POP-ART, CHHiP and STAMPEDE – Where do we stand in Prostate Radiation

Dr. Gagan Saini, Delhi

Cancer Prostate – Heterogenous disease

- On the same day you can advise one patient for Watchful Waiting and discuss with another for Chemohormonal therapy!

Lymph node involvement risk

Partin nomograms

TABLE 42C.1. *Prediction of lymph node involvement*

Gleason score	PSA (ng/mL)																			
	0–4 Clinical stage					4.1–10.0 Clinical stage					10.1–20.0 Clinical stage					>20 Clinical stage				
	T1b	T1c	T2a	T2b	T2c	T1b	T1c	T2a	T2b	T2c	T1b	T1c	T2a	T2b	T2c	T1b	T1c	T2a	T2b	T2c
2–4	0	0	0	0	0	1	0	0	1	1	2	0	1	1	1	4	1	1	3	—
5	1	0	0	1	1	2	0	1	2	2	5	1	2	4	4	10	3	3	7	7
6	2	0	1	2	2	5	1	2	4	4	13	3	4	10	10	23	7	8	16	17
7	6	1	2	5	5	12	3	4	9	9	24	8	9	17	18	—	14	14	25	25
8–10	14	4	5	10	10	23	8	9	16	17	40	16	17	29	29	51	24	24	36	35

PSA, prostate-specific antigen.
Note: Numbers represent probability (%); dash represents lack of sufficient data to calculate probability.
Modified from Partin AW, Kattan MW, Subong EN, et al. Combination of prostate-specific antigen, clinical stage and Gleason score to predict pathological stage in men with localized prostate cancer. *JAMA* 1997;277:1445.

- < 15% low
- 15-35% intermediate
- >35% high

Partin 1997, Roach 1993

TABLE 4. *Site of positive LNs detected by radio guided surgery*

Lymphadenectomy Region	No. Node Pos (%)
Internal iliac artery	4[illegible] (23.7)
External iliac vein	3[illegible] (16.9)
Obturator fossa	32 (15.5)
Internal iliac artery + external iliac vein	1[illegible] (9.2)
Internal iliac artery, external iliac vein + obturator fossa	1[illegible] (9.2)
Internal iliac artery + obturator fossa	13 (6.3)
Internal iliac artery + other	15 (7.3)
External iliac vein + obturator fossa	[illegible] (4.4)
Other (presacral, pararectal, paravesical +/or other combinations)	16 (7.7)

Weckerman et al. J Urol 2007

original reports

Prostate-Only Versus Whole-Pelvic Radiation Therapy in High-Risk and Very High-Risk Prostate Cancer (POP-RT): Outcomes From Phase III Randomized Controlled Trial

Vedang Murthy, MD[1]; Priyamvada Maitre, MD[1]; Sadhana Kannan, MSc[2]; Gitanjali Panigrahi, MSc[1]; Rahul Krishnatry, MD[1]; Ganesh Bakshi, MCh[3]; Gagan Prakash, DNB[3]; Mahendra Pal, DNB[3]; Santosh Menon, MD[4]; Reena Phurailatpam, MSc[5]; Smruti Mokal, MSc[2]; Dipika Chaurasiya, BSc[1]; Palak Popat, DNB[6]; Nilesh Sable, MD[6]; Archi Agarwal, DNB[7]; Venkatesh Rangarajan, DNB[7]; Amit Joshi, DM[8]; Vanita Noronha, DM[8]; Kumar Prabhash, DM[8]; and Umesh Mahantshetty, MD[1]

- Randomized trial comparing prophylactic whole-pelvic nodal radiotherapy (WPRT) to prostate-only radiotherapy (PORT) in high-risk prostate cancer.

Methods

- This phase III, single center, randomized controlled trial enrolled eligible patients undergoing radical radiotherapy
  - Node-negative prostate adenocarcinoma
  - Estimated nodal risk of 20%.
- Randomization was 1:1 to PORT (68 Gy/25# to prostate) or whole-pelvic radiotherapy (WPRT, 68 Gy/25# to prostate, 50 Gy/25# to pelvic nodes, including common iliac)
- computerized stratified block randomization
  - Stratified by Gleason score
  - Type of androgen deprivation
  - PSA at diagnosis
  - Prior transurethral resection of the prostate

Methods

- All patients received image-guided, intensity-modulated radiotherapy and minimum 2 years of androgen deprivation therapy.
- The primary end point was 5-year biochemical failure-free survival (BFFS), and secondary end points were disease-free survival (DFS) and overall survival (OS).

