21ST INTERNATIONAL ULTMANN CHICAGO LYMPHOMA SYMPOSIUM™

Special Considerations in Treating Patients with Lymphoma – Impact of Patient Age: AYA Patients

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THE UNIVERSITY OF CHICAGO MEDICINE & BIOLOGICAL SCIENCES

Disclosures

Advisory board: Seagen, Kite Pharma

Speakers' bureau: Research to Practice

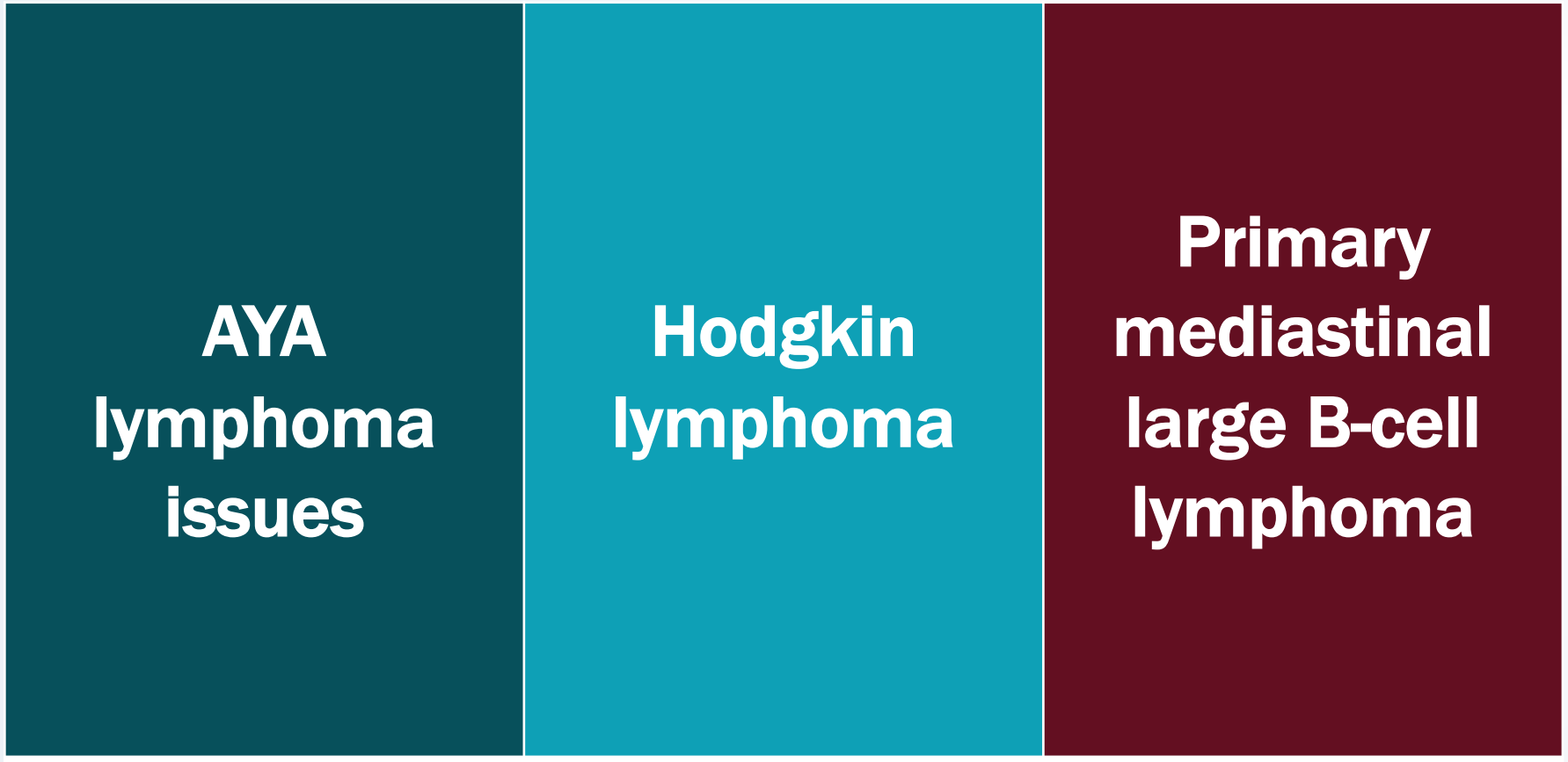
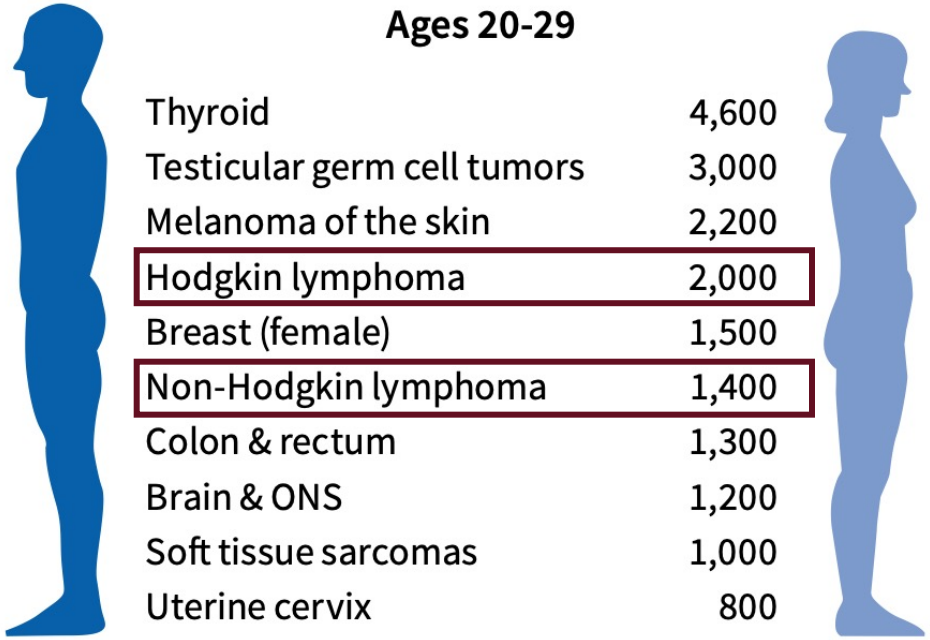

AYA lymphoma issues
Hodgkin lymphoma
Primary mediastinal large B-cell lymphoma

Figure S2. Leading Sites of New Cancer Cases in AYAs, Both Sexes Combined – 2020 Estimates

Estimated New Cases

Ages 15-19		Ages 20-29		Ages 30-39	
Thyroid	800	Thyroid	4,600	Breast (female)	11,100
Hodgkin lymphoma	800	Testicular germ cell tumors	3,000	Thyroid	9,000
Brain & ONS	500	Melanoma of the skin	2,200	Melanoma of the skin	5,500
Non-Hodgkin lymphoma	500	Hodgkin lymphoma	2,000	Colon & rectum	4,100
Testicular germ cell tumors	400	Breast (female)	1,500	Testicular germ cell tumors	3,100
Acute lymphoid leukemia	400	Non-Hodgkin lymphoma	1,400	Uterine cervix	3,000
Bone tumors	400	Colon & rectum	1,300	Non-Hodgkin lymphoma	2,700
Soft tissue sarcomas	400	Brain & ONS	1,200	Kidney	2,400
Melanoma of the skin	200	Soft tissue sarcomas	1,000	Uterine corpus	2,000
Acute myeloid leukemia	200	Uterine cervix	800	Brain & ONS	1,800



ONS = other nervous system. Estimates are rounded to the nearest 100 and exclude basal cell and squamous cell skin cancers, benign and borderline brain, and in situ carcinoma of any kind. Ranking is based on modeled progress and may differ from the most recent observed data.

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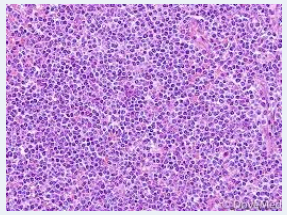
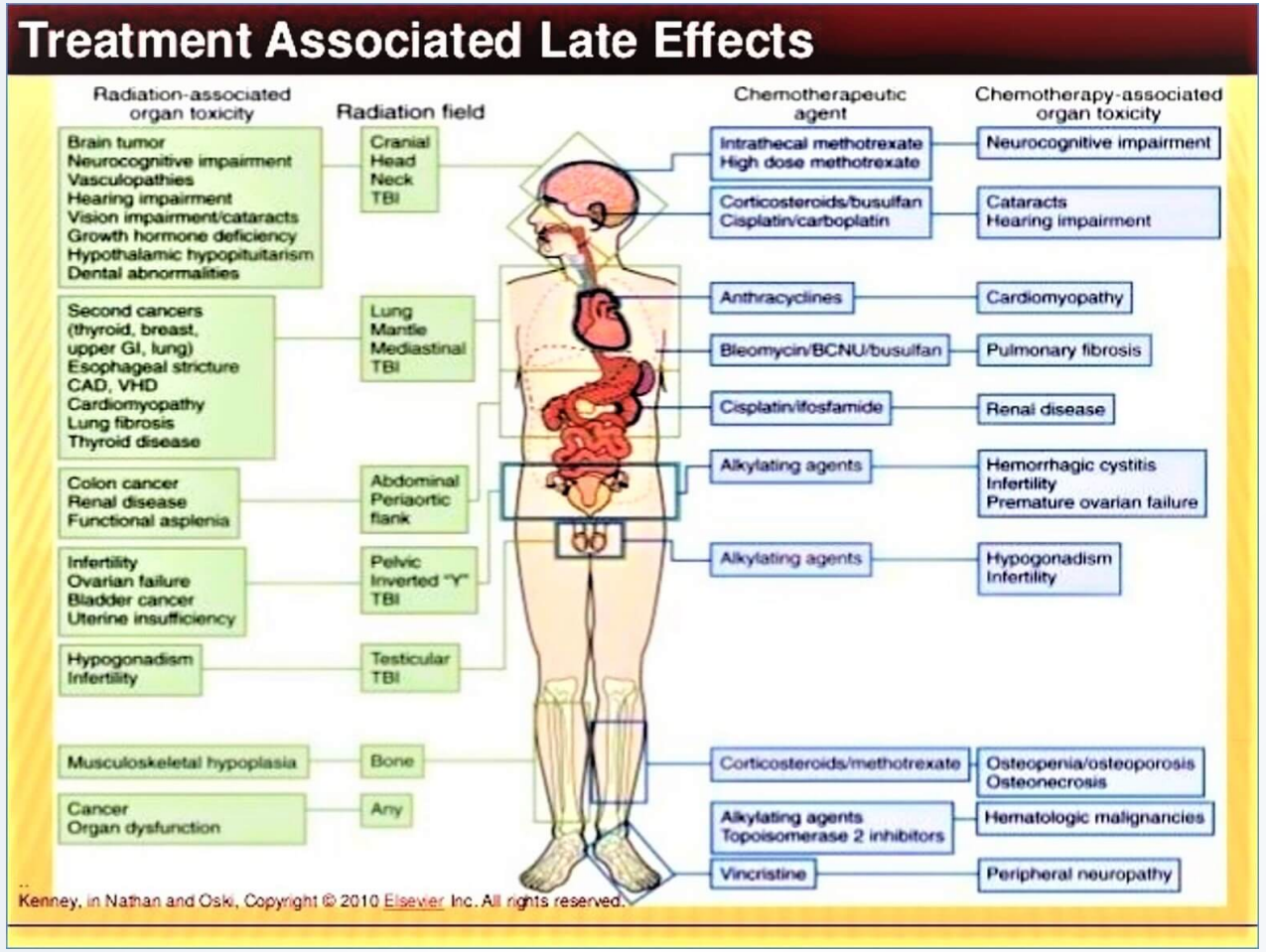
What are key issues in AYA treating patients with lymphoma?

