

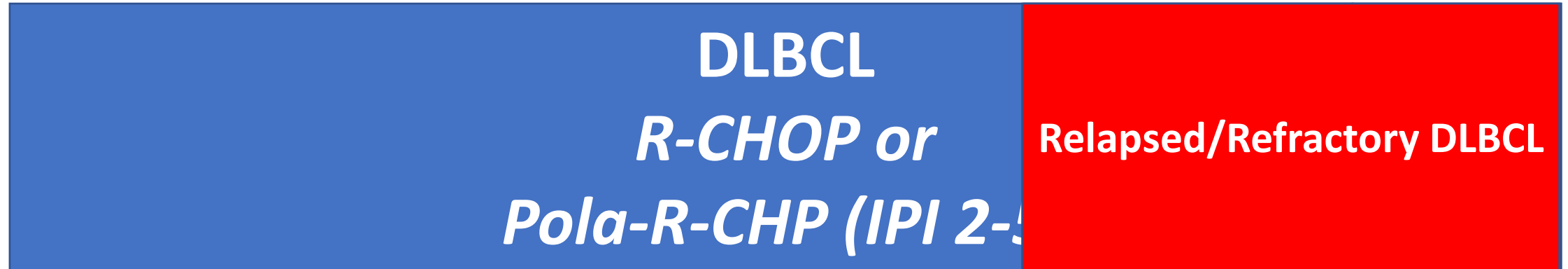
RT for Incomplete Response or Salvage Treatment of DLBCL

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Dana-Farber/Brigham Cancer Center
Harvard Medical School



**4th ILROG Educational Conference:
Radiotherapy in Modern Management of Haematological Malignancies**

Background



DLBCL
R-CHOP or
Pola-R-CHP (IPI 2-5)

Relapsed/Refractory DLBCL

- 1) If refractory, or relapse within 1 year → CAR T therapy (*ZUMA-7, TRANSFORM*)
- 2) If relapse > 1 year and transplant candidate → second line chemotherapy followed by transplant
- 3) If relapse > 1 year and not transplant candidate → CAR T therapy (*TRANSCEND PILOT*)
- 4) If not CAR T or transplant candidate, or additional relapses after CAR T therapy:
immunochemotherapy, Pola-R-Benda, Tafa-len, Bispecifics, Selinexor, Lonca, allo transplant, clinical trial, palliative RT

Background

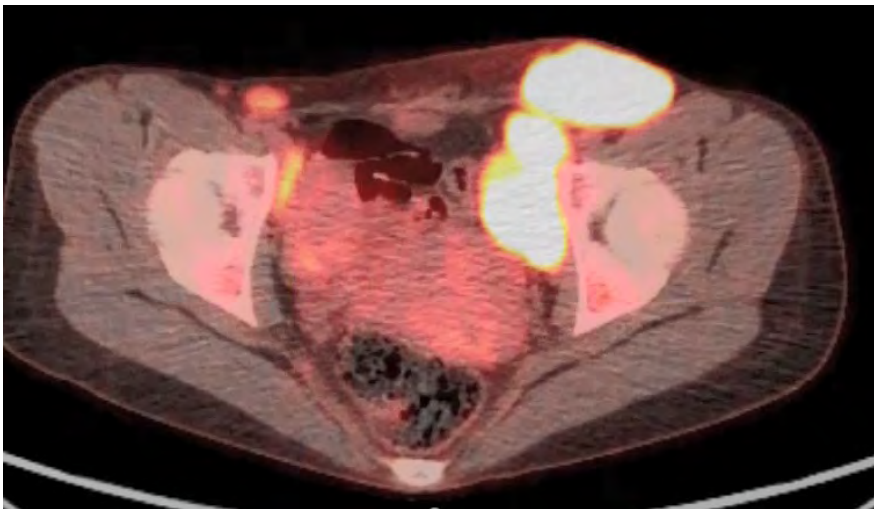
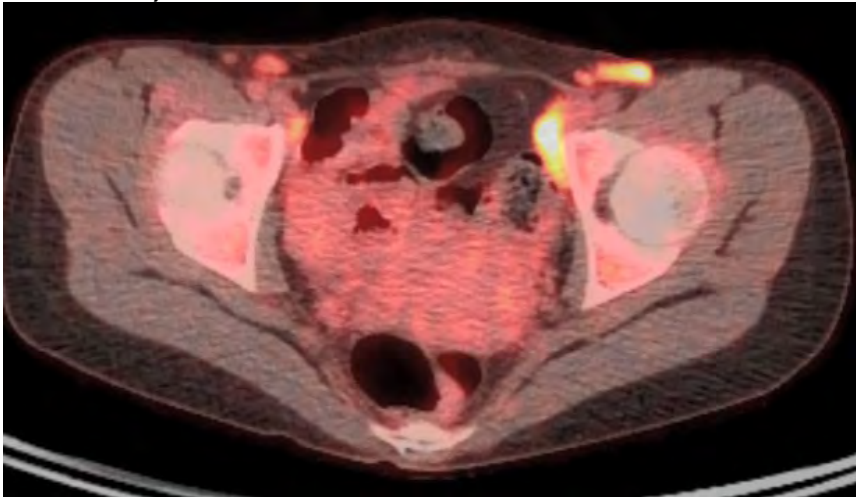
DLBCL
R-CHOP or
R-CHP (IPI 2-5)

12-25% will
have a good PR
but with
residual FDG
avidity
(Deauville 4/5)

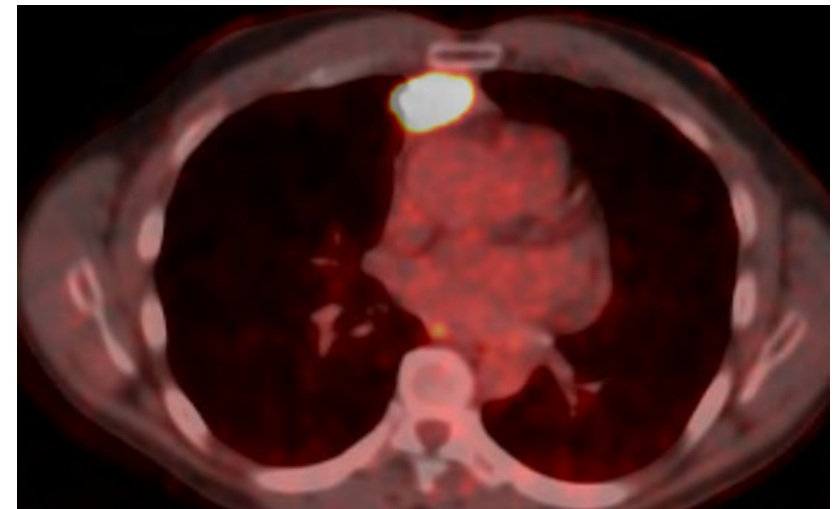
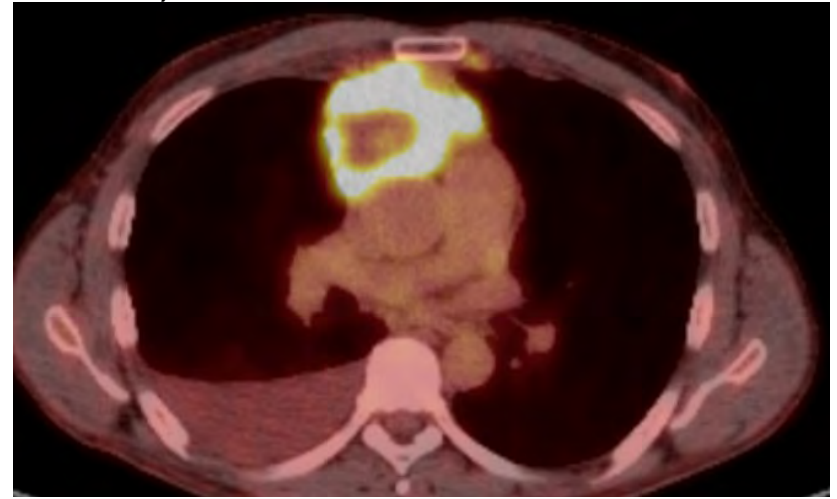
10-15% will
have primary
refractory
disease

Case Examples of Deauville 5

Case A, Deauville 5

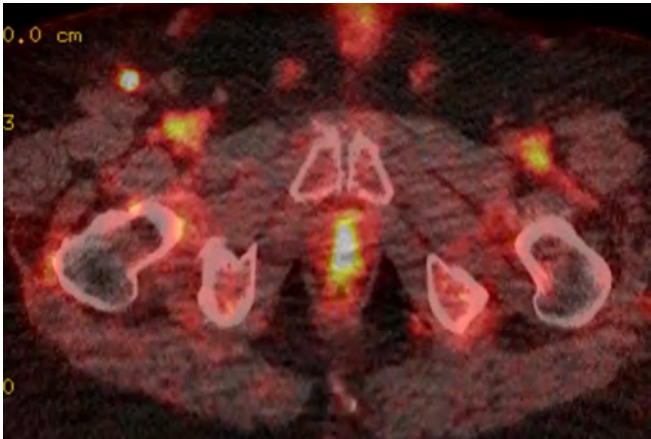
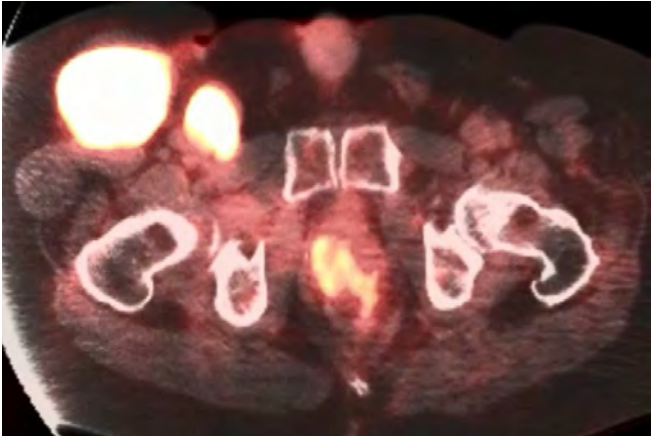


Case B, Deauville 5

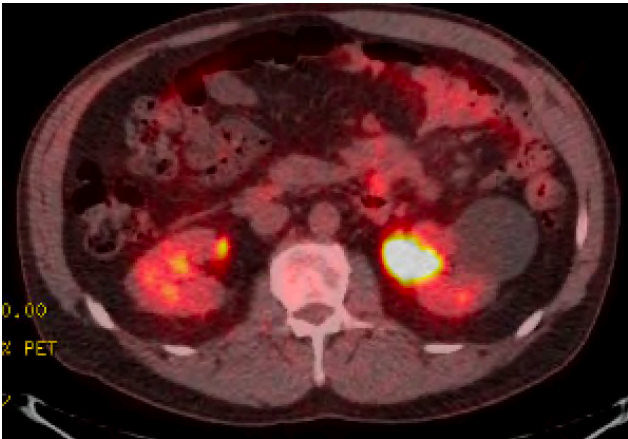
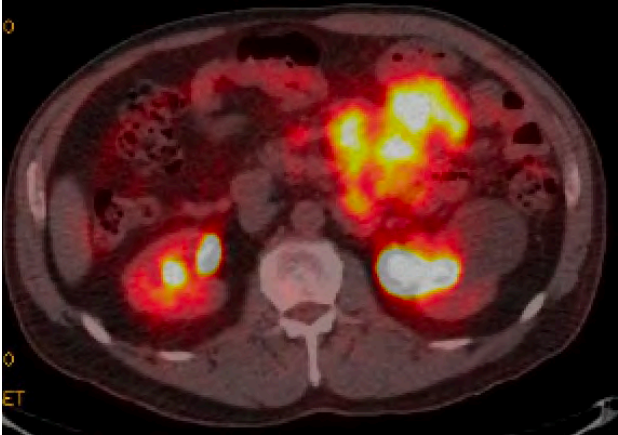