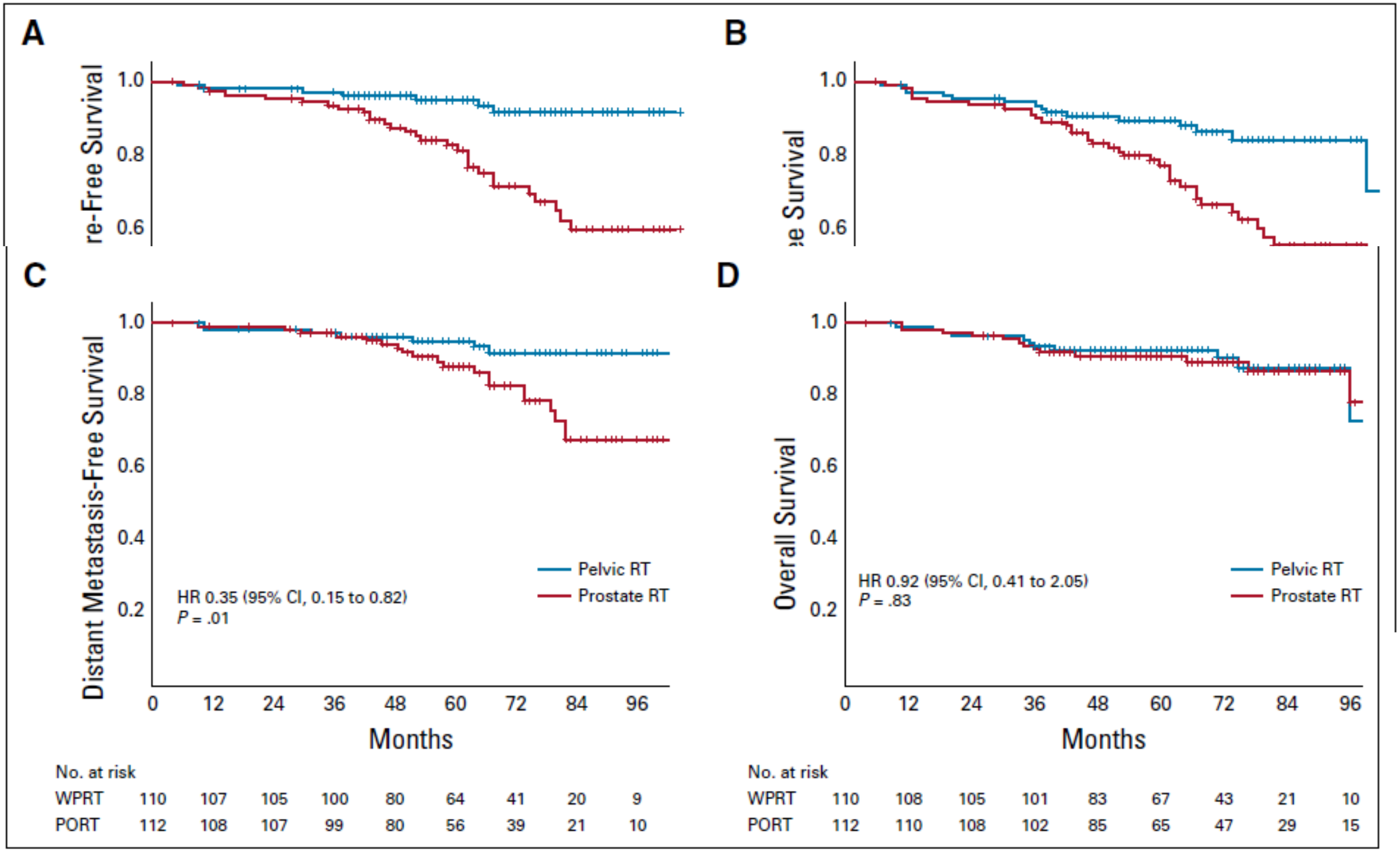
Methods

- Magnetic resonance imaging for prostate, contrast-enhanced computed tomography (CT) scan of abdomen and pelvis, technetium-99 bone scan, or positronemission tomography (PET) CT with fluoride-18 or gallium- 68 prostate-specific membrane antigen (PSMA) scans
- Key eligibility criterion was
  - the risk of pelvic node involvement of at least 20%, estimated using Roach formula
  - clinical stage T1-T3a with Gleason 8-10 and any PSA
  - Gleason 7 with PSA. 15 ng/mL
  - Gleason 6 with PSA. 30 ng/mL
  - Stage T3b-T4a with any GS and any PSA were eligible for inclusion.
  - estimated life expectancy of at least 5 years
  - ability to receive long-term ADT or undergo surgical castration
- All patients signed informed consent before being enrolled in the trial.

TABLE 1. Baseline Characteristics

Characteristic	All Patients (N = 222), N (%)	PORT (n = 112), N (%)	WPRT (n = 110), N (%)
Median age, years	66	66	66
Median PSA, ng/mL	28.2	27.4	29.9
Nodal risk, %[a]			
≤ 40%	119 (53.6)	60 (53.6)	59 (53.6)
> 40%	103 (46.4)	52 (46.4)	51 (46.4)
Gleason grade group			
1	22 (9.9)	11 (9.8)	11 (10)
2	38 (17.1)	20 (17.9)	18 (16.4)
3	53 (23.9)	25 (22.3)	28 (25.5)
4	53 (23.9)	26 (23.2)	27 (24.5)
5	56 (25.3)	30 (26.8)	26 (23.6)
ADT			
Orchiectomy	42 (18.9)	26 (23.2)	16 (14.5)
Medical	180 (81.1)	86 (76.8)	94 (85.5)
History of TURP			
Yes	60 (27)	30 (26.8)	30 (27.3)
No	162 (73)	82 (73.2)	80 (72.7)
Tumor stage			
T1	2 (0.9)	1 (0.9)	1 (0.9)
T2	46 (20.7)	19 (17)	27 (24.5)
T3a	70 (31.5)	38 (33.9)	32 (29.1)
T3b	86 (38.7)	44 (39.3)	42 (38.2)
T4	18 (8.1)	10 (8.9)	8 (7.3)

Abbreviations: ADT, androgen deprivation therapy; PORT, prostate-only radiotherapy; PSA, prostate-specific antigen; TURP, transurethral resection of prostate; WPRT, whole-pelvic radiotherapy.


A
re-Free Survival
1.0
0.8
0.6
B
e Survival
1.0
0.8
0.6
C
Distant Metastasis-Free Survival
1.0
0.8
0.6
0.4
0.2
HR 0.35 (95% CI, 0.15 to 0.82)
P = .01
Pelvic RT
Prostate RT
0 12 24 36 48 60 72 84 96
Months
No. at risk
WPRT 110 107 105 100 80 64 41 20 9
PORT 112 108 107 99 80 56 39 21 10
D
Overall Survival
1.0
0.8
0.6
0.4
0.2
HR 0.92 (95% CI, 0.41 to 2.05)
P = .83
Pelvic RT
Prostate RT
0 12 24 36 48 60 72 84 96
Months
No. at risk
WPRT 110 108 105 101 83 67 43 21 10
PORT 112 110 108 102 85 65 47 29 15

