Should interim restaging FDG-PET change the planned management of DLBCL

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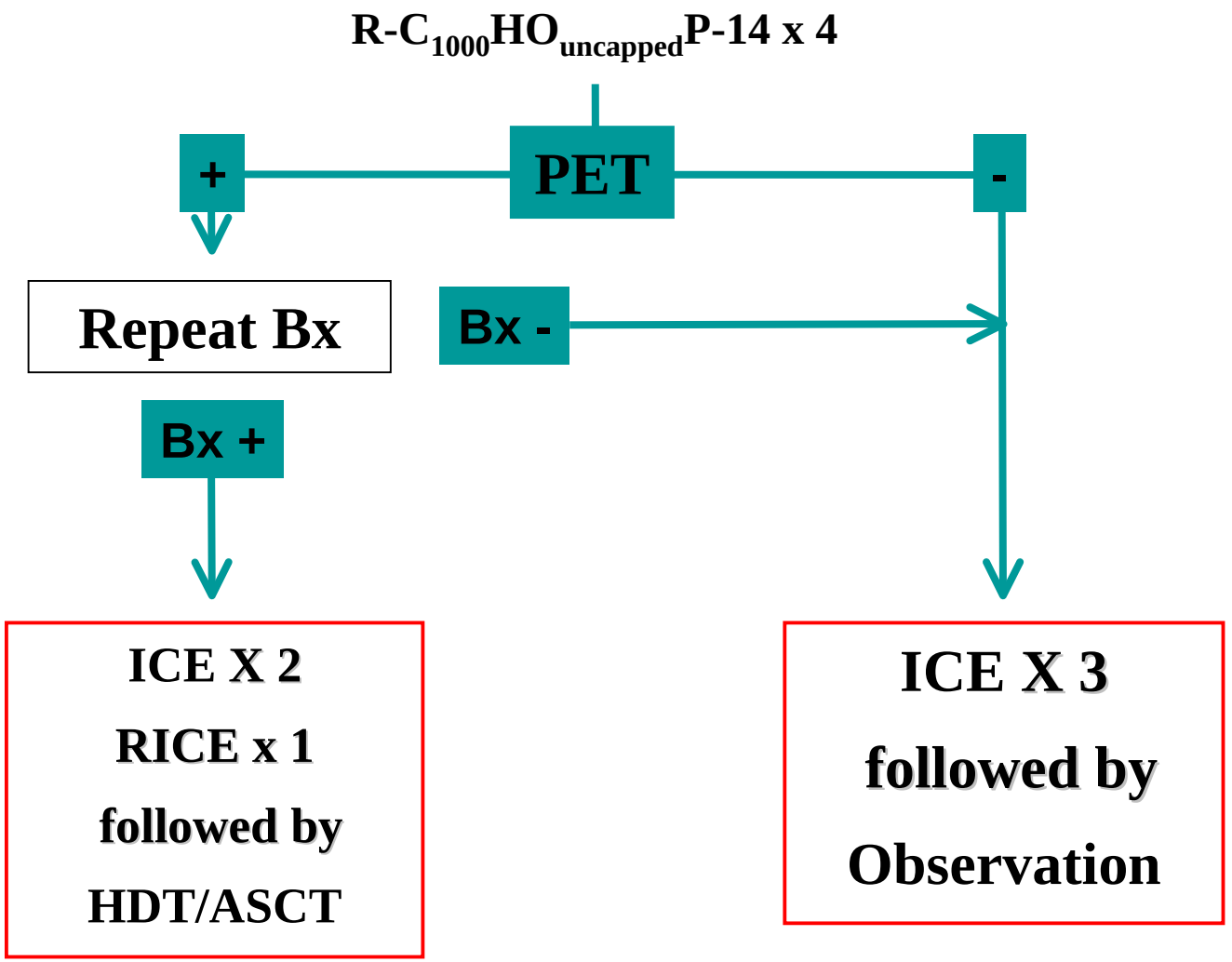
MSKCC 01-142: DLBCL: Risk Adapted for Therapy

CS IIX, III or IV disease, age-adjusted IPI 1, 2, or 3 Risk Factors, Transplant Eligible



