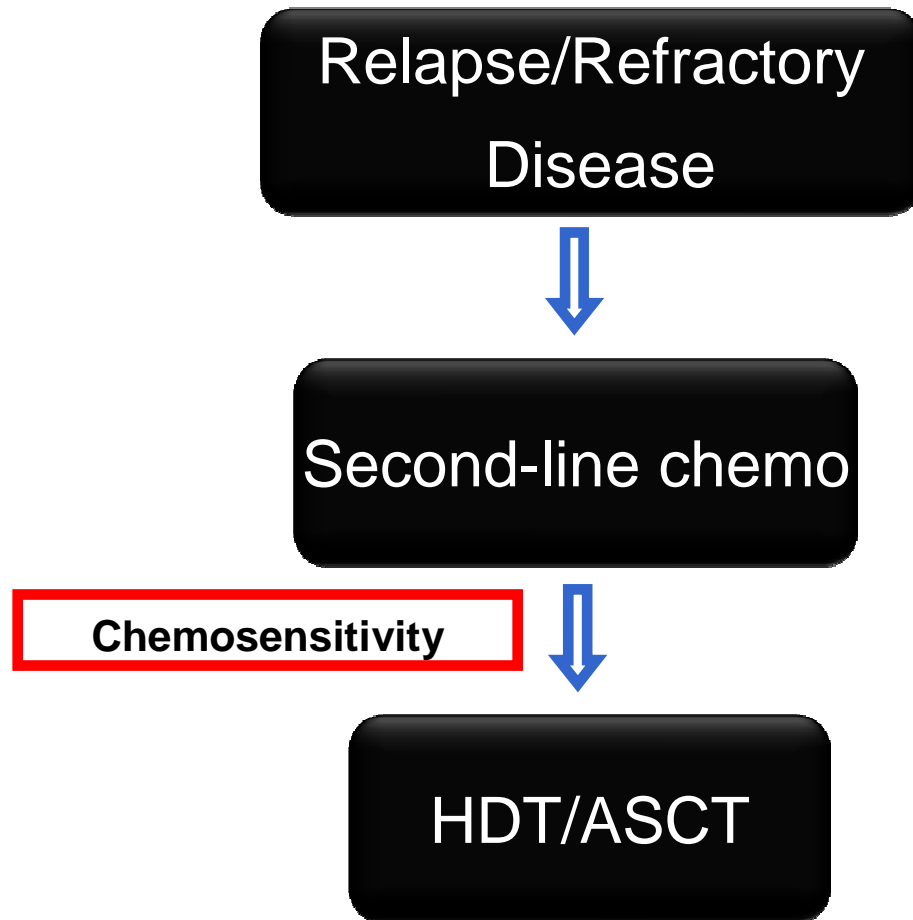


# PET in relapsed and refractory Hodgkin lymphoma

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# HL pathway



Schmitz, et al. Lancet. 2002.

Lynch, et al. Lancet. 1993

# Lesson learned from our first 3 studies 1985-2004

- **Intensive RT as part of transplant conditioning is safe and effective**
  - Goodman K, Moskowitz CH, Riedel E, Serrano V, Gulati S, and Yahalom J. Long-term outcome and quality of life of survivors of ASCT for relapsed and refractory Hodgkin Lymphoma. *J Clin Oncol.* 2008 Nov 10; 26(32):5240-7.
- **3 pre-salvage therapy risk factors predict outcome**

Moskowitz CH, Nimer SD, Portlock CS, Straus DJ, Hedrick EE, Gonzalez M, Walits J, Trippett TM Zelenetz AD, and Yahalom J. A 2-step comprehensive chemoradiotherapy program for relapsed and refractory Hodgkin's disease: intent to treat analysis and development of a prognostic model. *Blood* 2001, 97:616-623.
- **Normalization of functional imaging pre-ASCT is associated with a survival advantage; however to achieve this, tailored salvage therapy may be required**
  - Moskowitz CH, Yahalom J, Zelenetz AD, Zhang Z, Filippa D, Teruya-Feldstein J, Kewalramani T, Moskowitz AJ, Rice RD, Maragulia J, Vanak J, Trippett T, Hamlin P, Horowitz S, Noy A, O'Connor OA, Portlock C, Straus D and Nimer SD. High-dose chemo-radiotherapy for relapsed or refractory Hodgkin lymphoma and the significance of pre-transplant functional imaging. *Journal/Br J Haematol* 2010; 148 (6): 890-897.

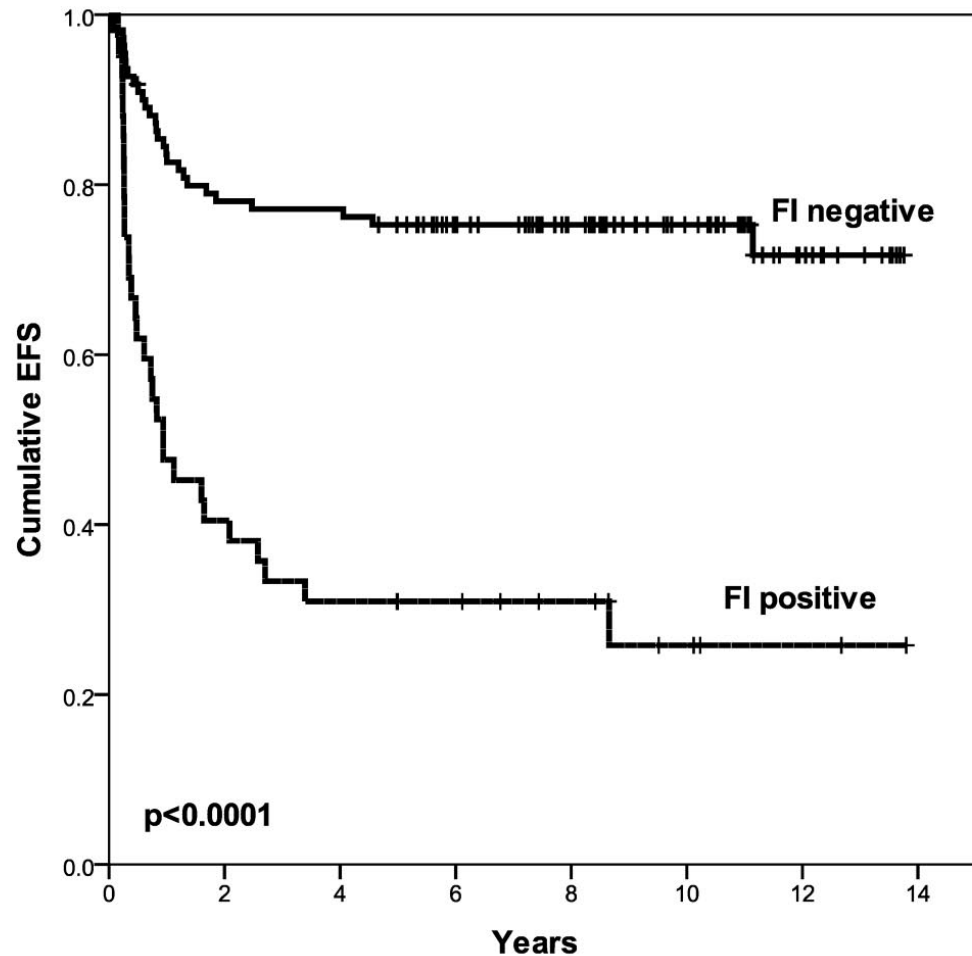
# Prognostic significance of pre-ASCT PET in HL