Re

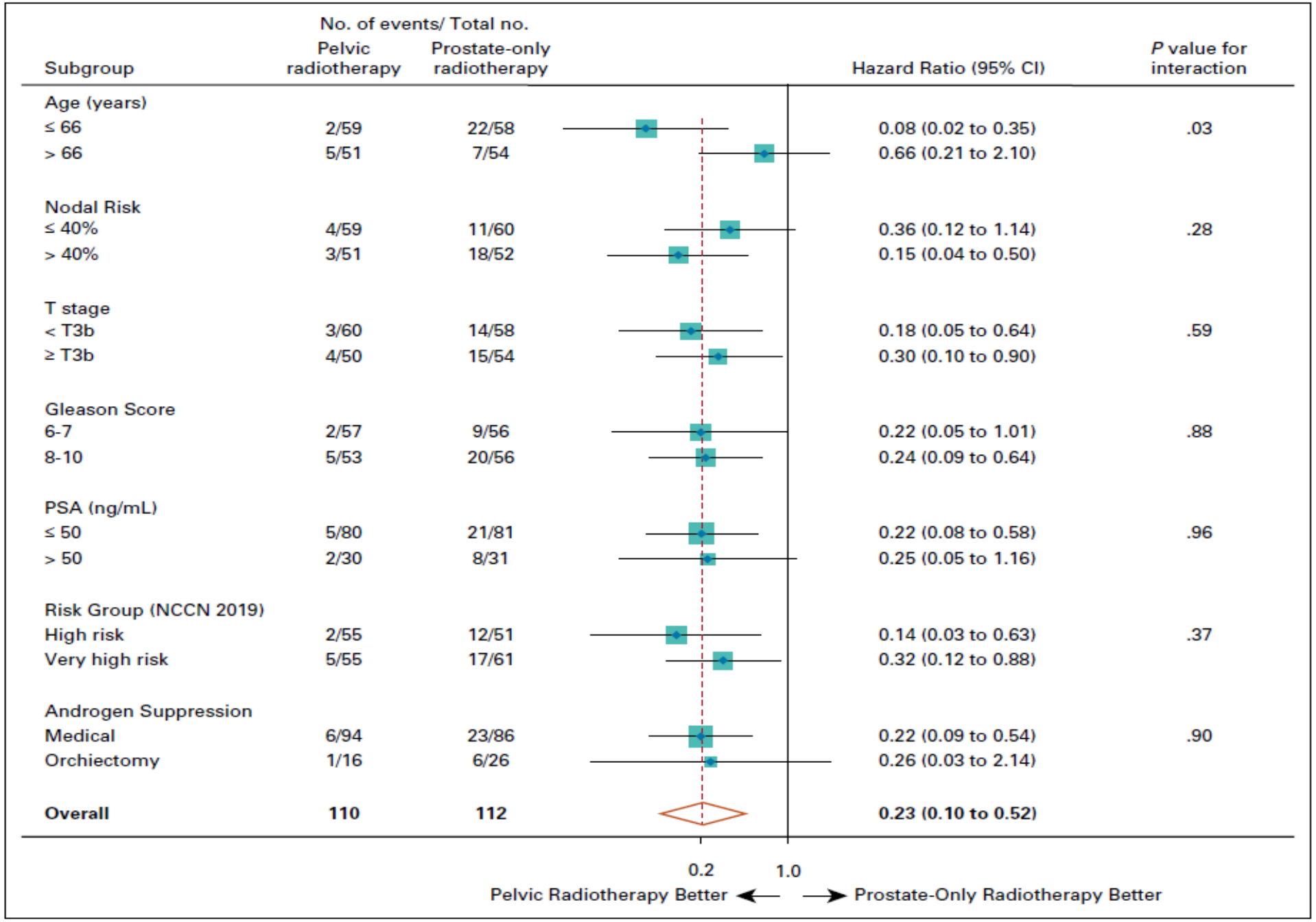


FIG 3. Subgroup analysis for biochemical failure-free survival. NCCN, National Comprehensive Care Network; PSA, prostate-specific antigen.

Results - toxicity

TABLE 2. Cumulative Late Toxicity (RTOG)

RTOG Grade	All Patients (N = 222), N (%)	PORT (n = 112), N (%)	WPRT (n = 110), N (%)	*P* (grade 0-1 *v* grade ≥ II)
GU				
0	85 (38.3)	45 (40.2)	40 (36.4)	.02
I	105 (47.3)	57 (50.9)	48 (43.6)	
II	28 (12.6)	8 (7.1)	20 (18.2)	
III	4 (1.8)	2 (1.8)	2 (1.8)	
GI				
0	138 (62.2)	74 (66.1)	64 (58.2)	.28
I	70 (31.5)	33 (29.5)	37 (33.6)	
II	12 (5.4)	5 (4.5)	7 (6.4)	
III	2 (0.9)	0 (0)	2 (1.8)	

Abbreviations: GU, genitourinary; PORT, prostate-only radiotherapy; RTOG, Radiation Therapy Oncology Group; WPRT, whole-pelvic radiotherapy.

Table 2 Unadjusted and Adjusted Hazard Ratios for All-Cause Mortality for Each Patient and Treatment Factor

	n	Deaths	Univariate			Multivariate		
			HR	95% CI	*P*	AHR	95% CI	*P*
Age, Years	3709	561	1.06	1.05-1.08	<.001	1.06	1.04-1.08	<.001
PSA (logarithm), ng/mL	3709	561	1.08	0.96-1.22	.21	1.08	0.95-1.22	.24
Gleason Score								
6	1787	257	ref	—	—	—	—	—
7	1422	190	1.15	0.95-1.39	.14	1.14	0.94-1.37	.20
8-10	500	114	1.77	1.42-2.20	<.001	1.63	1.30-2.05	<.001
2014 AJCC Tumor Category								
1	1968	261	ref	—	—	—	—	—
2	1663	271	0.94	0.79-1.12	.47	0.92	0.77-1.09	.31
3	78	29	1.00	0.67-1.49	.99	0.95	0.64-1.42	.80
Presence of Comorbidity	989 versus 2720	173 versus 388	1.25	1.04-1.50	.01	1.18	0.99-1.42	.07
Test of Interaction								
ADT versus no ADT	2723 versus 986	429 versus 132	0.84	0.67-1.05	.13	0.71	0.57-0.90	.004
RT treatment volume (WPRT vs. PSV RT)	622 versus 3087	142 versus 419	0.65	0.43-0.99	.046	0.58	0.38-0.89	.012
ADT × RT volume	3709	561	1.43	0.89-2.28	.14	1.61	1.00-2.58	.048
Additional Comparisons								
WPRT versus PSV RT	136 versus 850	31 versus 101	0.65	0.43-0.99	.046	0.58	0.38-0.89	.012
PSV RT with ADT versus PSV RT	2237 versus 850	318 versus 101	0.84	0.67-1.05	.13	0.71	0.57-0.90	.004
WPRT with ADT versus PSV RT	486 versus 850	111 versus 101	0.78	0.60-1.03	.08	0.67	0.50-0.88	.005
WPRT with ADT versus WPRT	486 versus 136	111 versus 31	1.20	0.80-1.81	.38	1.15	0.76-1.74	.51
WPRT with ADT versus PSV RT + ADT	486 versus 2237	111 versus 318	0.93	0.75-1.16	.52	0.93	0.75-1.16	.53
WPRT versus PSV RT with ADT	136 versus 2237	31 versus 318	0.78	0.53-1.14	.19	0.81	0.55-1.19	.29

Abbreviations: ADT = androgen deprivation therapy; AHR = adjusted hazard ratio; AJCC = American Joint Commission on Cancer; HR = hazard ratio; PSA = prostate-specific antigen; PSV RT = prostate and seminal vesicle radiotherapy; ref = reference; RT = radiotherapy; WPRT = whole-pelvis radiotherapy.

Phase II
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By M. Roach II , R.K. Valicenti,

