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JW MARRIOTT CHICAGO  
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*This activity is jointly provided by:*



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# Key Updates in Early-Stage Hodgkin Lymphoma

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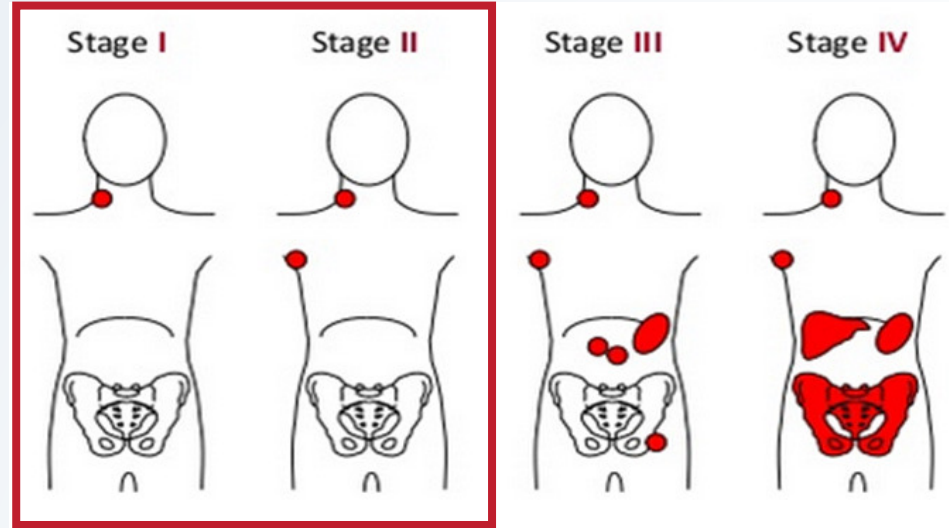
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# Disclosures

	Consulting	Research Funding
Kite Pharma		
Pfizer		
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Genentech		
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Caribou Biosciences		
Lyell Immunopharma		
CRISPR Therapeutics		
Morphosys AG		
Repare Therapeutics		
Artiva Biosciences		
Newave		
AstraZeneca		

# Early-Stage (ES) Classical Hodgkin's Lymphoma (cHL)



**Unfavorable Risk Factors for Stage I-II Hodgkin Lymphoma**

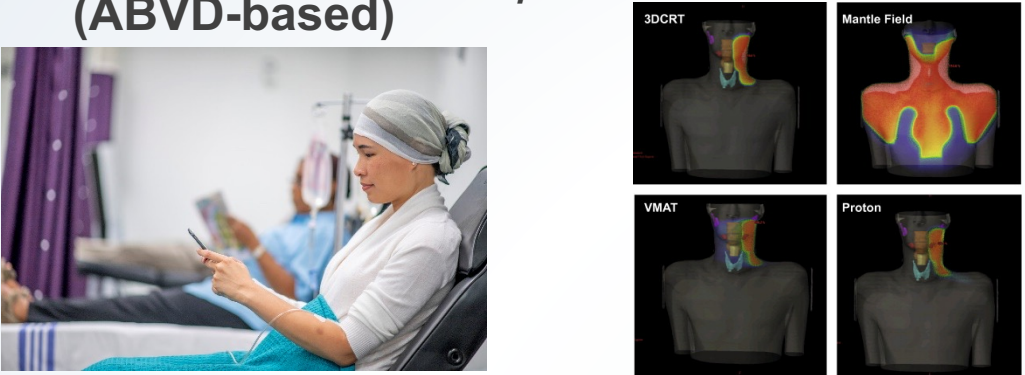
Risk Factor	GHSB	EORTC	NCCN
Age		≥50 years	
ESR and B symptoms	≥50 mm/hr if A; ≥30 mm/hr if B	≥50 mm/hr if A; ≥30 mm/hr if B	≥50 mm/hr or any B symptoms
Mediastinal mass <sup>n</sup>	MMR >0.33	MTR >0.35	MMR >0.33
# Nodal regions	≥3*	≥4*	≥4
E lesion	any		
Bulky <sup>n</sup>			>10 cm

GHSB = German Hodgkin Study Group  
 EORTC = European Organization for  
 Research and Treatment of Cancer

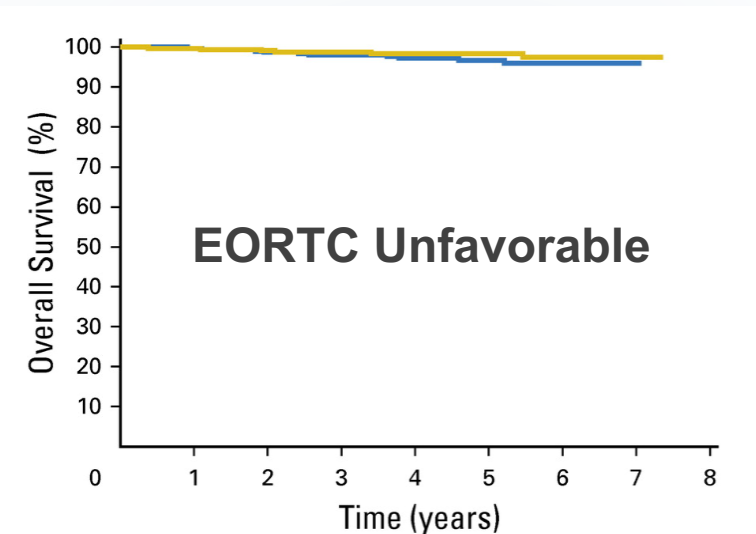
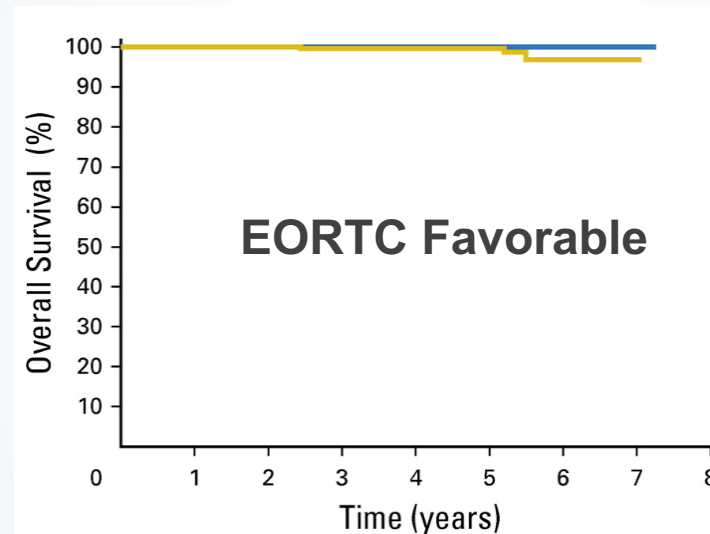
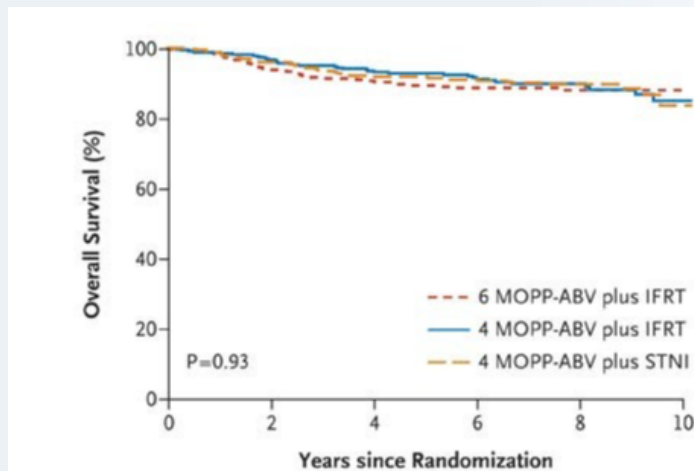
MMR = Mediastinal mass ratio, maximum width of mass/maximum intrathoracic diameter as measured on chest radiograph (CXR)  
 MTR = Mediastinal thoracic ratio, maximum width of mediastinal mass/intrathoracic diameter at T5-6 as measured on CXR

