IN PURSUIT OF *YOUR CURE.*™

# Relapsed /Refractory Hodgkin Lymphoma 2024

Craig Moskowitz, MD
Physician in Chief for Clinical Affairs & Clinical Research, Oncology Service Line
Sylvester Comprehensive Cancer Center
Professor of Medicine, Miller School of Medicine
University of Miami Health System

SYLVESTER COMPREHENSIVE CANCER CENTER
UNIVERSITY OF MIAMI HEALTH SYSTEM

NCI Cancer Center
A Cancer Center Designated by the National Cancer Institute

## Disclosures..

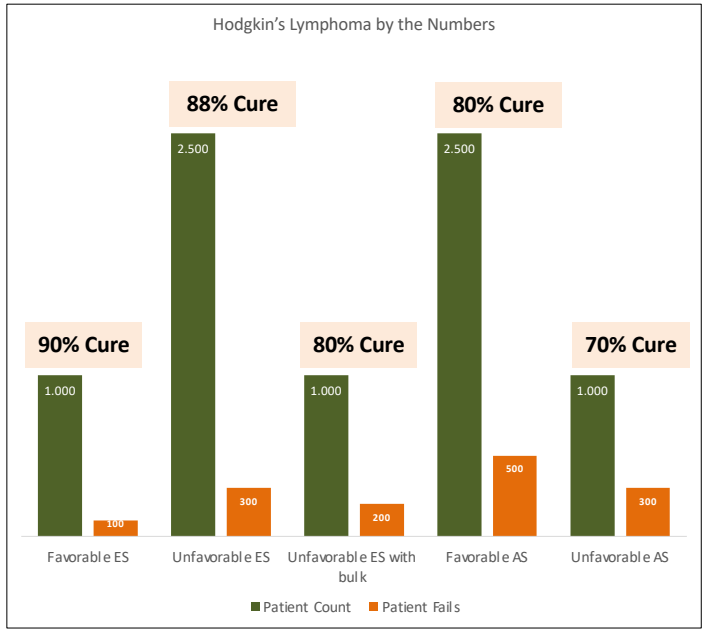
Research support-ADC therapeutics, Merck, Seattle Genetics, Astra Zeneca

Scientific Advisory Board-ADC therapeutics, Merck, Takeda, Merck, Seattle Genetics, Astra Zeneca. Incyte, Genmab

SYLVESTER COMPREHENSIVE CANCER CENTER
UNIVERSITY OF MIAMI HEALTH SYSTEM

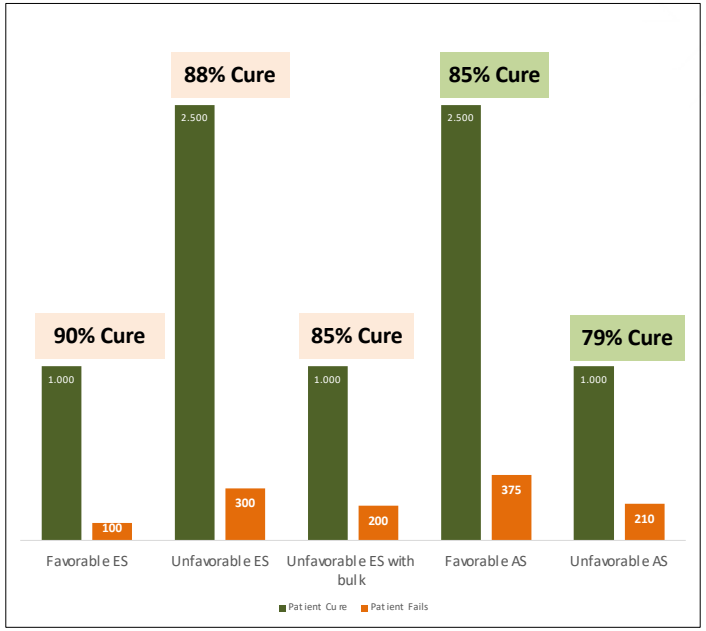
# Hodgkin Lymphoma by the Numbers

**Optimal upfront treatment 8,500 patients (Pre BV)**



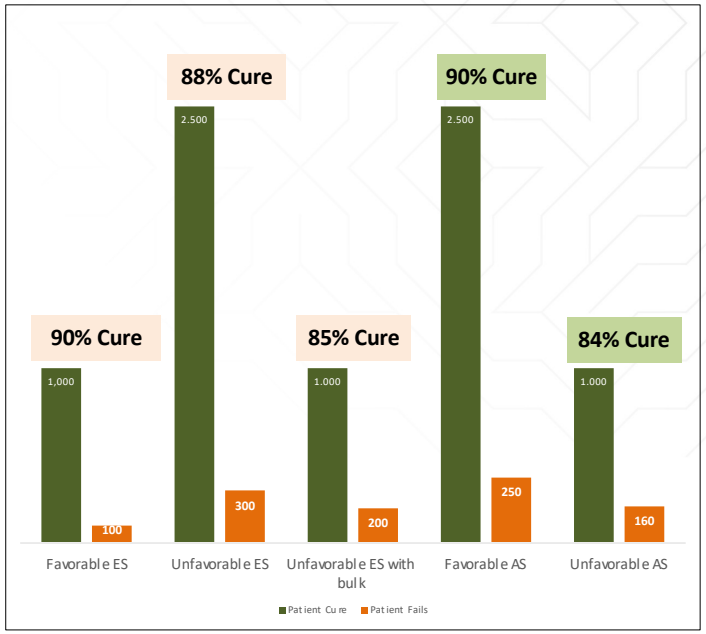

1400 pts need SLT

**Optimal upfront treatment 8,500 patients (post BV)**




1135 pts need SLT

**Optimal upfront treatment 8,500 patients (post CPI)**




1010 pts need SLT

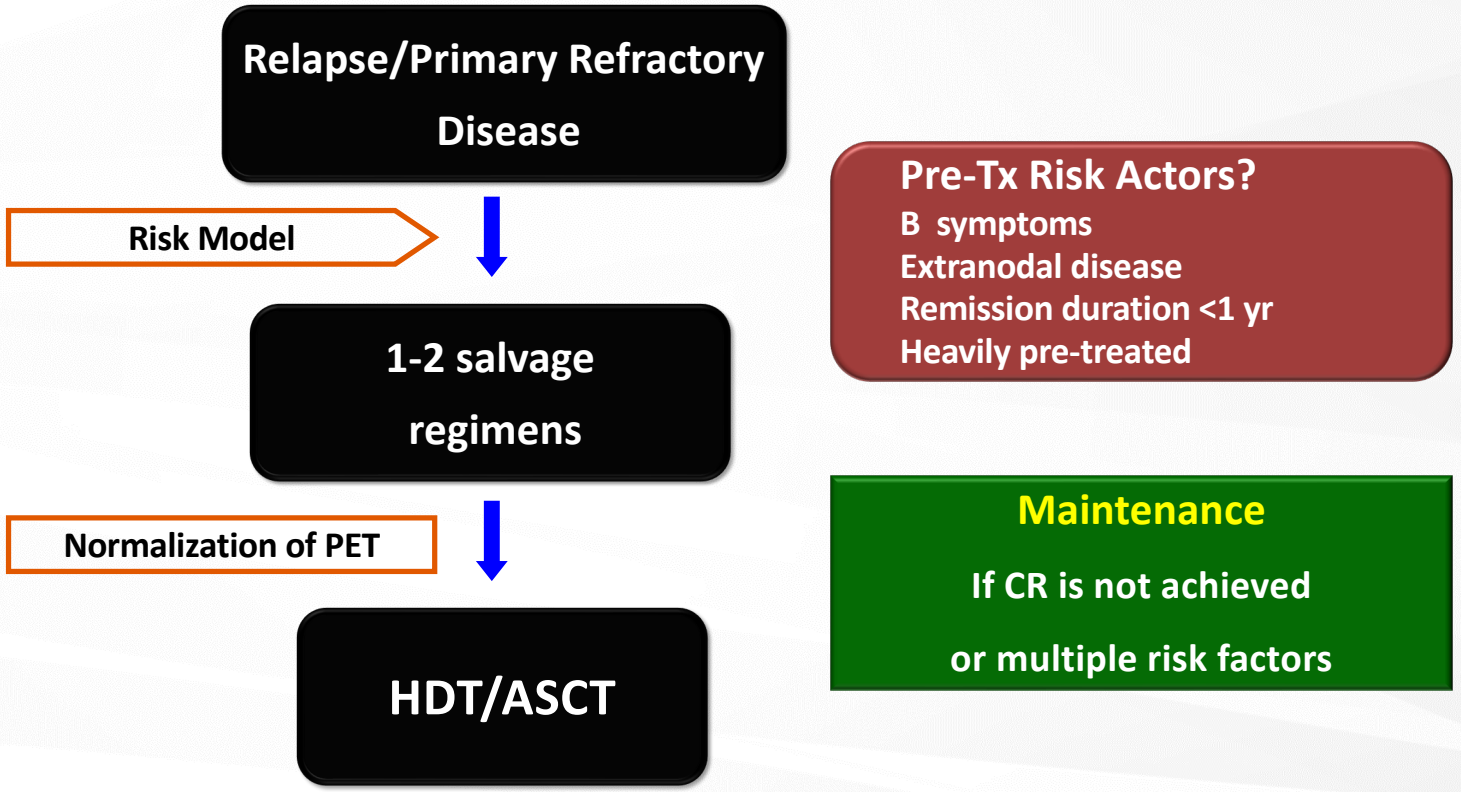
**700 patients ≥70 excluded**

SYLVESTER COMPREHENSIVE CANCER CENTER
UNIVERSITY OF MIAMI HEALTH SYSTEM
IN PURSUIT OF *YOUR CURE.*®

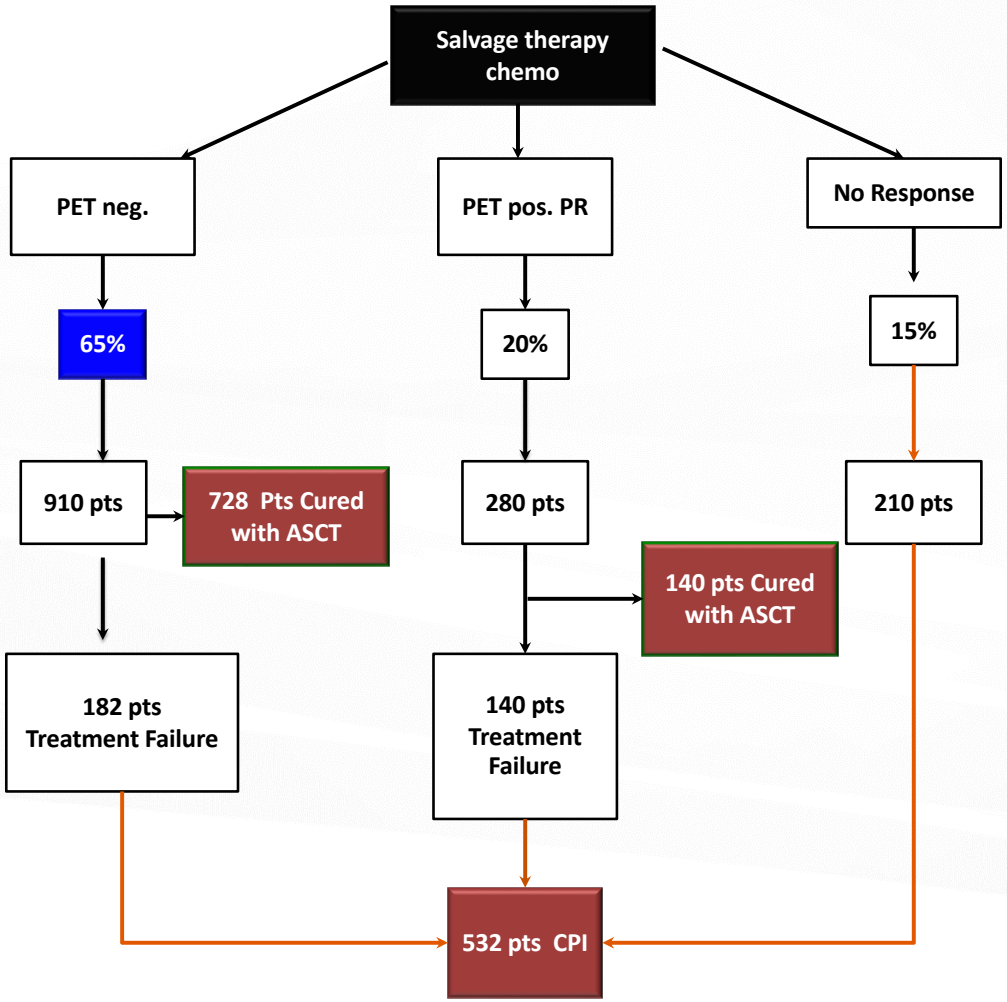
# Has clinical research gone in the wrong direction?