1.WP RT N & CHT

2.PO RT N & CHT

3.WP RT AHT

4.PO RT AHT

Risk of LN involvement of more than 15%

JCO 2003

Int. J. Radiation Oncology Biol. Phys., Vol. 69, No. 3, pp. 646–655, 2007

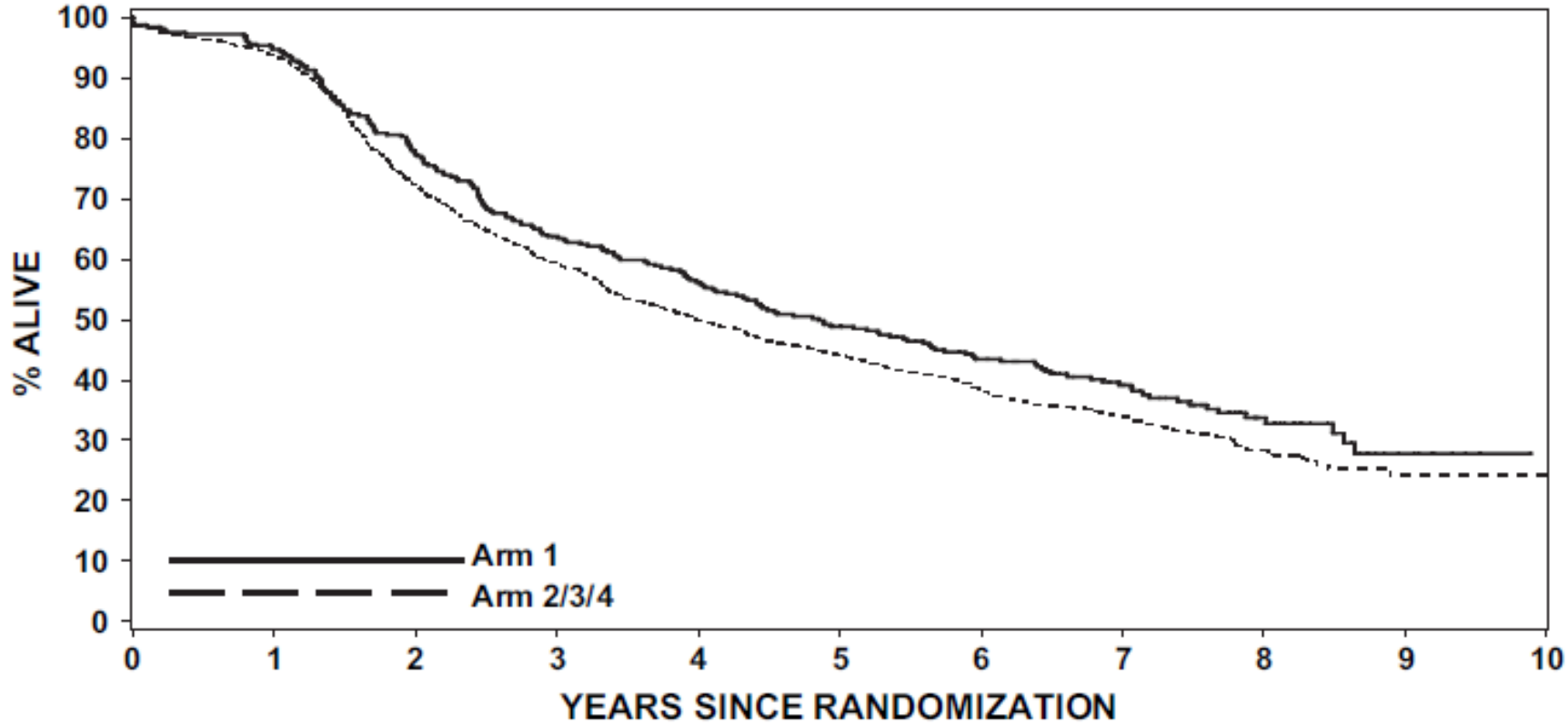


Fig. 7. Progression-free survival using protocol definition of biochemical failure for Arm 1 vs. Arms 2–4.

International Journal of Radiation Oncology biology • physics

www.redjournal.org

Clinical Investigation

Is There a Role for Pelvic Irradiation in Localized Prostate Adenocarcinoma? Update of the Long-Term Survival Results of the GETUG-01 Randomized Study

Pascal Pommier, MD, PhD,* Sylvie Chabaud, PhD,† Jean-Leon Lagrange, MD, PhD,‡ Pierre Richaud, MD,§ Elisabeth Le Prise, MD,‖ Jean-Philippe Wagner, MD,¶ David Azria, MD, PhD,# Veronique Beckendorf, MD,** Jean-Philippe Suchaud, MD,†† Valerie Bernier, MD,‡‡ David Perol, MD,† and Christian Carrie, MD, PhD*

IJROBP 2015

Table 1 Patient and treatment characteristics

Characteristic	Pelvis + prostate (n=225)	Prostate only (n=221)	*P*
Prognostic group (stratification), n (%)			.727
Low-risk	48 (21.3)	44 (19.9)	
High-risk	177 (78.7)	177 (80.1)	
Age at diagnosis (y)			.812
Mean (SD)	68.8 (5.0)	68.9 (4.9)	
Median (range)	69.8 (52.6-75.6)	69.9 (49.2-75.8)	
Stage T, n (%)			.648
1	56 (25.1)	48 (21.9)	
2	113 (50.7)	111 (50.7)	
3	54 (24.2)	60 (27.4)	
PSA (μg/L)			.359
Mean (SD)	16.3 (16.5)	15.0 (14.7)	
Median (range)	12.0 (0.2-144)	11.0 (1.3-150)	
Gleason score (GS), n (%)			.432
≤6	114 (50.9)	106 (48.6)	
7	82 (36.6)	91 (41.7)	
8-10	28 (12.5)	21 (9.6)	
RT dose to prostate/pelvis (Gy)			
Mean (SD)	22.32 (1.8)/46.14 (1.1)	68.08 (5.8)	
Median (range)	22 (18-28)/46 (44-50)	68.4 (4-76)	
RT dose to pelvis + prostate (Gy)			.369
Mean (SD)	68.45 (2.0)	68.08 (5.8)	
Median (range)	68.4 (63;74)	68.4 (4;76)	
RT dose to the prostate* (Gy)			.286
<70	138 (61.6)	121 (56.3)	
≥70	86 (38.4)	94 (43.7)	
LNI risk† (%)			.364
<15	115 (51.3)	124 (56.8)	
15-35	83 (37.1)	76 (34.9)	
>35	26 (11.6)	18 (8.3)	
Concomitant HT in patients stratified as high risk	97 (57.5)	102 (59.7)	.261

Abbreviations: HT = hormonal therapy; LNI = lymph node involvement; PSA = prostate-specific antigen; RT = radiation therapy; SD = standard deviation.

* Total dose.

† LNI risk = risk of LNI using the Roach formula: 2/3 PSA + [(GS − 6) × 10].

260

Radiation Therapy Oncology Group (RTOG) 9413: A Randomized Trial Comparing Whole Pelvic Radiation Therapy (WPRT) to Prostate Only (PORT) and Neoadjuvant Hormonal Therapy (NHT) to Adjuvant Hormonal Therapy (AHT)

M. Roach,[1] D. Hunt,[2] C.A. Lawton,[3] I. Hsu,[1] R.A. Lustig,[4] M. Seider,[5]
J.U. Christopher,[6] C.R. Thomas,[7] W.U. Shipley,[8] and H. Sandler[9]; [1]UCSF

Conclusions: RTOG 9413 continues to demonstrate that NHT+WPRT improves BF compared to NHT+PORT supporting the rationale for RTOG 0924. Studies are underway to determine whether misclassification bias or other causes explain the excess deaths from SCs observed in the post hoc analysis.

