Korean J Urol Oncol 2021;19(1):1-15
https://doi.org/10.22465/kjuo.2021.19.1.1

OPEN ACCESS
Review Article

Expert Group Consensus Opinion on Prostate Cancer Diagnosis and Management in India: Part 2 of 2

Amit Ghose[1], Makarand Khochikar[2], Ravindra Sabnis[3], Naveen Magendra Parmar[4], Indranil Purkait[4]

[1]Apollo Gleneagles Hospitals Limited, Kolkata, India
[2]Department of Uro-Oncology, Siddhi Vinayak Ganapati Cancer Hospital, Miraj, India
[3]Department of Urology, Muljibhai Patel Urological Hospital, Nadiad, India
[4]Medical Affairs and Clinical Research, Ipca Laboratories Ltd., Mumbai, India

With limited/no guidelines on prostate cancer (PCa) diagnosis and management currently in India, this consensus statement has been developed to evaluate Indian literature and current clinical practices to assist healthcare professionals across India in the diagnosis and management of patients with PCa. A group of leading PCa experts from across India convened at the 2019 CAP summit in Kolkata, India, to vote on 42 consensus statements on PCa diagnosis and management. In the subsequent meeting, an expert panel discussed on the consensus results. On the basis of the voting results and the subsequent expert panel discussion, 5 of 42 statements were deleted and 37 were accepted and retained in the final draft, which is divided into 2 parts. This paper covers part 2, which describes in detail the remaining 21 of 37 statements on locally advanced PCa and metastatic PCa with varying degrees of support from the panel. The consensus statement extrapolated from Indian scientific evidences, regional clinical experiences, and international guidelines will serve as a reference guide for clinicians across India in the diagnosis and management of PCa. **(Korean J Urol Oncol 2021;19:1-15)**

Key Words: Prostate cancer · Guideline · Prostate-specific antigen · Prostatectomy · Consensus

INTRODUCTION

Prostate cancer (PCa) is the second most common cancer and the sixth leading cause of cancer death in men worldwide.[1] The data on true incidence of PCa in India is limited as this entity is not a notifiable disease, and there are very few population-based cancer registries in India.[2] PCa had the fifth highest incidence rate in India in 2016 (4.8/100,000).[3] Compared with western countries, the prevalence of PCa in India was previously considered to be lower; however, with increasing migration of rural population to urban areas, increasing awareness, changing life style and easy access to medical facility, more cases of PCa are being detected, suggesting that India is not very far behind western countries in the prevalence rate of PCa.[1]

Hence, having a consensus on various issues related to PCa is important. This would enable early diagnosis and cure in early PCa, achieve optimum control, quality of care and provide relief in advanced PCa cases. Today, much has been achieved for curing early PCa using radical robotic prostatectomy and RT, along with huge advances in chemo-

Received October 26, 2020, Accepted November 3, 2020
Corresponding Author: Naveen Magendra Parmar
Medical Affairs and Clinical Research, Ipca Laboratories Ltd., 142-B, Charkop Rd, Charkop Industrial Estate, Charkop, Kandivali West, Mumbai 400067, Maharashtra, India
Email: naveenparmar95@gmail.com
Tel: +91-9867423441
ORCID: https://orcid.org/0000-0002-5452-7006

therapy, hormone therapy, and salvage radiotherapy (SRT) for advanced disease.

MATERIALS AND METHODS

Pan-India urology experts convened at the 2019 CAP summit for a 2-day (24–25 May 2019) consultative meeting at Kolkata, India, under the aegis of Board of Education, Urological Society of India. Of the 4 major areas defined for discussion as a part of the consensus process (Fig. 1), namely PCa diagnosis, early PCa, locally advanced prostate cancer, and metastatic PCa, the former 2 have been discussed in part 1 manuscript while the latter 2 have been discussed in this paper (i.e., part 2). In each of the sections, the issues were determined according to perceived clinical importance. A total of 42 consensus statements were designed and voting of 28 experts was taken with the help of voting pads. Each major area was discussed on various international guidelines and evidences, followed by voting on consensus statements. The grade of evidence and the level of agreement were based on voting results (Table 1). When the proportion of those who voted was 80% or higher, the statement was regarded as strongly accepted. The result of the consensus and manuscript version 1 was discussed with an expert panel of 13 members (Table 2) in the consensus board meeting (CBM) on 29 November 2019, before preparing the final manuscript draft. The meeting resulted in deletion of 5 statements according to the practicability of recommendations. This manuscript is the outcome of the expert group discussion and consensus and comprises 21 statements on locally advanced PCa and metastatic PCa.

RESULTS

1. Locally Advanced PCa

1) Statement No. 1

Should radical prostatectomy (RP) be considered as a management option for men with high-risk (D'Amico) cN1 cM0 PCa?

Literature review: Kulkarni et al.[4] analysed PCa-specific survival (PCS), biochemical recurrence-free survival (BRFS), and metastasis-free survival (MFS) in 56 high-risk lymph node-positive PCa patients who underwent RP (Table 3). Engel et al.[5] revealed that if RP was abandoned because of lymph node-positivity, there was a 2-fold increased risk of death, compared to men who received RP. The overall survival (OS) rate at 10 years was 64% for patients who received RP versus 28% for those who did not. Multivariate analysis demonstrated RP as a strong independent predictor of survival (hazard ratio [HR], 2.04; 95% confidence interval [CI], 1.59–2.63; $p < 0.0001$). RP provides accurate pathological staging in men with high-risk PCa, thus allowing better stratification of patients for further therapy.

Consensus: Should radical prostatectomy be considered as a management option for men with high-risk (D'Amico)

Table 1. Grading system for consensus statement

Voting percentage	Recommendation strength
>80%	Strong
60%–80%	Moderate
50%–60%	Weak

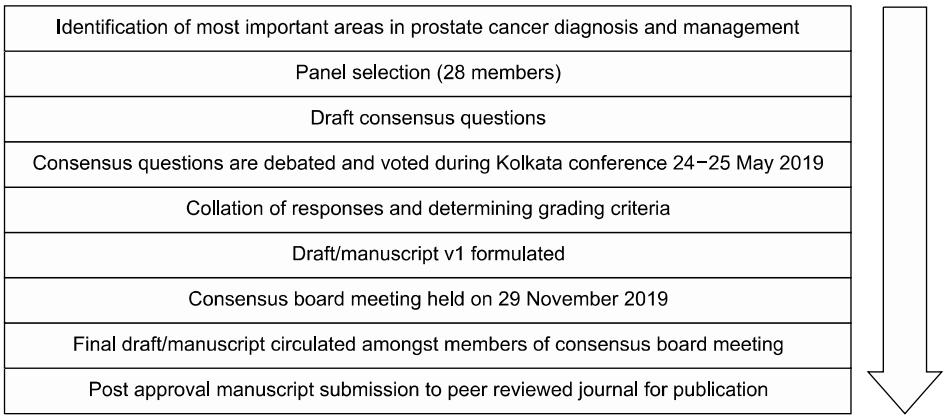

Fig. 1. Consensus process flow.

cN1 cM0 PCa? (yes: 82.1%, no:10.7%, no response: 7.1%). The expert committee recommended RP to be a part of the multi-modality management in men with high-risk (D'Amico) cN1 cM0 PCa.

2) Statement No. 2

Should neo-adjuvant androgen deprivation therapy (ADT) be considered for men with high-risk (D'Amico) cN1 cM0 PCa prior to radical prostatectomy?