Reference	n	PET neg definition	PFS/EFS PET pos	PFS/EFS PET neg
Gentzler, et al. BJH 2014	32	Deauville 2**	52%	85%
Akhtar, et al. BMT 2013	141	< Mediastinal blood pool	49%	74%
Devillier, et al. Haematologica 2012	111	Harmonization	23%	79%
Smeltzer, et al. BBMT 2011	46	Harmonization	41%	82%
Mocikova, et al. Leukemia&Lymphoma 2011	76	Harmonization	36%	73%
Moskowitz, et al. Blood 2010*	153	Harmonization	31%	75%
Jabbour, et al. Cancer 2007*	211	< Background	27%	69%

\*Publications included gallium scans

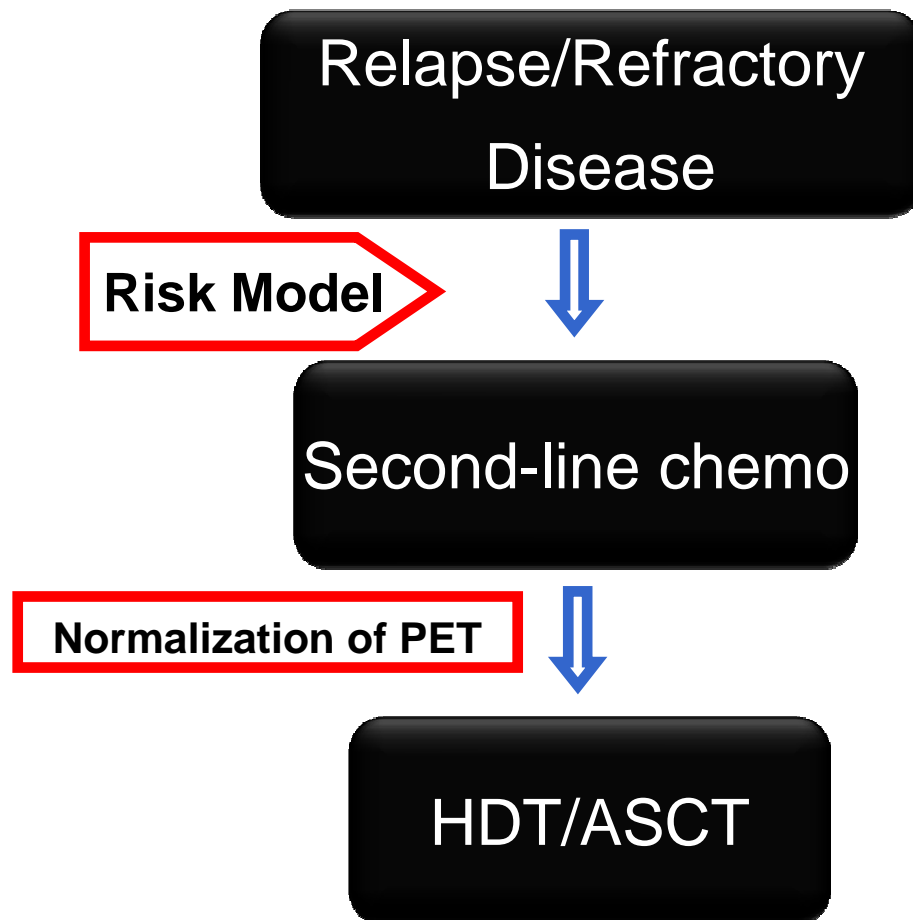
\*\*Results similar when PET negative defined as Deauville 3

# Pretransplant functional imaging in rel/ref HL (1994-2003)



- Risk adapted therapy administered based upon risk factors:
  - B symptoms
  - Extranodal disease
  - Relapse < 1 year
- Pre-transplant functional imaging was the most significant determinant of outcome