Case Examples of Deauville 4-5

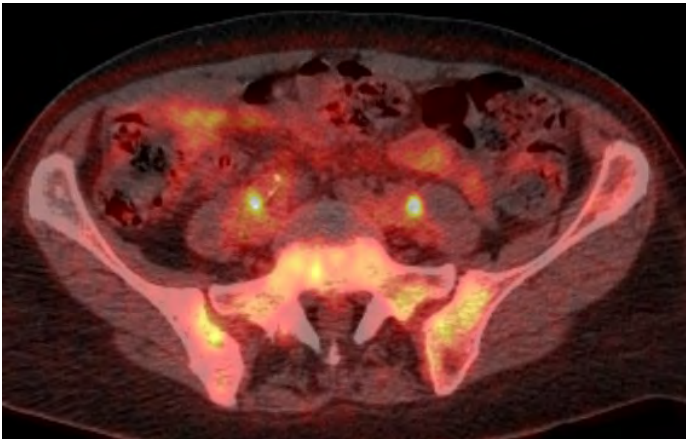
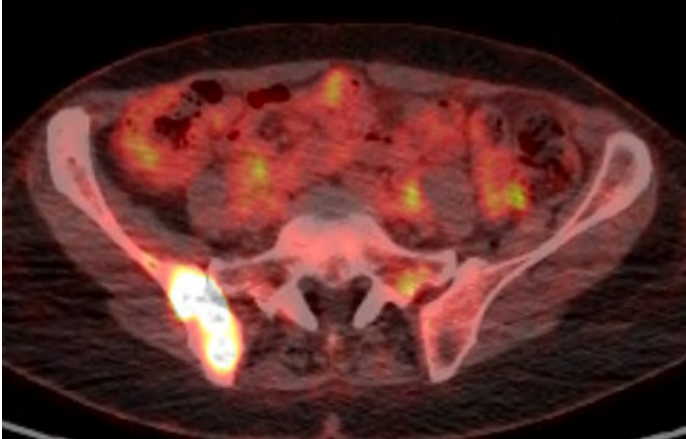
Case C, Deauville 5



Case D, Deauville 4



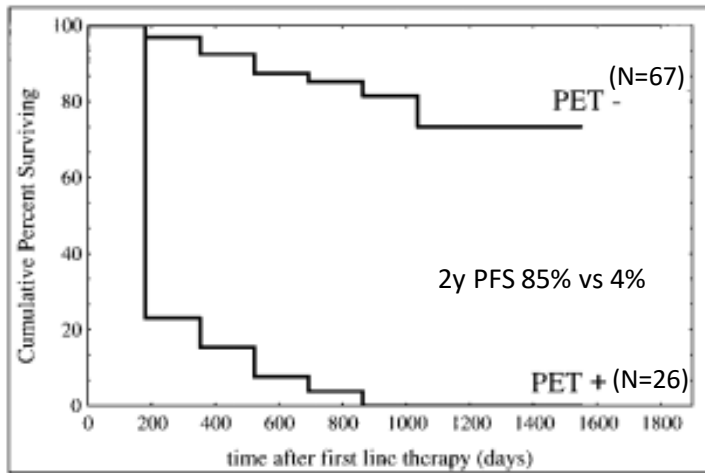
Case E, Deauville 4



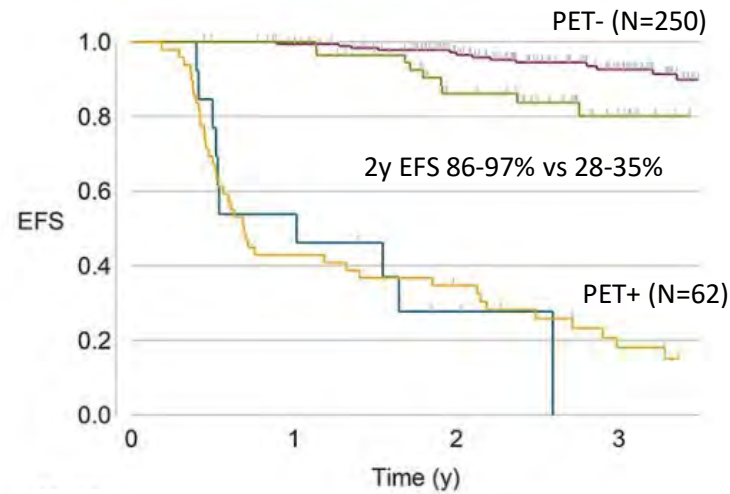
Options:

- Close observation; repeat PET-CT in 2-3 months
- ISRT alone
- CAR-T +/- bridging therapy

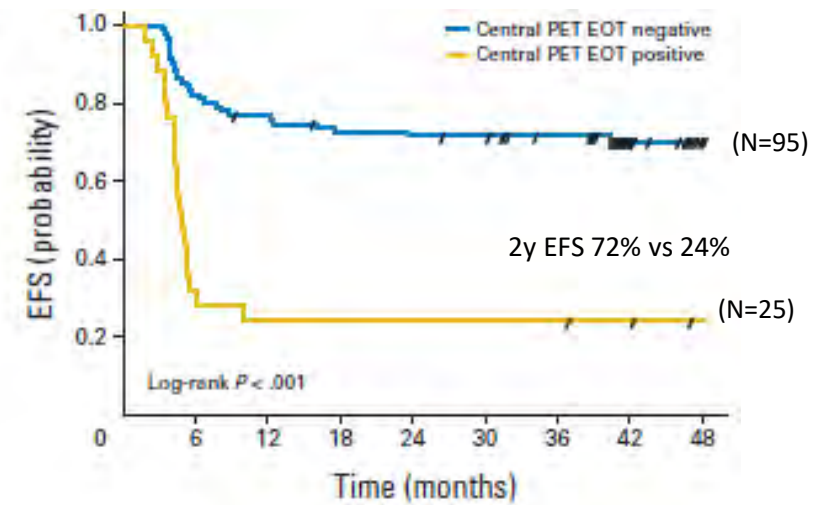
What is the prognosis of patients with DLBCL with residual PET avidity at EOT?