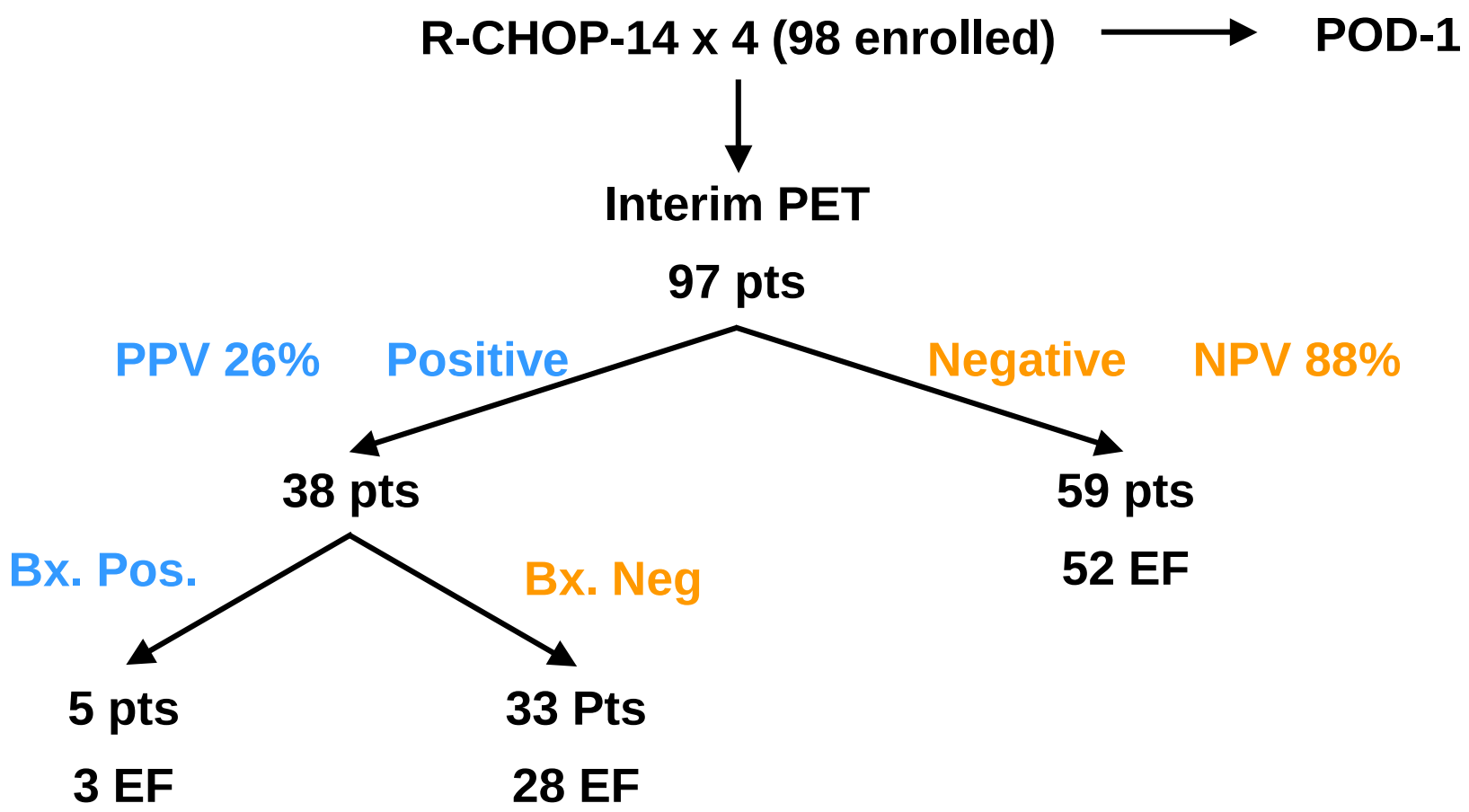
- Prospective, biopsy controlled determination of "positive PET"
- Therapy interval 2 weeks
- PET 10-14 days post cycle 4
- Treatment is adapted by biopsy, not PET
- No radiation therapy permitted except for testicular disease
- IT methotrexate for aaHR, paranasal sinus, testis, BM

MSKCC 01-142: Patient Characteristics

Characteristic		
N		98
Gender	Male	57
	Female	41
Median age		47
	Range	20-65
>60		16
KPS <80		32
LDH >normal		85
CS	IV	64
aaIPI	LR	Excluded
	LIR	21
HIR		49 } 79%
	HR	28 }