Literature review: Owing to limited Indian studies, other literature was evaluated to identify the role of neo-adjuvant ADT. A cochrane review[6] compared neo-adjuvant or adjuvant ADT combined with primary therapy (RT or RP) versus primary therapy alone in patients with localised or locally advanced PCa. Neo-adjuvant ADT before RP did not improve OS (odds ratio [OR], 1.11; p=0.69). However, a significant improvement was observed in parameters like pathological staging, organ-confined rates, and lymph node involvement. Longer duration of neo-adjuvant ADT (6 or 8 months) use prior to RP was associated with a significant reduction in positive surgical margins (OR, 0.56; 95% CI, 0.39–0.80; p=0.002).[6] In patients receiving neo-adjuvant treatment prior RP, a decrease in postoperative positive surgical margins is observed along with reduced biochemical recurrence (BCR) although no effect has been observed on global or cancer-specific survival.[7]

Consensus: Should neo-adjuvant ADT be considered for men with high-risk (D'Amico) cN1 cM0 PCa prior to radical prostatectomy? (yes: 39.2%, no: 53.5%, no response: 7.1%). The expert committee of CBM expressed a very weak recommendation for considering neo-adjuvant ADT in men with high-risk PCa.

3) Statement No. 3

In men with a detectable prostate-specific antigen (PSA) postprostatectomy, and pN1 cM0 disease, would you offer adjuvant docetaxel chemotherapy if fit enough?

Literature review: No Indian data exists on the use of adjuvant docetaxel chemotherapy postprostatectomy. In the Scandinavian PCa group 12 trial,[8] 459 patients received 6 cycles of adjuvant docetaxel every 3 weeks or surveillance post-RP. No significant difference was observed in time to BCR (PSA＞0.5 ng/mL) between the arms, and the restricted mean survival time was 43 months (docetaxel arm) and 46 months (surveillance arm) (p=0.06). After a median follow up of 56.8 months, biochemical progression happened in 44.8% men in the docetaxel arm versus 38.9% in the surveillance arm.[8] Lin et al.[9] evaluated the efficacy of adjuvant docetaxel and prednisone versus standard follow-up after RP. At a median follow-up of 62.4 months,

Table 2. Consensus board meeting members and their speciality

Name	Speciality
Dr. Amit Ghose	Urologist
Dr. Ajay Kumar	Urologist
Dr. Anant Kumar	Urologist
Dr. Aneesh Srivastava	Urologist
Dr. C. Mallikarjuna	Urologist
Dr. Makarand Khochikar	Urologist
Dr. N. P. Gupta	Urologist
Dr. Prem Kumar	Urologist
Dr. Rajeev Kumar	Urologist
Dr. Ravindra Sabnis	Urologist
Dr. S. K. Raghunath	Urologist
Dr. S. K. Singh	Urologist
Dr. Sudhir Rawal	Urologist

Table 3. Univariate analysis assessing impact of pathological variables on PCS, BRFS, and MFS at 5, 7, and 10 years of follow-up[4]

Pathological stage	PCS (%)			BRFS (%)			MFS (%)		
	5 Years	7 Years	10 Years	5 Years	7 Years	10 Years	5 Years	7 Years	10 Years
OC	94.7	94.7	88	91.1	78.8	74.2	94.9	90.9	90.9
PT3a+ LN-	87	75	75	72	58.7	50.3	86	81.3	59.1
PT3b+ LN-	80.9	72.8	54	40.7	28.8	23.8	72.4	61.3	39.9
LN+	89.5	75.3	57.8	75	40.3	21.6	75	65.7	34.2
p-value		0.05			0.000			0.001	

PCS: prostate cancer-specific survival, BRFS: biochemical recurrence-free survival, MFS: metastasis-free survival, OC: organ confined, PT: pathological tumor, LN: lymph node.

progression-free survival (PFS) in the 2 groups was 55.5 versus 45.6 months (log-rank p=0.26). Overall, 67% of patients in the chemotherapy arm experienced at least 1 grade 3 adverse event.[9] However, only node-negative men with postoperative PSA of 0.1 ng/mL were included in this study.[9]

Consensus: In men with a detectable PSA postprostatectomy, and pN1 cM0 disease, would you offer adjuvant docetaxel chemotherapy if fit enough? (yes: 21.4%, no: 67.8%, no response: 10.7%). The expert committee suggested that this statement should have a strong recommendation instead of a moderate.

4) Statement No. 4

In men with an undetectable PSA following radical prostatectomy (and good urinary continence), would you recommend adjuvant radiotherapy (ART) to the prostate bed-only?

Literature review: A cochrane review evaluated the effect of ART following RP in high-risk PCa patients compared with RP alone. ART following RP did not affect OS at 5 years (risk difference [RD], 0.00; 95% CI, 0.03−0.03), but improved survival at 10 years (RD, -0.11; 95% CI, -0.20 to -0.02). ART did not improve PCa-specific mortality at 5 years (RD, -0.01; 95% CI, -0.03 to 0.00). ART did not reduce metastatic disease at 5 years (RD, -0.00; 95% CI, -0.04 to 0.03), but reduced it at 10 years (RD, -0.11; 95% CI, -0.20 to -0.01). It improved BRFS at 5 years (RD, -0.16; 95% CI, -0.21 to -0.11) and 10 years (RD, -0.29; 95% CI, -0.39 to -0.19).[10] The ARO 96-02 study primarily compared 3 groups of PCa patients who achieved an undetectable PSA after RP. Patients who did not achieve an undetectable PSA were moved to SRT arm. Patients in the wait-and-see arm, ART arm, and SRT arm had a 10-year OS rate of 86%, 83%, and 68% respectively.[11]

Consensus: In men with an undetectable PSA following radical prostatectomy (and good urinary continence), would you recommend ART to the prostate bed-only? (yes: 7.14%, no: 89.28%, no response: 3.57%).

5) Statement No. 5

In men with an undetectable PSA following radical prostatectomy (and good urinary continence), would you recommend adjuvant ADT?

Literature review: In a retrospective Indian study, prognostic risk grouping, node positivity, and high initial PSA emerged as significant factors that influenced decisions regarding ADT prescription.[12] Rajput and Sehgal[13] stated that adjuvant ADT benefit has been observed only for those having metastatic disease. Thus, adjuvant ADT is recommended only for the patients with evidence of metastatic disease having early time to PSA recurrence, rapid PSA doubling time, and adverse pathological features. In another study, patients with locally advanced disease who underwent RP, the median follow-up was 9.7 years. There were no statistically significant differences between the bicalutamide and placebo groups with respect to PFS (HR, 0.85; 95% CI, 0.71−1.01; p=0.065) or OS (HR, 1.03; 95% CI, 0.84−1.26; p=0.817). Overall, 98% node-negative patients did not appear to benefit from postsurgery adjuvant treatment.[14] In a survey conducted in the United Kingdom, as a sole trigger factor, 70% of urologists considered a detectable postoperative PSA alone as an important deciding factor for adjuvant treatment.[15]

Consensus: In men with an undetectable PSA following radical prostatectomy (and good urinary continence), would you recommend adjuvant ADT? (yes: 3.57%, no: 85.71%, no response: 10.71%)

6) Statement No. 6

In men with a detectable PSA immediately postsurgery, but no risk factors for persistent pelvic disease, would you offer ART?

Literature review: Murthy et al.[16] studied the practice pattern of prostate RT among radiation oncologist in India. In his survey, including 126 oncologists, 86% reported using ART for high-risk pathological features after RP as their standard practice. Early SRT was practised as standard by 14% of oncologists. However, 43% of respondents observed an increasing trend of patients being offered early salvage treatment in the last 5 years. Another study evaluated patients treated with postoperative RT with a median follow-up of 32.5 months. In patients with locally advanced PCa (pT3/4), BRFS was similar in the ART and early SRT groups (HR, 0.21; 95% CI, 0.02−1.79; p=0.15). SRT administered at early PSA rise might be as effective as postoperative ART in patients with locally advanced PCa.[17]

Consensus: In men with a detectable PSA immediately postsurgery, but no risk factors for persistent pelvic disease,

would you offer ART? (yes: 50%, no: 35.71%, no response: 14.2%). The expert committee also defined 'immediately' as detectable PSA levels of more than 0.2 ng/mL within 12 weeks.

7) Statement No. 7.

In men with an undetectable PSA following radical prostatectomy (and good urinary continence), who subsequently develop a PSA recurrence, would you recommend SRT to the prostate bed-only?