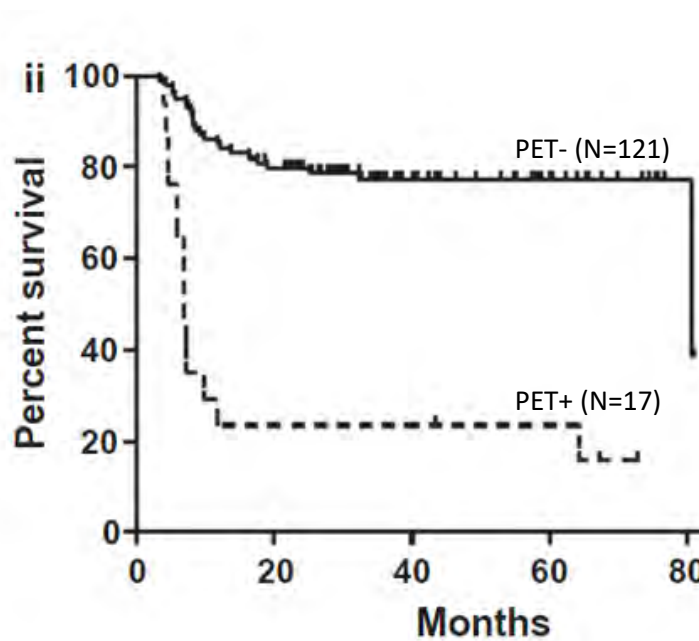
Spaegen. JCO 2001



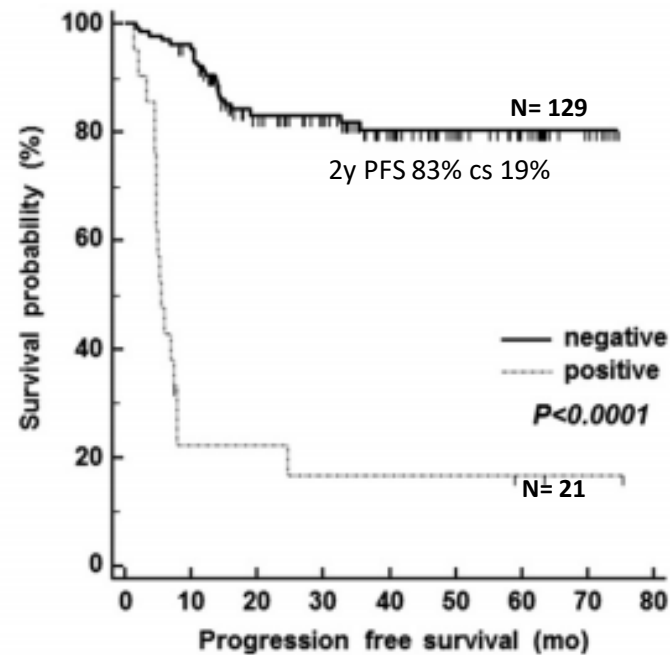
Carr. J Nucl Med 2014



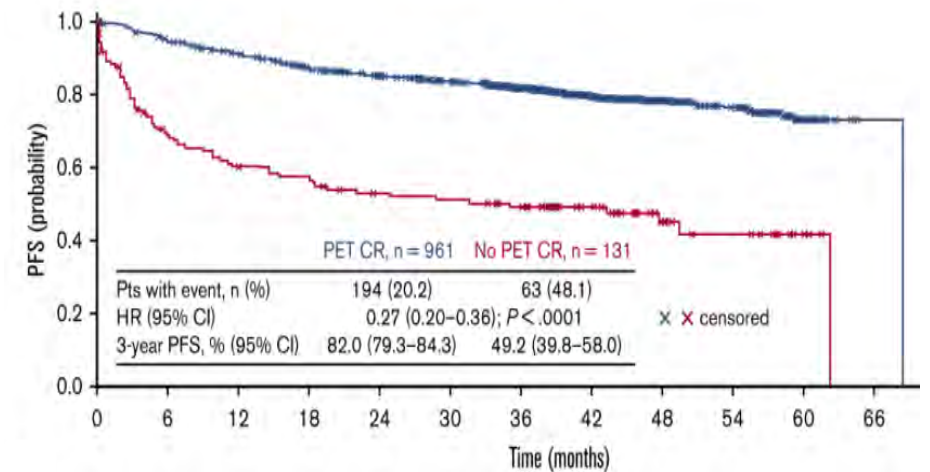
Mamot. JCO 2015



Bishton et al. BJH 2016



Kim. Leuk Lymph 2018



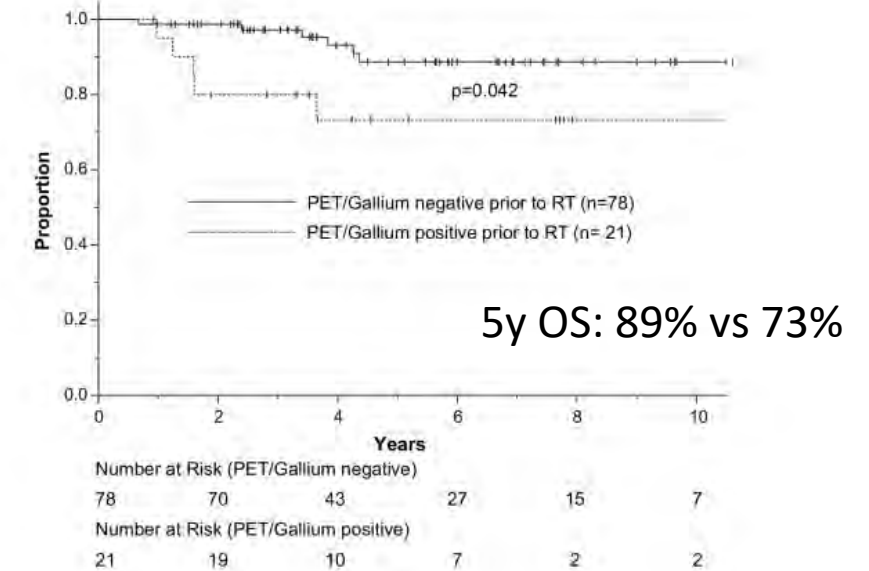
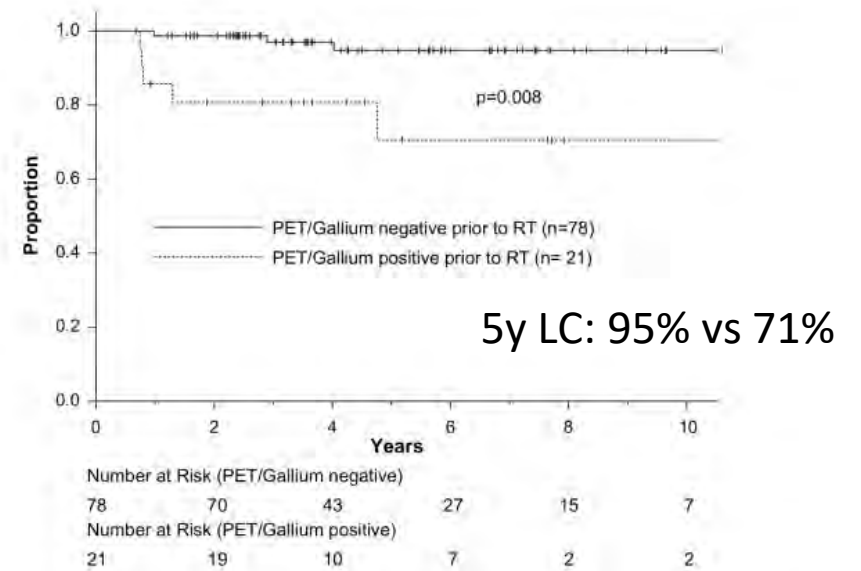
Kostakoglu. Blood Adv 2021

Is RT alone an effective modality for patients with PR and residual PET avidity (Deauville 4-5) after R-CHOP?

The impact of radiation therapy in patients with diffuse large B-cell lymphoma with positive post-chemotherapy FDG-PET or gallium-67 scans

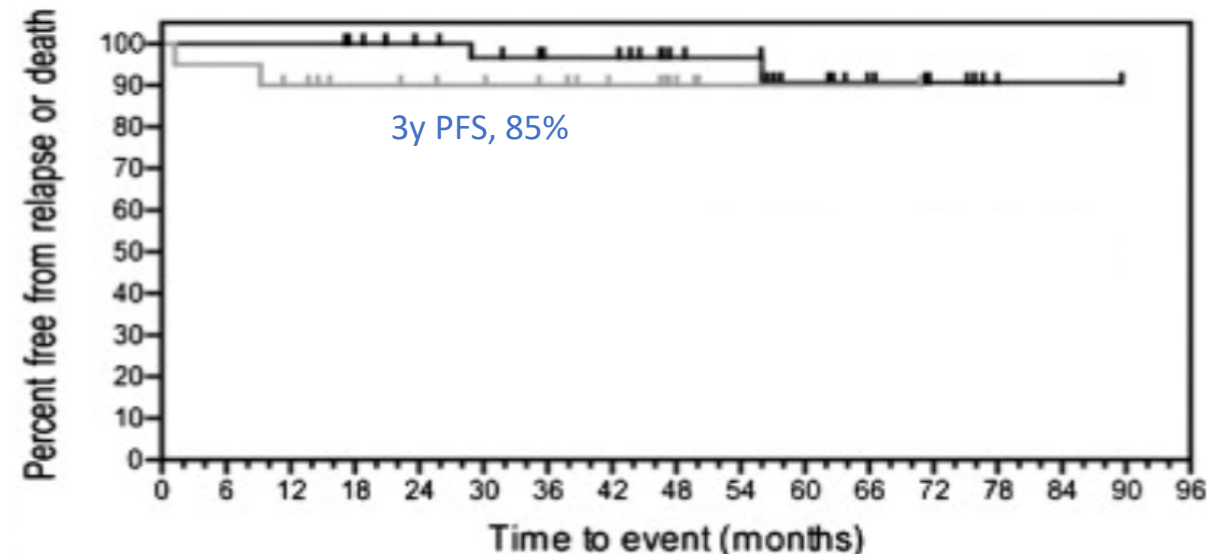
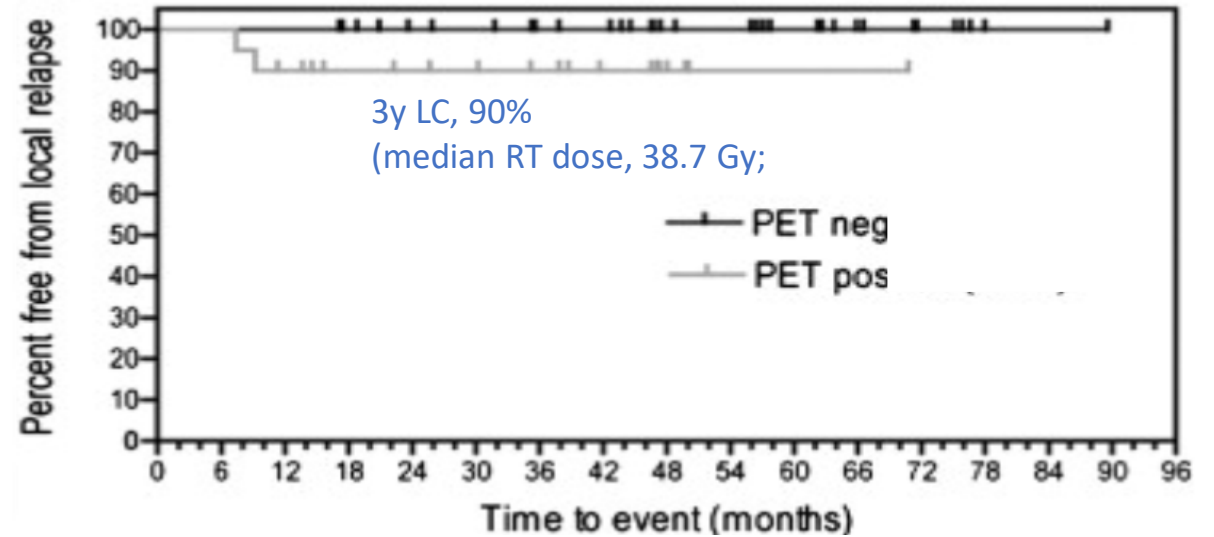
J. A. Dorth¹, J. P. Chino¹, L. R. Prosnitz¹, L. F. Diehl², A. W. Beaven², R. E. Coleman³ & C. R. Kelsey^{1*}

Departments of ¹Radiation Oncology; ²Medicine, Division of Medical Oncology; ³Radiology, Division of Nuclear Medicine, Duke University Medical Center, Durham, USA



Combined Modality Treatment for PET-Positive Non-Hodgkin Lymphoma: Favorable Outcomes of Combined Modality Treatment for Patients With Non-Hodgkin Lymphoma and Positive Interim or Postchemotherapy FDG-PET

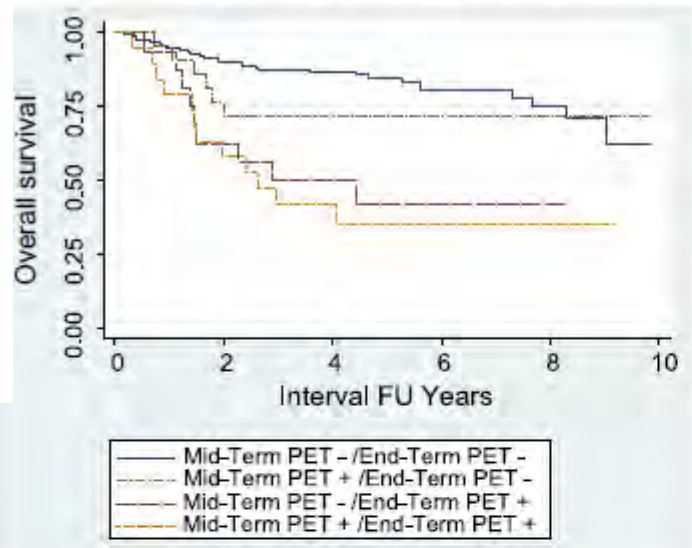
Lia M. Halasz, M.D.,* Heather A. Jacene, M.D.,† Paul J. Catalano, Sc.D.,‡
Annick D. Van den Abbeele, M.D.,† Ann LaCasce, M.D.,§ Peter M. Mauch, M.D.,
and Andrea K. Ng, M.D., M.P.H.¶



