

4<sup>th</sup> edition

# Unmet challenges in high risk hematological malignancies: from bedside to clinical practice

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Starhotels Majestic

*Scientific board:*

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**Minimizing toxicity and preserving efficacy in early-stage  
Hodgkin lymphoma  
- the chemoimmunotherapy perspective**

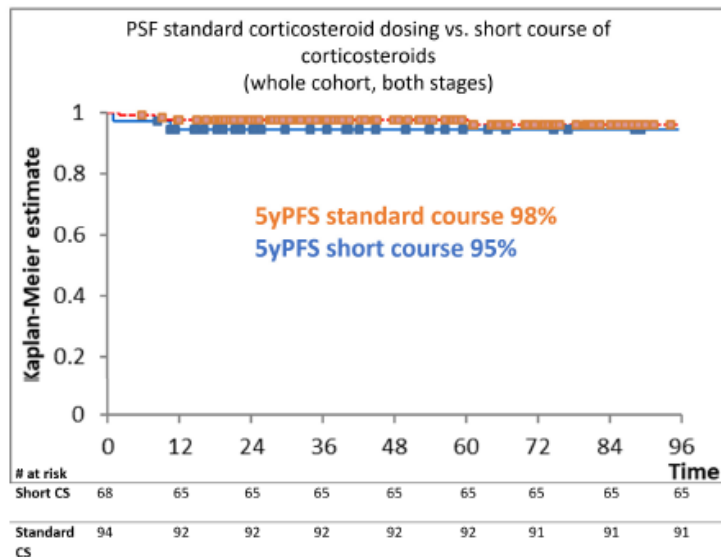
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# Affiliations & Conflict of Interest Disclosure

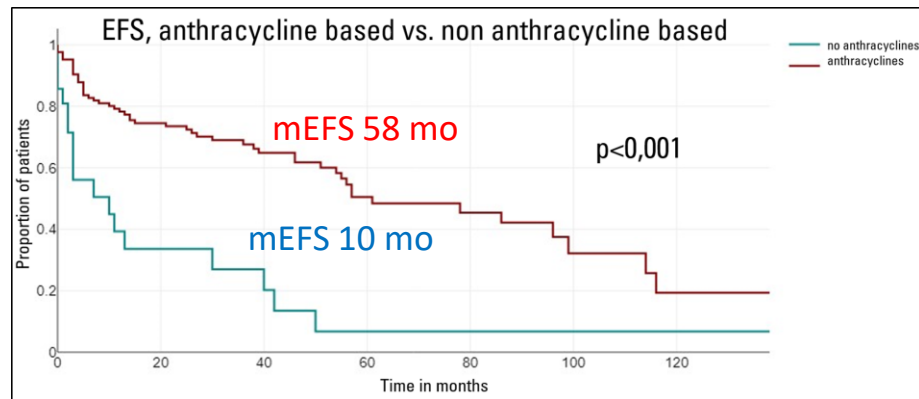


- Roche
- Abbvie
- Takeda
- Johnson & Johnson
- Astra-Zeneca
- BeOne
- Eli Lilly
- Sobi
- Novartis / Sandoz
- Pfizer
- Swixx

## Younger and fit



## Elderly and unfit



## Younger and fit

Table 3. Early and late toxicities (whole cohort, osteoarticular events excluded).

Emergency Hospitalization during Front Line Treatment	Short Course Corticosteroids	Standard Course Corticosteroids	p Value
	% (No/Total)	% (No/Total)	
Hospitalization (for any reason)	53 (33/68)	46 (43/94)	0.75
Febrile neutropenia	43 (29/68)	38 (36/94)	0.62
Treatment related death	0	2% (2/94)	/
<b>Late effects</b>			
Secondary neoplasms	4 (3/68)	2 (2/94)	0.65

Table 4. Osteoarticular adverse events.

Duration of Corticosteroid Treatment	Patient Designation	Description of Events	CTCAE Grade	Comment
short	Pt No 19	femoroacetabular impingement, osteitis pubis, sacroileitis, ischiofemoral collision	3	affecting every-day living and limiting self-care
	Pt No 20	Mb Freiberg	3	right foot
	Pt No 68	periarthritis humeroscapularis	2	right sided; had right supraclavicular lymphadenopathy at diagnosis
standard	Pt No 78	coxarthrosis	2	bilateral
	Pt No 111	AVN	3	hip, right
	Pt No 112	humeroscapular arthrosis	2	bilateral, dominantly left, initially had lymphadenopathy in left neck regions
	Pt No 141	tendinitis humeroscapularis; osteoporosis with pathological fractures	3	right hand side, initial lymphadenopathy on both sides of neck
	Pt No 142	AVN	3	hips, bilateral
	Pt No 143	periarthritis humeroscapularis	2	bilateral, had mediastinal irradiation

Abbreviations: Pt = patient; AVN = avascular hip necrosis; CTCAE = Common Terminology Criteria for Adverse Events.