Characteristic	
CD10	26/91
BCL6	60/89
MUM1	36/87
P53	38/82
Cell of Origin*	
GC	40%
Non-GC	30
PMLBL	30
Indeterminate	4
Median Ki-67 (MIB1)	63%
≥ 80%	37

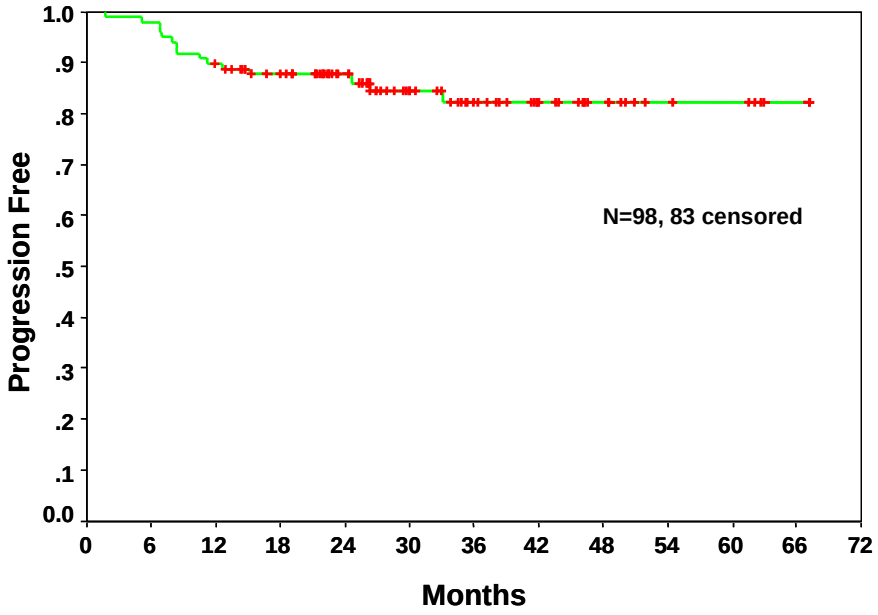
DLBCL: Risk adapted therapy
MSKCC 01-142