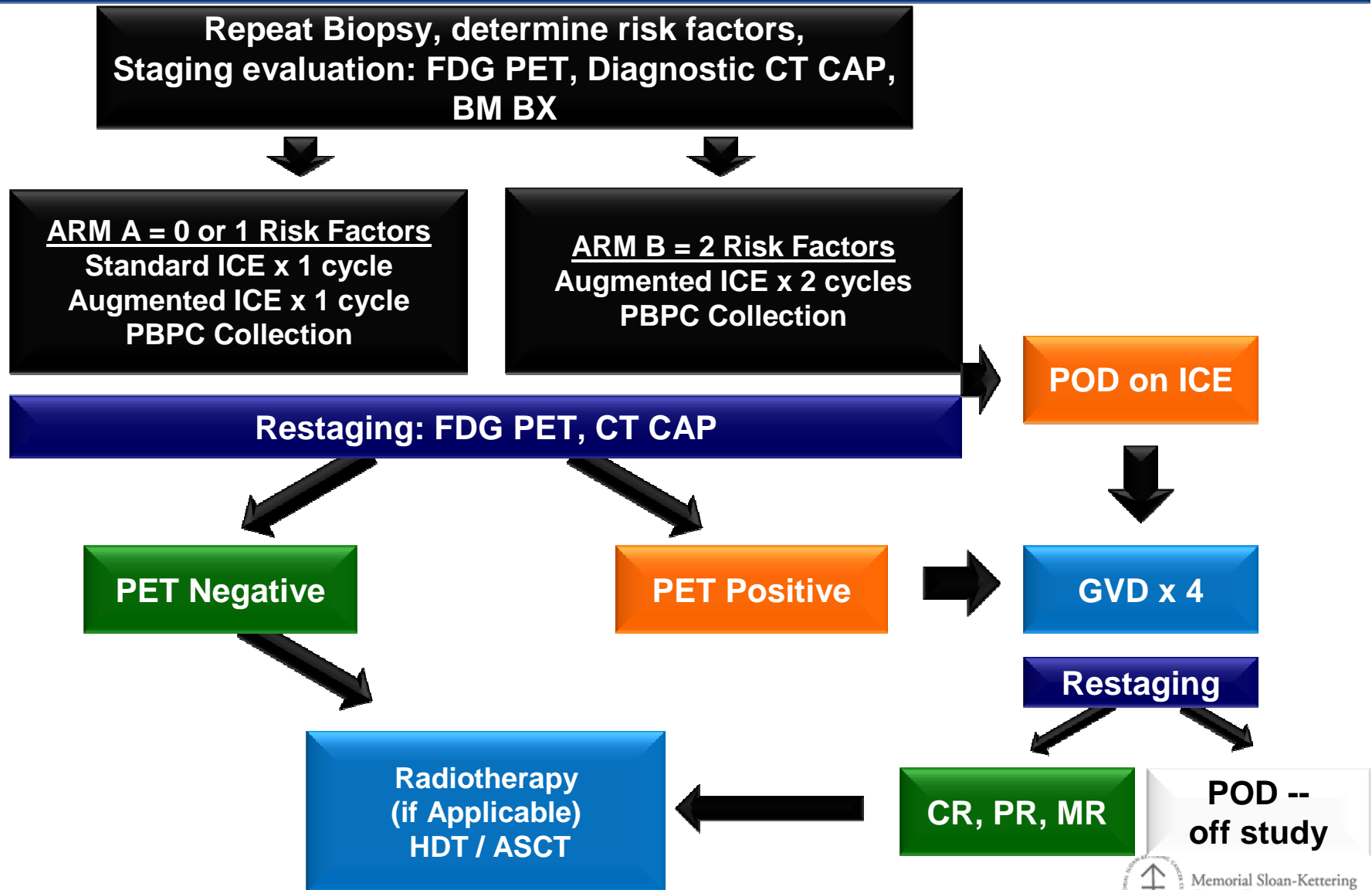
# HL pathway



## MSKCC Model

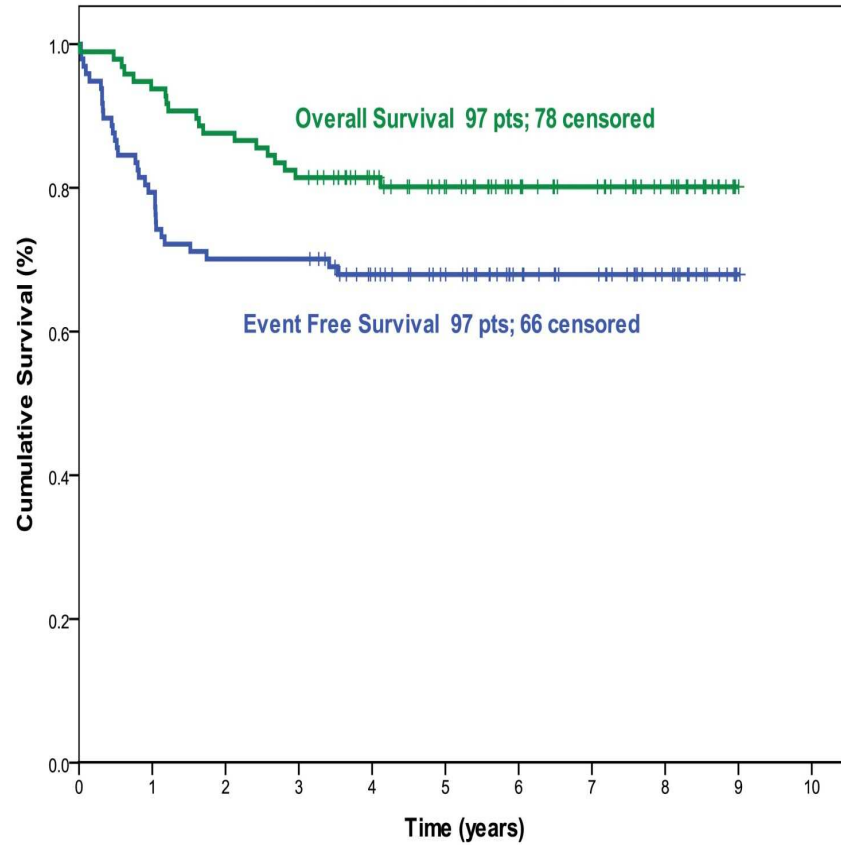
- B symptoms
- Extranodal disease
- Remission duration <1 yr.

