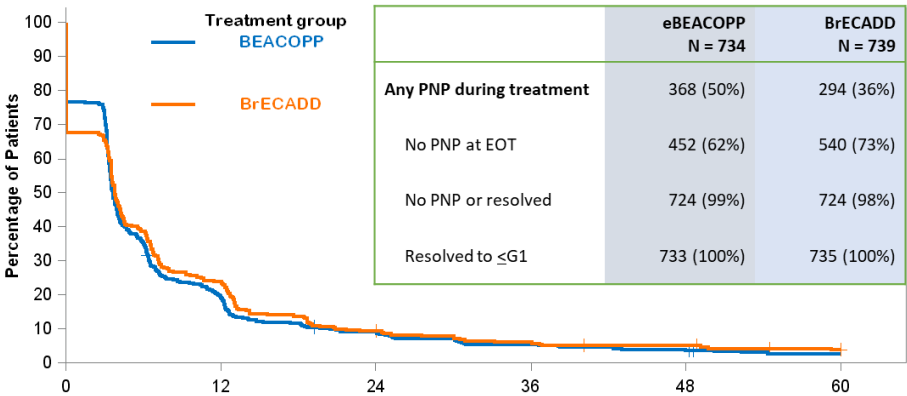
Second malignancies

		eBECOPP N=734	BrECADD N=739	ITT N=1473
Second malignancies		19 (3%)	21 (3%)	40 (3%)
Type of malignancy	AML/MDS	6 (1%)	1 (<1%)	7 (<1%)
	NHL	2 (<1%)	8 (1%)	10 (1%)
	Solid tumor	9 (1%)	11 (1%)	20 (1%)
	Other hematological malignancy	2 (<1%)	1 (<1%)	3 (<1%)
Year of event	2016-2023 (pre-publication)	16/19 (84%)	21/21 (100%)	37/40 (93%)
	2024	3/19 (16%)	0/21 (0%)	3/40 (8%)

Low rate of secondary malignancies.
Lower rate of AML/MDS likely driven by omission of procarbazine.

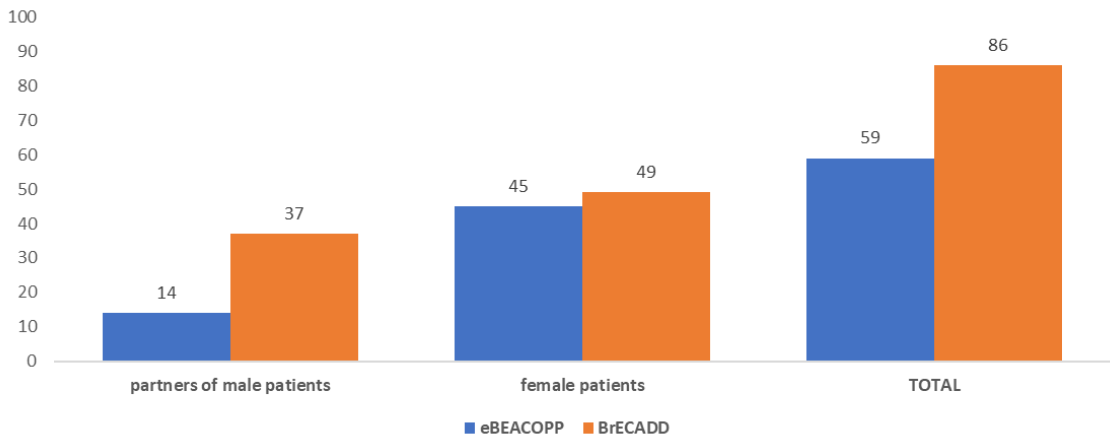
Time to PNP resolution

Only patients with PNP during therapy



Almost all patients recover from peripheral neuropathy

Childbirth at 5y mFU



More children born in the BrECADD arm

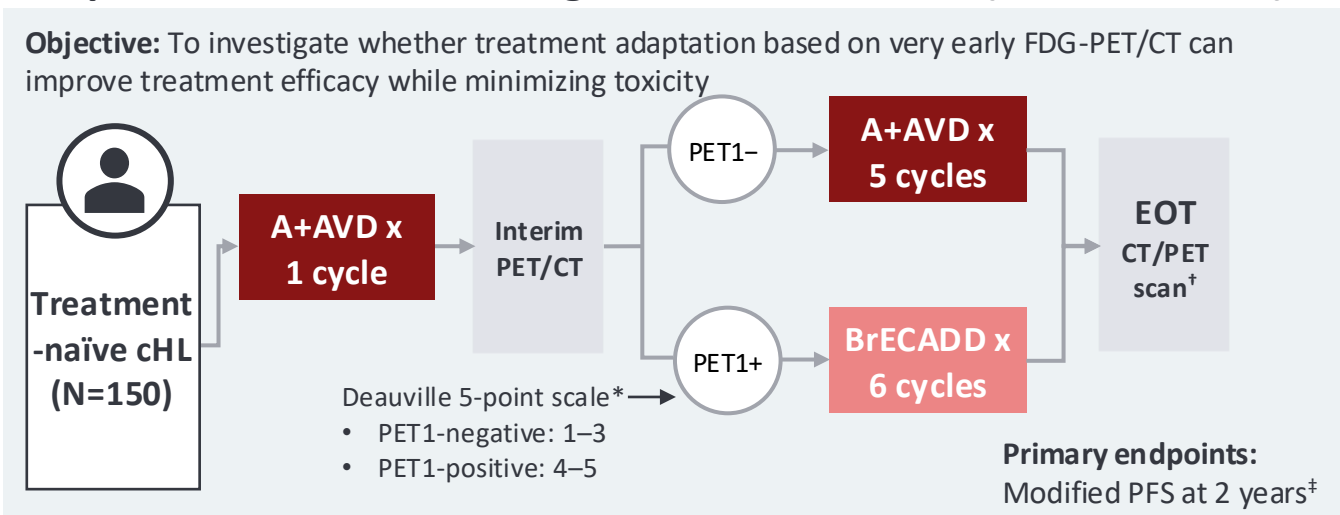
COBRA: Intensification with BRECADD

EORTC COBRA study:

Very early FDG-PET response-adapted therapy for advanced cHL

Study design

Prospective, multicenter, single-arm Phase 2 trial (NCT03517137)



Baseline characteristics

CHARACTERISTIC		N=150
Sex, %	Male	54
Age, years	Median (range)	32 (18–60)
Ann Arbor clinical staging, %	IIB / IIIA / IIIB	15 / 11 / 15
	IVA / IVB	23 / 37