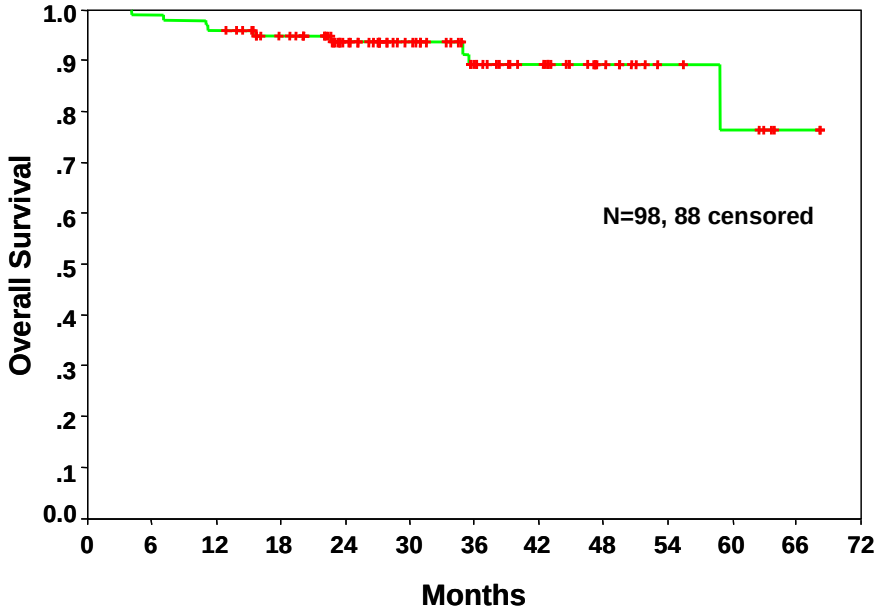
Total of 10 patients dead of disease

MSKCC 01-142: Outcomes

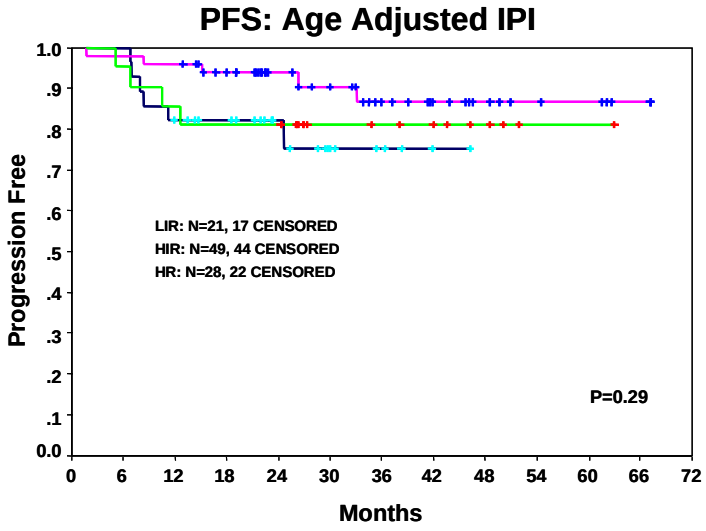
Progression Free Survival

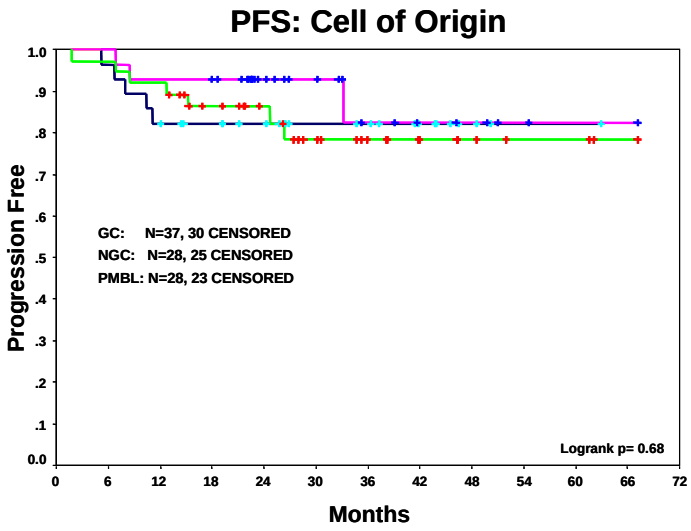


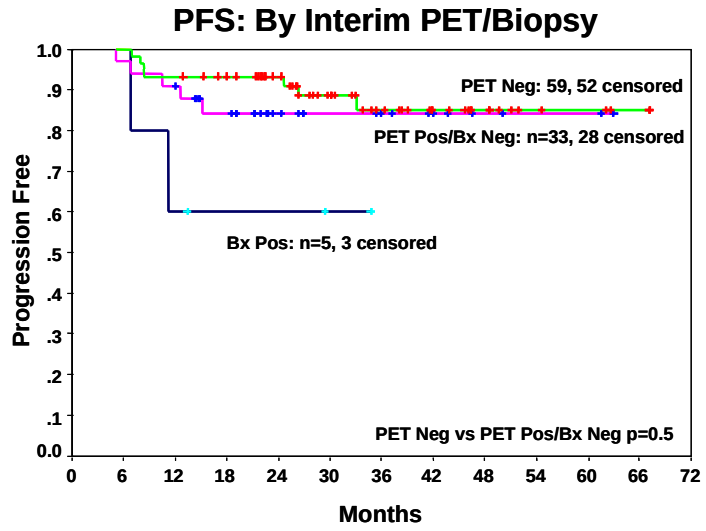
Overall Survival

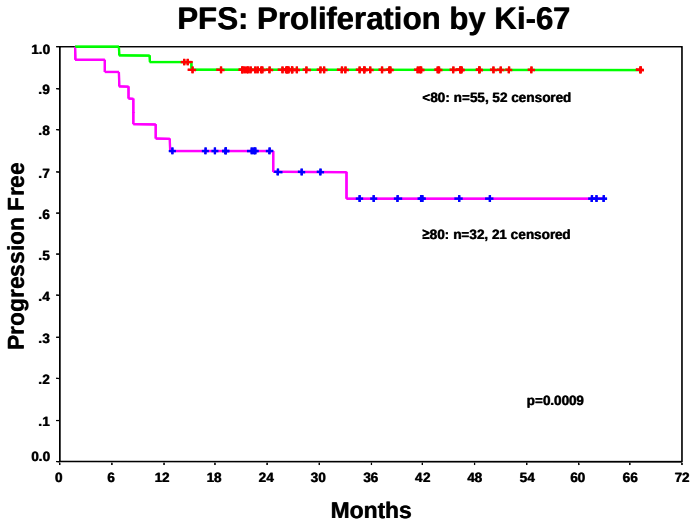


MSKCC 01-142: Outcome By Previously Identified Prognostic Factors









What Explains the Frequency of False Positive Interim PET Scans in This Study?

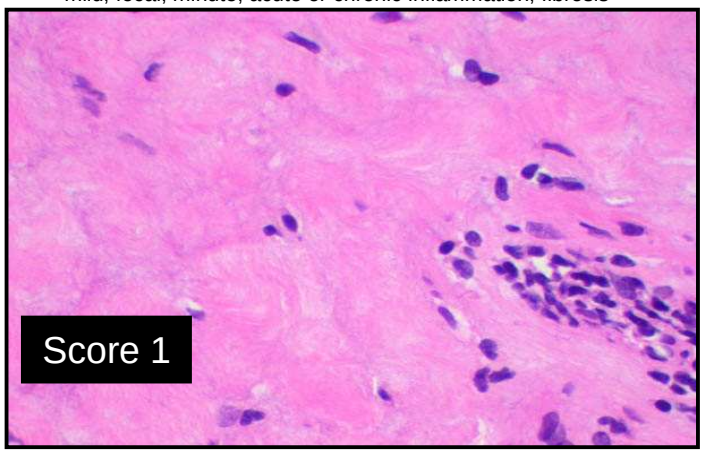