# ES cHL Is A Highly Curable Disease

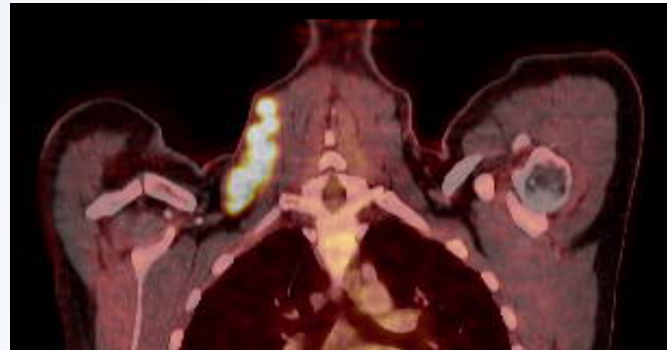
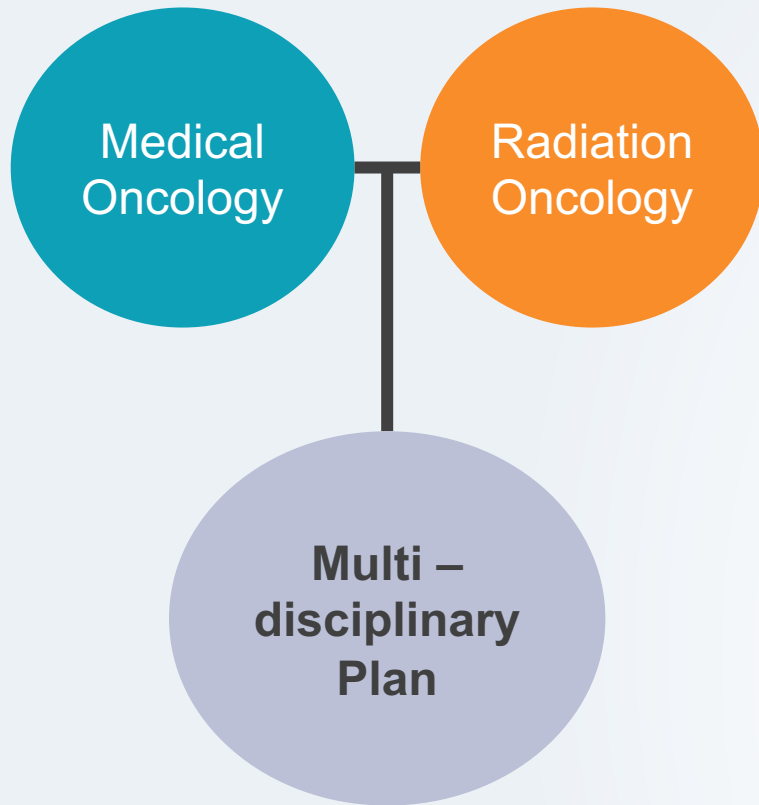
**Chemotherapy (ABVD-based) +/- Radiation**



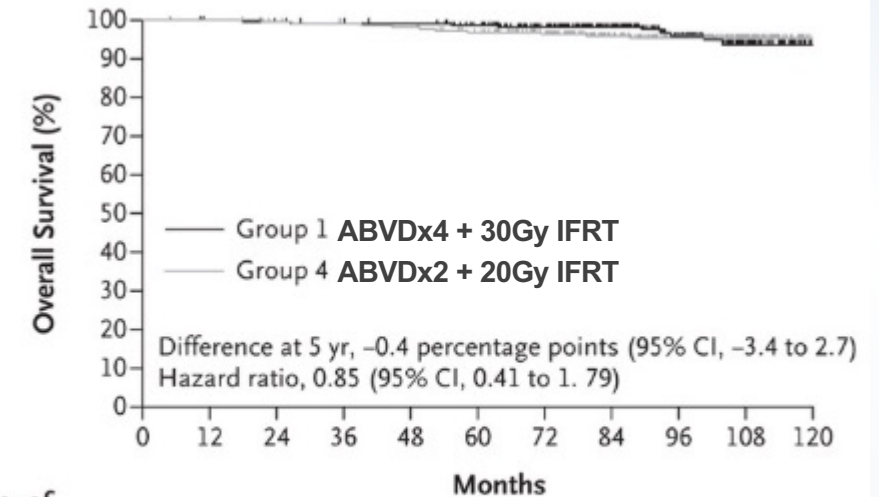
The image shows a patient in a hospital bed on the left. On the right, there are four radiation therapy planning diagrams: 3DCRT, Mantle Field, VMAT, and Proton.



# To Radiate or To Not Radiate?



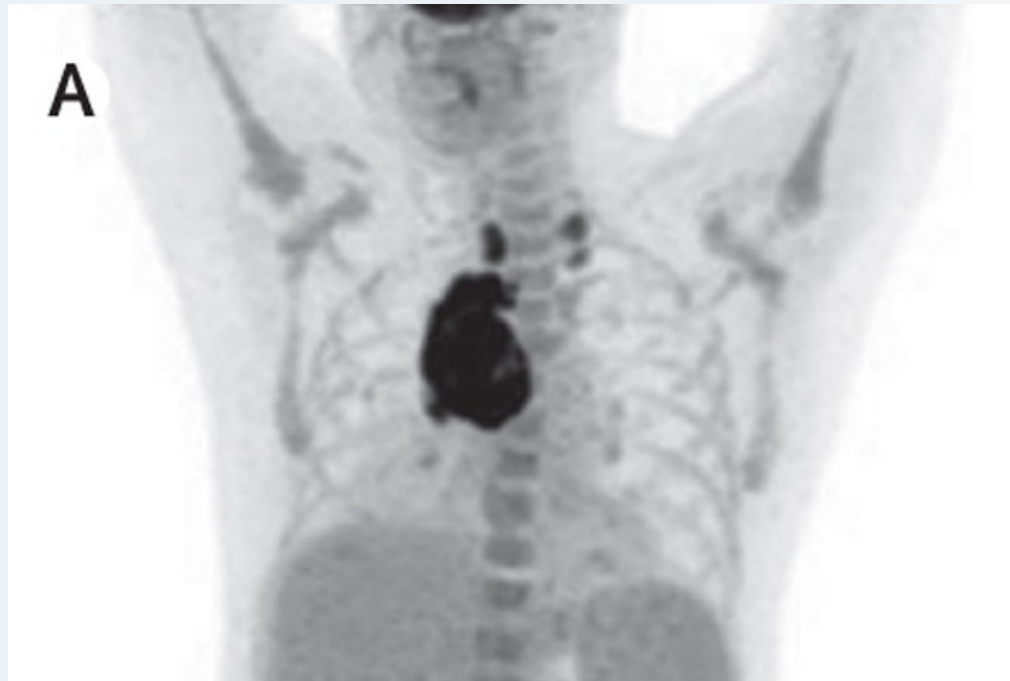
## HD10 GHSG Favorable



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

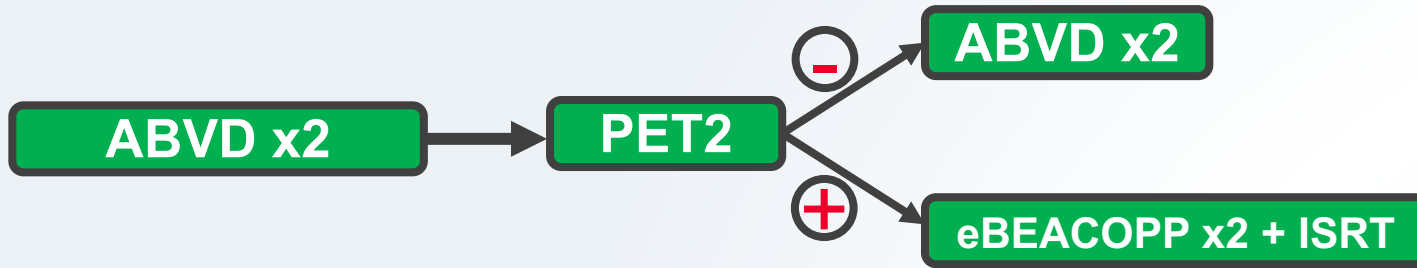
# Not All ES Favorable Disease Are Equal