# MSKCC Protocol 04-047 for relapsed and refractory Hodgkin Lymphoma

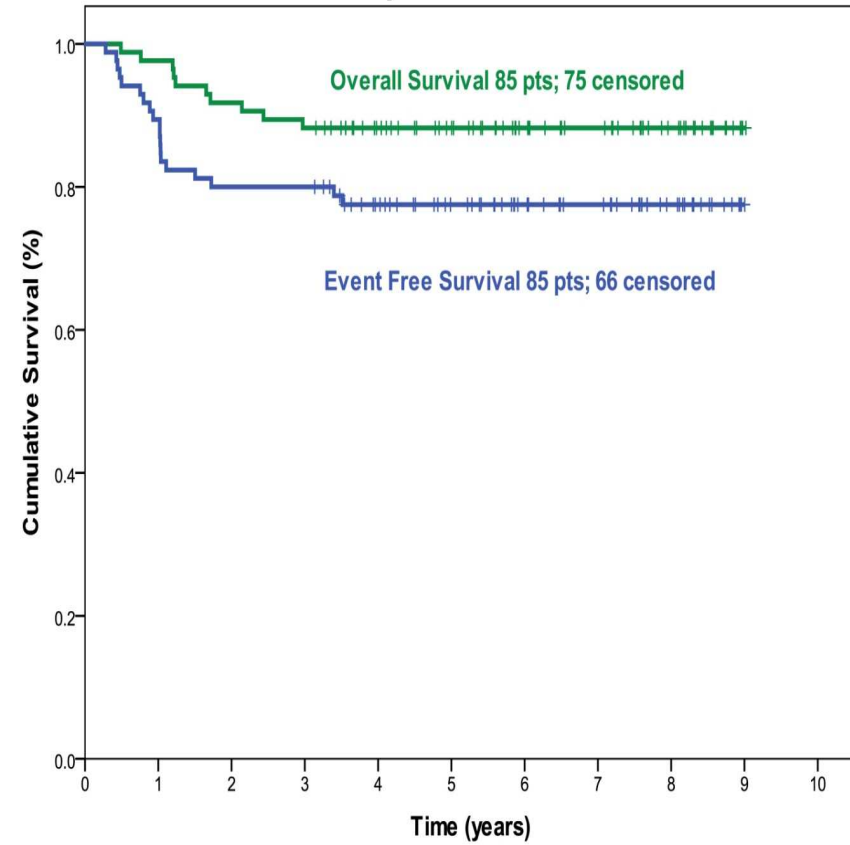


# Survival Curves 04-047

### Intent to Treat Cohort

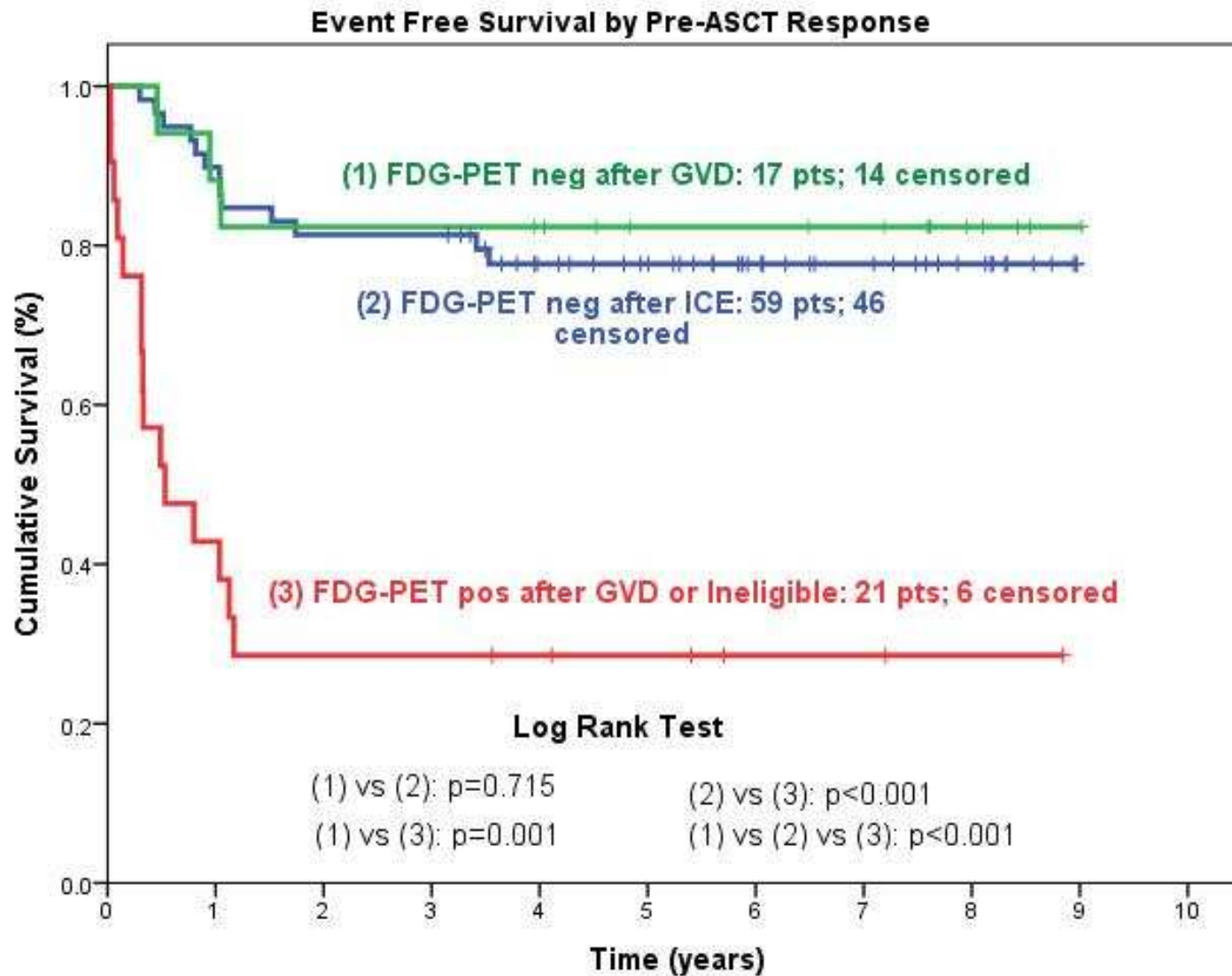


### Transplanted Patients

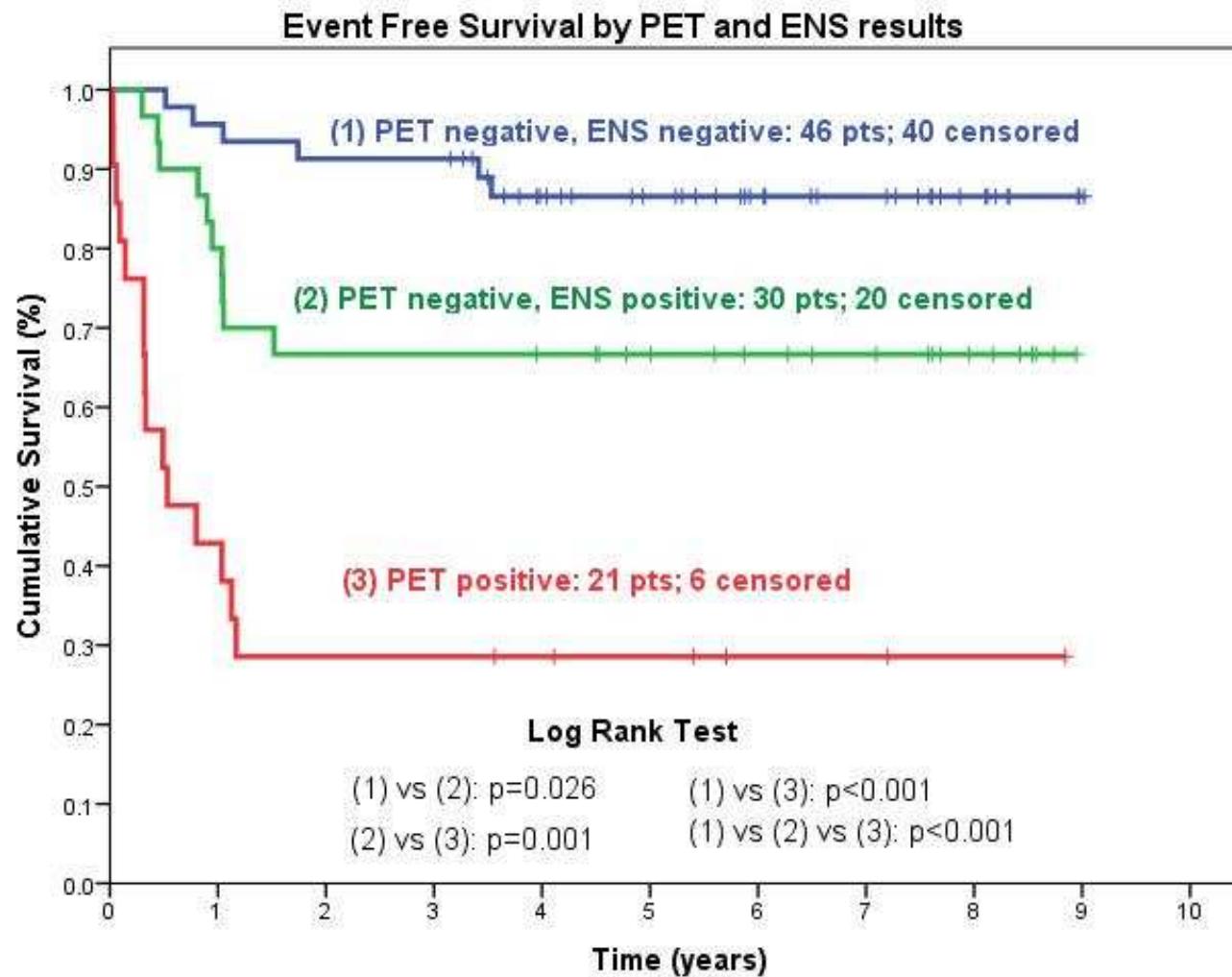




# Pre-ASCT Response



# FDG-PET and ENS



# Brentuximab vedotin (BV) as salvage therapy in rel/ref HL: **Rationale**

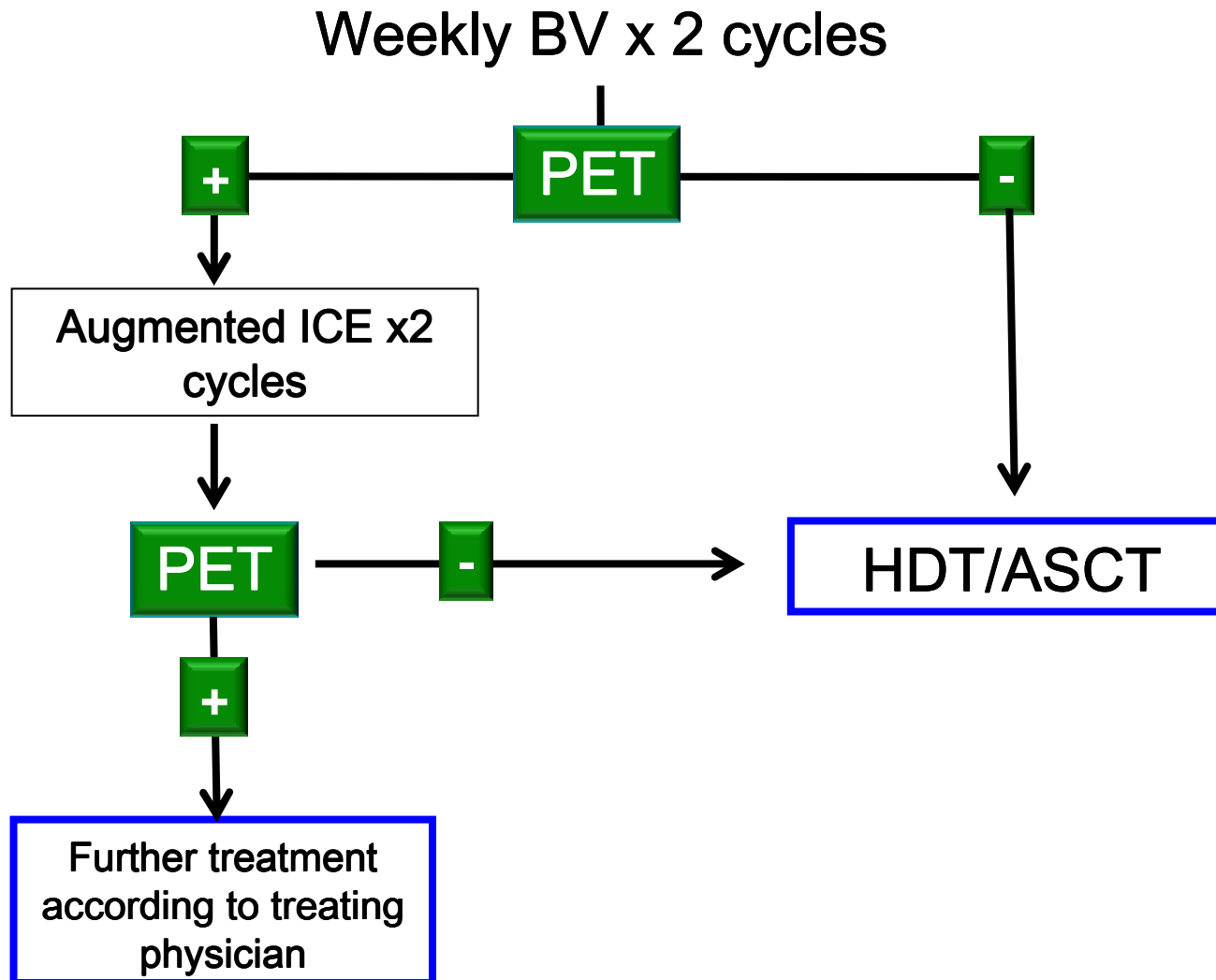
- **Current salvage regimens (i.e ICE, DHAP) are myelosuppressive, toxic**
- **Brentuximab vedotin is well tolerated and highly active in HL following transplant failure**
- **Pre-transplant FDG-PET is highly predictive of post-transplant outcome**