- **Differences with prior analyses of Spaepen and Haioun:**
  - **Dose dense therapy forces PET scan to be done within 14 days of therapy, median 12 days**
  - **All patients received rituximab**

- **Does residual inflammation explain the false positives?**

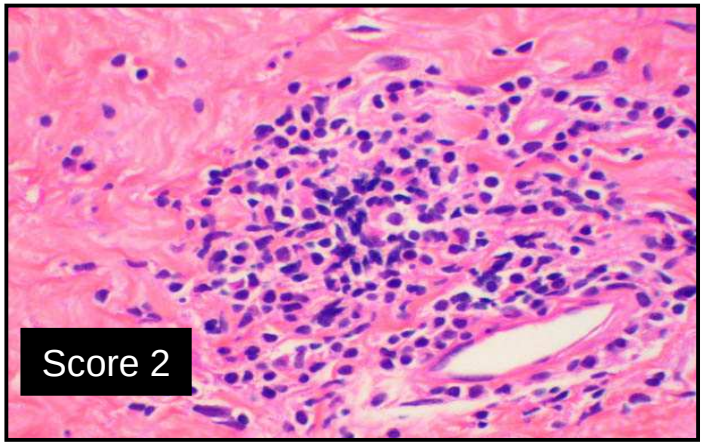
Spaepen et al. Ann Oncol 2002;13:1356-1363; Haioun et. Al, Blood 2005 106(4)

Inflammation Score for Interim Biopsies

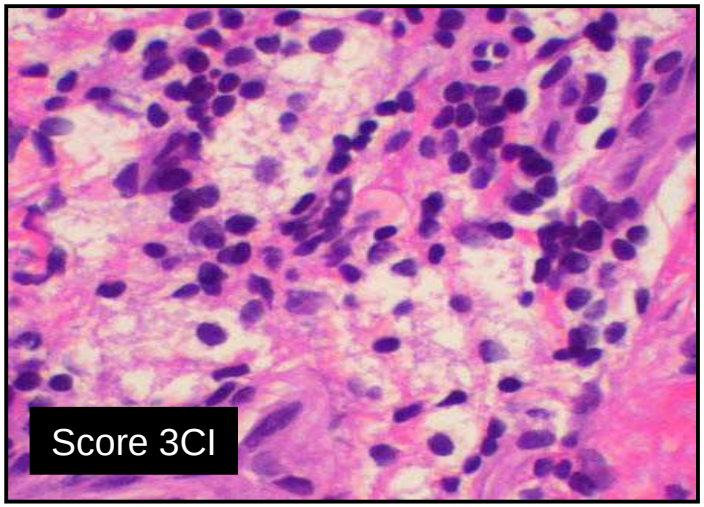
mild, focal, minute, acute or chronic inflammation, fibrosis