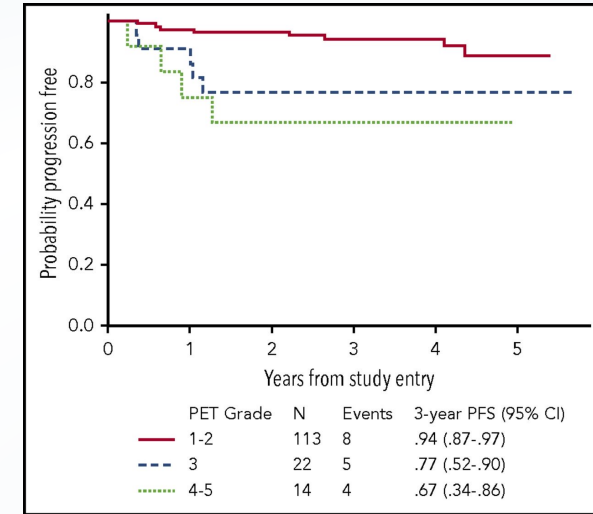
	EORTC Nodal Regions	GHSG Nodal Regions
R Cervical/Supraclavicular		
R ICL/Subpectoral		
R Axilla		
L Cervical/Supraclavicular		
L Infraclavicular/Subpectoral		
L Axilla		
Mediastinum		
R Hilum		
L Hilum		

# Radiation Free Treatment Strategies for ES cHL

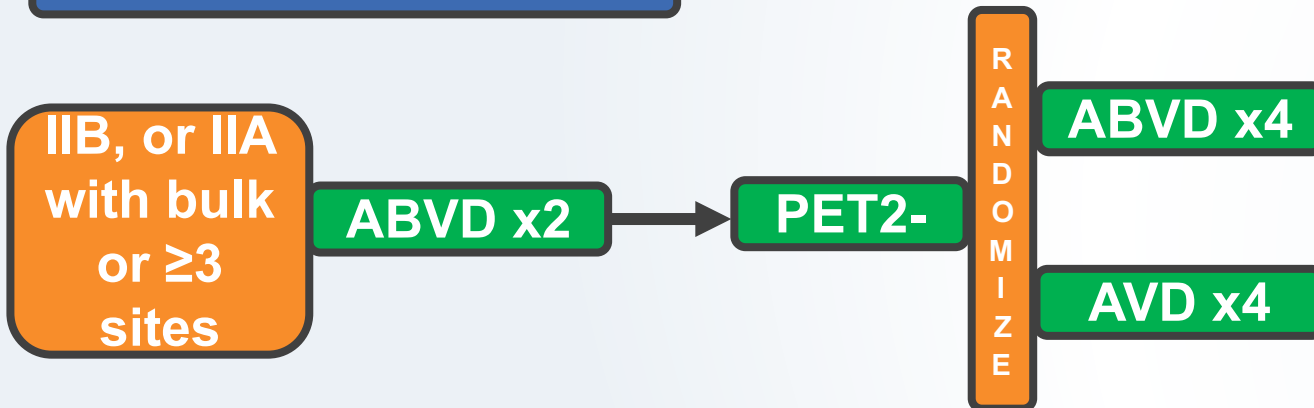
CALGB 50604



Straus DJ et al. Blood (2018) 132;10: 1013-1021.

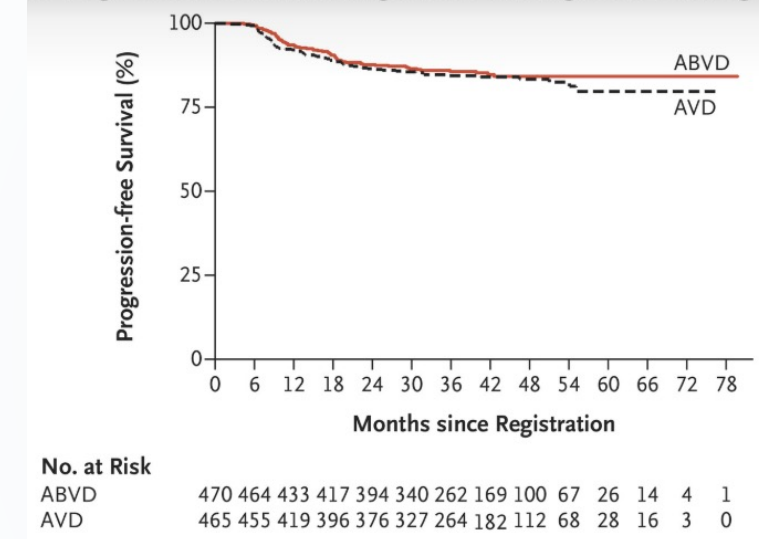


RATHL

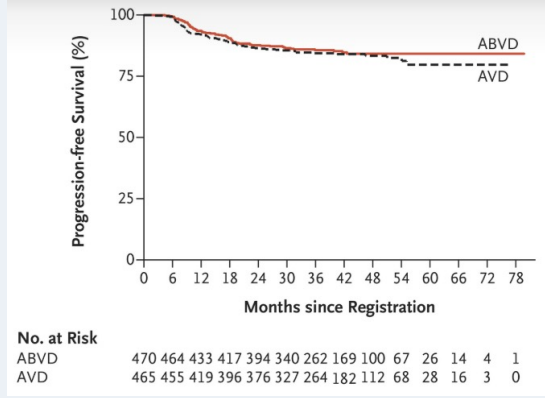


Johnson P et al. NEJM (2016) 374: 2419-2429.

A Progression-free Survival among Patients with Negative PET Findings



A Progression-free Survival among Patients with Negative PET Findings



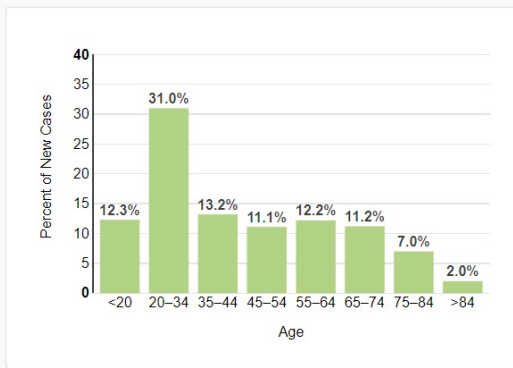
Johnson P et al. NEJM (2016) 374: 2419-2429.  
 Straus DJ et al. Blood (2018) 132;10: 1013-1021.  
 Seer database: <https://seer.cancer.gov/statfacts/html/hodg.html>

**Continue to Improve Cure Rates**

**PET2 Positive**

**What Are Some of The Remaining Questions/Unmet Needs?**

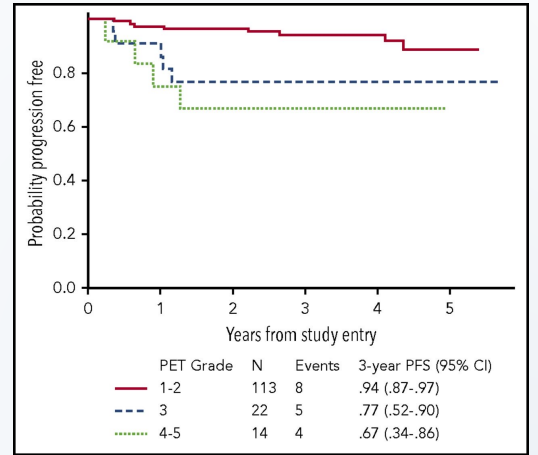
**Eliminate/Reduce Chemotherapy and Radiation Therapy Exposure**



