HIGHLIGHTS IN EMATOLOGIA

TREVISO
7-8 NOVEMBRE 2025

LINFOMA DI HODGKIN
CHE COSA C'È DI NUOVO IN TERMINI PROGNOSTICI?

Alessandro Broccoli
IRCCS Azienda Ospedaliero-Universitaria di Bologna, Policlinico «Sant'Orsola-Malpighi»
Department of Medical and Surgical Sciences, University of Bologna, Italy
Institute of Hematology «L. e A. Seràgnoli», Bologna, Italy

Disclosures: ALESSANDRO BROCCOLI

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Gilead				X	X	X
Merck	X					X
Janssen	X			X		X
Takeda		X		X	X	X
Kyowa Kirin	X			X	X	X
Incyte						X
Recordati						X
Astra Zeneca				X	X	
Roche				X		X
GlaxoSmithKline		X		X	X	
BeOne	X			X	X	X
Eli Lilly						X
SOBI				X		
SERB Pharma		X			X	

Prognostication for early- and advanced-stage Hodgkin lymphoma

- Prognostic models based on pre-treatment factors can help identify patients with early- and advanced-stage classic Hodgkin lymphoma who are at increased risk of relapse (or death).
- In early-stage disease, EORTC and GHSG classifications have been followed for the past 40-50 years.
- Original EORTC early-stage prognostic factors date back to early ‘70s, when staging laparotomy and mantle radiation (alone) were the predominant ways of treatment.
- In advanced-stage disease, the International Prognostic Score (IPS7) had been a standard index in classic Hodgkin lymphoma for 25 years.
- Performance of IPS7 decreased when analyzed in patients treated in a more recent era, and is almost surpassed when regimens containing newer drugs are applied frontline (poor calibration).
- Updated analyses with modern clinical trial and registry (real-world data) is desired.

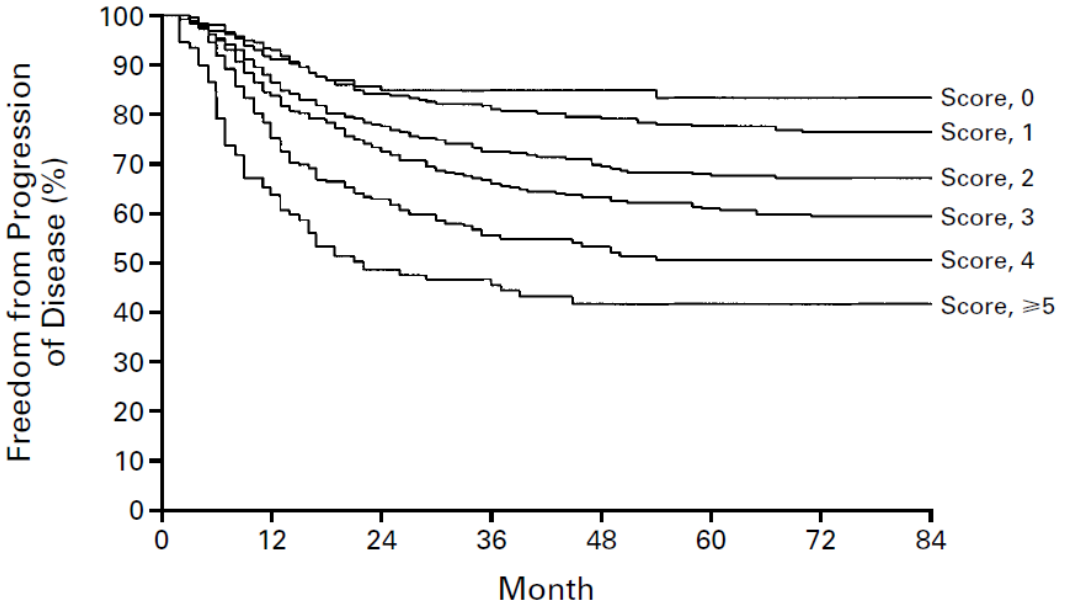
Evens AM. *Hematol Oncol (18 ICML meeting abstracts)*, 2025; 43(S2): e70066

A PROGNOSTIC SCORE FOR ADVANCED HODGKIN'S DISEASE

DIRK HASENCLEVER, PH.D., AND VOLKER DIEHL, M.D.,
FOR THE INTERNATIONAL PROGNOSTIC FACTORS PROJECT ON ADVANCED HODGKIN'S DISEASE*

THE FINAL COX REGRESSION MODEL.

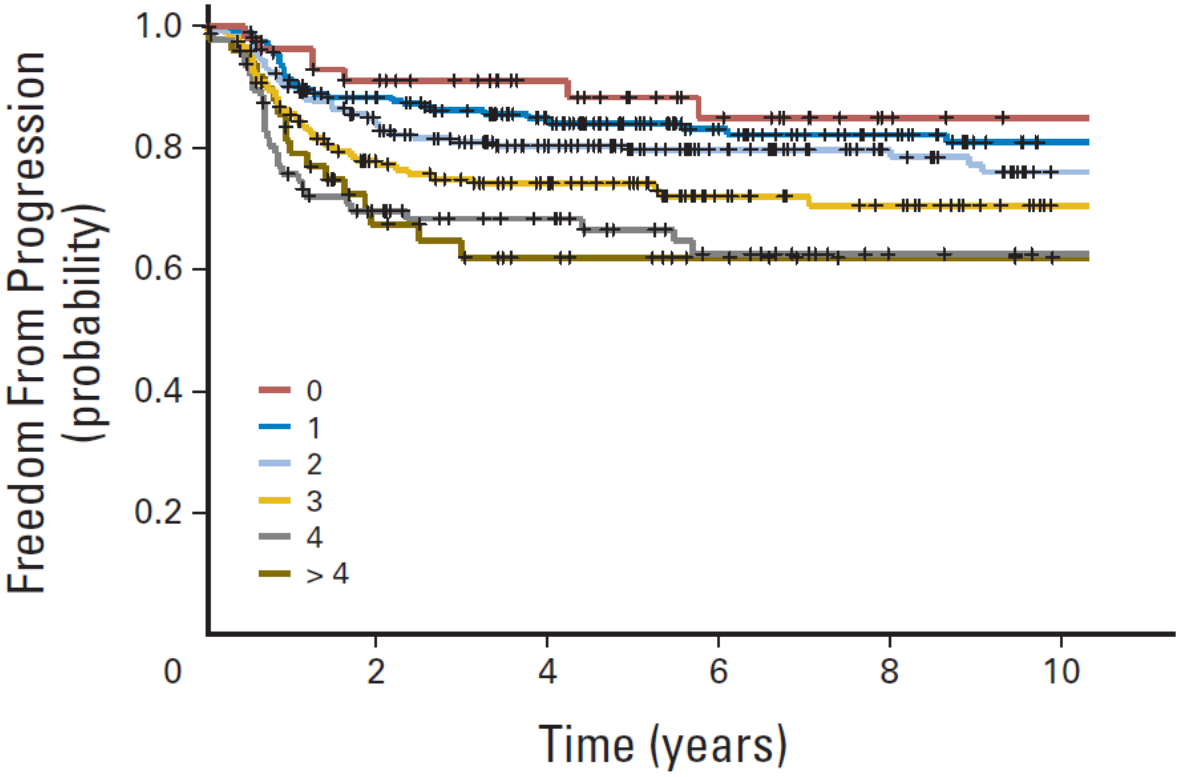
FACTOR	LOG HAZARD RATIO	P VALUE	RELATIVE RISK
Serum albumin, <4 g/dl	0.40±0.10	<0.001	1.49
Hemoglobin, <10.5 g/dl	0.30±0.11	0.006	1.35
Male sex	0.30±0.09	0.001	1.35
Stage IV disease	0.23±0.09	0.011	1.26
Age, ≥45 yr	0.33±0.10	0.001	1.39
White-cell count, ≥15,000/mm³	0.34±0.11	0.001	1.41
Lymphocyte count, <600/mm³ or <8% of white-cell count	0.31±0.10	0.002	1.38

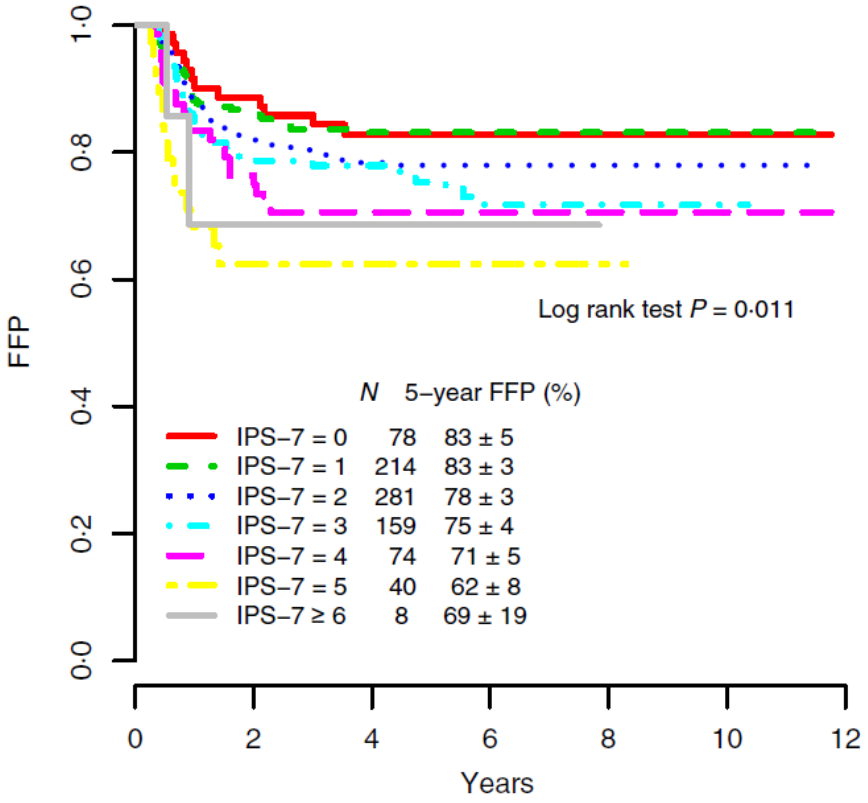


Treatments started **before January 1992**. More than 75 percent of the patients were treated with standard doxorubicin-containing regimens; 20 percent received MOPP or a similar regimen. Sixty percent of the patients received no radiotherapy. Thirty-three percent received full or selected involved field irradiation; 2 percent underwent more extensive irradiation with a mantle or inverted-Y field, and 5 percent underwent subtotal or total nodal irradiation.