Literature review: Other studies were evaluated for this statement owing to lack of Indian literature on the use of SRT in patients developing PSA recurrence following RP. In a retrospective study of 2,460 patients receiving SRT, the 5-year biochemical control rate was 71%, 63%, 54%, 43%, and 37% for pre-SRT PSA levels of 0.01–0.2 ng/mL, 0.21–0.50 ng/mL, 0.51–1.0 ng/mL, 1.01–2.0 ng/mL, and >2.0 ng/mL ($p<0.001$) respectively.[18] The RAVES and RADICAL trials assessed SRT in post-RP patients with PSA levels more than 0.1–0.2 ng/mL. It showed a 5-year BRFS rate of 88%.[19,20] A meta-analysis on the impact of BCR after RP reported SRT to be favourable for OS and PCa-specific mortality. In particular, SRT should be initiated in patients with rapid PSA kinetics after RP and with a PSA cutoff of 0.4 ng/mL.[21]

Consensus: In men with an undetectable PSA following radical prostatectomy (and good urinary continence), who subsequently develop a PSA recurrence, would you recommend SRT to the prostate bed-only? (yes: 46.4%, no: 53.6%, no response: 0%). The expert committee recommends to providing early SRT for PSA levels below 0.4 ng/mL.

8) Statement No. 8

In men with an undetectable PSA following radical prostatectomy (and good urinary continence), who subsequently develop a PSA recurrence, what imaging would you recommend?

Literature review: In a study of post-RP patients by Natarajan et al.,[22] the detection rates for ^{68}Ga-prostate-specific membrane antigen (PSMA) positron emission tomography/computed tomography (PET/CT) at various PSA levels were 23%, 50%, and 82% for PSA <1, 1–2, and >2 ng/mL, respectively, with an overall detection rate of 56%. About 50% of the patients with nodal metastases identified in ^{68}Ga-PSMA PET/CT in the post-RP group were negative on a CT scan by size criteria. Thus, early identification of relapse using PSMA PET may offer the option of further targeted therapy with curative intent. In another Indian study, in the post-RP cohort, the detection rate of ^{68}Ga-PSMA PET/CT was 39.3% for PSA 0.2 to <0.5 ng/mL, 47.3% for PSA 0.5 to <1 ng/mL, 68.4% for PSA 1 to <2 ng/mL, and 93.1% for PSA ≥2 ng/mL.[23] Only one study compared ^{68}Ga-PSMA PET/CT with whole-body magnetic resonance imaging (MRI) in patients with BCR of PCa following RP. ^{68}Ga-PSMA PET/CT detected 100% of the lesion in 71.4% of patients, while whole-body MRI detected 23.2% lesion in 39.3% of patients.[24]

Consensus: In men with an undetectable PSA following radical prostatectomy (and good urinary continence), who subsequently develop a PSA recurrence, what imaging would you recommend? (MRI: 7.1%, PSMA PET: 92.9%, no response: 0%).

9) Statement No. 9

Is there a PSA value above which you would consider offering SRT?

Literature review: It is estimated that about 30% of patients undergoing RP develop an increase in PSA after radical surgery.[25] Taguchi et al.[26] studied pT2-3N0M0 PCa men who underwent SRT for post-RP BCR at 3 timings. During follow-up (median, 70 months), 20%, 23%, and 44% of patients failed biochemically in the ultra-early SRT (PSA values≥0.2 ng/mL), early SRT (before PSA reached 0.5 ng/mL) and delayed SRT (after PSA reached 0.5 ng/mL) groups respectively. No survival benefit of ultra-early SRT compared with early SRT was observed, whereas delayed SRT was associated with worse prognosis. The results support use of SRT after 2 consecutive PSA values ≥0.2 ng/mL and before reaching 0.5 ng/mL. A 2014 meta-analysis evaluated 10 retrospective studies (Table 4) looking at BRFS based on early- or late-SRT. They found that the 5-year BRFS was 71.1% after early SRT (PSA<0.5 ng/mL).[27]

Consensus: Is there a PSA value above which you would consider offering SRT? (0.2: 60.71%, 0.4: 28.57%, any rise: 7.1%, no response: 3.5%). The expert committee in the CBM was of the opinion that the statement should have a strong recommendation for the PSA value of 0.2 ng/mL.

Table 4. Oncologic outcomes[27]

Study	No. of patients	Nodal involvement	PSA pre-RT (ng/mL), (range)	Follow-up (range)	Fraction BRFS at specific time points
Bernard et al.[52]	69	pN0	0.32 (0.1–0.49)	8 yr (0.6–15 yr)	5 yr: 79.8%
Liauw et al.[53]	34	pN0	0.27 (0.05–0.5)	72.4 mo (5.2–136.3 mo)	5 yr: 71%
Terai et al.[54]	21 of 37	N0	<0.15	31.9 mo (34.3–69.8 mo)	5 yr: 80%
Briganti et al.[55]	390	pN0	<0.5, <0.3	40.6 mo	2 yr: 92.8%, 5 yr: 81.8%
Stephenson et al.[56]	181	pN0	0.4 (0.3–0.4)	33 mo (15–56 mo)	6 yr: 48%, 5 yr: 61%, 3 yr: 69%
Ost et al.[57]	48	pN0/cN0	0.3 (0.1–0.5)	53 mo (18–132 mo)	5 yr: 77.1%
Goenka et al.[58]	143	pN0	<0.5	60 mo (4–221 mo)	5 yr: 48%

PSA: prostate-specific antigen, RT: radiation therapy, BRFS: biochemical recurrence-free survival.

10) Statement No. 10

Should patients with high-risk PCa (STAMPEDE criteria) receiving ADT+RT, also be offered 6 cycles of docetaxel chemotherapy (CT) up front?

Literature review: In RTOG 0521 trial, at a median follow-up of 5.7 years, 4-year OS was 89% for the control arm versus 93% with the addition of docetaxel (p=0.034; HR, 69%). There were 59 deaths in the ADT+RT arm and 43 in the ADT+RT+CT arm, with fewer deaths resulting from PCa in the ADT+RT+CT arm versus the ADT+RT arm (23 versus 16 deaths, respectively). The 6-year rate of distant metastasis was 14% for ADT+RT and 9.1% for ADT+RT+CT (HR, 0.60; 95% CI, 0.37–0.99; 2-sided p=0.044). The 6-year disease-free survival rate was 55% for ADT+RT and 65% for ADT+RT+CT (HR, 0.76; 95% CI, 0.58–0.99; 2-sided p=0.043). Of all patients who received CT in the RTOG 0521 trial, 65% suffered from ≥grade 3 adverse effects (AEs) definitely or probably related to treatment.[28] STAMPEDE trial also evaluated addition of docetaxel to ADT and RT (Table 5, Fig. 2).[29]

Consensus: Should patients with high-risk PCa (STAMPEDE criteria) receiving ADT+RT, also be offered 6 cycles of docetaxel chemotherapy up front? (yes: 28.6%, no: 71.4%, no response: 0%)

11) Statement No. 11

Should patients with high-risk PCa (STAMPEDE criteria) receiving ADT+RT, also be offered 2 years of abiraterone+prednisolone?

Literature review: In a study by Sydes et al.,[30] 189 of 566 patients (14%) were allocated to standard of care (SOC)+docetaxel+prednisone (DocP), and 377 (28%) to SOC+abiraterone acetate+prednisone (AAP). HR of <1 favours SOC+AAP and HR >1 favours SOC+DocP. With a median follow-up of 4 years, 149 deaths were reported. The HR for OS was 1.16 (95% CI, 0.82–1.65); for failure-free survival, HR was 0.51 (95% CI, 0.39–0.67); for PFS HR was 0.65 (95% CI, 0.48–0.88); for MFS HR was 0.77 (95% CI, 0.57–1.03); for PCS HR was 1.02 (95% CI, 0.70–1.49); and for symptomatic skeletal events HR was 0.83 (95% CI, 0.55–1.25). In the safety population, the proportion reporting grades 3, 4, and 5 AEs was 36%, 13%, and 1% in the SOC+DocP arm, and 40%, 7%, and 1% in the SOC+AAP arm respectively; the prevalence rate was 11% at 1 and 2 years in both arms.[30]

Consensus: Should patients with high-risk PCa (STAMPEDE criteria) receiving ADT+RT, also be offered 2 years of abiraterone+prednisolone? (yes: 28.5%, no: 67.8%, no response: 3.5%).