General Hospital, Boston, MA; [9]Samuel Oschin Comprehensive Cancer Center, Cedars-Sinai Medical Center, Los Angeles, CA

ASTRO 2013

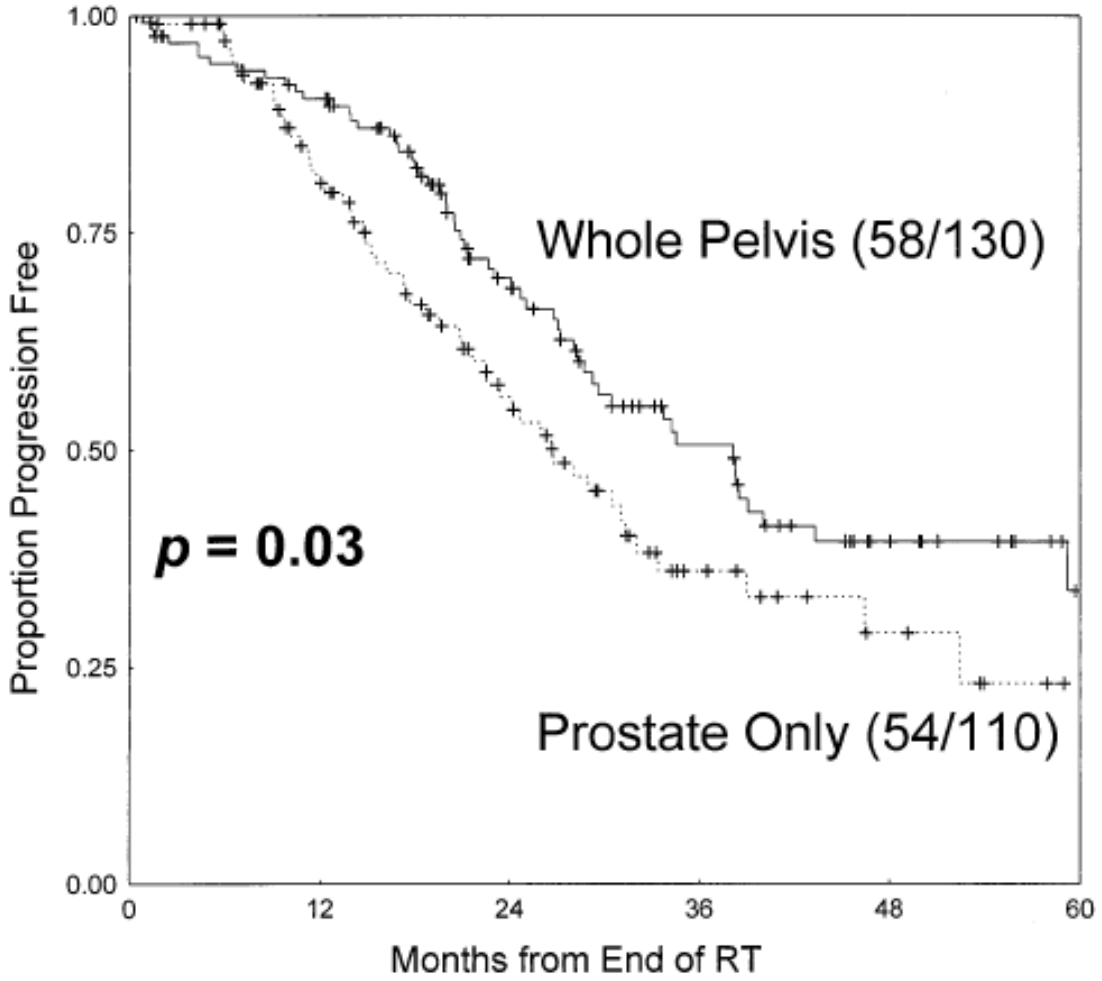


Fig. 3. Kaplan–Meier product limit progression-free survival curves for high-risk (2/3 iPSA + 10[(GS − 6) + (TG − 1.5)] ≥ 15) prostate cancer patients receiving whole pelvic irradiation followed by prostate-only boost or focal prostatic irradiation alone.

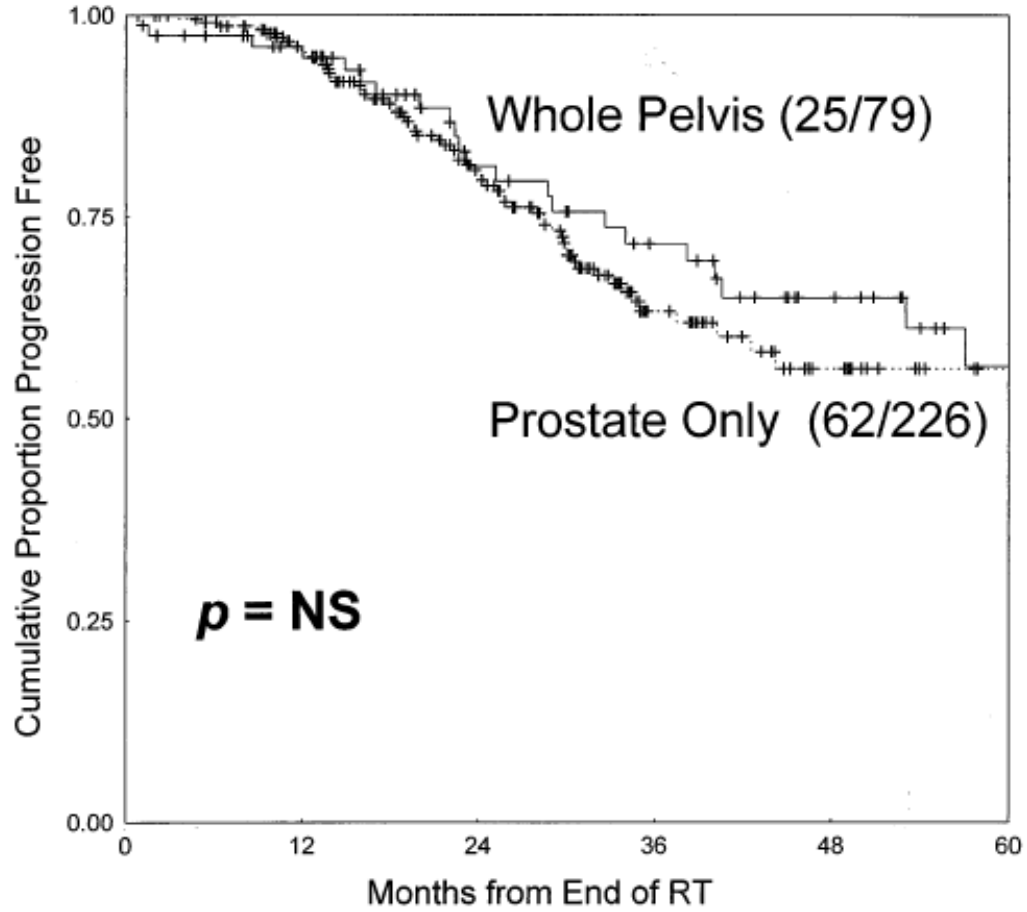


Fig. 4. Kaplan–Meier product limit progression-free survival curves for low-risk (2/3 iPSA + 10(GS − 6) < 15) prostate cancer patients receiving whole pelvic irradiation followed by prostate-only boost or focal prostatic irradiation.