Hasenclever D. *N Engl J Med*, 1998; 339: 1506-1514

Performance of IPS7 in modern era



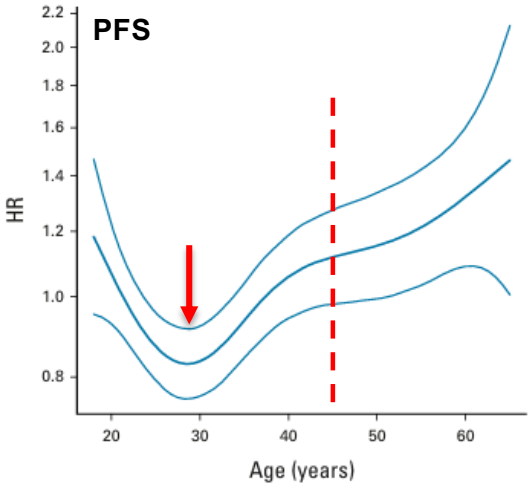


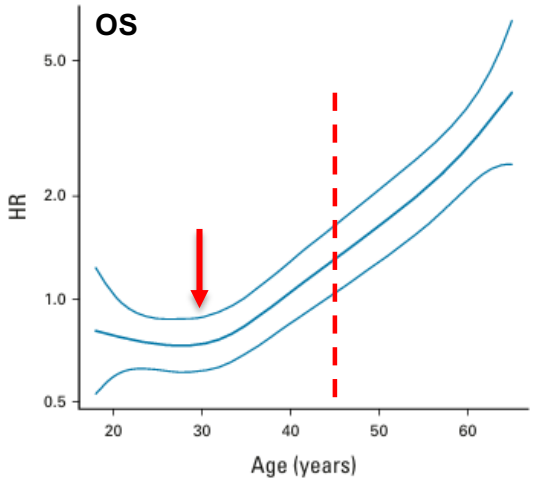
Moccia AA. *J Clin Oncol*, 2012; 30: 3383-3388 — Diefenbach C. *Br J Haematol*, 2015; 171: 530-538

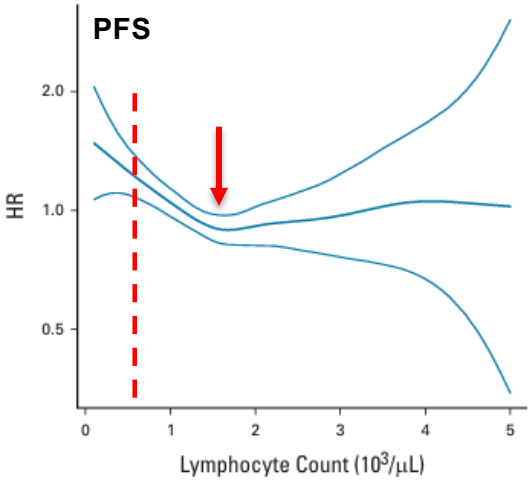
The Advanced-Stage Hodgkin Lymphoma International Prognostic Index: Development and Validation of a Clinical Prediction Model From the HoLISTIC Consortium

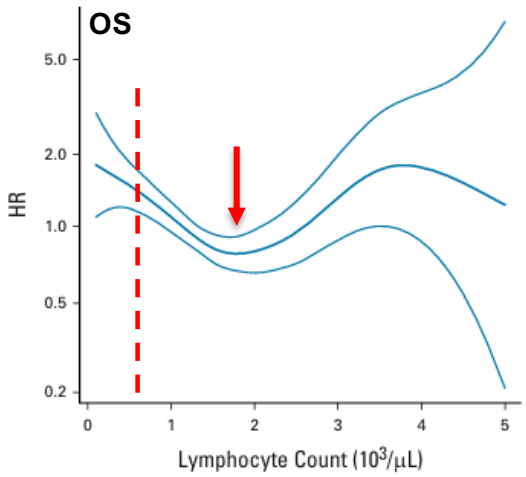
- **Why did IPS7 have to be refined?** Due to improvements in diagnostic accuracy, use of PET in more accurate stage definition, optimization of drug dosing and treatment dose intensity, treatment adaptation according to early PET results, improved post-relapse salvage treatment modalities.
- **How was it performed?**
  - A population of adult patients with newly diagnosed classic Hodgkin lymphoma aged 18-65 years and with advanced stage (IIB, III, IV).
  - Model developed on 4,022 patients from 8 clinical trials enrolling advanced-stage patients between 1996 and 2014; validated on 1,431 patients from 4 cancer registries (between 1996 and 2019).
- Continuous variables (e.g. age, laboratory parameters) were no more considered as dichotomized.
- **Novel non-linear relationships between age and absolute lymphocyte counts have been identified, along with unique prognostic variables significant for PFS versus OS**.
- An online calculator to assist clinicians and patients in estimating individualized prognosis.

Rodday AM. *J Clin Oncol*, 2023; 41: 2076-2086







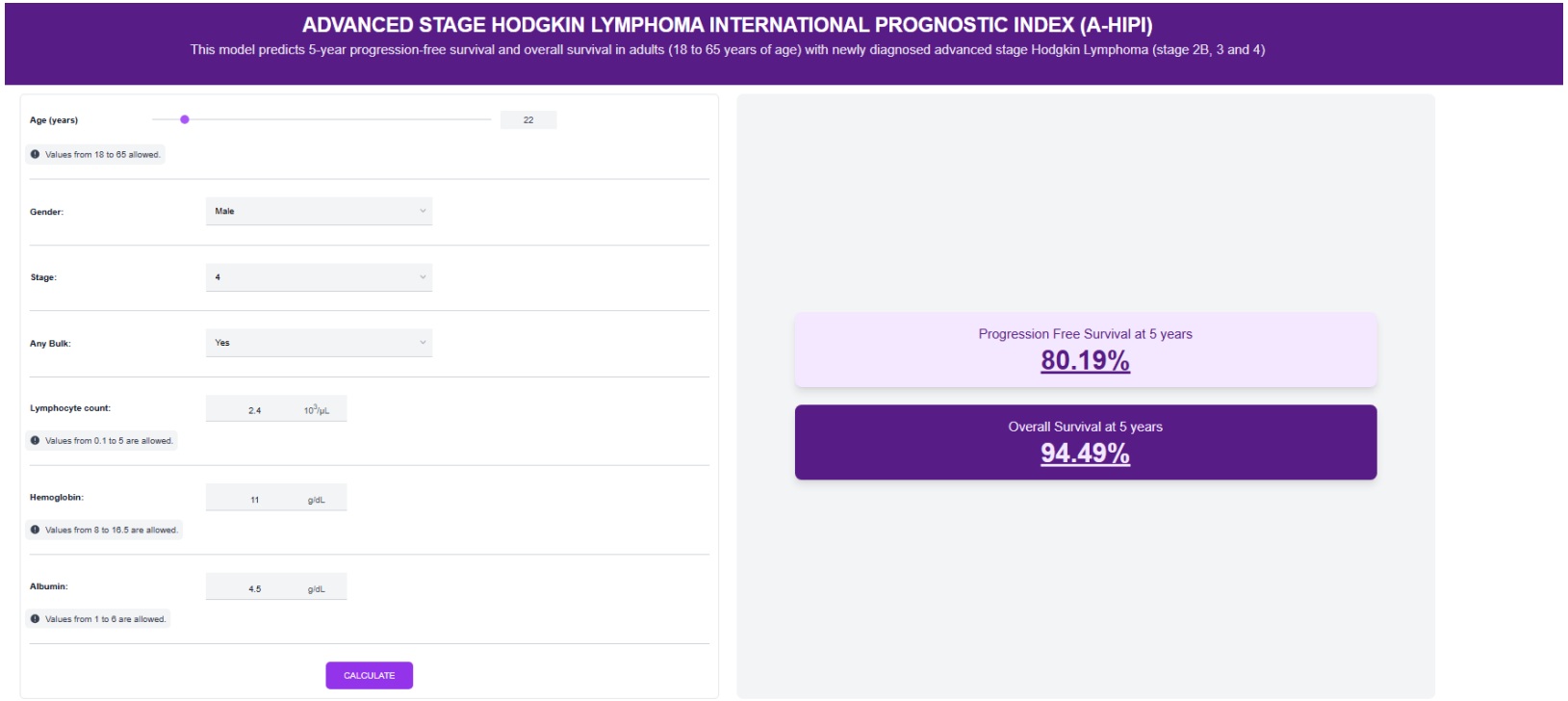


The Advanced-Stage Hodgkin Lymphoma International Prognostic Index: Development and Validation of a Clinical Prediction Model From the HoLISTIC Consortium

	5-year PFS HR (95% CI)	5-year OS HR (95% CI)
Age (years)		
Linear effect in 18 to 30 years	0.97 (0.95, 1.00)	0.98 (0.94, 1.02)
Linear effect in >30 years	1.02 (1.01, 1.02)	1.05 (1.04, 1.07)
Female	--	0.78 (0.61, 1.00)
Stage		
Stage IIB		
Stage III	1.23 (1.03, 1.48)	
Stage IV	1.53 (1.27, 1.83)	1.33 (1.04, 1.70)
Bulk	--	1.37 (1.05, 1.78)
Hemoglobin (g/dL)	--	0.88 (0.81, 0.96)
Albumin (g/dL)	0.74 (0.66, 0.82)	0.67 (0.53, 0.84)
Lymphocyte count (10^3/mm³)		
Linear effect in .1 to 2	0.75 (0.65, 0.87)	0.61 (0.46, 0.80)
Linear effect in 2 to 5	1.21 (0.96, 1.52)	1.49 (0.99, 2.22)

Rodday AM. *J Clin Oncol*, 2023; 41: 2076-2086

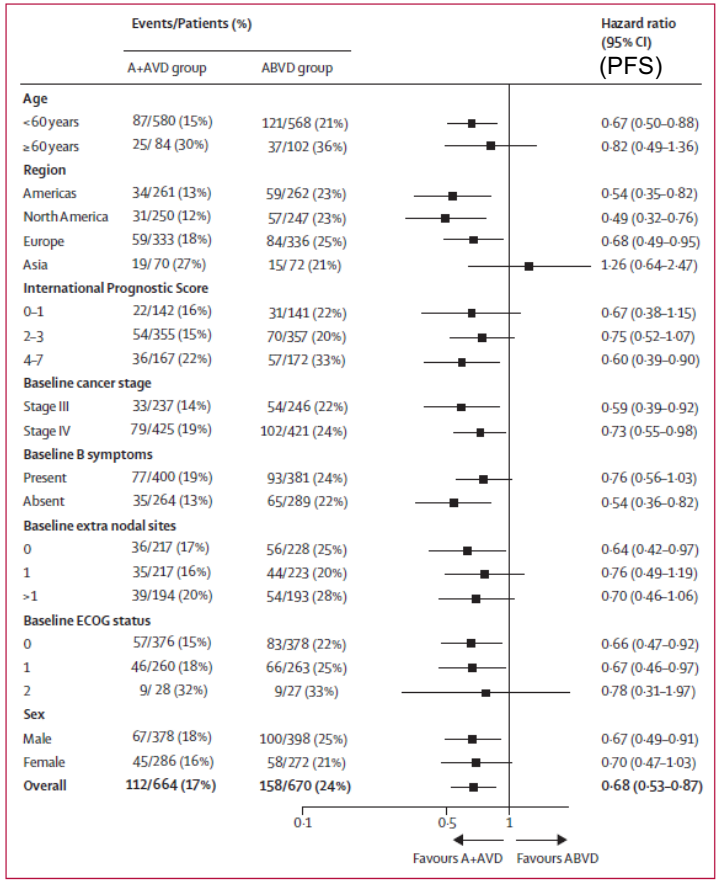
The Advanced-Stage Hodgkin Lymphoma International Prognostic Index: Development and Validation of a Clinical Prediction Model From the HoLISTIC Consortium



Rodday AM. *J Clin Oncol*, 2023; 41: 2076-2086 — https://holistic-calculator.web.app/

