«Grandangolo in radioterapia oncologica – Rimini 2015»

Prostate cancer, Lymphomas

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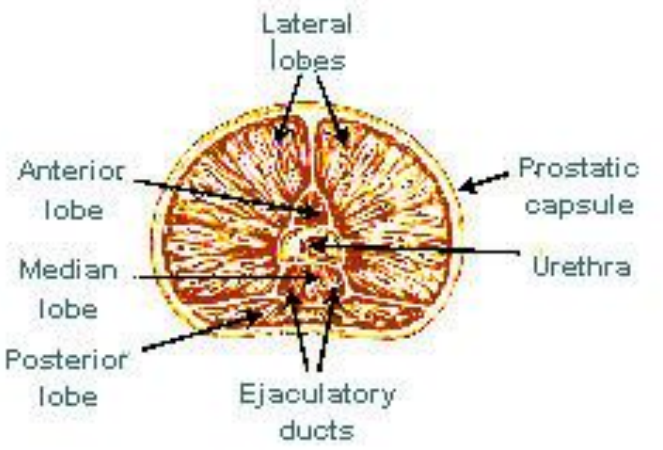
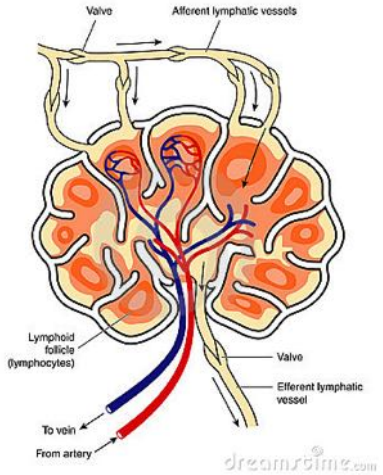
XXV CONGRESSO NAZIONALE AIRO 2015
PALACONGRESSI - Rimini, 7-10 novembre

Is there something in common between prostate cancer and lymphomas?





- ✓ *Overall, diseases with relatively good outcomes, the priority in both cases is that of selecting patients with good prognosis for de-intensified treatments*
- ✓ *In both cases, the better combination of drugs and radiation should be defined*
- ✓ *Finally, many new drugs became available in the last few years both for lymphomas and prostate cancer and should find their place in the therapeutic sequence*


Act One:
Lymphomas

Radiation therapy for lymphomas has been killed, at last, …in 2015 (or not?)

Curr. Treat. Options in Oncol. (2015) 16: 45
DOI 10.1007/s11864-015-0360-6

Lymphoma (JW Sweetenham, Section Editor)

Hodgkin Lymphoma: the Changing Role of Radiation Therapy in Early-Stage Disease—the Role of Functional Imaging

David J. Iberri, MD[1]
Richard T. Hoppe, MD[2]
Ranjana H. Advani, MD[3,*]

«Old» risk groups are no more sufficient to select patients categories suitable for de-intensification (or intensification) strategies… They are different …

Table 1. Unfavorable risk factors in early-stage CHL according to study group

Factor	European groups		North American groups	
	GHSG	EORTC	NCIC	NCCN
Age	–	≥50 years	≥40 years	–
ESR, B symptoms	>50 if A; >30 if B	>50 if A; >30 if B	>50 or any B symptoms	>50 or any B symptoms
Mediastinal bulk	MMR >0.33	MTR >0.35	MMR >0.33 or >10 cm	MMR >0.33
Nodal sites	>2	>3	>3	>3
Other	Any extranodal lesion	–	Mixed cellularity or lymphocyte-depleted histology	Any site >10 cm

MMR mediastinal mass ratio, *MTR* mediastinal thoracic ratio, *ESR* erythrocyte sedimentation rate, *GHSG* German Hodgkin Study Group, *EORTC* European Organization for Research and Treatment of Cancer, *NCIC* National Cancer Institute, Canada, *NCCN* National Comprehensive Cancer Network

Radiol med
DOI 10.1007/s11547-015-0581-6

DIAGNOSTIC IMAGING IN ONCOLOGY

Role of WB-MR/DWIBS compared to ^{18}F-FDG PET/CT in the therapy response assessment of lymphoma

Nicola Maggialetti[1] · Cristina Ferrari[3] · Carla Minoia[2] · Artor Niccoli Asabella[3] · Michele Ficco[4] · Giacomo Loseto[2] · Giacomina De Tullio[2] · Vincenza de Fazio[2] · Angela Calabrese[4] · Attilio Guarini[2] · Giuseppe Rubini[3] · Luca Brunese[1]

New tools to select patients
who do not need radiotherapy?
PET-CT remains the benchmark

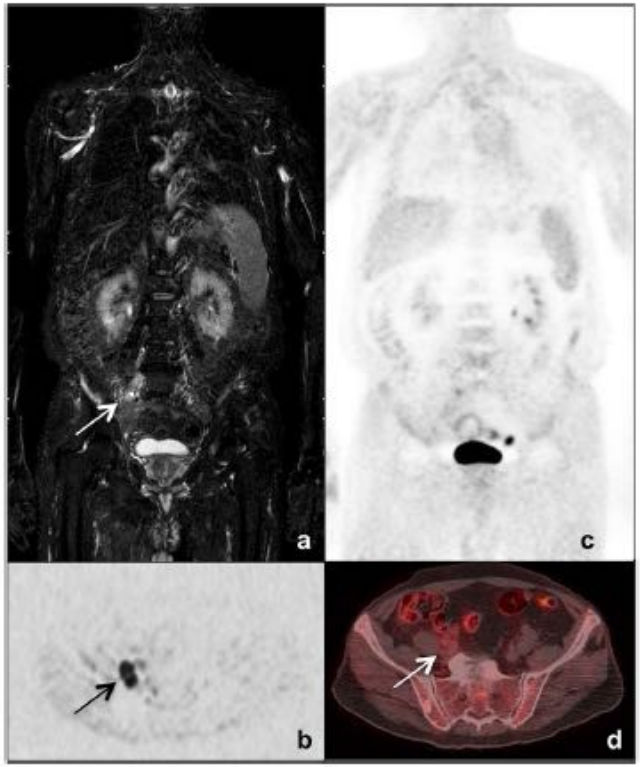


Fig. 1 Post-therapy WB-MR/DWIBS and ^{18}F-FDG PET/CT performed in a 78-year-old man affected by nodular sclerosis cHL, stage II. **a** Coronal WB-MR STIR sequence, **b** axial DWIBS image of the pelvis, **c** coronal WB PET and **d** axial fused PET/CT image of the pelvis. WB-MR/DWIBS shows residual nodes in the pelvic basin, in the right external iliac site, not detected byPET, even if enlarged lymph nodes are still visible on CT

Current response criteria utilizing PET/CT

Can RT be avoided in patients with a negative interim PET/CT?

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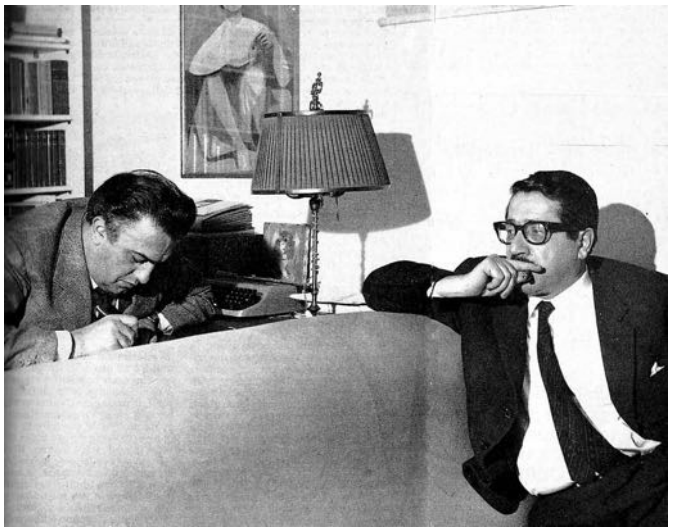
Current response criteria utilizing PET/CT



Clinical Investigation

Interim PET After Two ABVD Cycles in Early-Stage Hodgkin Lymphoma: Outcomes Following the Continuation of Chemotherapy Plus Radiotherapy

Gabriele Simontacchi, MD,* Andrea Riccardo Filippi, MD,† Patrizia Ciammella, MD,‡ Michela Buglione, MD,§ Calogero Saieva, MSc,‖ Stefano Maria Magrini, MD,§ Lorenzo Livi, MD,* Cinzia Iotti, MD,‡ Barbara Botto, MD,¶ Luca Vaggelli, MD,# Alessandro Re, MD,** Francesco Merli, MD,†† and Umberto Ricardi, MD†

International Journal of Radiation Oncology biology • physics

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Summary

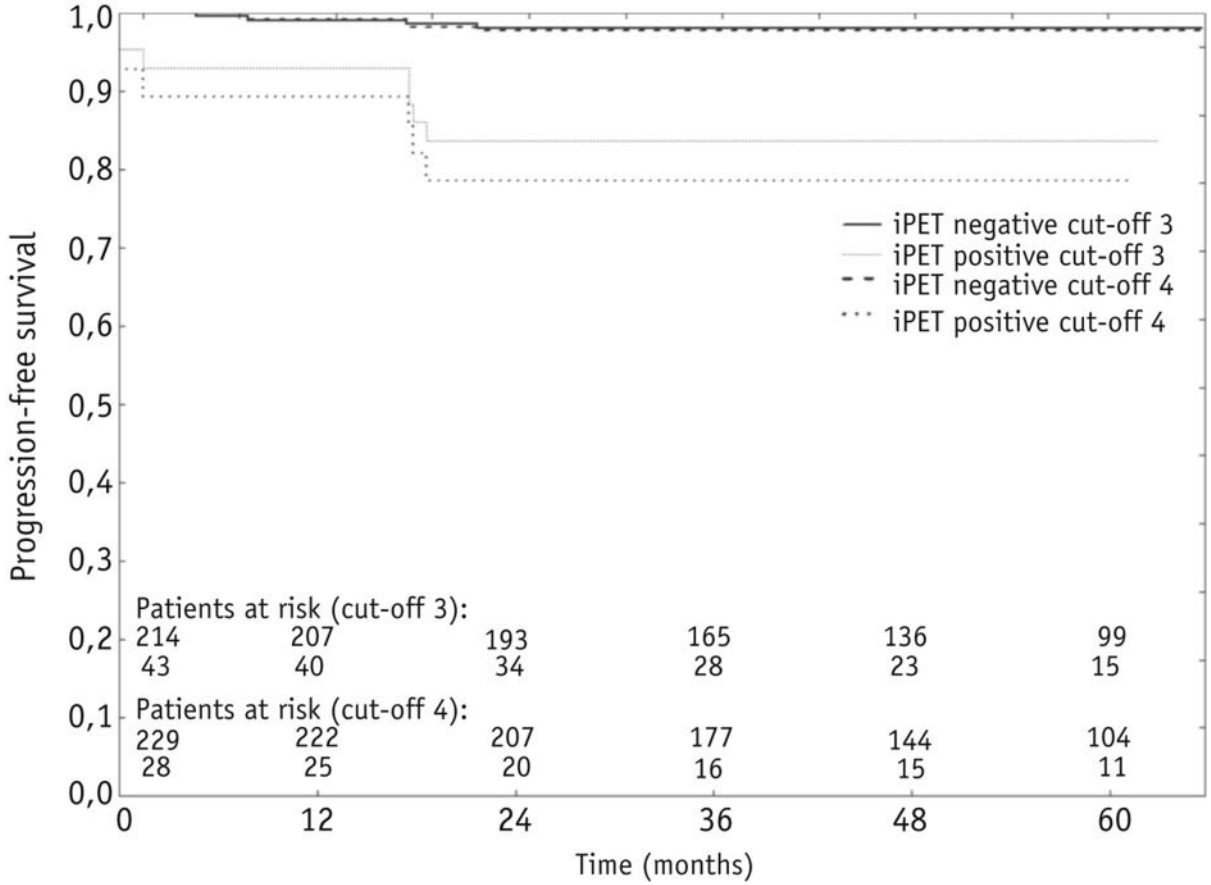
This study retrospectively analyzed a cohort of 257 stage I to IIAB Hodgkin lymphoma patients treated with chemotherapy plus radiation therapy, who underwent interim fluorodeoxyglucose-labeled positron emission tomography (i-FDG-PET) after the first 2 cycles of adriamycin, bleomycin, vinblastine, dacarbazine (ABVD) chemotherapy. i-FDG-PET resulted in a strong prognostic factor for both progression-free and overall survival. Continuation of chemotherapy followed by radiation therapy was able to achieve durable, complete remission in most of patients with interim FDG-PET positivity.

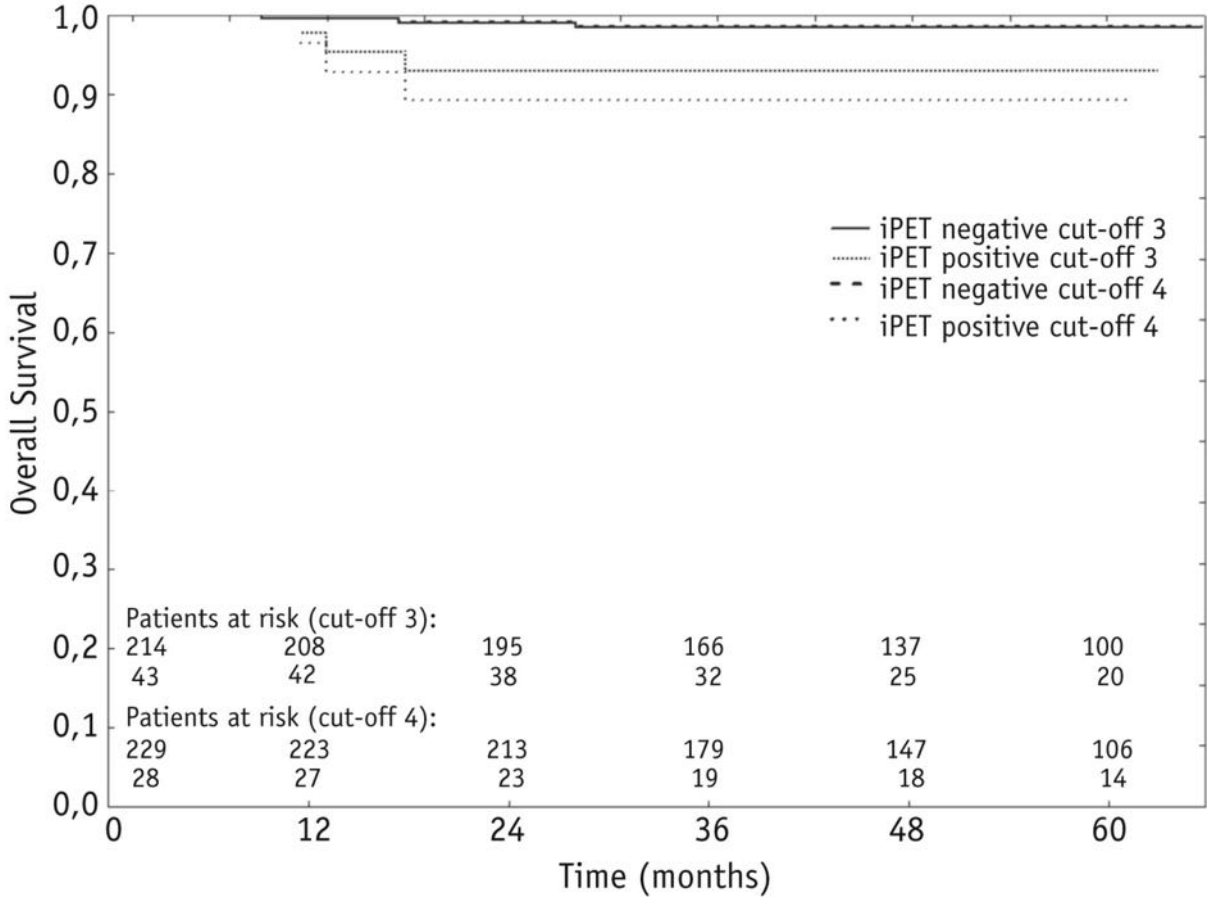
Purpose: This multicenter retrospective study was designed to evaluate the prognostic role of interim fluorodeoxyglucose-labeled positron emission tomography (i-FDG-PET) in a cohort of patients affected with early-stage Hodgkin lymphoma (HL) treated initially with adriamycin, bleomycin, vinblastine, dacarbazine (ABVD) chemotherapy followed by radiation therapy, and to assess the role of chemotherapy continuation plus radiation therapy for i-FDG-PET-positive patients.