12) Statement No. 12

Should all patients with high-risk (D'Amico) cN0 cM0 PCa receive ADT+RT to the prostate, seminal vesicles, and pelvic lymph nodes?

Literature review: Andic et al.,[31] analysed definitive external-beam radiotherapy (ExRT) arm, after risk adjustment according to ≥2-year ADT use. Not receiving pelvic lymphatic irradiation increased the risk of biochemical failure (p=0.048) than patients who received. Another retrospective study reported outcomes of patients with high-risk PCa who either underwent ExRT in combination with 9 months of ADT or underwent RP with pelvic lymph node sampling. The 3-year BRFS favored ExRT targeted to prostate and seminal vesicle without pelvic lymph node involvement (86.8% vs. 69.8%, p=0.001).[32]

Table 5. Characteristics of the included trials[29]

Trial (yr)	Stage	Sample size (n)	Median age (yr)	Median PSA (ng/mL)	T stage ≥3 (%)	Gleason score ≥8 (%)	Treatments		Median follow-up (mo)	Outcomes
							Experiment	Control		
STAMPEDE 2016	Metastatic, high-risk	690	65	65	81.8	71	ADT+RT+CT (3-weekly docetaxel 75 mg/m^2 for 6 cycles)	ADT+RT	43 months	OS, FFS, AEs
RTOG 0521 2015	High-risk	562	66	15	27	84	ADT+RT+CT (3-weekly docetaxel 75 mg/m^2 for 6 cycles)	ADT+RT	66 months	DFS, OS, AEs

ADT: androgen deprivation therapy, RT: radiation therapy, CT: chemotherapy, OS: overall survival, FFS: failure-free survival, AEs: adverse events, DFS: disease-free survival.

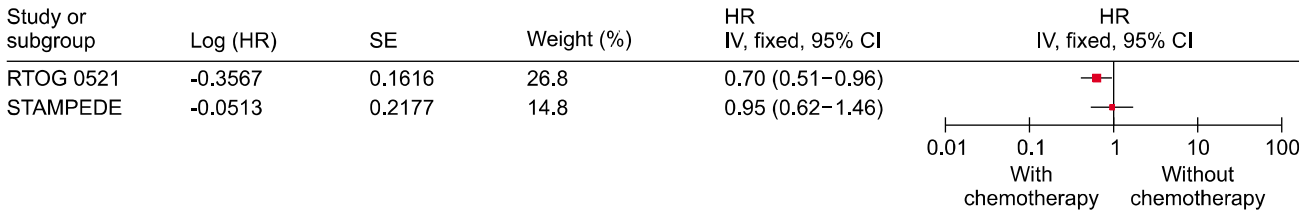

Fig. 2. Effects of additional chemotherapy on overall survival. HR: hazard ratio, SE: standard error, CI: confidence interval.

Consensus: Should all patients with high-risk (D'Amico) cN0 cM0 PCa receive ADT+RT to the prostate, seminal vesicles, and pelvic lymph nodes? (yes: 75%, no: 21.4%, no response: 3.5%)

13) Statement No. 13

Should all patients with cN1 cM0 PCa receive ADT+RT to the prostate, seminal vesicles, and pelvic lymph nodes?

Literature review: In a study conducted by Mallick et al.[33] in India, men with radiologically involved pelvic lymph nodes without distant metastases were treated with long-term ADT and hypo-fractionated RT to pelvic lymph nodes, prostate, and bilateral seminal vesicles. The 4-year biochemical control rate was 77.5% and the OS rate was 91%. Patients with residual enlarged nodes after 36 months of ADT and who required nodal boost had poorer biochemical control rates (4-year rate: 53.9% vs. 93.1%, $p<0.001$). Incidences of late grade 2+ gastrointestinal and genitourinary toxicities were 13.1% and 18%, respectively, with no grade 4 toxicities. Bryant et al.[34] studied the survival benefit of combined RT and ADT compared with ADT alone in node-positive PCa patients. The 5-year unadjusted cumulative mortality estimates favoured the ADT-RT group (all-cause mortality, 24% for ADT-RT vs. 42% for ADT; PCa-specific mortality, 18% vs. 27%; noncancer mortality, 6% vs. 21%).

Consensus: Should all patients with cN1 cM0 PCa receive ADT+RT to the prostate, seminal vesicles, and pelvic lymph nodes? (yes: 85.7%, no: 10.7%, no response: 3.5%)

14) Statement No. 14

In men with nonmetastatic PCa and a rising PSA post radical therapy (surgery or radiotherapy) is there a role for ADT monotherapy?

Literature review: Duchesne et al.[35] analysed immediate ADT versus delayed ADT for men with PSA relapse following RP or RT. Timing of delayed ADT was ≥2 years after BCR. Immediate ADT significantly improved OS compared with delayed ADT (5-year OS was 91.2% vs. 86.4%; p=0.047). Overall, 36% of patients had AEs in the study which required hospitalization. In another study, patients with BCR were managed by ADT, including 60% of

Summary of Recommendations on Locally Advanced PCa

S/N	Statement	Strength of recommendation
1	Should radical prostatectomy be considered as a management option for men with high-risk (D'Amico) cN1 cM0 PCa? Yes: 82.1%, no: 10.7%, no response: 7.1% Radical prostatectomy shouldbe considered as a management option for men with high-risk (D'Amico) cN1 cM0 PCa.	Strong
2	Should Neo-adjuvant ADT be considered for men with high-risk (D'Amico) cN1 cM0 PCa prior to radical prostatectomy? Yes: 39.2%, no: 53.5%, no response: 7.1% Neo-adjuvant ADT should not be considered for men with high-risk (D'Amico) cN1 cM0 PCa prior to radical prostatectomy.	Weak
3	In men with a detectable PSA postprostatectomy, and pN1 cM0 disease, would you offer adjuvant docetaxel chemotherapy if fit enough? Yes: 21.4%, no: 67.8%, no response: 0% In men with a detectable PSA postprostatectomy, and pN1 cM0 disease, we should not offer adjuvant docetaxel chemotherapy.	Moderate
4	In men with an undetectable PSA following radical prostatectomy (and good urinary continence), would you recommend ART to the prostate bed-only? Yes: 7.1%, no: 89.2%, no response: 3.5% In men with an undetectable PSA following radical prostatectomy (and good urinary continence), we should not recommend ART to the prostate bed-only.	Strong
5	In men with an undetectable PSA following radical prostatectomy (and good urinary continence), would you recommend adjuvant ADT? Yes: 3.5%, no: 85.7%, no response: 10.7% In men with an undetectable PSA following radical prostatectomy (and good urinary continence), we should not recommend adjuvant ADT.	Strong
6	In men with a detectable PSA immediately postsurgery, but no risk factors for persistent pelvic disease, would you offer ART? Yes: 50%, no: 35.7%, no response: 14.2% In men with a detectable PSA immediately postsurgery, but no risk factors for persistent pelvic disease, we should offer ART.	Weak
7	In men with an undetectable PSA following radical prostatectomy (and good urinary continence), who subsequently develop a PSA recurrence, would you recommend SRT to the prostate bed-only? Yes: 46.4%, no: 53.6%, no response: 0% In men with an undetectable PSA following radical prostatectomy (and good urinary continence), who subsequently develop a PSA recurrence, we should not recommend SRT to the prostate bed-only.	Weak
8	In men with an undetectable PSA following radical prostatectomy (and good urinary continence), who subsequently develop a PSA recurrence, what imaging would you recommend? MRI: 7.1%, PSMA PET: 92.9%, no response: 0% PSMA PET should be performed in a man with high-risk (D'Amico) cN0 cM0 PCa prior to receiving radical Hormone-Radiotherapy	Strong
9	Is there a PSA value above which you would consider offering SRT? 0.2: 60.71%, 0.4: 28.57%, any rise: 7.1, no response: 3.5% PSA value above 0.2 should be considered for offering SRT.	Moderate
10	Should patients with high-risk PCa (STAMPEDE criteria) receiving ADT+RT, also be offered 6 cycles of docetaxel chemotherapy upfront? Yes: 28.6%, no: 71.4%, no response: 0% Patients with high-risk PCa (STAMPEDE criteria) receiving ADT+RT, should not be offered 6 cycles of docetaxel chemotherapy upfront.	Moderate