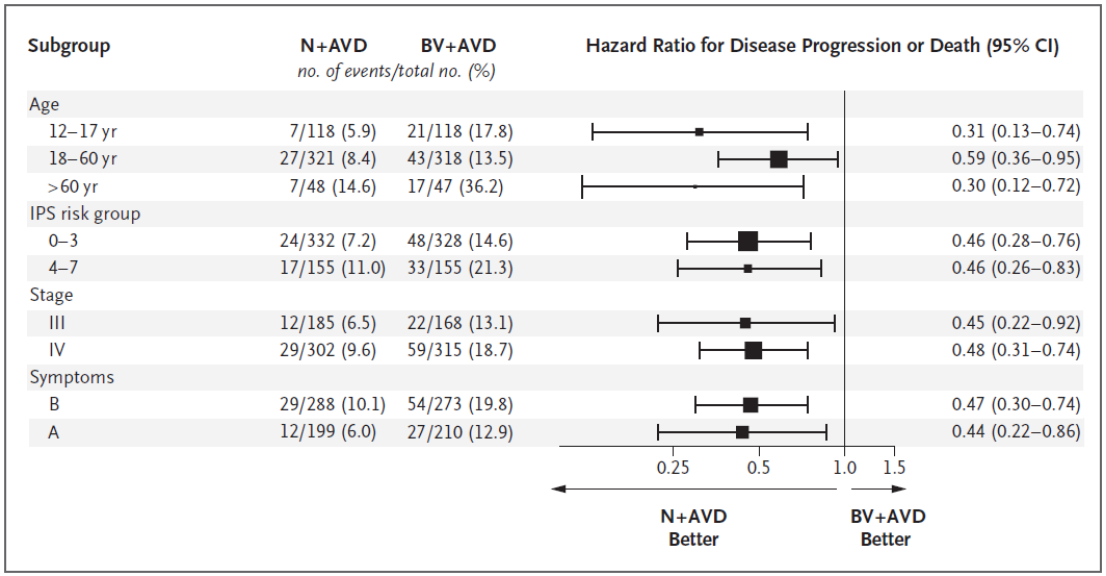
Significance of IPS7 in contemporary randomized clinical trials with new drugs (1)

A+AVD vs ABVD



	Events/Patients (%)		Hazard ratio (95% CI) (PFS)
	A+AVD group	ABVD group	
Age			
<60 years	87/580 (15%)	121/568 (21%)	0·67 (0·50–0·88)
≥60 years	25/ 84 (30%)	37/102 (36%)	0·82 (0·49–1·36)
Region			
Americas	34/261 (13%)	59/262 (23%)	0·54 (0·35–0·82)
North America	31/250 (12%)	57/247 (23%)	0·49 (0·32–0·76)
Europe	59/333 (18%)	84/336 (25%)	0·68 (0·49–0·95)
Asia	19/ 70 (27%)	15/ 72 (21%)	1·26 (0·64–2·47)
International Prognostic Score			
0–1	22/142 (16%)	31/141 (22%)	0·67 (0·38–1·15)
2–3	54/355 (15%)	70/357 (20%)	0·75 (0·52–1·07)
4–7	36/167 (22%)	57/172 (33%)	0·60 (0·39–0·90)
Baseline cancer stage			
Stage III	33/237 (14%)	54/246 (22%)	0·59 (0·39–0·92)
Stage IV	79/425 (19%)	102/421 (24%)	0·73 (0·55–0·98)
Baseline B symptoms			
Present	77/400 (19%)	93/381 (24%)	0·76 (0·56–1·03)
Absent	35/264 (13%)	65/289 (22%)	0·54 (0·36–0·82)
Baseline extra nodal sites			
0	36/217 (17%)	56/228 (25%)	0·64 (0·42–0·97)
1	35/217 (16%)	44/223 (20%)	0·76 (0·49–1·19)
>1	39/194 (20%)	54/193 (28%)	0·70 (0·46–1·06)
Baseline ECOG status			
0	57/376 (15%)	83/378 (22%)	0·66 (0·47–0·92)
1	46/260 (18%)	66/263 (25%)	0·67 (0·46–0·97)
2	9/ 28 (32%)	9/27 (33%)	0·78 (0·31–1·97)
Sex			
Male	67/378 (18%)	100/398 (25%)	0·67 (0·49–0·91)
Female	45/286 (16%)	58/272 (21%)	0·70 (0·47–1·03)
Overall	**112/664 (17%)**	**158/670 (24%)**	**0·68 (0·53–0·87)**

N+AVD vs A+AVD

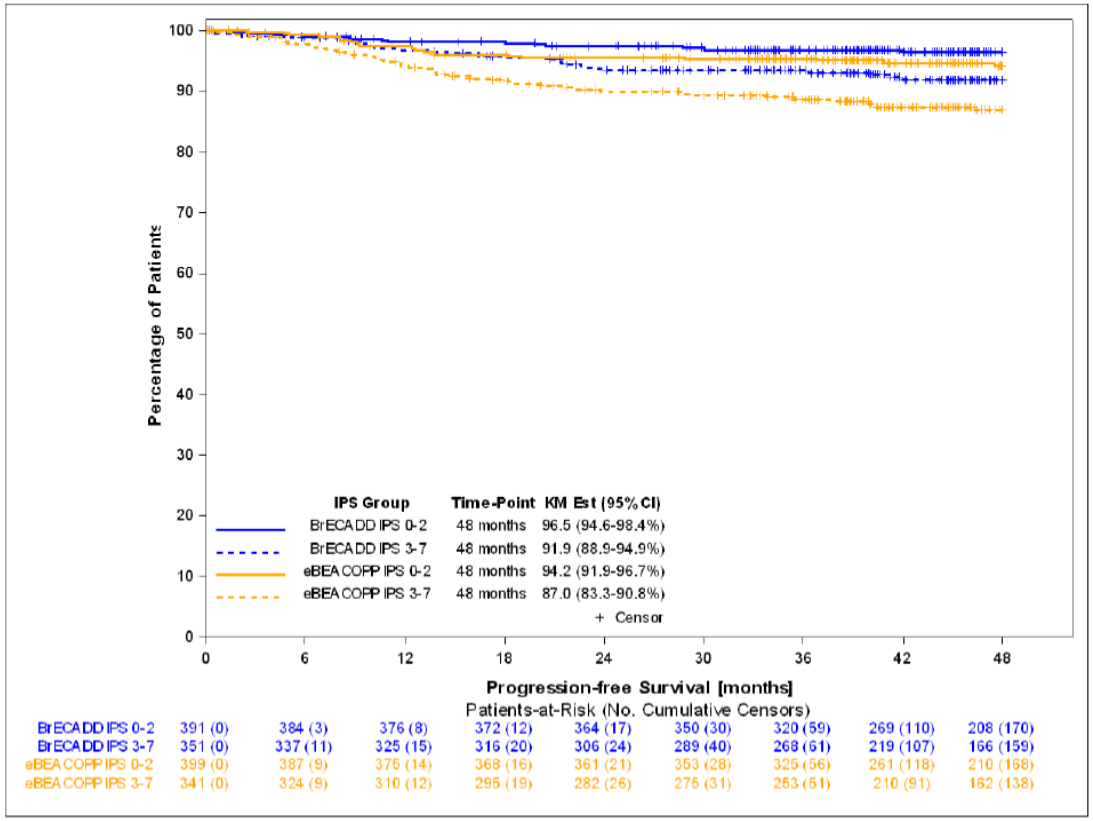


Subgroup	N+AVD	BV+AVD	Hazard Ratio for Disease Progression or Death (95% CI)
	no. of events/total no. (%)		
Age			
12–17 yr	7/118 (5.9)	21/118 (17.8)	0.31 (0.13–0.74)
18–60 yr	27/321 (8.4)	43/318 (13.5)	0.59 (0.36–0.95)
>60 yr	7/48 (14.6)	17/47 (36.2)	0.30 (0.12–0.72)
IPS risk group			
0–3	24/332 (7.2)	48/328 (14.6)	0.46 (0.28–0.76)
4–7	17/155 (11.0)	33/155 (21.3)	0.46 (0.26–0.83)
Stage			
III	12/185 (6.5)	22/168 (13.1)	0.45 (0.22–0.92)
IV	29/302 (9.6)	59/315 (18.7)	0.48 (0.31–0.74)
Symptoms			
B	29/288 (10.1)	54/273 (19.8)	0.47 (0.30–0.74)
A	12/199 (6.0)	27/210 (12.9)	0.44 (0.22–0.86)

Straus DJ. *Lancet Haematol*, 2021; 8: e410-e421 — Herrera AF. *N Engl J Med*, 2024; 391: 1379-1389

Significance of IPS7 in contemporary randomized clinical trials with new drugs (2)

BrECADD vs eBEACOPP



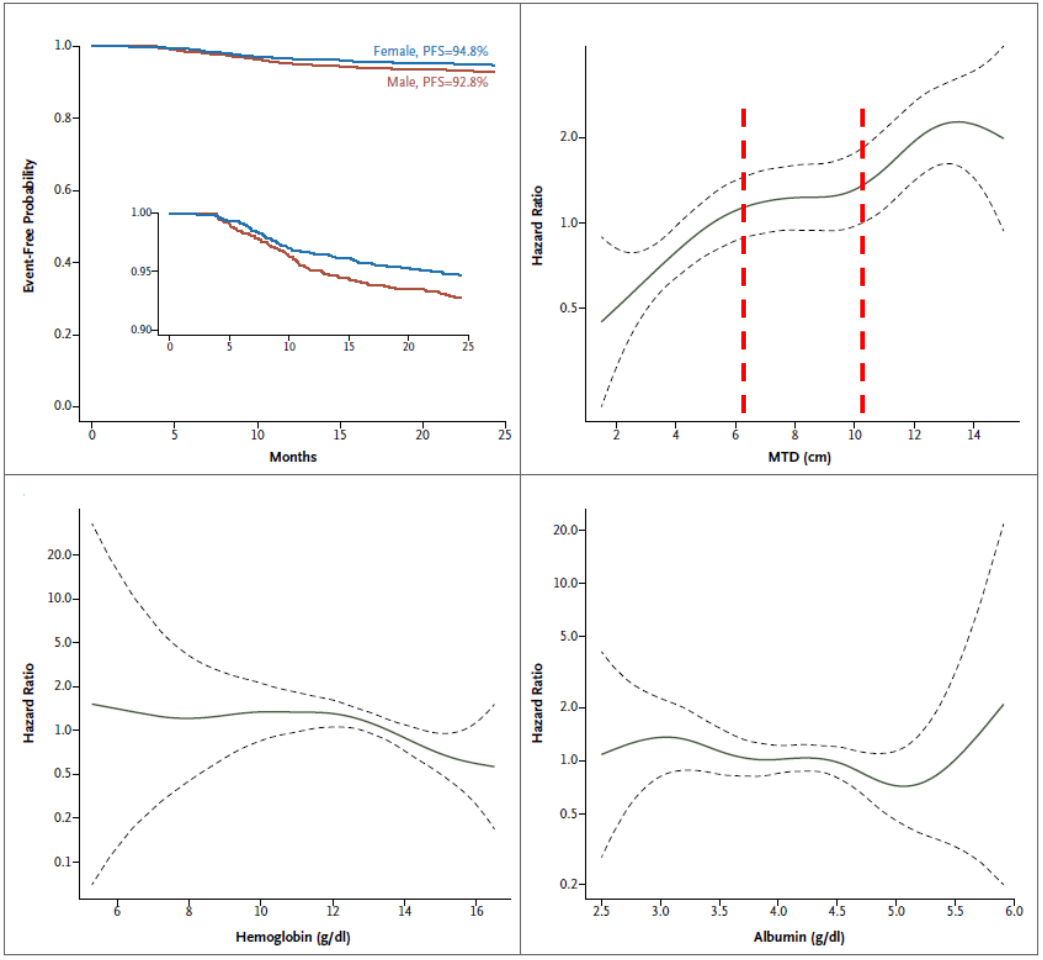
Borchmann P. *Lancet*, 2024; 404: 341-352