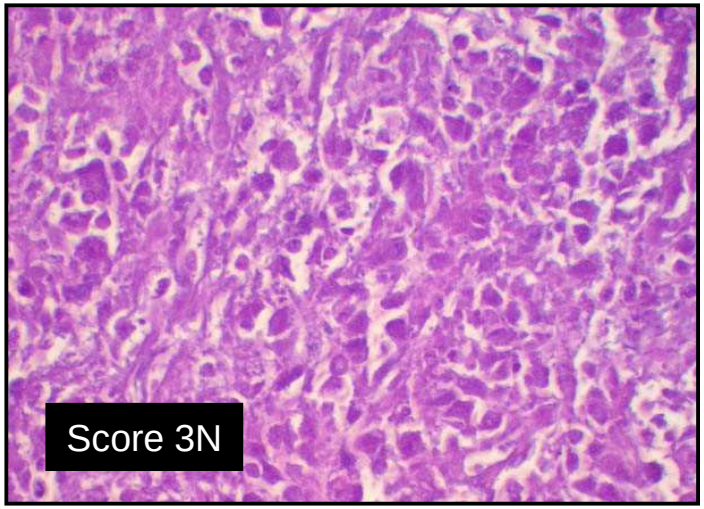
moderate inflammation with macrophages



marked inflammation



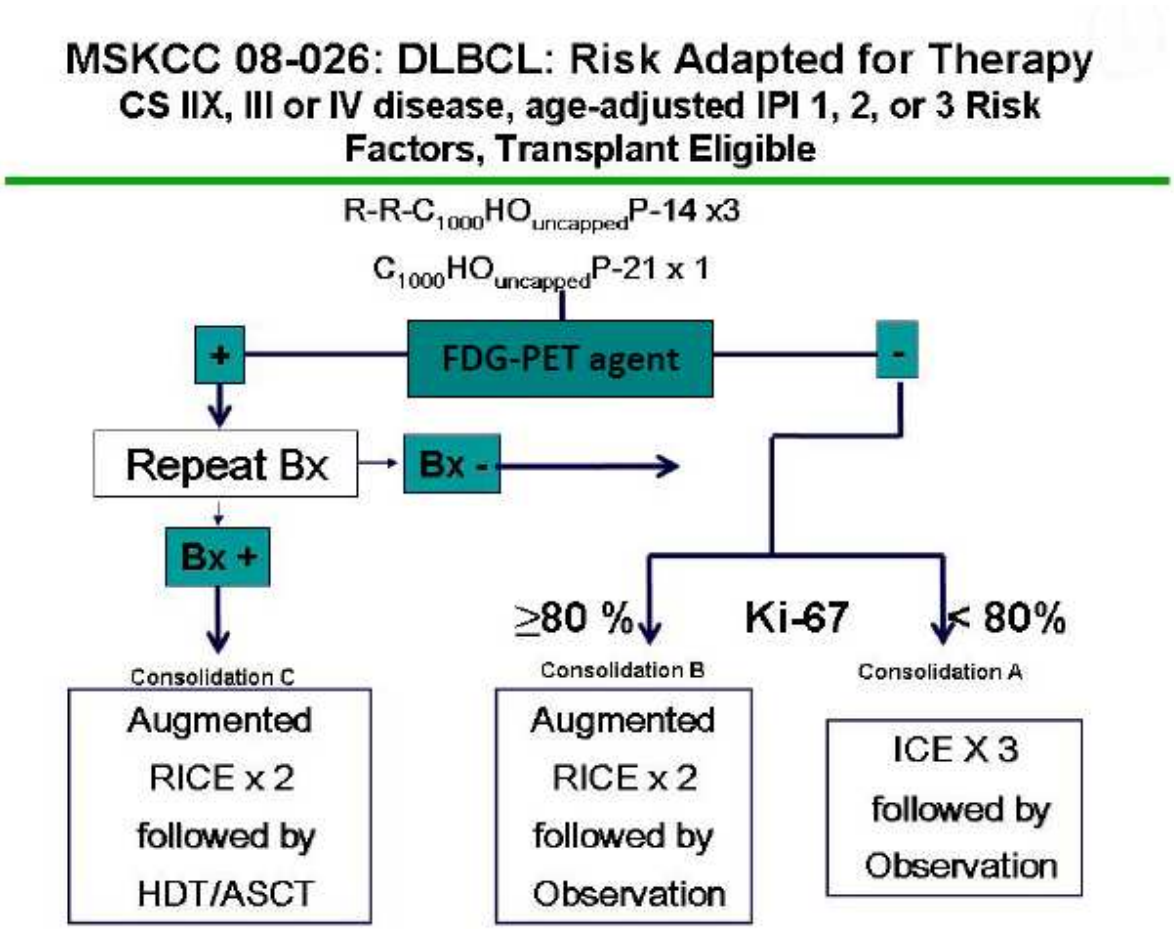
marked necrosis



Inflammatory Score and $SUV_{INTERIM}$

Inflammatory Score	N	$SUV_{INTERIM}$ (Median/ Range)	Residual DLBCL
1	14	3.5 1.5-11.5	0
2	3	3 2.5-11.5	0
3	14	3.4 2-14	4

Schema


MSKCC 08-026: DLBCL: Risk Adapted for Therapy
CS IIX, III or IV disease, age-adjusted IPI 1, 2, or 3 Risk Factors, Transplant Eligible
R-R-C1000HOuncappedP-14 x3
C1000HOuncappedP-21 x 1
FDG-PET agent
+
-
Repeat Bx
Bx -
Bx +
≥80 %
Ki-67
< 80%
Consolidation C
Augmented RICE x 2 followed by HDT/ASCT
Consolidation B
Augmented RICE x 2 followed by Observation
Consolidation A
ICE X 3 followed by Observation

Accrual and Current Status

- **Total accrual: 35 patients (3/10/2010)**
- **Patients actively being treated: 3**
- **Patients in follow-up: 27**
  - **1 patient off-study for hydropneumothorax discovered on second FLT PET**
- **Consolidation Accrual:**
  - **Consolidation A: 21 patients**
  - **Consolidation B: 8 patients**
  - **Consolidation C: 1 patient**
  - **Undetermined: 3 patients**
  - **Did not proceed to Consolidation therapy: 2 patients**

Patient Characteristics

- **Median age at outset: 51years (range: 21-71)**
- **63% female**
- **10/35 patients with PMBL**
- **aaIPI***
  - **All three risk factors (HR): 12**
  - **Two risk factors (HIR): 11**