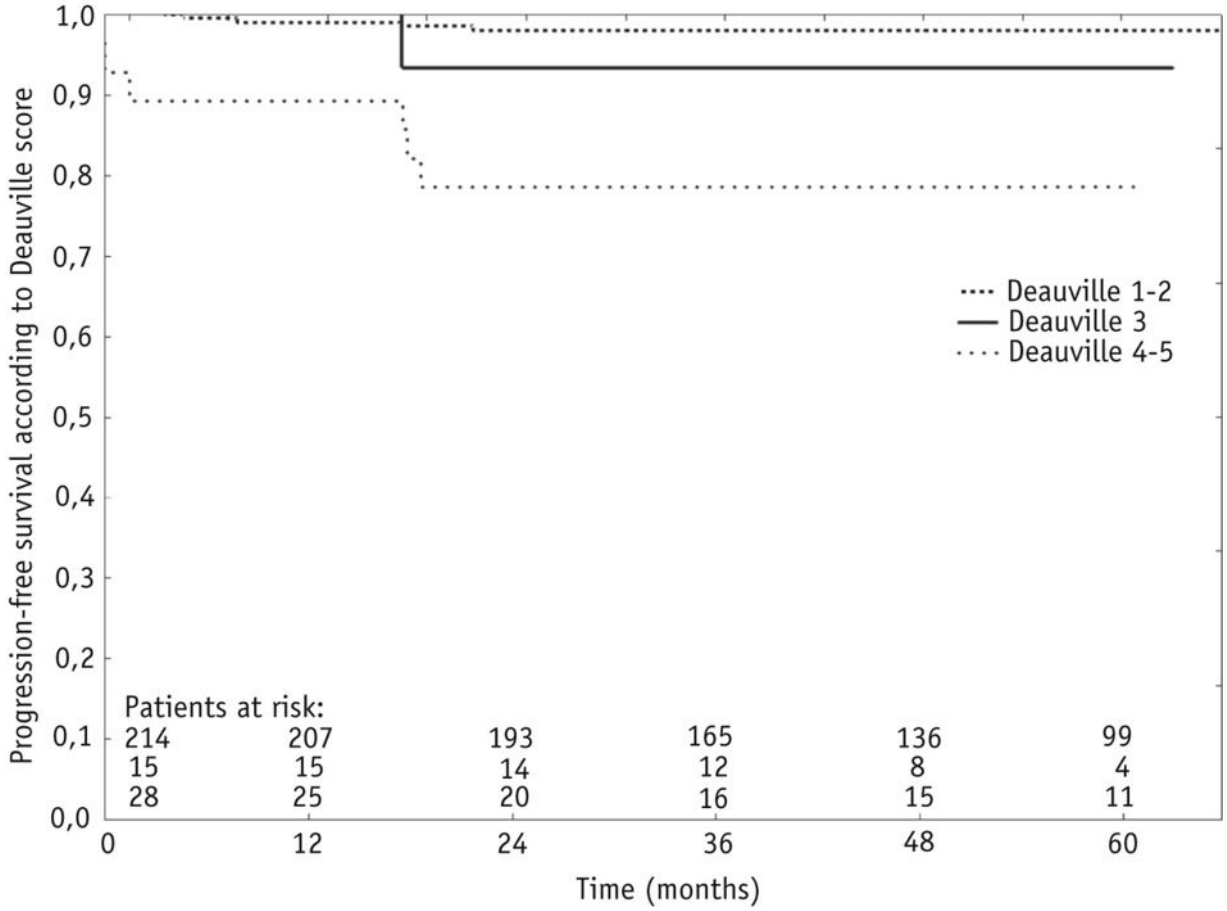
Methods and Materials: Data from 257 patients were retrieved from 4 hematology and radiation oncology departments. Inclusion criteria were stage I to IIAB HL, "intention-to-treat" AVBD plus radiation therapy, and FDG-PET at diagnosis and after the first 2 ABVD cycles. All i-FDG-PET scans underwent blinded local review by using the Deauville 5-point scoring system; patients were stratified as negative or positive using 2 Deauville score cutoff values, ≥ 3 or ≥ 4.

Results: Median follow-up time was 56 months (range: 9-163 months); 5-year overall survival (OS) and disease-specific survival (DSS) for the whole cohort were 97.5% and 98.3%, respectively. Five-year progression-free survival (PFS) was 95.6%. After i-FDG-PET revision, 43 of 257 patients (16.7%) had a positive i-FDG-PET (Deauville scores: 3-5). Five-year PFS rates for i-FDG-PET-negative and i-FDG-PET-positive patients were 98.1% and 83.7%, respectively, if using a Deauville score cutoff of 3, and 97.7% and 78.6%, respectively, if using a cutoff of 4 ($P = .0001$). Five-year OS for i-FDG-PET-negative and i-FDG-PET-positive patients was 98.5% and 93.0%, respectively, if using a cutoff of 3, and 98.6% and 89.3%, respectively, if using a cutoff of 4 ($P = .029$ and $P = .002$). At univariate regression analysis, i-FDG-PET positivity was associated with worse OS and PFS. At multivariate analysis, performed only for PFS, i-FDG-PET positivity confirmed its negative impact ($P = .002$).

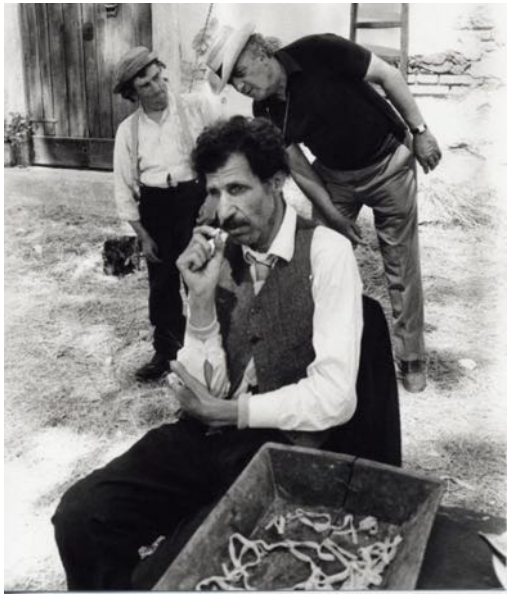
Conclusions: i-FDG-PET is prognostic for PFS and OS in early-stage HL patients treated with combined modality therapy; the continuation of chemotherapy followed by radiation therapy is able to obtain durable, complete remission in most i-FDG-PET-positive patients.


1,0
0,9
0,8
0,7
0,6
0,5
0,4
0,3
0,2
0,1
0,0
Progression-free survival
iPET negative cut-off 3
iPET positive cut-off 3
iPET negative cut-off 4
iPET positive cut-off 4
Patients at risk (cut-off 3):
214 207 193 165 136 99
43 40 34 28 23 15
Patients at risk (cut-off 4):
229 222 207 177 144 104
28 25 20 16 15 11
0 12 24 36 48 60
Time (months)


1,0
0,9
0,8
0,7
0,6
0,5
0,4
0,3
0,2
0,1
0,0
Overall Survival
iPET negative cut-off 3
iPET positive cut-off 3
iPET negative cut-off 4
iPET positive cut-off 4
Patients at risk (cut-off 3):
214 208 195 166 137 100
43 42 38 32 25 20
Patients at risk (cut-off 4):
229 223 213 179 147 106
28 27 23 19 18 14
0 12 24 36 48 60
Time (months)


Progression-free survival according to Deauville score
1,0
0,9
0,8
0,7
0,6
0,5
0,4
0,3
0,2
0,1
0,0
Deauville 1-2
Deauville 3
Deauville 4-5
Patients at risk:
214 207 193 165 136 99
15 15 14 12 8 4
28 25 20 16 15 11
0 12 24 36 48 60
Time (months)

Can RT be avoided in patients with a negative interim PET/CT?



In April 2014, the preplanned interim analysis of the H10 study (EORTC-LYSA-FIL) was published in JCO (32:1188-1194).

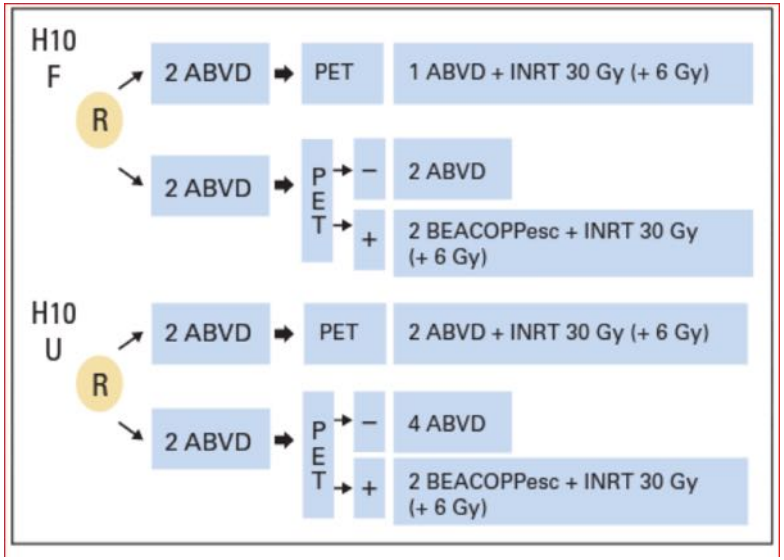
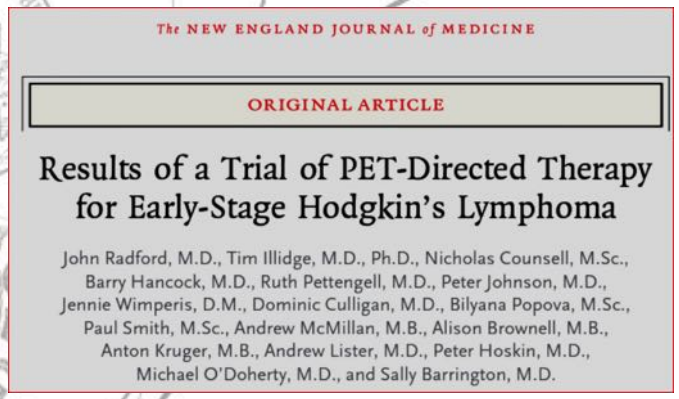


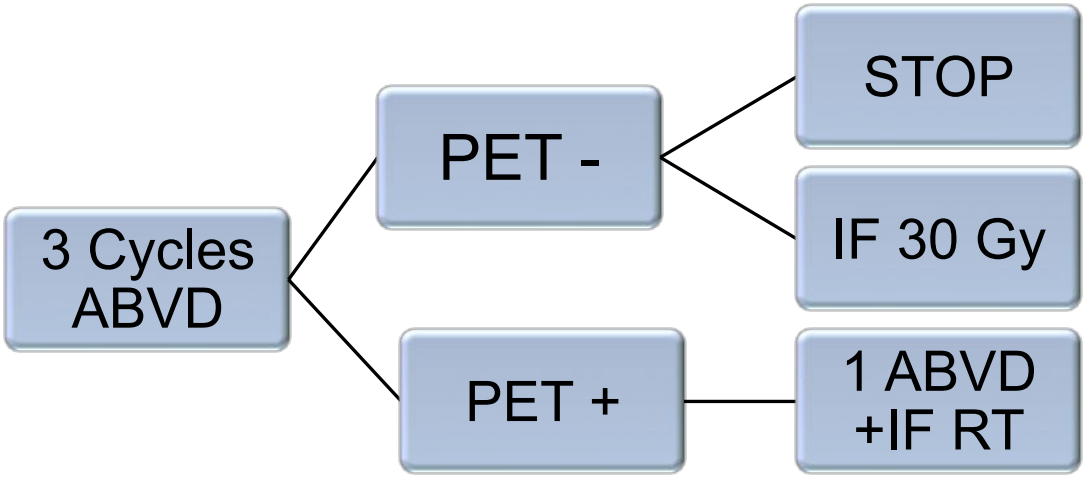
Table 2. Results of Interim Analysis in Patients With Early PET-Negative Disease

Subset	No. of Patients	No. of Observed Events	HR	Adjusted CI*	*P*†	1-Year PFS	
						%	Adjusted CI*
Favorable					.017		
Standard	188	1	1.00			100.00	
Experimental	193	9	9.36	2.45 to 35.73		94.93	91.89 to 96.85
Unfavorable					.026		
Standard	251	7	1.00			97.28	95.17 to 98.48
Experimental	268	16	2.42	1.35 to 4.36		94.70	92.11 to 96.46

Abbreviations: HR, hazard ratio; PET, positron emission tomography; PFS, progression-free survival.
*Confidence level adjusted to significance level used in interim test: 79.6% CI for favorable group and 80.4% CI for unfavorable group.
†One-sided Wald-test *P* value of superiority test.



The RAPID trial (UK, 2015)



N Engl J Med 2015;372:1598-607.
DOI: 10.1056/NEJMoa1408648

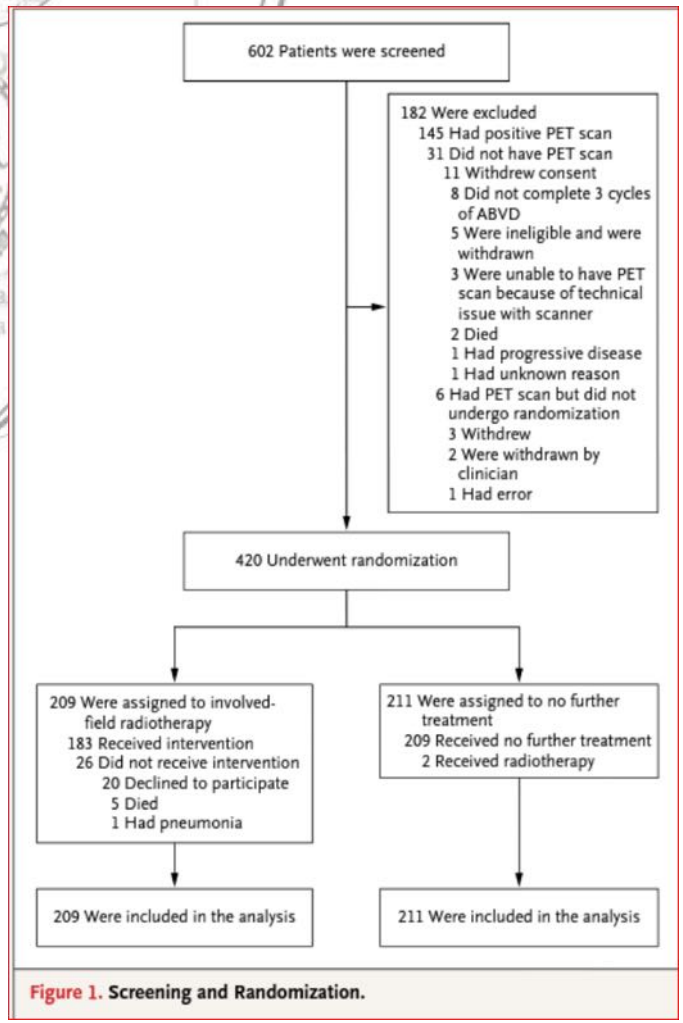


Figure 1. Screening and Randomization.

Table 2. Events of Disease Progression or Death.