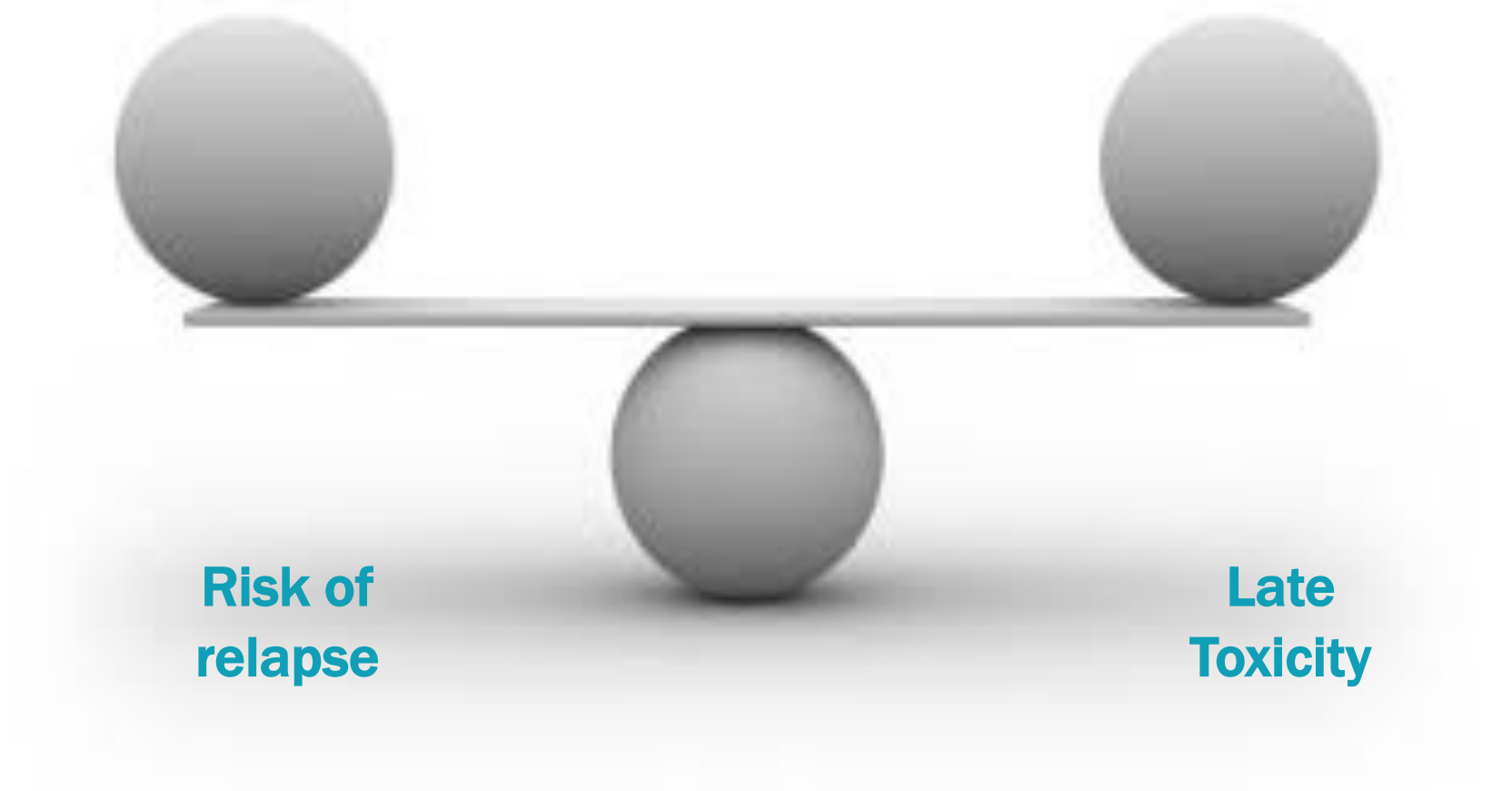


Disease specific issues

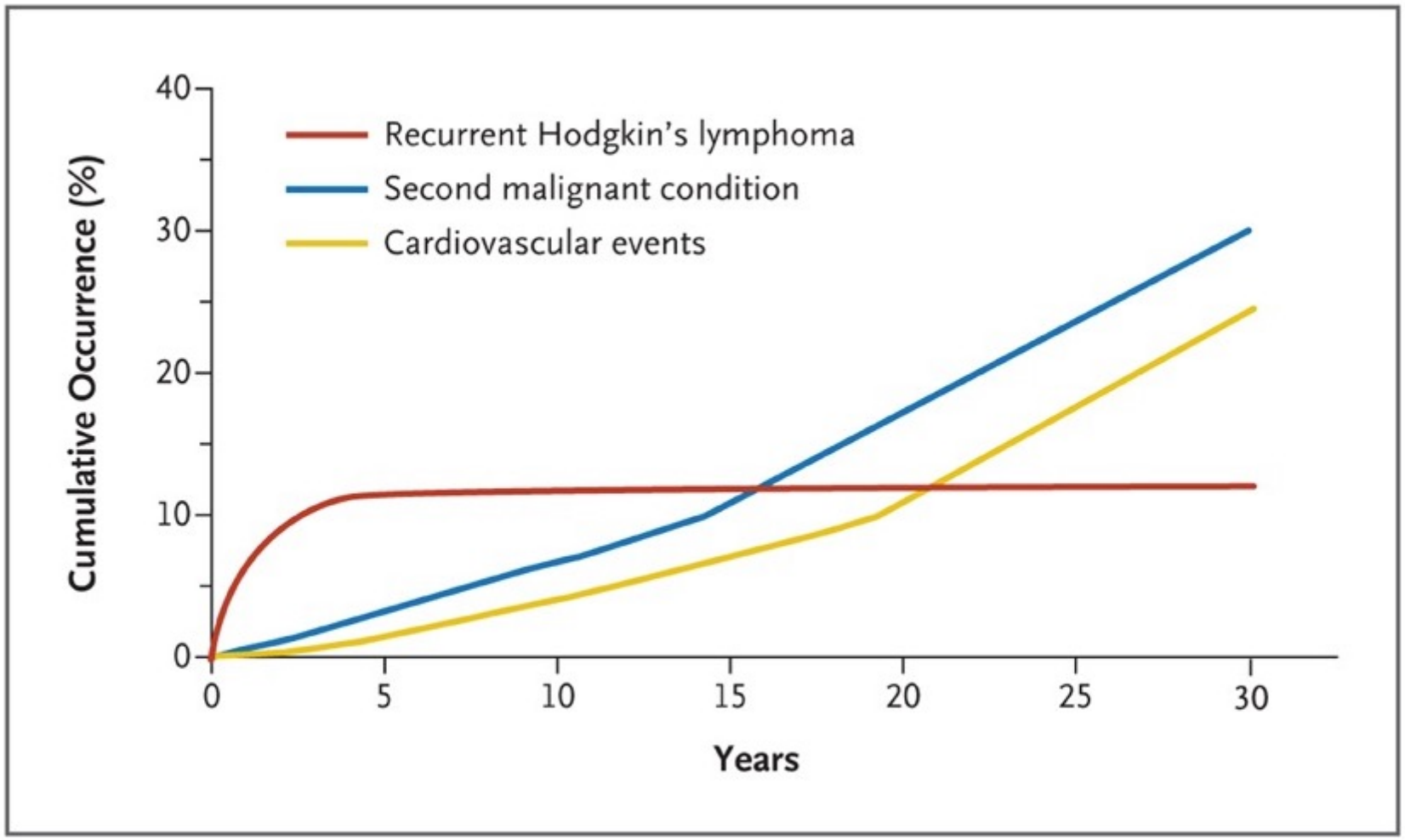


Psychosocial access to care/ adherence

Balancing risks in AYA lymphoma



Competing risks in early stage cHL



Armitage. NEJM 2010

RT related late effects

Secondary cancer:
Long latency
Increasing risk over time
Relates to dose and field

Secondary cancer:
Breast cancer (⬆️<30)
Lung 🚬
GI
Sarcoma
Thyroid

Cardiovascular disease:
CAD
Valvular
Pericardial
Conduction

RT associated risk of breast cancer in cHL survivors dependent on age, ovarian function, dose and volume of RT

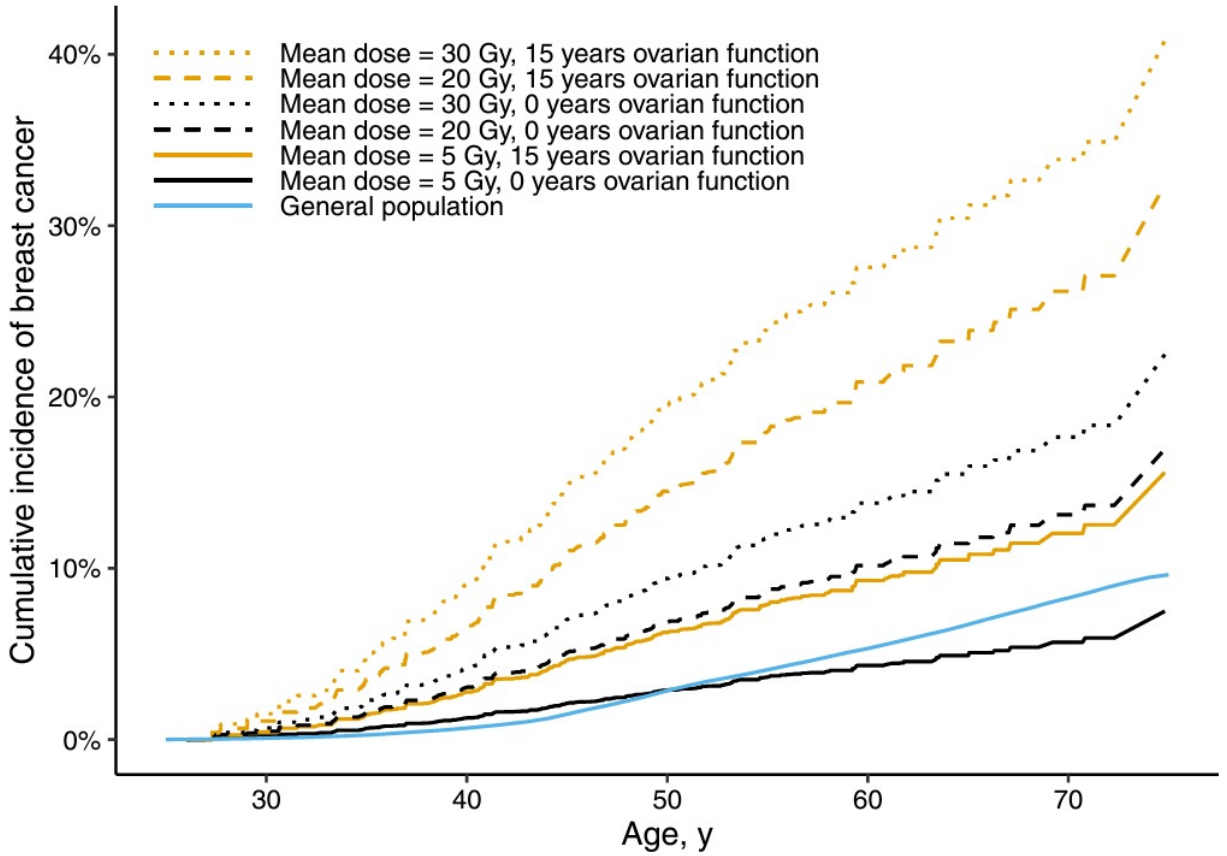


Figure 2. Cumulative incidence of breast cancer for a 5-year survivor of Hodgkin lymphoma treated at age 20 years, according to mean breast dose and duration of intact ovarian function. Case-control data were combined with information from the Hodgkin lymphoma survivors cohort (37), and cumulative incidence estimates were based on model (M1). Death and other cancers (except those treated with surgery only) were treated as competing events.