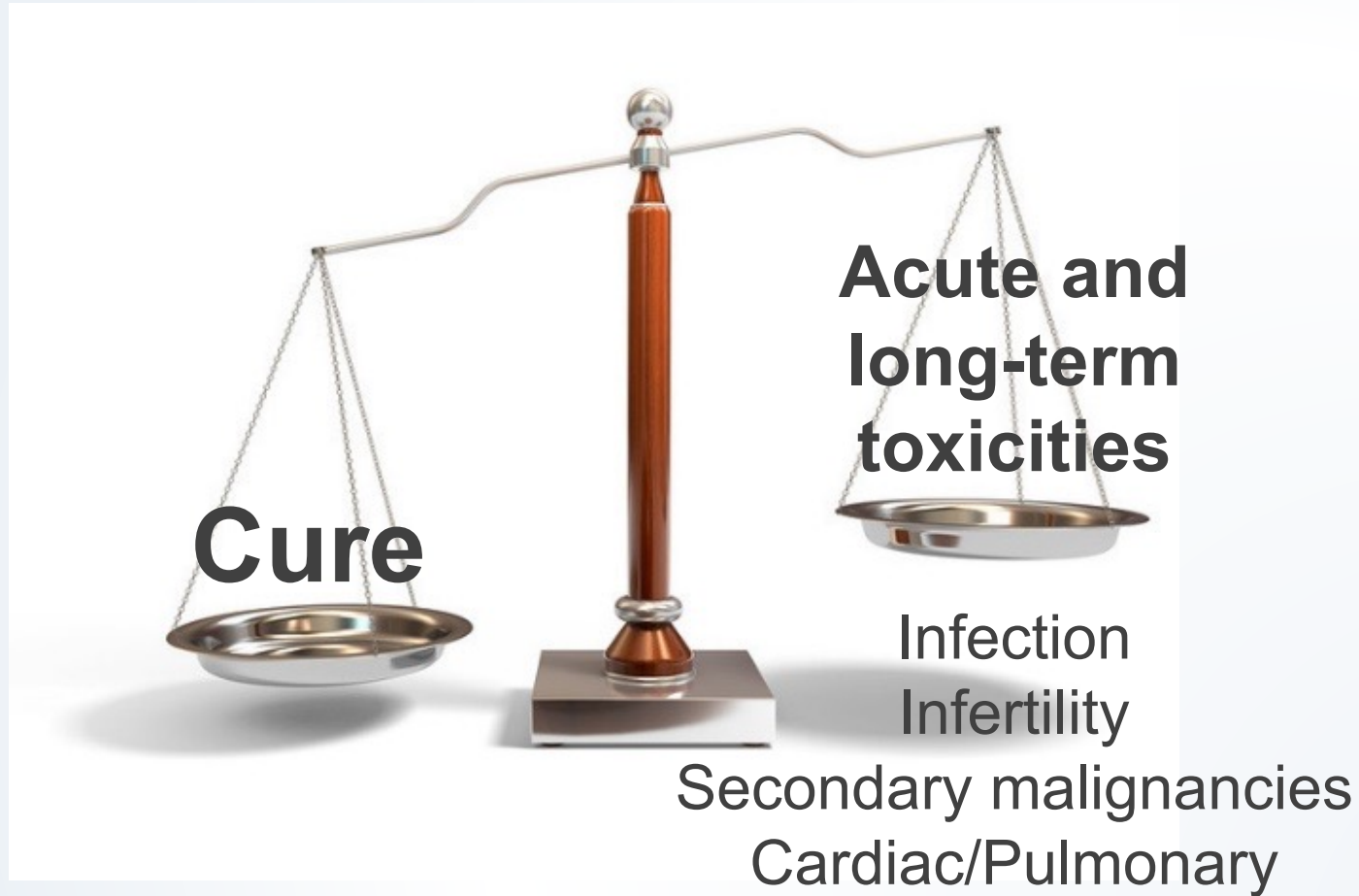
Hodgkin lymphoma is most frequently diagnosed among people aged 20-34.