Summary of Recommendations on Locally Advanced PCa

S/N	Statement	Strength of recommendation
11	Should patients with high-risk PCa (STAMPEDE criteria) receiving ADT+RT, also be offered 2 years of abiraterone+prednisolone? Yes: 28.5%, no: 67.8%, no response: 3.5% Patients with high-risk PCa (STAMPEDE criteria) receiving ADT+RT, should notbe offered 2 years of abiraterone+prednisolone.	Moderate
12	Should all patients with high-risk (D'Amico) cN0 cM0 PCa receive ADT+RT to the prostate, seminal vesicles, and pelvic lymph nodes? Yes: 75%, no: 21.4%, no response: 3.5% All Patients with high-risk (D'Amico) cN0 cM0 PCa should receive ADT+RT to the prostate, seminal vesicles, and pelvic lymph nodes.	Moderate
13	Should all patients with cN1 cM0 PCa receive ADT+RT to the prostate, seminal vesicles, and pelvic lymph nodes? Yes: 85.7%, no: 10.7%, no response: 3.5% All patients with cN1 cM0 PCa should receive ADT+RT to the prostate, seminal vesicles, and pelvic lymph nodes.	Strong
14	In men with nonmetastatic PCa and a rising PSA post radical therapy (surgery or radiotherapy) is there a role for ADT monotherapy? Yes: 82.1%, no: 17.9%, no response: 0% In men with nonmetastatic PCaand a rising PSA post radical therapy (surgery or radiotherapy), there is a role for ADT monotherapy	Strong

patients who underwent primary RP and 94% of patients who received primary RT.[36] The SWOG-JPR7 study evaluated intermittent versus continuous ADT in men with rising PSA following primary or salvage RT. The median OS was similar in both arms; 8.8 years in the intermittent group and 9.1 years in the continuous group (HR, 1.02). However, certain quality-of-life (QoL) issues improved with intermittent ADT.[37]

Consensus: In men with nonmetastatic PCa and a rising PSA post radical therapy (surgery or radiotherapy) is there a role for ADT monotherapy? (yes: 82.1%, no: 17.9%, no response: 0%)

2. Metastatic PCa

1) Statement No. 1

What is the optimum first-line androgen deprivation strategy for men with hormone-sensitive metastatic PCa in the Indian context?

Literature review: In a RCT by Rajesh and Nigam,[38] patients with osseous metastasis underwent bilateral orchiectomy with or without total androgen blockade. After a follow-up of 18 months; the mean percentage change in placebo group was 68% and flutamide group was 73% ($p > 0.05$). Hot flushes and diarrhoea occurred in 33.3% patients in the total androgen blockade group and 16.6% in placebo-controlled group. Another Indian study analysed surgical versus medical castration (leuprolide acetate) in metastatic PCa patients over 5 years. The OS was 45 months in medical castration arm and 41 months for surgical castration arm ($p > 0.05$). The cancer specific survival rate was 49 months and 44 months, respectively ($p > 0.05$).[39] There was no difference in QoL among those treated medically or surgically. Owing to high cost of ADT, 80% patients in India opt for surgical castration.[40]

Consensus: What is the optimum first-line androgen deprivation strategy for men with castration-sensitive metastatic PCa in the Indian context? (surgical castration: 67.8%, luteinizing hormone-releasing hormone [LHRH] analogues: 14.2%, LHRH antagonist: 7.1%, antiandrogen: 0%, no response: 10.7%).

2) Statement No. 2

What additional systemic therapy should be considered for men with hormone-sensitive metastatic PCa?

Literature review: In metastatic castration naive PCa patients with south Asian ethnicity, ADT+docetaxel and ADT+abiraterone achieved deeper serological response and reduced progression to castrate-resistant PCa compared to

ADT alone (Table 6).[41] LATITUDE trial randomized patients to receive ADT+abiraterone (1,000 mg daily)+prednisone (5 mg daily) or ADT+dual placebos. In the treatment arm, the risk of death reduced by 38% compared to the control arm (HR, 0.62; 95% CI, 0.51-0.76; p＜0.0001), while risk reduction in terms of progression was 53% compared to placebo (HR, 0.47; 95% CI, 0.39-0.55, p＜0.0001). The median OS was significantly longer in the treatment arm than in the control arm (not reached vs. 34.7 months) and median length of radiographic PFS was 33.0 months in the treatment arm versus 14.8 months in the control arm. Docetaxel was the most common post-progression treatment in both the groups.[42]

Consensus: What additional systemic therapy should be considered for men with hormone-sensitive metastatic PCa? (6 cycles docetaxel +/- prednisolone: 32.1%, abiraterone+prednisolone: 35.7%, none: 28.5%, no response: 3.5%). The expert committee recommends systemic therapy of abiraterone or docetaxel with moderate recommendation.

3) Statement No. 3

Is prostate radiotherapy indicated in low-volume hormone-sensitive PCa?

Literature review: In a meta-analysis, authors identified 2 completed (HORRAD and STAMPEDE) eligible trials. Pooled results of these trials showed no overall improvement in survival (HR, 0.92; 95% CI, 0.81-1.04; p=0.195) or PFS (HR, 0.94; 95% CI, 0.84-1.05; p=0.238) with prostate RT. There was an overall improvement in biochemical progression (HR, 0.74; 95% CI, 0.67-0.82; p=0.94×10 raise to -8) and failure-free survival (HR, 0.76; 95% CI, 0.69-0.84; p=0.64×10 raise to -7), equivalent to 10% benefit at 3 years. There was a 7% improvement in 3-year survival in men with fewer than 5 bone metastases. The effect of prostate RT varied with metastatic burden. This study concluded that prostate RT should be considered for men with metastatic hormone-sensitive PCa with a low metastatic burden.[43]

Consensus: Is prostate radiotherapy indicated in low-volume castration-sensitive PCa? (yes: 35.7%, no: 60.71%, no response: 3.5%)

4) Statement No. 4

What is the optimal first-line management option for men with Castration-resistant metastatic PCa in the Indian context?

Literature review: In a study by Shridhar et al.,[44] metastatic PCa patients with progressive disease following ADT

Table 6. Outcome analysis[41]

Outcome measure	ADT+ docetaxel	ADT+ abiraterone	ADT alone	Total
Sample size	28	18	30	76
Median follow-up (mo)	19	8	21	18
PSA decline ＞90%	24 (86%)	17 (94%)	22 (73%)	63 (83%)
Serological complete response, i.e., PSA<0.2 ng/mL	10 (36%)	9 (50%)	5 (17%)	24 (32%)
Progresses to CRPC	11 (39%)	2 (11%)	18 (60%)	31 (41%)

ADT: androgen deprivation therapy, PSA: prostate-specific antigen, CRPC: castrate-resistant prostate cancer.