Roberti S et al. J Natl Cancer Inst 2022

Breast cancer screening in HL

Table 2. Screen-Detected Abnormalities Leading to Biopsies

Scan Generating Biopsy	No. of Biopsies		
	Total	Positive	Negative
MRI and/or mammogram	63 in 45 patients*	18 (8 invasive, 9 DCIS, 1 phyllodes)	45 in 29 patients
MRI alone	25	5 (1 invasive, 3 DCIS, 1 phyllodes)	20 in 17 patients
Mammogram alone	21	6 (1 invasive, 5 DCIS)	15 in 10 patients
Both MRI and mammogram	17	7 (6 invasive, 1 DCIS)	10 in 6 patients

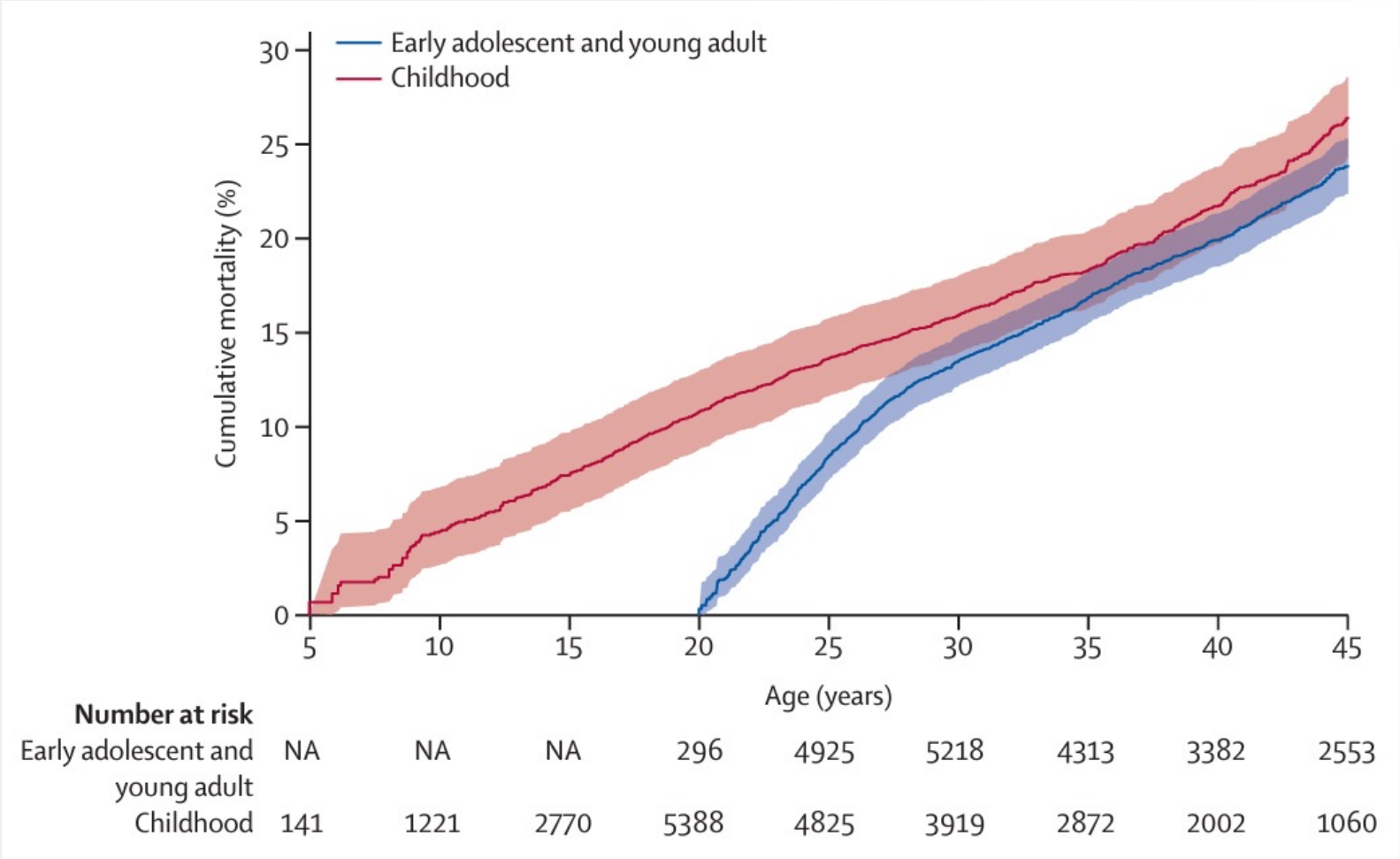
Abbreviations: DCIS, ductal carcinoma in situ; MRI, magnetic resonance imaging.
*One biopsy in 30 patients, two in 13 patients (six women had biopsies in both breasts), three biopsies in one patient (both breasts), and four biopsies in one patient (both breasts).

n= 148 women treated with chest RT
≤ age 35
> 8 years from therapy

	Sensitivity	Specificity
Mammography	68%	93%
MRI	67%	94%
Both	94%	90%

Ng et al. JCO 2013.

Late mortality and chronic health issues common: analysis from the Childhood Cancer Survivor Study



Number at risk									
Early adolescent and young adult	NA	NA	NA	296	4925	5218	4313	3382	2553
Childhood	141	1221	2770	5388	4825	3919	2872	2002	1060

early adolescent/ young adult survivors
n= 5804
35% with HL
10% with NHL

Suh et al. Lancet Oncol. 2020.

Premature ovarian failure

Low risk: Low risk (<25% decrease in likelihood of pregnancy/fertility-related outcome, or <25% increase in risk of infertility/infertility-related outcome)

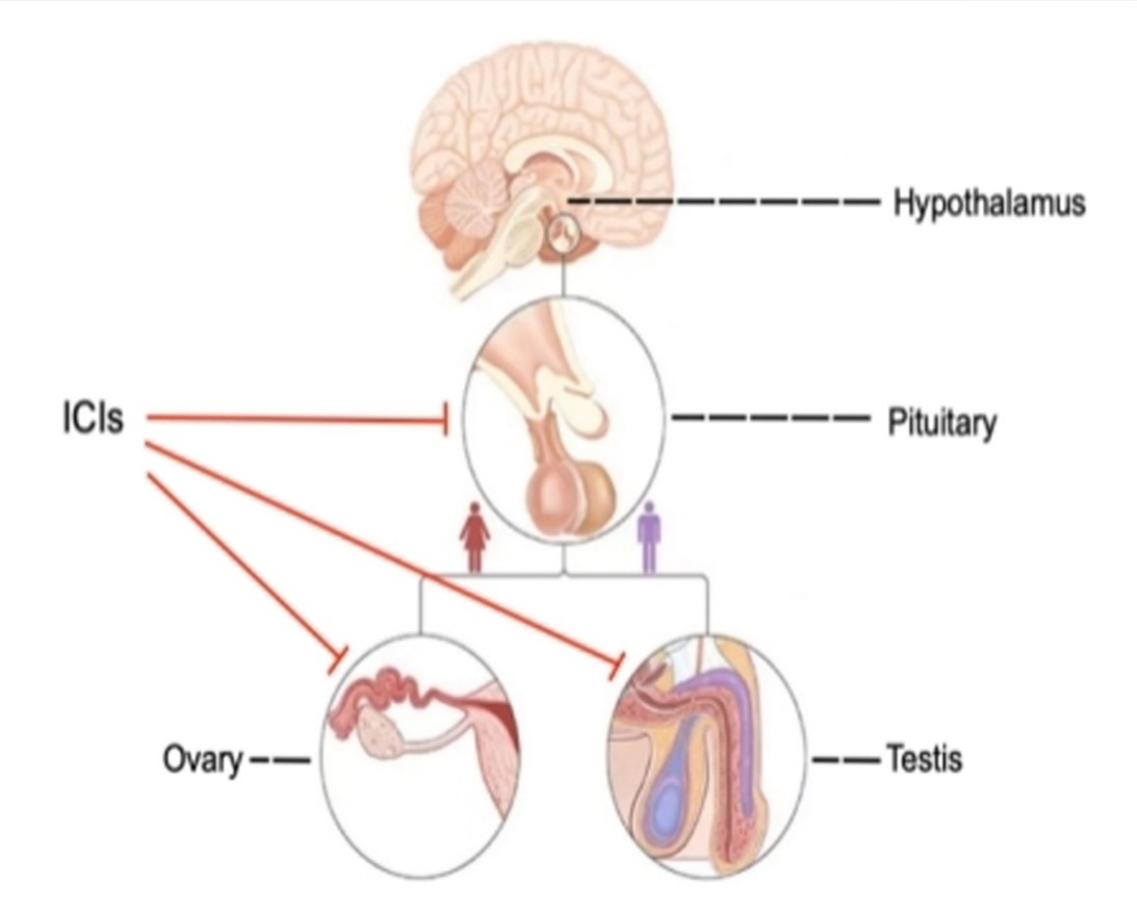
Intermediate risk: Intermediate risk (25–75% decrease in likelihood of pregnancy/fertility-related outcome, or 25–75% increase in risk of infertility/infertility-related outcome)

High risk: High risk (>75% decrease in likelihood of pregnancy/fertility-related outcome, or >75% increase in risk of infertility/infertility-related outcome)

Hodgkin Lymphoma	ABVD	16–35	Pregnancy	70% in survivors, 75% in controls[101]
		<40	Amenorrhea	3%–7%[96–98,100]
	BEACOPP	<40	Amenorrhea	40%–67%[96,98]
Non-Hodgkin Lymphoma	CHOP	17–40	Amenorrhea	5%*[102,103]
Leukemias, lymphomas, benign hematologic disorders	HCT conditioning (chemotherapy and/or TBI)	21–45	Pregnancy	Pregnancy rate <3%[115,116,156]; OR for not experiencing pregnancy = 35.9 (95% CI = 23.2 to 55.8) in combined male/female cohort, OR = 3.0 (95% CI = 1.3 to 6.9) for female sex[116]
	(Chemotherapy and/or TBI)	<18 (prepubertal)	Gonadal insufficiency	74-99%[118,192]