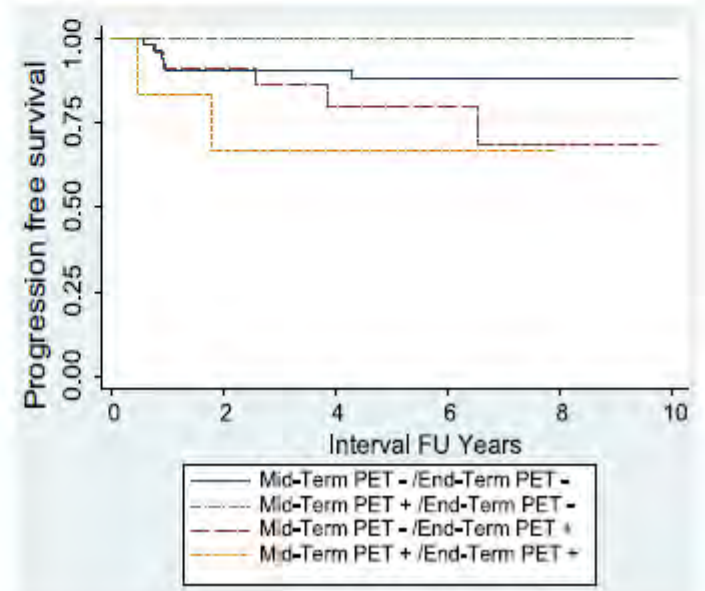
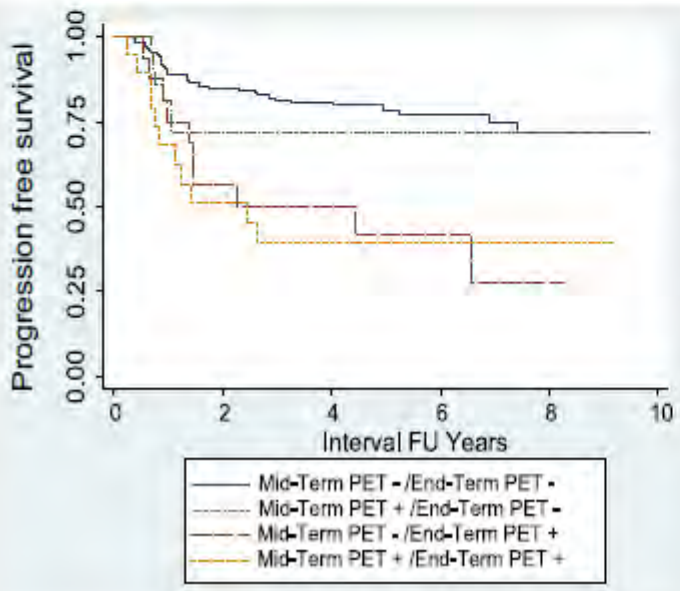
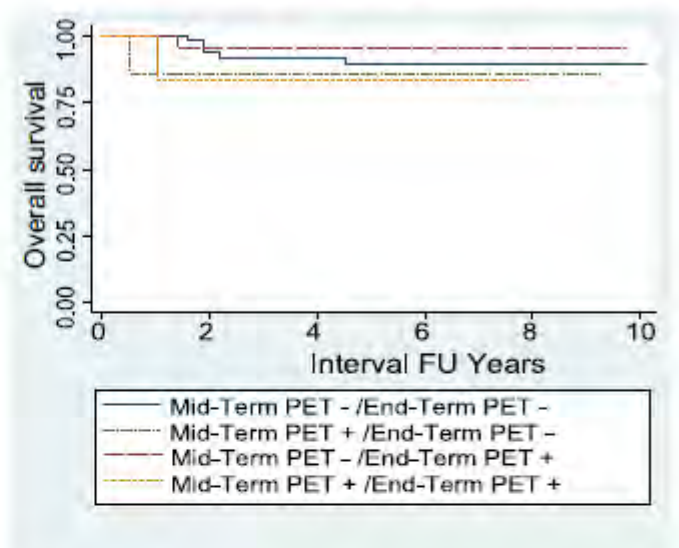
Positron Emission Tomography/Computed Tomography Findings During Therapy Predict Outcome in Patients With Diffuse Large B-Cell Lymphoma Treated With Chemotherapy Alone but Not in Those Who Receive Consolidation Radiation

Bouthaina S. Dabaja, MD,* Kenneth Hess, PhD,† Ferial Shihadeh, MD,* Donald A. Podoloff, MD,‡ L. Jeffrey Medeiros, MD,§ Osama Mawlawi, PhD,|| Isidora Arzu, MD, PhD,* Yasuhiro Oki, MD,¶ Fredrick B. Hagemeister, MD,¶ Luis E. Fayad, MD,¶ Valerie K. Reed, MD,* Aziza Kedir, BS,* Christine F. Wogan, MS,* and Alma Rodriguez, MD#

Patients given chemo only (n=206)



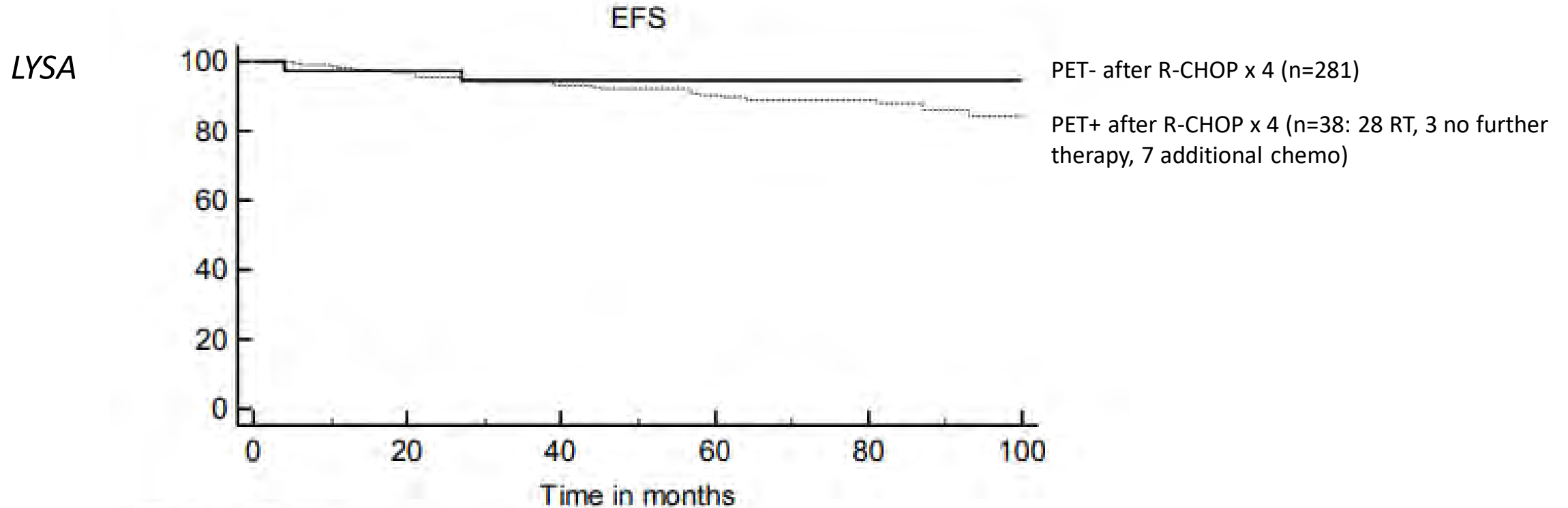
Patients given consolidn RT (n=88)



Studies on Omission of RT in Pts with PET CR

	LYSA <i>(Lamy. Blood 2018)</i>	SWOG S0014 <i>(Persky. JCO 2020)</i>	British Columbia <i>(Freeman. Blood 2021)</i>	Optimal >60 <i>Pfreundschuh. ICML/ASCO 2017)</i>
Study Design	Phase III non-inferiority trial (upper limit of 8% difference in 2y EFS)	Phase II trial (Historical 5y PFS of 85%)	Retrospective study	Phase II trial (Historical 2y PFS of 75%)
Patient Population	334 limited stage nonbulky (<7 cm)	132 limited stage nonbulky (<10 cm)	732 stage III/IV or stage I/II with B Sx or bulk (> 10 cm)	187 with bulky disease (>7.5 cm)
Treatment	R-CHOP-14 x 4-6 with PET after cycle 4 If PET CR: 40 Gy IFRT vs no RT If PET+ → off trial, majority received RT	R-CHOP 21 x 3 → PET If PET-CR, 1 more cycle of R-CHOP, no RT If PET+ → IFRT 36 Gy + 9 Gy boost	R-CHOP x 6-8 If PET-CR, no RT If PET + → RT 30-40 Gy	R-CHOP-14 vs R-CHLIP-14 If PET-CR, no RT If PET+ → 39.6 Gy
Results	5y EFS RT: 92% No RT: 89% HR, 0.61 (95%CI: 0.3-1.2)	PET CR pts: 5y PFS 89%/ 5y OS 91%	EOT PET CR pts: All pts: 3y TTP 83% Bulk (>10cm): 3y TTP 82%	2y PFS: 79%