Efficacy results

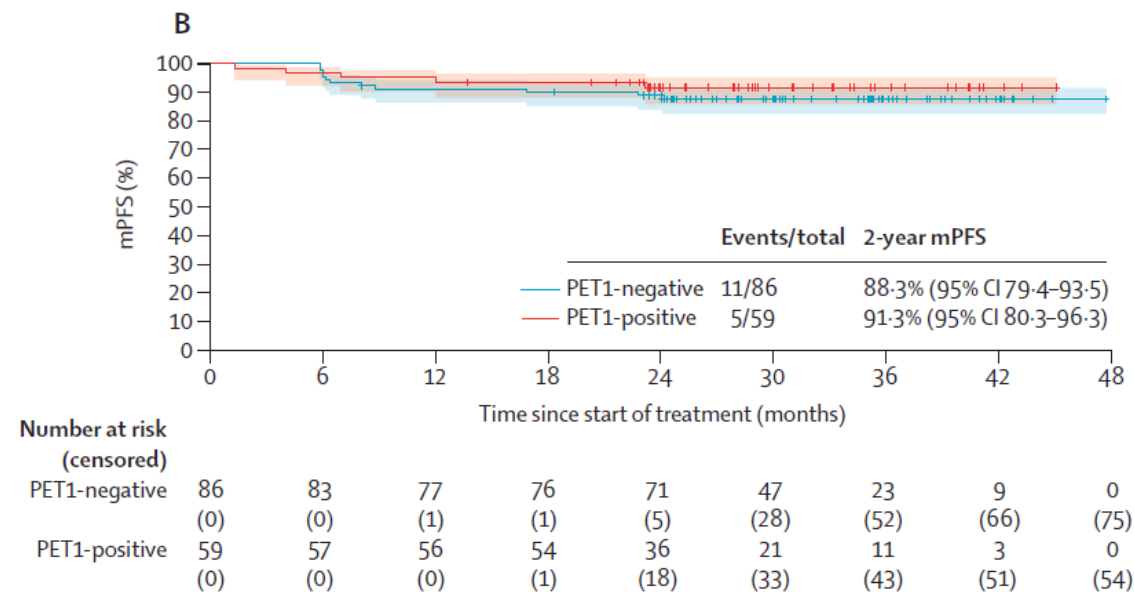
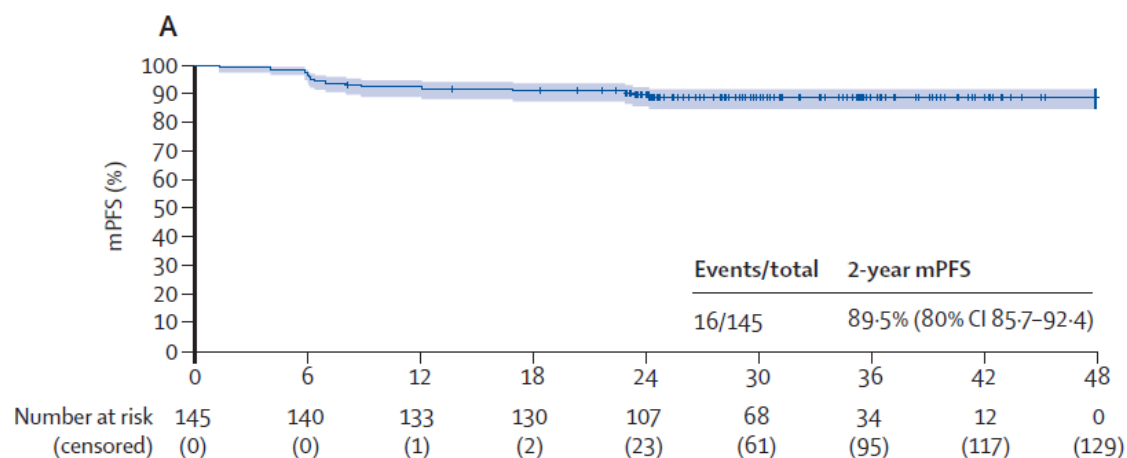
EFFICACY, %	n=145
Complete metabolic response (95% CI)	91 (85.2, 95.1)
2-year modified PFS (80% 2-sided CI)	89.5 (85.7, 92.4)
PET1-negative patients	88.3
PET1-positive patients	91.3

Safety results

SAFETY, %	N=150
TEAE	100
Grade 3/4	63
Grade 5	0
TRAE Grade 3/4	55
Serious TEAE	30

EORTC COBRA study:

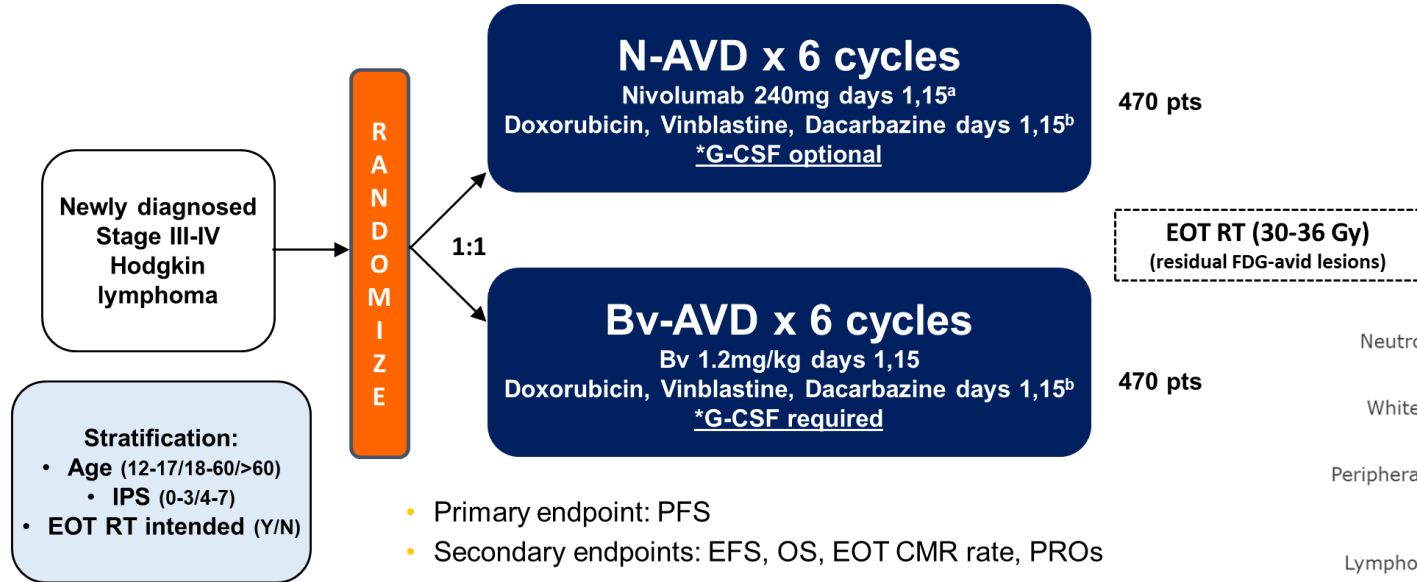
Very early FDG-PET response-adapted therapy for advanced cHL