Consider early referral to reproductive endocrinology
AMH levels correlate with ovarian reserve in women

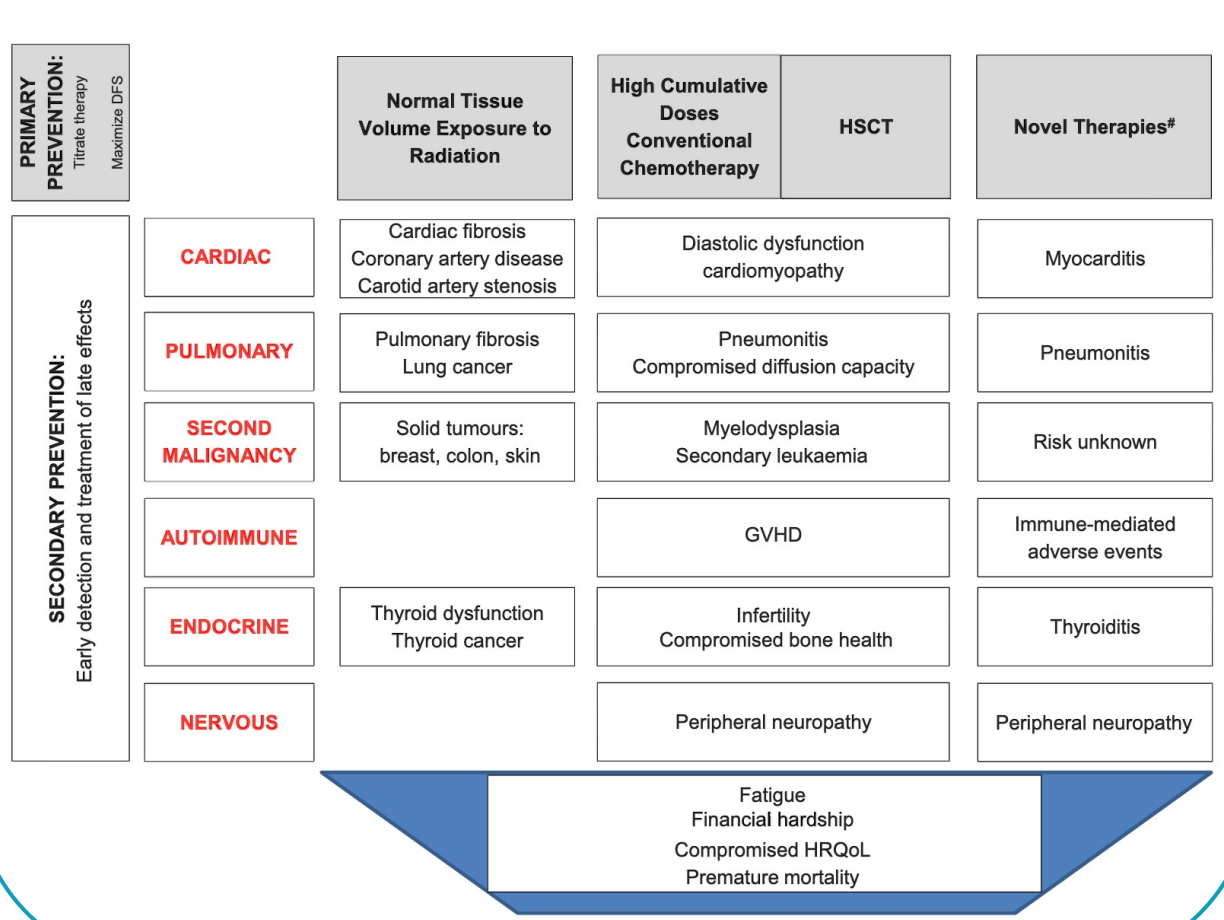
Poorvu et al. JNCI Cancer Spect 2019.



What about PD-1 inhibitors and fertility?

Tuerxun at al. Crit Rev Oncol Hematol. 2023

Survivorship issues in AYA patients



National Comprehensive Cancer Network®

NCCN Guidelines Version 2.2022
Adolescent and Young Adult (AYA) Oncology

NCCN Guidelines Index
Table of Contents
Discussion

SURVIVORSHIP

EXPOSURE	RECOMMENDATION See Screening Recommendations (AYAO-B)	
Any exposure	• Recommend a dental exam and cleaning every 6 mo for patients who received chemotherapy and/or radiation therapy	
Total body irradiation (TBI)	• Thyroid disease screening • Cardiovascular risk factor screening	• Screening for secondary malignant neoplasms (SMNs)
Cranial or craniospinal radiation	• Neuroendocrine axis screening • Neuropsychological evaluation • Ocular screening	• Audiologic evaluation for doses ≥30 Gy • Colorectal cancer screening (for lumbar and sacral spine)
Chest radiation	• Individual assigned female at birth: see Breast Cancer Screening • Cardiovascular risk assessment and screening	• Screening for cardiomyopathy • Screening for valvular heart disease • Pulmonary function screening
Neck radiation	• Thyroid disease screening	
Abdominal or pelvic radiation	• Colorectal cancer screening • Assessment of gonadal function	• Assessment for bowel incontinence • Screening for kidney or bladder disease
Intrathecal chemotherapy and high CNS penetrating systemic chemotherapy (high-dose methotrexate, Ara-C)	• Neuropsychological evaluation	
Alkylating agents	• Screening for kidney or bladder disease • Assessment of gonadal function	• Screening for treatment-related AML (t-AML) or myelodysplasia • Pulmonary function screening (for selected agents)
Anthracyclines	• Screening for cardiomyopathy • Screening for t-AML or myelodysplasia	
Bleomycin	• Pulmonary function screening	
Cisplatin/ carboplatin	• Cardiovascular risk assessment • Screening for kidney and/or bladder disease • Audiologic evaluation	• Screening for t-AML or myelodysplasia • Screening for peripheral neuropathy • Screening for gonadal function
Epipodophyllotoxins	• Screening for t-AML or myelodysplasia	

Castellino et al. Br J of Hematology 2019

Psychosocial late effects

Acute and persistent fatigue very common in HL survivors

Cognitive function
Anxiety
Mood disorders
Sexual dysfunction

Kreissl et al. Lancet Oncol. 2016

Table 1. Components of a multidisciplinary team for adolescents and young adults with Hodgkin lymphoma

	Clinician	Advanced practice provider	Nurse coordinator	Social worker	Psychology and psychiatry	Patient navigator	Fertility specialist
Diagnosis	X						
Treatment plan	X	X					
Side effect management	X	X	X				
Fertility	X	X					
Psychosocial concerns (work, school, relationships, family, and social life)	X		X	X	X	X	
Navigating the health system	X	X	X	X		X	
Treatment compliance	X	X	X	X			
Financial counseling & assistance			X	X		X	
Nutrition	X	X	X				
Connection to peer support				X		X	
General resource connection				X		X	
Survivorship	X	X	X	X		X	

Multi-disciplinary care critical in AYA lymphoma

Galloway et al. Curr Treat Option Onc 2021

Hodgkin lymphoma

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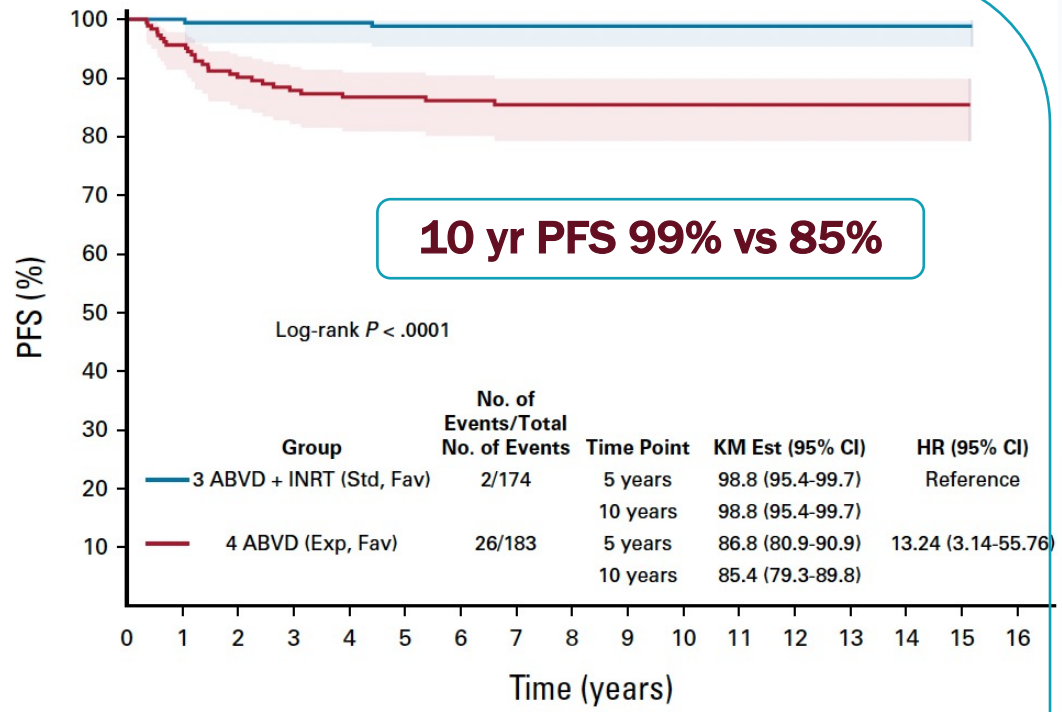
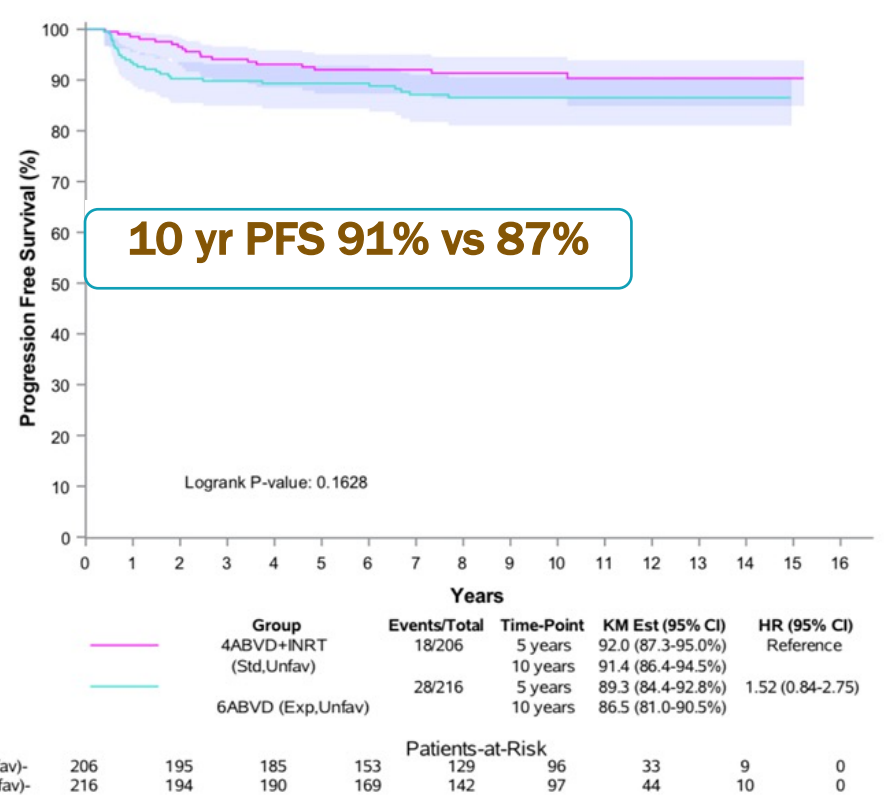
Early stage HL therapy