RT can be an effective modality for patients with EOT PET+ disease



Number at risk

Group: CR

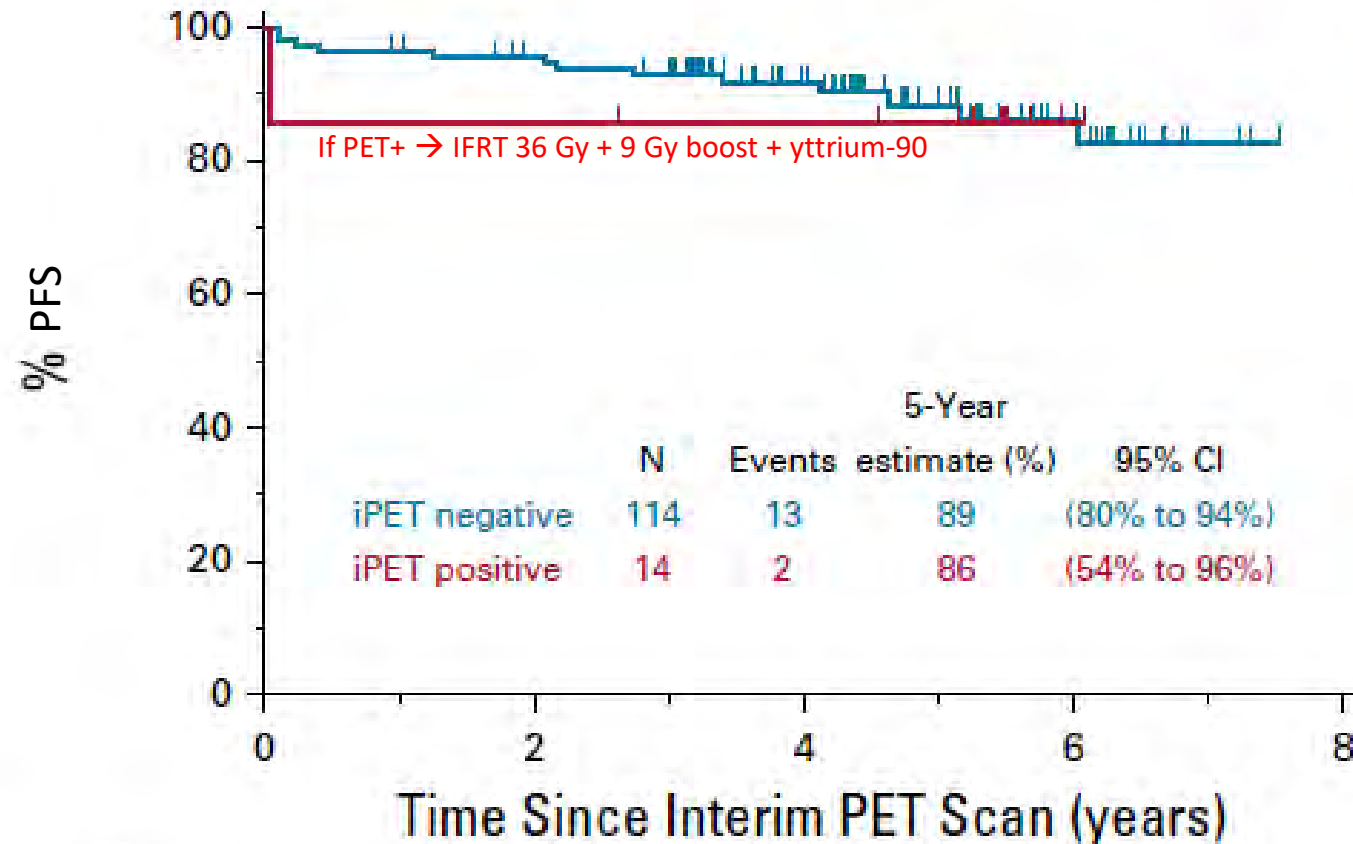
38 36 25 18 6 4

Group: PR

281 251 194 149 70 32

RT can be an effective modality for patients with EOT PET+ disease

SWOG S0014

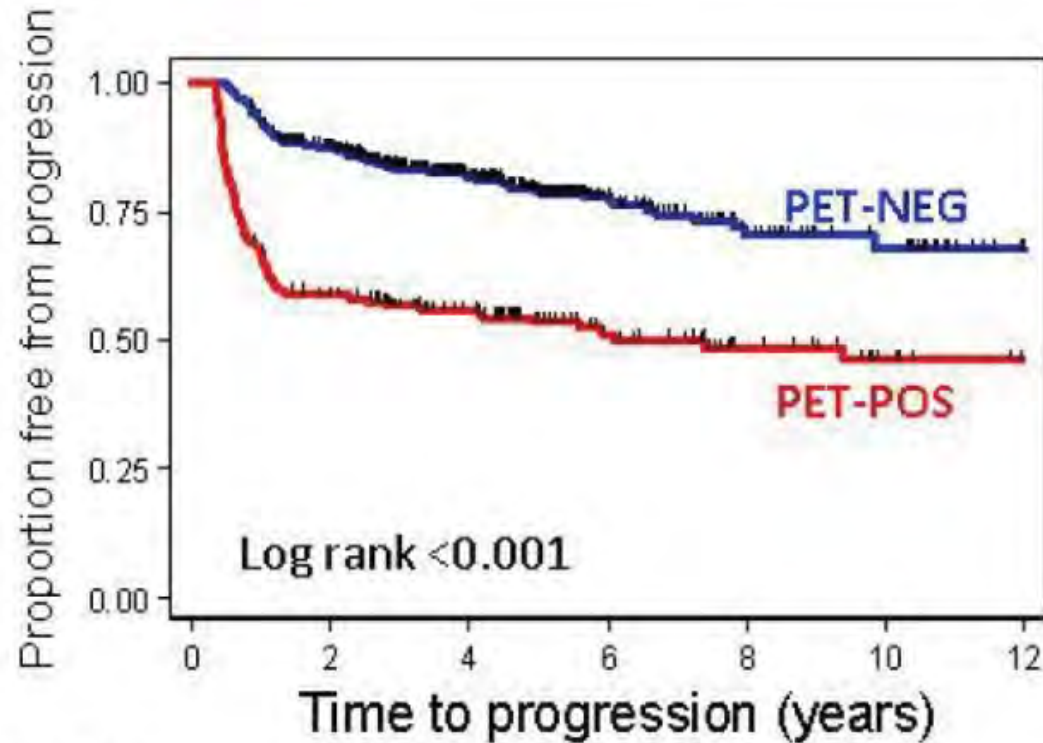


No. at risk:

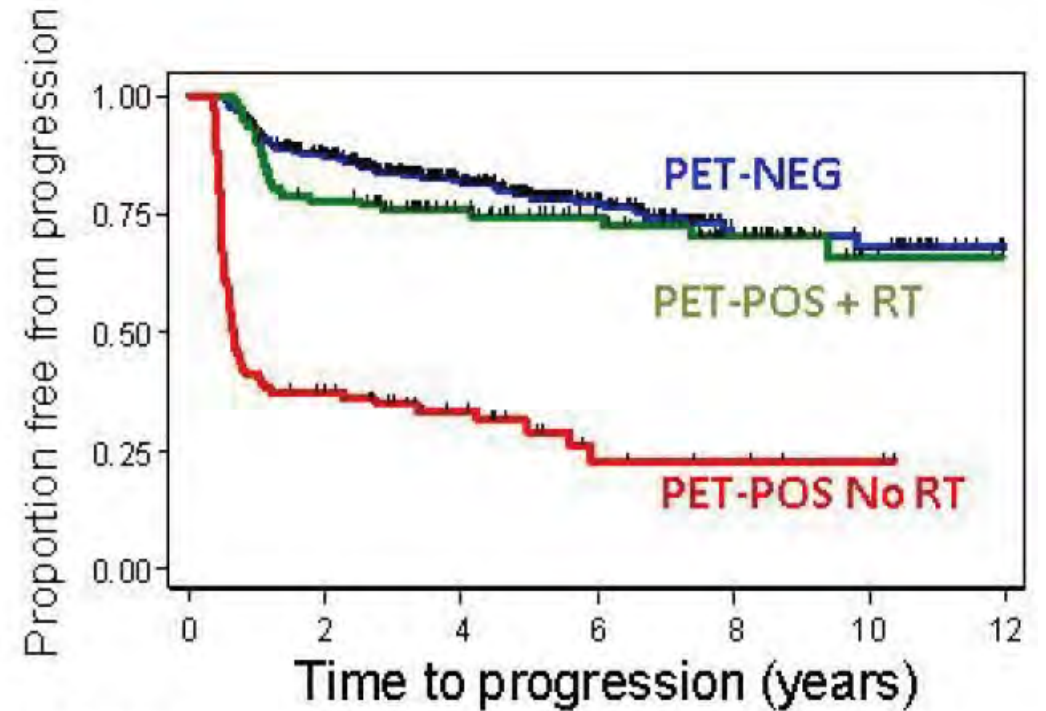
iPET negative	113	109	104	100	70	46	25	3	0
iPET positive	13	12	12	11	11	10	1	0	0

RT can be an effective modality for patients with EOT PET+ disease

BC Cancer Center



Number at risk		0	2	4	6	8	10	12
PET-NEG	517	420	239	104	47	28	8	
PET-POS	206	115	78	44	26	14	9	

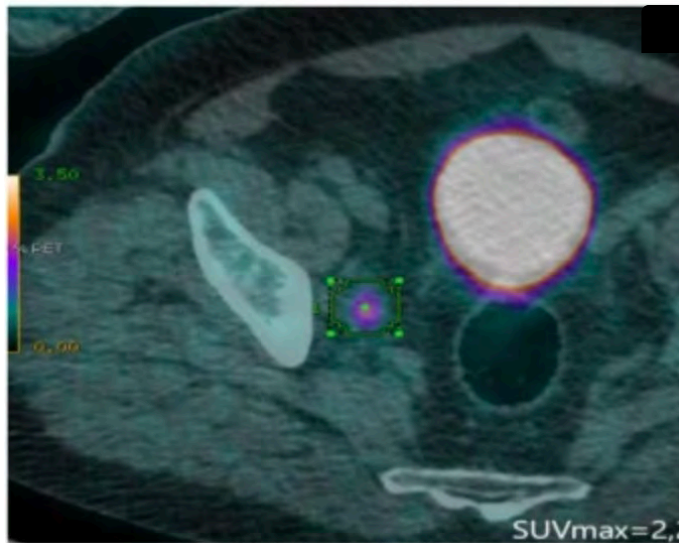
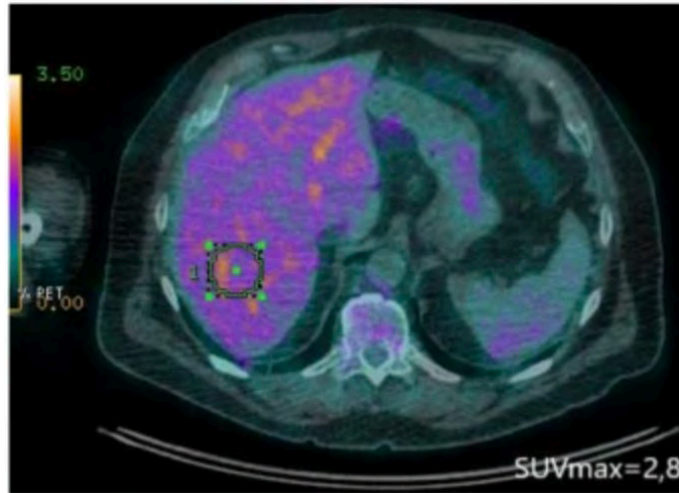


Number at risk		0	2	4	6	8	10	12
PET-NEG	517	420	239	104	47	28	8	
PET-POS+RT	109	82	58	37	21	11	8	
PET-POS No RT	97	33	20	7	5	3	1	

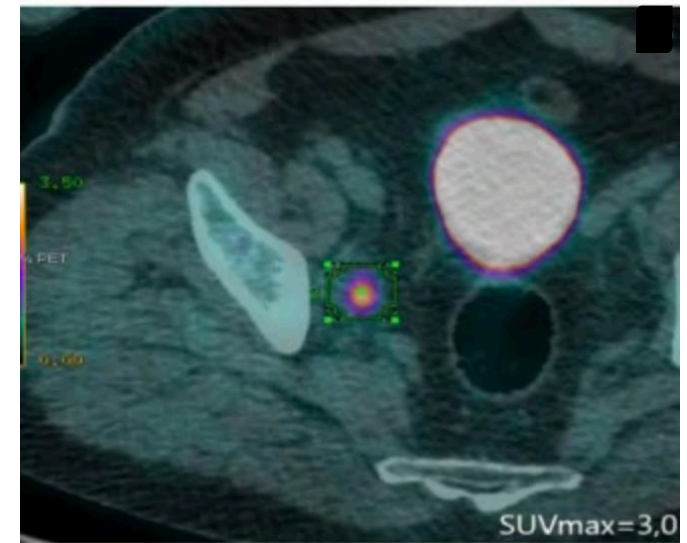
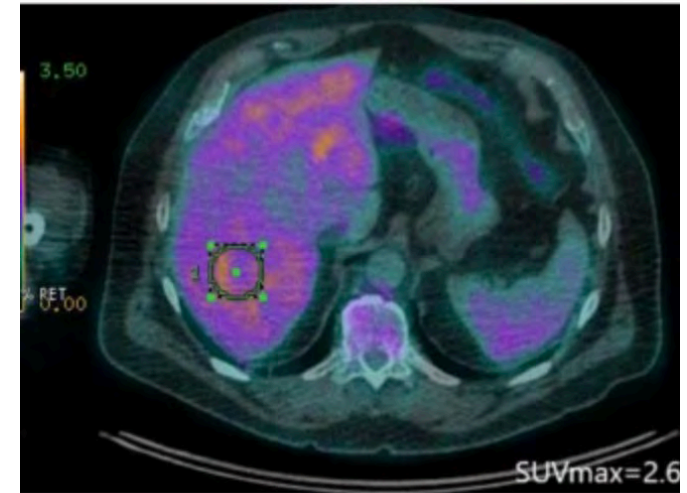
Use of Q.Clear in PET Interpretation for Lymphoma