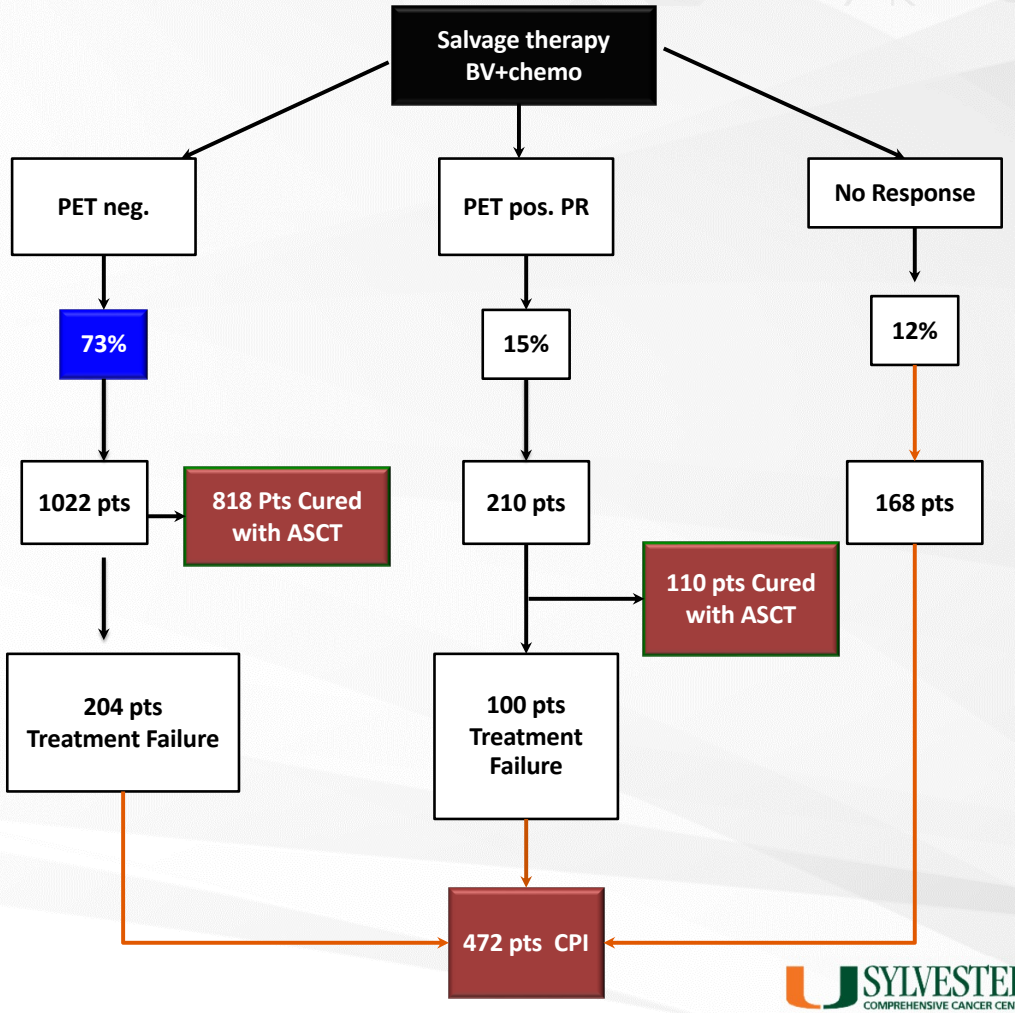
- **With optimal therapy less pts with ASHL need SLT/ASCT**
- **Reducing the number of cycles and the near elimination of ISRT for ESHL, more pts are relapsing**
- **Luckily in the second-line setting we are curing more patients!**
- **Don’t we want to cure more pts upfront?**

## A reasonable approach to relapsed/refractory Hodgkin lymphoma era of maintenance: 2014-2021



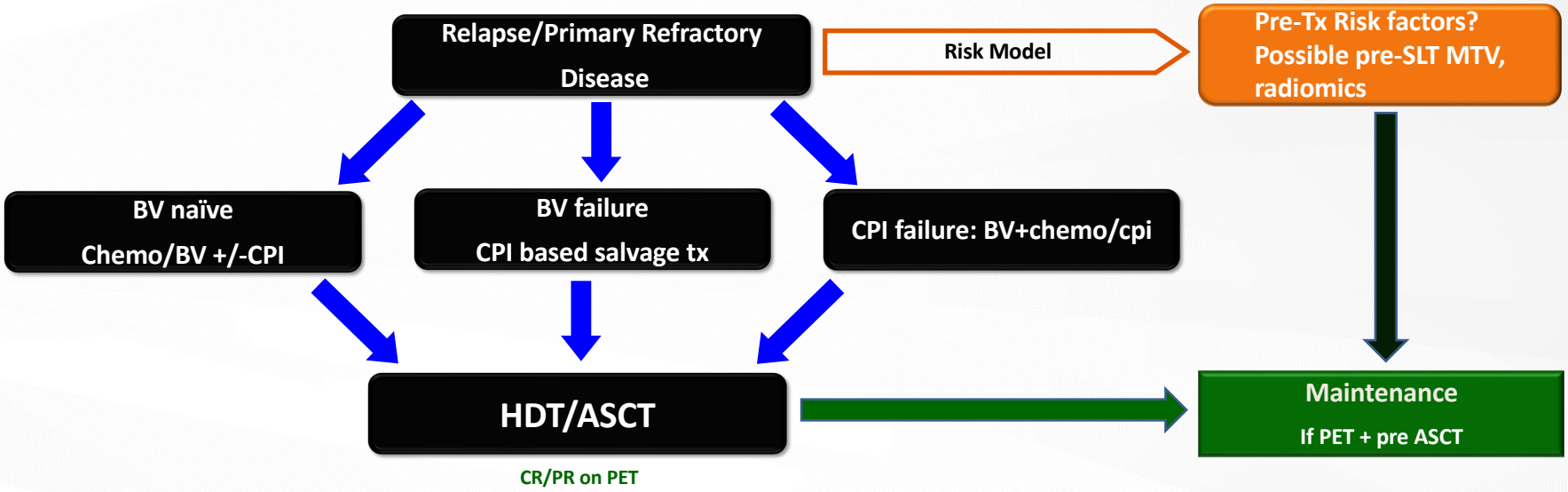
# Relapsed/Refractory HL: 1400 pts/year: and 65% are cured at time of AETHERA publication



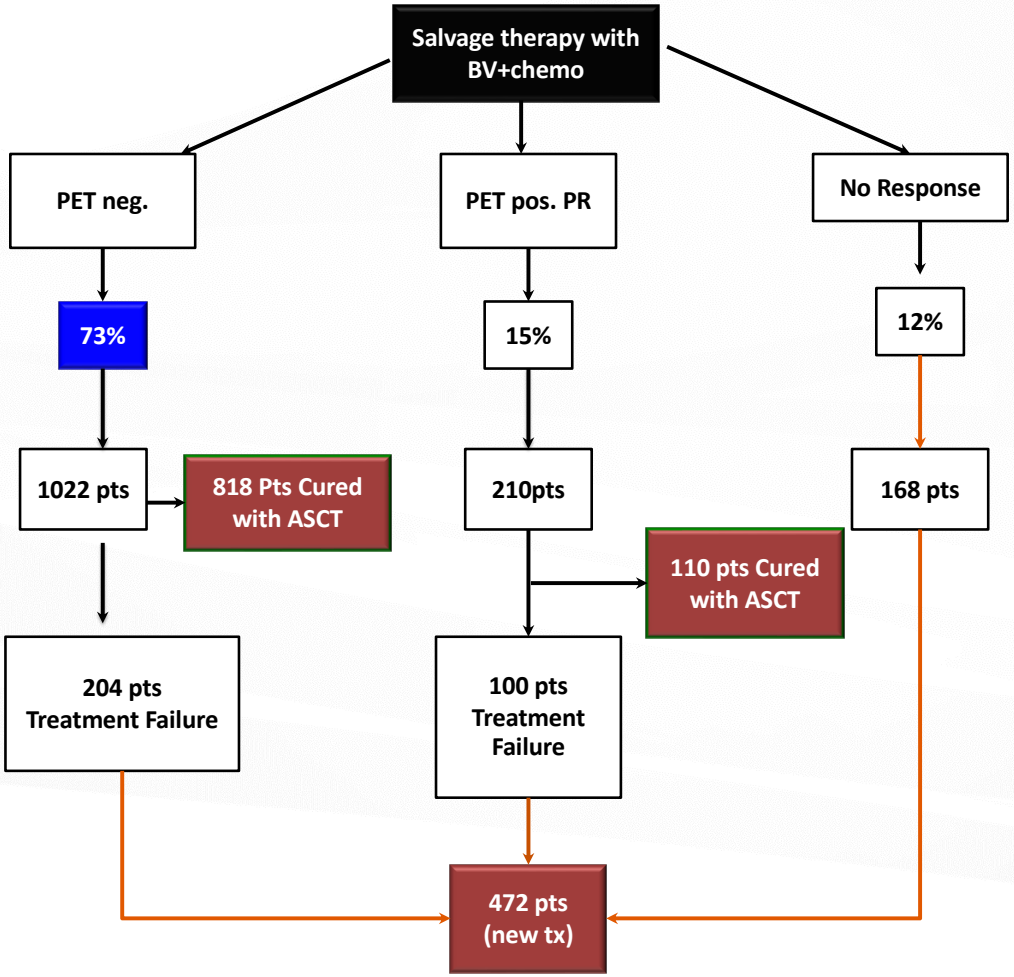




SYLVESTER COMPREHENSIVE CANCER CENTER
UNIVERSITY OF MIAMI HEALTH SYSTEM

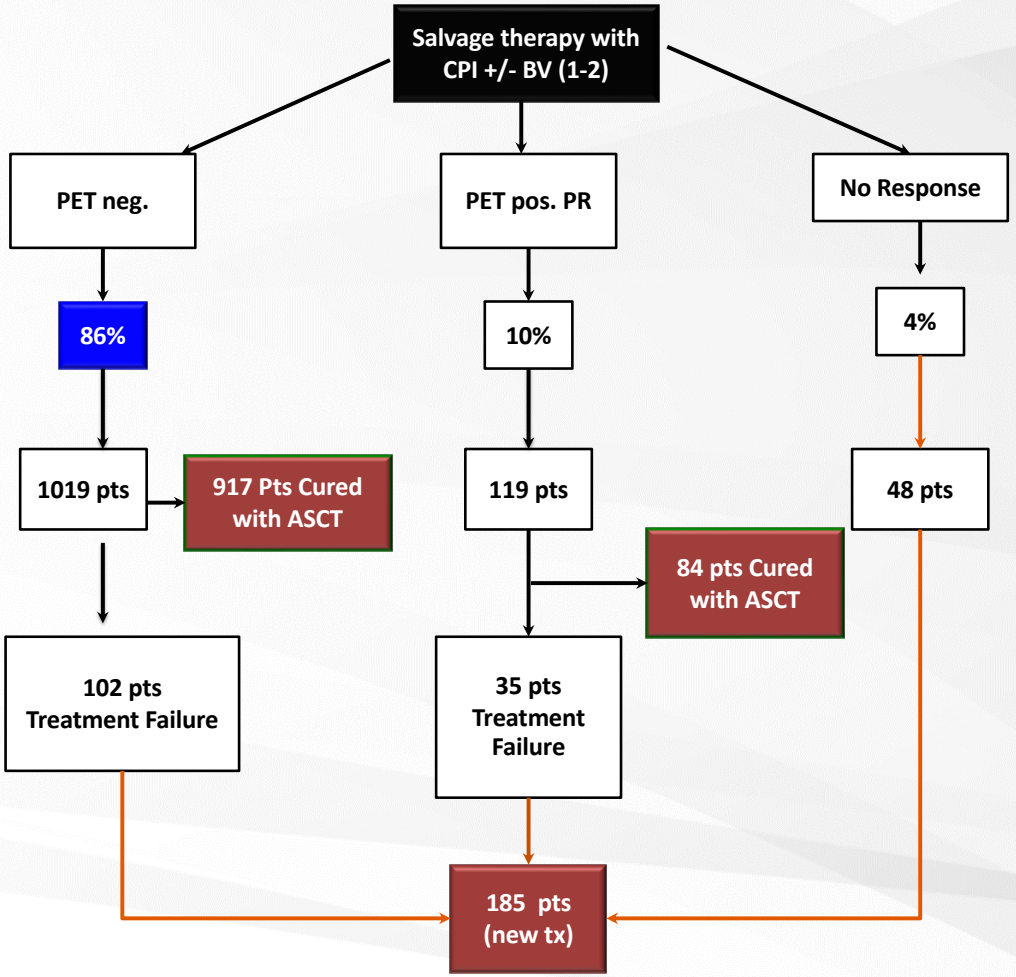
# A reasonable approach to relapsed/refractory Hodgkin lymphoma-2024