# Weekly Brentuximab vedotin – potential for earlier CRs with increased dose intensity

- **Phase I study evaluated weekly schedule for brentuximab vedotin**
  - **1.2 mg/kg weekly, 3 weeks on, 1 week off**
  - **41 patients; 86% with HL**
  - **CR rate 34%**
    - **12/14 CRs seen at first re-staging (8 weeks)**

# MSKCC 11-142: Relapsed/refractory HL

First TX following upfront therapy



# FDG-PET assessment

## Deauville criteria or 5 point scale

Score	FDG-PET/CT scan result
1	No uptake above background
2	Uptake $\leq$ mediastinum
3	Uptake $>$ mediastinum but $\leq$ liver
4	Uptake moderately more than liver uptake, at any site
5	Markedly increased uptake at any site or new sites of disease

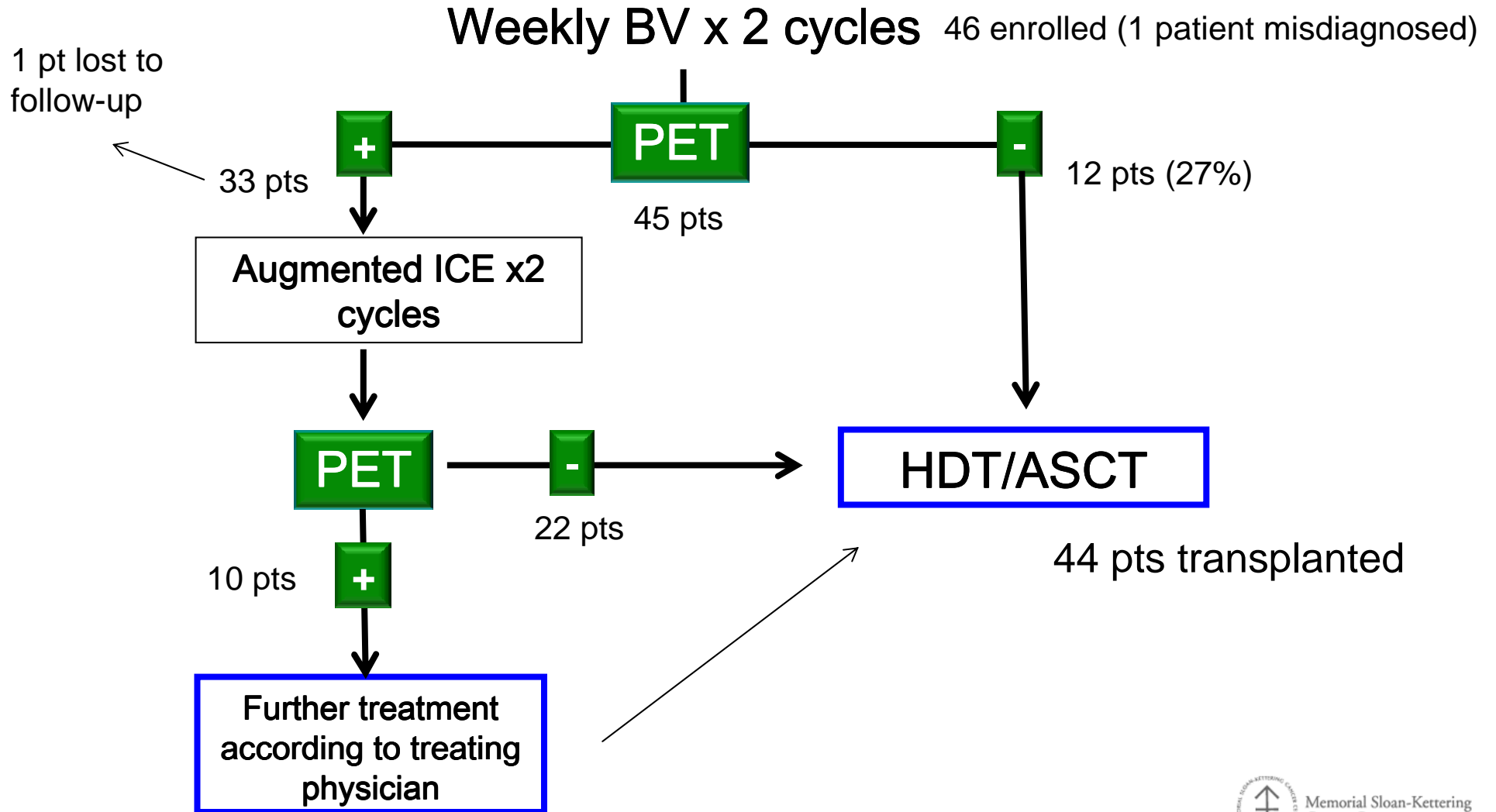
- Score of 1 or 2 = PET negative

# Patient characteristics

Characteristic	N=45
Male	25 (56%)
Median age (range)	31 (13-65)
Initial stage	I: 1 (2%) II: 20 (44%) III: 10 (22%) IV: 14 (31%)
Stage at enrollment	II: 20 (44%) III: 6 (13%) IV: 19 (42%)
Prior radiation	8 (18%)
Relapse > 1 year from initial Rx	7 (16%)
Relapse within 1 year of initial Rx	15 (33%)
Primary refractory	23 (51%)
Extranodal disease	19 (44%)
B symptoms	11 (24%)