**Median Age At Diagnosis**

**39**

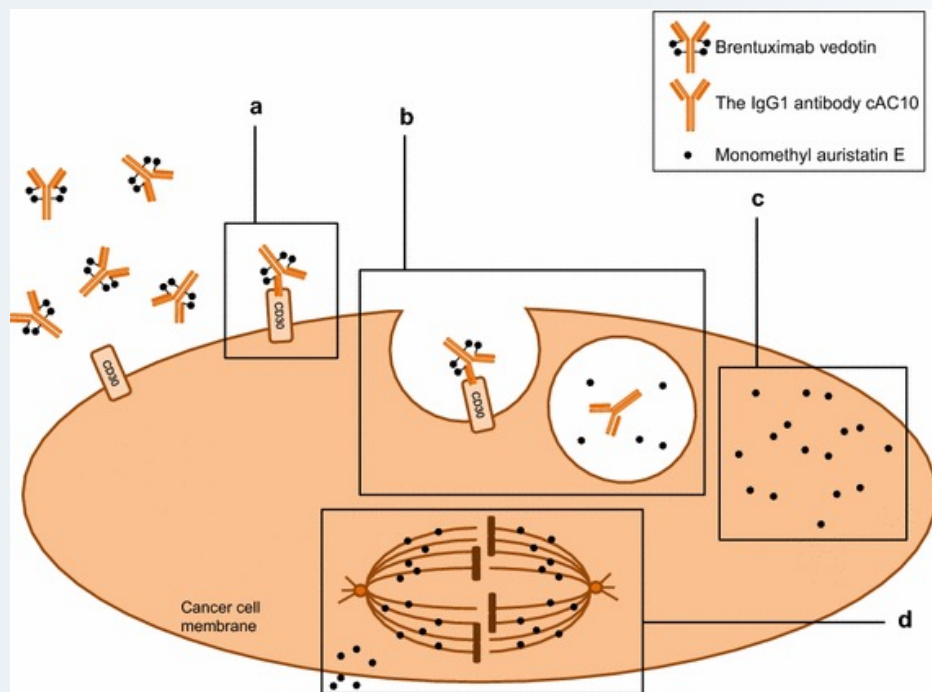


# A Balancing Act

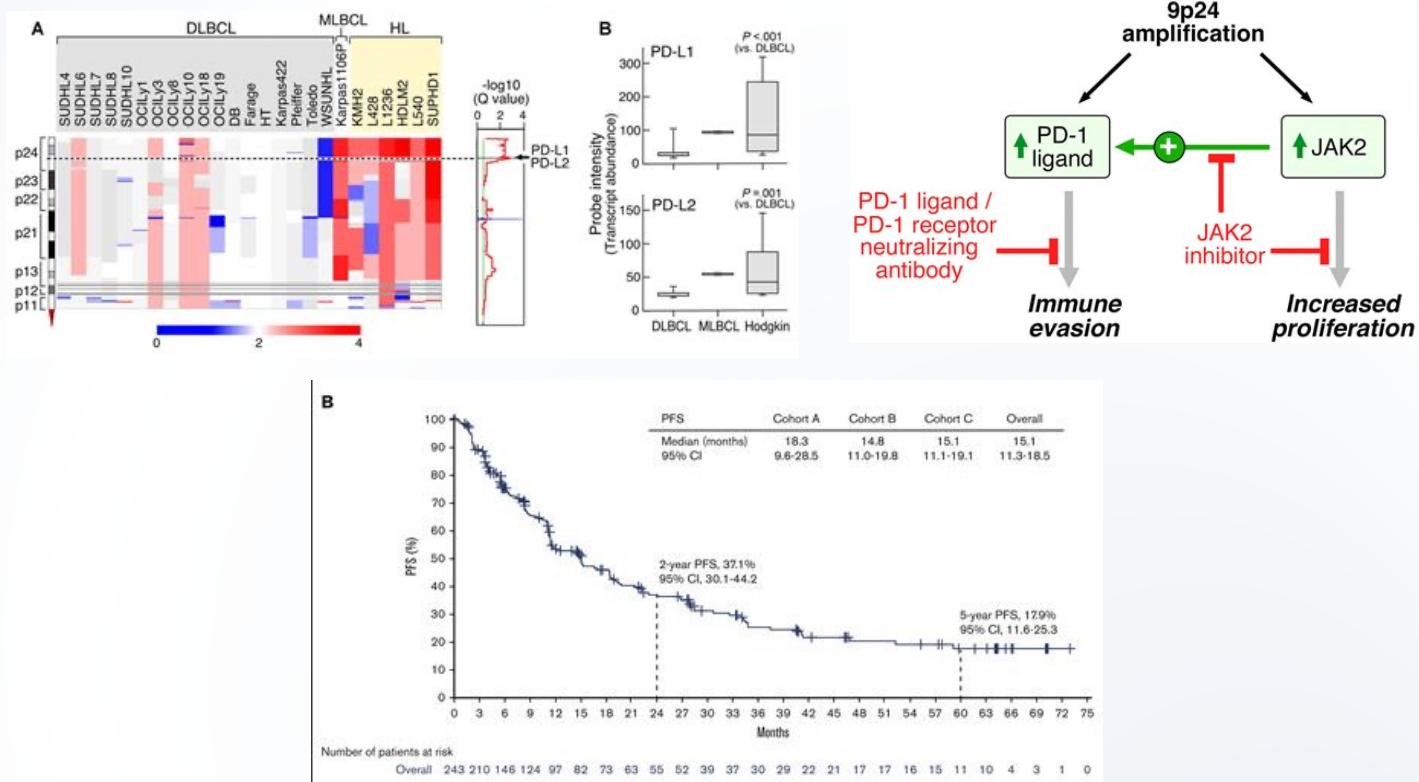


# Immunotherapeutic Targets in cHL

## Brentuximab Vedotin (BV)



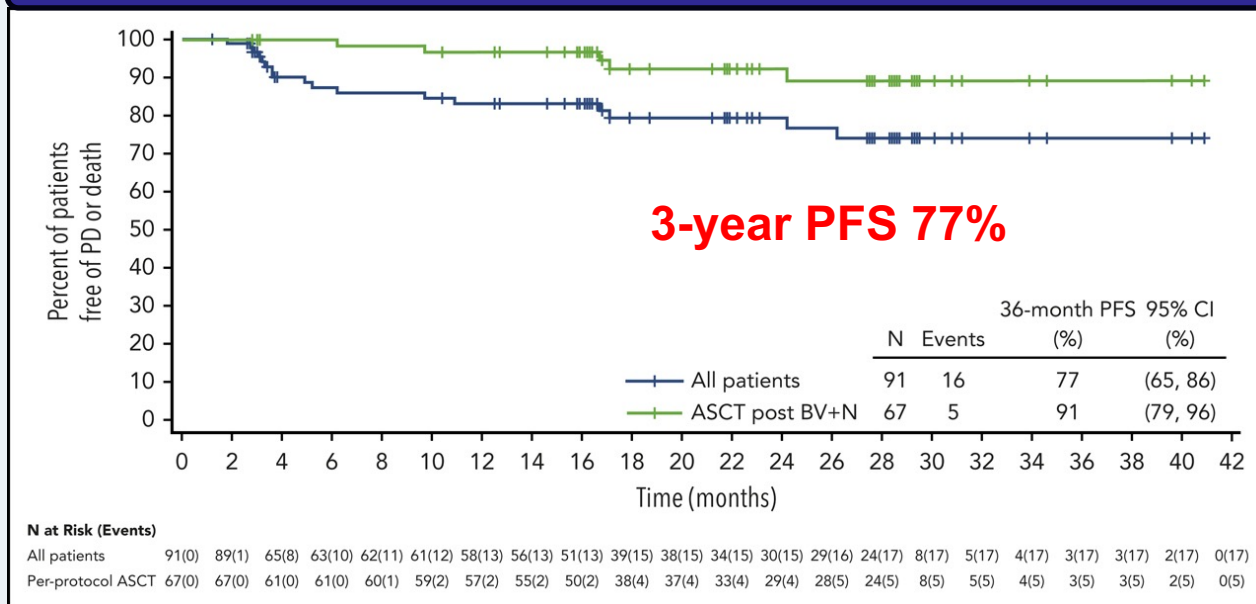
## Immune Checkpoint Blockade



Scott LJ. *Drugs* (2017) 77: 435-445.  
 Green MR et al. *Blood* (2010) 116; 17: 3268-3277.  
 Ansell S et al. *Blood Adv* (2023) 7;20: 6266-6274.

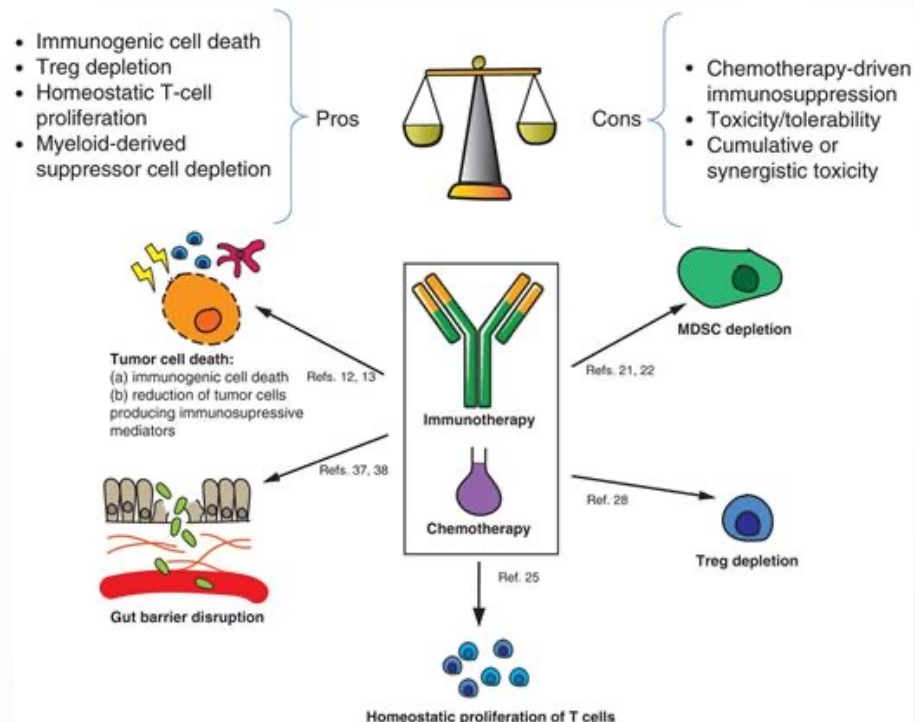
**Research Question:** How can we better utilize these novel therapies to **improve cure rates** while simultaneously **minimizing** long-term morbidity and treatment-related mortality by **reducing patient exposure** to radiotherapy and high cumulative doses of chemotherapy?

### Combination BV + Nivolumab in R/R cHL



**ORR 85%**  
**CR 67%**

### Chemo + Immune Checkpoint Blockade are Synergistic



Advani et al. Blood (2021) 138;6: 427-438.  
Salas-Benito D et al. Cancer Discovery (2021) 11;6: 1353-1367.

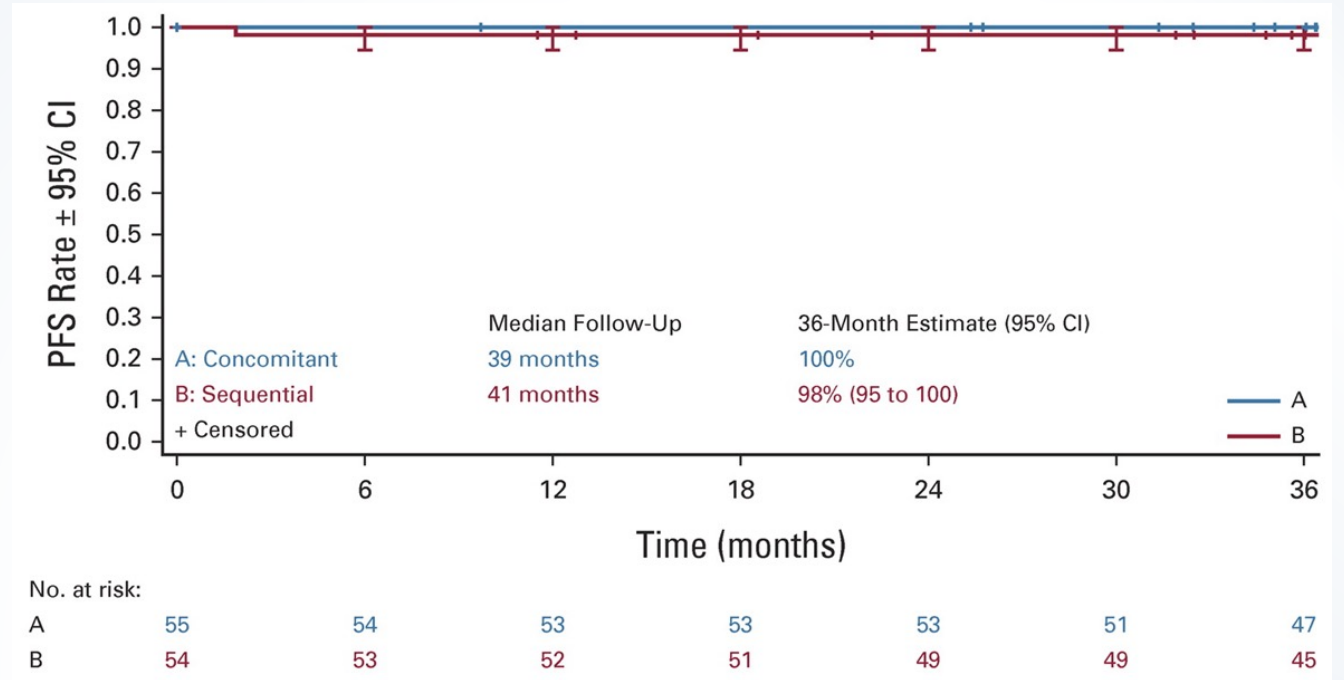
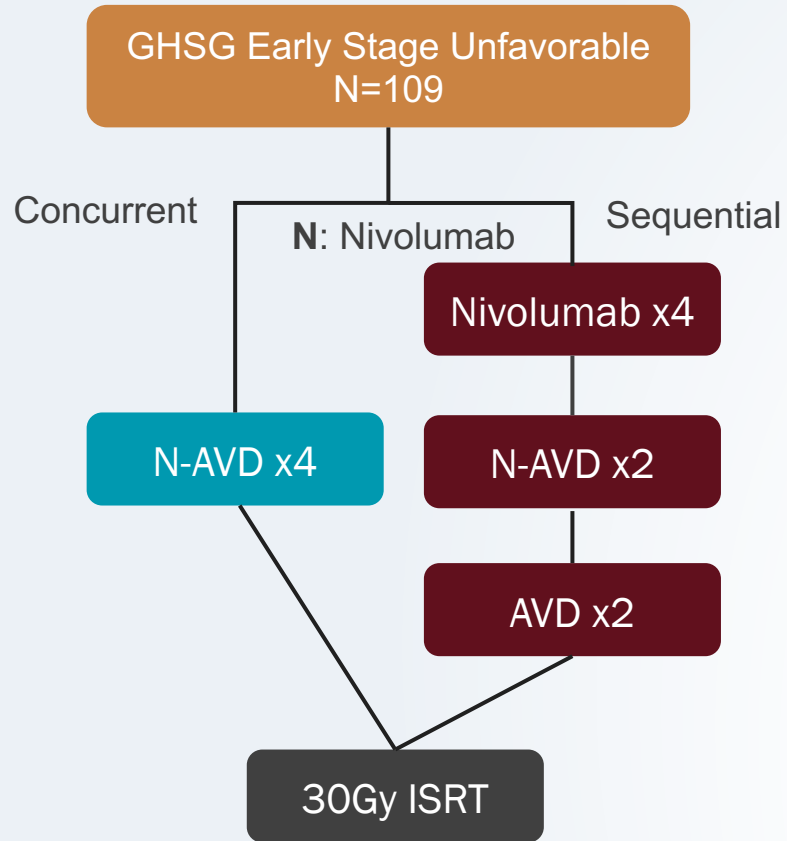
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# Concurrent Chemotherapy and Immunotherapy