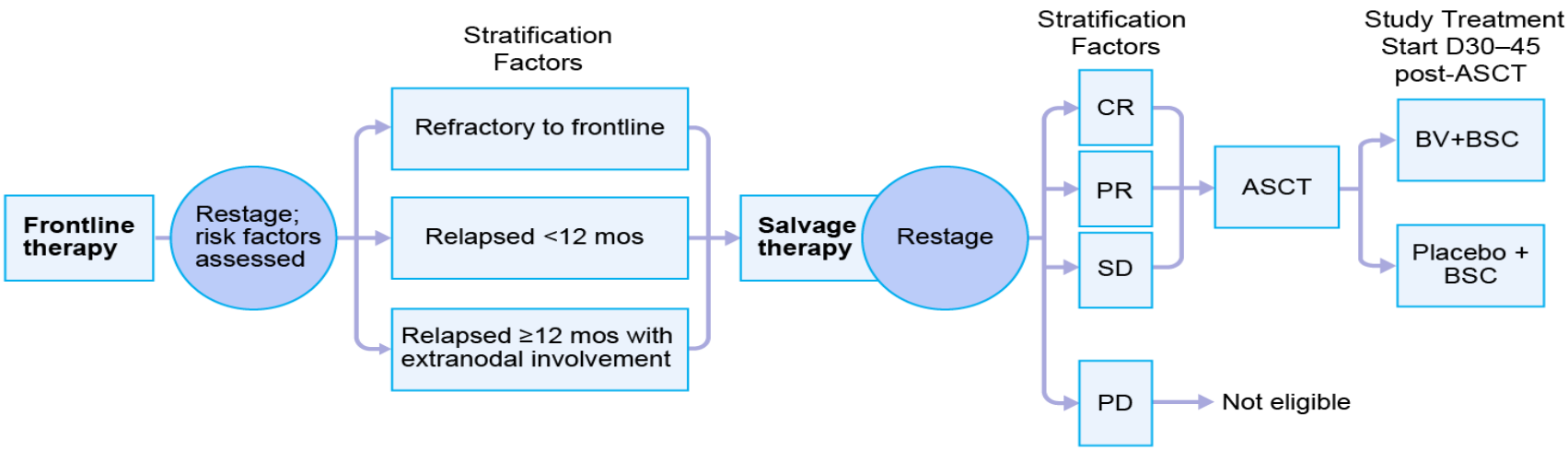
## 1400 pts/year vs




## 1185 pts/yr

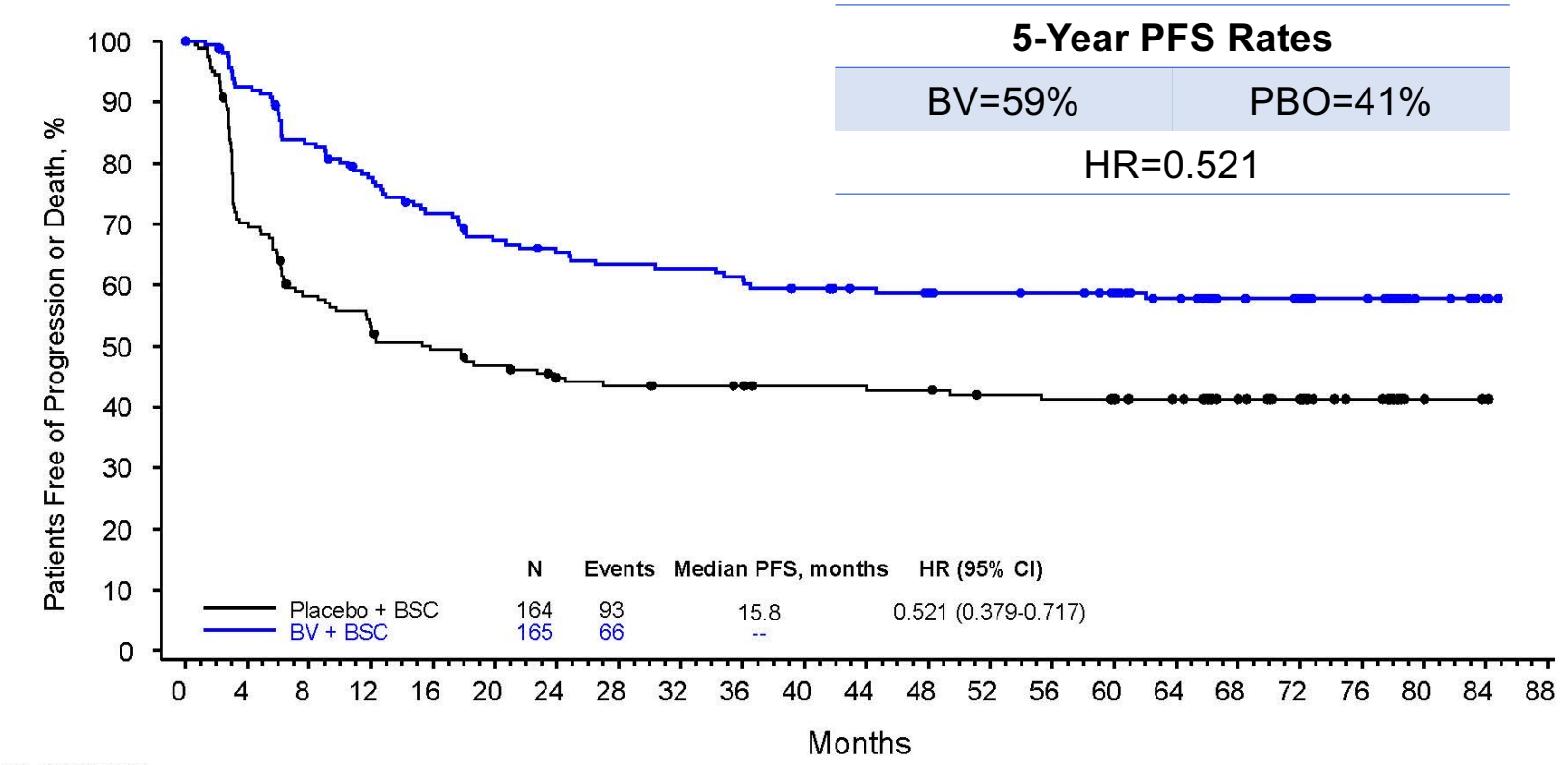


# AETHERA Trial Design




- Randomization was stratified by:
  - Risk factors after frontline therapy
  - Best clinical response to salvage therapy before ASCT
- 329 patients randomized to BV 1.8 mg/kg IV and BSC or PBO + BSC for up to 16 cycles, starting 30–45 days after ASCT
- Patients on the PBO+BSC arm with progressive disease had access to BV subsequent therapy on a separate study

# 5-Year PFS per Investigator: All Patients (N=329)




| 5-Year PFS Rates | |
|---|---|
| BV=59% | PBO=41% |
| HR=0.521 | |

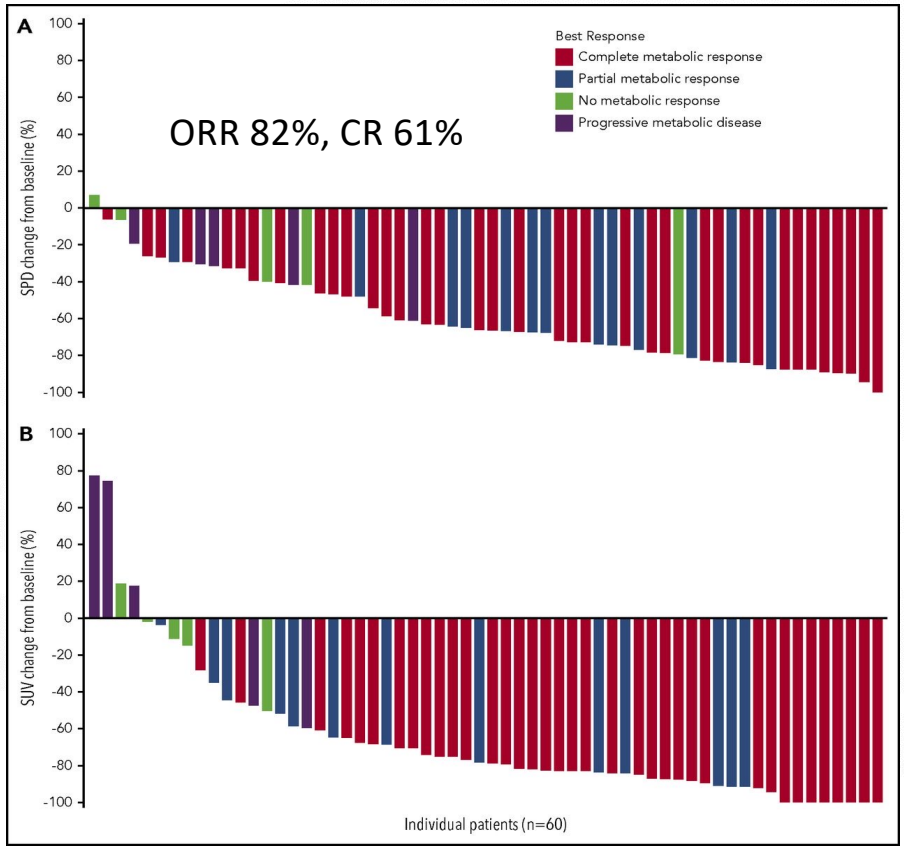
SYLVESTER COMPREHENSIVE CANCER CENTER
UNIVERSITY OF MIAMI HEALTH SYSTEM

# When evaluating patients for SLT/ASCT in 2024 the most important issues are

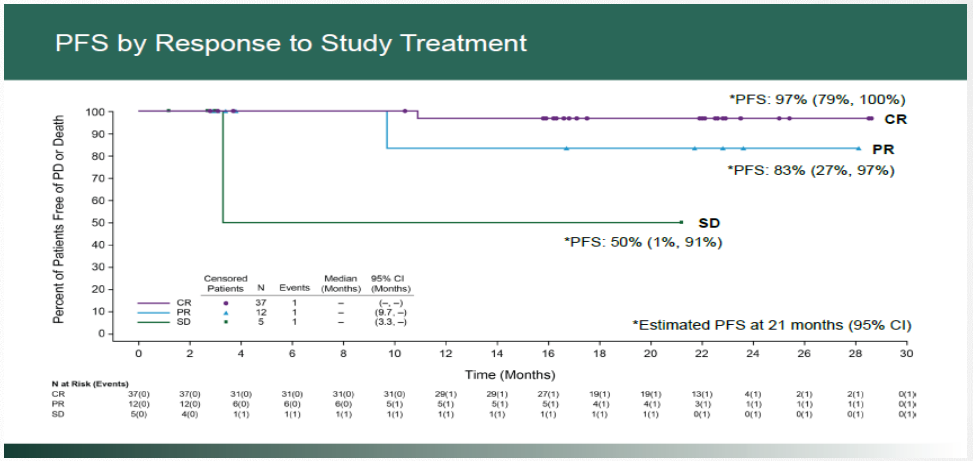
- Did the patient receive BV-AVD
- Did the patient receive N/P-AVD
- If the patient had ESHL was short course chemo alone administered?
  - Does the patient have low volume stage I/II nodal disease

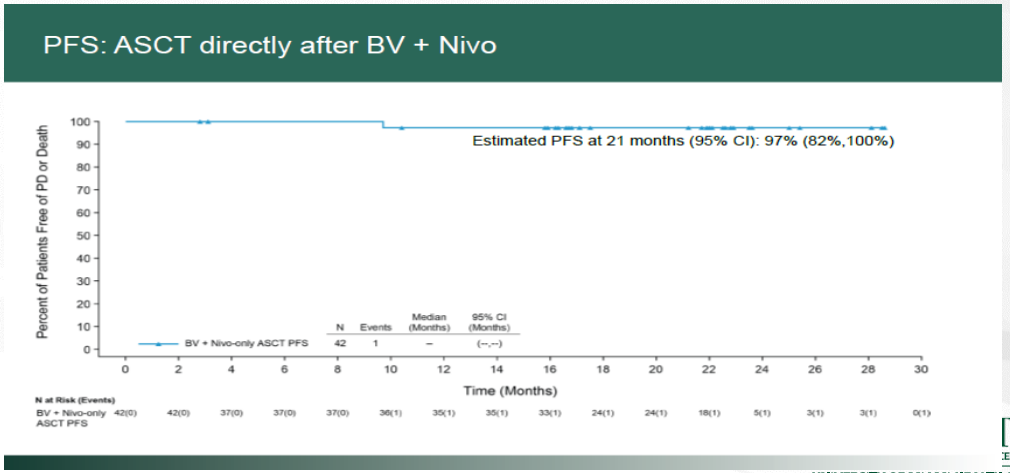
- Did the patient achieve a PET neg response after salvage chemotherapy
  - Was BV-based salvage chemotherapy used
  - Was CPI-based salvage chemotherapy used
  - Was BV/nivo salvage therapy used
  - Was standard platinum-based salvage chemotherapy used