## Elderly and unfit

Toxicities	No Pts/%
Hospitalization	45/126 (36%)
due to FN	20/109 (18%)
due to any kind of infection	29/109 (27%)
other acute toxicities	21/107 (20%)
Neutropaenia grade III-IV	65/129 (50%)
Anaemia grade III-IV	15/125 (50%)
Thrombocytopaenia grade III-IV	5/124 (4%)
<b>Other reported AEs of interest</b>	<b>No Pts</b>
Cardiac toxicity (i.e. acute event or worsening of previous condition, CTCAE grade III/IV)	12
Bleomycin lung toxicity	9
Nuropathy, any grade	18 (of 135)
Secondary malignancies	10 (in 8 Pts)
<b>Treatment related death</b>	<b>17 (11.7%)</b>

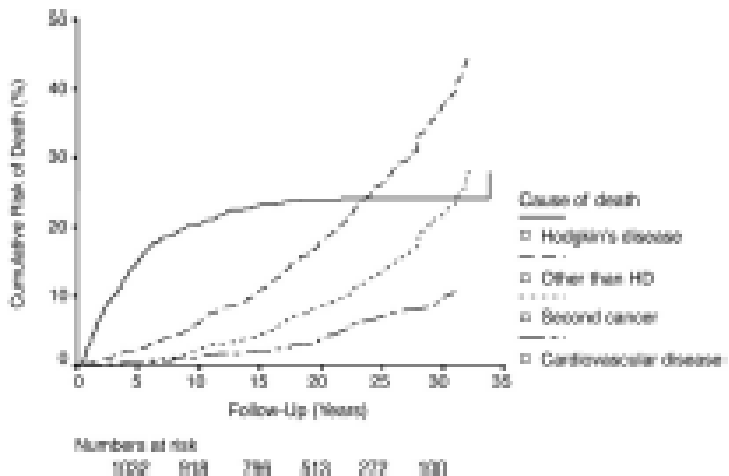


Fig 1. The actuarial risks of death from major disease categories. HD, Hodgkin's disease.

- secondary cancers
- heart disease
- infertility
- aseptic hip necroses
- thyroid disease
- chronic fatigue
- ...

Salvage treatment

Radiotherapy

Doxorubicin

Cyclophosphamide

Procarbazine

Bleomycin

Brentuximab vedotin , vinca alkaloids

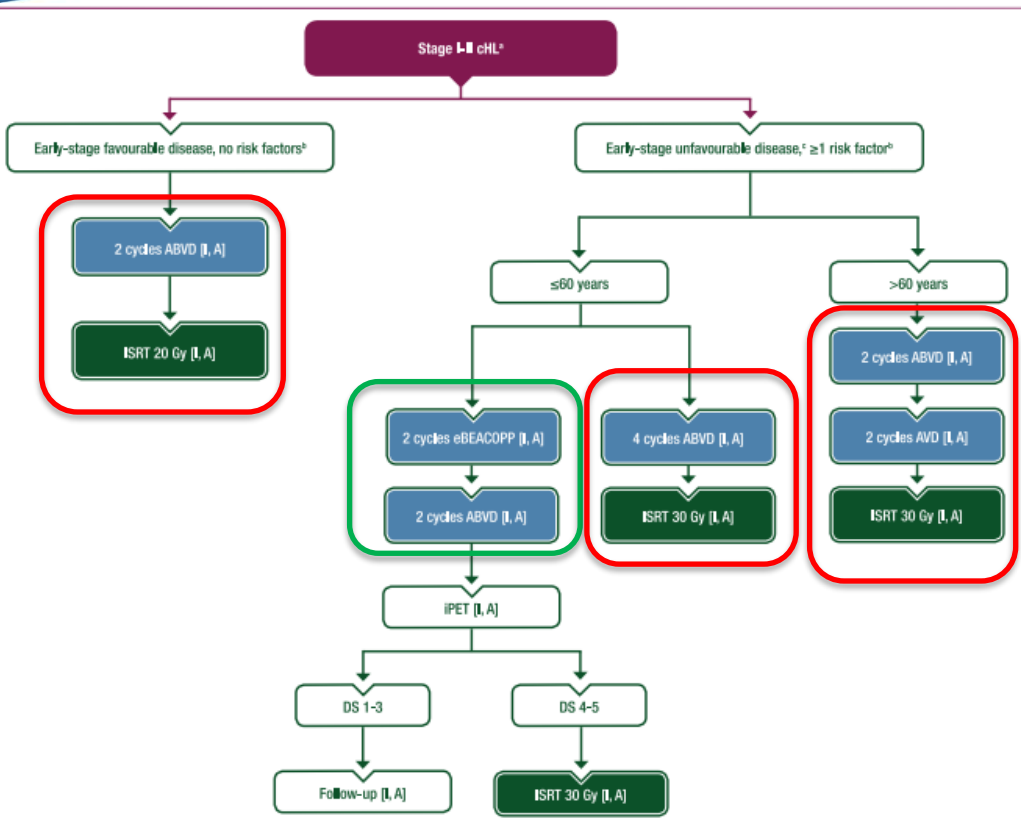
Early-stage cHL comes in 2 flavors:

- early **favorable**
- early **unfavorable**

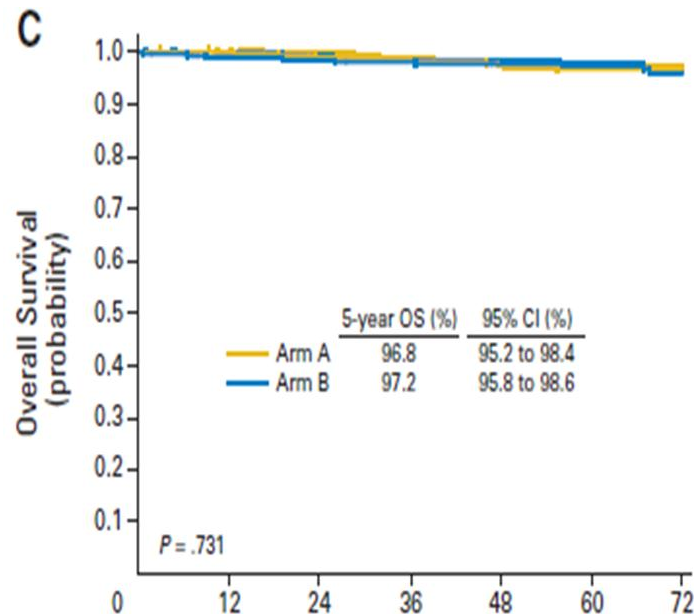
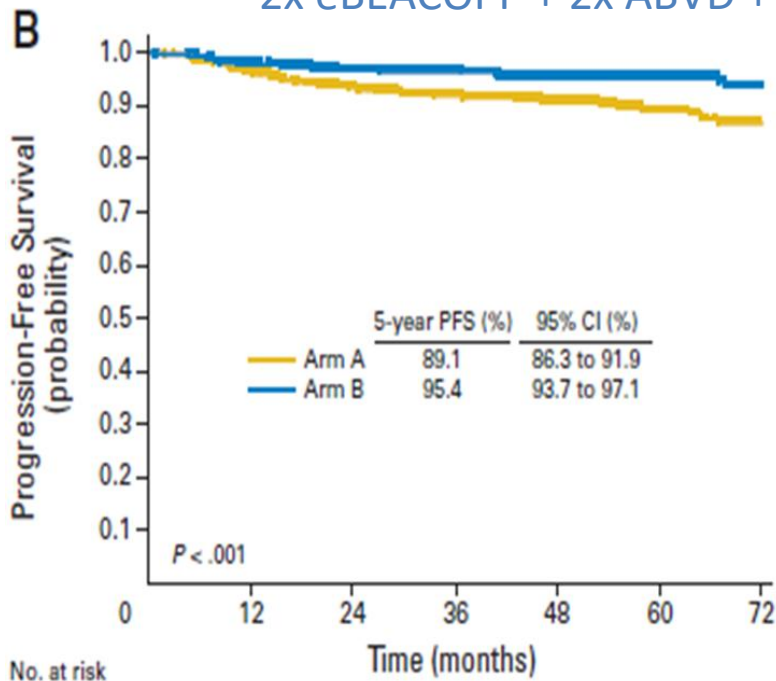
## GHSG criteria

	Stage (Ann Arbor)			
Risk Factors	IA, IB, IIA	IIB	IIIA, IIIB	IVA, IVB
None	Early favorable		Advanced	
≥ 3 LK- Areas	Early unfavorable			
Elevated ESR				
Large Mediastinal Mass				
Extranodal disease				

