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Metastasis-directed Therapy Prolongs Efficacy of Systemic Therapy and Improves Clinical Outcomes in Oligoprogressive Castration-resistant Prostate Cancer

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Abstract

Background: Available therapies for castrate-resistant prostate cancer (CRPC) confer minimal survival advantage; thus, there is interest in metastasis-directed therapy (MDT) for oligometastatic or oligoprogressive disease to improve outcomes. Here, we describe outcomes of oligoprogressive CRPC treated with stereotactic ablative radiotherapy (SABR).

Objective: To report outcomes of oligoprogressive CRPC treated with MDT using SABR.

Design, setting, and participants: Patients with oligoprogressive CRPC were retrospectively evaluated, and outcomes following MDT were reported. Outcomes were additionally compared with oligoprogressive CRPC treated with change in systemic therapy alone.

Intervention: SABR to oligoprogressive lesions.

Outcome measurements and statistical analysis: Outcomes of interest were time to prostate-specific antigen (PSA) failure, time to next intervention (TTNI), distant metastasis-free survival (DMFS), and overall survival. Survival analysis was performed using the Kaplan-Meier method, and univariable analysis and multivariable analysis (MVA) were performed.

Results and limitations: A total of 68 patients were included. After MDT, median time to PSA recurrence, TTNI, and DMFS were 9.7, 15.6, and 10.8 months, respectively. A total of 112 lesions were treated, and the cumulative incidences of local failure at 12 and 24 months were 2.1% and 13.8%, respectively. Factors associated with the risk of local recurrence on univariable analysis were age (hazard ratio [HR] 1.07, $p = 0.03$) and Gleason grade group (HR 2.20, $p = 0.07$). Compared with change in systemic therapy alone ($n = 52$), MDT ($n = 31$) was associated with improved median time to PSA failure (9.7 vs 4.2 months, $p = 0.066$)), TTNI (14.9 vs 8.8 months,

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$p = 0.025$), and DMFS (12.7 vs 8.9 months, p = 0.045), and remained associated with improved outcomes on MVA.

Conclusions: In a retrospective cohort of oligoprogressive CRPC patients, MDT was associated with favorable outcomes and improved cancer control as compared with change in systemic treatment alone. Future prospective trials are needed to confirm these findings.

Patient summary: In this report, we retrospectively analyzed outcomes of patients with oligoprogressive castrate-resistant prostate cancer treated with radiation therapy to progressing lesions. Our results suggest that treatment of these lesions with radiation therapy can result in sustained periods of disease-free survival and might add benefit in addition to systemic therapy at the time of progression. These results need to be verified in a prospective trial to identify the optimal integration of radiation therapy into metastatic castrate-resistant prostate cancer.

Introduction

First-line therapy for metastatic prostate cancer (PCa) is androgen deprivation therapy (ADT); however, PCa clones eventually become androgen insensitive heralding a castrate-resistant state [1,2]. Several systemic agents are used in the management of castrate-resistant PCa (CRPC) including supracastrating drugs (eg, enzalutamide), cytotoxic agents, immune modulating therapies, and radiopharmaceuticals, all of which confer a survival advantage of several months [3–9].

Despite improvements in systemic therapies, metastatic disease is still, generally, incurable. As such, there is interest in integrating local therapies in an attempt to improve outcomes, which has primarily been of interest in oligoprogressive disease, a category of oligometastases (five or fewer lesions) characterized by limited areas of treatment-resistant clones that expand in a background of otherwise stable or responding systemic disease.

Several trials have demonstrated improvements in progression-free survival (PFS) and overall survival (OS) with metastasis-directed therapy (MDT) of de novo or oligorecurrent metastatic disease [10–12]. Additionally, the STOMP trial established that stereotactic ablative radiotherapy (SABR), compared with observation, prolongs the time to initiation of ADT in oligorecurrent hormone-sensitive PCa (HSPC) [13]. However, much of the work involving MDT for oligometastatic PCa (OPCa) has involved men with HSPC with few reports in CRPC [14–16]. Given the modest benefit of systemic therapies in metastatic CRPC [4,6,7,17,18], maximizing the amount of time a responder can remain on a systemic agent is likely beneficial. Therefore, herein we report outcomes with the use of SABR in the treatment of oligoprogressive CRPC.