Current standard of care	Recent advances	On-going
ABVD chemotherapy PET adapted/individualized use of RT	Many phase 2 studies with encouraging PFS with less RT	Randomized study to assess impact of BV and PD-1 inhibitors

H10: Long term follow-up of PET 2 negative patients

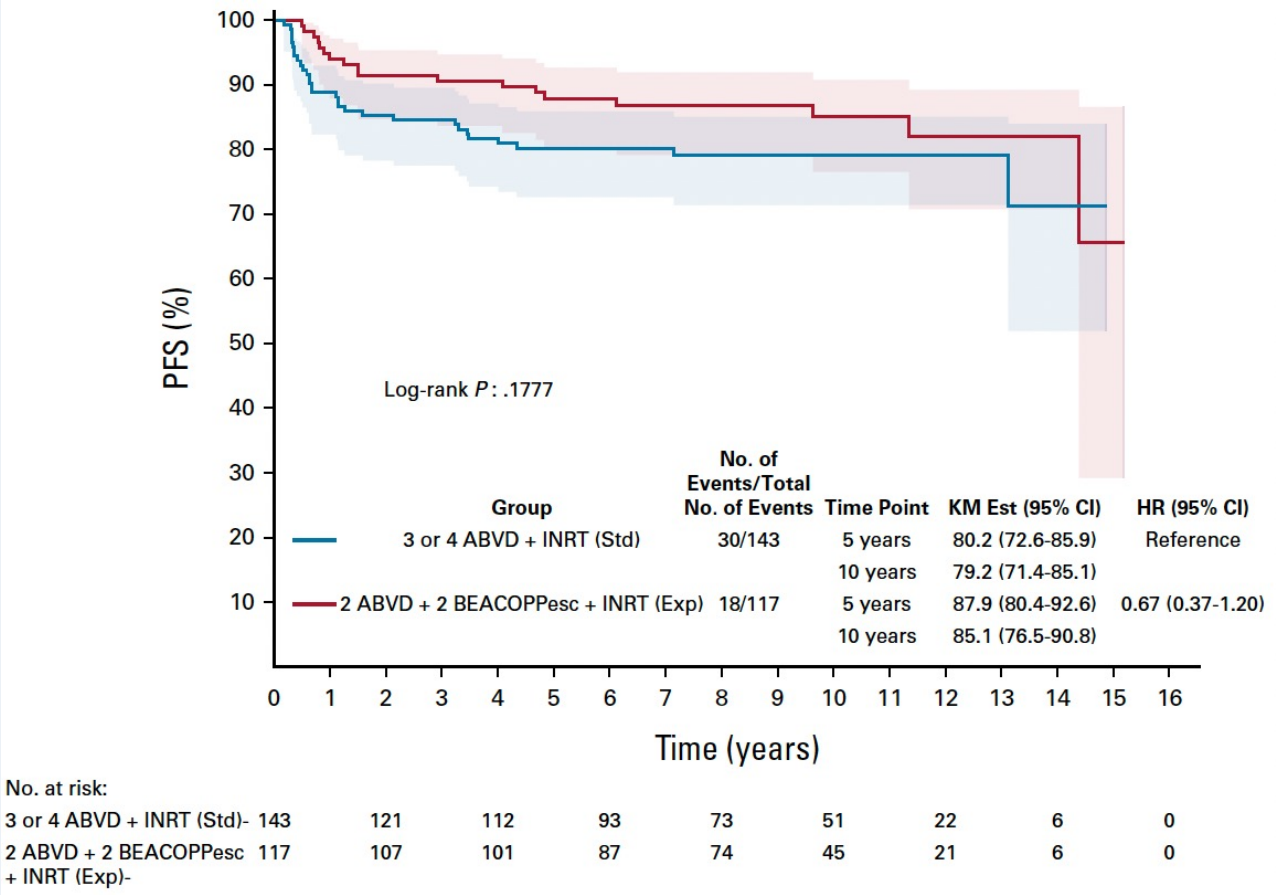
Positive PET = Deauville 3-5
81% of patients PET2 negative





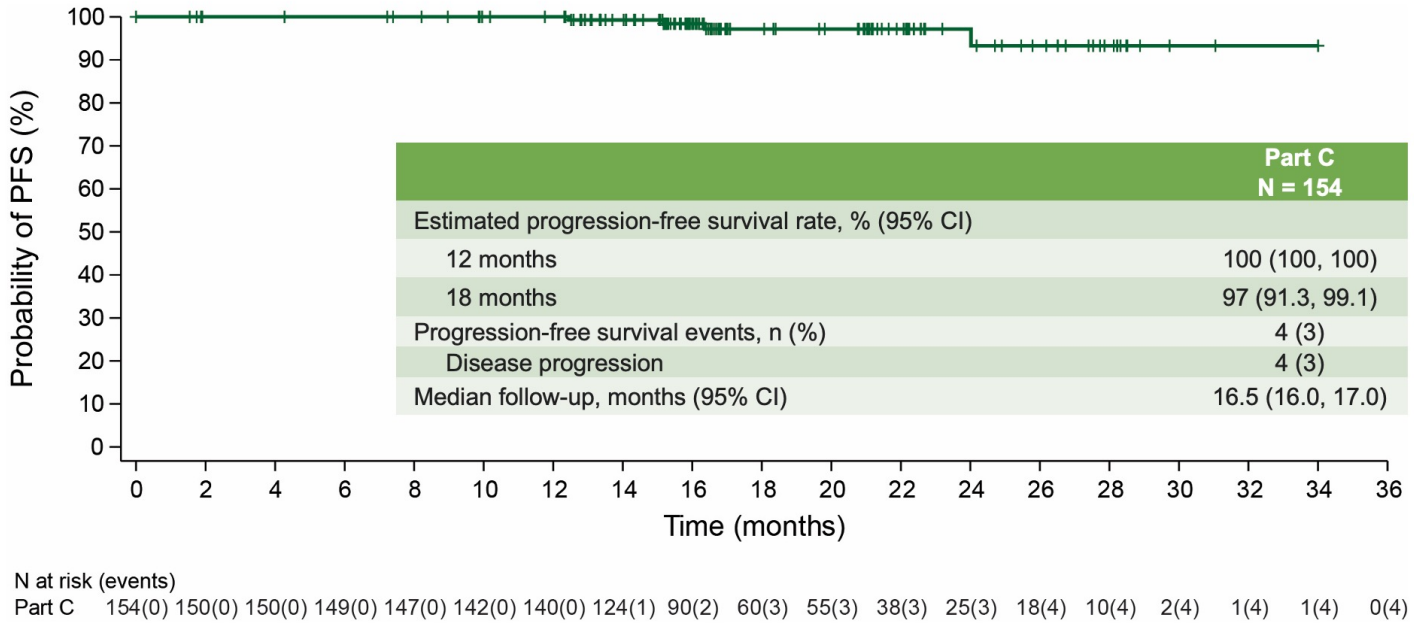
H10: long term follow-up of PET 2 positive patients

Positive PET = Deauville 3-5
19% of patients PET2 positive



10 yr PFS 80% vs 85%

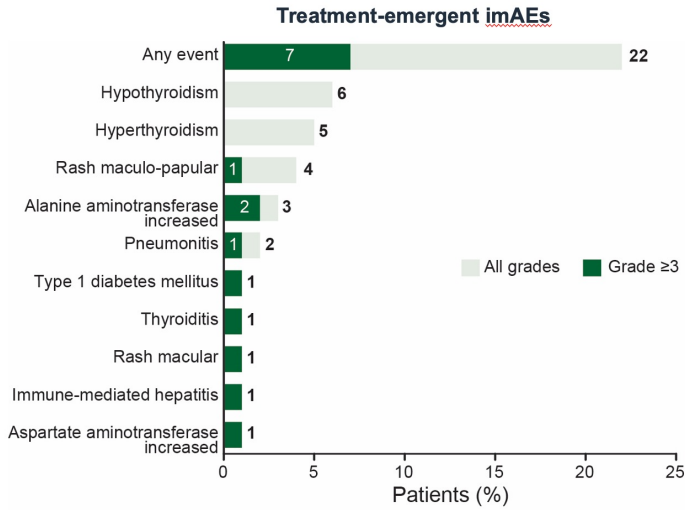
BV+Nivo plus AD x 4 in non bulky stage I/II stage HL



	Part C N = 154
Estimated progression-free survival rate, % (95% CI)	
12 months	100 (100, 100)
18 months	97 (91.3, 99.1)
Progression-free survival events, n (%)	4 (3)
Disease progression	4 (3)
Median follow-up, months (95% CI)	16.5 (16.0, 17.0)

N at risk (events)

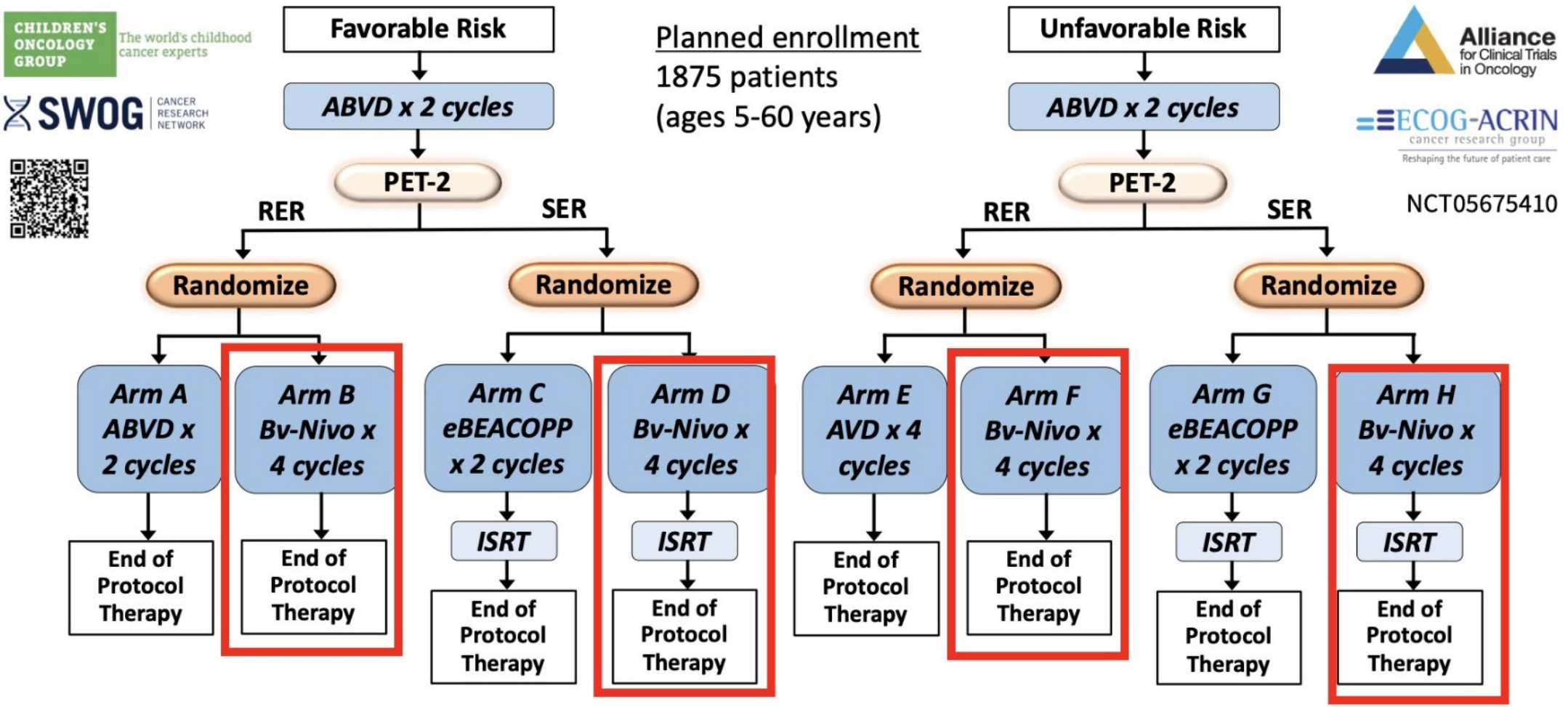
Part C	154(0)	150(0)	150(0)	149(0)	147(0)	142(0)	140(0)	124(1)	90(2)	60(3)	55(3)	38(3)	25(3)	18(4)	10(4)	2(4)	1(4)	1(4)	0(4)