# Phase I/II study BV + Nivolumab as 1st salvage



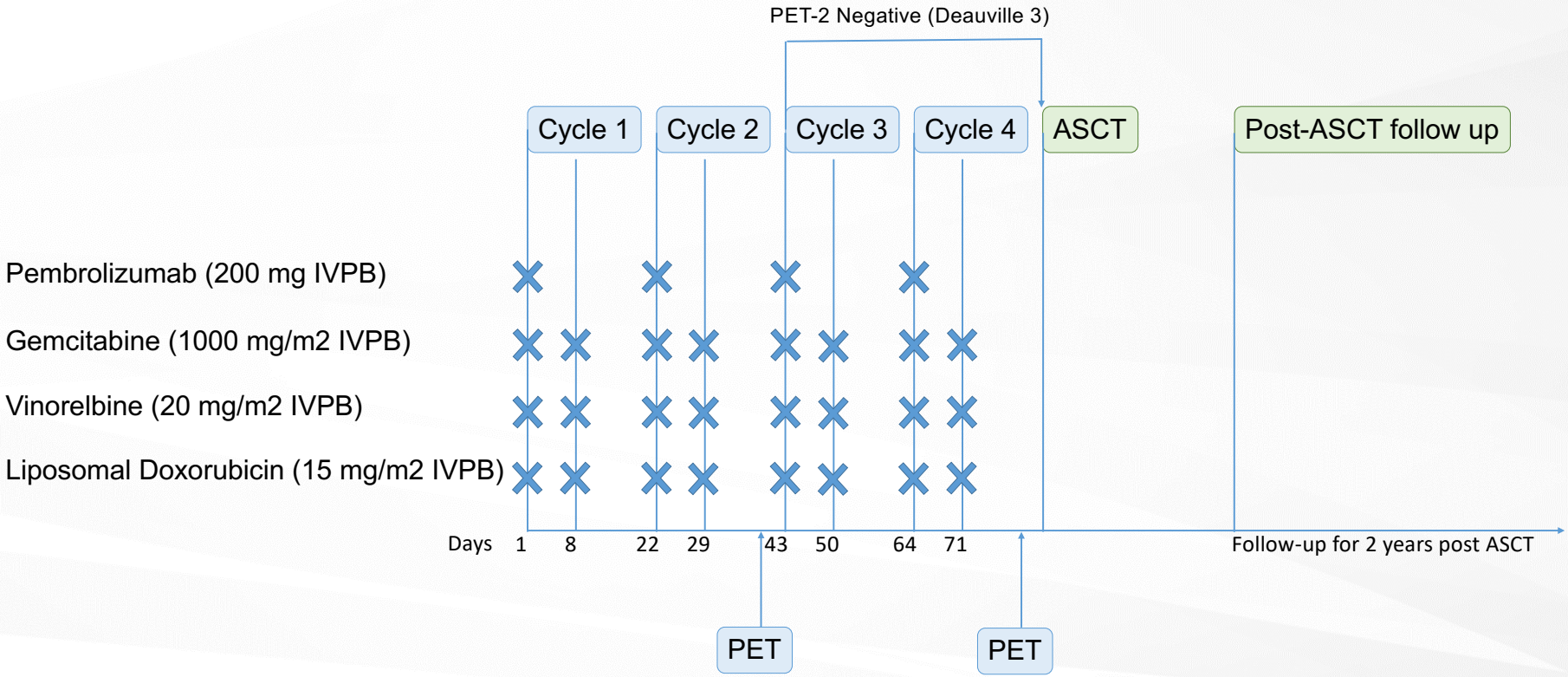

Advani et al Blood 2021




UNIVERSITY OF MIAMI HEALTH SYSTEM

# Pembro-GVD




**Exploratory: cytokines, metabolic tumor volume, ctDNA, 9p24.1 amplification, IHC staining for MHC-I, MHC-II, pd-1, pd-l1, pd-l2, beta-2 microglobulin**

SYLVESTER COMPREHENSIVE CANCER CENTER
UNIVERSITY OF MIAMI HEALTH SYSTEM

# Transplant Cohort: Accrual and Follow up Information

- Transplant Cohort

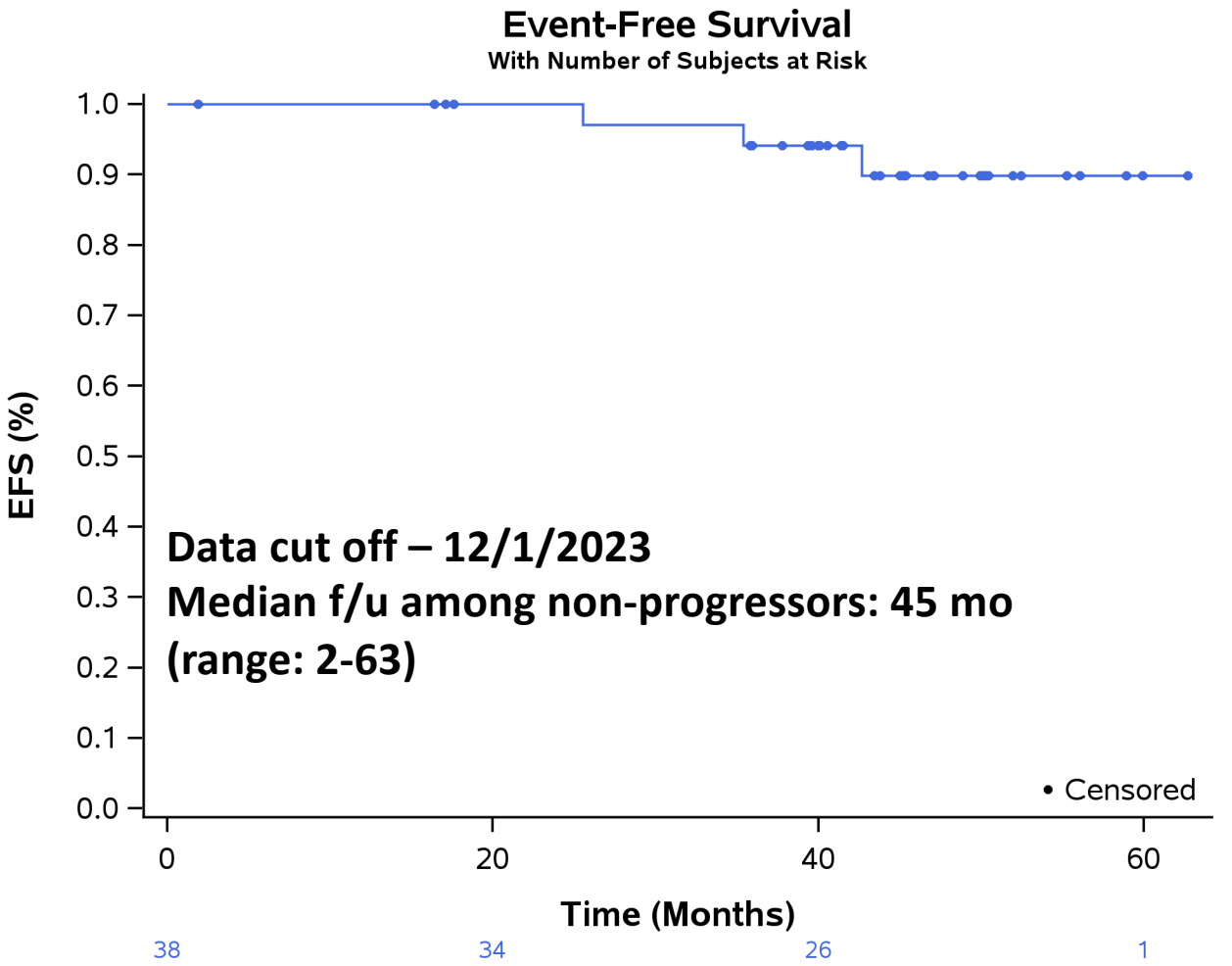
| Accrual | # of patients |
|---|---|
| Slots | 39 |
| Treated | 39 |
| Evaluable | 38 |
| Received transplant | 36 (2 not receiving) |

1 patient has relapsed, and 2 patients passed away due to unrelated reason

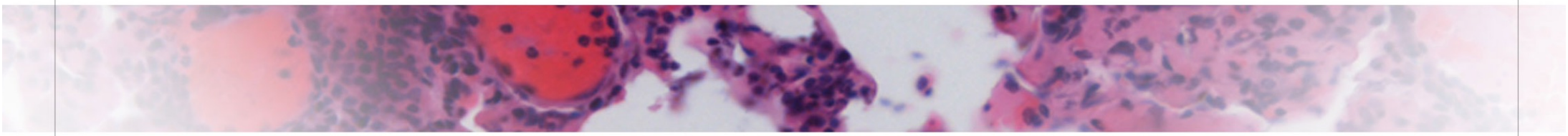
SYLVESTER COMPREHENSIVE CANCER CENTER
UNIVERSITY OF MIAMI HEALTH SYSTEM

# ITT Curve (Transplant Cohort): Follow up

- n=38 evaluable patients
- ORR: 100%
- CR: 95% (92% after 2 cycles)
- 1 relapse, 2 late deaths (unrelated)
- 30mo EFS: 97%



American Society *of* Hematology
Helping hematologists conquer blood diseases worldwide



# #182: PD-1 Blockade before Autologous Stem Cell Transplantation Improves Outcomes in Relapsed/Refractory Classic Hodgkin Lymphoma: Results from a Multicenter Cohort

**Sanjal H. Desai, MBBS**[1,2], Reid W. Merryman, MD[3], Harsh Shah, DO[4*], Levi D. Pederson, MS[2*], Susan M. Geyer, PhD[2], Nivetha Ganesan[5*], Tiffany Chang, MS[5*], Tamer Othman, MD[6], Ayo S Falade, MD, MBA[3], Gunjan L. Shah[5], Urshila Durani, MD, MPH[7], Kelsey Baron, MD[4], Shin Yeu Ong, MD, FRCPath[8*], Stephen M Ansell[7], Philippe Armand, MD, PhD[9], Siddharth Ivengar, MD[10*], Ivana Micallef, MD[2*], Alison Moskowitz, MD[5], Alex F. Herrera, MD[11], Robert Stuver, MD[5] and Matthew Genveh Mei, MD[11*]

# Methods:

- Consecutive adult patients with R/R cHL who underwent autologous stem cell transplant (ASCT) between 2010 and 2021 at 5 United States academic institutions were included.

- Demographics and clinical variables were recorded at relapse by electronic health records review.

- Study Objectives:
  - Progression free survival (PFS): time from ASCT to progression or death
  - Overall survival (OS): time from ASCT to death

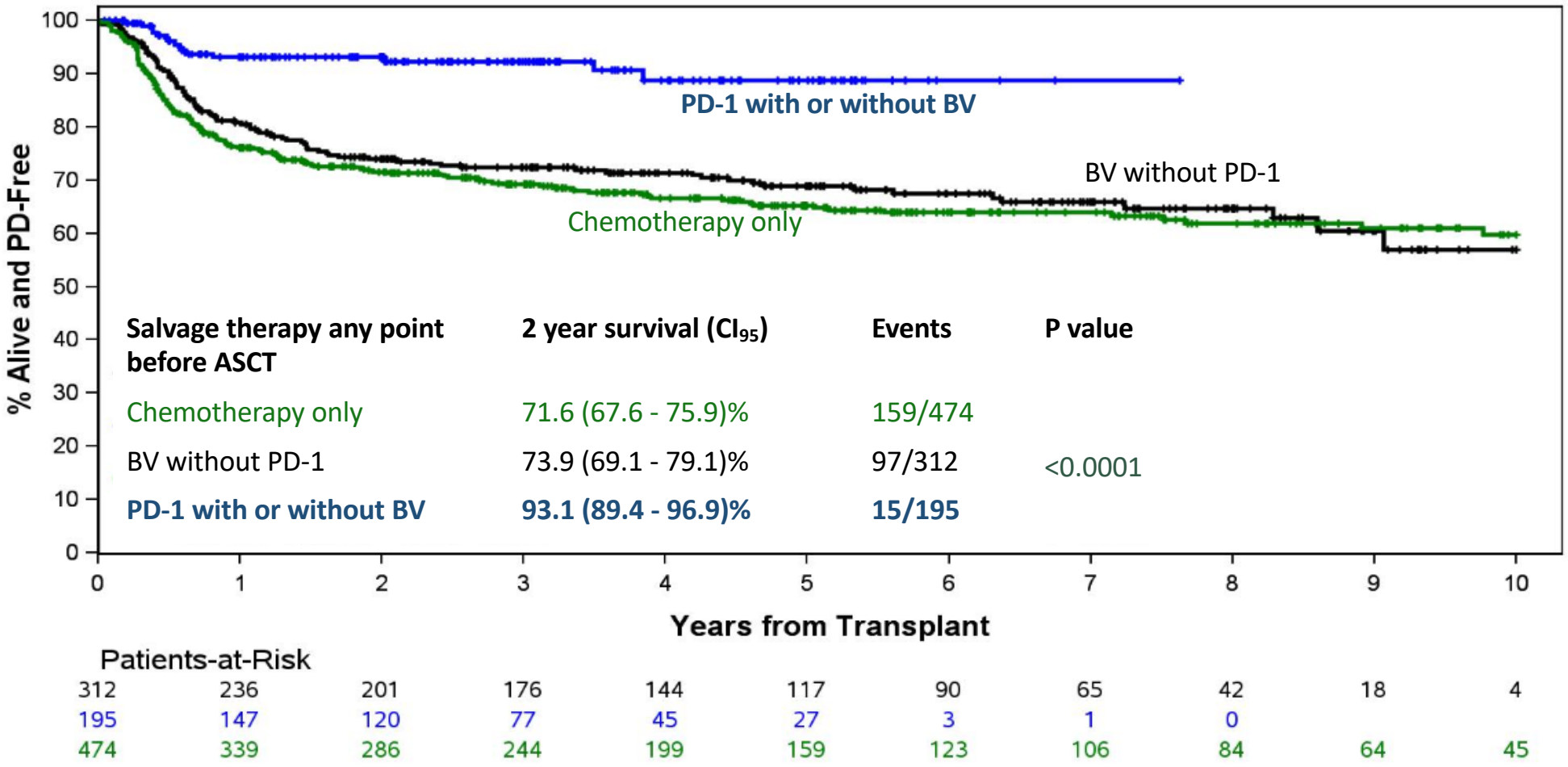
- Association of risk features with post-ASCT outcomes was assessed using univariable and multivariable COX proportional hazard ratio.