Patients and methods

Patient population

Following institutional review board approval, we reviewed our retrospectively collected databases of OPCa patients treated with SABR at the Johns Hopkins Hospital and Mayo Clinic from January 2013 through 2019. The inclusion criteria were men with CRPC and imaging demonstrating oligoprogressive metastatic disease defined as five or fewer progressing lesions. Progressive lesions were defined as newly identified lesions, growth of a lesion on anatomic imaging (i.e., computed tomography/magnetic resonance imaging), or increased uptake in a lesion on nuclear/molecular imaging (i.e., bone scan or positron emission tomography) in combination with rising prostate-specific antigen (PSA). Patients could have greater than five total metastases so long as additional lesions were stable.

Patients were typically seen every 3–6 months following SABR with repeat history, physical examination, PSA, and serum testosterone. Imaging was also often repeated every 6–12 months or sooner if warranted by symptoms or change in PSA dynamics. The decision regarding changes to a patient's treatment paradigm and new interventions following SABR, including a change in systemic therapy or repeat SABR, was typically taken in a multidisciplinary manner and usually at the time of disease progression. Treatment details for the cohort have been described previously for both institutions [19,20]. In order to assess the impact of SABR relative to systemic therapy, a cohort of patients treated with only a change of systemic therapy at the time of oligoprogression was included for comparison, which consisted of contemporary medical oncology patients treated at the xxx Johns Hopkins Hospital.

Statistical analysis

Summary statistics were calculated for patients and lesions. Chi-square test, Fisher's exact test, *t* test, or Wilcoxon rank sum test were used to compare variables. Survival analysis was conducted for PSA failure, time to next intervention (TTNI), distant metastasis-free survival (DMFS), and OS. PSA failure was as per Scher et al [21] and defined as follows: (1) an initial decline from baseline PSA was observed, a PSA increase of $\geq$25% and $\geq$2 ng/mL above the nadir, or an increase of $\geq$25% and greater than the pretreatment PSA value; (2) no initial decline from baseline if the baseline PSA was $\geq$2 ng/mL, a PSA increase of $\geq$ 25% and $\geq$ 2 ng/mL above the baseline, or a PSA increase of $\geq$ 2 ng/mL if the baseline

PSA was <2 ng/mL; or (3) initiation of new systemic therapy. Events for TTNI included any change to current therapy (including repeat SABR). DMFS was defined as the development of a new metastatic lesions or death. Median time to PSA relapse, TTNI, DMFS, and OS were calculated using the Kaplan-Meier method and compared using the log rank test. Univariable and multivariable Cox regression (MVA) analyses were conducted for TTNI, DMFS, and PSA failure. Variables included in the MVA were ones significant on univariable analysis as well as those with high a priori belief to be associated with outcomes while keeping the model limited to approximately one variable per 10 events. Rates of local failure were calculated using cumulative incidence function curves, and defined as any increase in size or radiotracer avidity of the treated lesion, subsequent use of a secondary local salvage therapy to the treated site, or the development of a new lesion within the initial 50% isodose line. Fine-Gray analysis was performed to evaluate factors associated with local recurrence. All statistical analyses were conducted using R, and $p < 0.05$ was considered statistically significant.

Results

Background characteristics

A total of 68 patients with oligoprogressive disease treated with MDT were included in the analysis, with median follow-up of 30.9 months (range, 4.40–54.6 months). Baseline characteristics of these patients are presented in Table 1.

Table 1 – Baseline characteristics.

Variable	*n*
Age (yr), median (IQR)	70.40 (62.60–73.80)
T stage [a], n (%)	
T1	2 (2.90)
T2	22 (32.40)
T3	35 (51.50)
T4	4 (5.90)
Tx	4 (5.90)
NA	1 (1.40)
N stage[a], n (%)	
N0	45 (66.20)
N1	17 (25.00)
NX	5 (7.40)
NA	1 (1.40)
M stage[a], n (%)	
M0	43 (63.20)
M1	11 (16.20)
MX	13 (19.10)
NA	1 (1.50)
Grade group[a], n (%)	
1	8 (11.80)
2	7 (10.30)
3	9 (13.20)
4	9 (13.20)
5	33 (48.50)
NA	2 (30)
iPSA (ng/mL)[a], median (IQR)	8.80 (4.92–27.60)
Number of metastases, n (%)	
1	28 (41.20)
2	15 (22.10)
3	7 (10.30)
4	4 (5.80)
5	5 (7.40)
6	2 (2.90)
7	1 (1.50)
8	3 (4.40)
9	0 (0)
10	2 (2.90)
11	1 (1.40)
Number oligoprogressive lesions treated, n (%)	
1	36 (52.90)
2	20 (29.40)
3	7 (10.30)
4	3 (4.40)
5	2 (3.00)
Pretreatment PSA (ng/mL), median (IQR)	3.50 (0.56–5.90)
Use of ADT, n (%)	68 (100)
Prior treatment with supracastrating drug, *n* (%)	38 (55.90)
Prior treatment with chemotherapy, *n* (%)	26 (38.20)
Number of prior systemic therapies, median (IQR)	3 (2–5)
Imaging, n (%)	
Conventional	19 (27.90)
Enhanced[b]	48 (70.60)
NA	1 (1.50)