Event	Negative PET Findings		Positive PET Findings (N=145)
	Radiotherapy (N=209)	No Further Treatment (N=211)	
	number of patients (percent)		
Alive without disease progression	193 (92.3)	187 (88.6)	127 (87.6)
Disease progression only	8 (3.8)	20 (9.5)	10 (6.9)
Died with disease progression	3 (1.4)	2 (0.9)	5 (3.4)
Died without disease progression	5 (2.4)	2 (0.9)	3 (2.1)

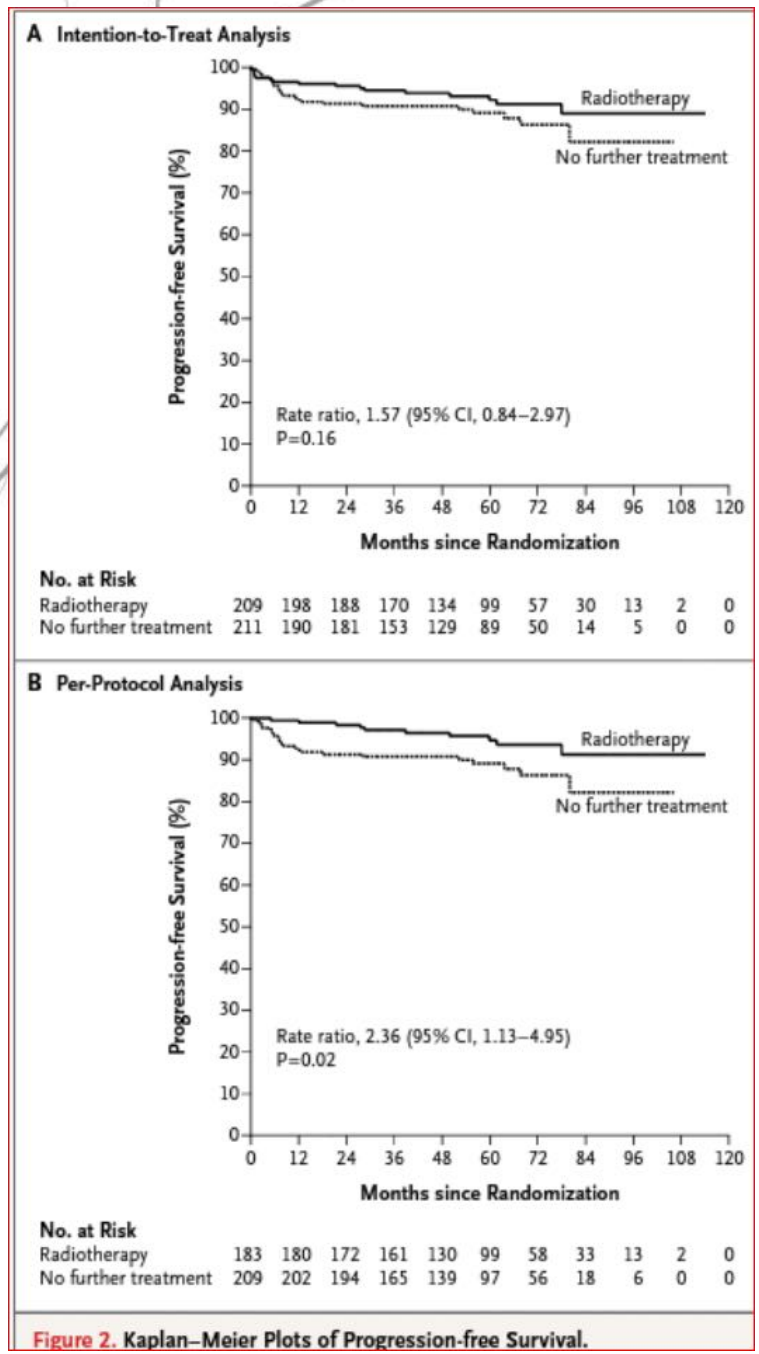


Figure 2. Kaplan–Meier Plots of Progression-free Survival.

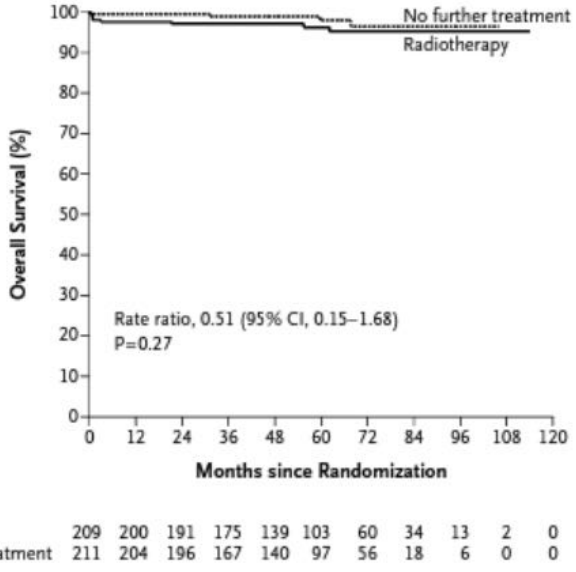


Figure 3. Kaplan–Meier Plot of Overall Survival.

Included are data from patients with negative PET findings who underwent randomization and were included in the intention-to-treat analysis (420 patients).

thebmj

BMJ 2015;350:h2190 doi: 10.1136/bmj.h2190 (Published 23 April 2015) Page 1 of 1

RESEARCH NEWS

PET after chemotherapy identifies Hodgkin's lymphoma patients who can avoid radiotherapy

In an accompanying editorial Dan Longo, from Harvard Medical School, Boston, and James Armitage, from the University of Nebraska Medical Center, Omaha, commented, "Clearly, both treatment strategies work."[2] They questioned whether a 4% difference in the rate of relapse was worth the added risk of radiotherapy. "Should 100 patients be exposed to radiation therapy to keep four from relapsing with no evidence of long term survival benefit?" they asked. Patients should be involved in making that decision after being informed of the risks and benefits, they advised.

The research group concluded that longer term follow-up was needed to see whether their response adapted approach leads to fewer second cancers, less cardiovascular disease, and improved overall survival when compared with a strategy that incorporates radiotherapy for all patients.

NO RT

5/8 DEATHS IN THE RT ARM IN PTS NOT HAVING RT

4/6 PTS WITH 2ND TUM DEATHS NOT TREATED WITH RT

6/6 PTS DEAD BECAUSE OF INFECTIOUS COMPLICATIONS HAD CHEMO

Table 3. Causes of Death.

PET Status, Sex, and Age at Registration	Time from End of Therapy to Death	Cause of Death
Negative PET findings, radiotherapy group		
Male, 71 yr*	3 wk	Pneumonia
Male, 70 yr*†	4 wk	Pneumonitis
Male, 62 yr*	7 wk	Cerebral hemorrhage
Female, 73 yr*†	9 wk	Pneumonitis
Male, 61 yr*‡	4 mo	Angioimmunoblastic T-cell lymphoma
Male, 28 yr§	20 mo	Myocardial fibrosis and heart failure
Female, 74 yr	54 mo	Hodgkin's lymphoma
Male, 67 yr	60 mo	Mycosis fungoides
Negative PET findings, group with no further treatment		
Female, 75 yr	3 wk	Bronchopneumonia
Female, 64 yr	31 mo	Small-cell carcinoma of lung
Male, 64 yr	60 mo	Diffuse large-B-cell lymphoma
Male, 51 yr	69 mo	Mantle-cell lymphoma
Positive PET findings		
Female, 60 yr	4 wk	Pneumonia
Male, 57 yr	10 mo	Pneumonia
Male, 55 yr	14 mo	Hodgkin's lymphoma
Male, 59 yr	19 mo	Hodgkin's lymphoma
Male, 46 yr	24 mo	Hodgkin's lymphoma
Male, 27 yr	25 mo	Diffuse large-B-cell lymphoma
Male, 74 yr	28 mo	Hodgkin's lymphoma
Male, 32 yr	64 mo	Meningitis

* Although randomly assigned to the radiotherapy group, this patient did not receive radiotherapy.
† The pneumonitis in this patient was probably caused by the bleomycin component of ABVD.
‡ After re-review of the histologic data at the time of recurrence, this patient was determined to have had angioimmunoblastic T-cell lymphoma at trial entry.
§ This patient had received a field of radiotherapy incorporating the heart.

? IF

International Journal of Radiation Oncology biology • physics
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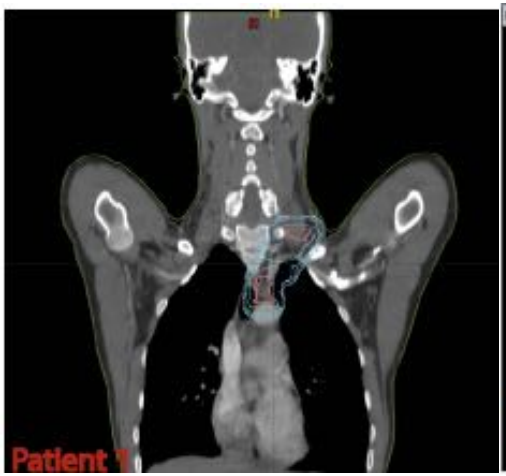
Clinical Investigation

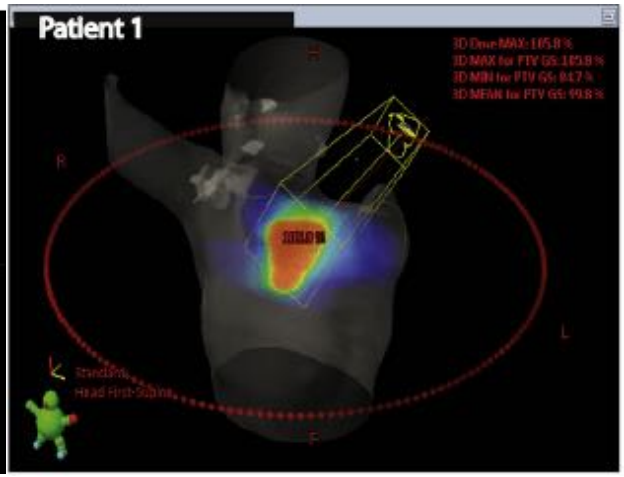
Radiation Therapy Planning for Early-Stage Hodgkin Lymphoma: Experience of the International Lymphoma Radiation Oncology Group

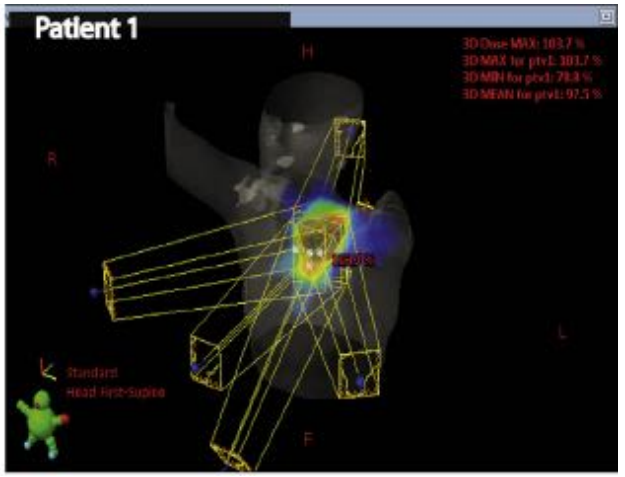
Maja V. Maraldo, MD, PhD,* Bouthaina S. Dabaja, MD,† Andrea R. Filippi, MD,‡ Tim Illidge, MD, PhD,§ Richard Tsang, MD,‖ Umberto Ricardi, MD,‡ Peter M. Petersen, MD, PhD,* Deborah A. Schut, MRT(T),* John Garcia, CMD,† Jayne Headley, CMD,§ Amy Parent, CMD,‖ Benoit Guibord, CMD,‖ Riccardo Ragona, MSc,† and Lena Specht, MD, DMSc*

*Departments of Clinical Oncology and Hematology, Rigshospitalet, University of Copenhagen, Denmark; †Department of Radiation Oncology, MD Anderson Cancer Center, Texas; ‡Department of Oncology, University of Torino School of Medicine, Torino, Italy; §Department of Oncology, Christie Hospital, Manchester, United Kingdom; and ‖Department of Radiation Oncology, Princess Margaret Cancer Centre, Toronto, Ontario, Canada

Estimated doses to OARs were comparable between centers. Adopting ILROG guidelines and implementing universal dose objectives could further standardize treatment techniques and contribute to lowering the dose to the OARs.







Int J Radiation Oncol Biol Phys, Vol. 92, No. 1, pp. 144–152, 2015

Table 2. PET/CT response-adapted therapy in early-stage CHL

Study	Treatment		PFS (ITT)	PFS (per protocol)	OS (ITT)
Published data of PET/CT response-adapted therapy in early-stage CHL					
UK RAPID [52••]	Standard:	3 × ABVD + 30 Gy IFRT if PET3 neg	94.6 % at 3y	97.1 % at 3y	97.1 % at 3y
	Experimental:	3 × ABVD + NFT if PET3 neg	90.8 % at 3y	90.8 % at 3y	99.0 % at 3y
		4 × ABVD + 30 Gy IFRT if PET3 pos	87.6 % at 5y	NR	94.5 % at 5y
EORTC H10F [54••]	Standard:	3 × ABVD + 30 Gy INRT	100 % at 1y[a]	NR	NR
	Experimental:	2 × ABVD + 2 × EB + 30 Gy INRT if PET2 pos	NR	NR	NR
		4 × ABVD + NFT if PET2 neg	94.9 % at 1y	NR	NR
EORTC H10U [54••]	Standard:	2 × ABVD + 30 Gy INRT	97.3 % at 1y[a]	NR	NR
	Experimental:	2 × ABVD + 2 × EB + 30 Gy INRT if PET2 pos	NR	NR	NR
		4 × ABVD + NFT if PET2 neg	94.7 % at 1y	NR	NR
New Trials of PET/CT response-adapted therapy in early-stage CHL					
Favorable risk trials					
CALGB 50604	Experimental:	2 × ABVD + 2 × EB + 30 Gy IFRT if PET2 pos			NCT01132807
		4 × ABVD + NFT if PET2 neg			
GHSG HD16	Standard:	2 × ABVD + 20 Gy IFRT			NCT00736320
	Experimental:	2 × ABVD + 20 Gy IFRT if PET2 pos			
		2 × ABVD + NFT if PET2 neg			
Unfavorable risk trials					
CALGB 50801	Experimental:	2 × ABVD + 4 × EB + 30 Gy IFRT if PET2 pos			NCT01118026
		6 × ABVD + NFT if PET2 neg			
GHSG HD17	Standard:	2 × EB + 2 × ABVD + 30 Gy IFRT			NCT01356680
	Experimental:	2 × EB + 2 × ABVD + 30 Gy INRT if PET4 pos			
		2 × EB + 2 × ABVD + NFT if PET4 neg			

NR not reported; *PFS* progression-free survival; *OS* overall survival; *ABVD* doxorubicin, bleomycin, vinblastine, dacarbazine; *EB* escalated bleomycin, etoposide, doxorubicin, cyclophosphamide, vincristine, procarbazine, prednisone; *IFRT* involved-field radiotherapy; *INRT* involved-node radiotherapy; *NFT* no further therapy; *ITT* intention-to-treat. PET2 and PET3 refer to interim PET/CT after 2 or 3 cycles of chemotherapy, respectively

[a]Data are for PET2-negative patients only

Thus, radiotherapy for Hodgkin's disease is …

2. Follicular lymphomas

Contents lists available at ScienceDirect

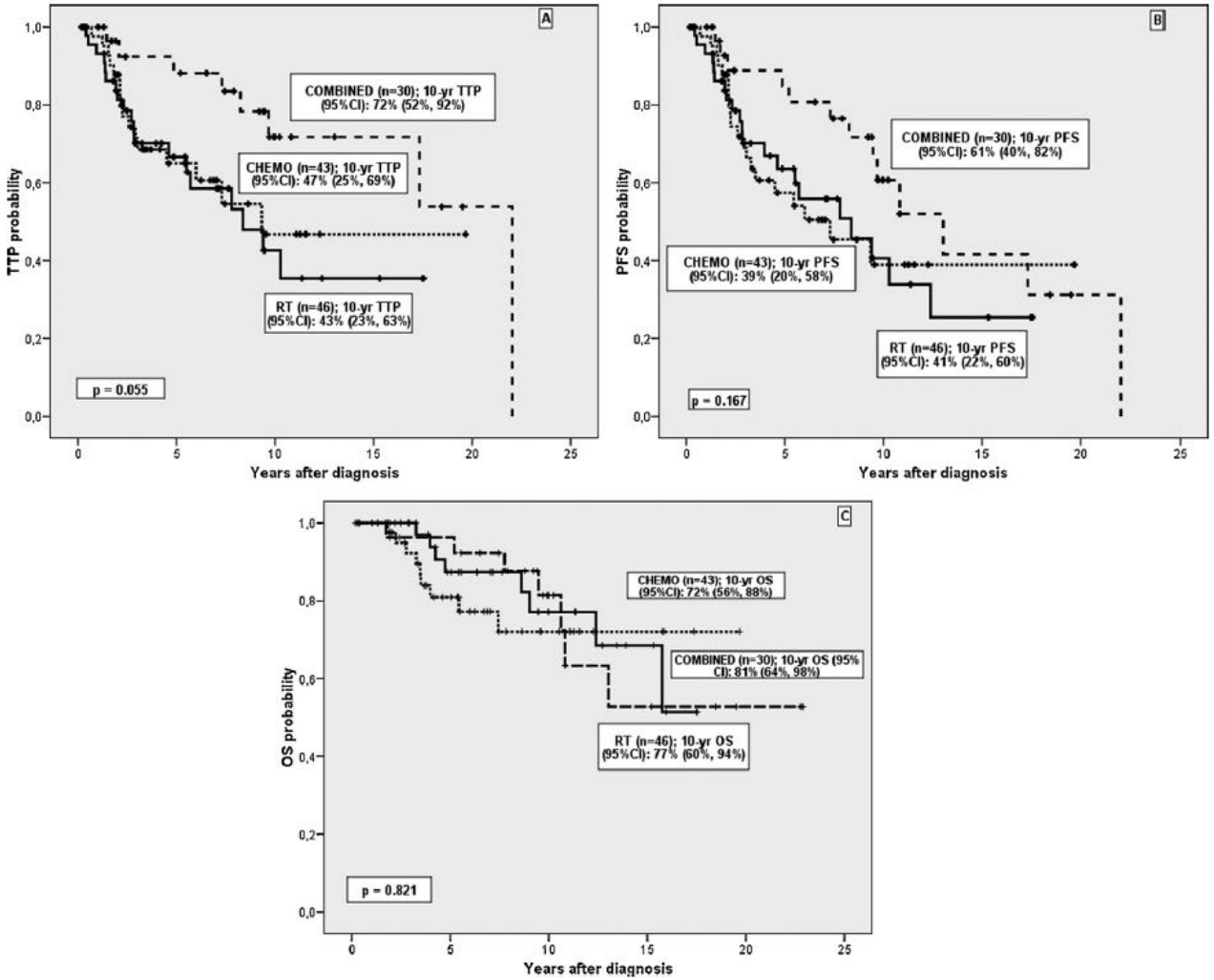
Leukemia Research

journal homepage: www.elsevier.com/locate/leukres

The long term follow-up of early stage follicular lymphoma treated with radiotherapy, chemotherapy or combined modality treatment