GHSG – German Hodgkin Study Group; HL – Hodgkin lymphoma; ESR - erythrocyte sedimentation rate

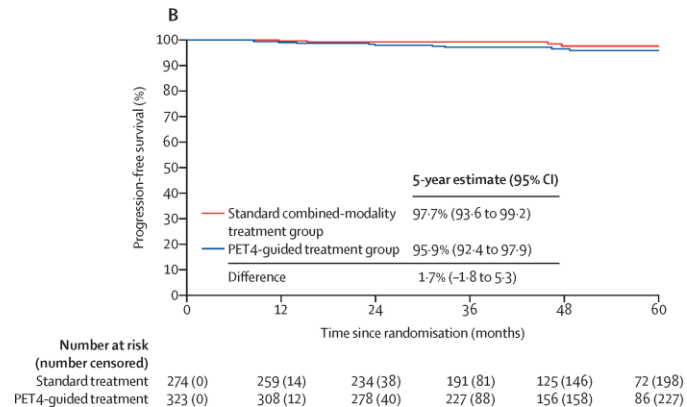
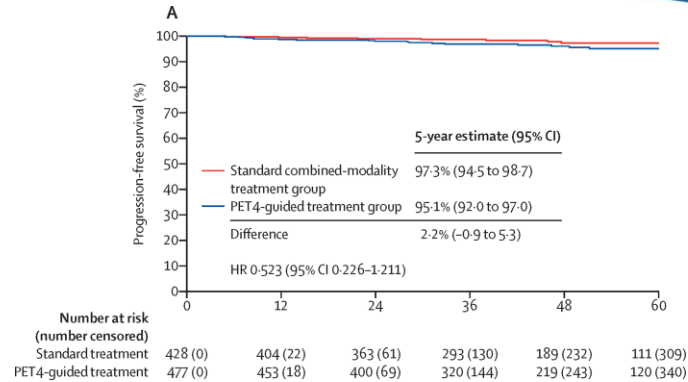


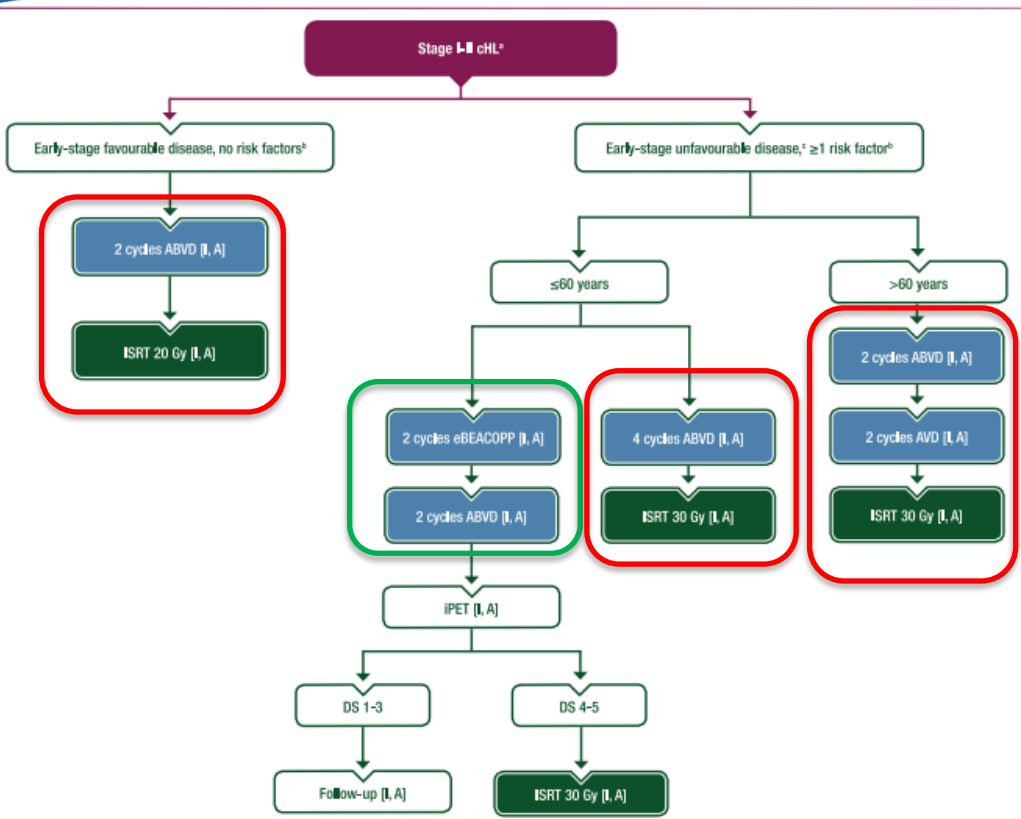
2x eBEACOPP + 2x ABVD + 30 Gy RT vs. 4x ABVD + 30 Gy RT