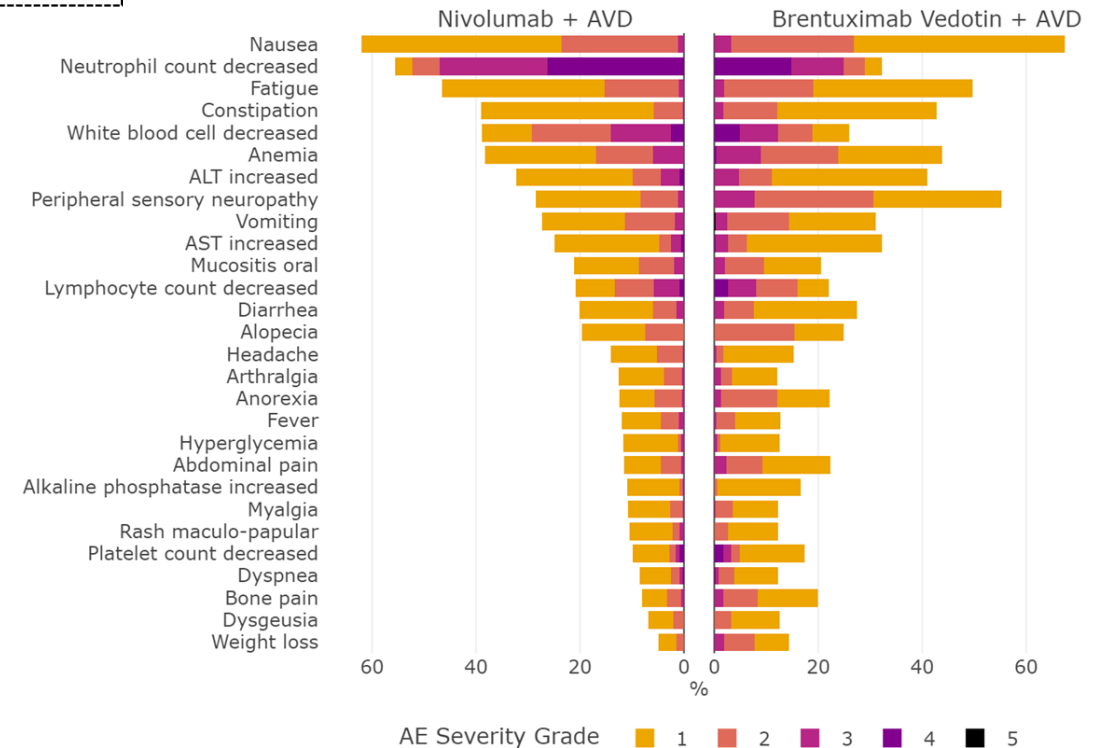
Very early FDG-PET response-adapted treatment led to very high efficacy, while sparing most patients intensive chemotherapy

SWOG1826: A-AVD vs. N-AVD

SWOG s1826 trial: A-AVD vs. N-AVD in newly diagnosed advanced cHL

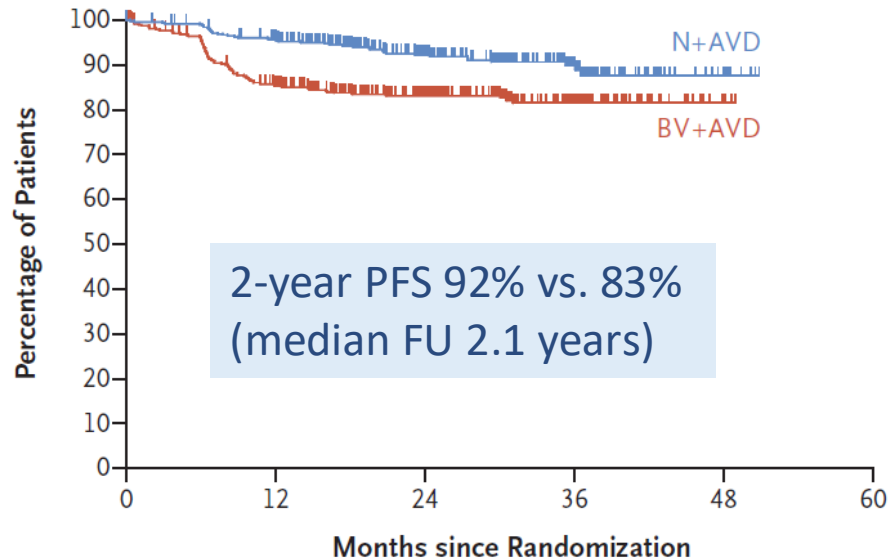


Toxicity	N-AVD n = 483			Bv-AVD n = 473		
	Gr 1 (%)	Gr 2 (%)	Gr ≥ 3 N (%)	Gr 1 (%)	Gr 2 (%)	Gr ≥ 3 N (%)
Peripheral sensory neuropathy	97 (20%)	35 (7%)	6 (1%)	117 (25%)	108 (23%)	37 (9%)
Peripheral motor neuropathy	12 (2%)	7 (1%)	1 (0%)	12 (3%)	17 (4%)	6 (1%)



SWOG s1826 trial: A-AVD vs. N-AVD in newly diagnosed advanced cHL

A Progression-free Survival



No. at Risk

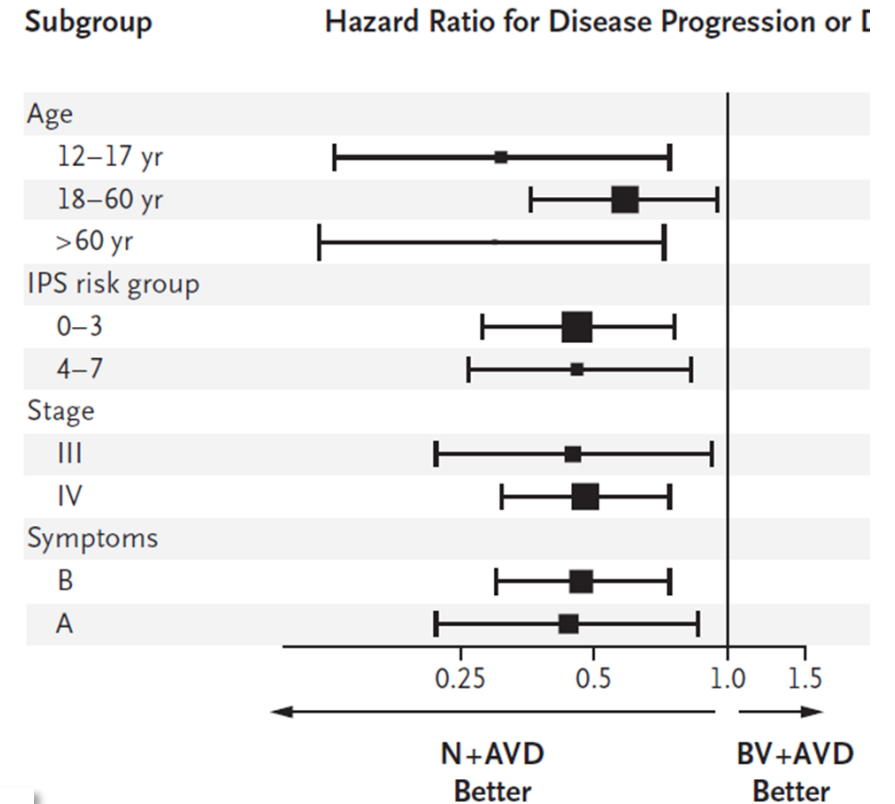
N+AVD	487	450	281	101	9	0
BV+AVD	483	392	244	97	7	0

	Disease Progression or Death <i>no. of patients</i>	2-Year Estimate for Progression-free Survival (95% CI)
		<i>percent</i>
N+AVD	41	92 (89–94)
BV+AVD	81	83 (79–86)

Hazard ratio, 0.45 (95% CI, 0.30–0.65)