Juan-Manuel Sancho[a,*], Olga García[a], Santiago Mercadal[b], Helena Pomares[b], Rubén Fernández-Alvarez[c], Eva González-Barca[b], Gustavo Tapia[d], Esther González-García[c], Miriam Moreno[a], Eva Domingo-Domènech[b], Marc Sorigué[a], José-Tomás Navarro[a], Cristina Motlló[a], Alberto Fernández-de-Sevilla[b], Evarist Feliu[a], Josep-Maria Ribera[a]

Leukemia Research 39 (2015) 853–858


A
COMBINED (n=30); 10-yr TTP (95%CI): 72% (52%, 92%)
CHEMO (n=43); 10-yr TTP (95%CI): 47% (25%, 69%)
RT (n=46); 10-yr TTP (95%CI): 43% (23%, 63%)
p = 0.055
TTP probability
Years after diagnosis
B
COMBINED (n=30); 10-yr PFS (95%CI): 61% (40%, 82%)
CHEMO (n=43); 10-yr PFS (95%CI): 39% (20%, 58%)
RT (n=46); 10-yr PFS (95%CI): 41% (22%, 60%)
p = 0.167
PFS probability
Years after diagnosis
C
CHEMO (n=43); 10-yr OS (95%CI): 72% (56%, 88%)
COMBINED (n=30); 10-yr OS (95% CI): 81% (64%, 98%)
RT (n=46); 10-yr OS (95%CI): 77% (60%, 94%)
p = 0.821
OS probability
Years after diagnosis

PLOS ONE | DOI:10.1371/journal.pone.0131158 July 6, 2015

RESEARCH ARTICLE

Radiotherapy Compared to Other Strategies in the Treatment of Stage I/II Follicular Lymphoma: A Study of 404 Patients with a Median Follow-Up of 15 Years

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‡ These authors also contributed equally to this work.
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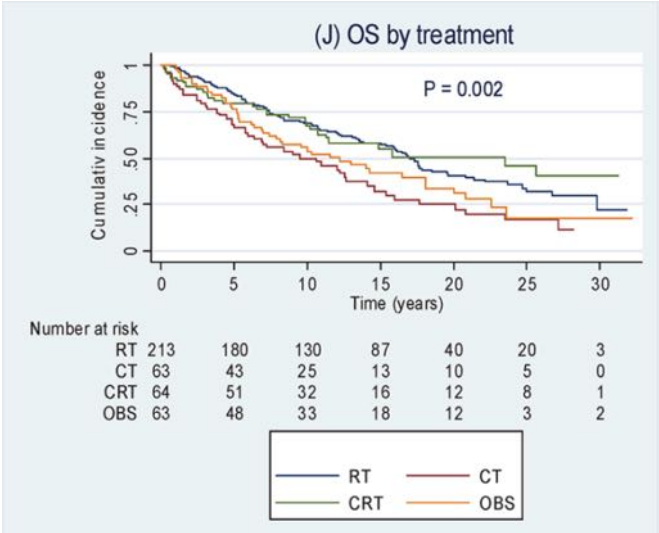
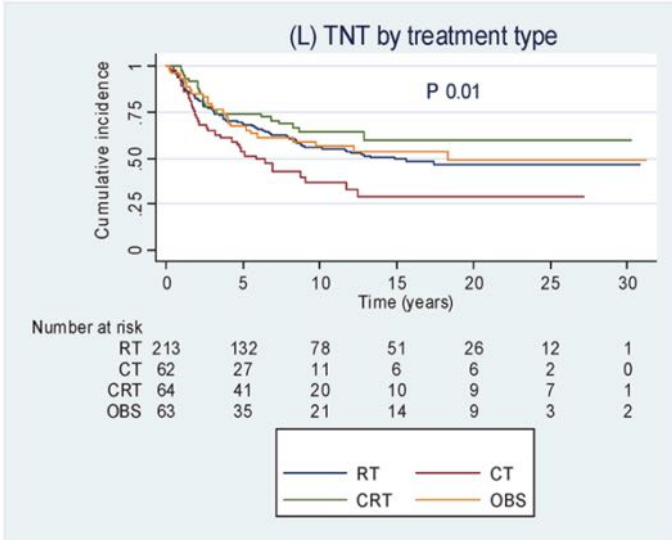


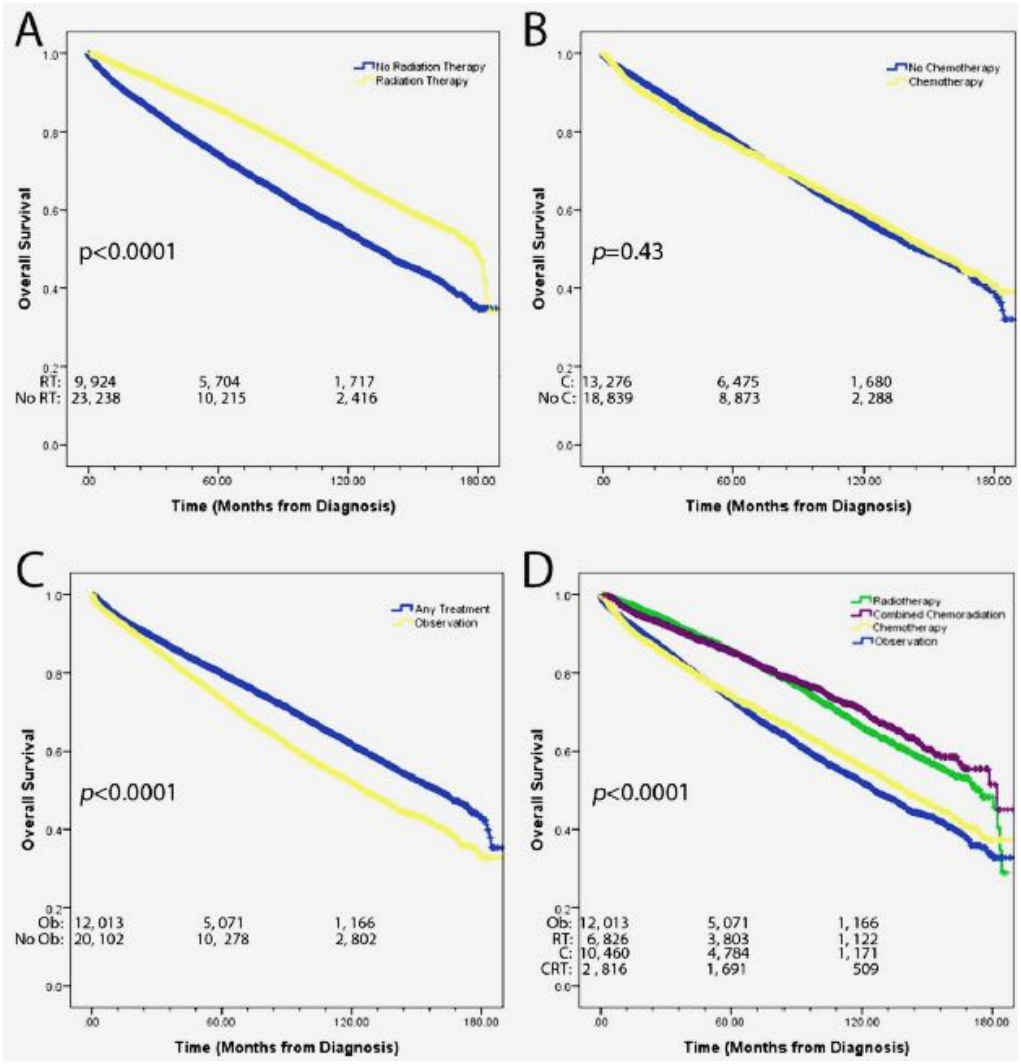


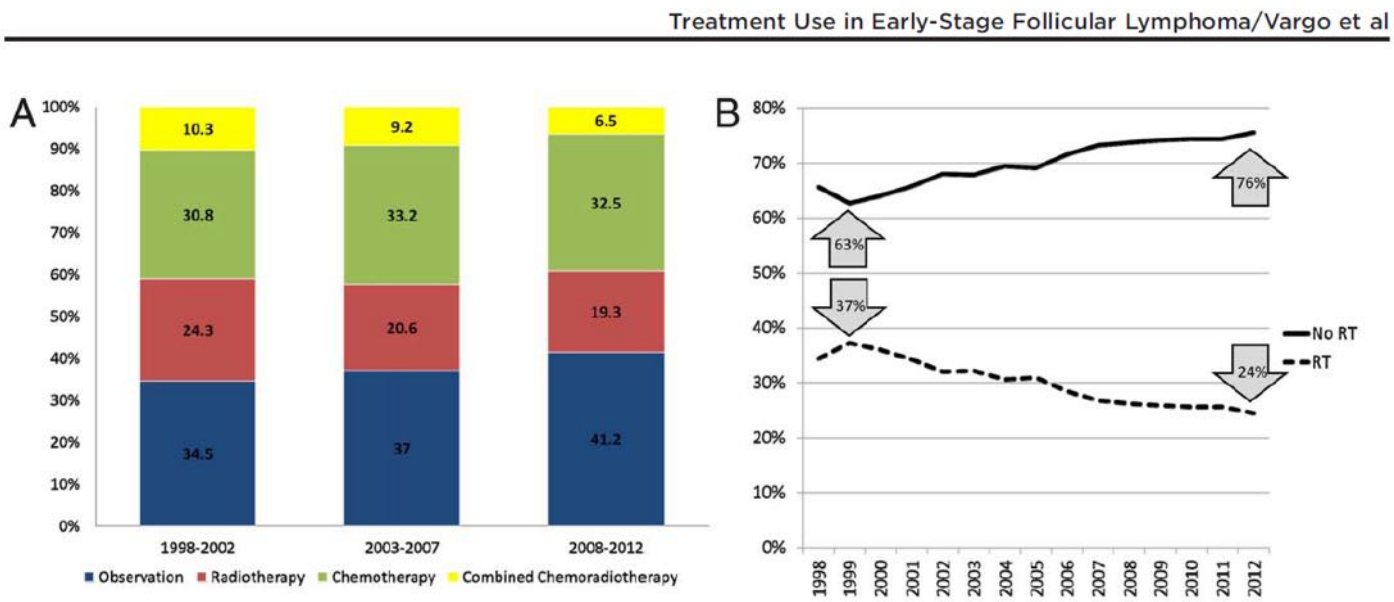
What Is the Optimal Management of Early-Stage Low-Grade Follicular Lymphoma in the Modern Era?

John A. Vargo, MD[1]; Beant S. Gill, MD[1]; Goundappa K. Balasubramani, PhD[2]; and Sushil Beriwal, MD[1]

National Cancer Database Data 1998-2012
36,961 Stage I-II, Grade 1-2 follicular lymphoma

Cancer, 2015; 121:3325-34.


A
No Radiation Therapy
Radiation Therapy
Overall Survival
p<0.0001
RT: 9, 924 5, 704 1, 717
No RT: 23, 238 10, 215 2, 416
Time (Months from Diagnosis)
B
No Chemotherapy
Chemotherapy
Overall Survival
p=0.43
C: 13, 276 6, 475 1, 680
No C: 18, 839 8, 873 2, 288
Time (Months from Diagnosis)
C
Any Treatment
Observation
Overall Survival
p<0.0001
Ob: 12, 013 5, 071 1, 166
No Ob: 20, 102 10, 278 2, 802
Time (Months from Diagnosis)
D
Radiotherapy
Combined Chemoradiation
Chemotherapy
Observation
Overall Survival
p<0.0001
Ob: 12, 013 5, 071 1, 166
RT: 6, 826 3, 803 1, 122
C: 10, 460 4, 784 1, 171
CRT: 2, 816 1, 691 509
Time (Months from Diagnosis)



«RT is an increasingly underused treatment approach in the era of modern therapy for patients with early-stage follicular lypmhomas. The use of RT appears to improve OS and should remain standard practice as encouraged by clinical practice guidelines…»

Thus, radiotherapy for follicular lymphomas is …

3. High grade lymphomas in the post-Rituximab era

✓ Open issues

- ✓ Redefining indications after widespread use of R-CHOP
- ✓ Role in advanced stage (bulky disease)
- ✓ Role in early stage in association with less chemotherapy
- ✓ Selection of patients for de-escalation with early PET
- ✓ Dose (30 vs 40 Gy)

Phase III 02-03 trial from the Lysa/Goelams group, presented at the 56th American Society of Hematology (ASH) Annual Meeting

Study Details

Depending on risk factors, patients received **4 or 6 consecutive cycles of R-CHOP14**, **followed or not** by **involved-field radiotherapy at 40 Gy** delivered 4 weeks after the last cycle of R-CHOP. All patients were evaluated by fluorodeoxyglucose–positron emission tomography (FDG-PET) at baseline, after 4 cycles of R-CHOP, and at the end of treatment. The recommendation was that **patients in partial response (tumor regression > 50% but a persistent positive FDG-PET) after cycle 4 receive an additional 2 cycles of R-CHOP followed by radiotherapy**. The primary objective was event-free survival 1 year after the last randomization.

There were **301 evaluable patients** (median age, 56 years), of whom 82% had normal LDH levels, 96% had no B symptoms, and the majority had an International Prognostic Index score of 1 to 2. The main tumor site was cervical lymph nodes, and 40% had extranodal sites.

No Additional Benefit of Radiotherapy

No significant benefit was observed in the cohort receiving radiotherapy after R-CHOP (n = 151) compared with the group receiving R-CHOP alone (n = 150). Complete response rates overall were 84%, and 14% of patients attained partial responses and three patients had stable disease.

In the intent-to-treat analysis, after 51 months' median follow-up, event-free survival at 5 years was 88%, with 88.4% for the radiotherapy arm and 87.3% for the R-CHOP alone arm (P = .13). Overall survival was 91% for the whole population and 92% for the radiotherapy arm and 90% for the R-CHOP–alone arm (P = .33),

By assignment group, **complete responses were observed in 82% after R-CHOP alone and 85% after R-CHOP plus radiotherapy; partial responses (PET-positive) were observed in 16% and 12**%, and stable disease was noted in one and two patients, respectively.
At the end of treatment, complete responses were observed in 93% and 95%, respectively. There were partial responses in seven patients treated with R-CHOP alone and one patient treated with R-CHOP plus radiotherapy, and stable disease was reported in two patients in the R-CHOP arm.
For the 43 patients who were partial responders after cycle 4, 37 (86%) received 2 additional cycles of R-CHOP plus radiotherapy, whereas 6 patients were treated with a different regimen, with or without radiotherapy. Of these 43 patients, 40 ultimately attained a complete response. After complete response, 5-year event-free survival was 89% in the R-CHOP–alone arm, and 91% in the R-CHOP plus radiotherapy arm.

“After 4 cycles of R-CHOP, adding 2 cycles plus radiotherapy for patients in partial response induced similar outcomes as compared to patients who obtained a complete response”

Relapses occurred in 12 patients (8%) in the R-CHOP–alone arm and 8 patients (5%) of the arm receiving R-CHOP plus radiotherapy, which was not a significant difference.

The median time to relapse was 21 months. **In the radiotherapy arm, none of these relapses occurred at the initial tumor site**, but in the R-CHOP–alone arm, 5 of 12 relapses occurred at that site. Altogether, nine patients developed progressive disease.

Role of radiotherapy in patients with early-stage diffuse large B cell lymphoma who had achieved complete remission after chemotherapy.