Shaping treatment according to risk factors and stage in Hodgkin lymphoma

Category	Features	Approach
Early-stage favorable	Stage I-II with no risk factors	ABVD x 2 + 20 Gy IFRT (non PET-adapted)[4] ABVD x 2 + 20 Gy IFRT (PET-adapted)[5] ABVD x 3 + 30 Gy IFRT (PET-adapted)[6]
Early-stage unfavorable	Stage I-II with risk factors[1-3] • Age ≥ 50 years (*) • Large mediastinal mass • B symptoms • ≥ 3 involved lymph node areas • Elevated ESR • Extranodal involvement	ABVD x 4 + 30 Gy IFRT (PET-adapted)[6] ABVD x 6 (PET-adapted)[6] ABVD x 2 → AVD x 4 (PET-adapted)[7]
Advanced stage	Stage II B with risk factors Stage III-IV	ABVD x 2 → AVD x 4 (PET2 negative)[7] ABVD x 2 → BEACOPP (PET2 positive)[8,9] A-AVD x 6 (non PET-guided)[10] N-AVD, BrECADD (non PET-guided)[11,12]

(*) EORTC only

1. Tubiana M. *Cancer Res*, 1971; 31: 1801-1810 — 2. Tubiana M. *Natl Cancer Inst Monogr*, 1973; 36: 513-530 — 3. Tubiana M. *Int J Radiat Oncol Biol Phys*, 1985; 11: 23-30
4. Engert A. *N Engl J Med*, 2010; 363: 640-652 — 5. Fuchs M. *J Clin Oncol*, 2019; 37: 2835-2845 — 6. Federico M. *J Clin Oncol*, 2024; 42: 19-25
7. Johnson P. *N Engl J Med*, 2016; 374: 2419-2429 — 8. Press OW. *J Clin Oncol*, 2016; 34: 2020-2027 — 9. Gallamini A. *J Clin Oncol*, 2018; 36: 454-462
10. Ansell SM. *N Engl J Med*, 2022; 387: 310-320 — 11. Herrera AF. *N Engl J Med*, 2024; 391: 1379-1389 — 12. Borchmann P. *Lancet*, 2024; 404: 341-352



An Individualized Prediction Model for Early-Stage Classic Hodgkin's Lymphoma

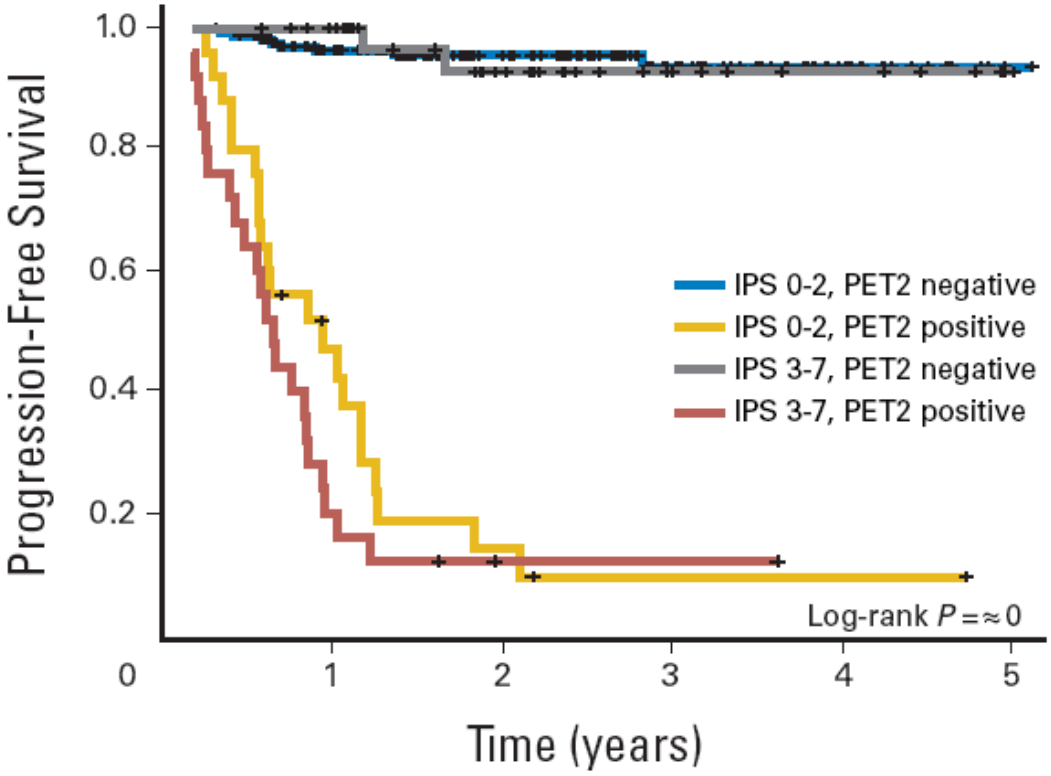
PFS-related variables

	Development (N=3000)	Validation 1 (N=1488)	Validation 2 (N=872)
Age (years), mean (SD)	34 (12)	34 (12)	38 (14)
Female sex	51%	53%	46%
Stage			
Stage I	23%	14%	25%
Stage IIA	55%	60%	46%
Stage IIB	22%	26%	30%
MTD, mean (SD)	6.5 (3.5)	6.5 (3.3)	5.3 (2.8)
Hemoglobin (g/dL), mean (SD)	13.0 (1.6)	13.1 (1.6)	13.4 (1.8)
Albumin (g/dL), mean (SD)	4.2 (0.5)	4.0 (0.5)	4.1 (0.5)
2-year PFS (KM)	93.7%	90.3%	91.6%

3,000 patients from 4 seminal early-stage trials with accrual from 1996 to 2011; two model validation cohorts with 2,360 patients from 5 cancer registries, diagnosed between 1996 and 2019 (treated with curative intent and outside clinical trials).

Rodday AM. *NEJM Evid*, 2025; 4: EVIDoa2500115

Predictive role of PET2 in Hodgkin lymphoma and its superiority to IPS7



	All	95% confidence level
All	260	---
True positive	33	---
True negative	203	---
False positive	12	---
False negative	12	---
Positive predictive value	0.73	0.68-0.79
Negative predictive value	0.94	0.92-0.97
Sensitivity	0.73	0.68-0.79
Specificity	0.94	0.92-0.97
Accuracy	0.91	0.87-0.94

Gallamini A. *J Clin Oncol*, 2007; 25: 3746-3752 — Gallamini A. *Haematologica*, 2014; 99: 1107-1113

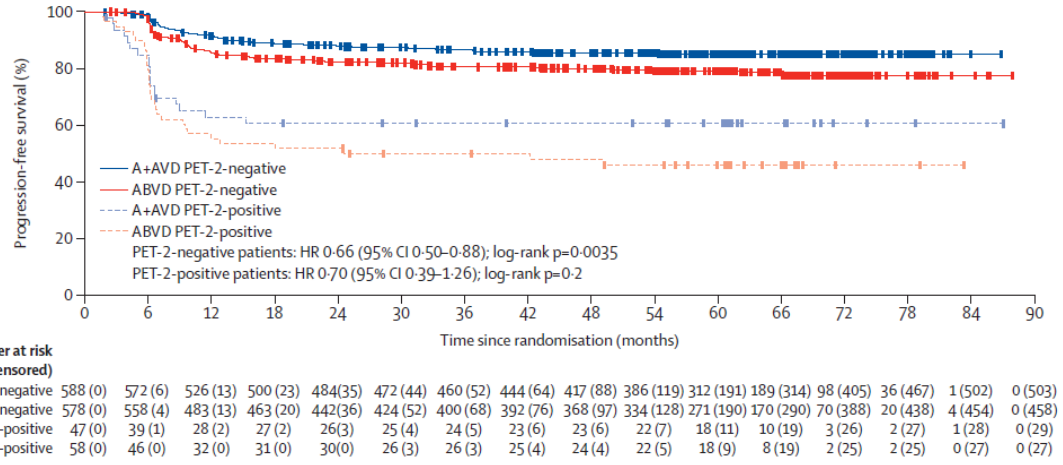
PET2-adapted treatment design in 4 clinical trials

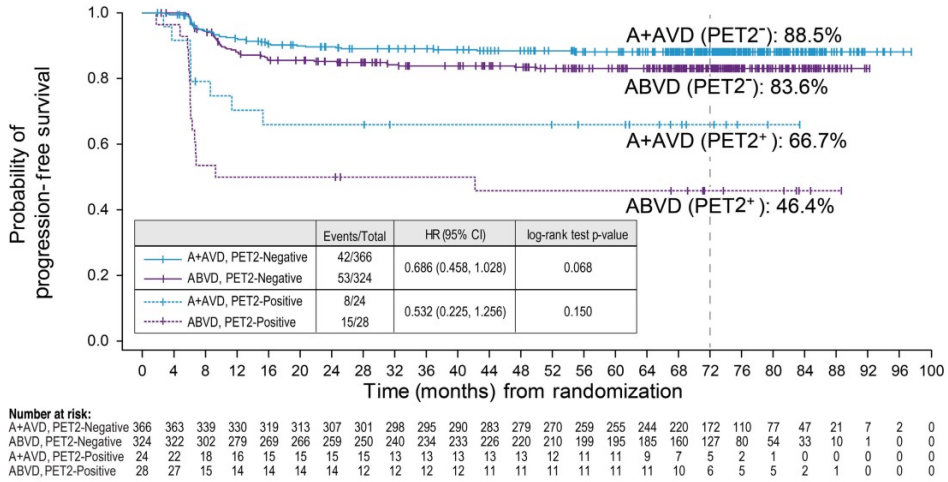
Study	Pts.	Clinical data	PET (+2) positive	Intensification (adherence)	Final PET neg	PFS	Toxicity (gr. 3-4)
Johnson[1] (2016)	1135	Age: 32 yrs Bulky: 33% B sympt: 61% Stage III-IV: 59%	16% (Deauville)	BEACOPP (95%)	74%	68% (3 yrs) [85% A(B)VD] Δ = 17%	Hematol: 72% Infections: 37%
Press[2] (2016)	331	Age: 32 yrs Bulky: 18% B sympt: 62% Stage III-IV: 100%	18% (Deauville)	BEACOPP (92%)	55%	64% (2 yrs) [82% ABVD] Δ = 18%	Hematol: NR Infections: 42%
Zinzani[3] (2016)	512	Age: 33 yrs Bulky: 35% B sympt: 64% Stage III-IV: 81%	20% (Juweid)	HDT HSCT (79%)	72%	74% (2 yrs) [81% ABVD] Δ = 7%	Hematol: 72% Infections: 16%
Gallamini[4] (2018)	780	age: 31 yrs Bulky: 58% B sympt: 81% Stage III-IV: 64%	19% (Deauville)	BEACOPP (99%)	54%	60% (3 yrs) [87% ABVD] Δ = 27%	Hematol: 76% Infections: 10%

1. Johnson P. *N Engl J Med*, 2016; 374: 2419-2429 — 2. Press OW. *J Clin Oncol*, 2016; 34: 2020-2027
3. Zinzani PL. *J Clin Oncol*, 2016; 34: 1376-1385 — 4. Gallamini A. *J Clin Oncol*, 2018; 36: 454-462

Is PET2 still informative in frontline approaches with new drugs?