SYLVESTER COMPREHENSIVE CANCER CENTER
UNIVERSITY OF MIAMI HEALTH SYSTEM

# Median follow up

| Salvage Therapy (any line) | Median follow up (years, 95% CI) |
|---|---|
| BV only without PD-1 | 5.3 (5.0-6.0) |
| PD-1 with or without BV | 2.8 (2.4-3.1) |
| Chemotherapy only | 5.3 (5.0-5.7) |

# Progression free survival



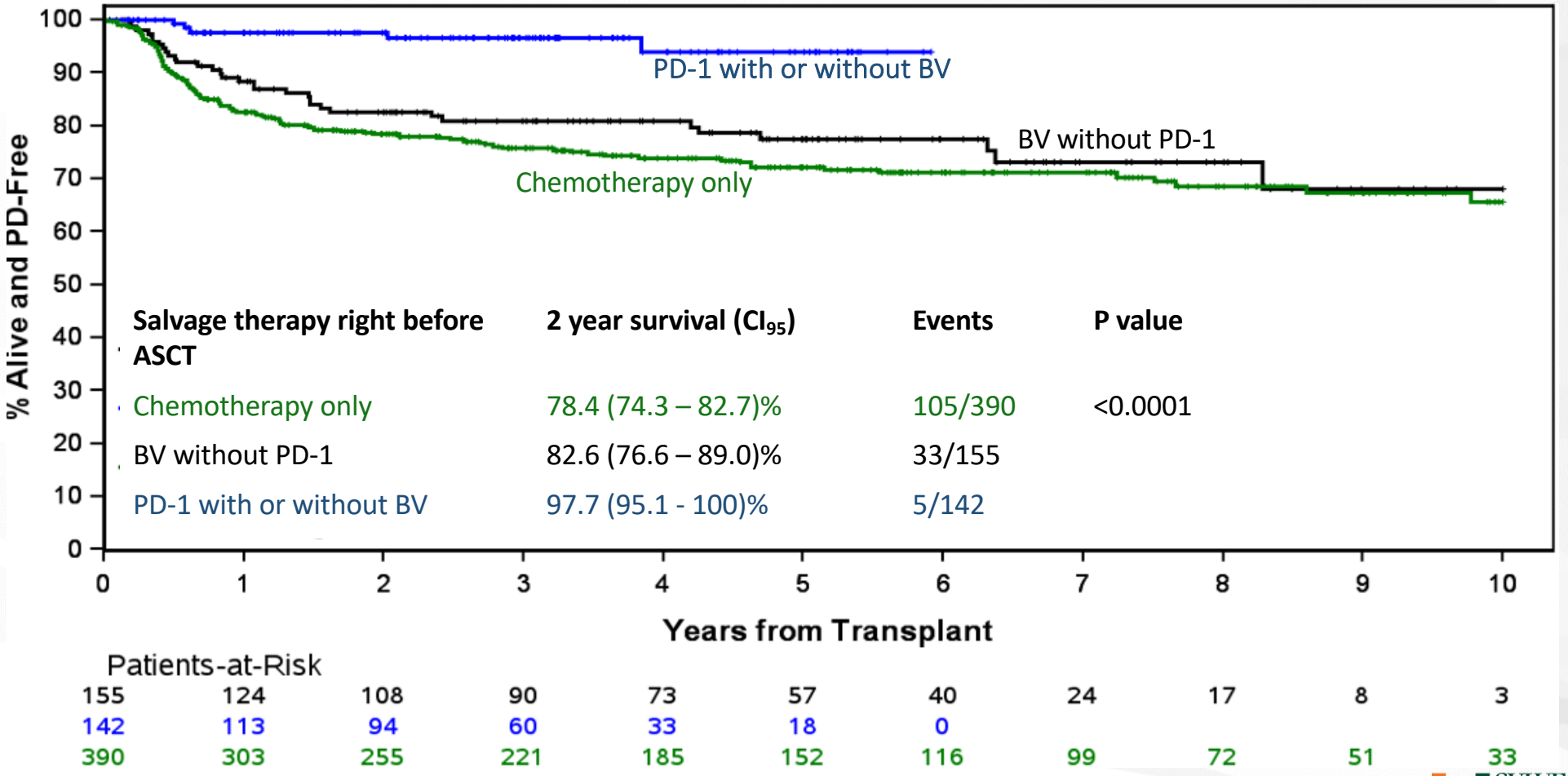

| Salvage therapy any point before ASCT | 2 year survival ($CI_{95}$) | Events | P value |
|---|---|---|---|
| Chemotherapy only | 71.6 (67.6 - 75.9)% | 159/474 | |
| BV without PD-1 | 73.9 (69.1 - 79.1)% | 97/312 | <0.0001 |
| **PD-1 with or without BV** | **93.1 (89.4 - 96.9)%** | **15/195** | |

Patients-at-Risk

| | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| 312 | 236 | 201 | 176 | 144 | 117 | 90 | 65 | 42 | 18 | 4 |
| 195 | 147 | 120 | 77 | 45 | 27 | 3 | 1 | 0 | | |
| 474 | 339 | 286 | 244 | 199 | 159 | 123 | 106 | 84 | 64 | 45 |

SYLVESTER COMPREHENSIVE CANCER CENTER
UNIVERSITY OF MIAMI HEALTH SYSTEM

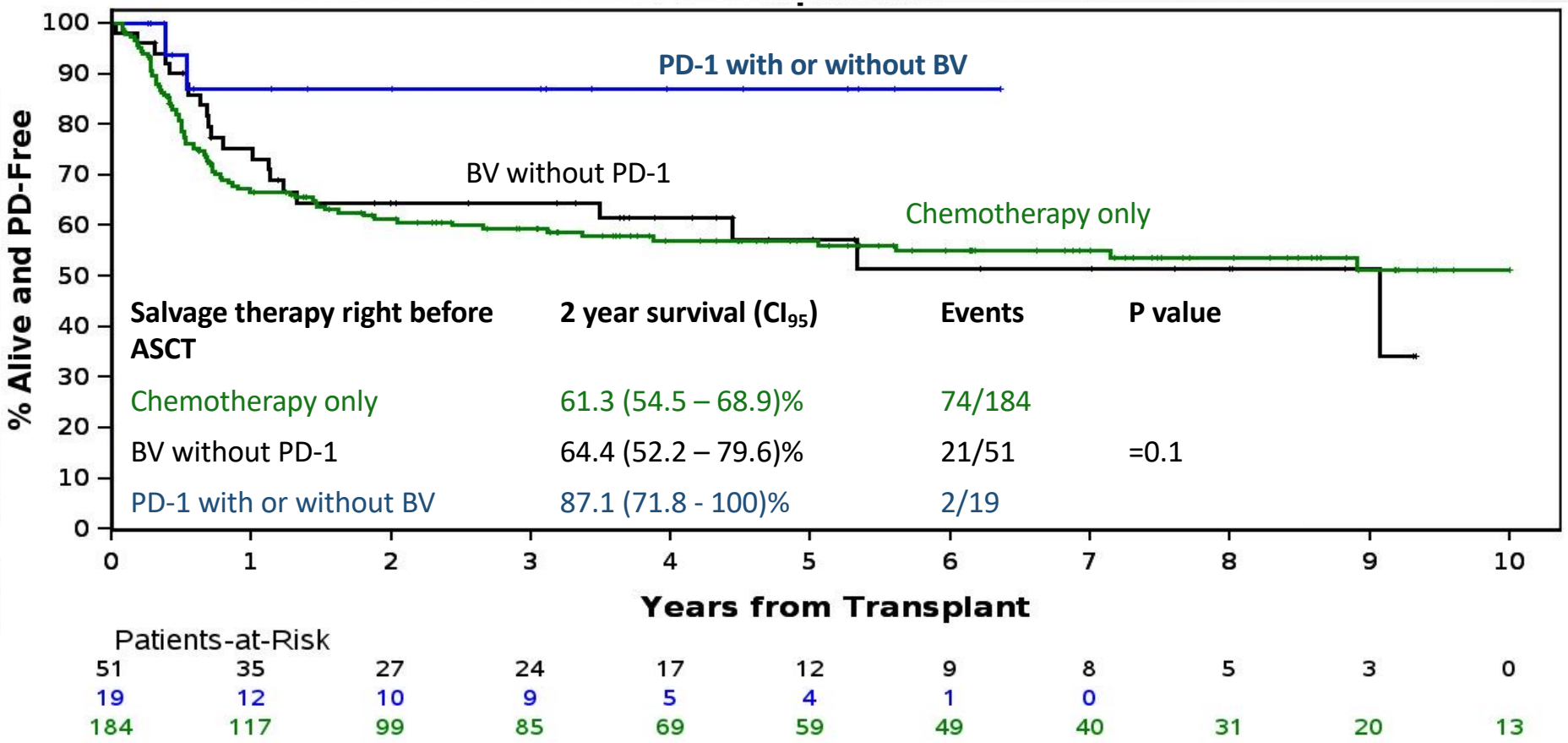
# PD-1 inhibitors improve PFS in PET- pts




| Salvage therapy right before ASCT | 2 year survival ($CI_{95}$) | Events | P value |
|---|---|---|---|
| Chemotherapy only | 78.4 (74.3 – 82.7)% | 105/390 | <0.0001 |
| BV without PD-1 | 82.6 (76.6 – 89.0)% | 33/155 | |
| PD-1 with or without BV | 97.7 (95.1 - 100)% | 5/142 | |