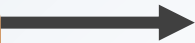
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# NIVAHL

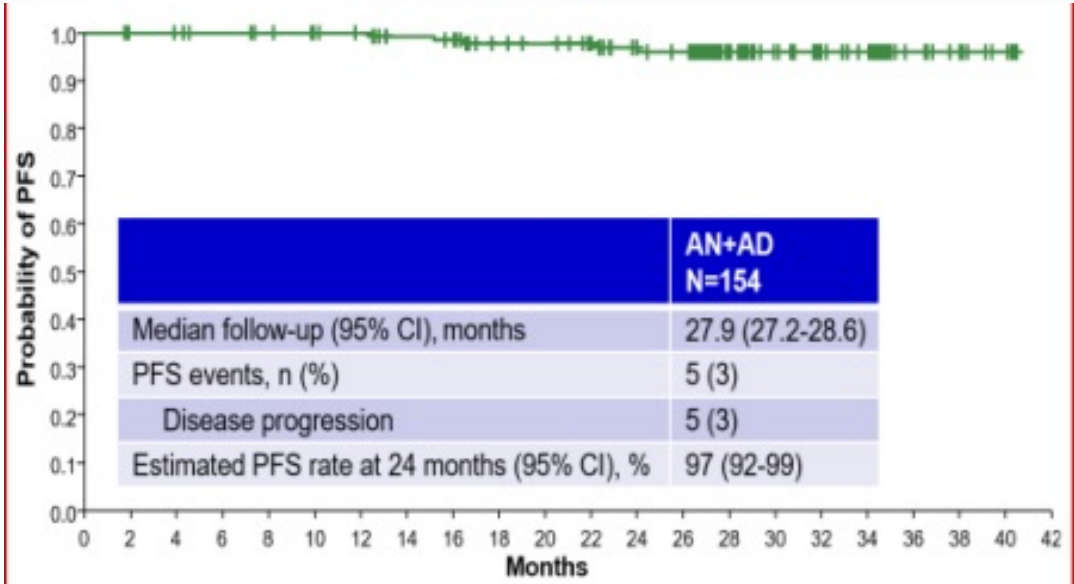
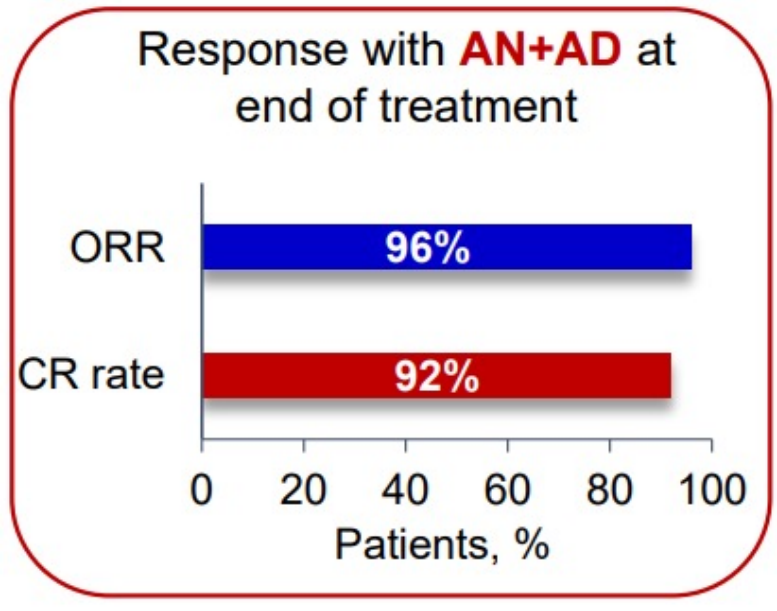


Brockelmann PJ et al. JCO (2023) 41 (6): 1193-1199.

**Non-Bulky Early Stage**  
**AN+AD x4**  
 (doxorubicin, nivolumab, BV, dacarbazine)



N=154	
Age	
• <60	130 (84%)
• ≥60	24 (16%)
GHSR Risk	
• Favorable	56 (36%)
• Unfavorable	97 (63%)