2015 ASCO Annual Meeting - J Clin Oncol 33, 2015 (suppl; abstr e19502)

Author(s): Yuan Zhu, Jianjiang Liu, et al., Hangzhou, China; Zhejian

Background: In the rituximab era, results of randomized trials and relevant studies focused on the role of consolidation radiotherapy (RT) in stage I–II diffuse large B cell lymphoma (DLBCL) were very few.
The objective of this study is to investigate the role of consolidation radiotherapy (RT) in patients with stage I–II diffuse large B cell lymphoma (DLBCL) who had achieved complete remission after chemotherapy.
Methods: Between January 2005 and December 2012, data for **376 patients with early stage DLBCL in complete remission after CHOP or R-CHOP** for at least three cycles were analyzed retrospectively. The median age was 53 years.
Patients were divided into four groups: the **R-CHOP group (93 patients), the R-CHOP+RT group (78 patients), the CHOP group (107 patients) and the CHOP+RT group (98 patients)**.
All patients used Involved –field radiotherapy and the total dosage ranged from 30 Gy to 56 Gy.
Results: During a **median follow-up of 53 months** (range 4–128 months), the 5-year actuarial rates for disease free survival (DFS) and overall survival (OS) across all 376 patients were 80.7% and 87.6%, respectively.
The 5-year DFS and OS of the R-CHOP+RT group were better than the R-CHOP group (5-year DFS: 94.9% vs. 88.1%, P = 0.030; 5-year OS: 97.9% vs. 86.0%, P = 0.026).
No significant DFS or OS benefits were observed between the CHOP+RT group and the CHOP group (5-year DFS: 74.2% vs. 71.4%, P = 0.623; 5-year OS: 74.2% vs. 71.4%, P = 0.623).
Conclusions: Our study indicates that consolidation radiotherapy can only improve DFS or OS of the patients with early stage DLBCL in complete remission after R-CHOP chemotherapy not CHOP regimen. All early stage patients are recommended to undergo rituximab-containing chemotherapy followed by consolidation radiotherapy.
Relevant randomized trials are needed to testify this question.

VOLUME 32 · NUMBER 11 · APRIL 10 2014

JOURNAL OF CLINICAL ONCOLOGY

ORIGINAL REPORT

Role of Radiotherapy to Bulky Disease in Elderly Patients With Aggressive B-Cell Lymphoma

Gerhard Held, Niels Murawski, Marita Ziepert, Jochen Fleckenstein, Viola Pöschel, Carsten Zwick, Jörg Bittenbring, Mathias Hänel, Sibylla Wilhelm, Jörg Schubert, Norbert Schmitz, Markus Löffler, Christian Rübe, and Michael Pfreundschuh

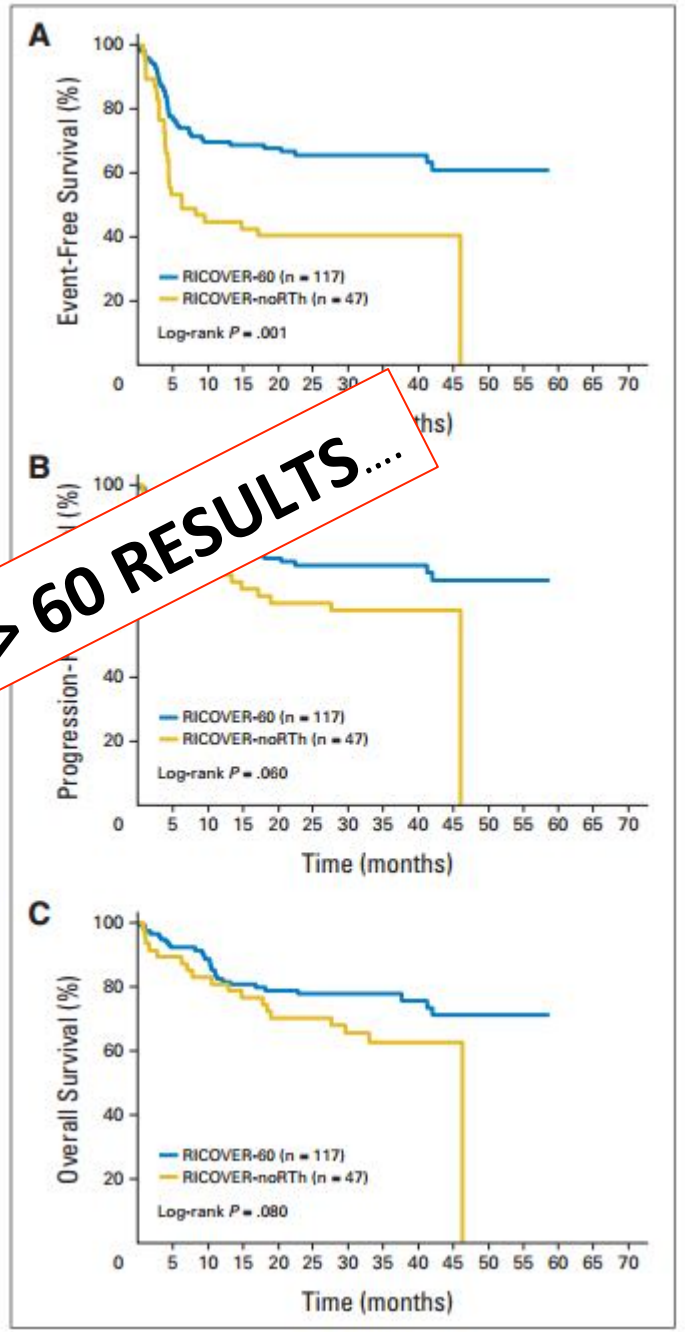
Abstract

Purpose R-CHOP (rituximab plus cyclophosphamide, doxorubicin, vincristine, and prednisone) is standard care for aggressive B-cell lymphoma. A prospective trial was conducted to investigate the role of additive radiotherapy (RT) to bulky and extralymphatic disease.

Patients and Methods The best arm of the RICOVER-60 trial (6×R-CHOP-1 [R-CHOP administered once every 2 weeks plus two additional ar rituximab] plus involved-field RT [36 Gy] to sites of initial bulky and extralymphatic involvement) was compared with a co immunochemotherapy but without RT in an amend -60 trial (RICOVER-noRTh) in a prospective fashion.

Results After a median observatio of 166 RICOVER-noRTh patients were evaluable. In a the intention-to-treat population adjusting for International Pr sk factors and age (> 70 years), event-free survival (EFS) of patients aky disease was inferior without additive RT (hazard ratio [HR], 2.1; 95% CI, 1.3 to 3.5; *P* = .005), with trends for inferior progression-free (PFS; HR, 1.8; 95% CI, 1.0 to 3.3; *P* = .058) and overall survival (OS; HR, 1.6; 95% CI, 0.9 to 3.1; *P* = .127). In a per-protocol analysis with 11 patients in RICOVER-noRTh excluded for receiving unplanned RT, multivariable analysis revealed HRs of 2.7 (95% CI, 1.3 to 5.9; *P* = .011) for EFS, 4.4 (95% CI, 1.8 to 10.6; *P* = .001) for PFS, and 4.3 (95% CI, 1.7 to 11.1; *P* = .002) for OS for patients not receiving RT to bulky disease.

Conclusion Additive RT to bulky sites abrogates bulky disease as a risk factor and improves outcome of elderly patients with aggressive B-cell lymphoma. Whether RT can be spared in patients with (metabolic) complete remission after immunochemotherapy must be addressed in appropriately designed prospective trials.



Awaiting OPTIMAL > 60 RESULTS....

Thus, radiotherapy for high grade lymphomas is …

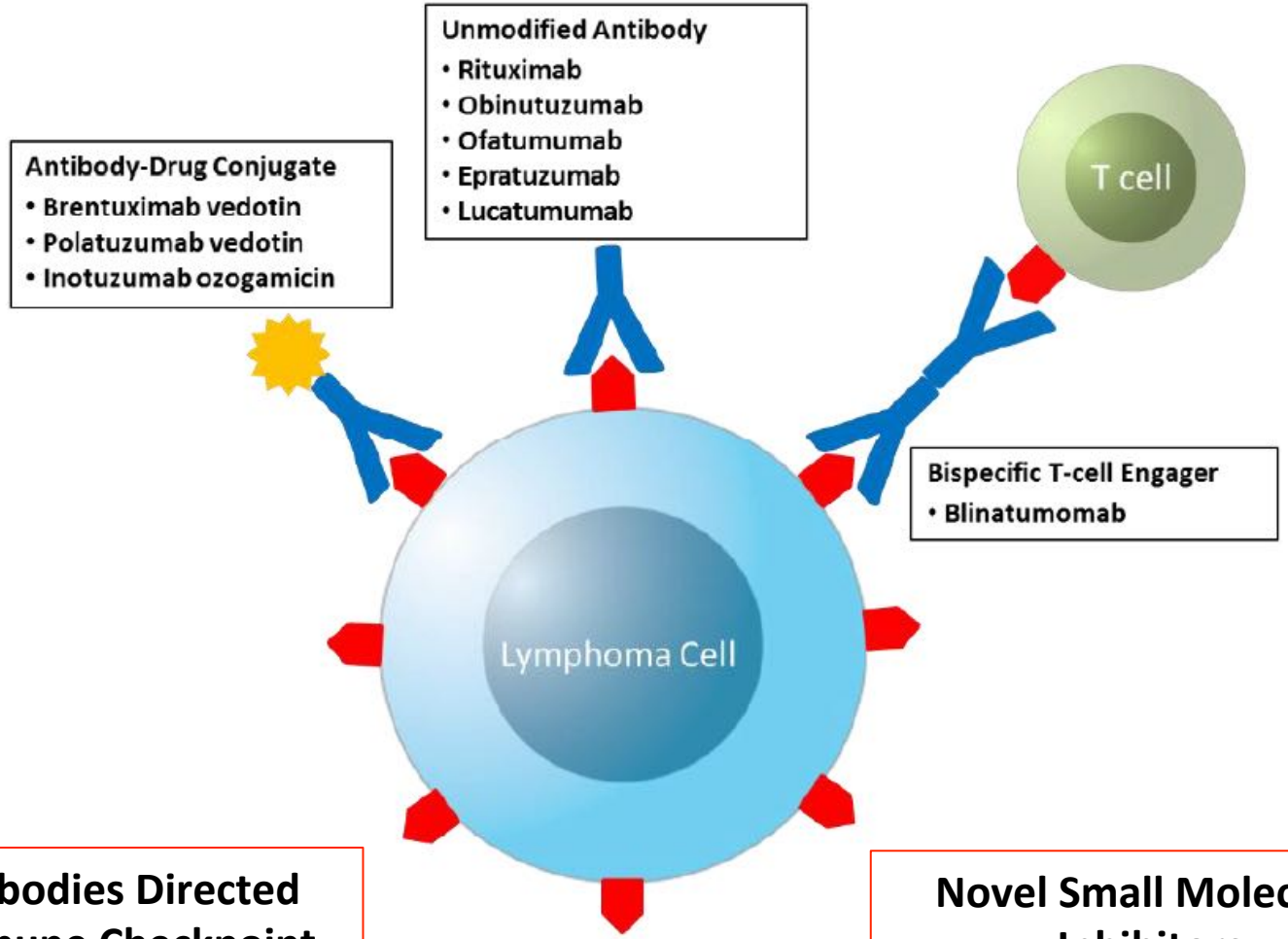
Is *chemotherapy* for lymphomas dying ?

Novel Targeted Agents in Hodgkin and Non-Hodgkin Lymphoma Therapy

Natalie S. Grover and Steven I. Park *

Pharmaceuticals **2015**, *8*, 607-636; doi:10.3390/ph8030607

There has been a recent emergence of **novel targeted agents** for treatment of Hodgkin and non-Hodgkin lymphoma. In particular, **antibodies and antibody-drug conjugates directed against surface antigens, agents that block immune checkpoint pathways, and small molecule inhibitors** directed against cell signaling pathways have shown significant promise in patients with relapsed and refractory disease and in the frontline setting. **With the development of these new therapies, cytotoxic chemotherapy may be avoided entirely in some clinical settings**. This review will present the latest information on these novel treatments in Hodgkin and non-Hodgkin lymphoma and will discuss both recently approved agents as well as drugs currently being studied in clinical trials.

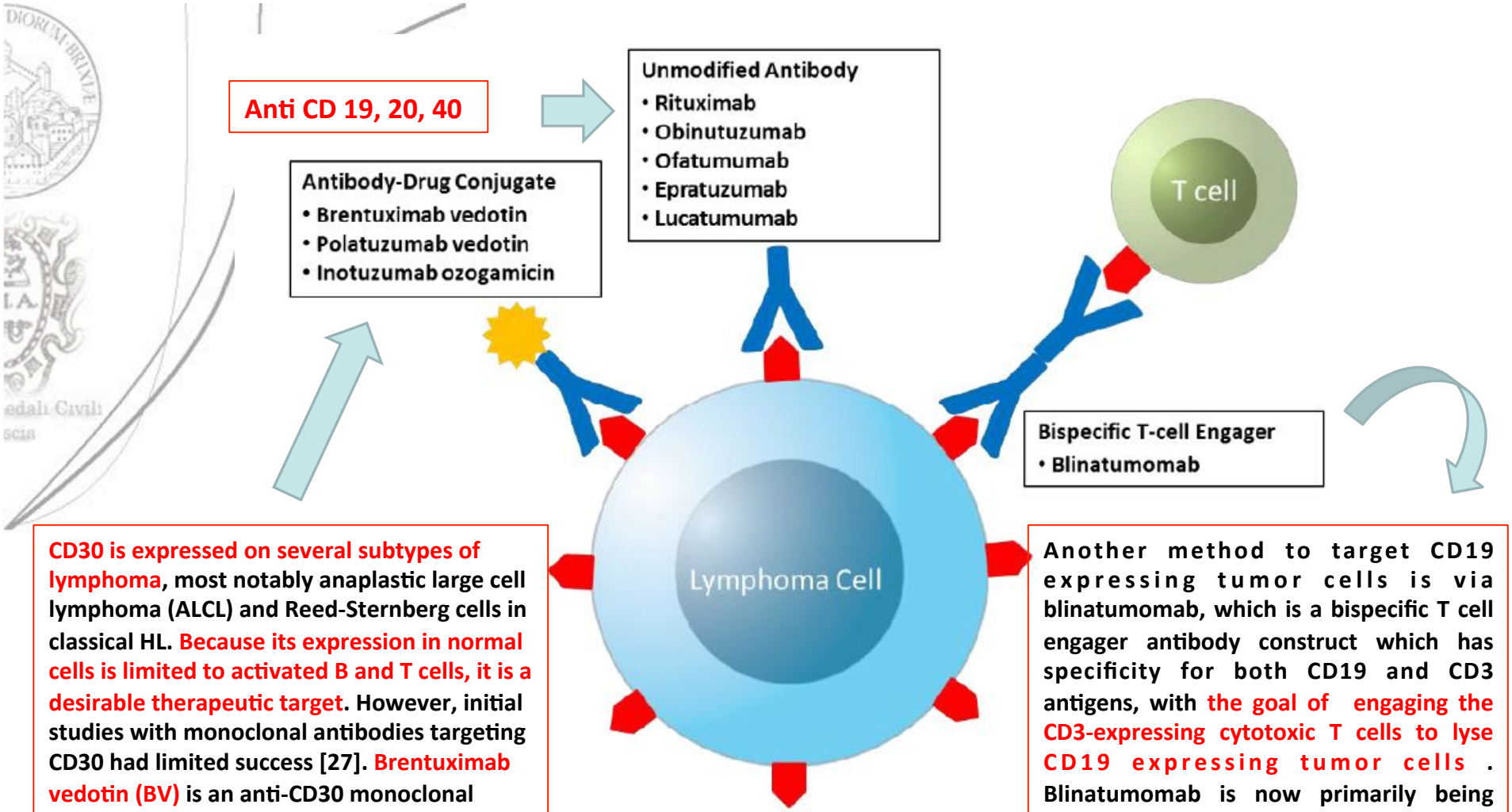


Novel Antibodies Directed against Immune Checkpoint Proteins

Ipilimumab (Anti-CTLA-4)
Pidilizumab (Anti-PD1)
Nivolumab (Anti-PD1)
Pembrolizumab (Anti-PD1)

Novel Small Molecule Inhibitors

Ibrutinib (BTK Inhibitor)
Idelalisib (PI3Kd Inhibitor)
Duvelisib (PI3Kgd Inhibitor)
TGR-1202 (PI3Kd Inhibitor)



CD30 is expressed on several subtypes of lymphoma, most notably anaplastic large cell lymphoma (ALCL) and Reed-Sternberg cells in classical HL. Because its expression in normal cells is limited to activated B and T cells, it is a desirable therapeutic target. However, initial studies with monoclonal antibodies targeting CD30 had limited success [27]. Brentuximab vedotin (BV) is an anti-CD30 monoclonal antibody which is linked to the antimicrotubule agent monomethyl auristatin E (MMAE). BV has shown remarkable effectiveness in both ALCL (as well as other peripheral T cell lymphomas) and HL. Current phase 3 trials are in progress which may dramatically change frontline therapy for both of these agents, similarly to rituximab in B-cell NHL.