SYLVESTER COMPREHENSIVE CANCER CENTER
UNIVERSITY OF MIAMI HEALTH SYSTEM

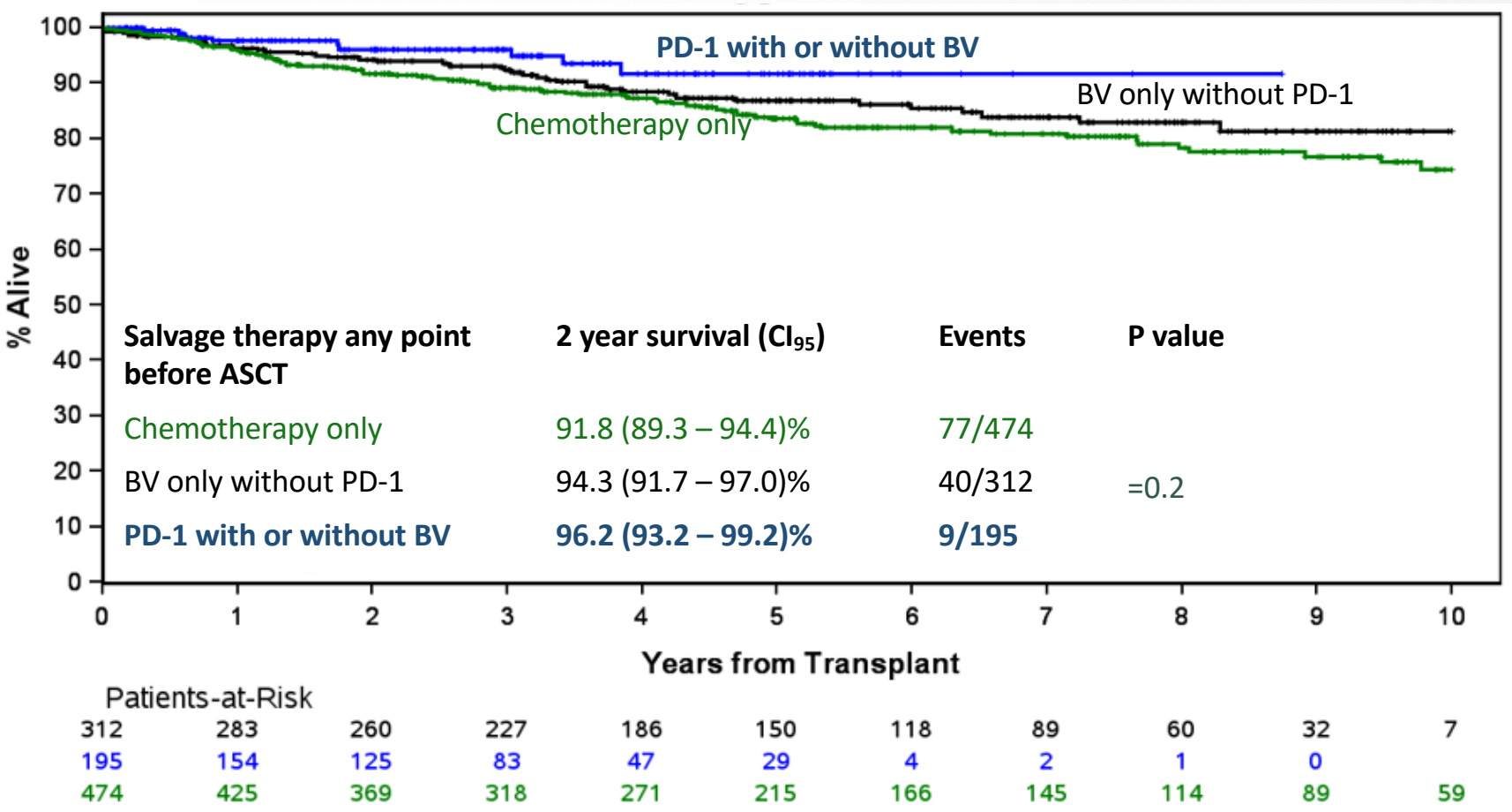
# PD-1 inhibitors improve PFS in PET+ pts




| Salvage therapy right before ASCT | 2 year survival ($CI_{95}$) | Events | P value |
|---|---|---|---|
| Chemotherapy only | 61.3 (54.5 – 68.9)% | 74/184 | |
| BV without PD-1 | 64.4 (52.2 – 79.6)% | 21/51 | =0.1 |
| PD-1 with or without BV | 87.1 (71.8 - 100)% | 2/19 | |

SYLVESTER COMPREHENSIVE CANCER CENTER
UNIVERSITY OF MIAMI HEALTH SYSTEM

# Overall survival



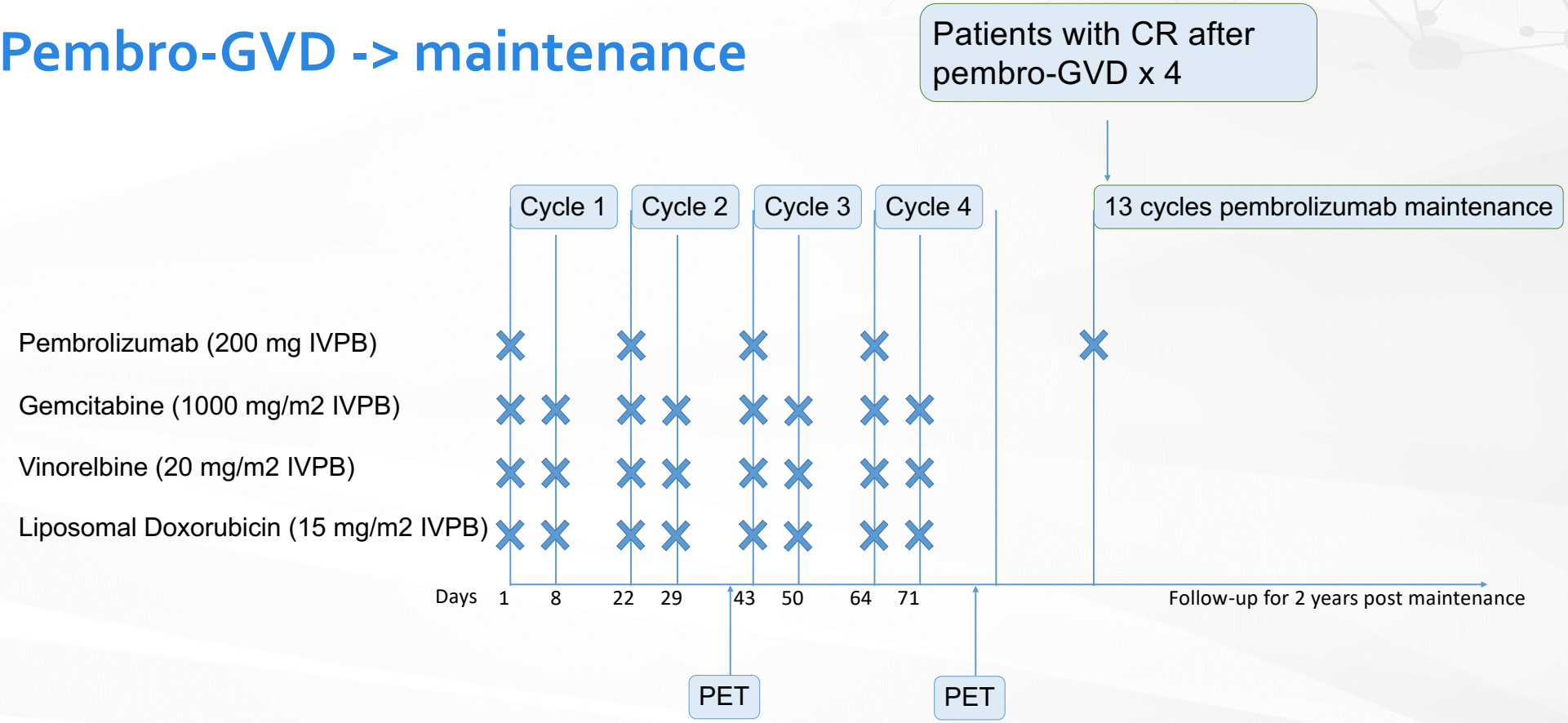

| Salvage therapy any point before ASCT | 2 year survival ($CI_{95}$) | Events | P value |
|---|---|---|---|
| Chemotherapy only | 91.8 (89.3 – 94.4)% | 77/474 | |
| BV only without PD-1 | 94.3 (91.7 – 97.0)% | 40/312 | =0.2 |
| **PD-1 with or without BV** | **96.2 (93.2 – 99.2)%** | **9/195** | |

SYLVESTER COMPREHENSIVE CANCER CENTER
UNIVERSITY OF MIAMI HEALTH SYSTEM

# Do relapsing patients require HDT/ASCT as part of second-line therapy?

SYLVESTER COMPREHENSIVE CANCER CENTER
UNIVERSITY OF MIAMI HEALTH SYSTEM

# Next cohort:
# Pembro-GVD -> maintenance



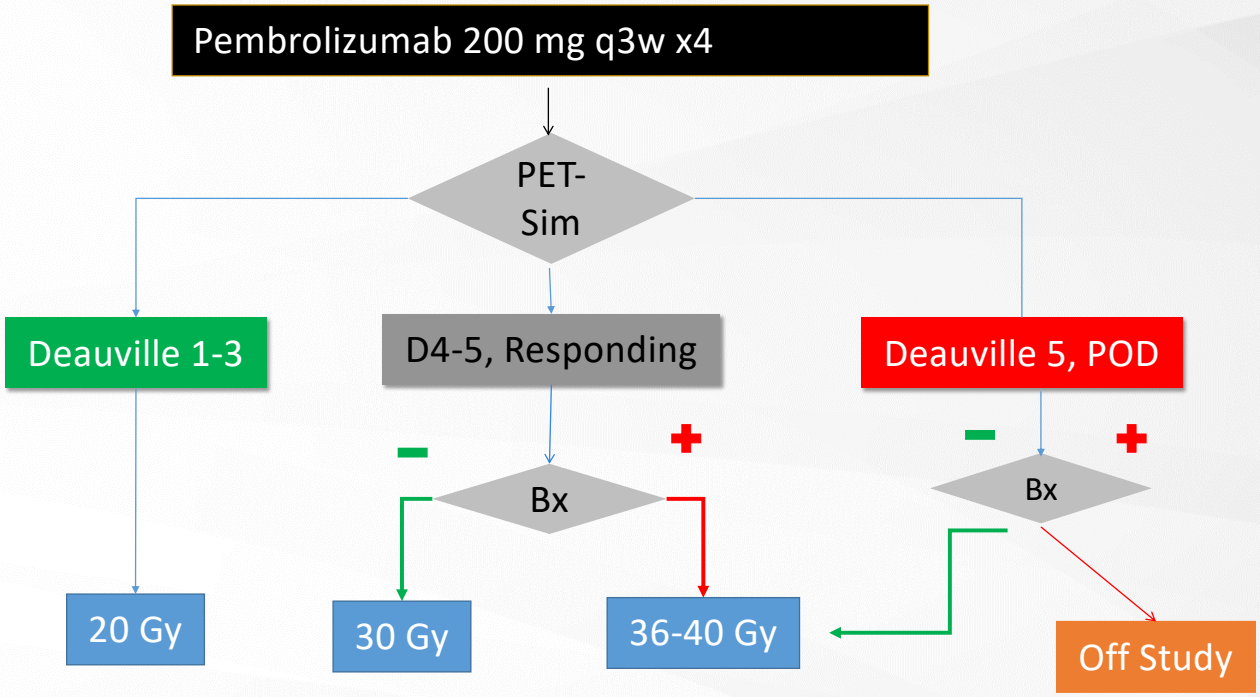

**Exploratory: cytokines, immune-cell subsets, metabolic tumor volume, ctDNA, 9p24.1 amplification, IHC staining for MHC-I, MHC-II, pd-1, pd-l1, pd-l2, beta-2 microglobulin**

Memorial Sloan Kettering Cancer Center

SYLVESTER COMPREHENSIVE CANCER CENTER
UNIVERSITY OF MIAMI HEALTH SYSTEM

# Pembro-RT

| Eligiblity |
| --- |
| Initial stage: I-IIA |
| Prior therapy: Chemo only or CMT with relapse outside field |
| Relapse stage: I-II |
| No bulk > 10 cm |
| ECOG 0-1 |




**Exploratory: cytokines, metabolic tumor volume, ctDNA, 9p24.1 amplification, IHC staining for MHC-I, MHC-II, pd-1, pd-l1, pd-l2, beta-2 microglobulin**

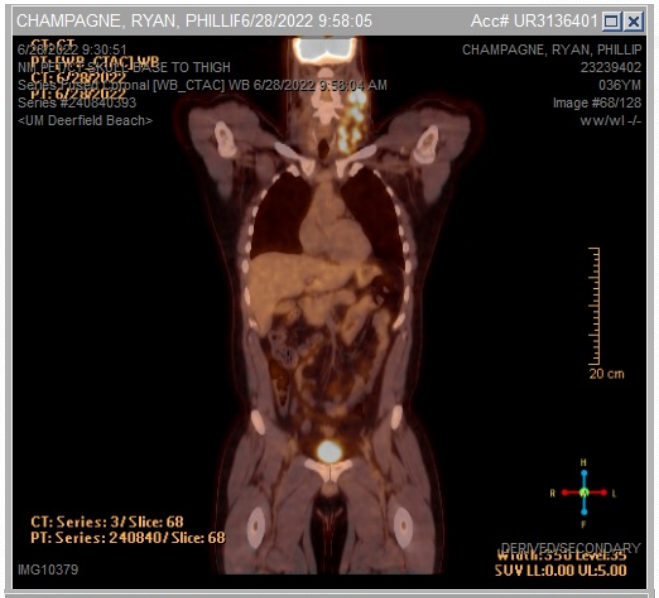
MSKCC protocol 17-054

SYLVESTER COMPREHENSIVE CANCER CENTER
UNIVERSITY OF MIAMI HEALTH SYSTEM

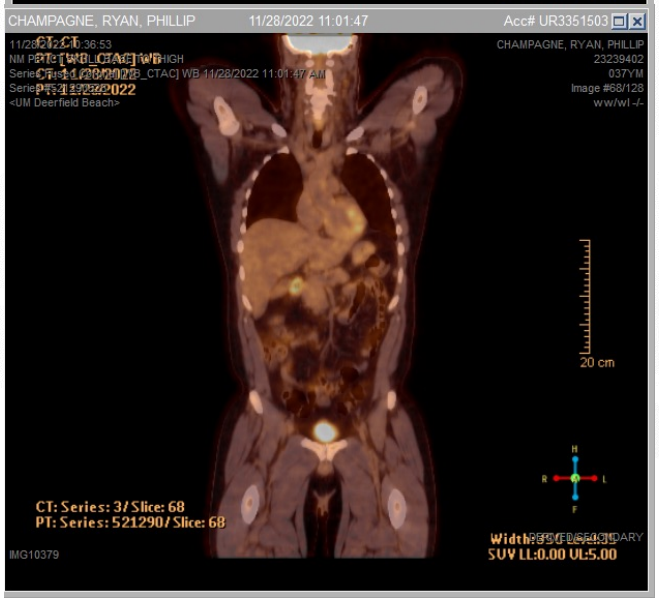
# Primary refractory Favorable ESHL

- 26 year-old male presents with stage 2 ESHL; ESR 40
- Largest nodal mass 4.6 cm in left neck
- DLCO 71%; history of smoking 1PPD
- Treatment as per CALGB, 4 cycles PET adapted however BV substituted for bleomycin
- PET 2-Deauville 3
- PET 4-Deauville 3