Table 7. Definition of oligometastatic disease used in representative studies of oligometastatic prostate cancer[48]

Study	Type	Sample size (n)	Location of metastases	Cutoff for oligometastases (n)
Jereczek-Fossa et al.[59]	P; SA	69	LN	≤1
Berkovic et al.[60]	P; SA	24	Bone or LN	≤3
Singh et al.[61]	R; NA	369	Any	≤5
Decaestecker et al.[62]	P; SA	50	Bone or LN	≤3
Ost et al.[63]	P; SA	119	Any	≤3
Ost et al.[64]	P; RA	62	Any	≤3
Schick et al.[65]	P; SA	50	NR	≤4

NR: not reported, P: prospective, R: retrospective, RA: randomized, SA: single arm, LN: lymph node.

were given docetaxel-based chemotherapy (78.82%) and the remaining 21.18% patients did not receive further treatment. The OS was 32.61±6.09 months in patients receiving docetaxel-based chemotherapy as compared to 12.83±2.40 months in patients with no treatment. In another retrospective Indian study, the OS rate in patients treated with abiraterone was 3–6 months for 45% patients. Thirty-two percent patients had more than 6 months of survival rate without progression, and 23% had progression after starting the drug.[45] In an Enzalutamide trial (PREVAIL), after 12 months of follow-up, radiographic PFS data for enzalutamide versus placebo was evaluated (median not reached vs. 3.9 months; 81% risk reduction; $p<0.001$). In an earlier interim analysis, median OS had been estimated as 32.4 months for enzalutamide versus 30.2 months for placebo.[46]

Consensus: What is the optimal first-line management option for men with Castration-resistant metastatic PCa in the Indian context? (abiraterone+pred: 53.5%, enzalutamide: 0%, abiraterone+pred OR enzalutamide: 14.2%, docetaxel: 28.5%, no response: 3.5%).

5) Statement No. 5

What is the definition of oligometastatic PCa?

Literature review: The biological definition of oligometastatic PCa is open to interpretation, no formal cutoff for "oligo" has been defined in the literature.[47] Clinical trials have generally used either 3 or 5 metastatic sites on conventional imaging as the cutoff to define oligometastatic disease (Table 7).[48]

Consensus: What is the definition of oligometastatic PCa? (4 or less skeletal: 89.2%, lymph nodal only: 0%, visceral only: 3.5%, no response: 7.1%)

6) Statement No. 6

What is the optimum management for men with oligometastatic PCa?

Literature review: The randomized CHAARTED trial first showed an OS benefit with the addition of docetaxel to ADT (median OS 57.6 months with docetaxel vs. 44.0 months with ADT alone, $p<0.001$).[49] A predefined subgroup analysis of long-term data concluded docetaxel to have an OS advantage in patients with high-volume (presence of visceral metastases and/or >4 bony metastases with at least 1 bony metastasis outside the spine or pelvis) but not in patients with low-volume disease.[48] The survival benefit of abiraterone in hormone-sensitive metastatic PCa was observed in 2 trials, STAMPEDE and LATITUDE. Grade 3 toxicity was experienced by 33% of patients in the ADT arm, and 47% of patients in the ADT+abiraterone arm in the STAMPEDE trial; with even higher rates of grade 3 toxicity were observed in the LATITUDE trial (48% in the ADT arm and 63% in the ADT+abiraterone arm).[41,50]

Consensus: What is the optimum management for men with oligometastatic PCa?

(ADT only: 35.7%, ADT+abiraterone: 39.2%, ADT+chemo: 17.8%, ADT+enzalutamide: 0%, no response: 7.1%). The expert committee suggested that with evolution, surgery or local RT may be considered along with ADT.

7) Statement No. 7

What imaging should men with a rising PSA and no evidence of metastatic disease on conventional imaging undergo?

Literature review: An Indian study included men, who underwent previous RP or RT. In the post-RP cohort, the detection rate of ^{68}Ga-PSMA PET/CT was 39.3% for PSA 0.2 to <0.5 ng/mL, 47.3% for PSA 0.5 to <1 ng/mL, 68.4% for PSA 1 to <2 ng/mL and 93.1% for PSA ≥2 ng/mL. In this group, local recurrence was identified in 28.73% and lymph nodal metastases in 65.1% of men. In the post-RT group, the detection rate was 88.8% for PSA 2 to <4 ng/mL and 100 % for PSA≥4 ng/mL. Local recurrence after RT was present in 79.5% of the group and 63.6% had lymph nodal metastases.[51] In the study of Natarajan et al.,[22] PSMA PET/CT revealed nodal metastases in 54% patients while CT scan showed pathological nodes only in 28% patients. In a study by Sawick et al.,[24] ^{68}Ga-PSMA PET/CT detected 56 of 56 lesions (100%) in 20 patients (71.4%), while whole-body MRI detected 13 lesions (23.2%) in 11 patients (39.3%). ^{68}Ga-PSMA PET/CT out-performed whole-body MRI in the detection of BCR in PCa patients after RP in this study.

Consensus: What imaging should men with a rising PSA and no evidence of metastatic disease on conventional imaging undergo? (PSMA PET/CT: 75%, whole-body MRI: 21.4%, no response: 3.5%). The expert committee was of the opinion that the statement should have strong recommendation.

Summary of Recommendations on Metastatic PCa

S/N	Statement	Strength of recommendation
1	What is the optimum first-line androgen deprivation strategy for men with castration-sensitive metastatic PCa in the Indian context? Castration: 67.8% LHRH analogues: 14.2% LHRH antagonist:7.1% antiandrogen:0% no response: 10.7% Castration is the optimum first-line androgen deprivation strategy for men with castration-sensitive metastatic PCa in the Indian context.	Moderate
2	What additional systemic therapy should be considered for men with Castration-sensitive metastatic PCa? 6 cycles docetaxel +/- prednisolone: 32.1%, abiraterone+prednisolone: 35.7%, none: 28.5%, no response: 3.5% Abiraterone+prednisolone should be considered for additional systemic therapy for men with Castration-sensitive metastatic PCa.	Weak
3	Is prostate radiotherapy indicated in low-volume castration-sensitive PCa? Yes: 35.7%, no: 60.71%, no response: 3.5% Prostate radiotherapy is not indicated in low-volume castration-sensitive PCa.	Moderate
4	What is the optimal first-line management option for men with Castration-resistant metastatic PCa in the Indian context? Abiraterone+pred: 53.5%, enzalutamide: 0%, abiraterone+pred OR enzalutamide: 14.2%, docetaxel: 28.5%, no response: 3.5% Abiraterone+pred isthe optimal first-line management option for men with Castration-resistant metastatic PCa in the Indian context	Weak
5	What is the definition of oligometastatic PCa? 4 or less skeletal: 89.2%, lymph nodal only: 0%, visceral only: 3.5%, no response: 7.1% 4 or less skeletal involvement should be the definition of oligometastatic PCa	Strong
6	What is the optimum management for men with oligometastatic PCa? ADT only: 35.7%, ADT+abiraterone: 39.2%, ADT+chemo:17.8%, ADT+enzalutamide: 0%, no response: 7.1% ADT+abiraterone is the optimum management for men with oligometastatic PCa	Weak
7	What imaging should men with a rising PSA and no evidence of metastatic disease on conventional imaging undergo? PSMA PET/CT: 75%, whole-body MRI: 21.4%, no response: 3.5% Men with a rising PSA and no evidence of metastatic disease on conventional imaging should undergo PSMA PET/CT scan	Moderate

REFERENCES

1. Jain S, Saxena S, Kumar A. Epidemiology of prostate cancer in India. Meta Gene 2014;2:596-605.
2. Hariharan K, Padmanabha V. Demography and disease characteristics of prostate cancer in India. Indian J Urol 2016;32:103-8.
3. Dhillon PK, Mathur P, Nandakumar A, Fitzmaurice C, Kumar GA, Mehrotra R, et al. The burden of cancers and their variations across the states of India: the Global Burden of Disease Study 1990-2016. Lancet Oncol 2018; 19:1289-306.
4. Kulkarni JN, Gunavanthe VS, Dhale A. Outcome of radical prostatectomy as primary treatment for high-risk prostate cancer patients. Indian J Cancer 2015;52:646-52.
5. Engel J, Bastian PJ, Baur H, Beer V, Chaussy C, Gschwend JE, et al. Survival benefit of radical prostatectomy in lymph node-positive patients with prostate cancer. Eur Urol 2010;57:754-61.
6. Kumar S, Shelley M, Harrison C, Coles B, Wilt TJ, Mason MD. Neo-adjuvant and adjuvant hormone therapy for localised and locally advanced prostate cancer. Cochrane Database Syst Rev 2006;(4):CD006019.
7. Srivatsa N, Nagaraja H, Shweta S, Raghunath SK. Radical prostatectomy for locally advanced prostate cancers—review of literature. Indian J Surg Oncol 2017;8:175-80.
8. Ahlgren GM, Flodgren P, Tammela TLJ, Kellokumpu-Lehtinen P, Borre M, Angelsen A, et al. Docetaxel versus surveillance after radical prostatectomy for high-risk prostate cancer: results from the prospective randomised, open-label phase 3 scandinavian prostate cancer group 12 trial. Eur Urol 2018;73:870-6.
9. Lin D, Garzotto M, Aronson W, Basler J, Beer T, Brophy M, et al. VA CSP#553 Chemotherapy after prostatectomy