Another method to target CD19 expressing tumor cells is via blinatumomab, which is a bispecific T cell engager antibody construct which has specificity for both CD19 and CD3 antigens, with the goal of engaging the CD3-expressing cytotoxic T cells to lyse CD19 expressing tumor cells . Blinatumomab is now primarily being studied and used in patients with ALL, promising results in relapsed/refractory aggressive lymphomas. Chimeric antigen receptor (CAR) T-cell therapy, which uses autologous infusion of genetically engineered T cells that express chimeric antigen receptors targeting surface antigens, like CD19, is being investigated for lymphoma treatment with promising preliminary data

.. Not yet, too….


Act Two:
Prostate Cancer

Medscape Medical News > Conference News

What's Hot at ASCO 2015?

Zosia Chustecka

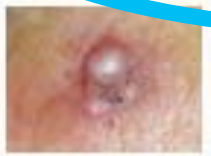
May 21, 2015

2 comments

EDITORS' RECOMMENDATIONS

Chemo Boost Reduces Relapse in High-Risk Wilms' Tumor

Chemo Upfront Ups Survival in Advanced Prostate Cancer



Vitamin B Derivative Reduces Risk for Further Skin Cancer

So here w
caught up
Oncology

Chicago is
more than
world are
president
scientific m

This year's
Transformi

This is key

Docetaxel ± ZA added to standard of care for hormone-naïve PCa: STAMPEDE results

James ND. J Clin Oncol 2015:33(15S):269s(abs.5001)

- RCT with novel multi-arm, multi-stage design
- Patient population: men with hormone-naïve PCa
  - Newly diagnosed
    - High-risk N0 M0 with ≥2 of: stage T3/4; PSA ≥40ng/ml; GS 8-10
    - N+ PCa
    - M+ PCa
  - Relapsing after RT or RP
    - ≥1 of: PSA ≥4ng/ml and rising with doubling time <6 mo; PSA ≥20ng/ml; N+ PCa; M+ PCa
- 4 arms are presented (pts recruited 2005-2013)

Standard of care (≥3 yrs ADT ± RT*)	N=1,184
ADT ± RT* + zoledronic acid (ZA)	N=593
ADT ± RT* + docetaxel (D; 75 mg/m^2, 6 cycles, with prednisone)	N=592
ADT ± RT* + ZA + D	N=593

* RT was encouraged for N0 M0 pts up to Nov 2011, then mandated

Data from oral presentation

Docetaxel ± ZA added to standard of care for hormone-naïve PCa: STAMPEDE results

James ND. J Clin Oncol 2015:33(15S):269s(abs.5001)

» Survival outcomes at median FU 42 mo

Intervention	Median OS				
	Standard of care	Standard of care + intervention	HR	95% CI	*P*
ZA	67 mo	80 mo	0.93	0.79-1.11	0.44
D	67 mo	77 mo	0.76	0.63-0.91	0.003
ZA + D	67 mo	72 mo	0.81	0.68-0.97	0.02

Adding docetaxel to ADT ± RT improves OS by average of 10 mo.
Adding ZA to ADT ± RT does not improve OS.
Adding ZA + docetaxel to ADT ± RT does improve OS, but there is no obvious benefit over adding docetaxel alone

Data from oral presentation

Docetaxel ± ZA added to standard of care for hormone-naïve PCa: STAMPEDE results

James ND. J Clin Oncol 2015:33(15S):269s(abs.5001)

» Outcomes in M+ (61% of pts) and M0 (39% of pts) subgroup: ADT±RT vs ADT±RT +D:

OS	HR (95% CI)
M+	0.73 (0.59-0.89)
M0	1.01(0.65-1.56)

FFS*	HR (95% CI)
M+	0.62 (0.54-0.73)
M0	0.57 (0.42-0.76)

43 mo vs 65 mo; *P*=0.002

*failure-free survival: first of PSA failure, local failure, LN failure, distant metastasis, PCa death

» Adverse events

AEs, Grade ≥3 (%)	ADT ± RT	ADT ± RT + D
Total	31	51
Febrile neutropenia	1	12
Neutropenia	1	12

Docetaxel should be considered for routine practice in fit men with newly diagnosed M+ PCa. It is too soon for a recommendation in men with high-risk M0 PCa

Data from oral presentation

ASCO GU 2015. ABSTRACT 140. Androgen deprivation therapy (ADT) plus docetaxel (D) versus ADT alone for hormone-naïve metastatic prostate cancer (PCa): Long-term analysis of the GETUG-AFU 15 phase III trial.

Gwenaelle Gravis et al.

ADT	ADT + D	p-value	Hazard ratio (95%CI)	
Overall population	N = 193	N = 192		
Median OS	46.5 [39.1-60.6]	60.9 [46.1-71.4]	0.44	0.9 [0.7-1.2]
Biological PFS	12.9 [11.9-17.7]	22.9 [19.5-28.4]	0.0021	0.7 [0.6-0.9]
HVD * Pts	N = 91	N = 92		
Median OS	35.1 [29.9-44.2]	39 [28-52.6]	0.35	0.8 [0.6-1.2]
Biological PFS	9.2 [8.3-12.2]	15.2 [12-21.2]	0.0039	0.6 [0.5-0.9]
LVD Pts	N = 102	N = 100		
Median OS	NR [61.8-NR]	83.1 [69.5-NR]	0.87	1 [0.6-1.5]
Biological PFS	22.4 [16.8-37]	40.9 [28.4-62.5]	0.0533	0.7 [0.5-1]

Conclusions: With longer follow-up, the addition of docetaxel to ADT did not significantly improve OS in patients with hormone-naïve metastatic prostate cancer. In the retrospective analysis using aligned definition of volume of metastasis as E3805, the HVD outcomes were similar to E3805 for ADT alone and there was a non-significant 4 months increase in OS with ADT+D, in this underpowered subset.

ADT alone vs ADT + docetaxel (D) for hormone-naïve M+ PCa: long-term results of the GETUG-AFU 15 trial

Gravis G. J Clin Oncol 2015:33(Suppl 7S):abs.140

- Multi-centre phase III trial; N=385 hormone-sensitive M+ PCa pts randomised to ADT alone vs ADT + D (75 mg/m² q3wk up to 9 cycles)
- Median FU: 83 mo

GETUG-AFU 15	ADT (N=193)	ADT + D (N=192)	HR	95% CI	*P*
Median OS	46.5 mo	60.9 mo	0.9	0.7-1.2	0.44
Biological PFS	12.9 mo	22.9 mo	0.7	0.6-0.9	0.002

CHAARTED*	ADT (N=393)	ADT + D (N=397)	HR	95% CI	*P*
Median OS	44 mo	57.6 mo	0.61	0.47-0.81	0.0003

*Sweeney C et al. J Clin Oncol 2014;35(5S):abstract LBA2

Data from oral presentation

ADT alone vs ADT + docetaxel (D) for hormone-naïve M+ PCa: long-term results of the GETUG-AFU 15 trial

Gravis G. J Clin Oncol 2015:33(Suppl 7S):abs.140

» Retrospective application of "extent of disease" criteria of CHAARTED to GETUG 15 data

Low-volume disease

GETUG-AFU 15	ADT (N=102)	ADT + D (N=100)	HR	95% CI	*P*
Median OS	NR	83 mo	1.0	0.6-1.5	0.87
Biological PFS	22 mo	41 mo	0.7	0.5-1.0	0.05

High-volume disease

GETUG-AFU 15	ADT (N=91)	ADT + D (N=92)	HR	95% CI	*P*
Median OS	35 mo	39 mo	0.8	0.6-1.2	0.35
Biological PFS	9 mo	15 mo	0.6	0.5-0.9	0.004

CHAARTED*	ADT		ADT + D		HR	95% CI	*P*
	N	OS	N	OS			
Low-volume	142	NR	134	NR	0.63	0.34-1.17	0.14
High-volume	251	32 mo	263	49 mo	0.60	0.45-0.81	0.0006

*Sweeney C et al. J Clin Oncol 2014;35(5S):abstract LBA2

Data from oral presentation

ADT alone vs ADT + docetaxel (D) for hormone-naïve M+ PCa: long-term results of the GETUG-AFU 15 trial

Gravis G. J Clin Oncol 2015:33(Suppl 7S):abs.140

» Multivariable analysis for OS:

	HR	95% CI	*P*
High- vs low-volume disease	1.76	1.27-2.41	<0.001
Elevated vs normal ALP	2.31	1.69-3.17	<0.001

» 80% of pts in the ADT arm and 45% of pts in the ADT + D arm received docetaxel beyond PSA progression

» The differences in outcomes between GETUG & CHAARTED will need to be further examined before practice can be changed. The outcomes of additional trials such as STAMPEDE (ASCO 2015) are awaited to further define the role of chemotherapy in hormone-naïve metastatic PCa

The addition of ADT to docetaxel in hormone-naïve M+ PCa pts does not significantly improve OS in the GETUG-AFU 15 trial

Data from oral presentation

The role of chemotherapy in hormone-naïve PCa

Based on presentation Tannock I at ASCO 2015

» Patient population in 3 trials

	Age (median, yrs)	M+ at presentation (% of pts)	High-volume mets (% of pts)
GETUG-AFU 15	64	71%	52%
CHAARTED	63	73%	65%
STAMPEDE	65	Most	Unknown

» These are not men with slowly progressive disease who develop metastases several yrs after diagnosis and local tx

Men with high-risk M+PCa, especially those presenting with metastases at or soon after diagnosis, who are judged fit to receive chemotherapy, should be offered 6 cycles of docetaxel in addition to ADT

Until longer FU of GETUG-AFU12, RTOG 0521 and STAMPEDE is available, men with M0 PCa who are to receive RT+ADT should not be offered additional docetaxel

RT + ADT ± docetaxel for high-risk localised PCa: results from RTOG 0521

Sandler HM. J Clin Oncol 2015:33:(abs.LBA5002)

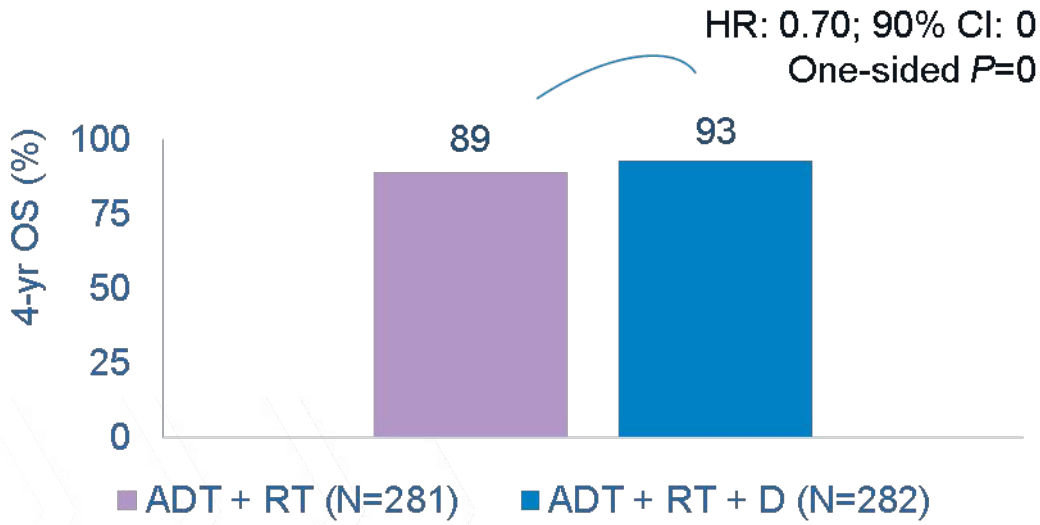
» Phase III RCT; N=563 high-risk PCa pts

Stage	GS	PSA
Any	≥9	<150
	7-8	≥20-150
≥T2	8	<20

randomisation

- ADT (24 mo) + RT (8 wks; 72.0-75.6 Gy) N=281
- ADT + RT + D (75 mg/m^2; 6 cycles + P (10 mg)) N=282

» Median FU: 6 yr



Predefined statistical criteria: detect improvement in 4-yr OS from 86% to 93%; HR: 0.49 not met → not a positive trial (yet) according to discussion

Data from oral presentation

RT + ADT ± docetaxel for high-risk localised PCa: results from RTOG 0521

Sandler HM. J Clin Oncol 2015:33:(abs.LBA5002)

	ADT + RT	ADT + RT + D	HR	95% CI	*P*
6-yr biochemical failure	74%	66%	0.81	0.58-1.11	0.19
6-yr DFS*	55%	65%	0.76	0.58-0.99	0.04

Cause of death	ADT + RT (N=59)	ADT + RT + D (N=43)
PCa-related	23	16
Due to protocol treatment	0	2
Other cause	24	16
Second primary cancer	12	5
Unknown	0	4

Worst overall AE grade, (possibly) related to tx (% of pts)

Gr	ADT + RT	ADT + RT + D
1	17	3
2	53	29
3	21	38
4	1	26
5	0	1

* disease-free survival: PSA failure, local failure, distant metastases or death due to any cause

Adj docetaxel to ADT + RT for pts with high-risk localised PCa might improve OS, however longer FU is needed and this is **not** the new standard of care

Data from oral presentation

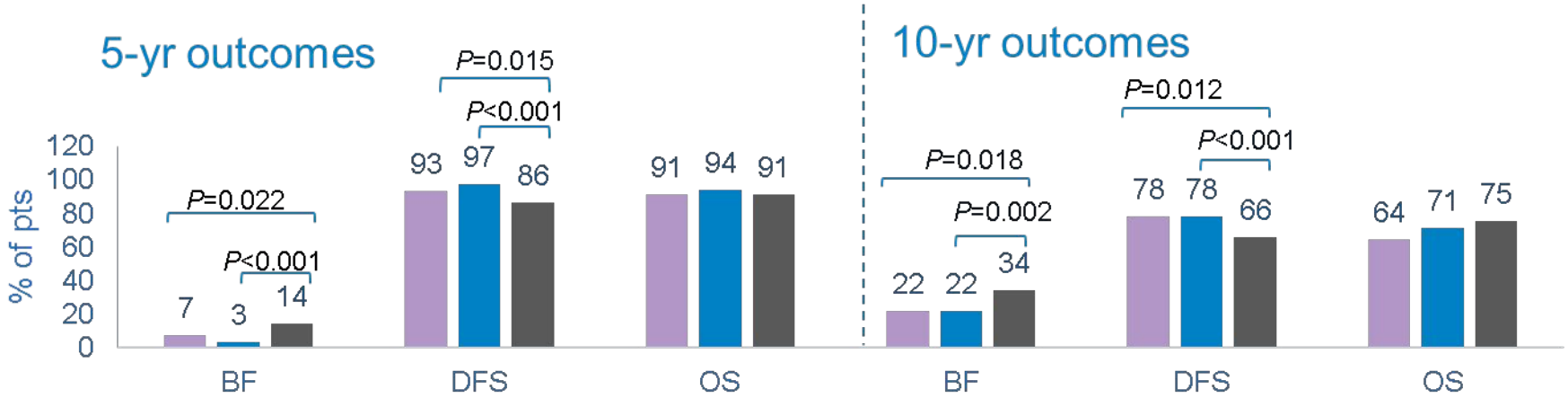
RT ± short-term ADT in pts with intermediate-risk PCa

Nabid A. J Clin Oncol 2015:33(15S):273s(abs.5019)

» Multi-centre, phase III, randomised PCS III trial; N=600 intermediate-risk PCa pts randomised to 1 of 3 arms:

ADT (6 mo) + RT (70 Gy) N=200	ADT (6 mo) + RT (76Gy) N=200	RT (76 Gy) N=200

» Median FU: 6.5 yr; 21.7% pts died; 1.2% pts died from PCa



BF: biochemical failure (nadir + 2 ng/ml); DFS: disease-free survival: OS: overall survival

6 mo ADT + RT (70 Gy and 76 Gy) improved DFS compared with RT (76 Gy); longer FU is needed for OS

Data from poster

Short-term ADT + RT as salvage tx for PSA-relapse after RP: results from GETUG-AFU 16 trial

Carrie C. J Clin Oncol 2015:33(15S):270s(abs.5006)

- French, multi-centre, randomised, open-label, phase III trial; N=742 pts with undetectable PSA for ≥6 mo after RP who had a PSA relapse, randomised to RT alone (66 Gy prostate ± 46 Gy pelvis) or RT + 6 mo ADT (2006-2010)
- Median FU: 63 mo
- Survival outcomes