ECHELON-1 was <u>not a PET2-adapted trial</u>. Patients with positive PET2 (Deauville 4 and 5) continued on treatment according to randomization. Patients with Deauville 5 at PET2 could be switched to another off-protocol treatment (e.g. escalation).



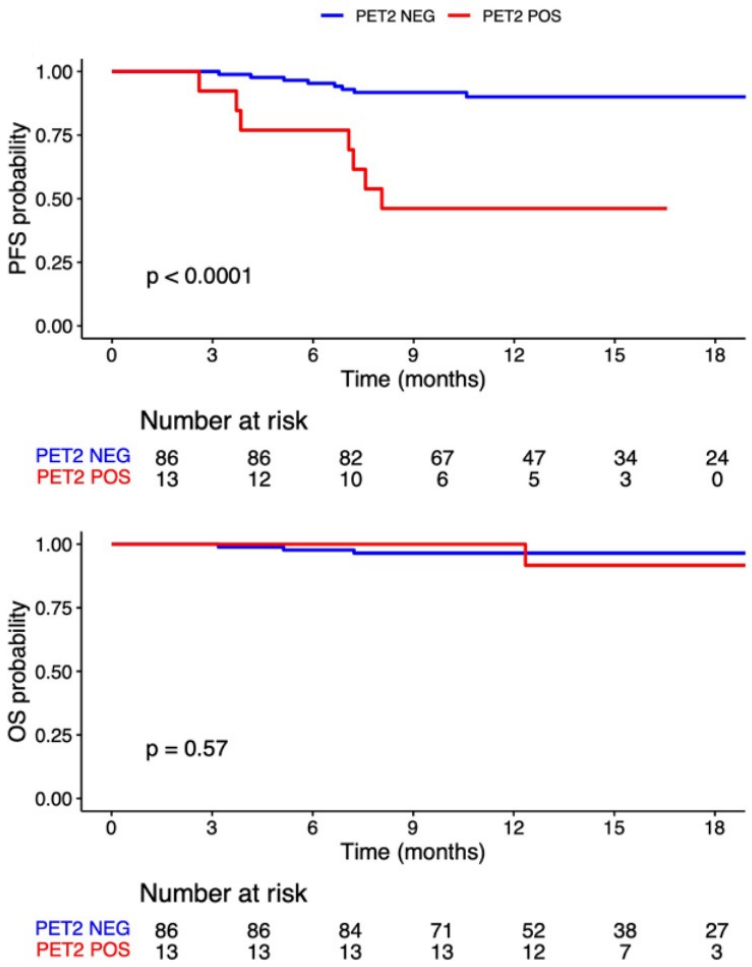


<u>All patients</u>	Deaths	Progression events	Death + Progression events
A-AVD PET2 negative	9/588 **(1.5%)**	76/588 **(12.9%)**	85/588 **(14.5%)**
ABVD PET2 negative	26/578 **(4.5%)**	94/578 **(16.3%)**	120/578 **(20.8%)**
A-AVD PET2 positive	0/47 **(0)**	18/47 **(38.3%)**	18/47 **(38.3%)**
ABVD PET2 positive	3/58 **(5.2%)**	28/58 **(48.3%)**	31/58 **(53.4%)**

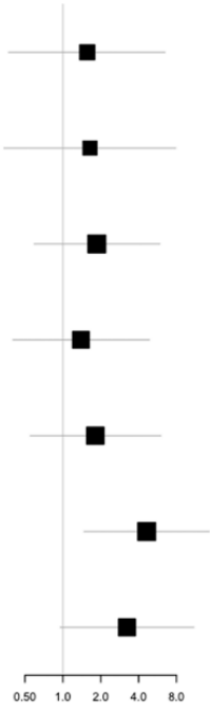
<u>Age 18-39</u>	Death + Progression events
A-AVD PET2 negative	42/366 **(11.5%)**
ABVD PET2 negative	53/324 **(16.4%)**
A-AVD PET2 positive	8/24 **(33.3%)**
ABVD PET2 positive	15/28 **(53.6%)**

Straus DJ. *Lancet Haematol*, 2021; 8: e410-e421 — Crosswell HE. *Haematologica*, 2024; 109: 982-987

Interim-PET predicts progression-free survival in stage IV Hodgkin lymphoma treated with upfront brentuximab vedotin-AVD



Variable	Comparison	HR	95% CI	p-value
Age	>65 vs <=65 years	1.56	0.37-6.49	0.542
B symptoms	Yes vs No	1.64	0.34-7.9	0.535
Extranodal involvement	>1 vs 0-1	1.86	0.59-5.91	0.293
Bulky	Yes vs No	1.39	0.4-4.88	0.607
Hasenclever score	>=4 vs <4	1.81	0.55-6.02	0.331
PET2 DS	Pos vs Neg	4.64	1.47-14.62	0.009 **
Treatment delay for neutropenia	Yes vs No	3.23	0.95-11	0.061

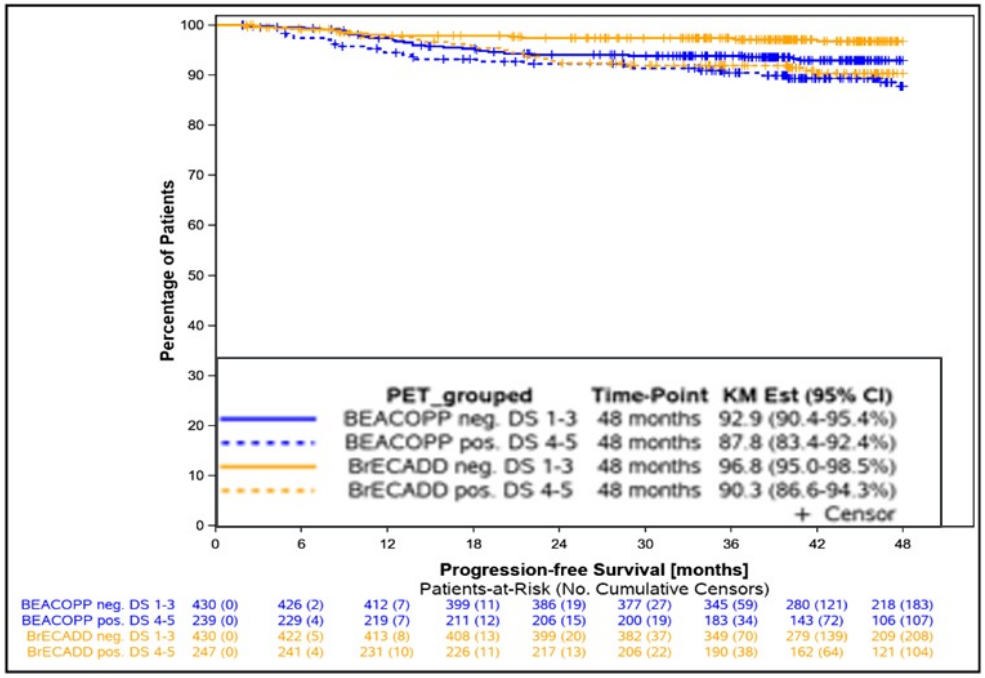


Rusconi C. *Leuk Lymphoma*, 2025; 66: 879-887

Is PET2 still informative in frontline approaches with new drugs?

HD21 (BrECADD vs eBEACOPP) is a PET2-adapted trial in which PET2-negative patients receive 2+2 cycles of either BrECADD or eBEACOPP according to randomization, whereas PET2-positive patients receive 2+4 cycles of therapy.

BrECADD vs eBEACOPP



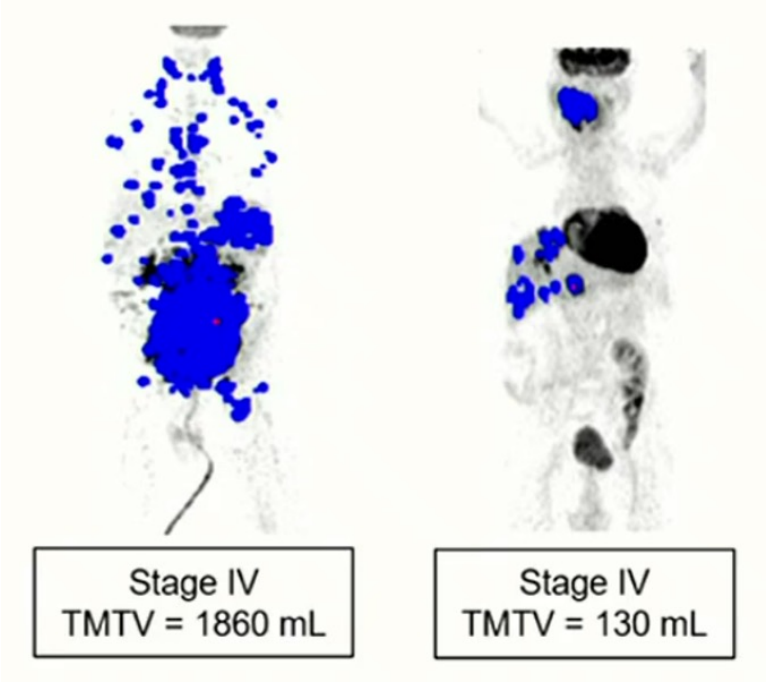
	BV-AVD	PET Adapted BrECADD	Nivo-AVD
Median f/u	**73 months**	**48 months**	25 months
PFS	83%	94.3%	92%
iPET neg	**85%**	**96.8%**	NA
iPET pos	**60.6%**	**90.3%**	NA
# cycles	6	**4-6**	6
OS	93.4%	98.6%	99%

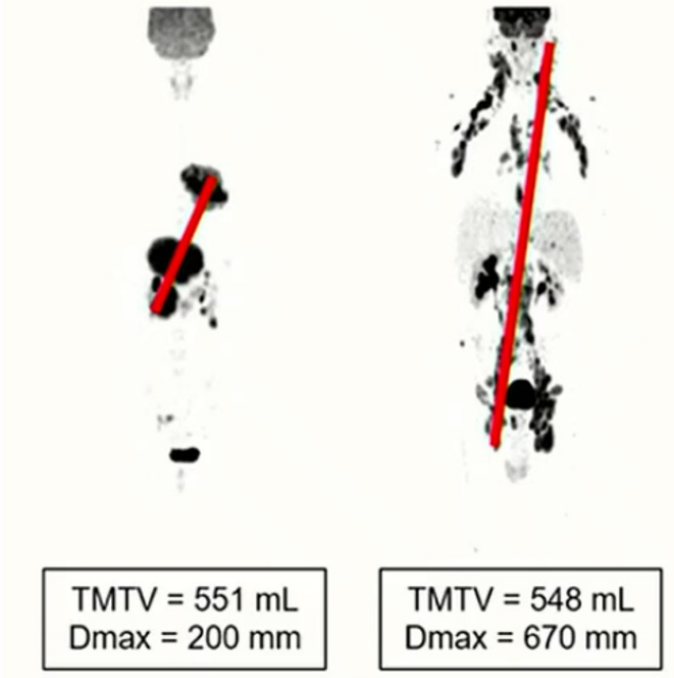
Borchmann P. *Lancet*, 2024; 404: 341-352 — Schroers-Martin JG. *Hematology Am Soc Hematol Educ Program*, 2024; 2024: 511-516

Prognostic parameters upon baseline PET scan

Baseline PET features could provide additional prognostic parameters in various lymphoma subtypes:

- tumor burden quantification: Total Metabolic Tumor Volume (TMTV);
- tumor dissemination: Distance maximum (Dmax) as the largest distance between two lesions.