# MSKCC 11-142

45 evaluable patients





# Deauville response to salvage therapy

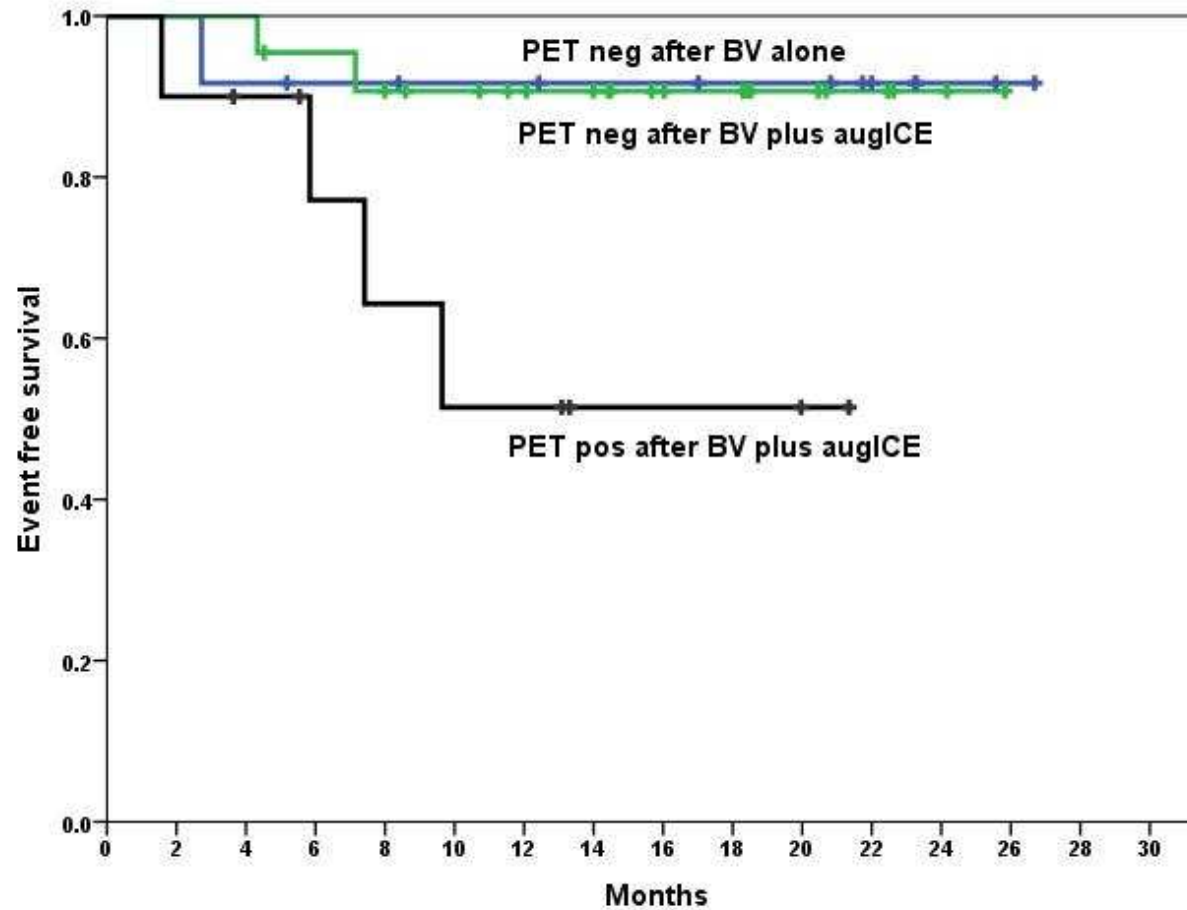
**BV (n=45)**

Deauville score	n
1	4
2	8
3	8
4	21
5	4

**AugICE (n=32)**

Deauville score	n
1	8
2	14
3	2
4	8
5	

# EFS according to treatment and PET status



# Path to ASCT for PET positive patients

Patient	Deauville Score		Stage at relapse	Post-augICE treatment	Time since ASCT	Status
	After BV	After augICE				
1	4	4	IIA	IFRT -> PR BEAM	16 months	NED
2	4	3	IVA	CBV	23 months	NED
3	4	4	IIB	IFRT -> CR BEAM	9 months	NED
4	4	4	IIISA	IFRT -> CR BEAM		Relapsed at 9 months
5	5	4	IIA	IFRT -> PR CBV		Relapsed at 7 months
6	4	4	IIA	IFRT -> PR BEAM	17 months	NED
7	4	4	IVA	R-BEAM		Relapsed at 8 months
8	4	4	IIXA	IFRT -> CR CBV	24 months	NED
9	3	3	IIA	CBV		Relapsed at 6 months
10	5	4	IVB	augICE#3-> PR CBV		Progression at 6 weeks

# Summary

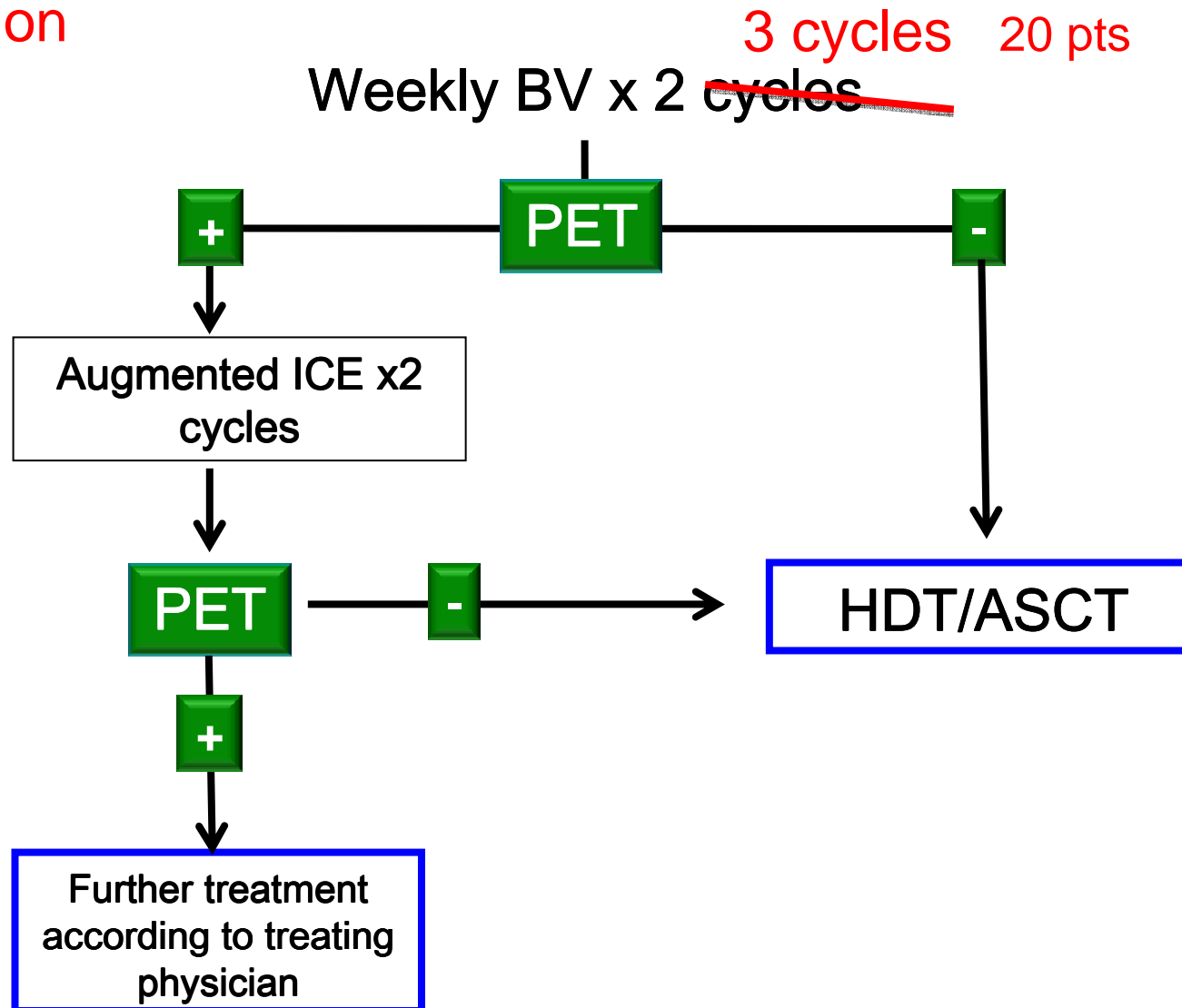
- **76% CR rate achieved with PET adapted sequential therapy with BV and augmented ICE**
- **27% patients avoided ICE salvage therapy**
- **44 transplants completed**
  - **Median time since transplant: 19 months (range 6-29 months)**