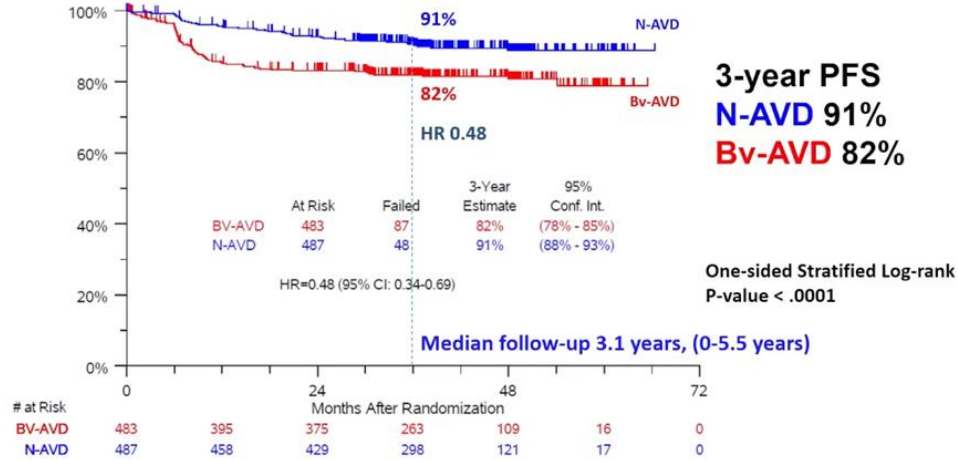
	Death <i>no. of patients</i>	2-Year Estimate for Overall Survival (95% CI)
		<i>percent</i>
N+AVD	7	99 (97–100)
BV+AVD	14	98 (96–99)

Hazard ratio, 0.39 (95% CI, 0.15–1.03)

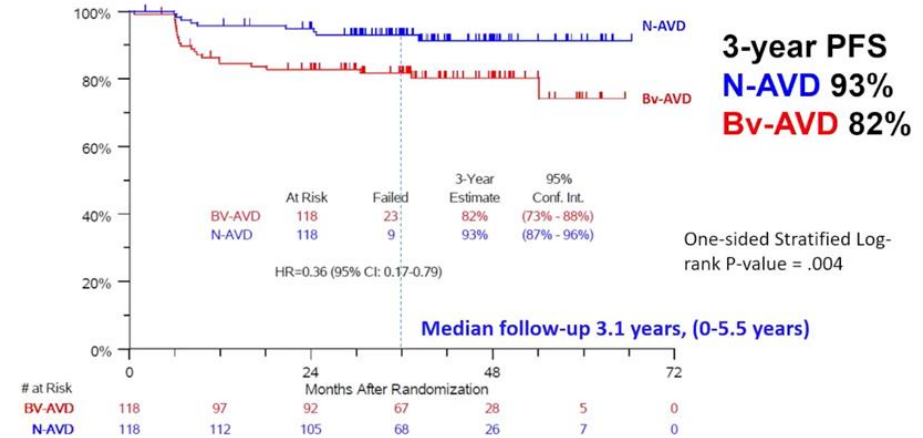


SWOG s1826 trial: ASH 2025 update (Herrera A, et al.)

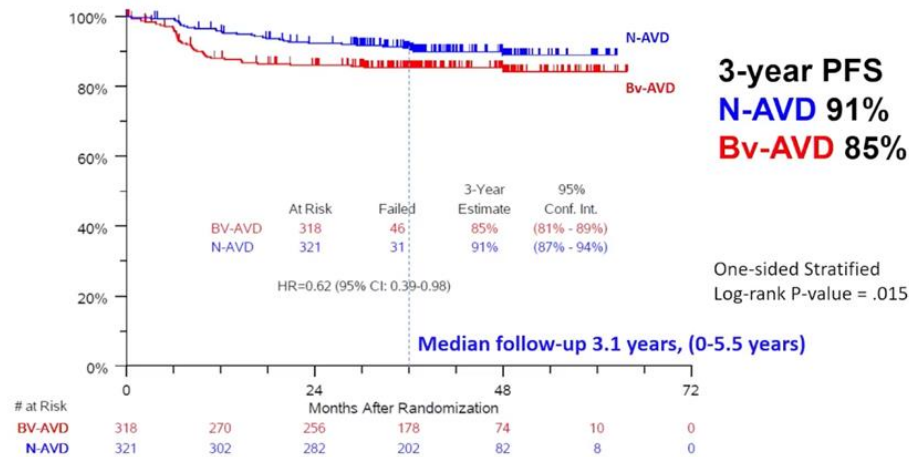
PFS benefit of N-AVD sustained with 3y follow-up