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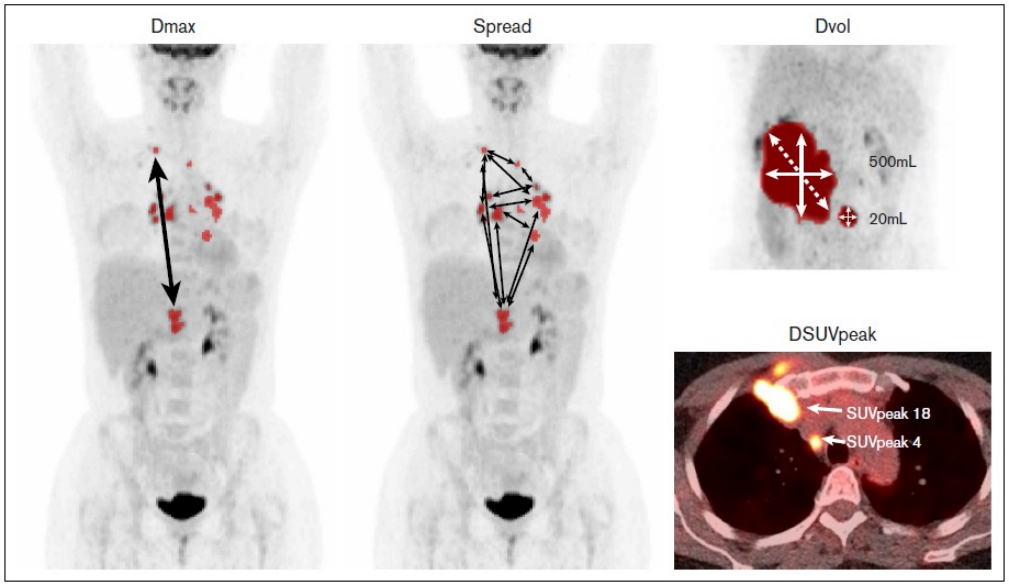
A radiomics glossary



Variable	Definition
MTV	Metabolic tumor volume; The FDG-avid tumor volume
TLG	Total lesion glycolysis; MTV multiplied by SUVmean
SUVmean	The mean SUV value of the VOI
SUVmax	The SUV of the voxel with the highest SUV within the VOI
SUVpeak	The SUV of the 3mL with the highest SUV within the VOI (global peak)
$TLR_{SUVmean}$	Tumor to liver ratio of the lesional SUVmean and the liver SUVmean
$TLR_{SUVpeak}$	Tumor to liver ratio of the lesional SUVpeak and the liver SUVmean
Number of lesions	The number of separated lesion selections within the VOI
Dmax	The maximum distance between two lesions
DmaxBulk	The maximum distance between the largest lesion and any other lesion
Spread	The sum of the distance between all lesions
SpreadBulk	The sum of the distance between the largest lesion and all other lesions
Dvol	The difference in volume between the largest and the smalles lesion
VolSpread	The sum of the differences in volume between all lesions
VolSpreadBulk	The sum of the differences in volume between the largest lesion and all other lesions
DSUVmax	The difference in SUVmax between the lesion with the highest SUVmax and the lesion with the lowest SUVmax
DSUVmaxSum	The sum of the differences in SUVmax of all lesions
DSUVmaxBulk	The differences in SUVmax between the largest lesion and all other lesions
DSUVmaxSumBulk	The sum of the differences in SUVmax between the largest lesion and all other lesions
DSUVmaxSumHot	The sum of the differences in SUVmax between the lesion with the highest SUVmax and all other lesions
DSUVpeak	The difference in SUVpeak between the lesion with the highest SUVpeakmax and the lesion with the lowest SUVpeak
DSUVpeakSum	The sum of the differences in SUVpeak of all lesions
DSUVpeakBulk	The differences in SUVpeak between the largest lesion and all other lesions
DSUVpeakSumBulk	The sum of the differences in SUVpeak between the largest lesion and all other lesions
DSUVpeakSumHot	The sum of the differences in SUVpeak between the lesion with the highest SUVpeak and all other lesions

Driessen J. *Blood Adv*, 2023; 7: 6732-6743

Prognostic value of baseline metabolic tumor volume in early-stage Hodgkin lymphoma in the standard arm of the H10 trial

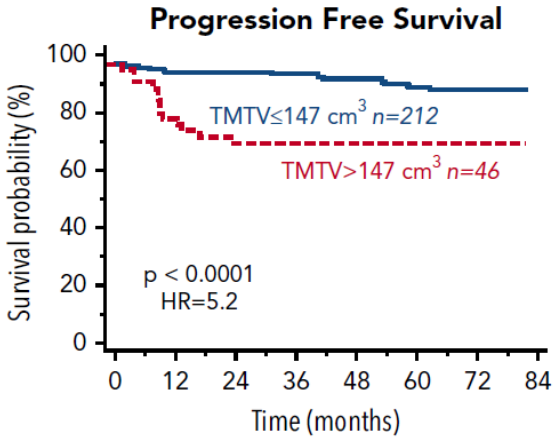
Characteristics	Total population (N = 258)	Low TB TMTV ≤147 cm³ (n = 212)	High TB TMTV >147 cm³ (n = 46)	P
Median age (range), y	31 (15-71)	32 (15-71)	27 (17-63)	.009
Age ≥50 y (%)	34 (13)	31 (15)	3 (7)	.22
Male, n (%)	129 (50)	104 (49)	25 (54)	.62
Nodular sclerosis histology n (%)	207 (80)*	168 (79)	37 (80)	.68
Ann Arbor stage II, n (%)	198 (77)	157 (74)	41 (89)	.03
B symptoms, n (%)	85 (33)	60 (28)	25 (54)	.001
Median ESR (interquartile range), mm/h	26	23 (12-50)	49 (26-72)	.0001
≥4 Involved sites, n (%)	28 (11)	17 (8)	11 (24)	.004
Bulk mediastinum (M/T ≥ 0.35), n (%)	62 (24)	34 (16)	29 (63)	<.0001
U EORTC, n (%)	157 (61)	117 (55)	40 (87)	.0001
U GSHG, n (%)	177 (69)	133 (63)	44 (96)	<.0001
U NCCN, n (%)	164 (64)	121 (57)	43 (93)	<.0001
Positive iPET2 (DS 4-5), n (%)	21 (8)	13 (6)	8 (17)	.028

M/T, mass/thoracic ratio.

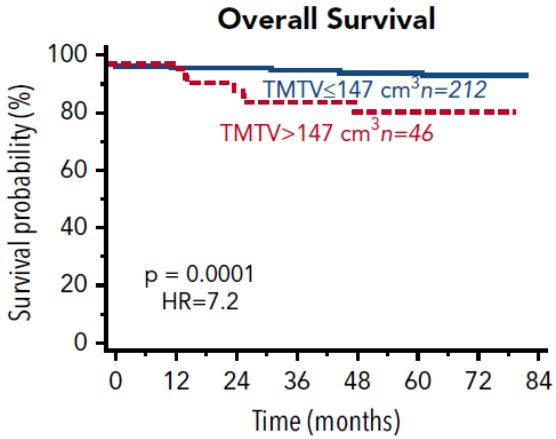
*Data not available for 2 patients.

Cottereau AS. *Blood*, 2018; 131: 1456-1463

Prognostic value of baseline metabolic tumor volume in early-stage Hodgkin lymphoma in the standard arm of the H10 trial



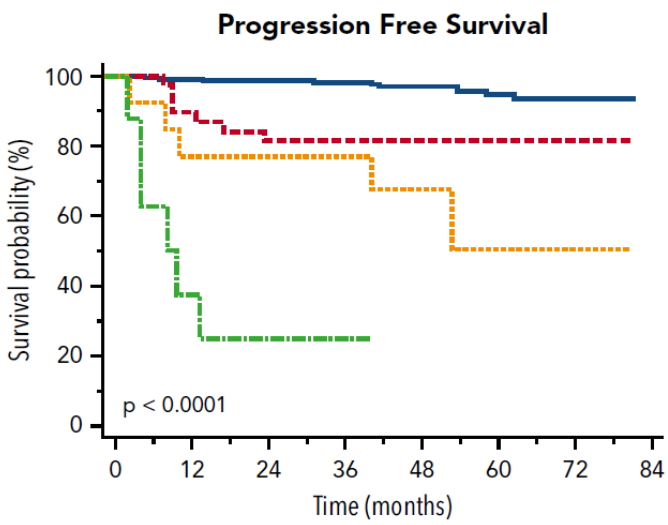
	Events	censored	5y PFS (95% CI) months	Log-rank p value
TMTV≤147cm^3(n=212)	14 (7%)	198 (93%)	92 % (90-94)	
TMTV>147cm^3(n=46)	13 (28%)	33 (72%)	71 % (65-77)	< 0.0001

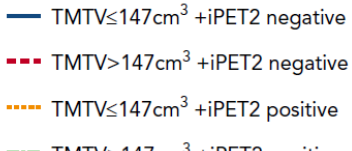


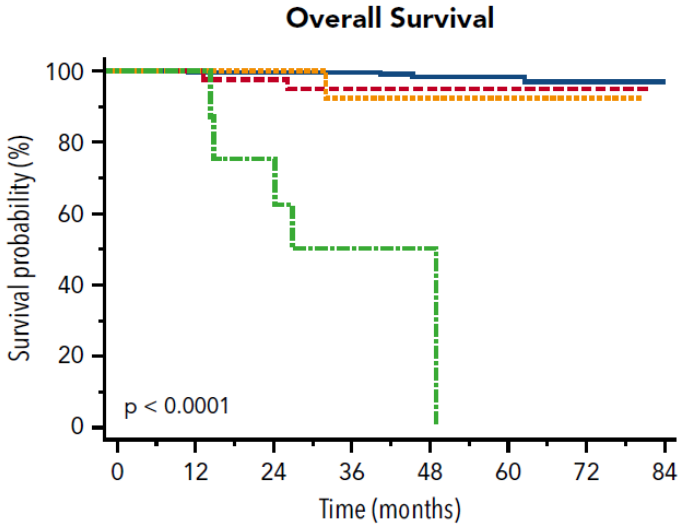
	Events	censored	5y PFS (95% CI) months	Log-rank p value
TMTV≤147cm^3 (n=212)	5 (2%)	207 (98%)	98 % (97-99)	
TMTV>147cm^3 (n=46)	7 (15%)	39 (85%)	83 % (77-89)	= 0.0001

Cottereau AS. *Blood*, 2018; 131: 1456-1463

Prognostic value of baseline metabolic tumor volume in early-stage Hodgkin lymphoma in the standard arm of the H10 trial