- Deauville score determination is based on OSEM (ordered subsets expectation maximization) reconstruction algorithm
- Q.Clear, new PET reconstruction algorithm with:
 - reduced background noise
 - increased SUVmax
 - increased sensitivity
 - Using Q.Clear may alter lymphoma response assessment

Use of Q.Clear in PET Interpretation for Lymphoma



OSEM: Deauville 3, negative



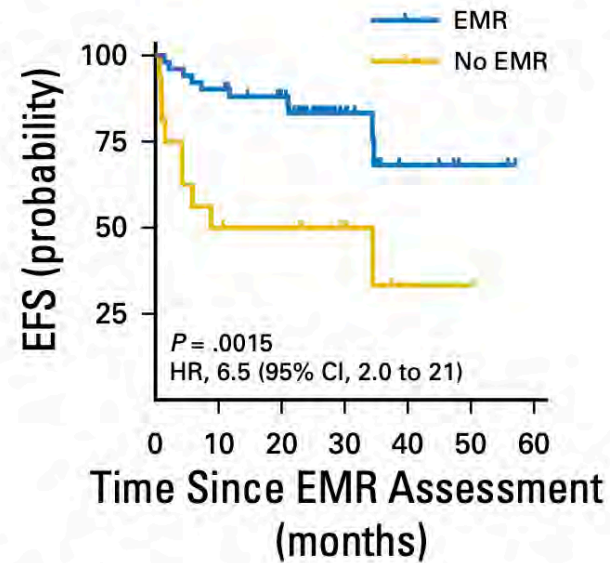
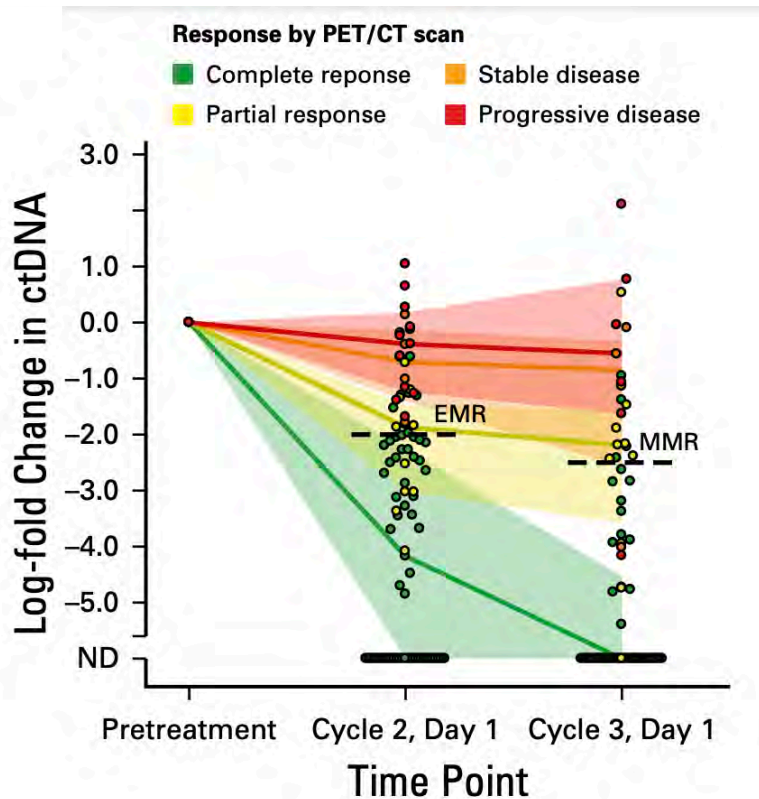
Q.Clear: Deauville 5, positive

Use of Q.Clear in PET Interpretation for Lymphoma

Deauville score		Q.Clear				
		1	2	3	4	5
OSEM	1	-	-	-	-	-
	2	-	27	3	-	-
	3	-	-	25	6	1
	4	-	-	-	1	1
	5	-	-	-	-	6

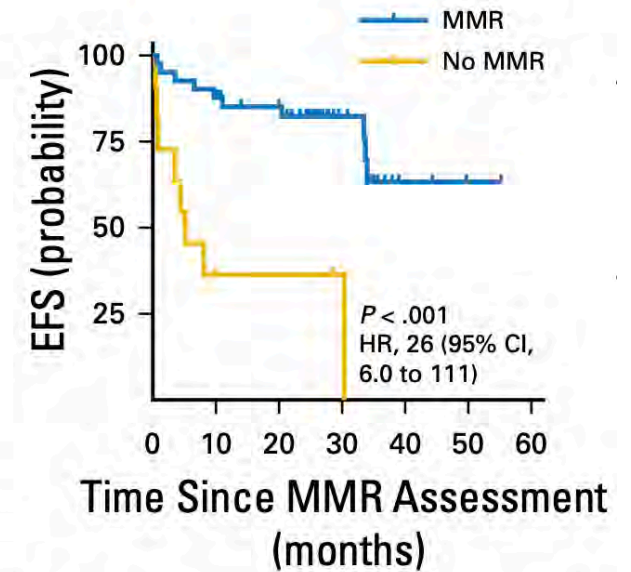
Ongoing efforts to improve response assessment:
MTV/TLG
ctDNA

ctDNA May Augment PET in Response Assessment



No. at risk:

EMR	51	46	38	15	5	2	0
No EMR	16	8	7	4	1	1	0



No. at risk:

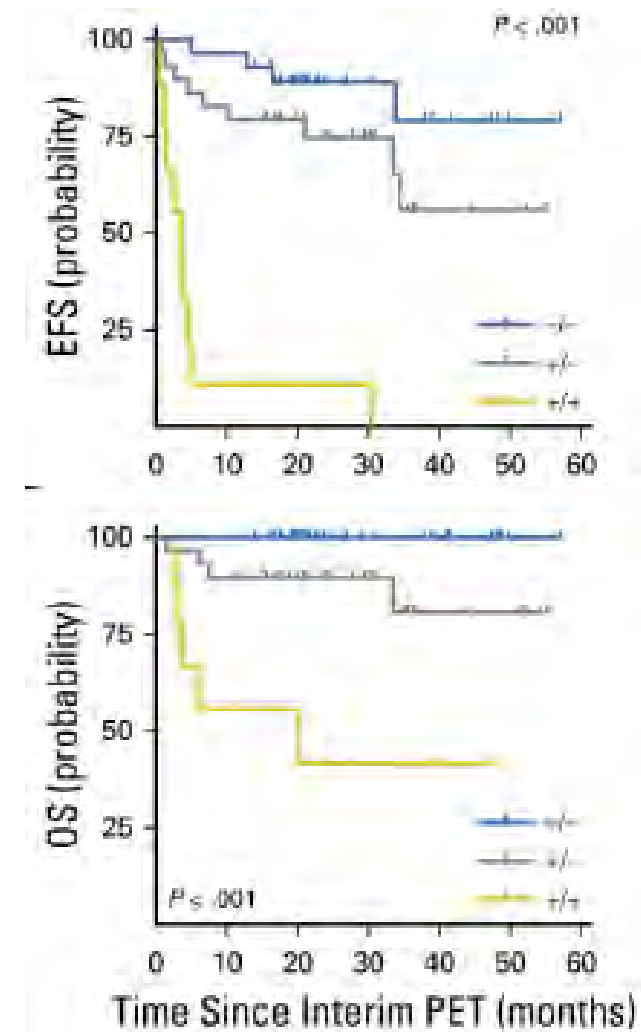
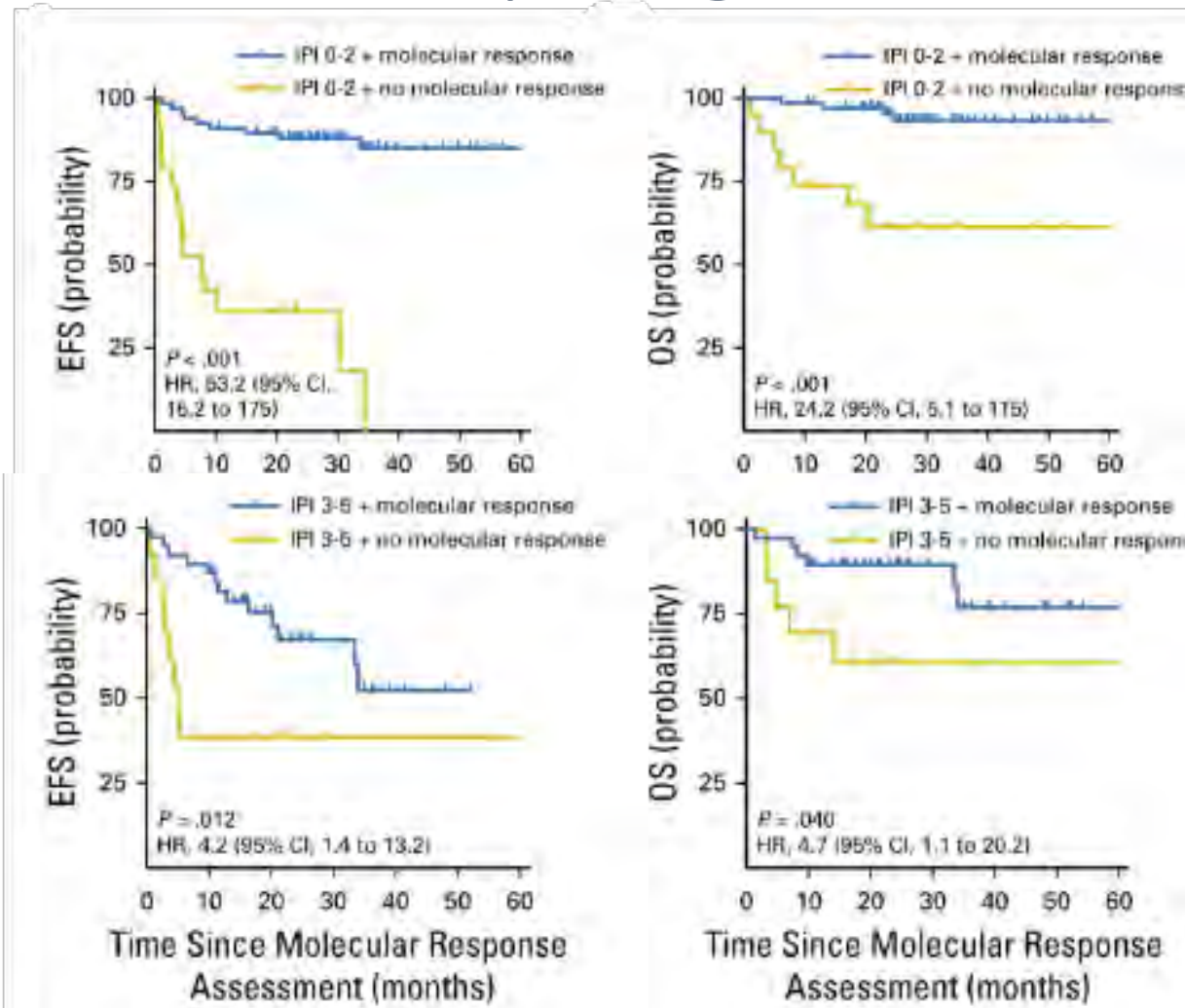
MMR	41	36	31	14	3	1	0
No MMR	11	4	3	1	0	0	0