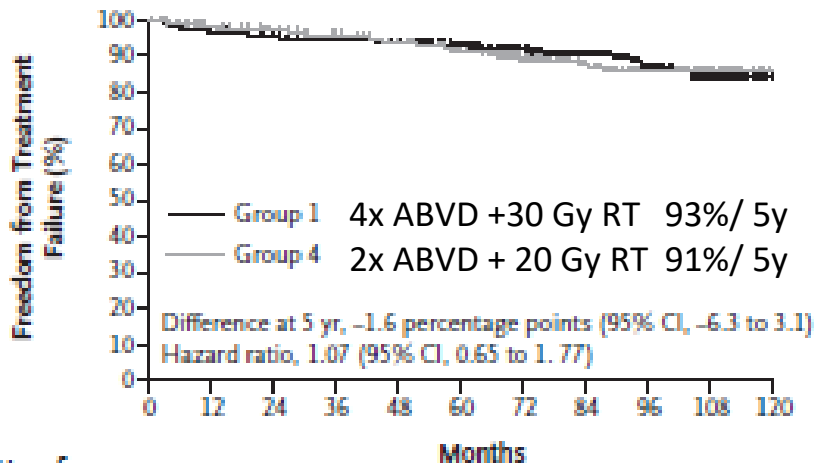


In pts. with localised unfavorable disease RT can safely be avoided if they are PET- after 2x eBEACOPP + 2x ABVD



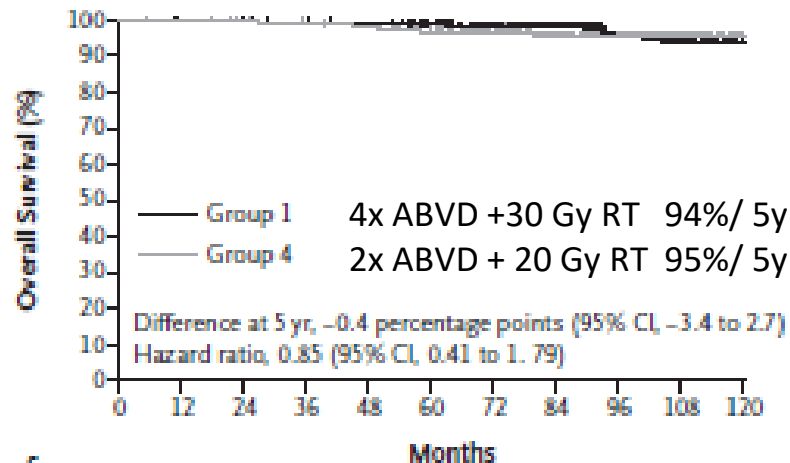


## C Comparison of Groups 1 and 4



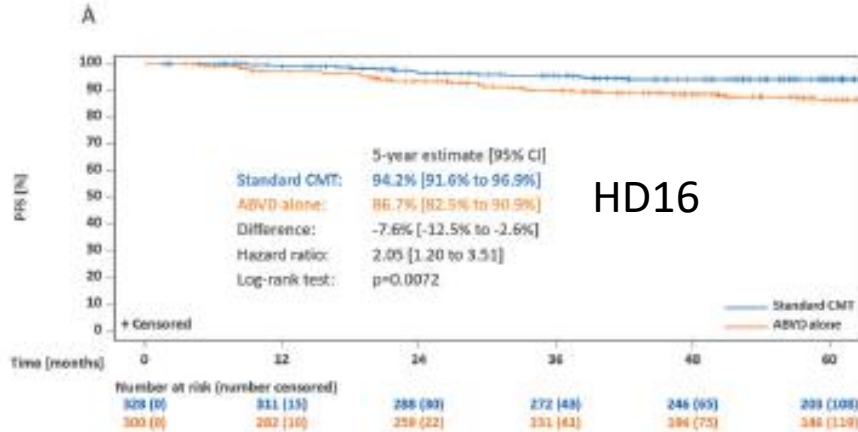
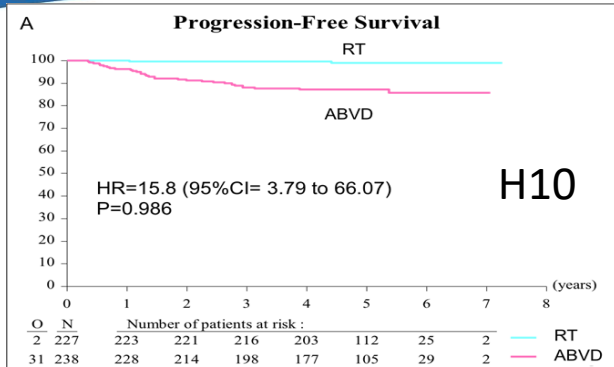
No. of Patients at Risk