Number at risk

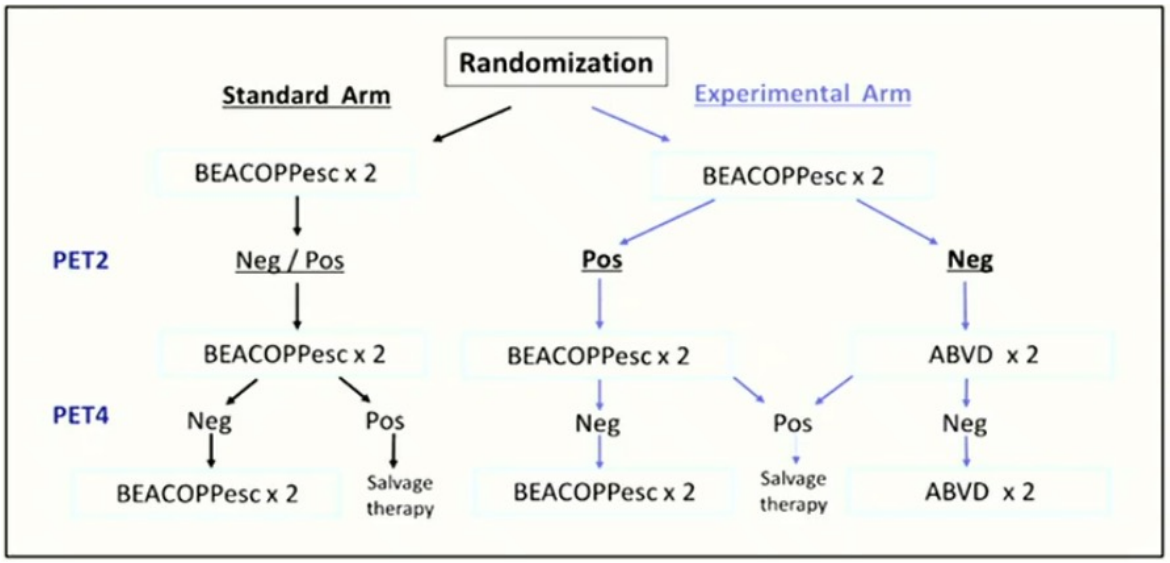
TMTV≤147cm^3 +iPET2 negative	199	195	193	178	137	79	14	0
TMTV>147cm^3 +iPET2 negative	38	34	31	27	17	13	4	0
TMTV≤147cm^3 +iPET2 positive	13	10	10	9	7	2	1	0
TMTV>147cm^3 +iPET2 positive	8	3	2	2	0	0	0	0

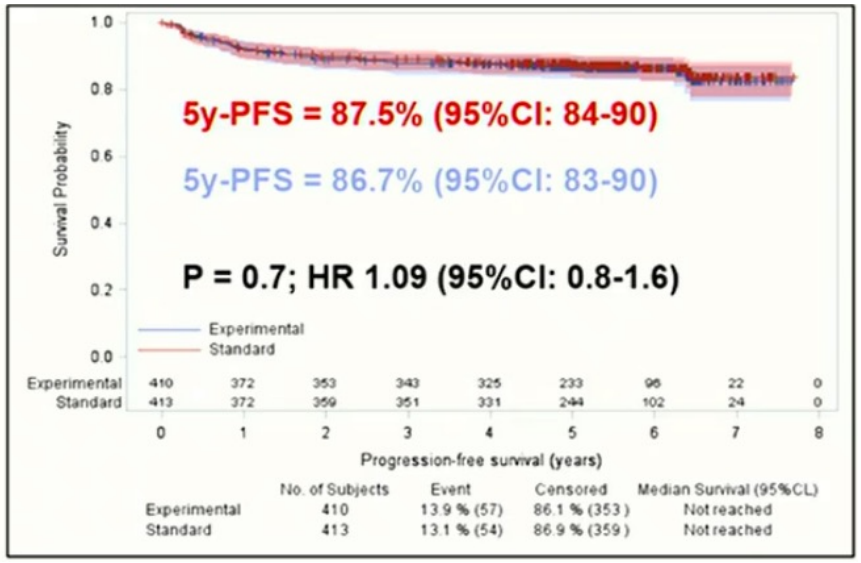
Number at risk

TMTV≤147cm^3 +iPET2 negative	199	196	195	181	139	82	16	1
TMTV>147cm^3 +iPET2 negative	38	38	37	32	20	16	6	0
TMTV≤147cm^3 +iPET2 positive	13	13	13	11	9	3	1	0
TMTV>147cm^3 +iPET2 positive	8	8	6	4	1	0	0	0

Cottereau AS. *Blood*, 2018; 131: 1456-1463

PROGNOSTIC VALUE OF BASELINE TOTAL METABOLIC TUMOR VOLUME (TMTV) AND TUMOR SPREAD (Dmax) IN ADVANCED HODGKIN LYMPHOMA: ANCILLARY STUDY OF THE AHL2011 TRIAL





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PROGNOSTIC VALUE OF BASELINE TOTAL METABOLIC TUMOR VOLUME (TMTV) AND TUMOR SPREAD (Dmax) IN ADVANCED HODGKIN LYMPHOMA: ANCILLARY STUDY OF THE AHL2011 TRIAL

	Median (IQR)	Cutoff	% patients (out of the 721 pts)
TMTV (mL)	210 (123-390)	220	**48%** with high TMTV (≥220)
Dmax (mm^{-1})	220 (160-335)	325	**26%** with high Dmax (≥325)

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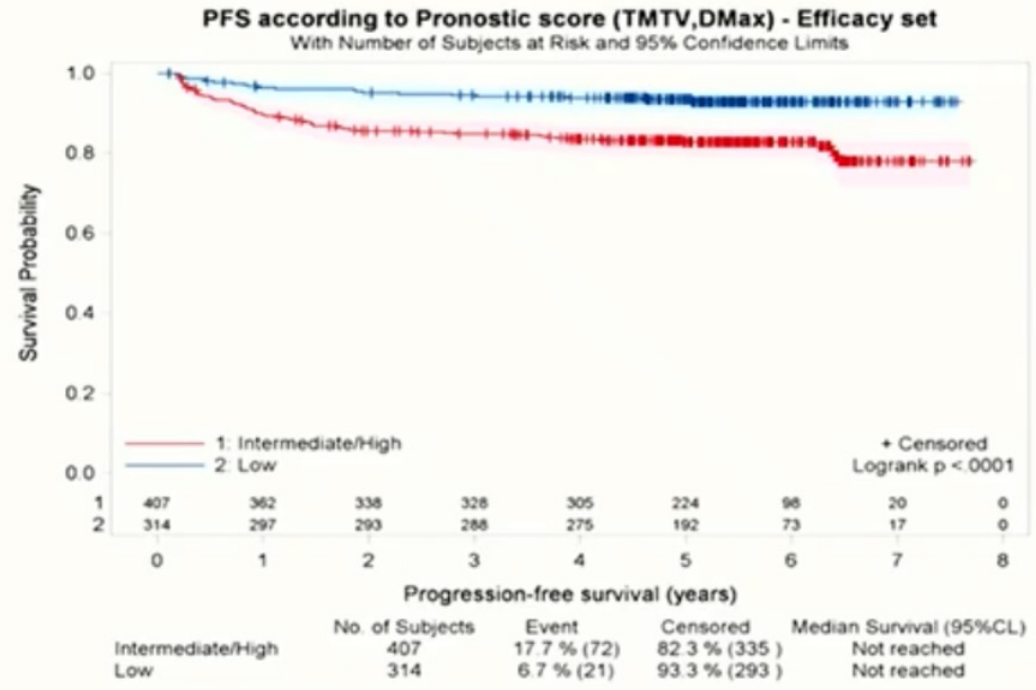
PROGNOSTIC VALUE OF BASELINE TOTAL METABOLIC TUMOR VOLUME (TMTV) AND TUMOR SPREAD (Dmax) IN ADVANCED HODGKIN LYMPHOMA: ANCILLARY STUDY OF THE AHL2011 TRIAL

Two subgroups of patients are identifyable:

- **patients with low TMTV and low Dmax**;
- **patients with either high TMTV and/or high Dmax**.



5-year PFS: 92% vs 83.4%,
HR=2.2 [95%CI: 1.4-3.6],
p<0.001

Kanoun S. *Hematol Oncol (18 ICML meeting abstracts)*, 2025; 43(S3): e70093

PROGNOSTIC VALUE OF BASELINE TOTAL METABOLIC TUMOR VOLUME (TMTV) AND TUMOR SPREAD (Dmax) IN ADVANCED HODGKIN LYMPHOMA: ANCILLARY STUDY OF THE AHL2011 TRIAL

	TMTV		Dmax	
	Low TMTV (<220mL)	High TMTV (≥220mL)	Low Dmax (<325mm^{-1})	High Dmax (≥325mm^{-1})
PET2 positive*	**10% (n=37)**	**16% (n=57)**	**11% (n=58)**	**19% (n=36)**
PET2 negative*	90% (n=337)	84% (n=290)	89% (n=473)	81% (n=154)
P-value (Fisher exact test)	0.011		0.008	

*In AHL trial, PET2 evaluations were centrally reviewed and interpreted using modified Deauville score (partial response if residual uptake > 140% liver background)

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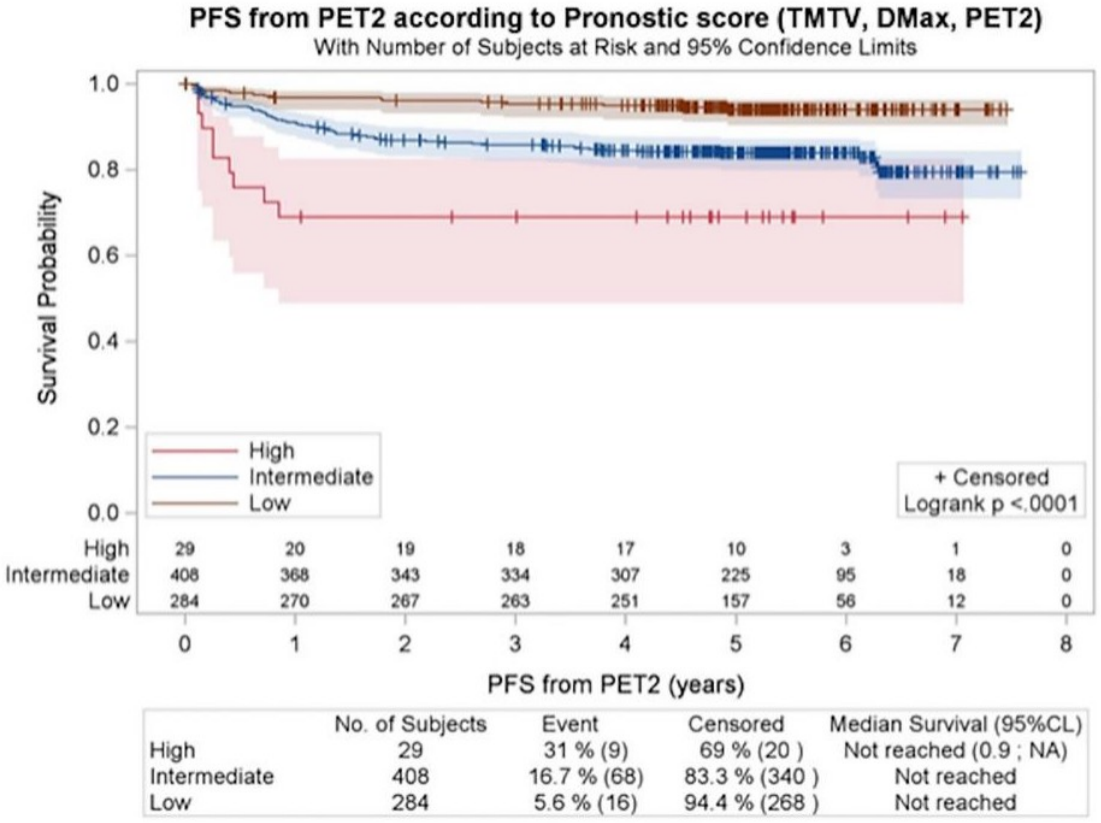
PROGNOSTIC VALUE OF BASELINE TOTAL METABOLIC TUMOR VOLUME (TMTV) AND TUMOR SPREAD (Dmax) IN ADVANCED HODGKIN LYMPHOMA: ANCILLARY STUDY OF THE AHL2011 TRIAL