ADT = androgen deprivation therapy; iPSA = initial PSA; IQR = interquartile range; NA = not applicable; PSA = prostate-specific antigen; PSMA = prostate-specific membrane antigen.
[a] At the time of initial diagnosis.
[b] Enhanced imaging included fluciclovine, choline, and PSMA PET/CT.

Clinical outcomes following MDT

Following therapy, 73.5% of patients experienced a decline or stability in PSA. The median PSA nadir following MDT was 0.50 ng/mL (range, 0–48.40 ng/ml), representing a median decline of 71% (range, −100% to +196.90%; Fig. 1). Following MDT median time to PSA recurrence was 9.67 months (95% CI, 6.77 – 13.30), median TTNI was 15.60 months (95% CI, 13.80– 21.10), and median DMFS was 10.83 months (95% CI, 7.47 – 13.57; Fig. 2A–C). The median time to progression of untreated lesions was 7.43 months (95% CI 3.87 – not reached). A total of 16 deaths occurred and median OS was not yet reached, but two year OS was 90.20% (Fig. 2D). Factors associated with PSA failure, DMFS, and TTNI on univariable analysis are reported in Supplementary Tables 1 and 2, and include the number of prior systemic treatments and the National Comprehensive Cancer Network risk group; however, these did not remain significant on MVA (Table 2).

Patients who had consolidation of both progressive and stable lesions appeared to have better outcomes. The median time to PSA failure (11.77 months [95% confidence interval {CI} 9.48–19.10] vs 6.22 months [95% CI 3.63–12.50], $p = 0.004$), TTNI (19.20 months [95% CI 15.00–31.30] vs 13.10 months [95% CI 9.30–16.80], $p = 0.01$), and DMFS (11.77 months [95% CI 9.29–17.30] vs 7.43 months [95% CI 3.87–12.70], $p = 0.01$) were all improved with total consolidation of disease. However, those who did not have full consolidation of metastases had higher disease volume at the time of treatment (median of five metastases vs one metastasis, $p < 0.001$). MDT appeared to prolong the time patients could remain on the current systemic agents at the time of oligoprogression: Fifty-five (80.90%) patients remained on the same systemic therapy at the time of

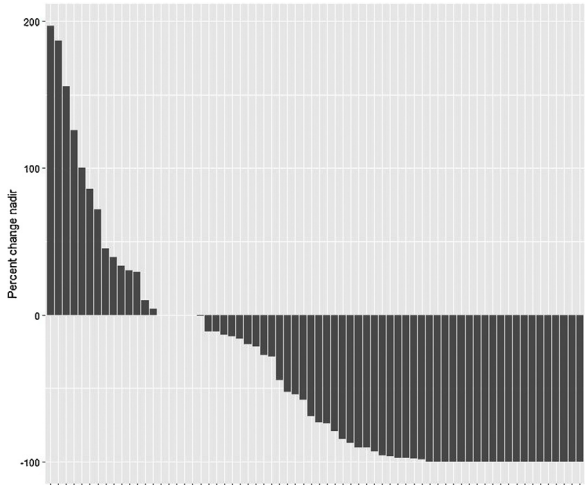

Fig. 1 – Waterfall plot of PSA change following radiation therapy. PSA = prostate-specific antigen.