Imp

- Lack of optimal patient selection,
- radiotherapy technique
- volume and dose
- inadequate duration of ADT for high-risk disease

- In conclusion, prophylactic WPRT using a contemporary dose and technique along with long-term ADT for high-risk and very high-risk prostate cancer resulted in a large and significantly improved BFFS and DFS as compared with PORT,
- Did not impact OS.
- Until the long-term outcomes of the ongoing trials are reported, prophylactic pelvic radiotherapy should be routinely considered for these patients

Conventional versus hypofractionated high-dose intensity-modulated radiotherapy for prostate cancer: 5-year outcomes of the randomised, non-inferiority, phase 3 CHHiP trial

David Dearnaley, Isabel Syndikus, Helen Mossop, Vincent Khoo, Alison Birtle, David Bloomfield, John Graham, Peter Kirkbride, John Logue, Zafar Malik, Julian Money-Kyrle, Joe M O'Sullivan, Miguel Panades, Chris Parker, Helen Patterson, Christopher Scrase, John Staffurth, Andrew Stockdale, Jean Tremlett, Margaret Bidmead, Helen Mayles, Olivia Naismith, Chris South, Annie Gao, Clare Cruickshank, Shama Hassan, Julia Pugh, Clare Griffin, Emma Hall, on behalf of the CHHiP Investigators*

Summary

Background Prostate cancer might have high radiation-fraction sensitivity that would give a therapeutic advantage to hypofractionated treatment. We present a pre-planned analysis of the efficacy and side-effects of a randomised trial comparing conventional and hypofractionated radiotherapy after 5 years follow-up.

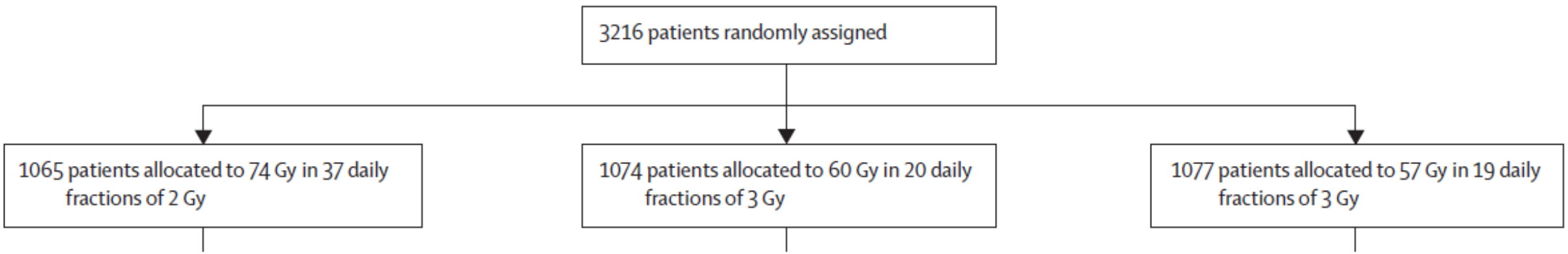
Lancet Oncol 2016; 17: 1047–60

Published Online
June 20, 2016

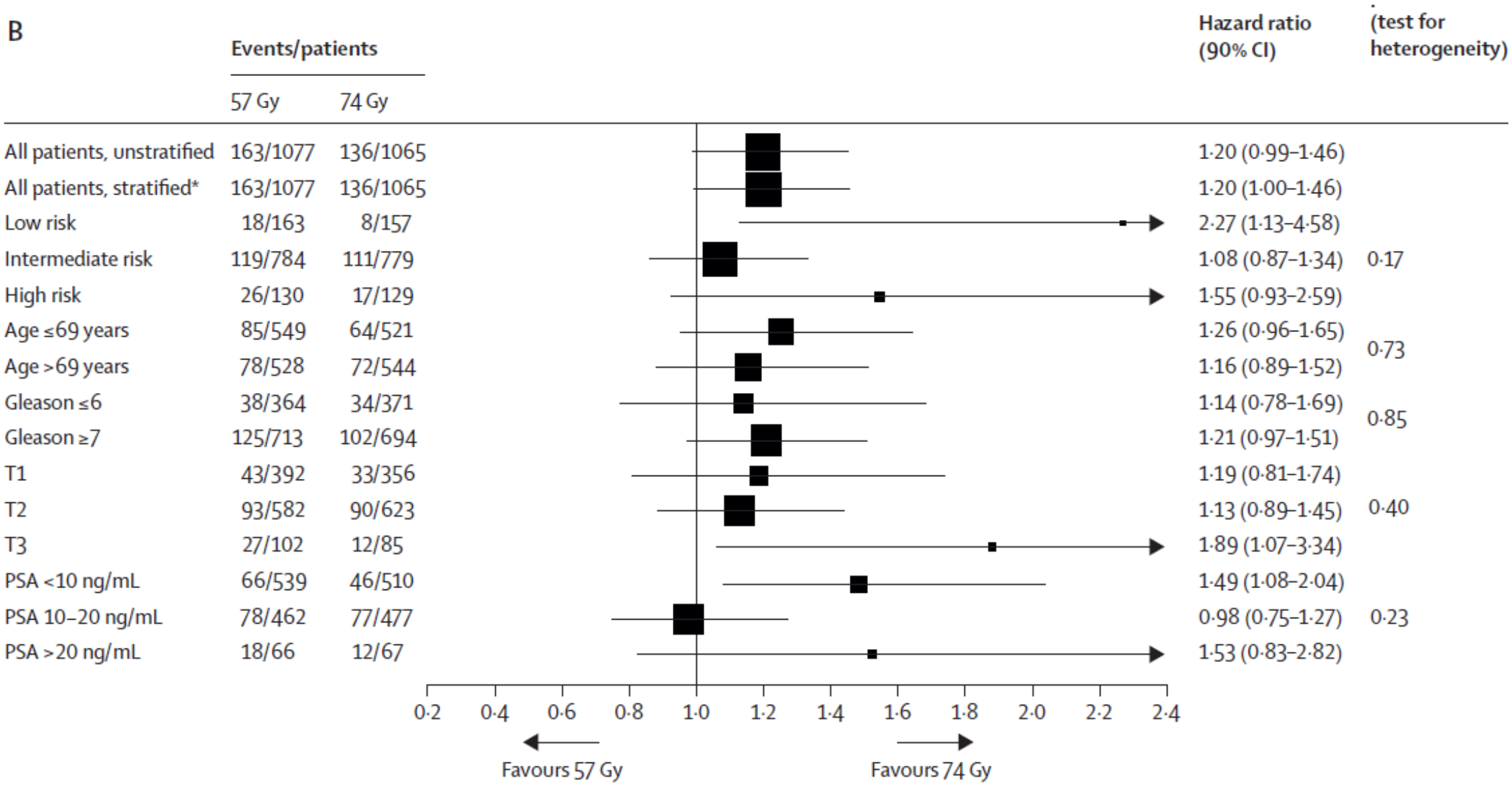
Methods

- CHHiP is a randomised, phase 3, non-inferiority trial
- localised prostate cancer (pT1b–T3aN0M0)
- Patients were randomly assigned (1:1:1) to conventional (74 Gy delivered in 37 fractions over 7·4 weeks) or one of two hypofractionated schedules (60 Gy in 20 fractions over 4 weeks or 57 Gy in 19 fractions over 3·8 weeks)
- all intensity-modulated techniques
- Most patients were given radiotherapy with 3–6 months of neoadjuvant and concurrent androgen suppression.
- The primary endpoint was time to biochemical or clinical failure; the critical hazard ratio (HR) for non-inferiority was 1·208.