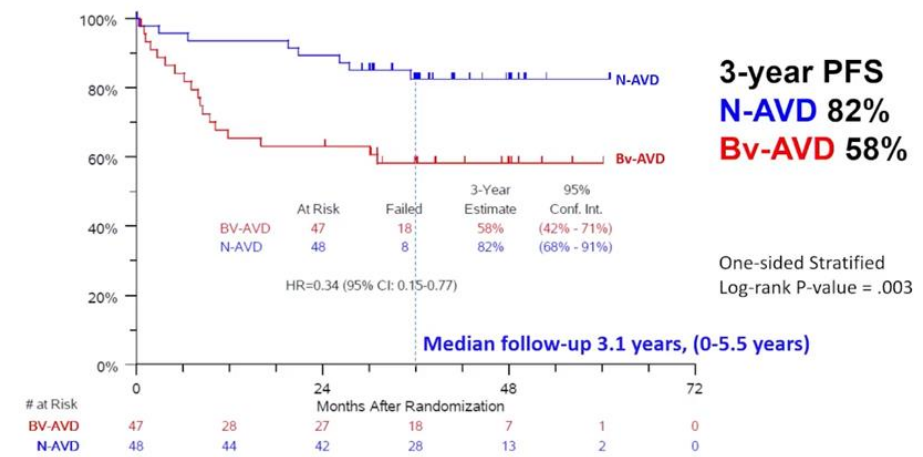
N-AVD prolongs PFS in adolescents



N-AVD prolongs PFS in 18-60 year-old adults

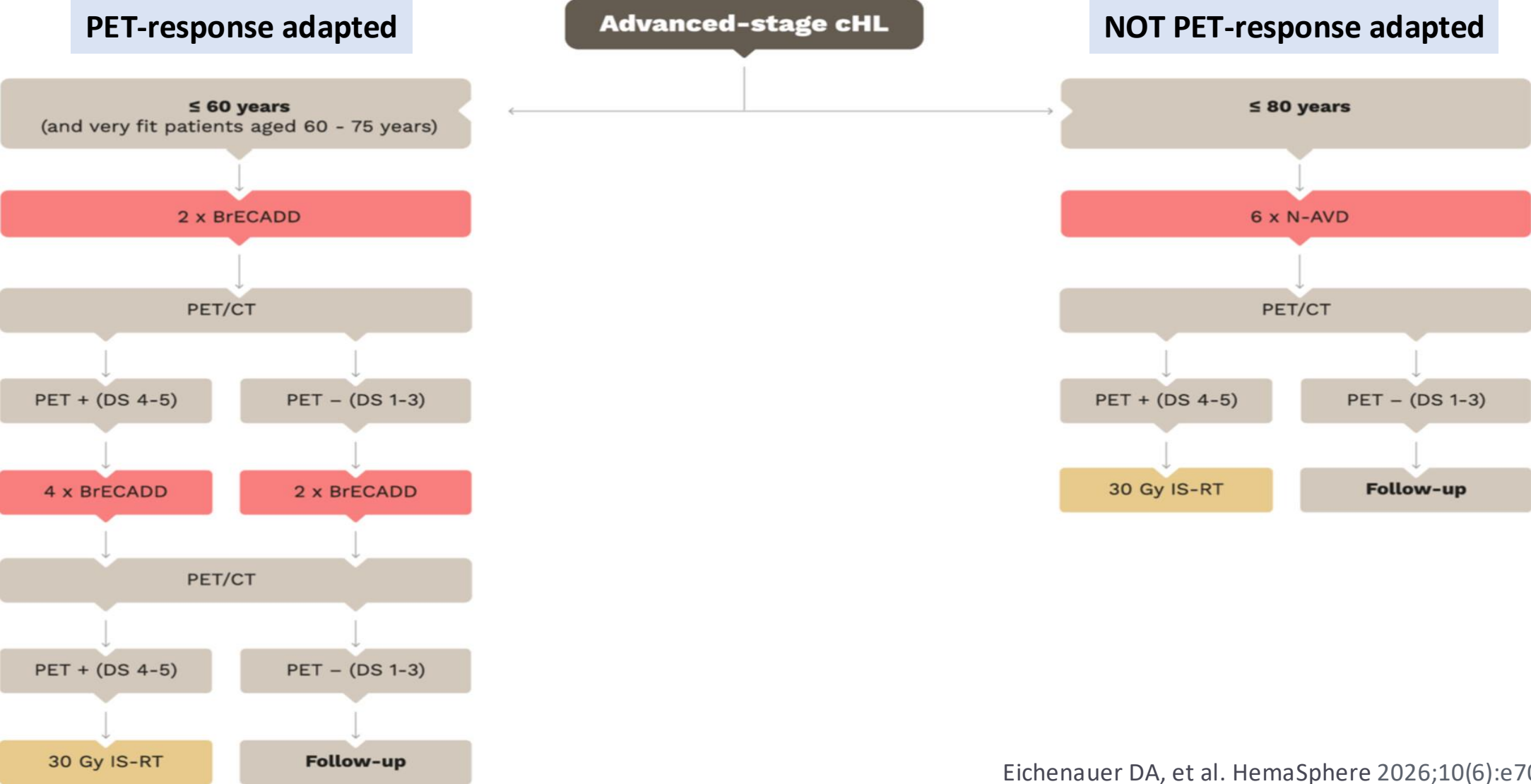


N-AVD prolongs PFS in older adults

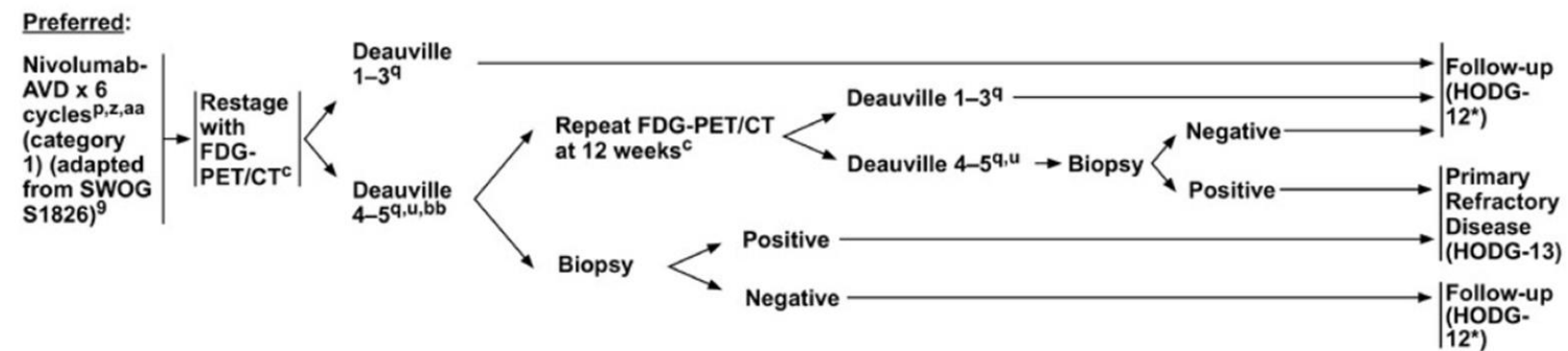


Current guidelines and conclusions

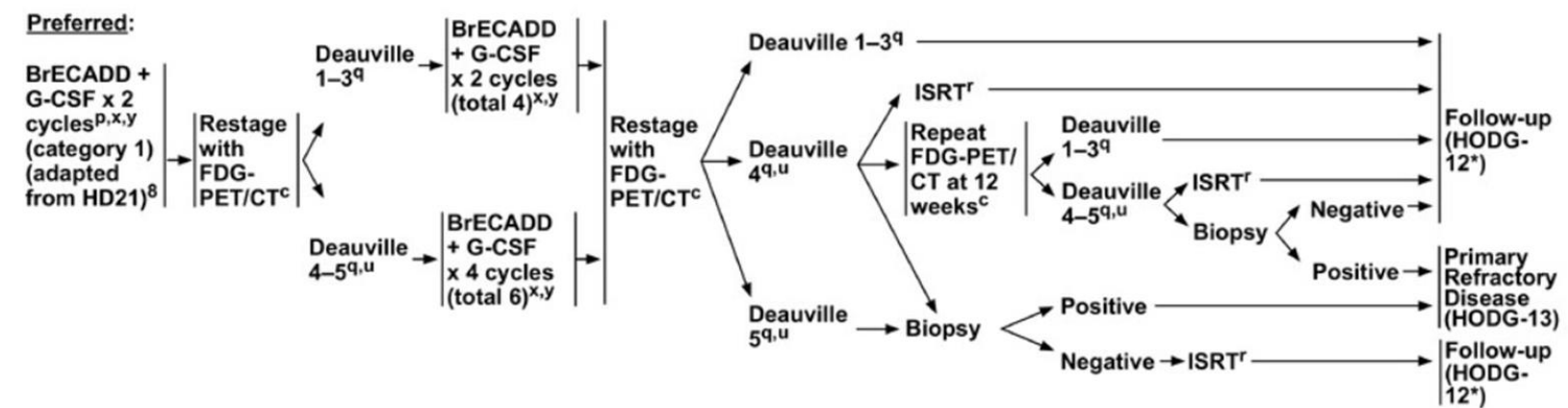
Hodgkin lymphoma: 2026 EHA Clinical Practice Guidelines for diagnosis, treatment, and follow-up