Primary endpoint

	RT (N=373)	RT + ADT (N=369)	HR	95% CI	*P*
5-yr PFS	62%	80%	0.50	0.38-0.66	<0.0001
5-yr OS	95%	96%	0.66	0.36-1.22	0.18

- QoL outcomes: evolution between inclusion and yr 1 (% of pts) (by QLQ-C30)

	RT	RT + ADT
Worsened	26%	35%
Stable	56%	48%
Improved	19%	17%

EORTC questionnaire to assess QoL of cancer pts

Data from oral presentation

Short-term ADT + RT as salvage tx for PSA relapse after RP: results from GETUG-AFU 16 trial

Carrie C. J Clin Oncol 2015:33(15S):270s(abs.5006)

» Toxicity outcomes

Grade ≥3 toxicity	RT (N=373)	RT + ADT (N=369)
Acute genitourinary	1.1%	0.8%
Acute gastrointestinal	0.3%	0.3%
Late genitourinary	7.8%	7.2%
Late gastrointestinal	1.4%	1.7%
Late cardiac	0.3%	0.3%

RT + short-term ADT vs RT alone as salvage tx for PSA relapse after RP significantly improved PFS without increasing grade ≥3 toxicity. After 63 mo median FU, there was no difference in OS

Data from oral presentation

NRG ONCOLOGY

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press release

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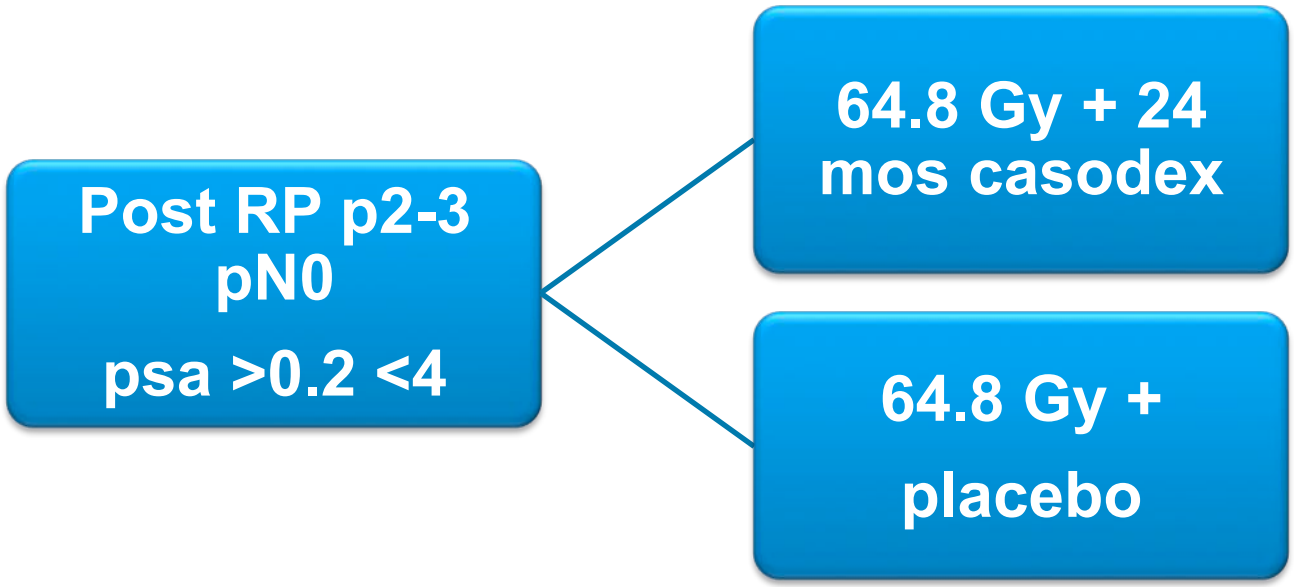
Under Embargo Until
Monday, October 19, 2015
2:43 PM Central Time

Contact: Nancy Fredericks • Office: 215.717.2769 • Mobile: 610.715.7707

The Randomized NRG Oncology RTOG 9601 Protocol Reports That Men With Prostate Cancer Who Have a PSA Recurrence Following Radical Prostatectomy Have Improved Survival With the Addition to Salvage Radiotherapy of a Long-term Course of Antiandrogen Therapy Compared With Salvage Radiotherapy Alone

Report of NRG Oncology/RTOG 9601, A Phase III Trial in Prostate Cancer: Anti-androgen Therapy (AAT) with Bicalutamide During and After Radiation Therapy (RT) in Patients Following Radical Prostatectomy (RP) with pT2-3pN0 Disease and an Elevated PSA

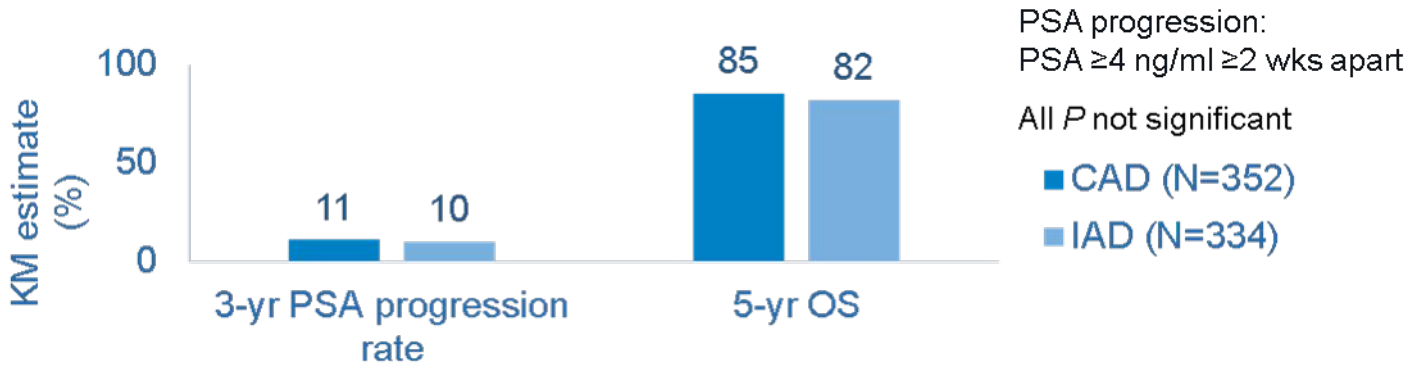


From 3/98 to 3/03, 761 eligible patients (median age 65) were randomized to RT + AAT (384) or RT + placebo (377). 248 patients (33%) were pT2pN0 and 513 patients (67%) were pT3pN0. 671 patients (88%) had a PSA nadir after RP of < 0.5 ng/ml. 649 patients (85%) had an entry PSA value of <1.6, 112 patients (15%) had an entry PSA of 1.6-4. Median follow up was 12.6 years. The actuarial overall survival at 10 years was 82% for RT plus AAT and 78% for RT + placebo and a hazard ratio of 0.75 (95% CI: 0.58-0.98) with a 1-sided p-value of 0.018 (2-sided p-value = 0.036). PSA progression was defined as a PSA > 0.5 ng/ml in patients whose treatment resulted in an undetectable PSA or, if not, when the PSA rose 0.3 ng/ml above the entry PSA. Freedom from PSA Progression (FFP) estimated at 10 years was 46% for RT + AAT and 30% for RT + placebo ($p < 0.001$). The 12-year incidences of PC central-reviewed deaths were 2.3% for RT + AAT and 7.5% for RT + placebo ($p<0.001$).The cumulative incidence of metastatic PC at 12 years was less in the RT + AAT arm, 14% (51 patients),vs 23% (83 patients) in the RT + placebo arm ($p<0.001$). Late Grade III and Grade IV toxicity were similar in the AAT and placebo arms. By category the combined Grade III plus Grade IV toxicities for RT +AAT and RT +placebo were: for bladder 7.0% vs 6.7%, bowel 2.7% vs 1.6%. Gynecomastia (mostly all Grades I and II) differed significantly by treatment arm, 70% and 11%. In the RT +AAT arm Grade III was the highest liver toxicity observed which occurred in <1% of patients.

Intermittent vs continuous ADT in relapsing or locally advanced PCa: results from the ICELAND study

Schulman C. J Urol 2015:193(4S):e938(abs.MP73-20)

- Multi-centre phase IIIb trial
- N=932 pts with relapsing M0 or locally advanced PCa
- N=701 pts with PSA ≤1 ng/ml after 6 mo of induction HT randomised to IAD or CAD with leuprorelin for 36 mo
- Median number of injections during randomised phase:
  - CAD: 12 injections vs IAD: 3 injections



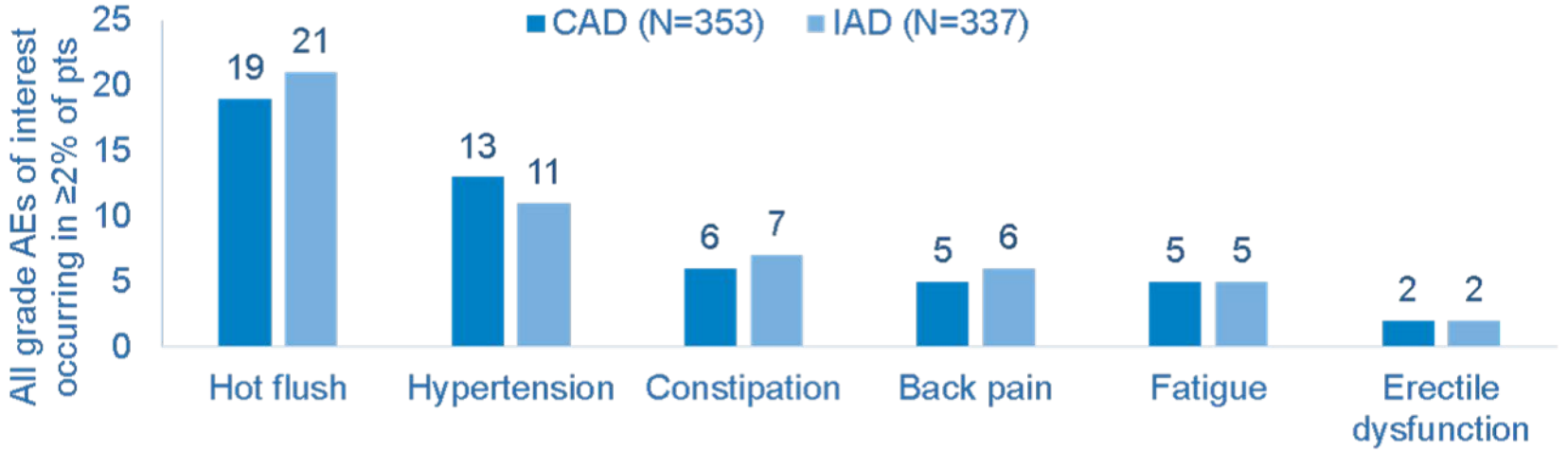
- No differences in mean PSA levels over time and QoL outcomes between both groups

Data from poster

Intermittent vs continuous ADT in relapsing or locally advanced PCa: results from the ICELAND study

Schulman C. J Urol 2015:193(4S):e938(abs.MP73-20)

	CAD (N=353)	IAD (N=337)
Grade ≥3 TEAE	28%	28%
Death	3%	5%
Discontinuation due to TEAE	5%	7%



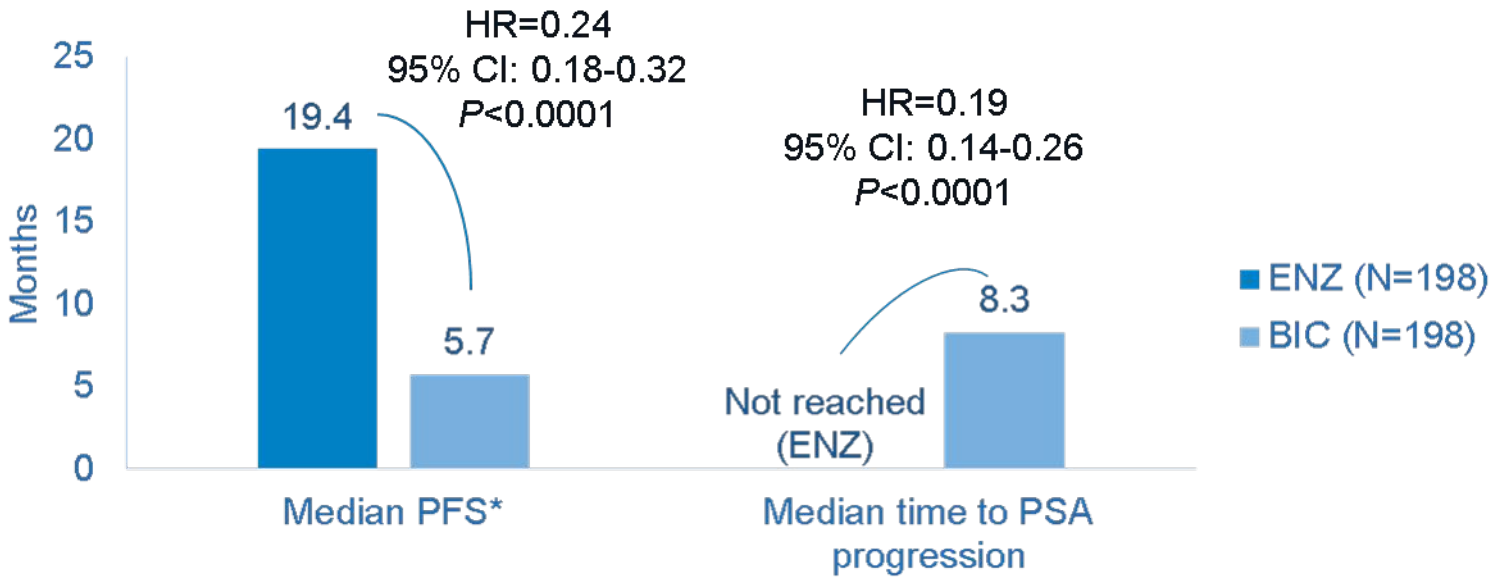
IAD and CAD seem to result in comparable efficacy, tolerability and QoL outcomes in pts with non-metastatic locally advanced or relapsing PCa

Data from poster

Enzalutamide (ENZ) vs bicalutamide (BIC) in M0 or M1CRPC: results from the STRIVE trial

Penson D. J Urol 2015:193(4S):e499(abs.PII-LBA10)

- Multi-centre phase II trial (2012-2014)
- N=396 pts with asymptomatic/mildly symptomatic progressive M0 or M1 CRPC randomised to ENZ (160 mg/d) or BIC (50 mg/d)



*primary endpoint, PSA progression or radiographic progression or death

Data from oral presentation

Enzalutamide (ENZ) vs bicalutamide (BIC) in M0 or M1CRPC: results from the phase II STRIVE trial

Penson D. J Urol 2015:193(4S):e499(abs.PII-LBA10)

» Results by baseline population (M0 and M1 CRPC subgroups)

	M0 CRPC			M1 CRPC		
	ENZ (N=70)	BIC (N=69)	HR (95% CI)	ENZ (N=128)	BIC (N=129)	HR (95% CI)
Median PFS (mo)	NR	8.6	0.24 (0.14-0.42)	16.5	5.5	0.24 (0.17-0.34)
Median rPFS* (mo)	NR	NR	0.24 (0.10-0.56)	NR	8.3	0.32 (0.21-0.50)
Median time to PSA progression (mo)	NR	11.1	0.18 (0.10-0.34)	24.9	5.7	0.19 (0.13-0.28)
PSA response ≥50% (%)	91	42	-	76	25	-

NR: not reached
*time from randomisation to first objective evidence of radiographic progression or death from any cause

Data from oral presentation

Enzalutamide (ENZ) vs bicalutamide (BIC) in M0 or M1CRPC: results from the phase II STRIVE trial

Penson D. J Urol 2015:193(4S):e499(abs.PII-LBA10)

Safety outcomes	ENZ (N=197)	BIC (N=198)
Serious AEs	29%	28%
Any grade ≥3 AEs	36%	36%
Cardiac grade ≥3 AEs	5%	4%
Seizure	0.5%	0%
Most common TEAE (≥10%)*	**ENZ (N=197)**	**BIC (N=198)**
Fatigue	38%	28%
Hot flushes	16%	10%
Fall	14%	8%
Dizziness	12%	7%
Hypertension	12%	5%

*more frequently reported in ENZ arm and ≥5% difference with BIC arm

ENZ for M0 or M1 CRPC seems more effective than BIC in terms of PFS, rPFS, time to PSA progression and PSA response rates

Data from oral presentation

Enzalutamide (ENZ) vs bicalutamide (BIC) in mCRPC: results from the TERRAIN trial

Shore N. J Urol 2015:193(4S):e496(abs.PII-LBA4)