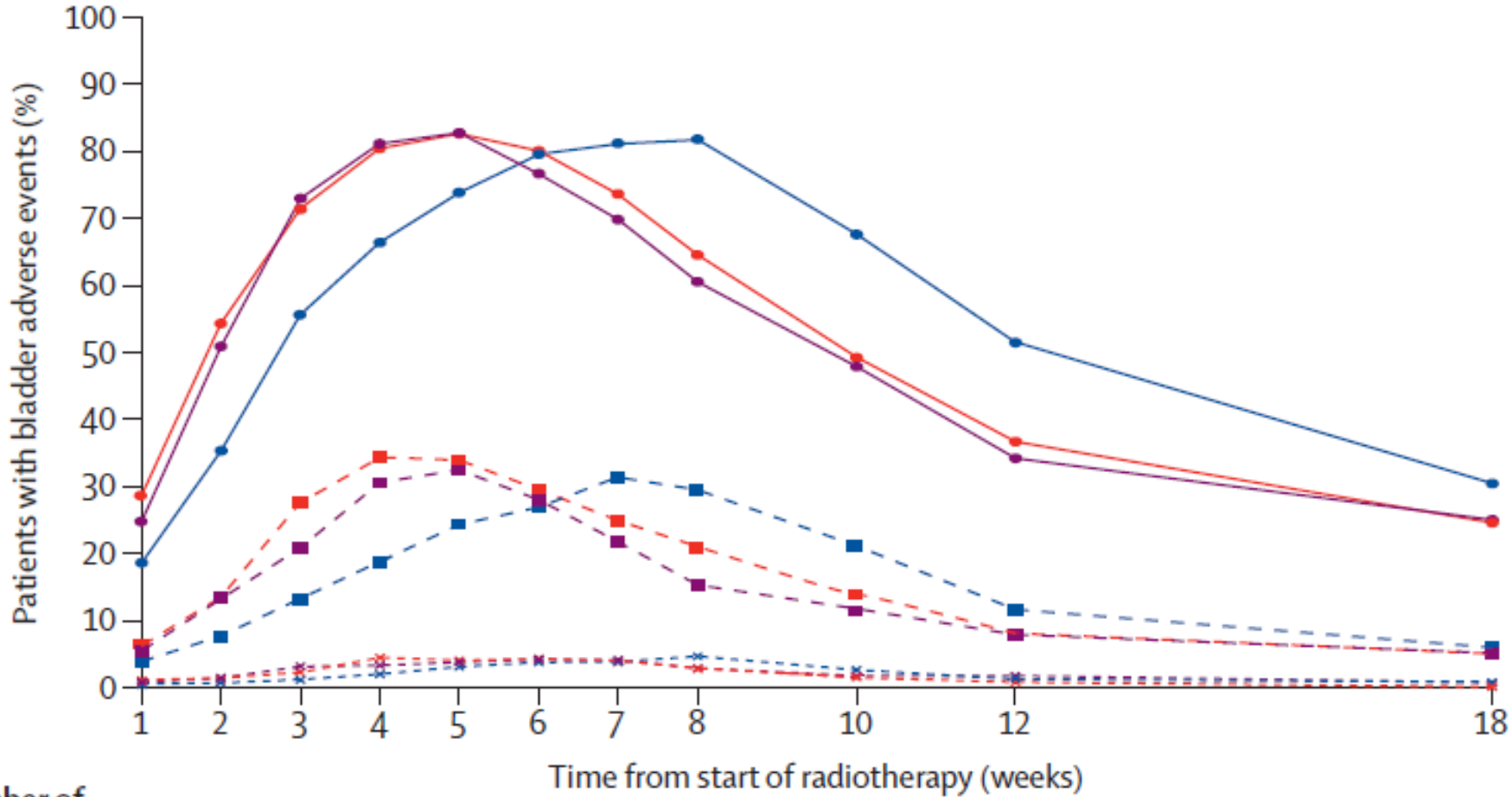
- Eligibility
  - PSA concentration of less than 40 ng/mL
  - Risk of lymph node involvement less than 30%
  - risk of seminal vesicle involvement less than 30%
- Patients were ineligible
  - if they had both T3 tumours and a Gleason score of 8 or higher
  - life expectancy of less than 10 years.


3216 patients randomly assigned
1065 patients allocated to 74 Gy in 37 daily fractions of 2 Gy
1074 patients allocated to 60 Gy in 20 daily fractions of 3 Gy
1077 patients allocated to 57 Gy in 19 daily fractions of 3 Gy

B


Events/patients
57 Gy
74 Gy
Hazard ratio (90% CI)
(test for heterogeneity)
All patients, unstratified 163/1077 136/1065 1·20 (0·99–1·46)
All patients, stratified* 163/1077 136/1065 1·20 (1·00–1·46)
Low risk 18/163 8/157 2·27 (1·13–4·58)
Intermediate risk 119/784 111/779 1·08 (0·87–1·34) 0·17
High risk 26/130 17/129 1·55 (0·93–2·59)
Age ≤69 years 85/549 64/521 1·26 (0·96–1·65) 0·73
Age >69 years 78/528 72/544 1·16 (0·89–1·52)
Gleason ≤6 38/364 34/371 1·14 (0·78–1·69) 0·85
Gleason ≥7 125/713 102/694 1·21 (0·97–1·51)
T1 43/392 33/356 1·19 (0·81–1·74)
T2 93/582 90/623 1·13 (0·89–1·45) 0·40
T3 27/102 12/85 1·89 (1·07–3·34)
PSA <10 ng/mL 66/539 46/510 1·49 (1·08–2·04)
PSA 10–20 ng/mL 78/462 77/477 0·98 (0·75–1·27) 0·23
PSA >20 ng/mL 18/66 12/67 1·53 (0·83–2·82)
0·2 0·4 0·6 0·8 1·0 1·2 1·4 1·6 1·8 2·0 2·2 2·4
Favours 57 Gy
Favours 74 Gy

Toxicity



Numl
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Number of patients											
74 Gy	703	700	698	699	694	689	691	666	685	638	682
60 Gy	709	701	710	696	668	673	662	659	695	643	696
57 Gy	702	708	704	692	665	670	654	660	688	633	679

Conclusion

- Hypofractionated radiotherapy using 60 Gy in 20 fractions is non-inferior to conventional fractionation using 74 Gy in 37 fractions and is recommended as a new standard of care for external-beam radiotherapy of localized prostate cancer.