	No. of Subjects	Event	Censored	Median Survival (95%CL)
High	29	31 % (9)	69 % (20)	Not reached (0.9 ; NA)
Intermediate	408	16.7 % (68)	83.3 % (340)	Not reached
Low	284	5.6 % (16)	94.4 % (268)	Not reached

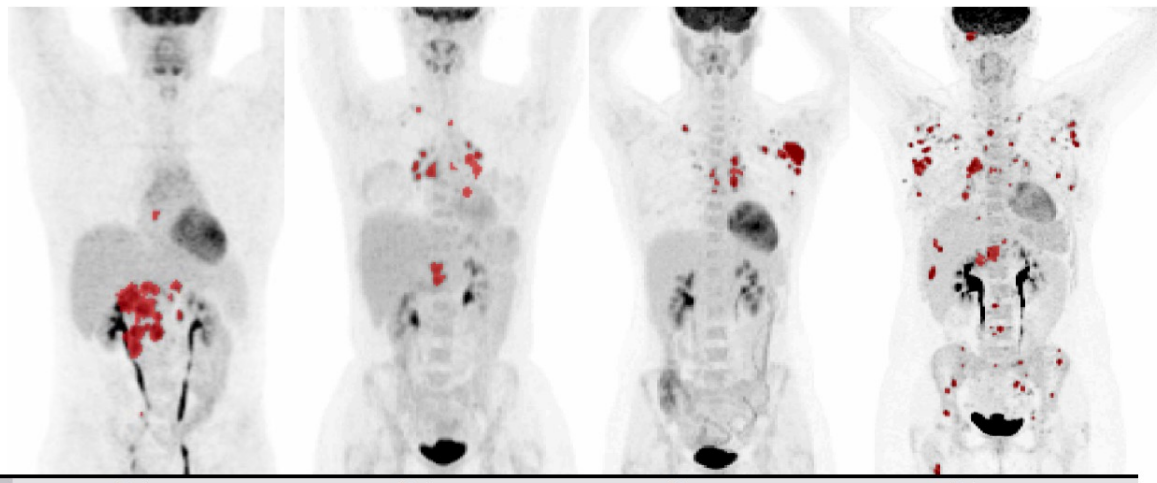
	No of pts (%)	5-year PFS	PFS event rate
0 risk factor	284 (39%)	94%	6%
1 or 2 risk factors	408 (57%)	84%	17%
3 risk factors	29 (4%)	69%	31%

Kanoun S. *Hematol Oncol (18 ICML meeting abstracts)*, 2025; 43(S3): e70093

Prognostic model using ^{18}F-FDG PET radiomics predicts progression-free survival in relapsed/refractory Hodgkin lymphoma

	Training (n = 113)		Validation (n = 69)		Total (n = 182)		
	No.	%	No.	%	No.	%	*P* value
Study							<.001
BV-DHAP	58	51	0	0	58	32	
BV-ICE	55	49	0	0	55	30	
ICE-GVD	0	0	69	100	69	38	
Female sex	61	54	32	46	93	51	.319
Median age, (range)	30 (13-65)		34 (18-66)		31 (13-66)		.175
Primary refractory	55	50	25	37	80	45	.062
Ann Arbor stage							.002
I	10	9	1	1	11	6	.042
II	46	41	43	62	89	49	.004
III	19	17	2	3	21	12	.004
IV	38	34	23	33	61	34	.970
Extranodal disease	44	39	25	36	69	38	.715
B symptoms	28	25	7	10	35	20	.011

-2.472 – [2.478 * (Relapsed=1, refractory=0)] + [1.010 * (B symptoms = 1, no B symptoms =0)] – [0.384 * log(MTV in uL)] + [0.413 * log(Spread)] + [2.409 * log(SUVmean/liverSUVmean)].

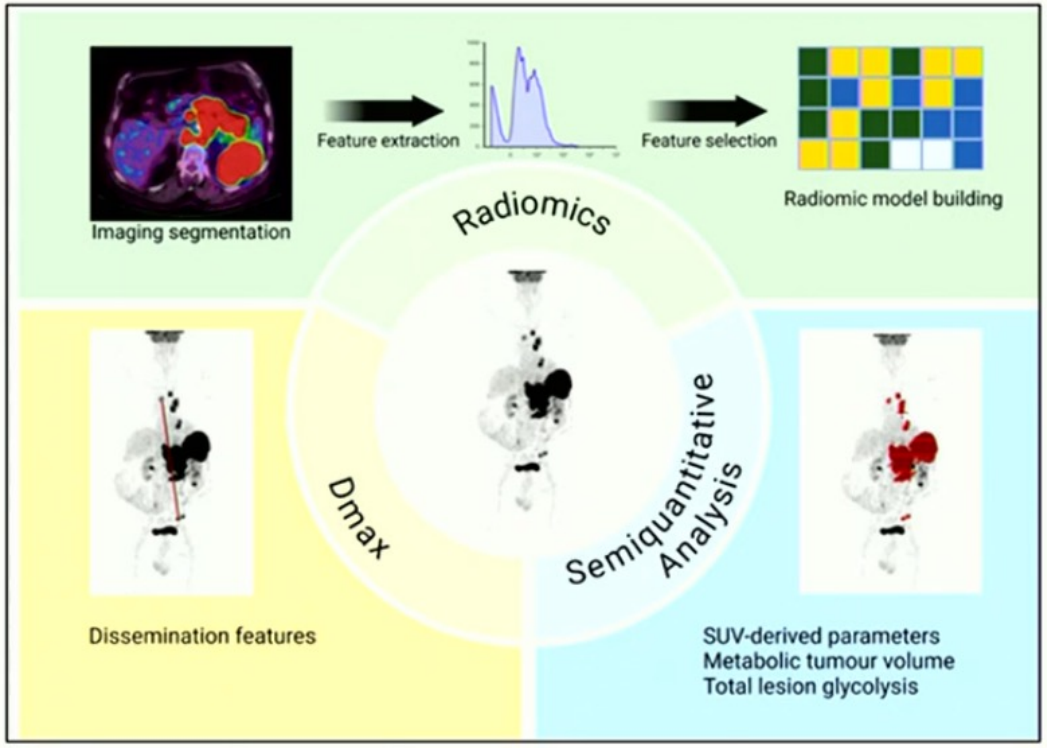


	A	B	C	D
R/R status	Relapse	Relapse	Refractory	Relapse
B symptoms	No	No	Yes	No
Stage	IV	III	IV	IV
$TLR_{SUVmean}$	3.06	2.43	4.59	4.48
MTV (mL)	81.6	11.0	23.9	47.3
Spread (cm)	194	411	677	39576
Model score	**0.03**	**0.05**	**0.88**	**0.46**
Outcome	**No PD**	**No PD**	**PD 3m after ASCT**	**PD 12m after ASCT**

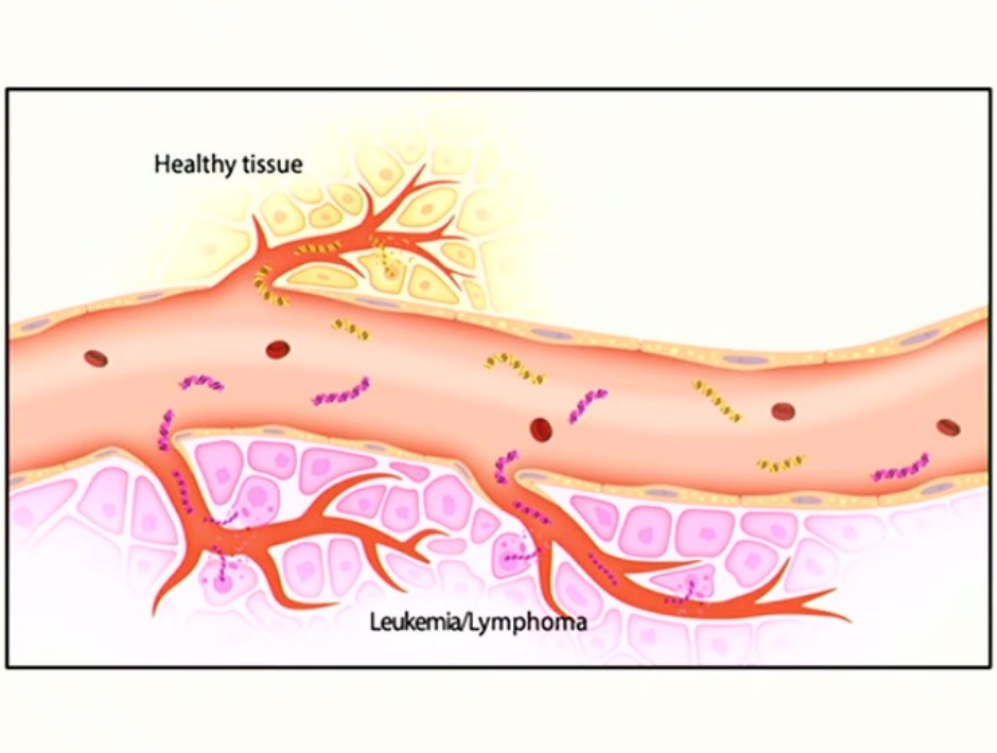
Ann Arbor stage: not part of the final model as outperformed by spread.
TLR: tumor to liver ratio.

Driessen J. *Blood Adv*, 2023; 7: 6732-6743

PET parameters



Circulating tumor DNA (ctDNA)



Prognostication for early- and advanced-stage Hodgkin lymphoma… What's new?

- Prognostic models built upon continuous variables better stratify patients according to risk in both advanced- and early-stage disease.
- These models are complex, but can be easily applied at bedside by using tools available online.
- Models based on binary cutoffs are nowadays outdated and reduce their performance in the era of new drugs (e.g. brentuximab vedotin, checkpoint inhibitors) used frontline.
- *Interim* PET scan maintains its value if PET-adapted strategies are adopted (e.g. stage IIB, III), although its predictive value may be questioned when new drugs are applied frontline.
- New PET parameters (*radiomics*) evaluated at baseline may offer new prognostic interpretations and emerge as novel predictive factors, both in treatment naïve and relapsed/refractory patients.