SABR with a median TTNI of 15.60 months (95% CI 14.57–21.10), which was not significantly different from the TTNI of those who changed systemic therapy (13.50 months, 95% CI 4.37–not reached, $p = 0.60$). Additionally, the median time to PSA failure (9.67 months [95% CI 6.37–13.20] vs 7.43 months [95% CI 3.27–not reached], $p = 0.53$), DMFS (13.17 months (95% CI 7.43–not reached] vs 9.73 months [95% CI 7.34–13.30], $p = 0.45$), and OS (median not reached, $p = 0.29$) were also not significantly different.

Lesional outcomes

A total of 119 lesions were treated: 88 (73.94%) bone, 23 (19.33%) nodal, and eight (6.73%) visceral. Lesions were most commonly located in the spine ($n = 31$, 26.05%) or pelvis ($n = 31$, 26.05%). The median biological equivalent dose using an alpha/beta ratio of 3 was 130.0 Gy. The estimated cumulative incidences of local failure at 12 and 24

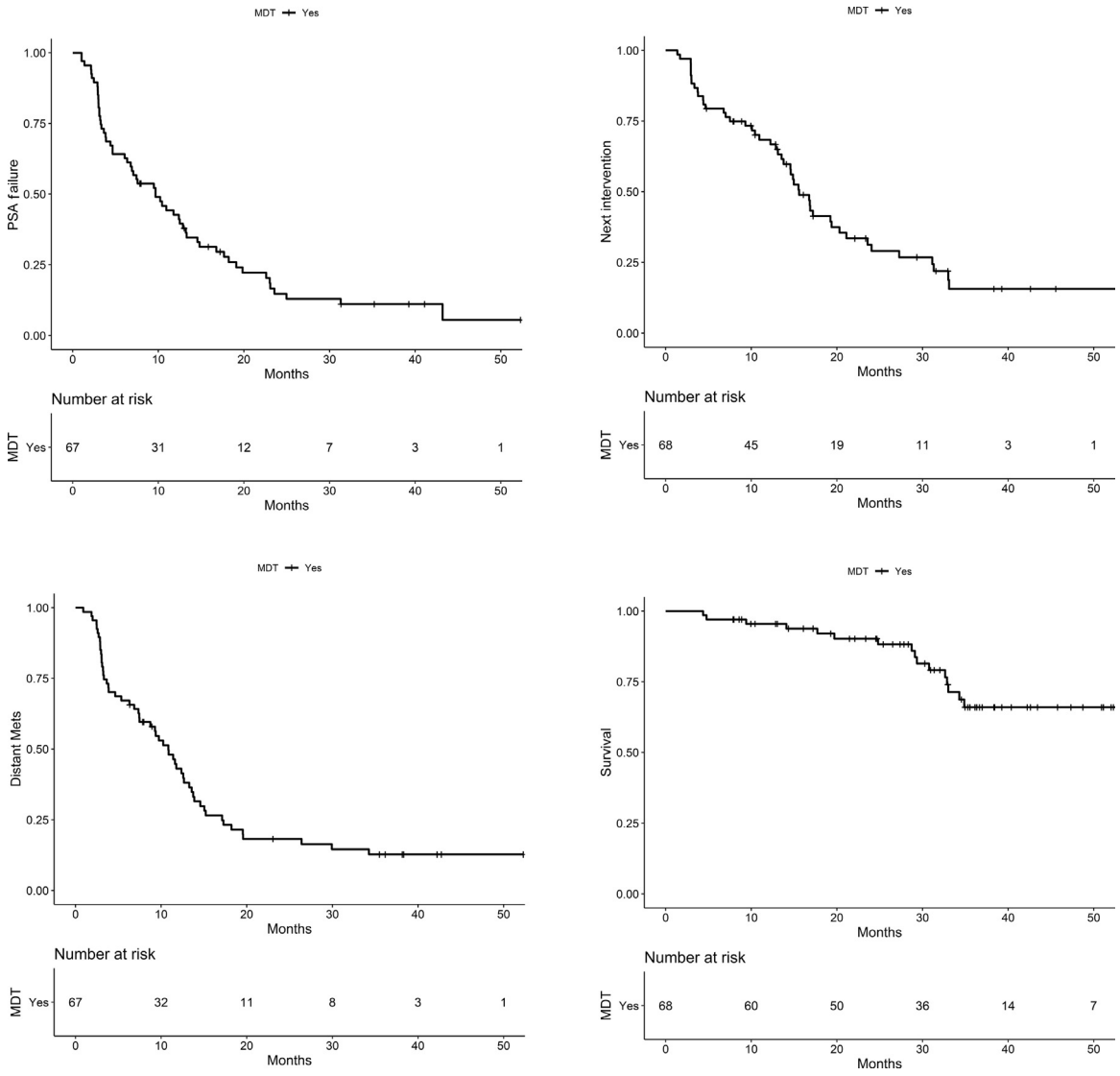

Fig. 2 – (A) PSA failure, (B) time to next intervention, (C) distant metastasis-free survival, and (D) overall survival, for the whole population. MDT = metastasis-directed therapy; Mets = metastasis; PSA = prostate-specific antigen.

Table 2 – Multiple variable analysis for factors associated with PSA failure, time to next intervention, and distant metastasis-free survival.

Covariate	Comparison	PSA failure		TTNI		DMFS	
		HR (95% CI)	*p* value	HR (95% CI)	*p* value	HR (95% CI)	*p* value
MDT alone cohort		Number of events = 57		Number of events = 47		Number of events = 55	
Number of mets at treatment		1.03 (0.92–1.14)	0.62	1.09 (0.98–1.22)	0.11	1.03 (0.92–1.14)	0.62
Number of systemic treatments		1.11 (0.97–1.28)	0.13	1.12 (0.96–1.32)	0.11	1.11 (0.97–1.28)	0.13
Pretreatment PSA		1.00 (0.98–1.02)	0.97	1.00 (0.98–1.01)	0.94	1.00 (0.98–1.02)	0.97
Imaging	Enhanced vs conventional	1.27 (0.66–2.43)	0.47	1.28 (0.65–2.54)	0.47	1.27 (0.66–2.43)	0.47