- Double-blind, phase II trial
- N=375 chemo-naïve pts with asymptomatic or mildly symptomatic, progressive mCRPC randomised to ENZ (160 mg/d) or BIC (50 mg/d)

Efficacy	ENZ (N=184)	BIC (N=191)	HR	95% CI	*P*
Median PFS*	15.7 mo	5.8 mo	0.44	0.34-0.57	<0.001
Pts achieving ≥90% PSA decrease	56%	5%	-	-	-
Time to ≥90% PSA decrease from baseline	5.4 mo	Not reached	13.9	7.2-26.8	-
Pts with FACT-P total score response**	33%	23%	-	-	-
Time to FACT-P total score deterioration***	13.8 mo	8.5 mo	0.64	0.46-0.88	0.007

*primary endpoint defined as not experiencing radiographic progression, skeletal-related events, change to new anti-neoplastic therapy or death; **10-point increase from baseline; ***10-point decrease from baseline

Data from oral presentation

Enzalutamide (ENZ) vs bicalutamide (BIC) in mCRPC: results from the TERRAIN trial

Shore N. J Urol 2015:193(4S):e496(abs.PII-LBA4)

» Median duration on ENZ: 11.7 mo – on BIC: 5.8 mo

Grade ≥3 AE	ENZ (N=183)	BIC (N=189)
Fatigue	1.1%	1.1%
Back pain	2.7%	1.6%
Hot flushes	0	0
Nausea	0	0
Hypertension	7.1%	4.2%
Constipation	1.1%	0.5%
Diarrhoea	0	1.1%
Decreased weight	0.5%	0.5%
Pain in extremities	1.1%	0.5%
Arthralgia	1.1%	1.1%

ENZ seems associated with greater efficacy vs BIC in pts with asymptomatic or mildly symptomatic mCRPC

Data from oral presentation

Timing of ADT in PCa pts with biochemical relapse following ≥1 curative therapy: TOAD trial results

Duchesne GM. J Clin Oncol 2015:33(15S):270s(abs.5007)

- Australian, phase III RCT (VCOG, PR 01-03 / TROG, 03.06 trial); N=293 PCa pts with PSA relapse following ≥1 curative tx (N=261) or newly diagnosed asymptomatic PCa unsuitable for curative tx (N=32) enrolled (2004-2012)
- Randomisation:

Arm A: Delayed ADT
N=151
Triggers for tx: symptoms or
PSA DT <6 mo or
PSA DT <12 mo + PSA >10 ng/ml
Metastases or
PSA >60 ng/ml

Relapse group

Newly diagnosed

Arm B: Immediate ADT
N=142
Either continuous or intermittent

Original target accrual:
750 pts in total (not met)

- Median FU: 5 yr
- Delayed ADT arm: 35% pts started ADT before 2 yrs; 41% pts did not start ADT within study period
- ADT-related symptoms: 47% pts in delayed arm; 78% pts in immediate arm
- Immediate ADT improved OS by approximately 10% at 5 years (median not yet reached in both arms)

Data from oral presentation

Timing of ADT in PCa pts with biochemical relapse following ≥1 curative therapy: TOAD trial results

Duchesne GM. J Clin Oncol 2015:33(15S):270s(abs.5007)

» Efficacy outcomes (Cox regression analysis, immediate ADT vs delayed ADT)

	HR	95% CI	*P*
Overall survival (unadjusted)	0.55	0.30-1.00	0.05
Overall survival (adjusted)	0.54	0.27-1.06	0.07
PCa-specific survival	0.50	0.18-1.60	0.26
Time to first local progression	0.51	0.34-0.76	<0.01
Time to first metastatic disease	0.54	0.32-0.90	0.02
Time to castration resistance	1.20	0.94-1.53	0.14
Time to first PCa complication	0.78	0.54-1.11	0.16

Primary endpoint

Immediate ADT might improve OS in selected men with PSA relapse after ≥1 primary tx or in men ineligible to curative tx.
Longer FU is needed for clear conclusions

Data from oral presentation

NRG ONCOLOGY

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press release

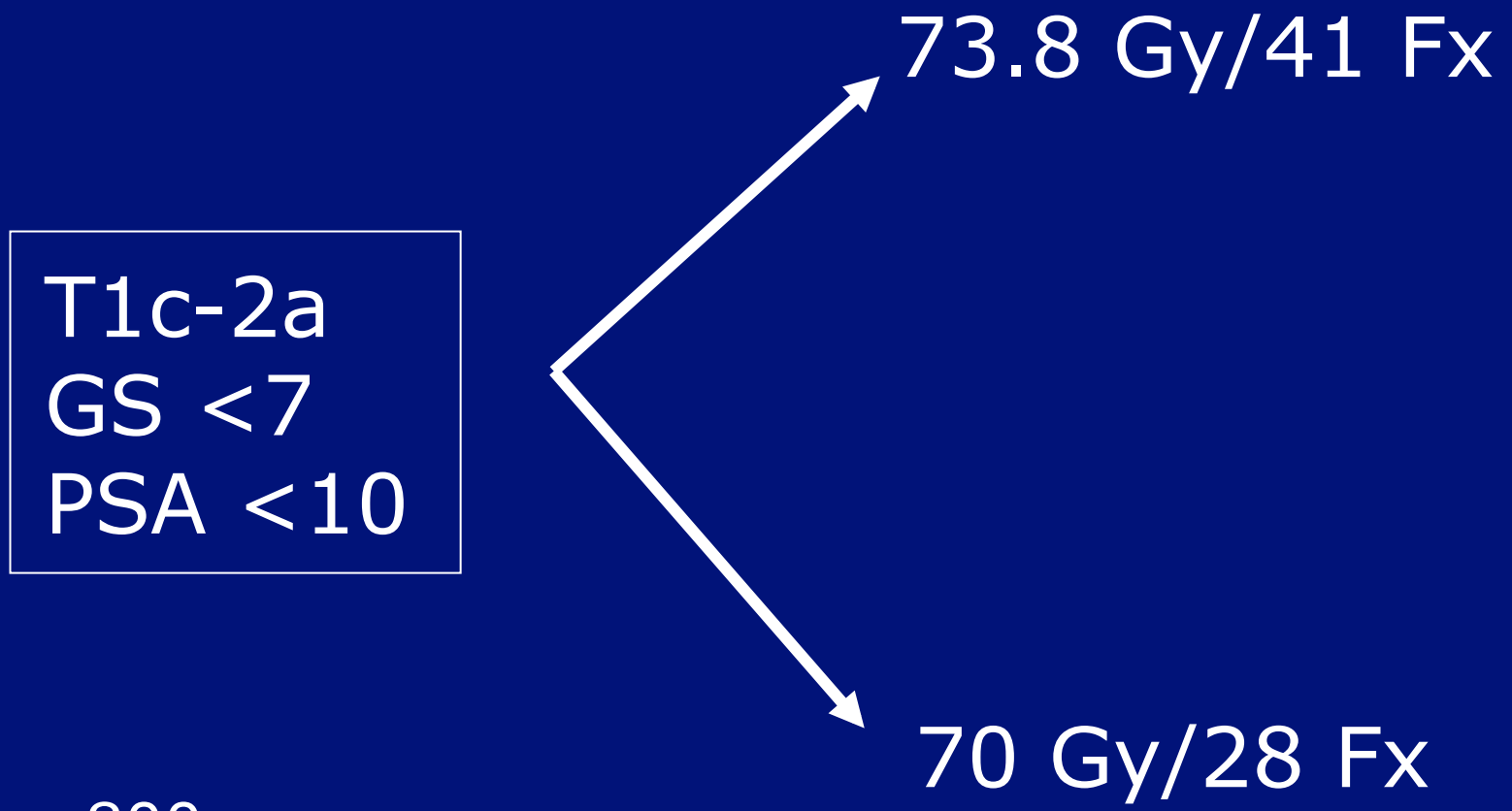
Four Penn Center • 1500 JFK Blvd, Suite 1020 • Philadelphia, PA 19103
Phone: 215-854-0770 • Fax: 215-854-0716

Under Embargo Until
Monday, October 19, 2015
2:57 PM Central Time

Contact: Nancy Fredericks • Office: 215.717.2769 • Mobile: 610.715.7707

The Treatment of Men With Low-Risk Prostate Cancer Using a Shortened Radiotherapy Schedule Has Similar Efficacy as Treatment With the Longer Conventional Radiotherapy Schedule

RTOG 0415 Schema



n=800
Endpoint is 5 Year BFFF
Non-inferiority margin 7% (Control 85%, Exp 78%)

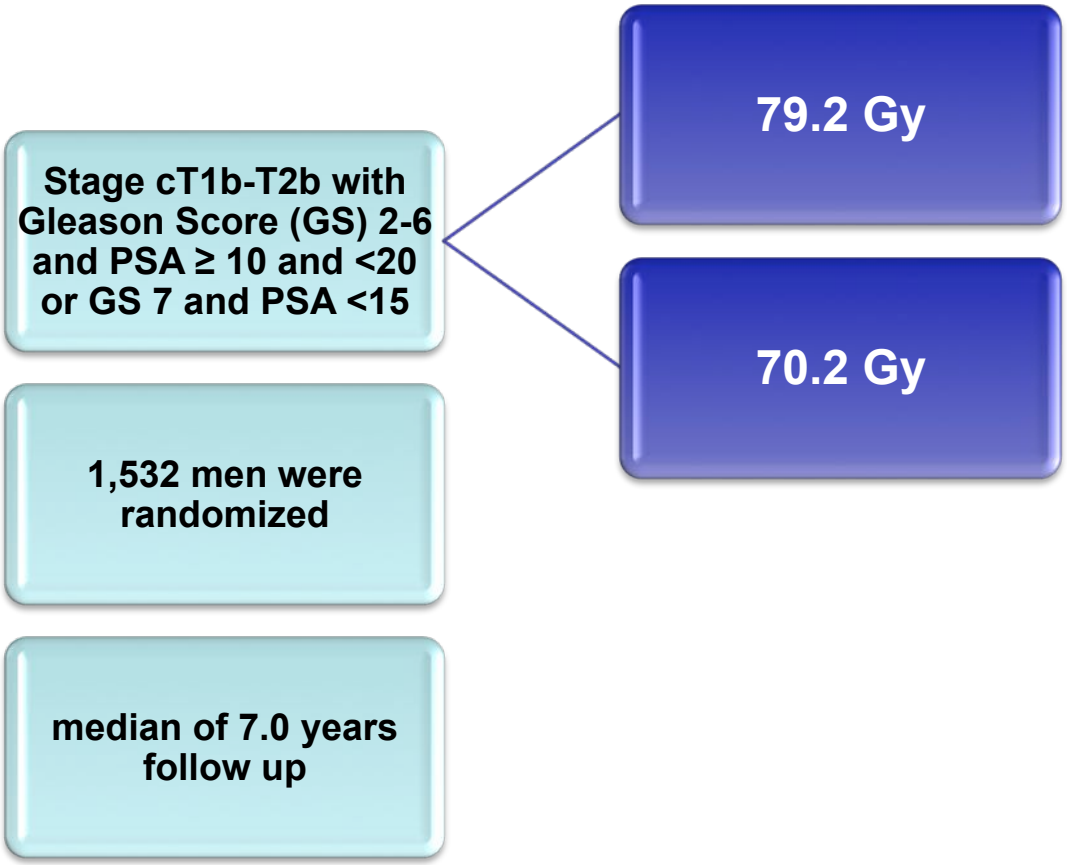
ASTRO 2015

American Society for Radiation Oncology (ASTRO) confirm that these patients can be treated with a shortened (or hypofractionated) course of radiotherapy (70 Gy of radiation delivered in 28 fractions over 5.6 weeks) and experience the same level of cancer control as those treated with a conventional course of radiotherapy (73.8 Gy of radiation delivered in 41 fractions over 8.2 weeks). Conducted by the Radiation Therapy Oncology Group (RTOG), now conducting research as NRG Oncology, RTOG 0415 analyzed data from 1,092 patients diagnosed with low-risk prostate cancer who were randomized to either the hypofractionated schedule arm (550 patients) or the conventional schedule arm (542 patients).

At a median patient follow-up of 5.8 years, 185 disease-free survival events (the primary end point) had occurred (86 in the hypofractionated schedule arm; 99 in the conventional schedule arm). Mild side effects (grade 2) were slightly higher in patients assigned to the hypofractionated arm, but more severe, late grade 3 gastrointestinal (GI) and genitourinary (GU) events were no different (GI, 4.1 percent [70 Gy] vs. 2.4 percent [73.8 Gy]; GU, 3.5 percent [70 Gy] vs. 2.1 percent [73.8 Gy], respectively).

Lee emphasizes that these toxicities are physician-reported results, which do not always reflect the patients' experiences accurately. To answer the important question regarding what patients thought about their treatment, in the future, the investigators will analyze patient-reported quality of life data collected during the study. Next steps also include the evaluation of economic data to assess resource savings.

ASCO GU 2015- RTOG 0126



Results: **5 and 10-yr rates of OS** are 88% and 67% with 79.2Gy and 89% and 66% with 70.2Gy (p=0.87; HR (95%CI)=0.98 (0.79,1.21).

BF rates at 5 and 10 yr are 25% (16%) and 30% (26%) with 79.2Gy and 40% (21%) and 45% (43%) with 70.2Gy (both p<0.0001).
LP rates at 5 and 10-yr are 1% and 4% with 79.2Gy and 2% and 8% with 70.2Gy (p=0.0059; HR (95%CI)=0.46 (0.27,0.81)).
DM rates at 5 and 10 yr are 2% and 5% with 79.2Gy and 3% and 8% with 70.2Gy (p=0.026; HR (95%CI)=0.57 (0.35,0.94)).
The high dose arm had lower rate of salvage therapy, 13.5% vs 21%, p=0.0002.
The 10 yr rates for time to late grade ≥ 2 GI/GU are 22%/15% with 79.2Gy and 16%/10% with 70.2Gy (p=0.0063/p=0.001).

Conclusions: **Despite significant improvement in BF, DM, and LP rates, dose escalation did not improve OS. Patients receiving high dose radiation experience more late toxicity.**

THE ASCO POST

PARP Inhibitor Olaparib Produces High Response Rate in Metastatic Prostate Cancer With DNA Repair Defects

By **Matthew Stenger**

Posted: 11/6/2015 3:09:05 PM
Last Updated: 11/6/2015 3:09:05 PM

In a phase II trial reported in *The New England Journal of Medicine*, Mateo et al found that the PARP inhibitor olaparib (Lynparza) produced a high response rate in patients with previously treated metastatic castration-resistant prostate cancer with tumors exhibiting defects in DNA repair genes.

Study Details

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genes.

Study Details

In the trial, 50 patients were treated with olaparib at 400 mg twice daily. All patients had received prior treatment with docetaxel, 98% with abiraterone (Zytiga) or enzalutamide (Xtandi), and 58% with cabazitaxel.

The primary endpoint was response rate, defined as objective response, reduction in prostate-specific antigen level of ≥ 50%, or confirmed reduction in circulating tumor cell count from ≥ 5 per 7.5 mL of blood to <5/7.5 mL. Targeted next-generation sequencing, exome and transcriptome analysis, and digital polymerase chain reaction testing were performed on tumor biopsies from all patients.

Response Rates

Overall, response was observed in 16 of 49 evaluable patients (response rate = 33%, 95% confidence interval = 20%–48%). Next-generation sequencing identified homozygous deletions, deleterious mutations, or both in DNA-repair genes, including *BRCA1/2*, *ATM*, Fanconi's anemia genes, and *CHEK2*, in 16 (335) of the 49. Of these, 14 (88%, $P < .001$ vs patients negative for biomarkers) had a response to olaparib, including each of seven patients with *BRCA2* loss (four with biallelic somatic loss, three with germline mutations) and four of five with *ATM* aberrations.

Median radiologic progression-free survival was 9.8 months in biomarker-positive patients vs 2.7 months in biomarker-negative patients ($P < .001$). Median overall survival was 13.8 vs 7.5 months ($P = .05$).

The most common grade 3 or 4 adverse events were anemia (20%) and fatigue (12%).

The investigators concluded: “Treatment with the PARP inhibitor olaparib in patients whose prostate cancers were no longer responding to standard treatments and who had defects in DNA repair genes led to a high response rate.”

Johann de Bono, MB, ChB, PhD, of the Institute of Cancer Research is the corresponding author for the *New England Journal of Medicine* article.

The study was supported by Cancer Research UK, AstraZeneca, and others. For full disclosures of the study authors, visit www.nejm.org.

The content in this post has not been reviewed by the American Society of Clinical Oncology, Inc. (ASCO®) and does not necessarily reflect the ideas and opinions of ASCO®.

Grazie per l'attenzione!