Group 1	298	277	264	255	239	217	167	121	74	35	3
Group 4	299	275	265	252	239	199	151	110	66	28	4

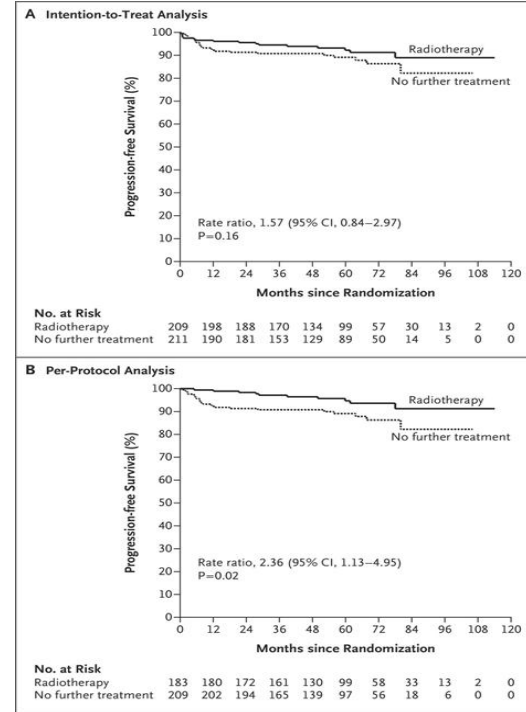


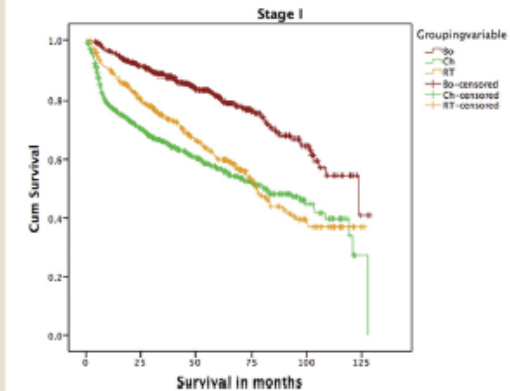
No. of Patients at Risk

Group 1	298	293	289	286	283	271	240	182	116	63	12
Group 4	299	298	293	289	285	273	241	182	122	64	16



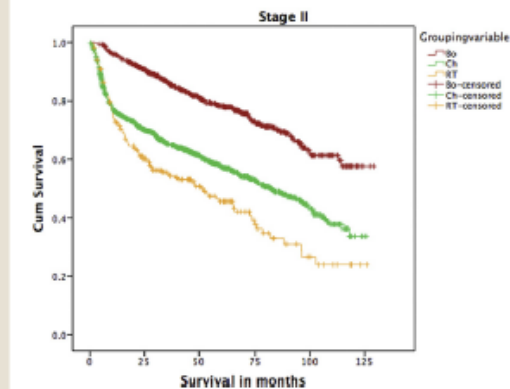
## RAPID



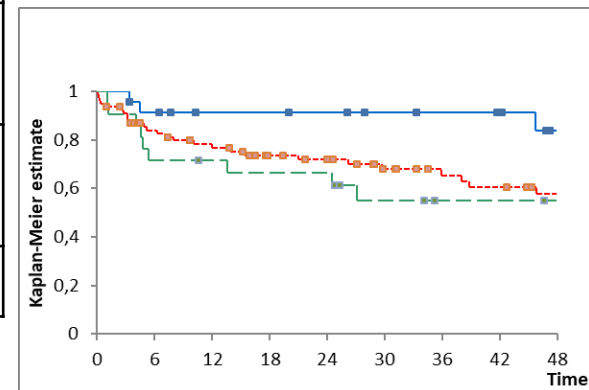
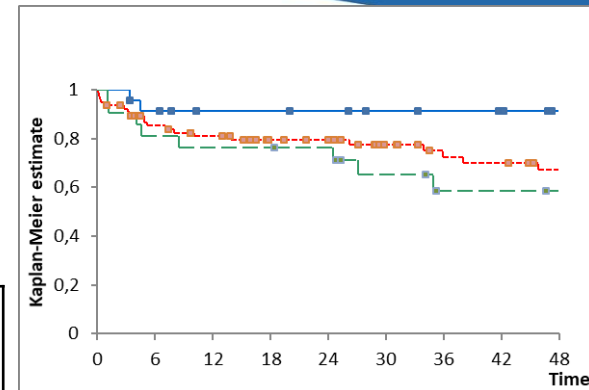