# Additional BV combinations under evaluation in the pre-transplant setting

- **Brentuximab vedotin combined with DHAP phase I/II in relapsed/refractory Hodgkin lymphoma (Europe)**
- **Brentuximab vedotin combined with ICE in relapsed/refractory Hodgkin lymphoma (Washington)**

# MSKCC 11-142

## Expansion

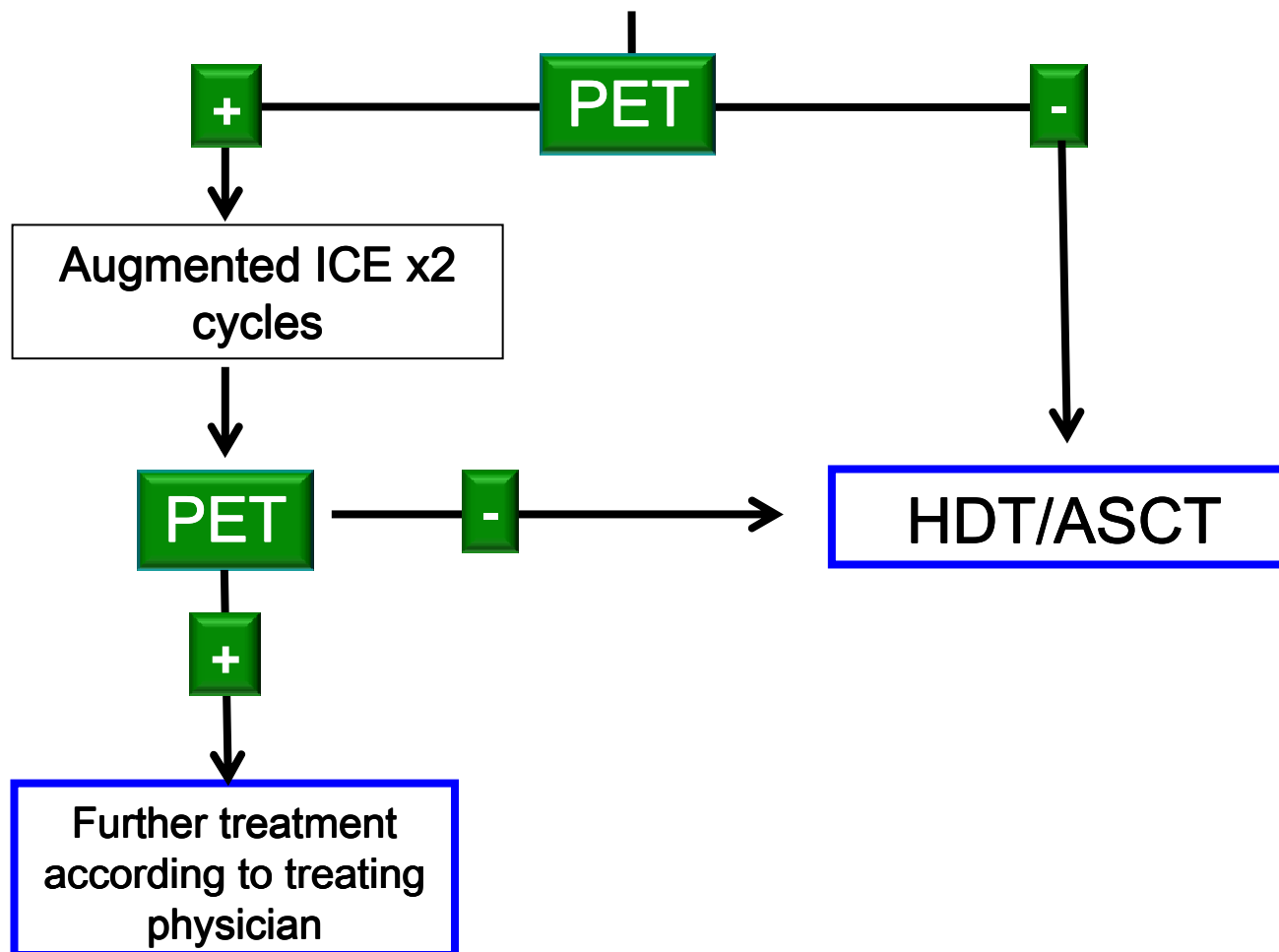


# Moving forward

## Developing novel combinations within the setting of PET-adapted salvage therapy

Novel BV combinations

~~Weekly BV x 2 cycles~~



# Acknowledgements

## **MSKCC Lymphoma Service**

- **John Gerecitano**
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