Hodgkin Lymphoma, Version 1.2026, NCCN Clinical Practice Guidelines In Oncology



NOT PET-response adapted



PET-response adapted

ABVD and BV-AVD still recommended for certain situations

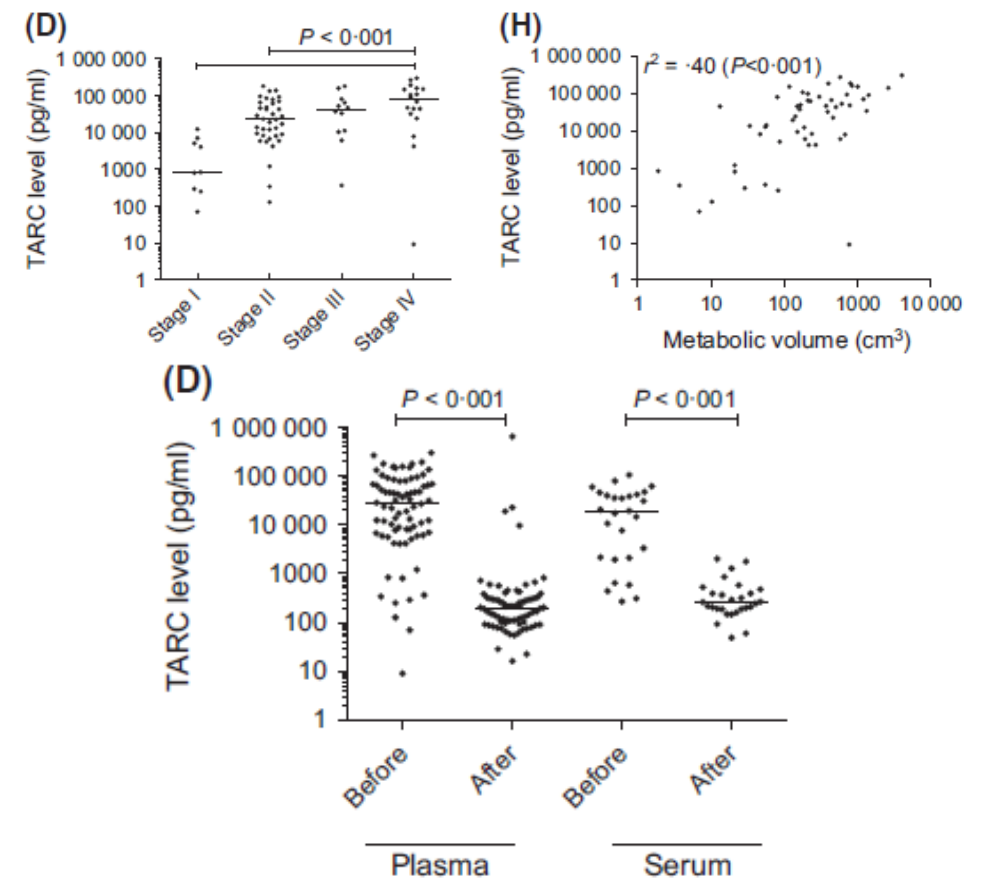
Future developments

TARC and ctDNA with or without interim PET

TARC in Hodgkin lymphoma

- 103 consecutive HL patients, consecutively included in a single-centre study
- Authors compared the dynamics of sGalectin-1, sCD163 and sCD30 with TARC
- Baseline TARC levels clearly elevated in 93% of patients, and correlated to stage and metabolic tumor volume
- There was no correlation with changes in sGalectin-1, sCD163 and sCD30 and clinical treatment response in individual patients
- TARC remained high in 6 out of 7 non-responsive patients and decreased in 95 out of 96 responsive patients

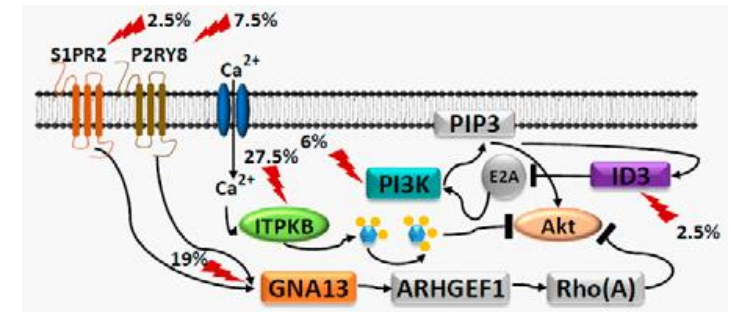
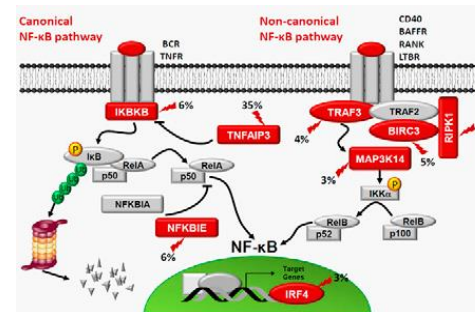
TARC: A chemokine highly expressed on HRS cells - contributes to the inflammatory HL microenvironment, promoting tumor initiation, maintenance, and progression



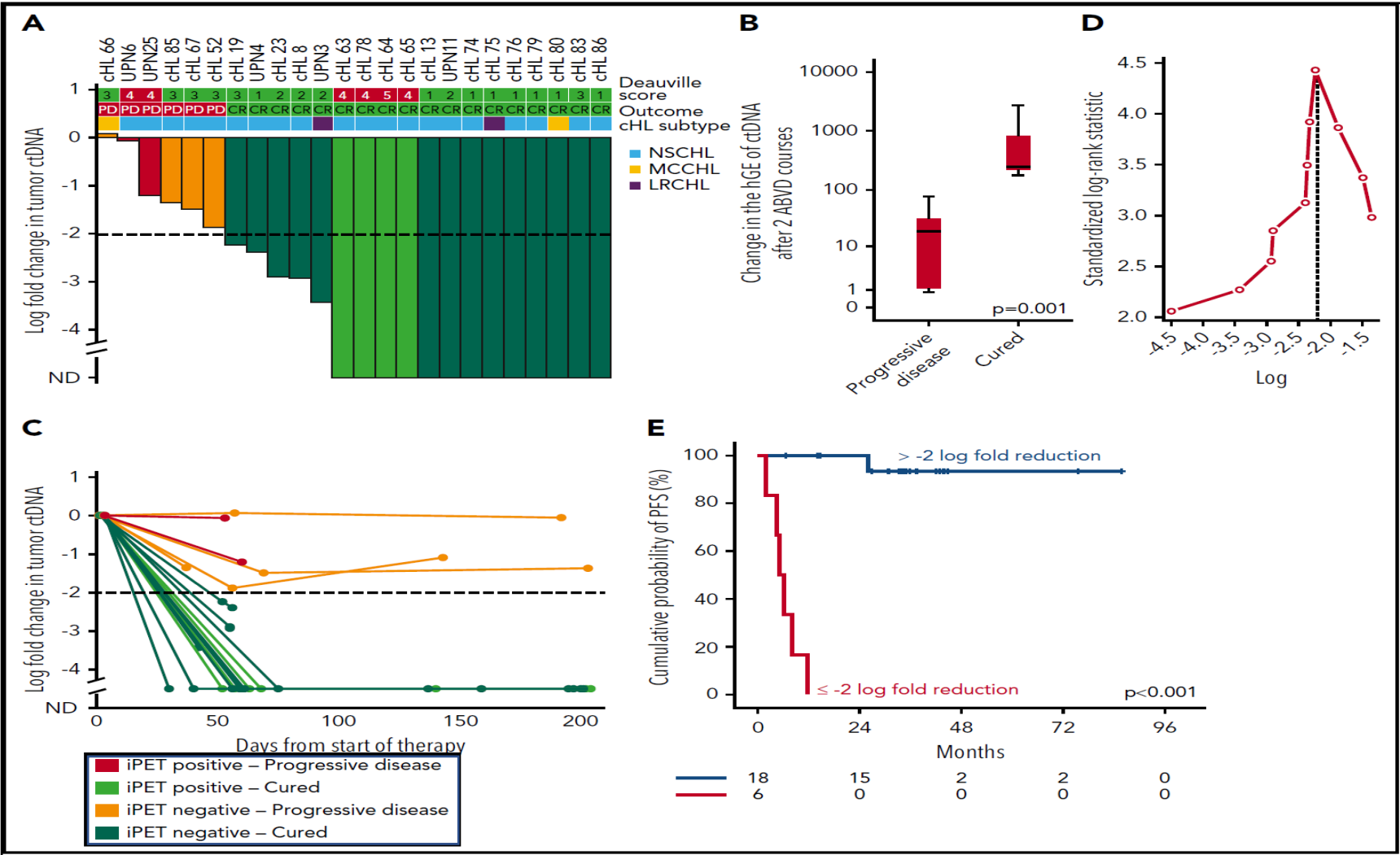
ctDNA in Hodgkin lymphoma

- Analysis of ctDNA from previously untreated (n = 80) and r/r (n = 32) cHL, plus ctDNA from plasma during ABVD treatment (after 1 cycle) and at the end of treatment (n = 24)
- Nonsynonymous somatic mutations detected in 81.2% of cases
- The most commonly mutated genes (>20%) were consistent with well-described activation of signaling pathways in cHL:

- STAT6 (JAK/STAT – cytokine signaling)
- TNFAIP3 (NF-κB)
- ITPKB (PI3K-AKT)



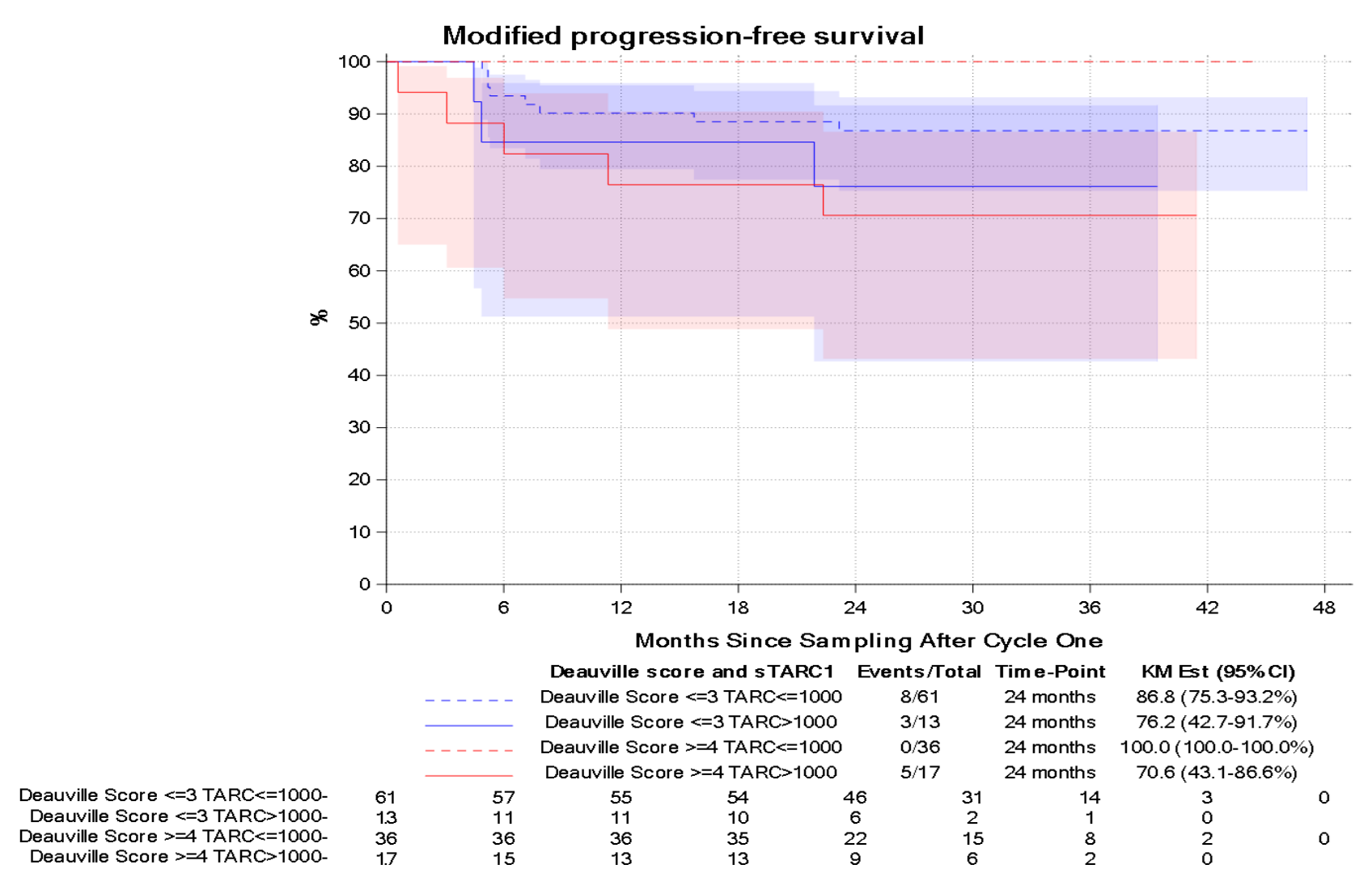
A quick, 100-fold drop in ctDNA levels was highly prognostic



SWOG s1826 trial: Interim PET vs. ctDNA

- **PET2 is still prognostic in N-AVD: 3-year PFS 84% vs. 93%**
- Analysis of the first 388 patients on the trial with baseline, cycle 3 day 1 (C3D1) and end-of-therapy (EOT) plasma samples (and germline DNAs)
- All had PET/CT at the same time points
- 375/388 (97%) had detectable clustered variants at baseline
- Clinical characteristics and survival were comparable to the entire trial cohort
- Pts with detectable ctDNA at C3D1 had significantly inferior outcomes in the full 375 pt cohort (FC) and both Tx arms:
 - 3y PFS ctDNA⁺ vs ctDNA⁻: Full cohort 61% vs 89%
 - N-AVD 71% vs 93%
 - BV-AVD 50% vs 84%
- In the cohort of patients with detectable ctDNA, PET2 did not have independent prognostic value

Early PET and TARC in the COBRA trial



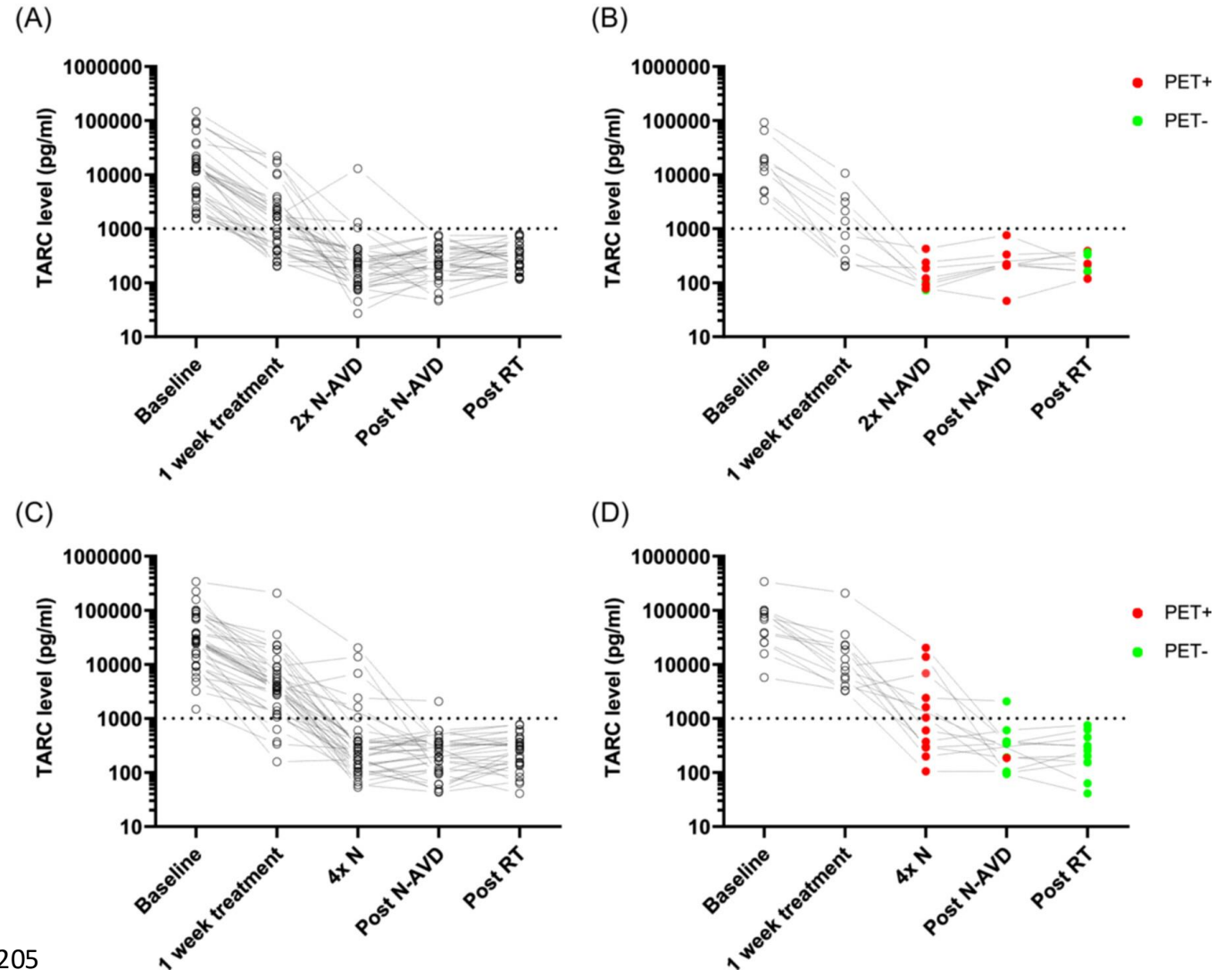
sTARC dynamics and PET response NIVAHL (early unfavourable HL)