Journal of Clinical Oncology®
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Meeting Abstract | 2020 Genitourinary Cancers Symposium

PROSTATE CANCER - LOCALIZED

Eight-year outcomes of a phase III randomized trial of conventional versus hypofractionated high-dose intensity modulated radiotherapy for prostate cancer (CRUK/06/016): Update from the CHHiP Trial.

David P. Dearnaley, Clare Griffin, Isabel Syndikus, Vincent Khoo, Alison Jane Birtle, Ananya Choudhury, ...

- pre-planned analysis of 8 year outcomes.

- With BCF rates over 80%, long-term follow-up confirms that 60Gy/20f is non-inferior to 74Gy/37f. Late side effects were very low across all groups. These results support the continued use of 60Gy/20f as standard of care for men with localised PCa

Trials Comparing Hypofractionated radiotherapy versus conventional radiotherapy

Study	Year	Country	n	TNM or risk group	RT	Design	Schedule	ADT	Outcomes
Aluwini et al	2015–2016	Netherlands	410	T_{1b}-$T_4N_{X-0}M_{X-0}$ intermediate- to high-risk	Most IMRT	Hypofractionated versus conventional	64.6Gy (19 fractions within 6.5wks)	Yes	OS, BF acute and late adverse events
			410				78Gy (39 fractions within 8wks)		
Arcangeli et al	2010–2017	Italy	83	≥T_{2c}, Gleason ≥7 PSA ≥20ng/ml high-risk	3D-CRT	Hypofractionated versus conventional	62Gy (20 fractions of 3.1Gy, 5wks)	Yes	OS, BF, PCaSS acute and late adverse events
			85				80Gy (40 fractions of 2Gy, 8wks)		
Pollack et al	2007–2013	US	154	T_1-T_3, Gleason ≥5 intermediate- to high-risk	IMRT	Hypofractionated versus conventional	70.2Gy (26 fractions of 2.7Gy)	Yes	OS, BF late adverse event
			153				76Gy (38 fractions of 2Gy)		
Marzi et al	2009	Italy	57	≥T_{2c}, Gleason7-10 PSA>10ng/ml high-risk	3D-CRT	Hypofractionated versus conventional	62Gy (20 fractions of 3.1Gy)	Yes	late adverse event
			57				80Gy (40 fractions of 2Gy)		
Strigary et al	2009	Italy	80	localized prostate cancer high-risk	3D-CRT	Hypofractionated versus conventional	62Gy (20 fractions of 3.1Gy)	Yes	acute adverse event
			52				56Gy (16 fractions of 3.5Gy)		
			80				80Gy (40 fractions of 2Gy, 8wks)		
Catton et al	2017	Canada	608	intermediate-risk	IMRT	Hypofractionated versus conventional	60Gy (20 fractions of 3Gy)	Yes	BF, PCaSS acute and late adverse events
		Australia							
		France	598				78Gy (39 fractions of 2Gy)		

OS Overall survival, *BF* Biochemical failure, *ADT* Androgen deprivation therapy, *PCaSS* Prostate cancer-specific survival, *IMRT* Intensity-modulated radiation therapy, *3D-CRT* Three-dimensional conformal radiotherapy, *PSA* Prostate-specific antigen

Important

- 80 % BFS rate in CHHIP trial
- 95% BFS in POP-ART
- Are we undertreating in CHHIP?? The LN risk was less than 30%, POP-ART had LN risk above 20%.
- Previous issue about hypofractionation in high risk Cap answered well in POP-art
- Now you have a protocol for treating pelvis as well
- POP-Art technically not only endorses WPRT but also guides Hypofractionation for high risk

What do the guidelines say?

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Special Article

Hypofractionated Radiation Therapy for Localized Prostate Cancer: Executive Summary of an ASTRO, ASCO, and AUA Evidence-Based Guideline

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Prostate cancer control outcomes: Impact of patient age, comorbi function

Toxicity and quality of life

Statement KQ1D
for EBRT, moder
offered regardless
anatomy, or urinar
should discuss the
for most existin
hypofractionation.

- **Recommend**
- **Quality of e**
- **Consensus:**

Statement KQ1E: Men should be counseled about the small increased risk of acute gastrointestinal (GI) toxicity with moderate hypofractionation. Moderately hypofractionated EBRT has a similar risk of acute and late genitourinary and late GI toxicity compared with conventionally fractionated EBRT. However, physicians should discuss the limited follow-up beyond 5 years for most existing RCTs evaluating moderate hypofractionation.

- **Recommendation strength:** Strong
- **Quality of evidence:** High
- **Consensus:** 100%

PRINCIPLES OF RADIATION THERAPY

Table 1: Below are examples of regimens that have shown acceptable efficacy and toxicity. The optimal regimen for an individual patient warrants evaluation of comorbid conditions, voiding symptoms and toxicity of therapy. Additional fractionation schemes may be used as long as sound oncologic principles and appropriate estimate of BED are considered.

See PROS-3, PROS-4, PROS-5, PROS-6, PROS-7, PROS-9, PROS-13, and PROS-G for other recommendations, including recommendations for neoadjuvant/concomitant/adjuvant ADT.

Regimen	Preferred Dose/Fractionation	NCCN Risk Group (✓ indicates an appropriate regimen option if radiation therapy is given)					
		Very Low and Low	Favorable Intermediate	Unfavorable Intermediate	High and Very High	Regional N1	Low Volume M1[a]
EBRT							
Moderate Hypofractionation (Preferred)	3 Gy x 20 fx 2.7 Gy x 26 fx 2.5 Gy x 28 fx	✓	✓	✓	✓	✓	
	2.75 Gy x 20 fx						✓
Conventional Fractionation	1.8–2 Gy x 37–45 fx	✓	✓	✓	✓	✓	
Ultra-Hypofractionation	7.25–8 Gy x 5 fx 6.1 Gy x 7 fx	✓	✓	✓	✓		
	6 Gy x 6 fx						✓
Brachytherapy Monotherapy							
LDR Iodine 125 Palladium 103 Cesium 131	145 Gy 125 Gy 115 Gy	✓	✓				
HDR Iridium-192	13.5 Gy x 2 implants 9.5 Gy BID x 2 implants	✓	✓				
EBRT and Brachytherapy (combined with 45–50.4 Gy x 25–28 fx or 37.5 Gy x 15 fx)							
LDR Iodine 125 Palladium 103 Cesium 131	110–115 Gy 90–100 Gy 85 Gy			✓	✓		
HDR Iridium-192	15 Gy x 1 fx 10.75 Gy x 2 fx			✓	✓		