(CAP) for high risk prostate carcinoma: a phase III randomized study. J Urol 2016;195:e1071.
10. Daly T, Hickey BE, Lehman M, Francis DP, See AM. Adjuvant radiotherapy following radical prostatectomy for prostate cancer. Cochrane Database Syst Rev 2011;(12): CD007234.
11. Wiegel T, Bartkowiak D, Bottke D, Thamm R, Hinke A, Stöckle M, et al. Prostate-specific antigen persistence after radical prostatectomy as a predictive factor of clinical relapse-free survival and overall survival: 10-year data of the ARO 96-02 trial. Int J Radiat Oncol Biol Phys 2015;91: 288-94.
12. Sharma K, Pande SC, Verma K, Goel S. Influencing factors while prescribing androgen deprivation therapy for carcinoma prostate in clinical practice: When literature is not enough! J Curr Oncol 2018;1:73-9.
13. Rajput R, Sehgal A. Endocrine manipulations in cancer prostate: a review. Indian J Endocr Metab 2012;16(Suppl S2):S199-204.
14. Iversen P, McLeod DG, See WA, Morris T, Armstrong J, Wirth MP. Casodex Early Prostate Cancer Trialists' Group. Antiandrogen monotherapy in patients with localized or locally advanced prostate cancer: final results from the bicalutamide Early Prostate Cancer programme at a median follow-up of 9.7 years. BJU Int 2010;105:1074-81.
15. Lee LW, Clarke NW, Ramani VA, Cowan RA, Wylie JP, Logue JP. Adjuvant and salvage treatment after radical prostatectomy: current practice in the UK. Prostate Cancer Prostatic Dis 2005;8:229-34.
16. Murthy V, Mallick I, Arunsingh M, Gupta P. Prostate radiotherapy in India: evolution, practice and challenges in the 21st century. Clin Oncol (R Coll Radiol) 2019;31: 492-501.
17. Vogel MME, Kessel KA, Schiller K, Devecka M, Gschwend JE, Weichert W, et al. Adjuvant versus early salvage radiotherapy: outcome of patients with prostate cancer treated with postoperative radiotherapy after radical prostatectomy. Radiat Oncol 2019;14:198.
18. Tendulkar RD, Agrawal S, Gao T, Efstathiou JA, Pisansky TM, Michalski JM, et al. Contemporary update of a multi-institutional predictive nomogram for salvage radiotherapy after radical prostatectomy. J Clin Oncol 2016;34: 3648-54.
19. Kneebone A, Fraser-Browne C, Delprado W, Duchesne G, Fisher R, Frydenberg M, et al. A phase III multi-centre randomised trial comparing adjuvant versus early salvage radiotherapy following a radical prostatectomy: results of the TROG 08.03 and ANZUP "RAVES" Trial. Int J Radiat Oncol Biol Phys 2019;105(1 Supplement):S37-8.
20. Parker C, Clarke NW, Cook A, Kynaston HG, Meidahl Petersen P, Cross W, et al. Timing of radiotherapy (RT) after radical prostatectomy (RP): first results from the RADICALS RT randomised controlled trial (RCT) [NCT00541047]. Ann Oncol 2019;30(suppl_5):v851-934.
21. Van den Broeck T, van den Bergh RCN, Arfi N, Gross T, Moris L, Briers E, et al. Prognostic value of biochemical recurrence following treatment with curative intent for prostate cancer: a systematic review. Eur Urol 2019;75: 967-87.
22. Natarajan A, Agrawal A, Murthy V, Bakshi G, Joshi A, Purandare N, et al. experience of Ga-68 prostate-specific membrane antigen positron emission tomography/computed tomography imaging in evaluation of biochemical recurrence in prostate cancer patients. World J Nucl Med 2019;18:244-50.
23. Seniaray N, Verma R, Khanna S, Belho E, Pruthi A, Mahajan H. Localization and restaging of carcinoma prostate by 68Gallium prostate-specific membrane antigen positron emission tomography computed tomography in patients with biochemical recurrence. Indian J Urol 2020;36: 191-9.
24. Sawicki LM, Kirchner J, Buddensieck C, Antke C, Ullrich T, Schimmöller L, et al. Prospective comparison of whole-body MRI and 68Ga-PSMA PET/CT for the detection of biochemical recurrence of prostate cancer after radical prostatectomy. Eur J Nucl Med Mol Imaging 2019; 46:1542-50.
25. Viani GA, Hamamura AC, Correa AC, de Arruda FT. Salvage radiotherapy for biochemical recurrence after radical prostatectomy: does the outcome depend on the prostate cancer characteristics? Int Braz J Urol 2019;45:237-45.
26. Taguchi S, Shiraishi K, Fukuhara H, Nakagawa K, Morikawa T, Naito A, et al. Optimal timing of salvage radiotherapy for biochemical recurrence after radical prostatectomy: is ultra-early salvage radiotherapy beneficial? Radiat Oncol 2016;11:102.
27. Pfister D, Bolla M, Briganti A, Carroll P, Cozzarini C, Joniau S, et al. Early salvage radiotherapy following radical prostatectomy. Eur Urol 2014;65:1034-43.
28. Rosenthal SA, Hu C, Sartor O, Gomella LG, Amin MB, Purdy J, et al. Effect of chemotherapy with docetaxel with androgen suppression and radiotherapy for localized high-risk prostate cancer: the randomized phase III NRG Oncology RTOG 0521 Trial. J Clin Oncol 2019;37:1159-68.
29. Chen J, Zhang X, Sun G, Zhao J, Liu J, Zhao P, et al. The effect of additional chemotherapy on high-risk prostate cancer: a systematic review and meta-analysis. Onco Targets Ther 2018;11:9061-70.
30. Sydes MR, Spears MR, Mason MD, Clarke NW, Dearnaley DP, de Bono JS, et al. Adding abiraterone or docetaxel to long-term hormone therapy for prostate cancer: directly randomised data from the STAMPEDE multi-arm, mul-