NCCN risk	High vs intermediate	0.62 (0.30–1.28)	0.20	1.12 (0.46–2.76)	0.80	0.62 (0.30–1.29)	0.20
MDT and change in sytemic therapy comparison		Number of events = 72		Number of events = 79		Number of events = 66	
MDT		0.40 (0.22–0.74)	0.003	0.35 (0.18–0.68)	0.002	0.38 (0.19–0.76)	0.01
Number of mets at treatment		1.21 (1.08–1.37)	0.001	1.17 (1.03–1.32)	0.01	1.22 (1.07–1.39)	0.002
Number of systemic treatments		1.13 (0.95–1.33)	0.17	1.08 (0.91–1.28)	0.40	1.16 (0.96–1.40)	0.12
Pretreatment PSA		1.004 (0.99–1.01)	0.38	1.01 (1.00–1.02)	0.15	1.002 (0.99–1.01)	0.61
Imaging	Enhanced vs conventional	1.55 (0.83–2.88)	0.17	1.72 (0.87–3.39)	0.12	1.35 (0.67–2.75)	0.40
NCCN risk	High vs intermediate	0.35 (0.17–0.72)	0.004	0.31 (0.15–0.64)	0.002	0.40 (0.19–0.87)	0.02

CI = confidence interval; DMFS = distant metastasis-free survival; HR =- hazard ratio; MDT = metastasis-directed therapy; NCCN = National Cancer Comprehensive Network; Num met = number of metastasis; PSA = prostate-specific antigen; TTNI = time to next intervention.
NCCN risk: this takes into account T stage, Gleason group, and initial PSA.

months were 2.10% and 13.80%, respectively. Factors associated with an increased risk of local recurrence on univariable analysis included increasing age (hazard ratio [HR] 1.07 [95% CI 1.01–1.14], $p = 0.03$) and increasing International Society of Urologic Pathologists grade group (HR 2.20 [95% CI 0.95–5.10], $p = 0.07$; Supplementary Tables 1 and 2).

Comparison to systemic agents alone

In order to assess the impact of MDT + systemic therapy relative to change in systemic therapy alone, we compared outcomes of 31 patients treated with SABR at Johns Hopkins Hospital with those of a cohort of 52 patients treated at the same institution who received a change in systemic therapy alone at the time of progression. Baseline characteristics for the two groups are detailed in Table 3.