40-mo OS

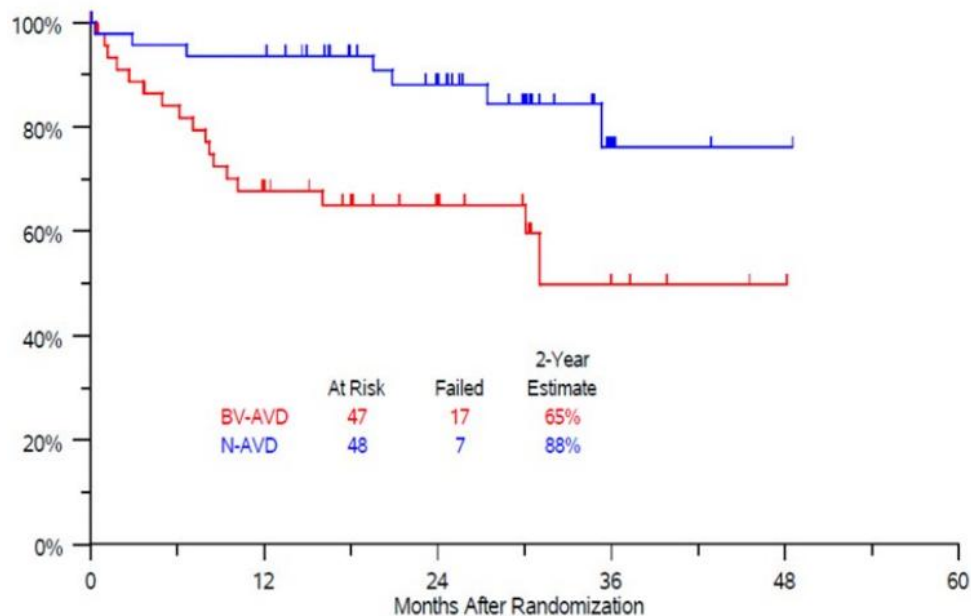
54%, 58%, 78%



	4-y PFS	4-y OS
Early-stage favorable	84%	91%
Early-stage unfavorable	55%	59%
Advanced stage	59%	67%



## &gt;60 years of age



Adapted from: Herrera AF, et al. N Engl J Med 2024;391:1379-1389. <https://doi.org/10.1056/NEJMoa2405888>

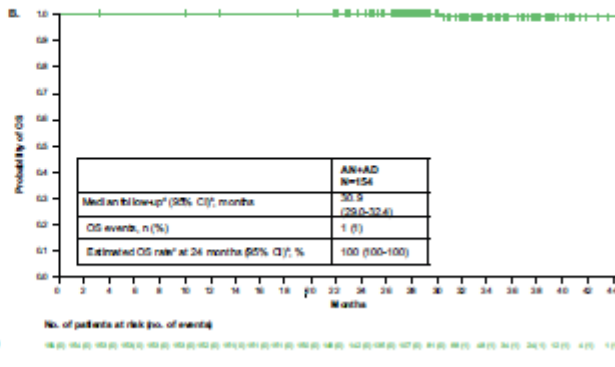
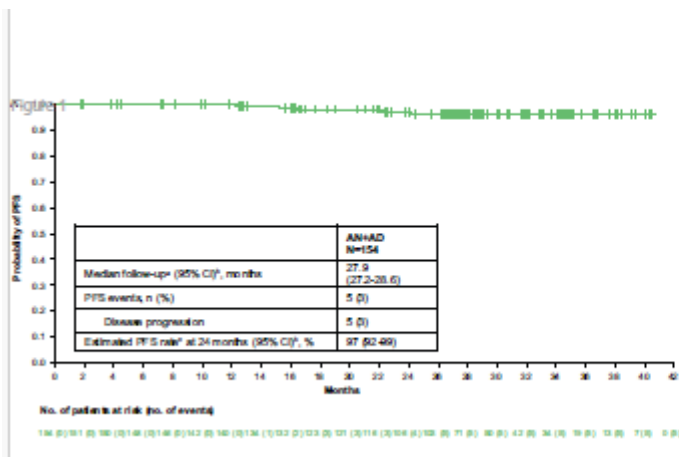
Regimen	N	% RT	PFS	Median FU
3x Pembro + 4 (ES) - 6 (AS) x AVD	EU 12 AS 18	0	100% / 3y	33 mo
4x Bv-Nivo-AD	ES nonbulky 154	1.3%	95% / 3y	31 mo
8x Bv-Nivo*	ES 16 AS 30	8.7%	mPFS 18 mo	20 mo
16x Bv-Nivo*	ES 4 AS 16 Unknown 1	0	52% / 3y	52 mo