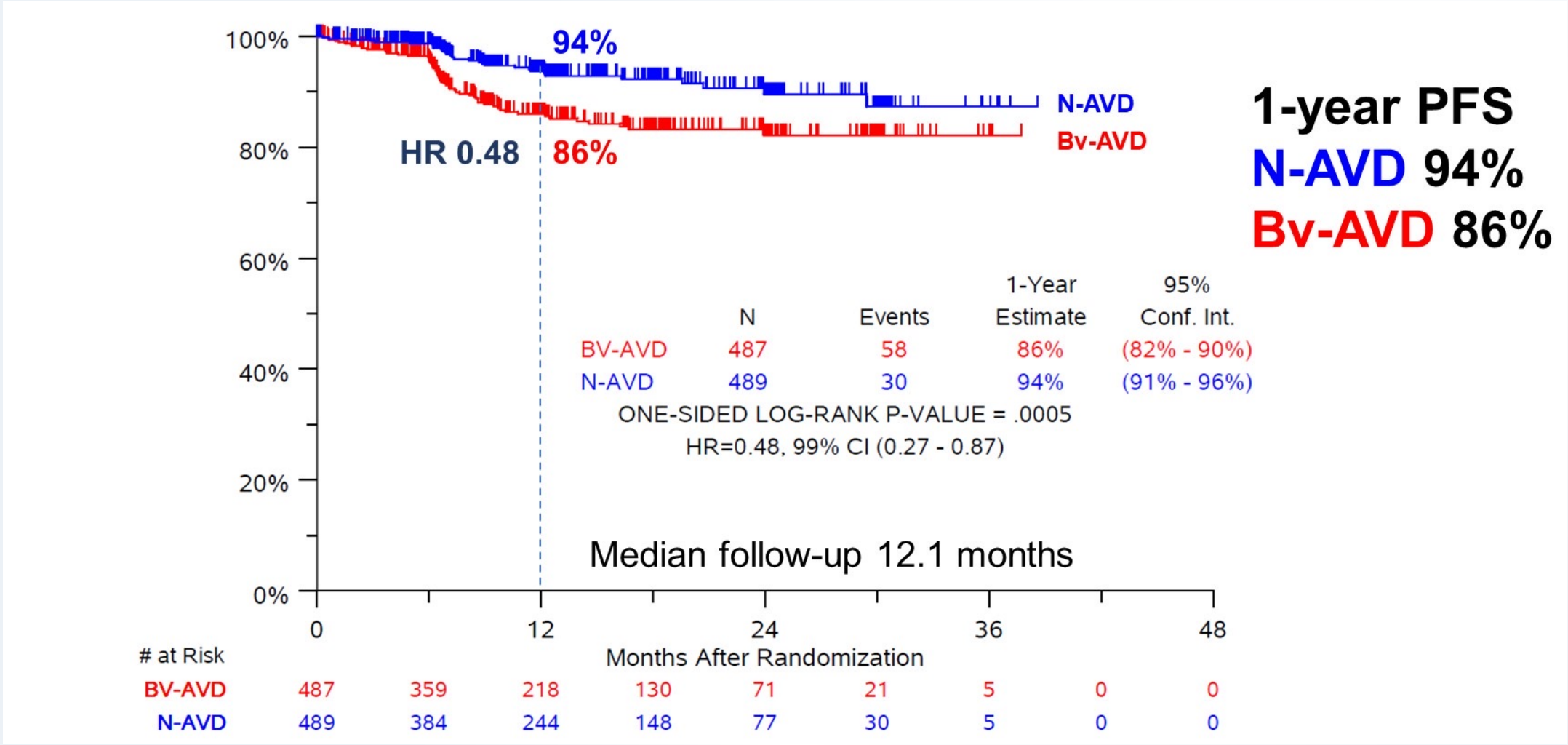
- The maximum grades for immune-mediated adverse events (imAEs) reported were primarily grade 1-2, and were consistent with the safety profile of nivolumab
- 4/154 (3%) had imAEs leading to discontinuation of nivolumab:
  - Pneumonitis (n=2), hepatitis (n=1), thyroiditis (n=1)

Abramson et al. ASH 2023

Standard therapy vs. immuno-oncology for children and adults with newly diagnosed stage I and II classic HL: AHOD 2131



Primary endpoint met: superior PFS of nivolumab-AVD vs BV-AVD



Herrera et al. ASCO 2023

Results favor N-AVD with regard short-term toxicities

	Received g-csf	Febrile neutropenia	Thyroid dysfunction	ALT increased	Peripheral sensory neuropathy	Peripheral motor neuropathy	Discontinued N or BV
N-AVD	54%	5%	10%	31%	29%	4%	11%
BV-AVD*	95%	7%	1%	41%	55%	7%	22%

* Growth factor support mandated per protocol

Herrera et al. ASCO 2023

PMBCL

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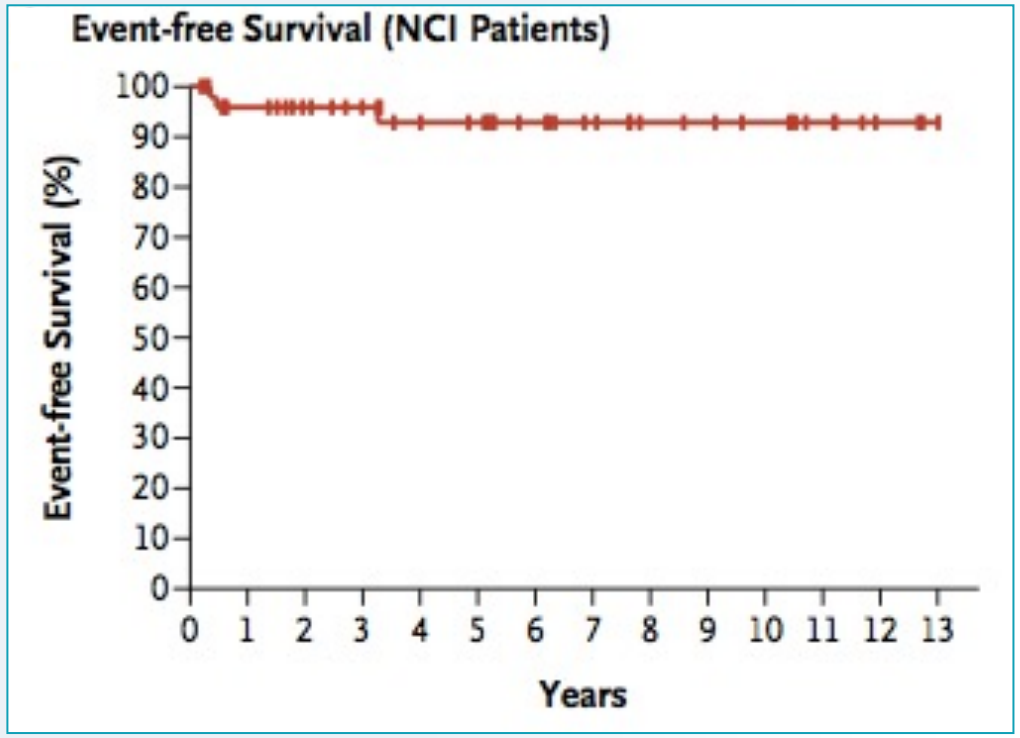
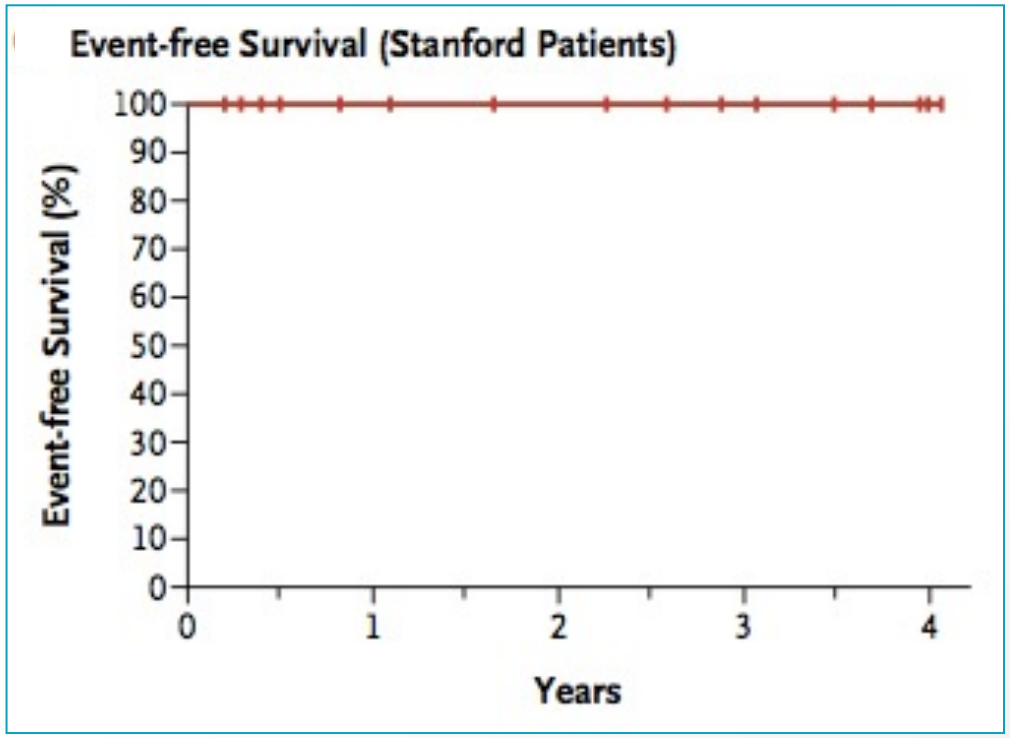
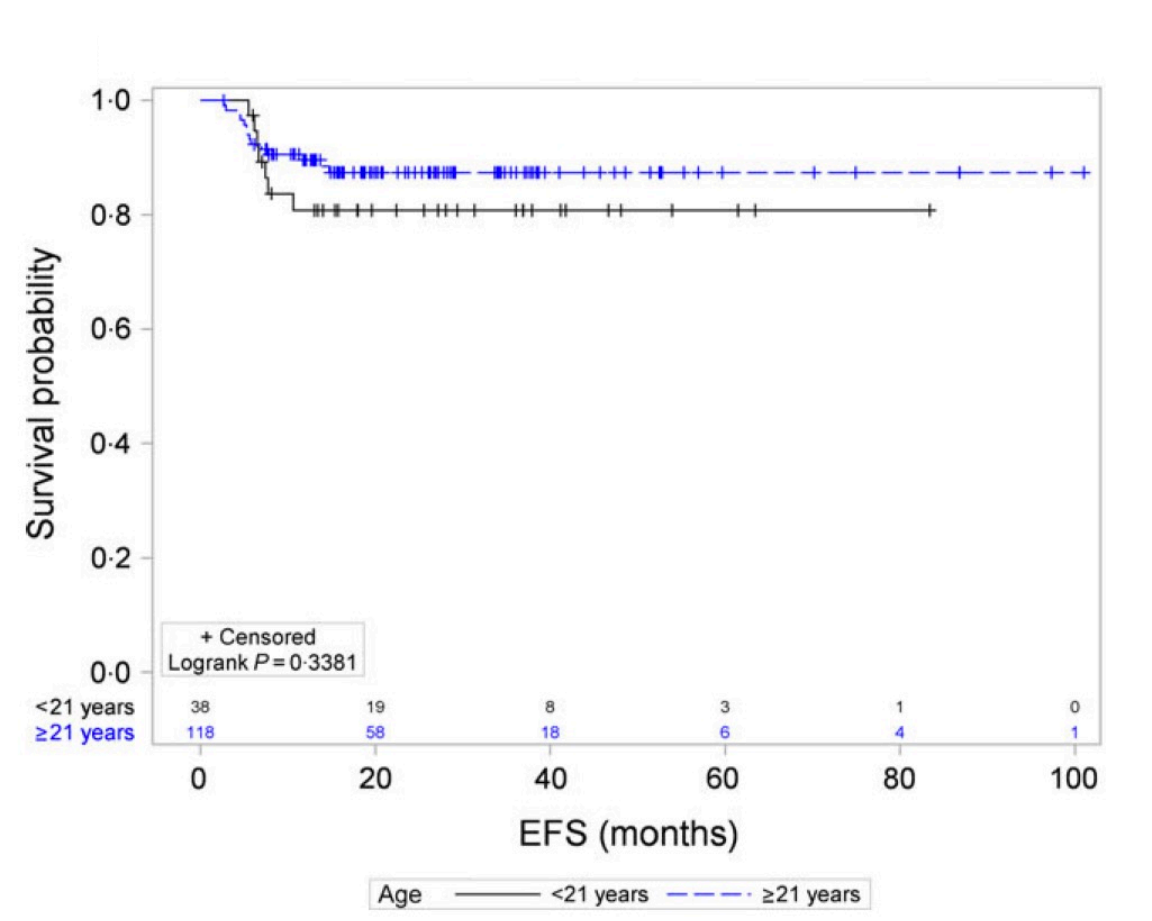
Dose adjusted REPOCH associated with very high EFS in prospective phase 2 study