The median time to PSA failure was longer with the addition of MDT (9.67 [6.37–17.67] vs 4.17 [3.27–9.53] months, $p = 0.07$); Fig. 3A). MDT was also associated with prolongation of TTNI (14.87 [10.93–20.30] vs 8.83 [7.47–11.20] months, $p = 0.03$) and DMFS (12.67 [10.80–19.50] vs 8.87 [5.80–14.20] months, $p = 0.05$; Fig. 3B and 3C). Two-year OS was 90.30% for those treated with MDT and 76.80% for those treated with systemic therapy only ($p = 0.46$; Fig. 3D). In order to confirm the addition of MDT in addition to change in systemic thearpy was driving the improvement in outcomes, we performed a sensitivity analysis excluding those who did not change systematic therapy at the time of MDT. These results demonstrated that the combination of MDT and change in systemic therapy compared with change in systemic therapy alone improved time to PSA failure (19.83 months [95% CI 6.90–not reached] vs 4.17 months [95% CI 3.27–9.53], $p = 0.05$), and DMFS (23.60 months [95% CI 14.60–not reached] vs 8.87 months [95% CI 5.80–14.20], $p = 0.007$), and trended towards improved TTNI (20.30 months [95% CI 7.00–not reached] vs 8.83 months [95% CI 7.47–11.20], $p = 0.079$) suggesting that the addition of MDT may improve outcomes beyond changes in systemic therapy.

Factors associated with oncologic outcomes on univariable analysis can be seen in Supplementary Tables 1 and 2. On MVA (Table 2), the use of MDT was associated with lower risks of PSA failure (HR 0.40, 95% CI 0.22–0.74, $p = 0.003$), TTNI (HR 0.35, 95% CI 0.18–0.68, $p = 0.002$), and DMFS (HR 0.38, 95% CI 0.19–0.76, $p = 0.01$). Higher number of metastases at treatment was also consistently associated with PSA failure (HR 1.21, $p = 0.001$), TTNI (HR 1.17, $p = 0.01$), and DMFS (HR 1.22, $p = 0.002$).

Discussion

Here, we report on a cohort of CRPC patients with oligoprogressive disease treated with MDT. Oncologic outcomes with regard to PSA failure, DMFS, and TTNI appear favorable, and MDT could possibly allow for continuation of current systemic therapy at progression. Additionally, when compared with a cohort of patients treated with change in systemic therapy alone, the addition of MDT appears to improve oncologic outcomes moderately.

There is great interest in integrating local therapies in the management of oligometastatic disease after several prospective trials, including POPSTAR, STOMP, and ORIOLE, demonstrated improved oncologic outcomes with MDT [13,22,23]. However, these three trials focused on castrate-sensitive OPCa, and less evidence exists for the use of SABR in oligometastatic CRPC. Triggiani et al's [24] study represents one of the largest oligoprogressive CRPC cohorts of 41 patients treated with MDT, and reported 1-year freedom from systemic therapy of 72.1% and 1-year distant PFS of 52.3%, both in line with our findings of TTNI of 68.7% and DMFS of 42.1% at 1 year. Other retrospective studies include those of Berghen et al [14], which included a cohort of 30 patients and reported median TTNI and PFS of 10

Table 3 – Baseline characteristics of groups that received and did not receive MDT.