N

EMR (Early molecular response): 2-log drop in ctDNA at start of cycle 2

MMR (Major molecular response): 2.5-log drop in ctDNA at start of cycle 3

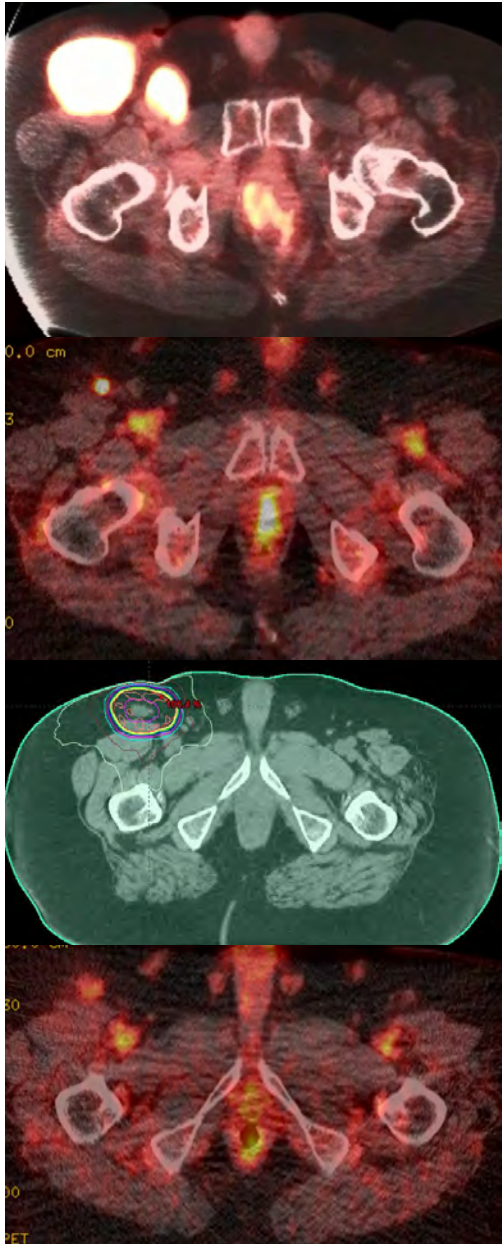
ctDNA May Augment PET in Response Assessment



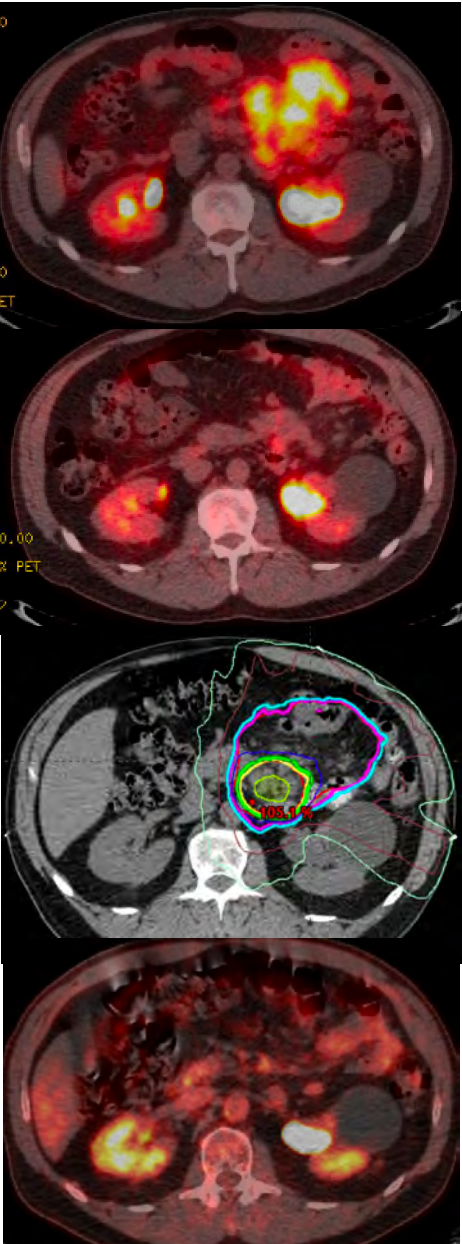
Molecular response predicted pt outcome independent of IPI and PET-response

Case Examples of Deauville 4-5

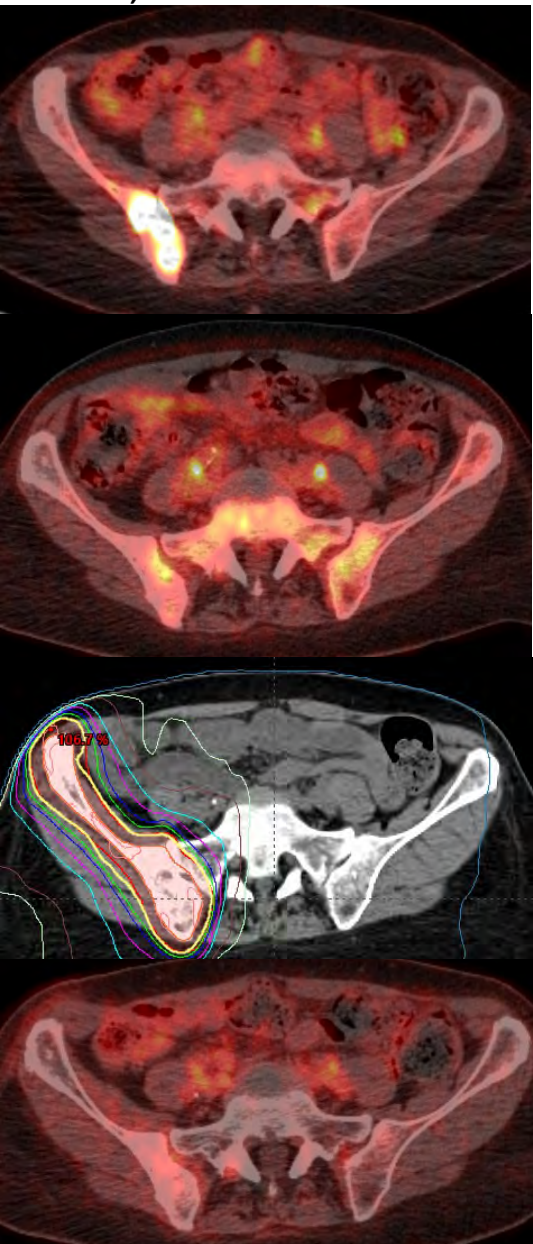
Case C, Deauville 5



Case D, Deauville 4



Case E, Deauville 4

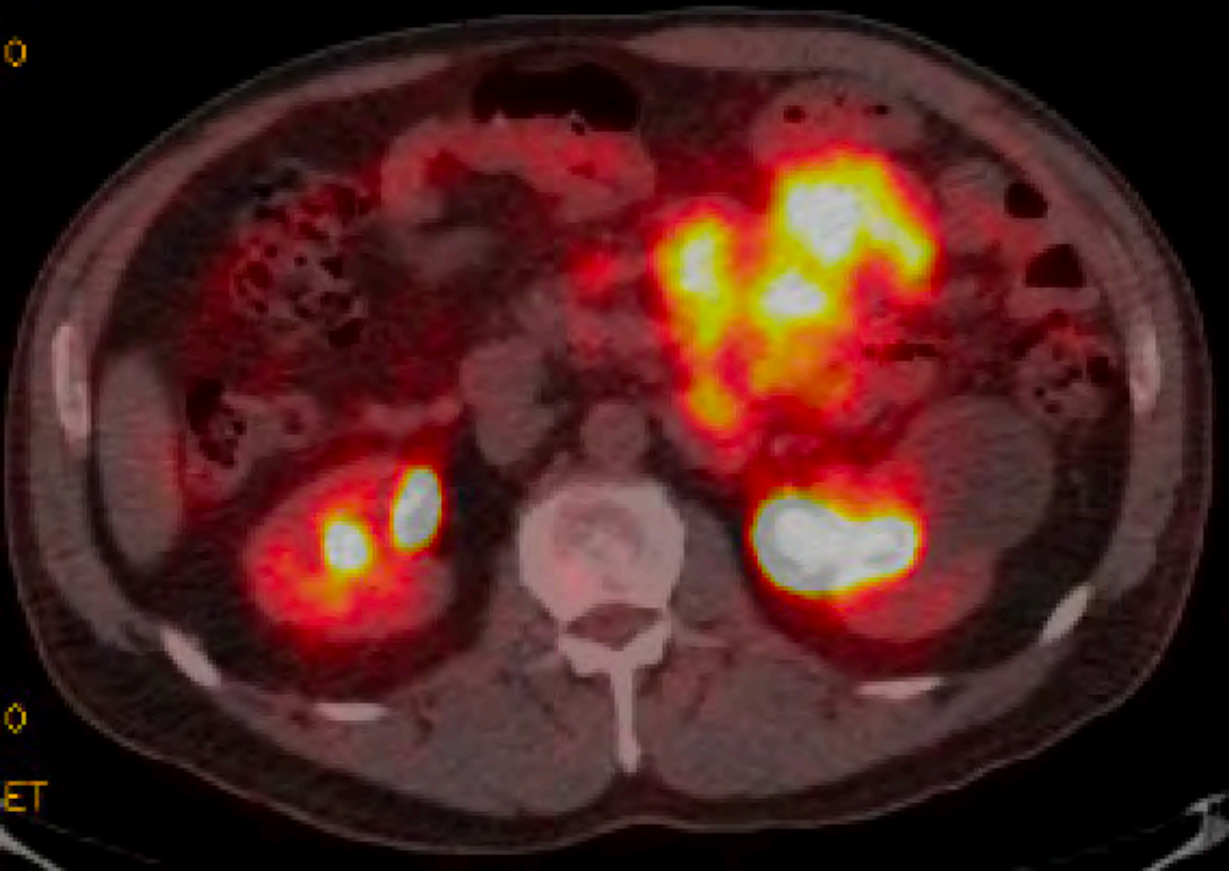


Take Home Messages

- EOT PET+ disease (Deauville 4/5) is a highly variable entity
- Those with overall responding disease without clearly refractory lymphoma, radiation therapy alone can be an effective modality, producing outcome similar to pts with EOT PET- disease
- RT doses range: 36-45 Gy
- Improvement in PET sensitivity and incorporation of molecular response may refine selection of patients for consolidation radiation therapy

Thank you!