ti-stage platform protocol. Ann Oncol 2018;29:1235-48.
31. Andic F, Izol V, Gokcay S, Arslantas HS, Bayazit Y, Coskun H, et al. Definitive external-beam radiotherapy versus radical prostatectomy in clinically localized high-risk prostate cancer: a retrospective study. BMC Urol 2019;19:3.
32. Arcangeli G, Strigari L, Arcangeli S, Petrongari MG, Saracino B, Gomellini S, et al. Retrospective comparison of external beam radiotherapy and radical prostatectomy in high-risk, clinically localized prostate cancer. Int J Radiat Oncol Biol Phys 2009;75:975-82.
33. Mallick I, Das A, Arunsingh M. Moderately. Hypofractionated radiotherapy in node-positive prostate cancer. Clin Oncol (R Coll Radiol) 2019;31:260-4.
34. Bryant AK, Kader AK, McKay RR, Einck JP, Mell LK, Mundt AJ, et al. Definitive radiation therapy and survival in clinically node-positive prostate cancer. Int J Radiat Oncol Biol Phys 2018;101:1188-93.
35. Duchesne GM, Woo HH, Bassett JK, Bowe SJ, D'Este C, Frydenberg M, et al. Timing of androgen-deprivation therapy in patients with prostate cancer with a rising PSA (TROG 03.06 and VCOG PR 01-03 [TOAD]): a randomised, multicentre, non-blinded, phase 3 trial. Lancet Oncol 2016;17:727-37.
36. Agarwal PK, Sadetsky N, Konety BR, Resnick MI, Carroll PR; Cancer of the Prostate Strategic Urological Research Endeavor (CaPSURE). Treatment failure after primary and salvage therapy for prostate cancer: likelihood, patterns of care, and outcomes. Cancer 2008;112:307-14.
37. Crook JM, O'Callaghan CJ, Duncan G, Dearnaley DP, Higano CS, Horwitz EM, et al. Intermittent androgen suppression for rising PSA level after radiotherapy. N Engl J Med 2012;367:895-903.
38. Rajesh R, Nigam DK. Bilateral orchiectomy versus total androgen blockade in the management of metastatic cancer prostate. Int Surg J 2016;3:841-5.
39. Purushothaman A, Kumar G, Gangadharan P, Roshni PR. A comparison of leuprolide acetate versus bilateral orchiectomy for patients with metastatic prostate cancer. Asian J Pharm Clin Res 2016;9:51-4.
40. Singh P, Agrawal T, Yadav S, Nayak B, Seth A, Dogra PN. A comparative study of the effects of medical versus surgical androgen deprivation therapy on health-related quality of life in patients with metastatic carcinoma prostate. Indian J Cancer 2018;55:148-53.
41. Sonthwal N, Hussain SM, Arya D, Batra S, Chaturvedi HK, Gupta A. Addition of docetaxel or abiraterone to androgen deprivation therapy in metastatic castration-naive prostate cancer in South Asian population. J Clin Oncol 2019;37:15_suppl:e16514.
42. Fizazi K, Tran N, Fein L, Matsubara N, Rodriguez-Antolin A, Alekseev BY, et al. Abiraterone plus Prednisone in Metastatic, Castration-Sensitive Prostate Cancer. N Engl J Med 2017;377:352-60.
43. Burdett S, Boevé LM, Ingleby FC, Fisher DJ, Rydzewska LH, Vale CL, et al. Prostate radiotherapy for metastatic hormone-sensitive prostate cancer: a STOPCAP systematic review and meta-analysis. Eur Urol 2019;76:115-24.
44. Shridhar CG, Rajendra BN, Murigendra BH, Bassappa BK. Docetaxel based treatment for metastatic castration-resistant prostate cancer-our early experience. Transl Biomed 2016;7:2.
45. James A, Vincent B, Sivadas A, Pavithran K. A study on the clinical outcome of abiraterone acetate in castration resistant prostate cancer patients. Int J Hematol Oncol Stem Cell Res 2018;12:4-7.
46. Beer TM, Armstrong AJ, Rathkopf DE, Loriot Y, Sternberg CN, Higano CS, et al. Enzalutamide in metastatic prostate cancer before chemotherapy. N Engl J Med 2014;371:424-33.
47. Gillessen S, Attard G, Beer TM, Beltran H, Bossi A, Bristow R, et al. Management of patients with advanced prostate cancer: the report of the Advanced Prostate Cancer Consensus Conference APCCC 2017. Eur Urol 2018;73:178-211.
48. Rao A, Vapiwala N, Schaeffer E, Ryan C. Oligometastatic prostate cancer: a shrinking subset or an opportunity for cure? Am Soc Clin Oncol Educ Book 2019;39:309-20.
49. Kyriakopoulos CE, Chen YH, Carducci MA, Liu G, Jarrard DF, Hahn NM, et al. Chemohormonal therapy in metastatic hormonesensitive prostate cancer: long-term survival analysis of the randomized phase III E3805 CHAARTED trial. J Clin Oncol 2018;36:1080-7.
50. James ND, de Bono JS, Spears MR, Clarke NW, Mason MD, Dearnaley DP, et al. Abiraterone for prostate cancer not previously treated with hormone therapy. N Engl J Med 2017;377:338-51.
51. Nikhil S, Ritu V, Sudhir K, Ankur P, Ethel B, Harsh M. 68Ga PSMA PET/CT in restaging of prostate cancer patients with biochemical recurrence. J Nucl Med 2019;60:Supplement 1:1560.
52. Bernard JR, Buskirk SJ, Heckman MG, Diehl NN, Ko SJ, Macdonald OK, et al. Salvage radiotherapy for rising prostate-specific antigen levels after radical prostatectomy for prostate cancer: dose-response analysis. Int J Radiat Oncol Biol Phys 2010;76:735-40.
53. Liauw SL, Webster WS, Pistenmaa DA, Roehrborn CG. Salvage radiotherapy for biochemical failure of radical prostatectomy: a single-institution experience. Urology 2003;61:1204-10.
54. Terai A, Matsui Y, Yoshimura K, Arai Y, Dodo Y. Salvage radiotherapy for biochemical recurrence after radical prostatectomy. BJU Int 2005;96:1009-13.
55. Briganti A, Wiegel T, Joniau S, Cozzarini C, Bianchi M,

Sun M, et al. Early salvage radiation therapy does not compromise cancer control in patients with pT3N0 prostate cancer after radical prostatectomy: results of a match-controlled multi-institutional analysis. Eur Urol 2012;62: 472-87.
56. Stephenson AJ, Scardino PT, Bianco FJ, Eastham JA. Salvage therapy for locally recurrent prostate cancer after external beam radiotherapy. Curr Treat Options Oncol 2004;5:357-65.
57. Ost P, De Troyer B, Fonteyne V, Oosterlinck W, De Meerleer G. A matched control analysis of adjuvant and salvage high-dose postoperative intensity-modulated radiotherapy for prostate cancer. Int J Radiat Oncol Biol Phys 2011;80:1316-22.
58. Goenka A, Magsanoc JM, Pei X, Schechter M, Kollmeier M, Cox B, et al. Long-term outcomes after high-dose post-prostatectomy salvage radiation treatment. Int J Radiat Oncol Biol Phys 2012;84:112-8.
59. Jereczek-Fossa BA, Piperno G, Ronchi S, Catalano G, Fodor C, Cambria R, et al. Linac-based stereotactic body radiotherapy for oligometastatic patients with single abdominal lymph node recurrent cancer. Am J Clin Oncol 2014;37:227-33.
60. Berkovic P, De Meerleer G, Delrue L, Lambert B, Fonteyne V, Lumen N, et al. Salvage stereotactic body radiotherapy for patients with limited prostate cancer metastases: deferring androgen deprivation therapy. Clin Genitourin Cancer 2013;11:27-32.
61. Singh D, Yi WS, Brasacchio RA, Muhs AG, Smudzin T, Williams JP, et al. Is there a favorable subset of patients with prostate cancer who develop oligometastases? Int J Radiat Oncol Biol Phys 2004;58:3-10.
62. Decaestecker K, De Meerleer G, Lambert B, Delrue L, Fonteyne V, Claeys T, et al. Repeated stereotactic body radiotherapy for oligometastatic prostate cancer recurrence. Radiat Oncol 2014;9:135.
63. Ost P, Jereczek-Fossa BA, As NV, Zilli T, Muacevic A, Olivier K, et al. Progression-free survival following stereotactic body radiotherapy for oligometastatic prostate cancer treatment-naive recurrence: a multi-institutional analysis. Eur Urol 2016;69:9-12.
64. Ost P, Reynders D, Decaestecker K, Fonteyne V, Lumen N, Bruycker AD, et al. Surveillance or metastasis-directed therapy for oligometastatic prostate cancer recurrence: a prospective, randomized, multicenter phase II trial. J Clin Oncol 2018;36:446-3.
65. Schick U, Jorcano S, Nouet P, Rouzaud M, Vees H, Zilli T, et al. Androgen deprivation and high-dose radiotherapy for oligometastatic prostate cancer patients with less than five regional and/ or distant metastases. Acta Oncol 2013; 52:1622-8.