Variable	MDT	No MDT	*p* value
	(*n* = 31)	(*n* = 52)	
Age (yr)	66 (53–84)	69.2 (41.3–85.2)	0.40
T stage[a], n (%)	2 (6.50)	2 (3.80)	0.98
T1	8 (25.80)	14 (26.90)	
T2	16 (51.60)	28 (53.80)	
T3	3 (9.70)	4 (7.70)	
T4	1 (3.20)	1 (1.90)	
Tx	1 (3.20)	3 (5.80)	
NA			
N stage[a], n (%)	20 (64.50)	34 (65.40)	0.55
N0	8 (25.80)	16 (30.80)	
N1	2 (6.50)	2 (3.80)	
Nx	1 (3.20)	0 (0)	
NA			
M stage[a], n (%)	17 (54.80)	39 (75.00)	0.11
M0	5 (16.10)	8 (15.40)	
M1	8 (25.80)	5 (9.60)	
Mx	1 (3.20)	0 (0)	
NA			
Gleason group [a], n (%)	2 (6.50)	4 (7.70)	0.53
1	2 (6.50)	3 (5.80)	
2	5 (16.10)	10 (19.20)	
3	9 (29.00)	7 (13.50)	
4	13 (41.90)	28 (53.80)	
5			
iPSA (ng/mL) [a]	9.50 (1.90–84.90)	11.5 (0.90–121.00)	0.19
Number of metastases, n (%)			0.23
1	6 (19.40)	12 (23.10)	
2	5 (16.10)	16 (30.80)	
3	6 (19.40)	11 (21.20)	
4	3 (9.70)	6 (11.50)	
5	5 (16.00)	2 (3.80)	
6	2 (6.50)	4 (7.70)	
7	1 (3.20)	1 (1.90)	
8	2 (6.50)	0 (0)	
11	1 (3.20)	0 (0)	
Number oligoprogressive lesions, n (%)	10 (32.30)	23 (44.20)	0.79
1	10 (32.30)	15 (28.80)	
2	6 (19.40)	8 (15.40)	
3	3 (9.70)	4 (7.70)	
4	2 (6.40)	2 (3.80)	
5			
Pretreatment PSA (ng/mL)	5.20 (0–95.80)	7.35 (0.10–143.90)	0.78
Progression after castrating drug, *n* (%)	31 (100)	52 (100)	
Progression after supracastrating drug, *n* (%)	18 (58.10)	17 (32.70)	0.04
Progression after chemotherapy, *n* (%)	8 (25.80)	15 (28.80)	0.96
Imaging, n (%)			0.01
Conventional	18 (58.10)	45 (86.50)	
Enhanced[b]	13 (41.90)	6 (11.50)	
NA	0 (0)	1 (1.90)	

iPSA = initial PSA; MDT = metastasis-directed therapy; NA = not applicable; PSA = prostate-specific antigen; PSMA = prostate-specific membrane antigen.
[a] At the time of initial diagnosis.
[b] Enhanced imaging included fluciclovine, choline, and prostate specific membrane antigen.

months, and Yoshida et al [15], who included a cohort of 23 patients and reported median time to PSA progression of 8.7 months. Finally, Deek et al [25] reported on a cohort of 28 men with oligoprogressive CRPC and documented biochemical PFS and TTNI of 7.2 and 12.2 months, respectively, while Moyer et al [20] reported on a cohort of 17 patients and documented distant PFS of 43% and 33% at 1 and 2 year, respectively. While retrospective evidence has demonstrated promising outcomes, prospective evaluation of MDT in oligoprogressive CRPC is still necessary.

Our study adds several important findings to the currently available literature surrounding oligoprogressive CRPC. First, our data suggest that MDT might be able to prolong the efficacy of current systemic therapy at progression, given that time to PSA failure and DMFS were similar between patients who changed and those who did not change systemic therapy at the time of MDT. Unlike metastatic HSPC, which typically follows an indolent disease course following PSA relapse [26], CRPC represents a more aggressive disease. While numerous systemic