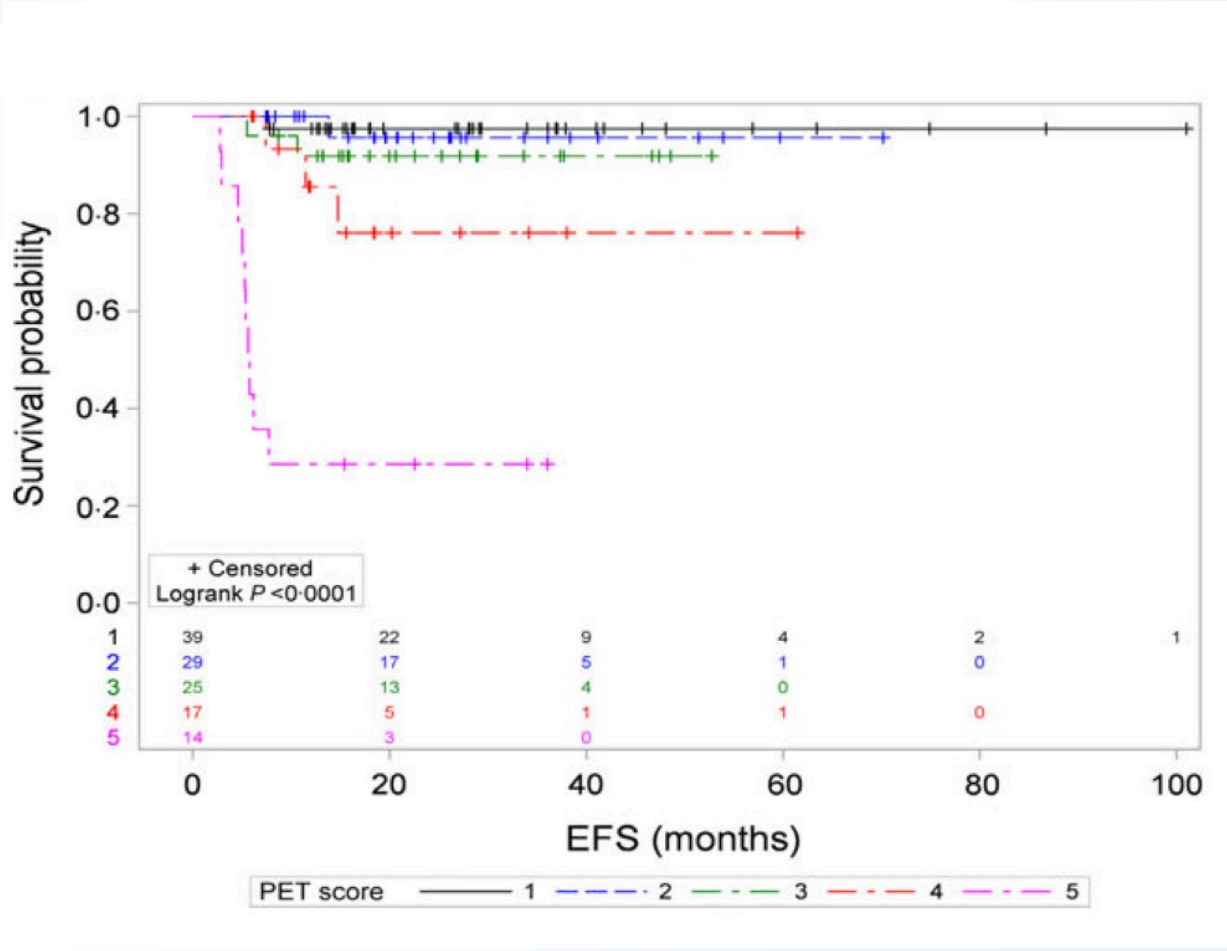




Dunleavy K et al. NEJM 2013

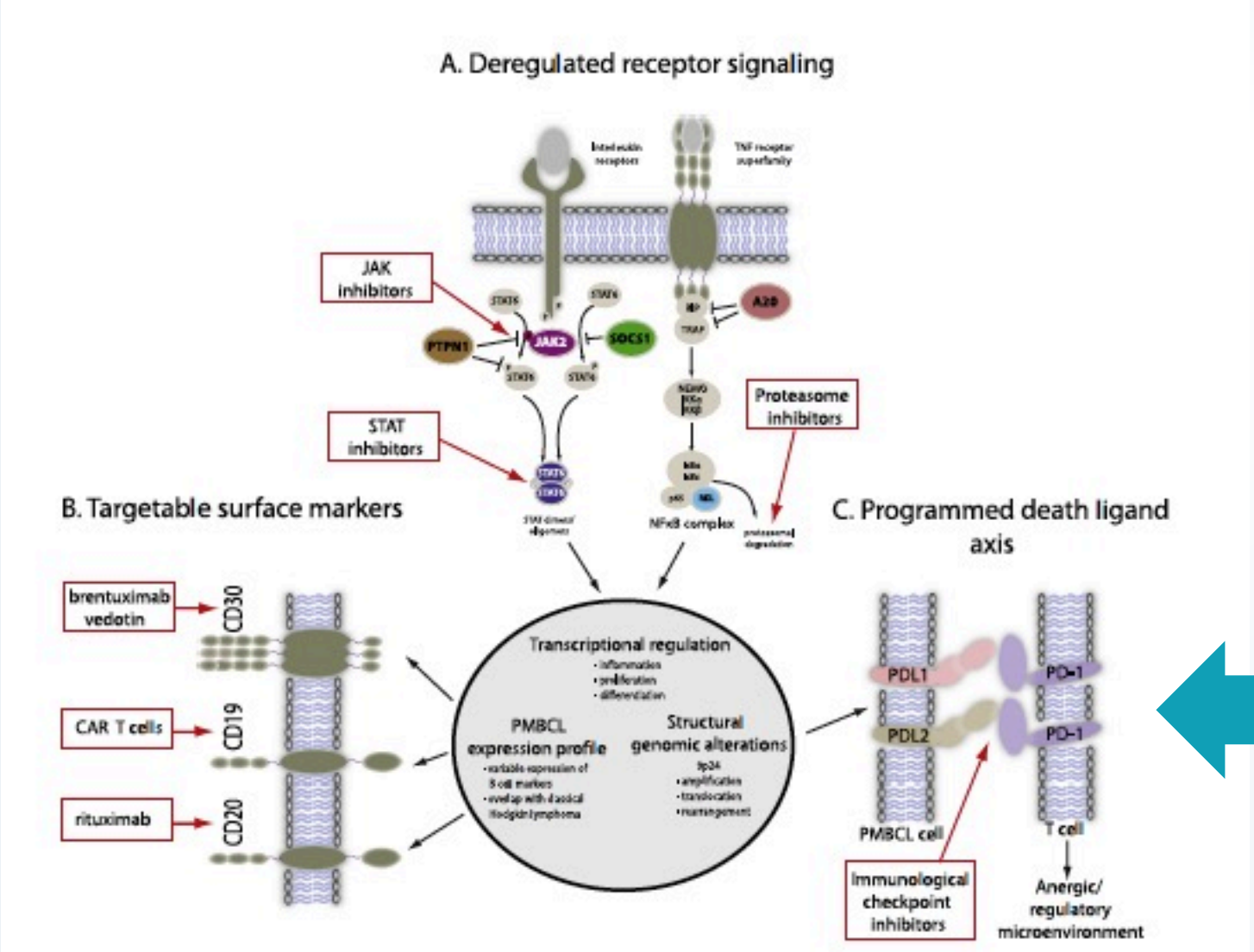
“Real world” outcomes with DA-REPOCH slightly less favorable than trial data