(A) All patients who received concomitant N-AVD (nivolumab, doxorubicin, vinblastine, dacarbazine) treatment.

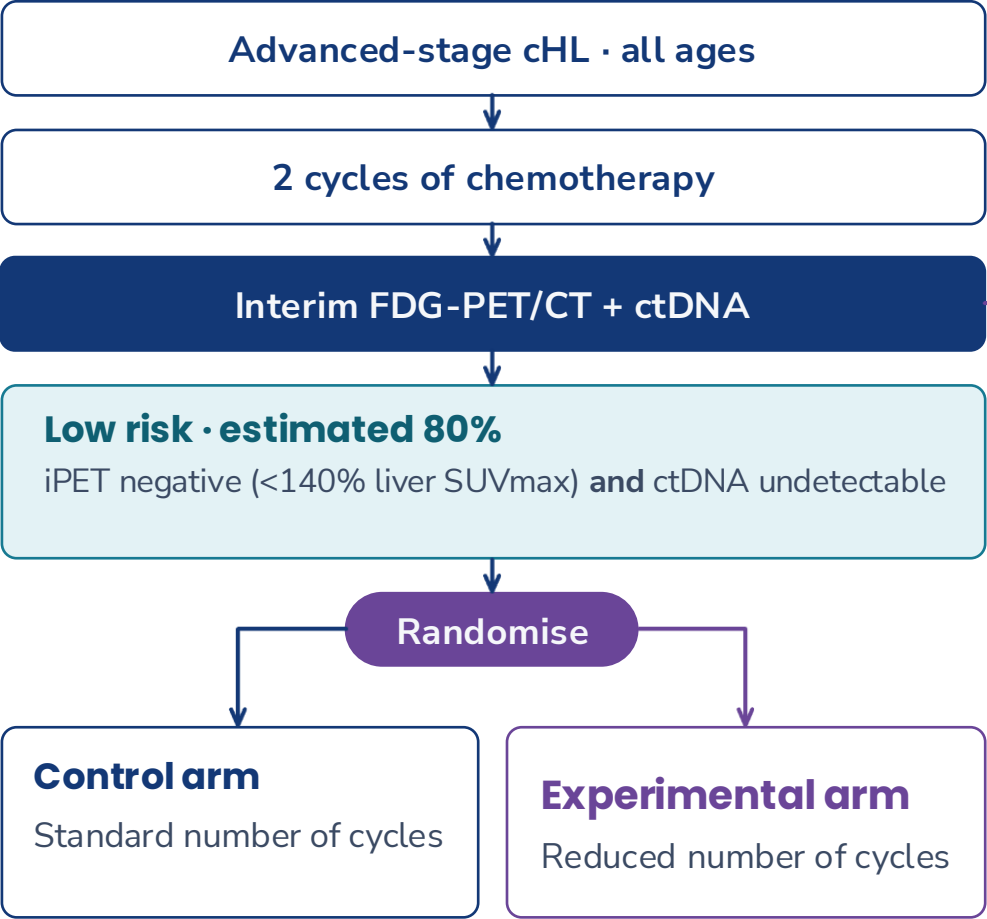
(B) Patients receiving concomitant N-AVD treatment with a positive PET scan based on Deauville score at a timepoint during or after treatment and the respective sTARC values.

(C) All patients who received sequential nivolumab and (N-)AVD treatment.

(D) Patients receiving sequential nivolumab and (N-)AVD with a positive PET scan based on Deauville score at a timepoint during or after treatment and the respective sTARC values.



TRIAL SCHEMA



Baseline PET-CT, ctDNA + germline DNA

Standard risk · estimated 20%
iPET positive (≥140% liver SUVmax) and/or
ctDNA detected
Treated per current protocols, followed on trial

Timing
ctDNA results take up to 3 weeks, so all patients
receive cycle 3. Randomisation happens before the
end of cycle 3.

	ABVD, BV-AVD, N-AVD	escBEACOPP, BrECADD	OEPA / DECOPDac
Control low-risk arm	6 cycles	4 cycles	2 OEPA + 4 DECOPDac
Experimental low-risk arm	4 cycles	3 cycles	2 OEPA + 2 DECOPDac

Summary

- Even in the era of novel therapies like BRECAD and N-AVD, there is need for individualised treatment and therefore for response-adapted treatment of Hodgkin lymphoma
- PET/CT is the cornerstone of staging and response assessment in lymphoma and will probably play the main role for many years to come
- sTARC and ctDNA seem to be more accurate for early prognostication and should be part of future response-adapted strategies



Phase 1 Unit, Haematology translational research team:

Simon Husby
Emil Kyvsgaard
Chiara Bancone

Phase 1 team, Clinical research unit, Department of Haematology, Rigshospitalet:

Tina Bjerg, Claudia Jensen,
Karina Juhls, Maria Lind, Chris Mathiasen, Sissel Brendes Olsen, Nikoline Rykind-Eriksen



Phase 1 Unit, Departments of Oncology and Haematology, Rigshospitalet:

Haematology consultants:

Caroline Riley
Claudia Schöllkopf

Oncology consultants:

Martin Højgaard
Kristoffer Rohrberg
Lise Høj Omland
Ulrik Lassen



Lymphoma and CLL team, Department of Haematology, Rigshospitalet:

Fazila Asmar
Mads Emil Bjørn
Peter de Nully Brown
Caspar da Cunha-Bang
Lisbeth Enggaard
Anne Ortved Gang
Jette Gørløv
Troels Hammer
Pär Josefsson
Carsten Niemann
Jindrich Mourek
Michael Pedersen
Caroline Riley
Dorte Tholstrup