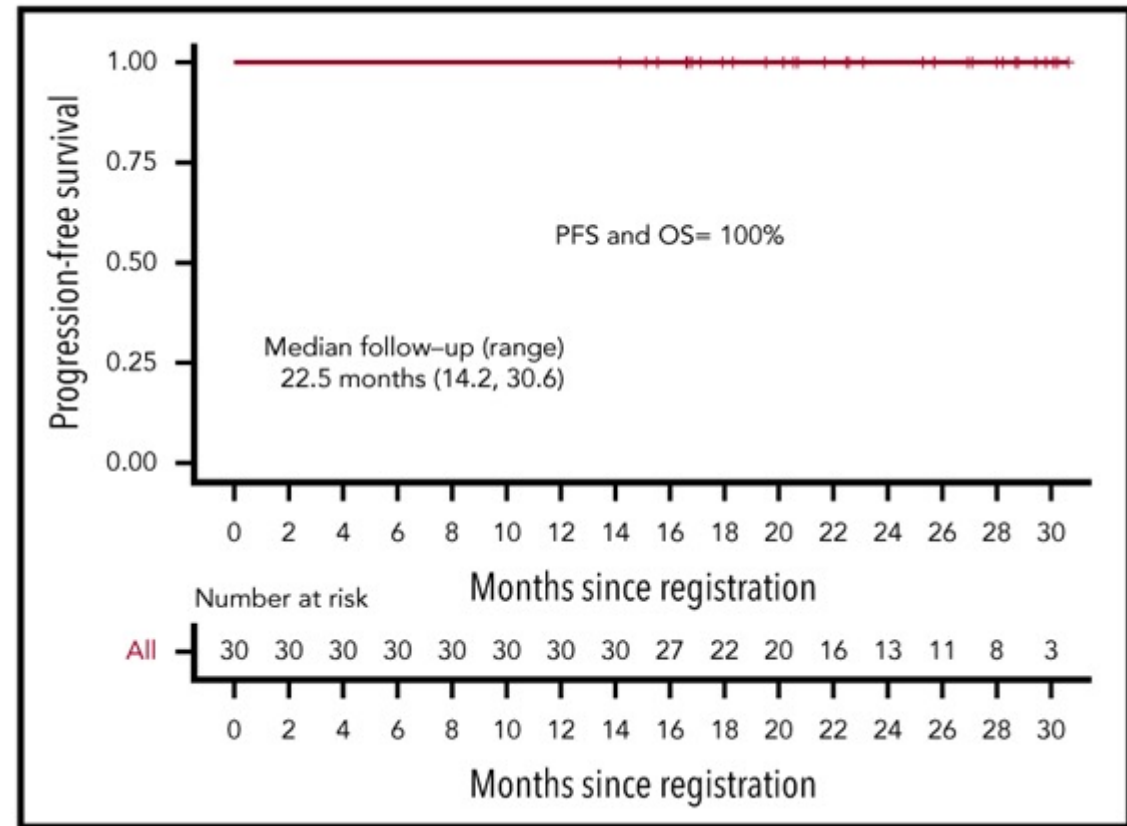
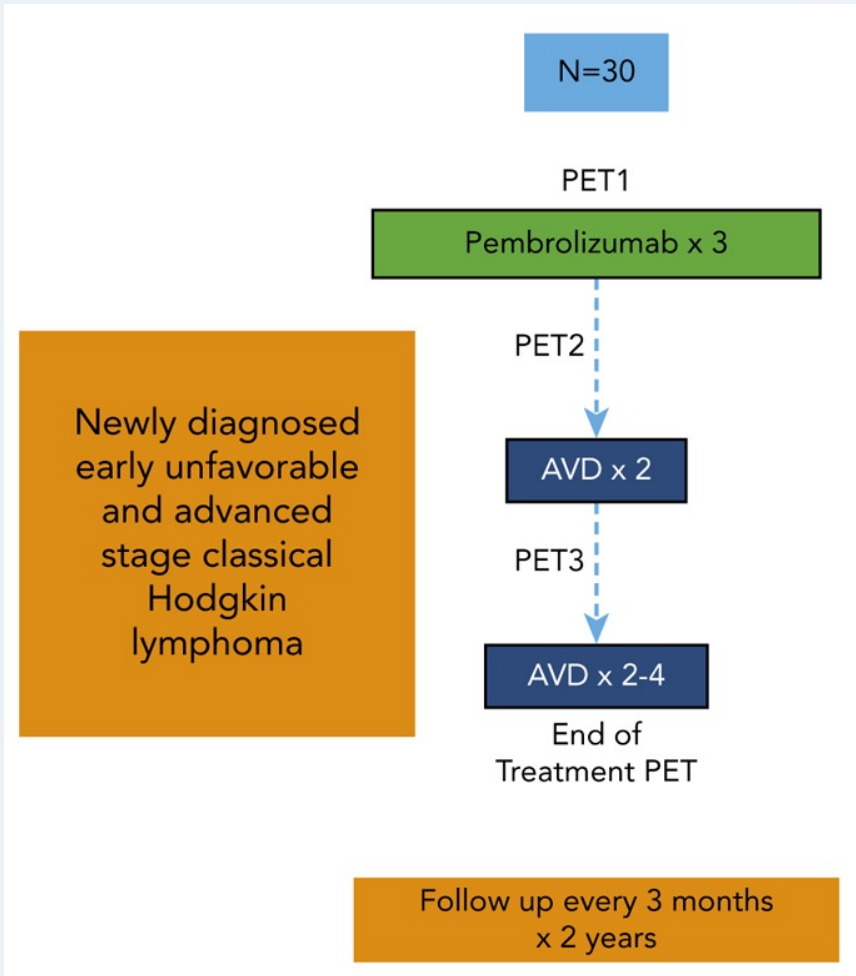
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# Sequential Chemotherapy and Immunotherapy

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# Sequential Pembrolizumab and Chemotherapy



Allen PB et al. Blood (2021) 137 (10): 1318-1326.

# NAHLCL

Key eligibility:  
Age  $\geq$  16  
Stage I/II  
PS  $\leq$  2

SOC ABVD  
x 2 cycles

PET

PET 2 –  
Deauville 1-3

Non bulky

Bulky  
 $\geq$ 7.5 cm  
mediastinal mass

A

B1

B2

BV-nivo  
x 3 cycles

ABVD x 2 cycles  
Nivo x q 2 weeks x 6

PET 2 +  
Deauville 4-5

C

BV-AVD  
x 4 cycles

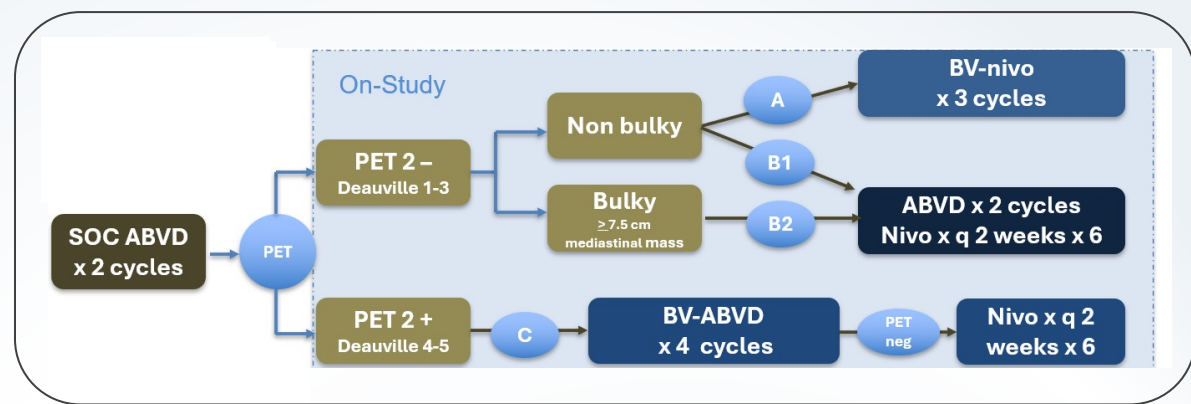
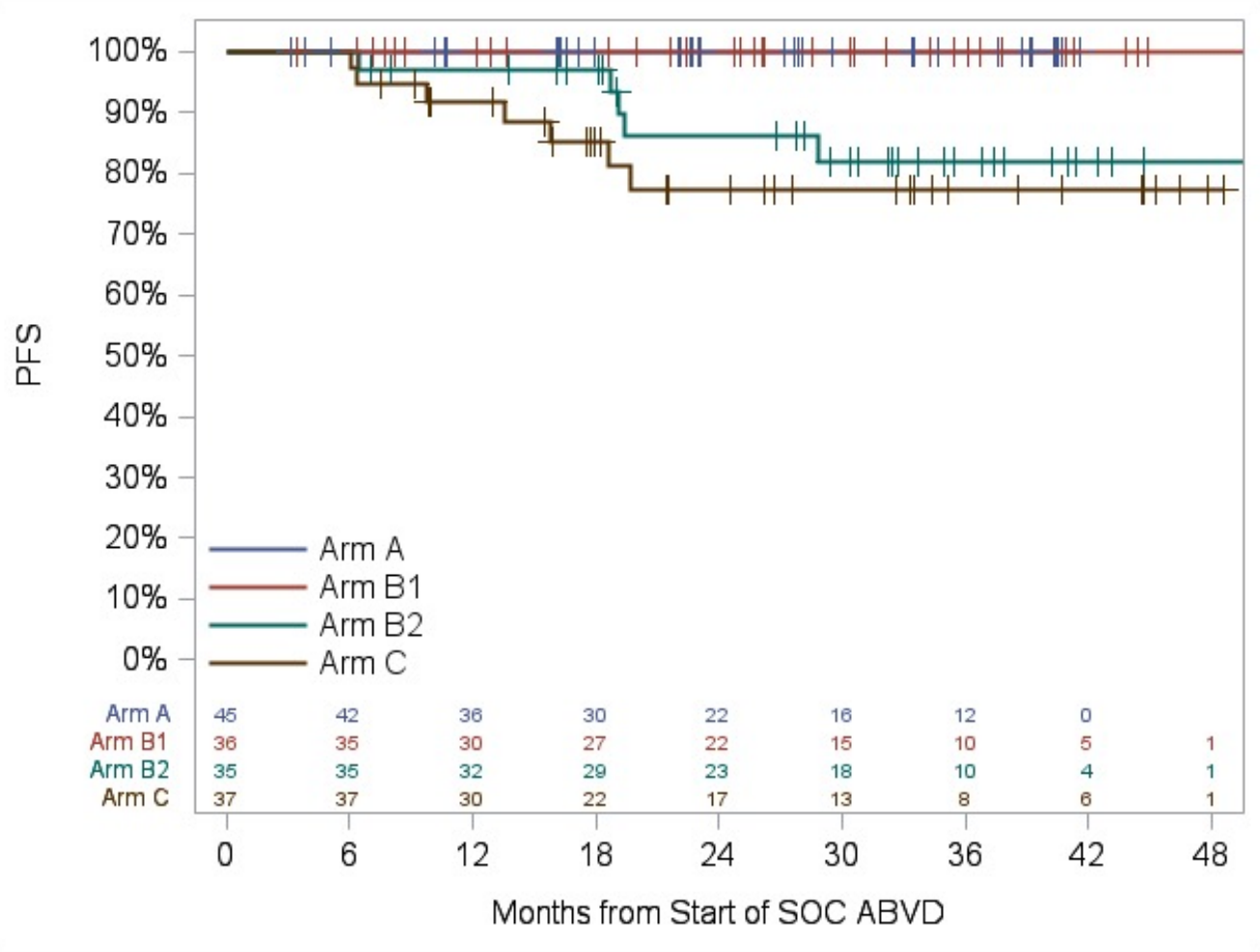
PET  
neg