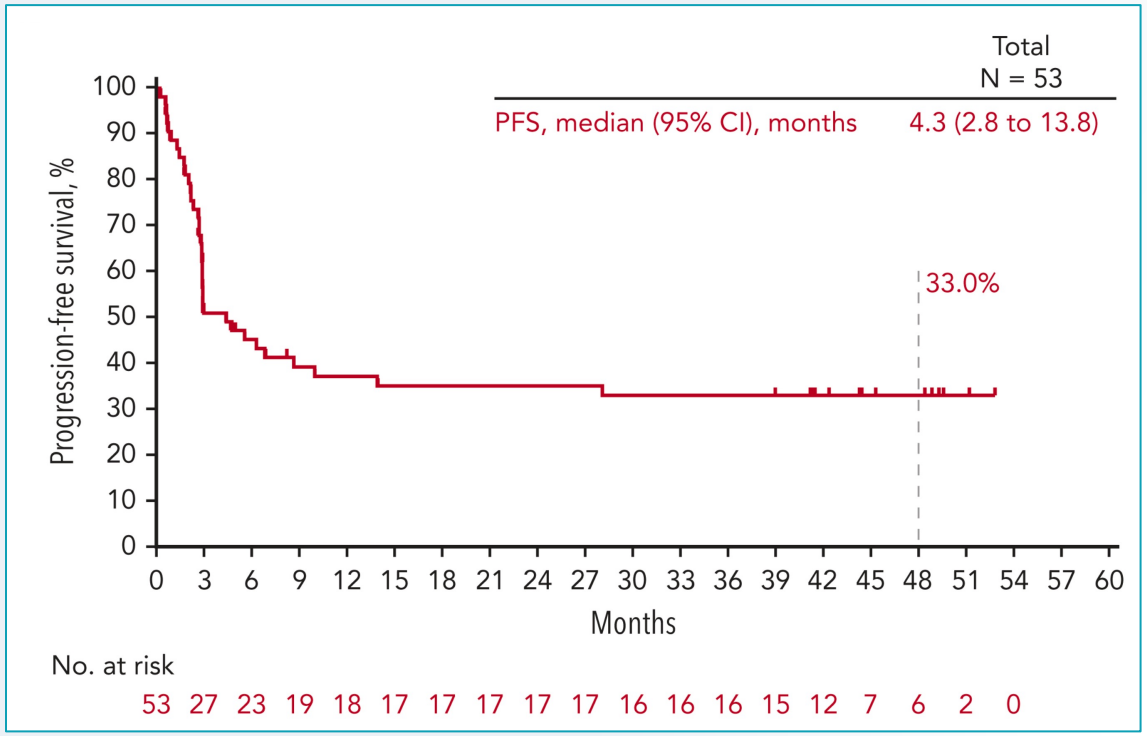
Giulino-Roth et al. Br J Hem 2017

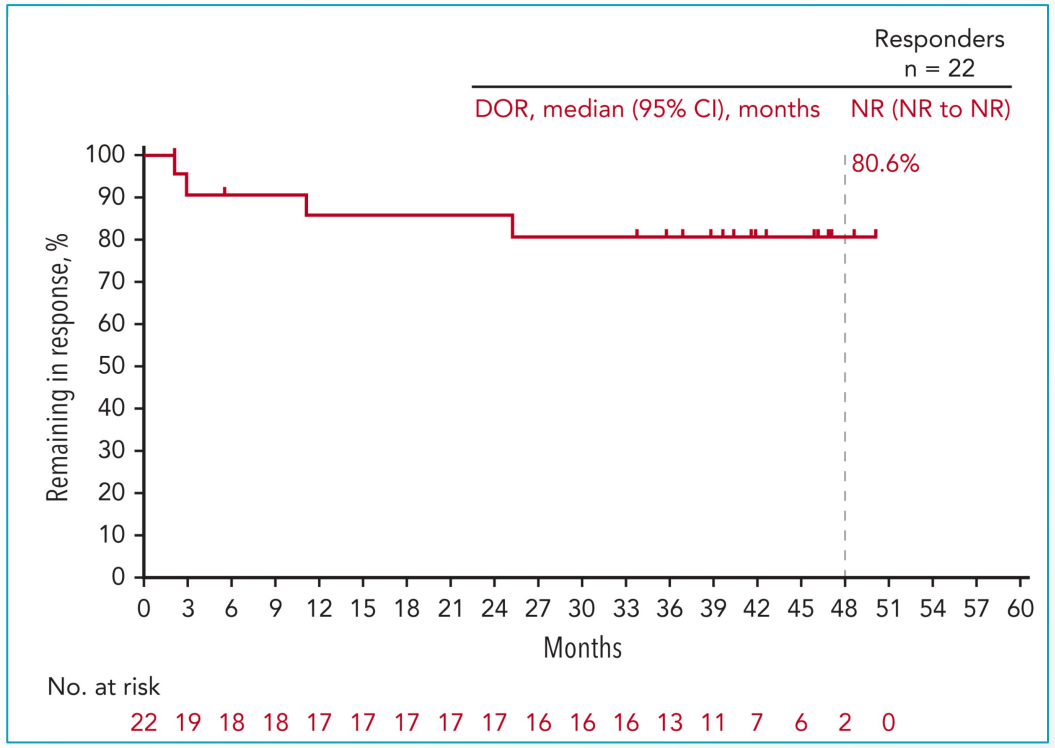
Biology of PMBCL and targeted agents



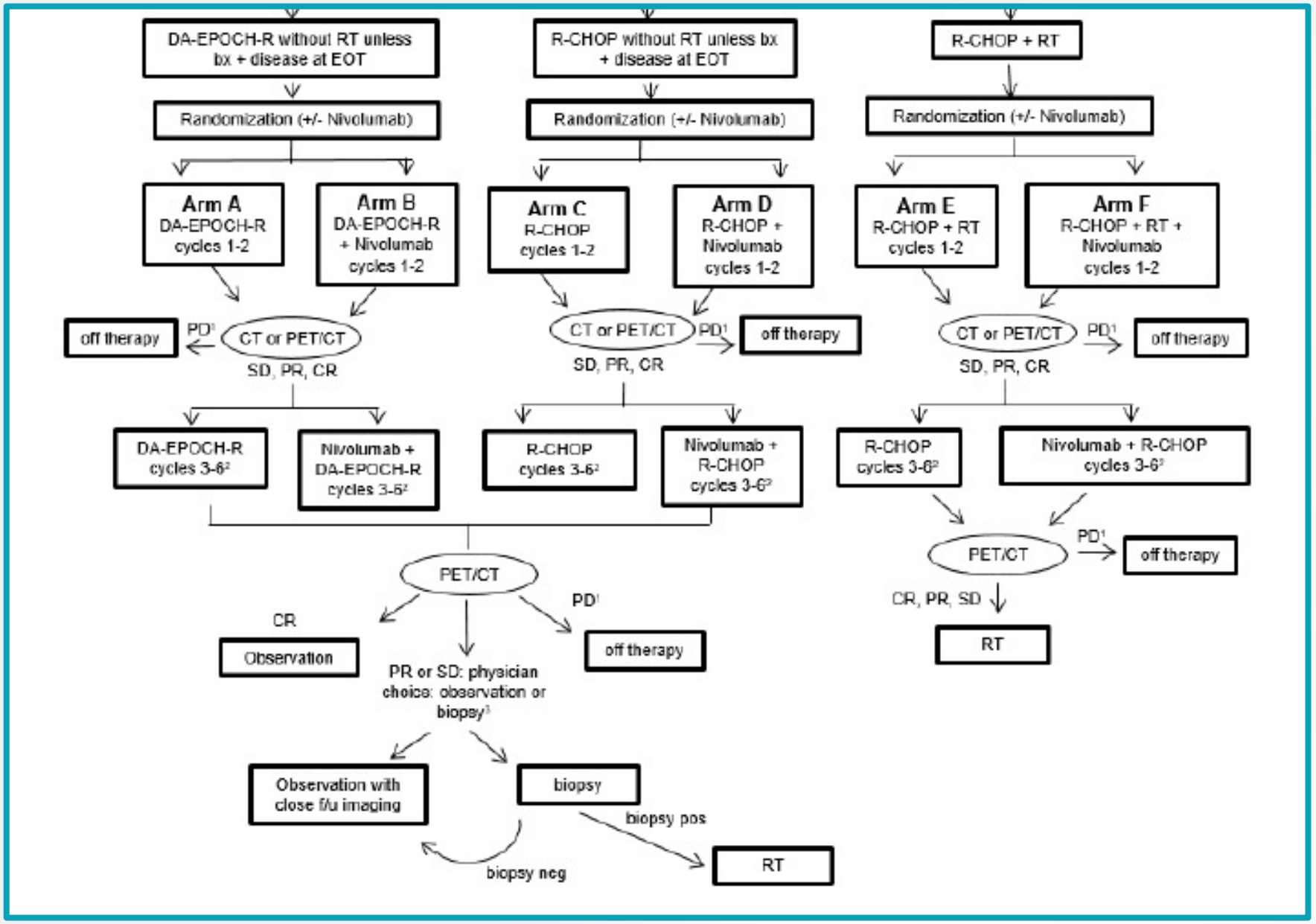
Dunleavy and Steidl. Sem in Hem 2015

Pembrolizumab with durable response in subset of relapsed/ref PMBCL





Zinzani et al, Blood 2023



ANHL1931: A Randomized Phase III trial of Nivolumab in Combination with Chemo-immunotherapy for the Treatment of Newly Diagnosed Primary Mediastinal B-cell Lymphoma

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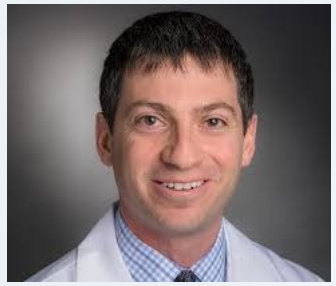

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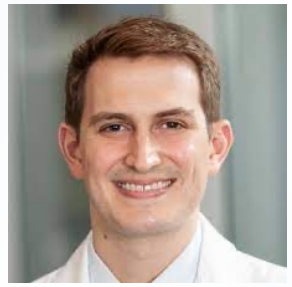

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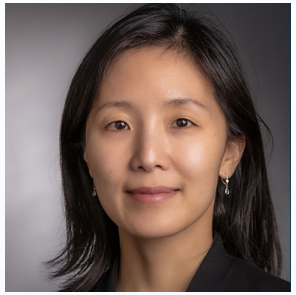

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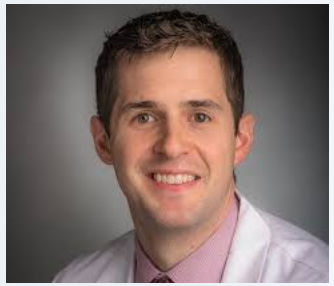

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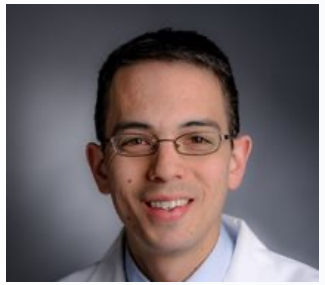

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THANK YOU!

Moccia et al. JCO. 2012