  - **One risk factor (LIR): 9**

***Need additional information to determine aaIPI for 3 patients**

Interim Restaging

- **Summary:** **30 patients have undergone 4 cycles of RR-CHOP14/CHOP21 followed by interim restaging scans (2 off-study before restaging, 3 currently receiving induction therapy)**

- **RESULTS:**
  - **13 / 30 (43%) had a positive FDG-PET scan**
  - **Biopsy location of PET-avid sites: mediastinal mass (5), lymph node (4), inguinal soft tissue (1), splenic nodule (1), colon (1), tonsil (1)**
  - **12 / 13 (92%) biopsies were negative**

DLBCL Summary

- **When R-X chemotherapy is administered, interim restaging FDG-PET negative patients have greater than an 80% 5 yr. PFS**
- **However, if the test is positive PFS ranges from 30-70%**

- **Clearly interim FDG-PET scans for patients are investigational!**

Lymphoma Disease Management

- Lymphoma Service
  - John Gerecitano
  - Paul Hamlin
  - Steve Horwitz
  - LiaPalomba
  - Craig Moskowitz
  - ArielaNoy
  - Carol Portlock
  - David Straus
  - Andrew Zelenetz
- Nuclear Medicine
  - Heiko Schoder
  - Neetha Pandit-Tasker
- Radiation Oncology
  - Joachim Yahalom
- Transplant Services
  - Matt Matasar
  - Craig Sauter
  - Craig Moskowitz
  - Juliet Barker
  - Hugo Castro-Malaspina
  - Miguel Perales
  - Jill Vanak
- Pathology
  - Julie Feldstein
  - Daniel Filippa
  - Cyrus Hedvat
  - Oscar Lin