Nivo x q 2  
weeks x 6

- Exclusion:
- No sensory > gr 1 PN
  - Any motor PN
  - No condition requiring prednisone > 10 mg/ immunosuppressive medications within 14 d

ABVD could be given prior to enrollment  
Randomization stratified between stage I vs II and A vs B sx  
Interim PET scored (Lugano 2014) per local review

LaCasce AS et al. 2024 ASH Annual Meeting Oral Abstract #459  
Slide Courtesy of Dr. Ann LaCasce



PFS (95% CI)	# of PD/Rel	18-month	24-month
Arm A (n=45)	0	100%	<b>100%</b>
Arm B1 (n=36)	0	100%	<b>100%</b>
Arm B2 (n=35)	5	97% (81-100%)	<b>86% (67-95%)</b>
Arm C (n=37)	7	85% (68-94%)	<b>77% (57-89%)</b>

No deaths reported thus far.  
 Median follow-up is 27.7 months (range 3.2-51.0).

# AHOD2131 TRIAL DESIGN

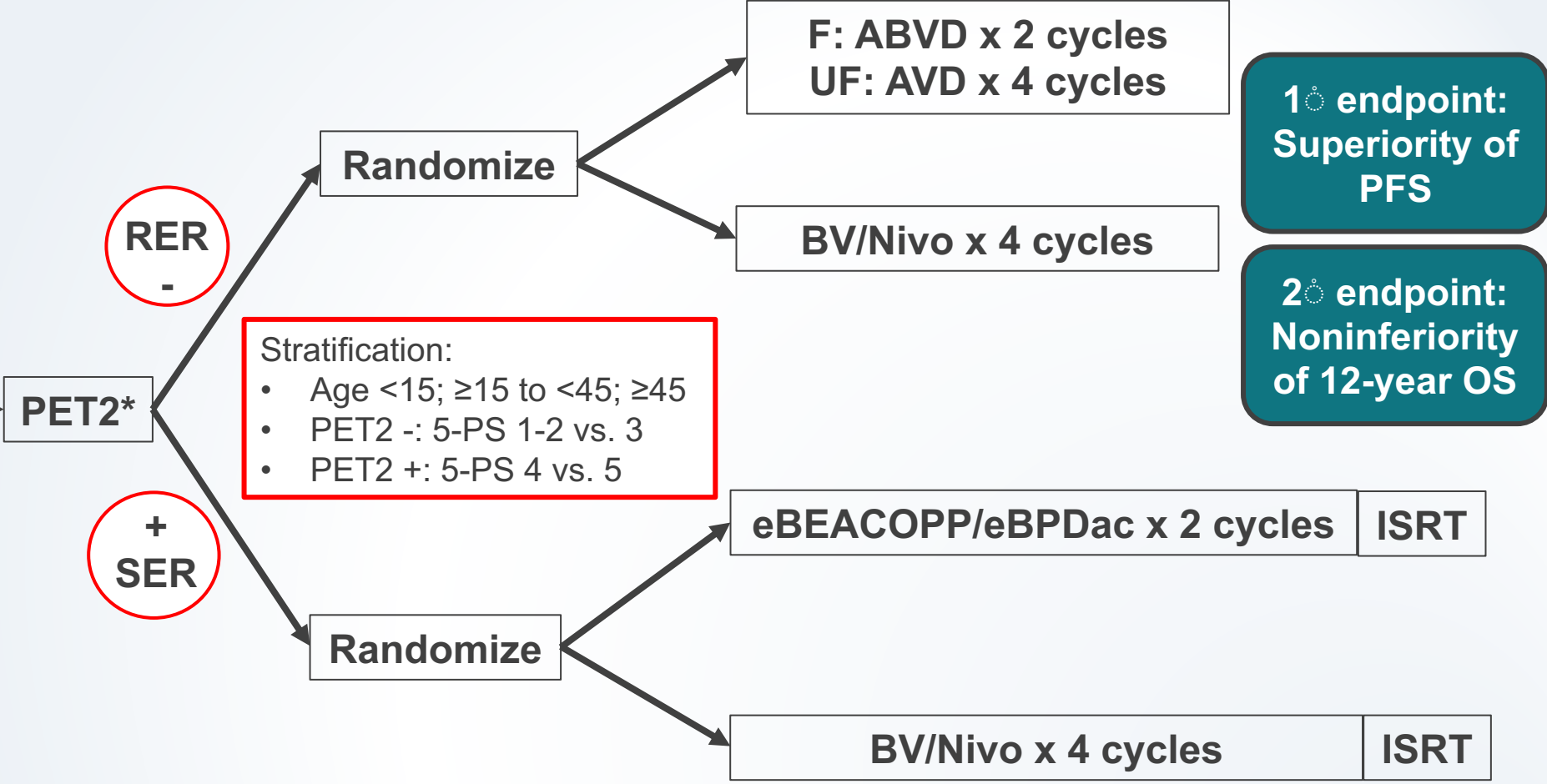
Sample Size Projections:  
 1875 enrolled over 5 years  
 1782 evaluable (1/3 F, 2/3 UF)

- EORTC Favorable (F) and Unfavorable (UF):
- Age  $\geq 50$
  - $>3$  nodal sites
  - ESR  $>50$  if A;  $>30$  if B
  - MTR  $>0.35$
  - Bulky  $\geq 10\text{cm}$

Newly diagnosed, previously untreated stage I or II cHL  
 Ages 5-60

\*Rapid central review  
 PET2-neg = 5-PS 1-3

Projected Numbers  
 PET2 neg (85%): N=1514  
 PET2 pos (15%): N=268



Stratification:

- Age  $<15$ ;  $\geq 15$  to  $<45$ ;  $\geq 45$
- PET2 -: 5-PS 1-2 vs. 3
- PET2 +: 5-PS 4 vs. 5

RER: Rapid Early Responders  
 SER: Slow Early Responders

# Conclusions

- **Multidisciplinary decision making** is key in determining the optimal treatment strategy for early-stage patients.
- Future clinical trials and development of new treatment paradigms for HL aim to **reduce exposure** to chemotherapy and radiotherapy to **minimize** acute and late term effects of treatment.
- Incorporation of **immunotherapy-based treatments** either as **concurrent** or **sequential** therapy with chemotherapy has changed and will continue to change the treatment landscape of HL.
- Sequential **ABVD** → **BV/Nivo** has demonstrated **100% PFS** for interim PET2 negative **early-stage HL** in a smaller phase II study and serves as support for the larger intergroup **AHOD2131** clinical trial.

# Thank you!



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