0.0 cm

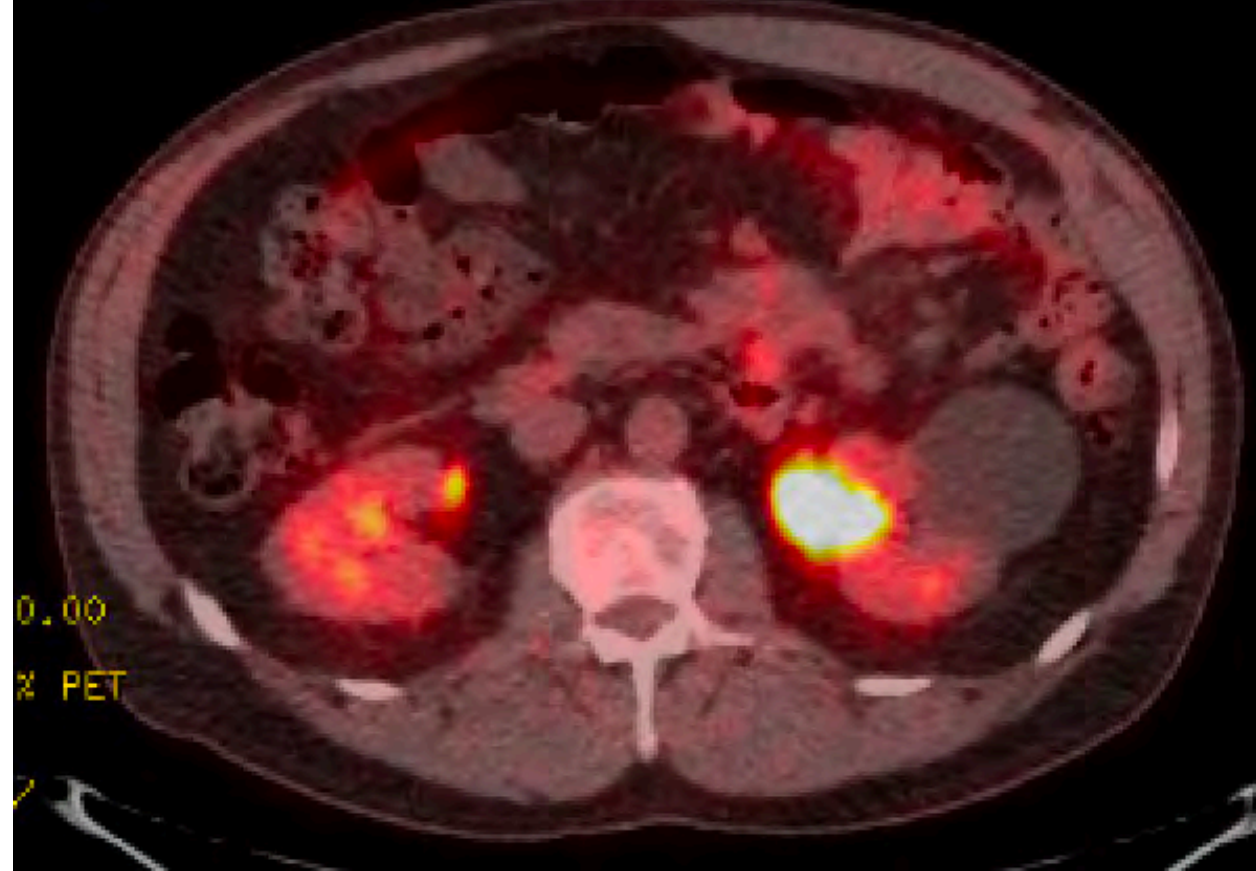


0

0

ET

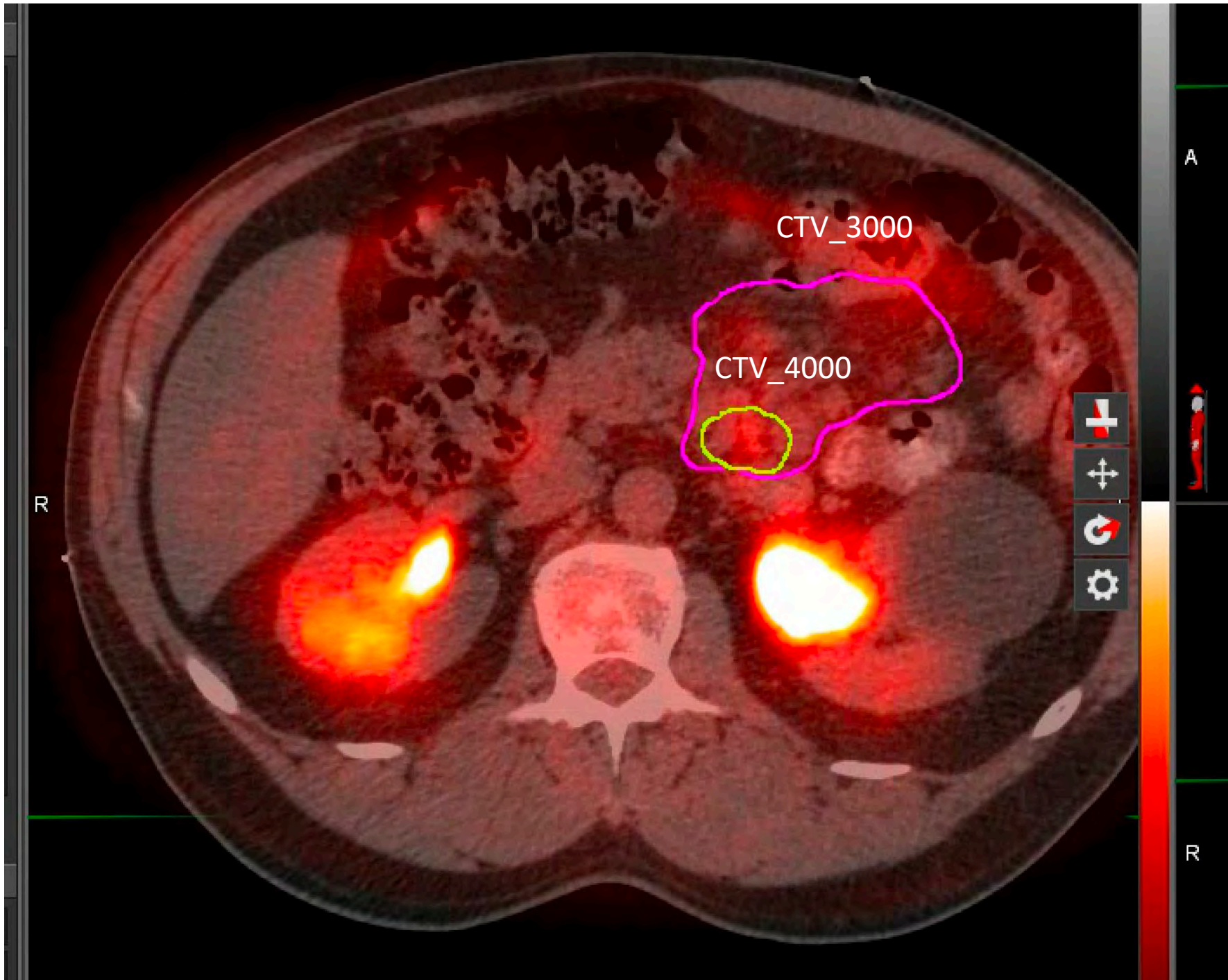
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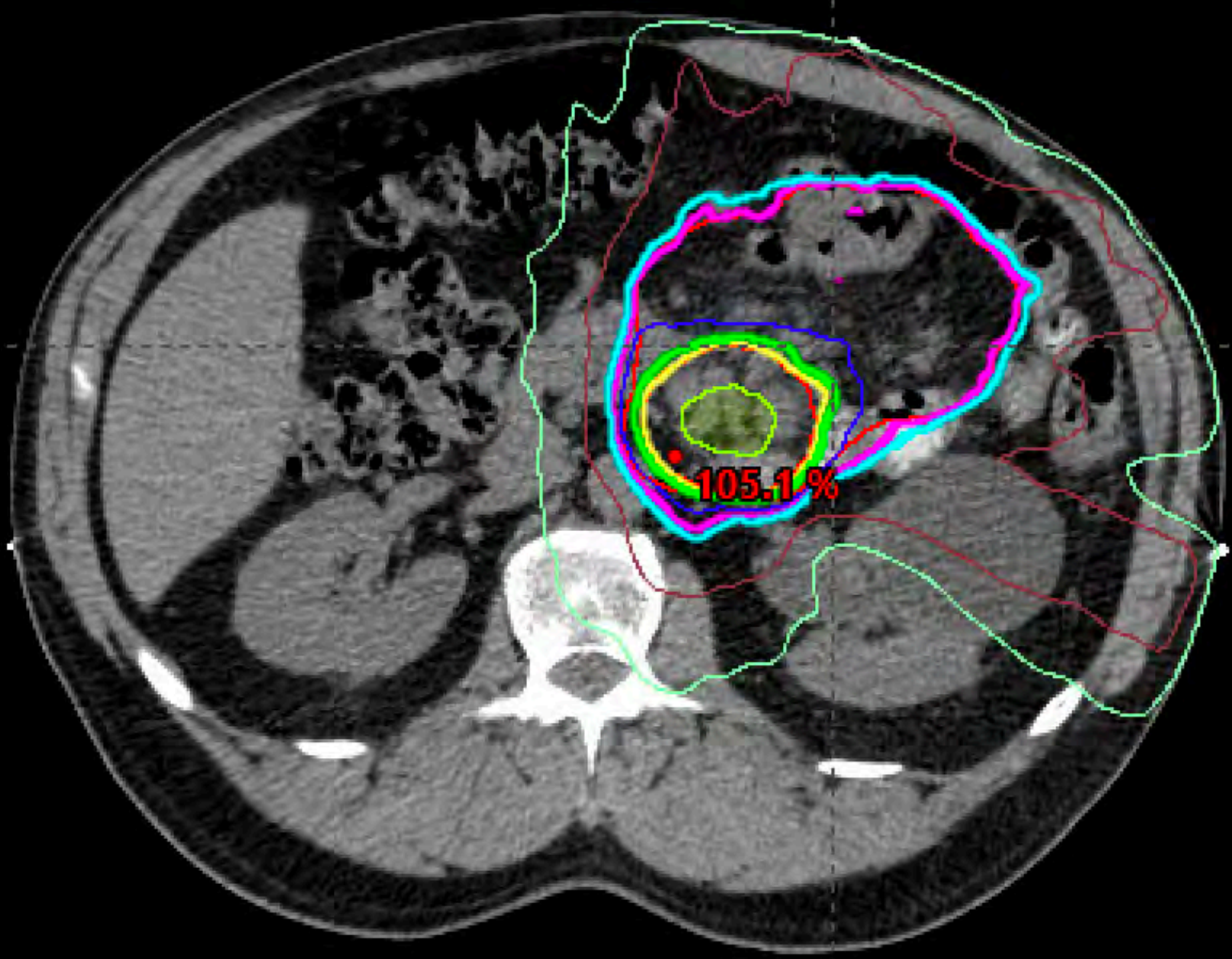


0.00

% PET

7





105.1%