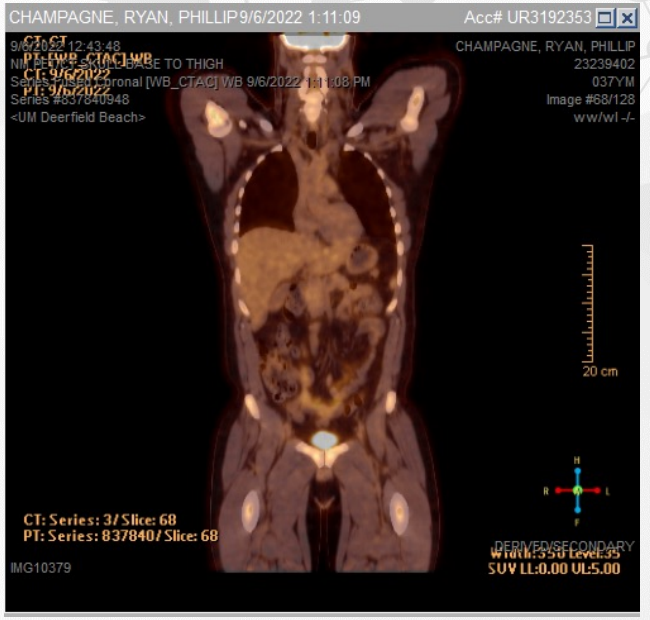
Baseline PET




EOT scan (after 4 cycles)

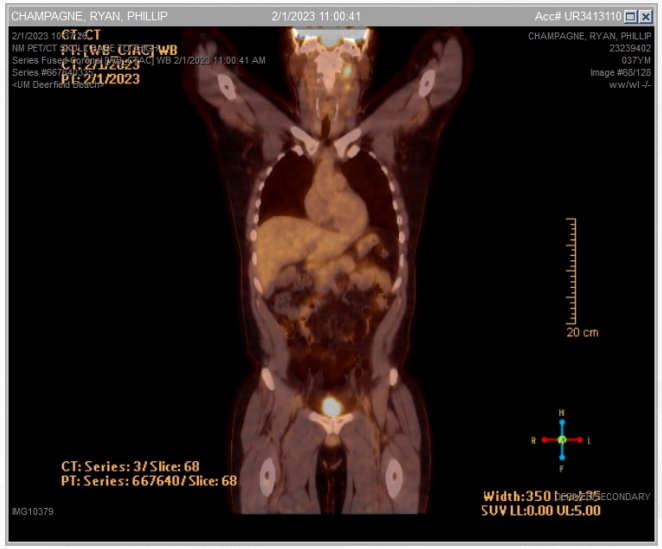



PET2



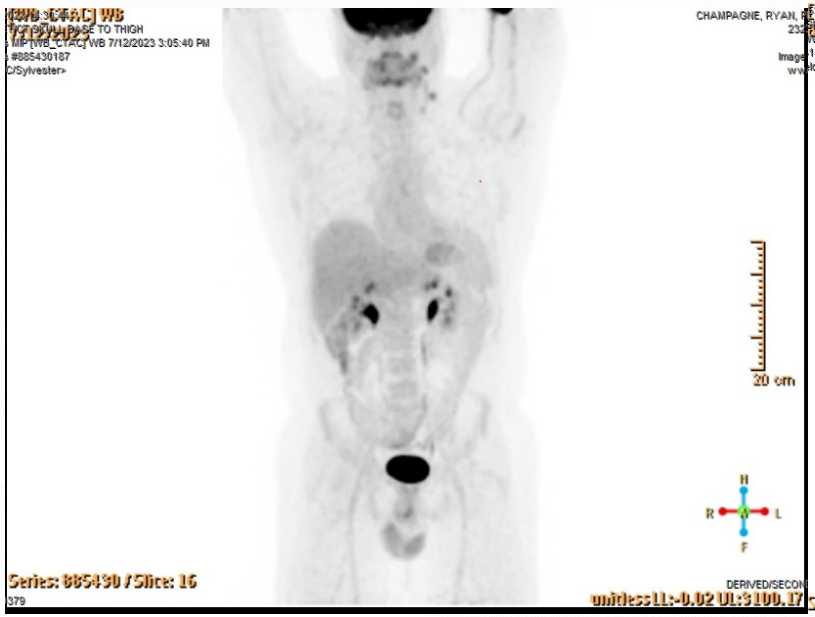

SYLVESTER COMPREHENSIVE CANCER CENTER
UNIVERSITY OF MIAMI HEALTH SYSTEM

- Patient calls 6 weeks later with new node; on exam about 1 cm
- Repeat PET 6 weeks later-POD; bx cHL
  - **HDT/ASCT**
  - **CMT**
  - **ISRT**

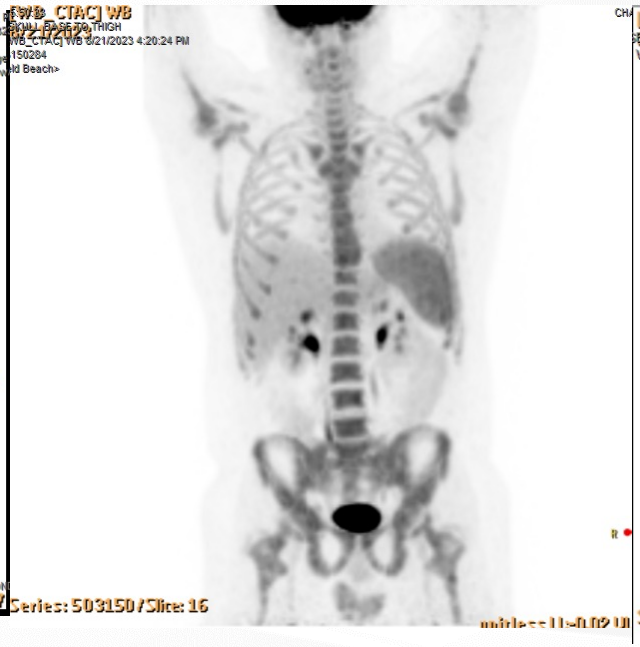


Pembro/ISRT study

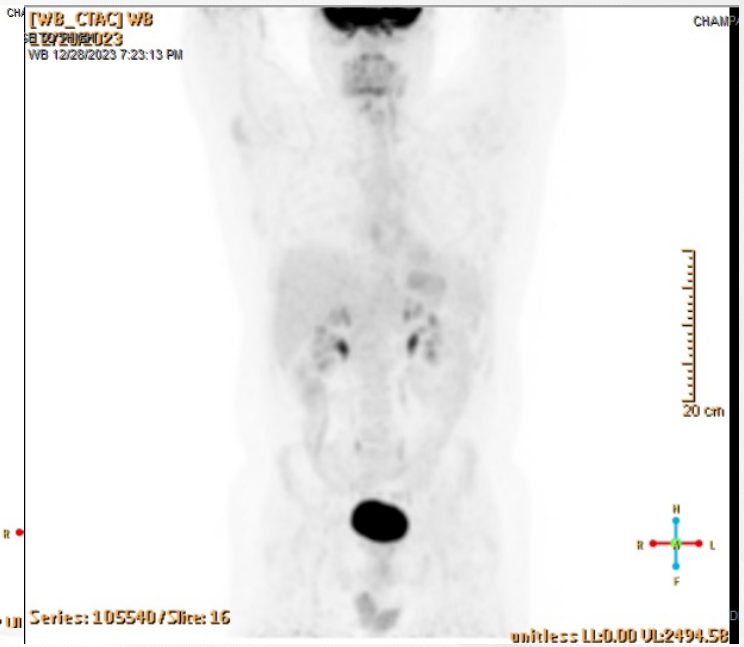
s/p Pembro x4




s/p ICE x2

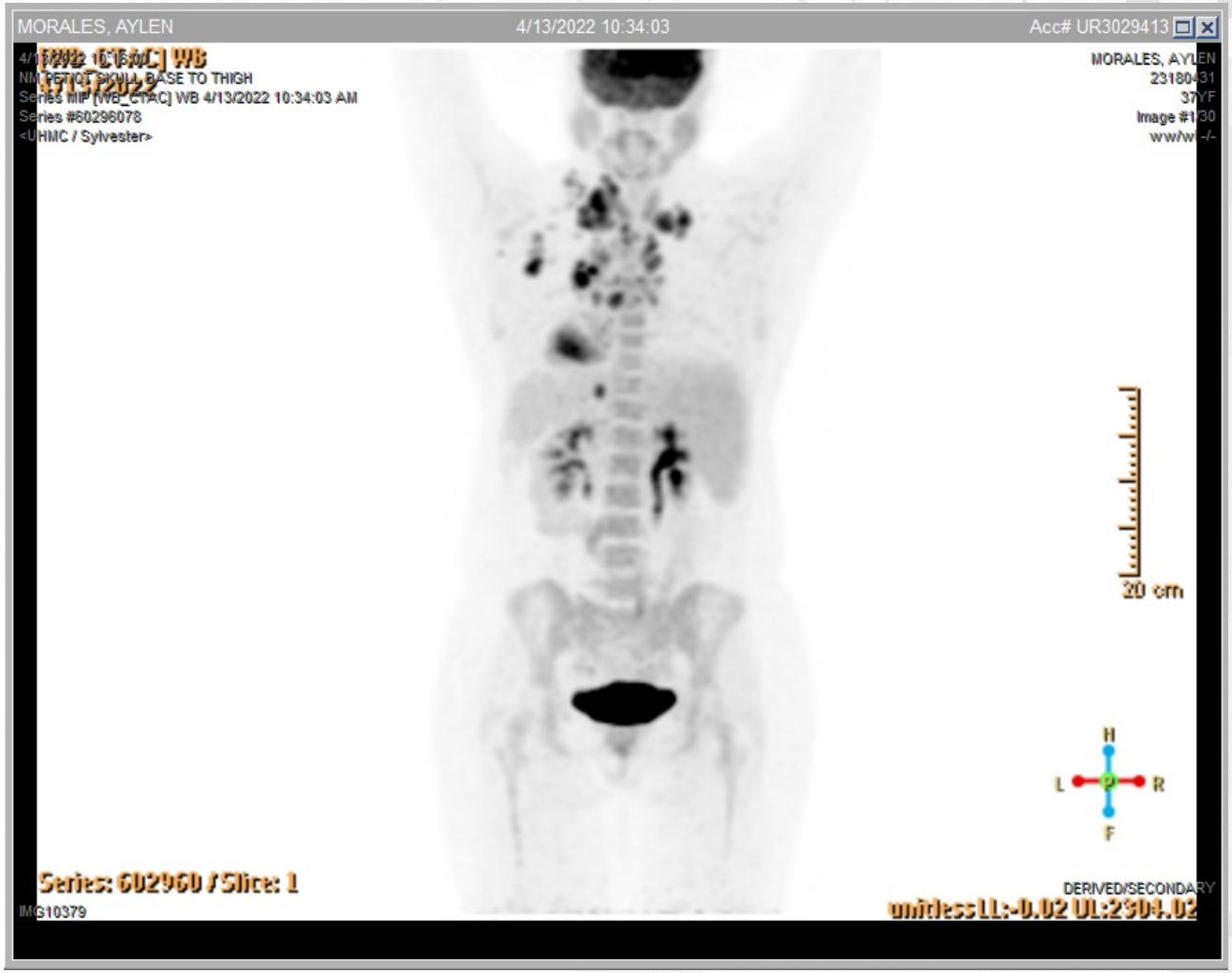



s/p ASCT day 180



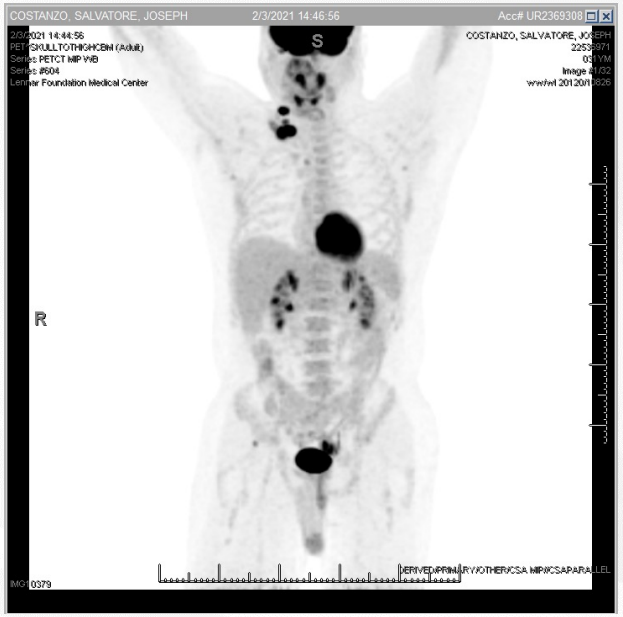

SYLVESTER COMPREHENSIVE CANCER CENTER
UNIVERSITY OF MIAMI HEALTH SYSTEM

37 year-old internist presented with favorable ASHL
Treated with 2 cycles of ABVD, interim PET Deauville 3; treated with 4 more cycles of ABVD