EU = early stage unfavorable; AS = advanced stage; ES = early stage

\* Elderly or unfit for chemotherapy

N=154, median age 31 y (range 18-77),  
early stage favorable 36%, early stage unfavorable 63%, unknown 1%

**2-y PFS favorable 100%, unfavorable 95%**



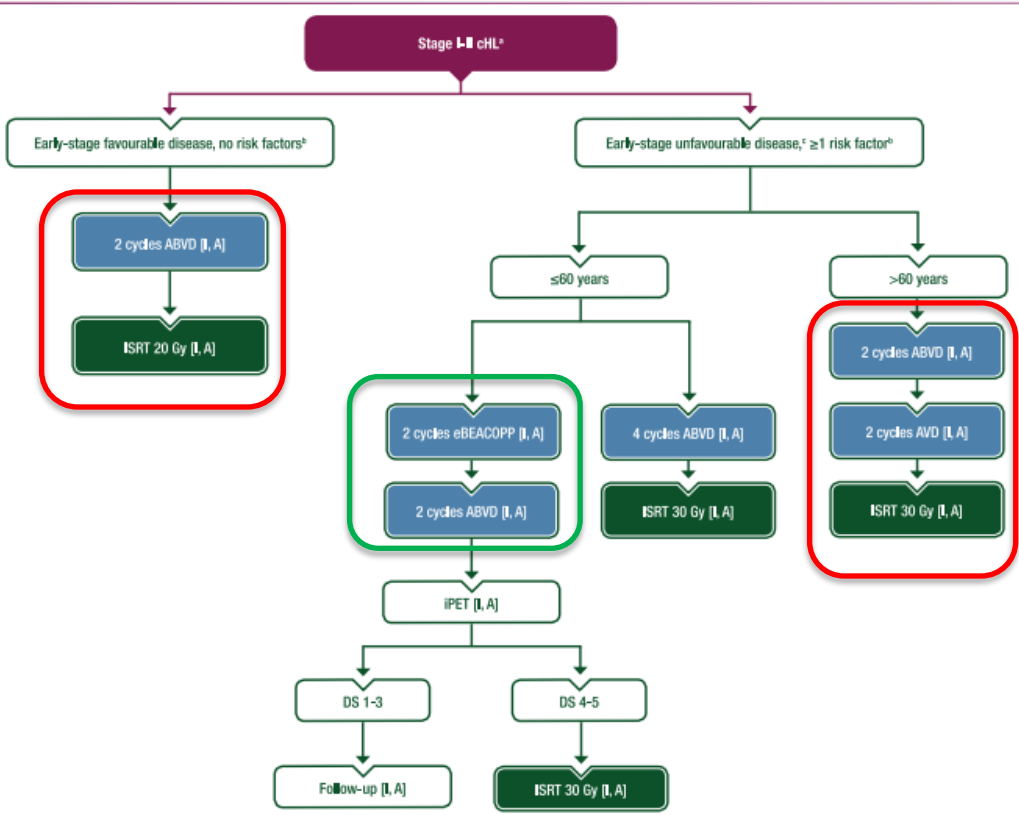
### Toxicity

FN	0
Neutropenia gr.≥3	9%
PN	47%
PN gr.≥3	3%
IMAE	22%
IMAE gr.≥3	8%

FN = febrile neutropenia

PSN = peripheral neuropathy

IMAE = immune-mediated adverse effects



2x eBEACOPP (or similar) + 2x ABVD is standard for EU pts <60y  
-RT needed only if PET+ after EOT

2x ABVD + 20 Gy INRT standard for EF pts

2x ABVD + 2x AVD + 30 Gy INRT standard for EU pts > 60y

4x PD1inh + AV/BvD more effective, less toxic  
Soon new standard of care!

With modern treatment of cHL, RT can be limited to pts. who are in  
PR after systemic therapy!



**Thank  
you!**