SYLVESTER COMPREHENSIVE CANCER CENTER
UNIVERSITY OF MIAMI HEALTH SYSTEM

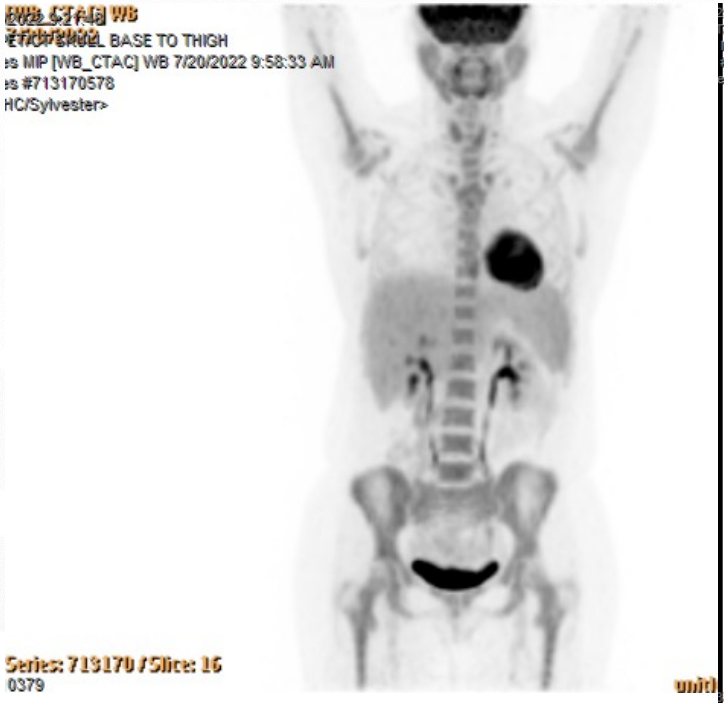
- PET is repeated 10 weeks later because pt palpates RSCN;  POD of disease bx confirms cHL
  - BV-ICE/ASCT
  - BV-Nivo/ASCT
  - P-GVD/ASCT
  - CMT



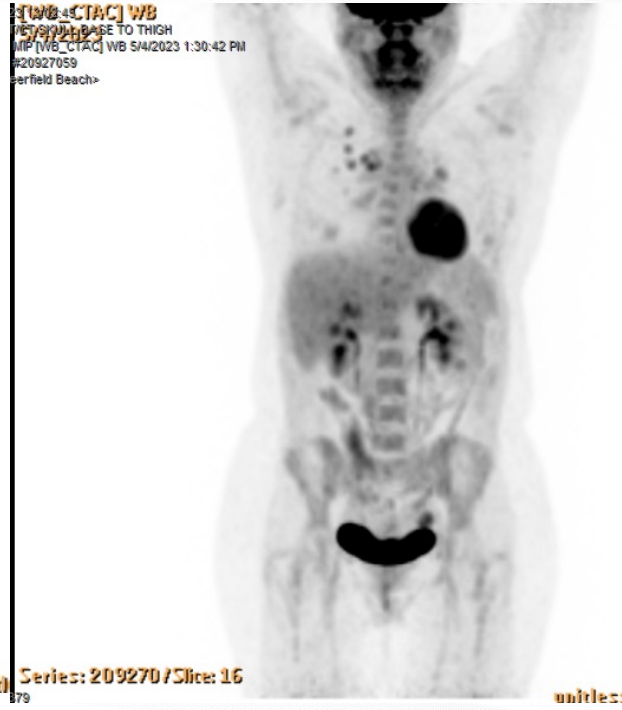

SYLVESTER COMPREHENSIVE CANCER CENTER
UNIVERSITY OF MIAMI HEALTH SYSTEM

P-GVD-P maintenance for one year

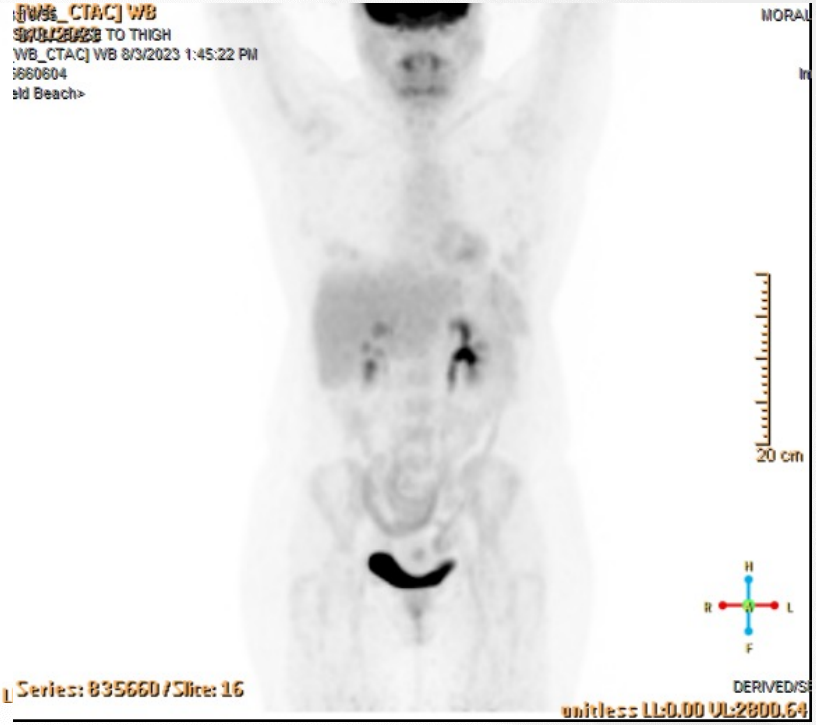
s/p PGVD x4




s/p 1 year pembro maintenance
Recovreing from covid




18 months post treatment



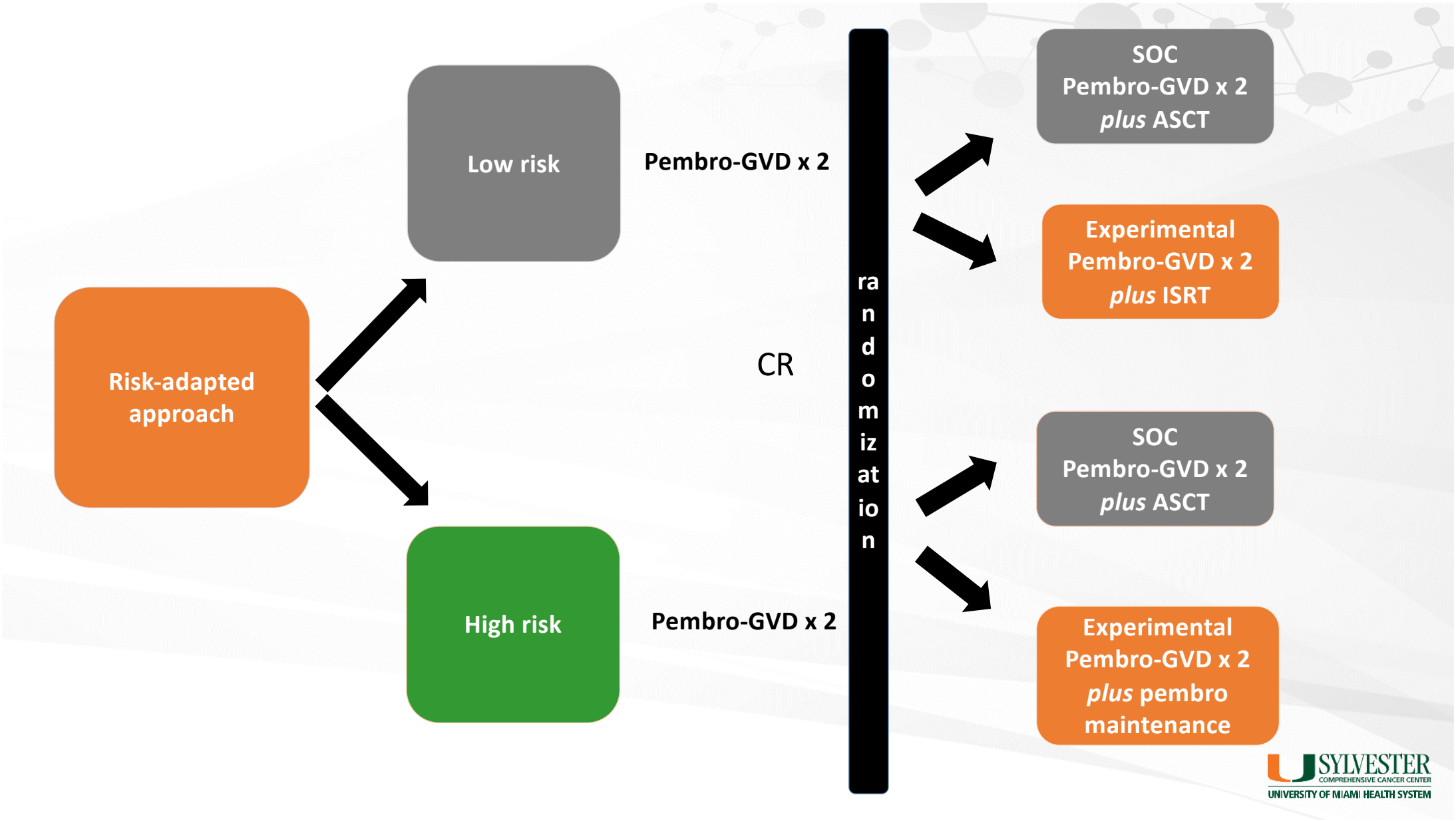

SYLVESTER
COMPREHENSIVE CANCER CENTER
UNIVERSITY OF MIAMI HEALTH SYSTEM

# Can the treatment paradigm be changed

- Not all salvage regimens are the same; consider efficacy, toxicity, easy of administration and cost
- Post-ASCT, BV should be standard for patients with multiple risk factors in BV naive pts or pts that have had a CR to BV based salvage but not 16 doses
- Research studies need to explore non-ASCT programs for favorable disease

- Off study I am in favor of withholding the salvage therapy/ASCT program until second relapse if patients have early-stage disease that relapses as early stage, if all the disease can be encompassed into a reasonable RT field using a novel agent and RT consolidation

- Excluding ASCT for any other pt group should not be done off study!


Risk-adapted approach
Low risk
Pembro-GVD x 2
High risk
Pembro-GVD x 2
CR
randomization
SOC
Pembro-GVD x 2
plus ASCT
Experimental
Pembro-GVD x 2
plus ISRT
SOC
Pembro-GVD x 2
plus ASCT
Experimental
Pembro-GVD x 2
plus pembro
maintenance
SYLVESTER
COMPREHENSIVE CANCER CENTER
UNIVERSITY OF MIAMI HEALTH SYSTEM

# I want to thank the HL patients for participating in these research studies over the past 30 years

**Lymphoma faculty at MSKCC where I spent 25 years of my life especially Joachim Yahalom who was the co-PI of all the pre-BV studies and Alison Moskowitz the co-PI of all the studies before I left in mid 2018 and now I am her co-PI!**

**Lastly, the lymphoma faculty at the University of Miami**

SYLVESTER COMPREHENSIVE CANCER CENTER
UNIVERSITY OF MIAMI HEALTH SYSTEM

# Lymphoma Service-Sylvester Comprehensive Cancer Center, University of Miami Health System

- Izidore Lossos
- Juan Alderuccio
- Alvaro Alencar
- Georgio Pongas
- Michelle Stanchina
- Juan Ramos
- Joe Rosenblatt
- Jonathan Schatz
- Craig Moskowitz

We see 1000 lymphoma consults each year

Griffen Cancer Research Building

Gemma, Dylan and Ethan

SYLVESTER COMPREHENSIVE CANCER CENTER
UNIVERSITY OF MIAMI HEALTH SYSTEM