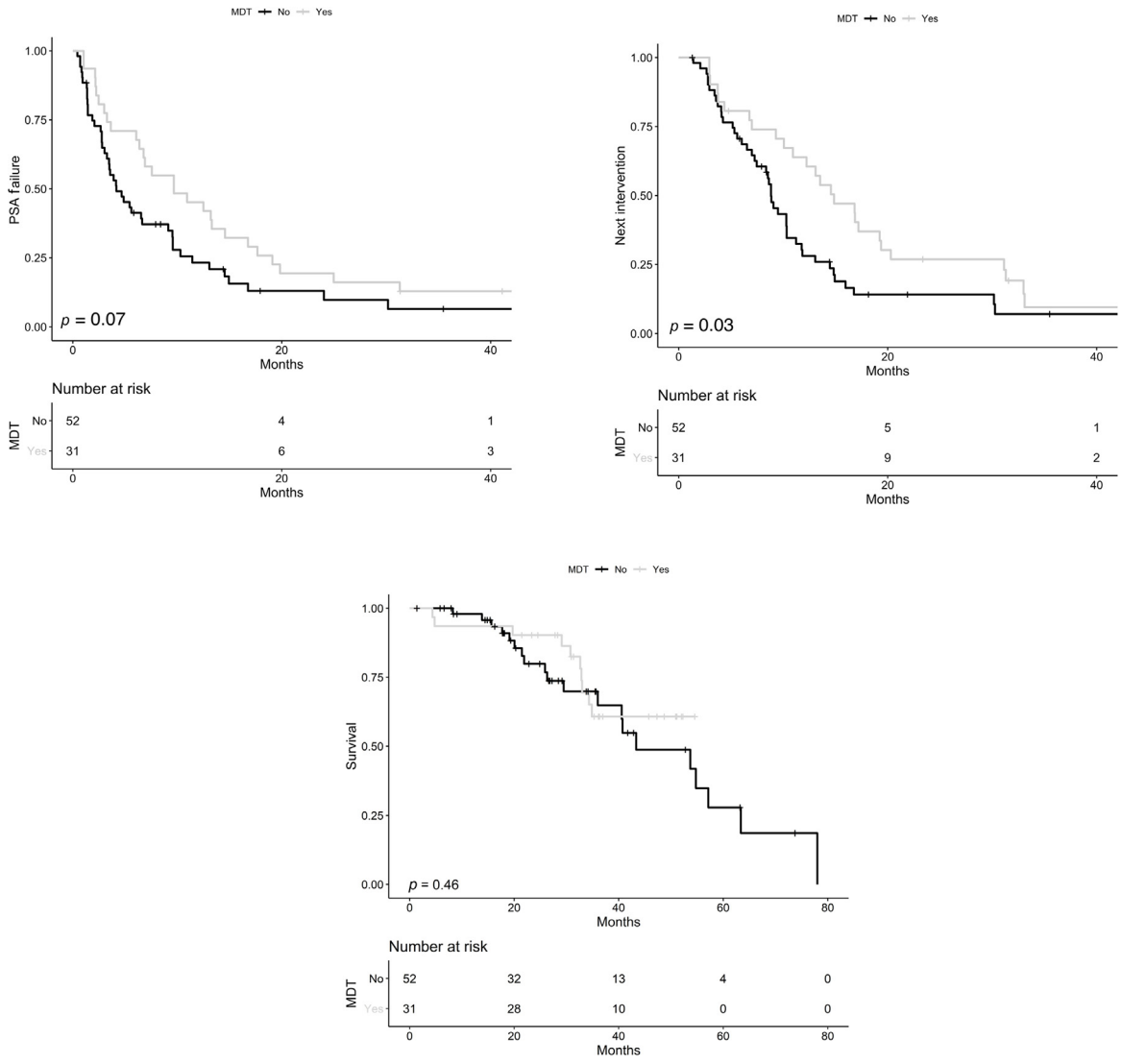

Fig. 3 – (A) PSA failure, (B) time to next intervention, (C) distant metastasis-free survival, and (D) overall survival, stratified by the use of metastasis-directed therapy. MDT = metastasis-directed therapy; Mets = metastasis; PSA = prostate-specific antigen.

therapies are approved for metastatic CRPC, the benefit seen in regard to OS is modest and PSA response rates range from 20% to 70% [4,6,7,17,18]. Therefore, when a sustained disease response occurs, continued maintenance of the systemic agent is desirable, and SABR might offer the ability to sterilize resistant clones and allow for continued prolonged periods of disease-free survival on the current systemic agent [27].

Compared with a contemporary retrospective cohort, our results suggest that the addition of MDT to change in systemic therapy at the time of oligoprogression results in modest improvements in oncologic outcomes. While comparison of retrospectively treated cohorts should be interpreted with caution, several prospective trials of oligometastatic disease demonstrated improvements in PFS and OS with the use of MDT. This raises the question of how MDT might be best integrated into the management of men with CRPC—currently the question of the ongoing phase II FORCE trial (NCT03556904) randomizing men with castrate-resistant OPCa to systemic therapy ± MDT and the DECREASE trial randomizing men to darolutamide ± MDT. Additionally, if prospectively performed trials validate the benefit of MDT in CRPC, there will also need to be efforts to identify who will most benefit from therapy. The number of metastases at progression was associated with clinical outcomes on MVA and suggests that those with low-volume disease might benefit most from local therapy, and thus advanced imaging techniques as well as blood-based biomarkers such as circulating tumor cells, circulating DNA, and immune markers might help choose patients ideal for MDT.

Our study has several limitations. First, as for any retrospective study, these findings are hypothesis generating and have to be viewed in the context of possible selection biases, such as referring healthier patients or those with fewer lesions for MDT. Therefore, prospective

testing is necessary before routine clinical use. Second, the oncologic outcomes in the group with systemic therapy alone appear to be worse than those documented in the currently available literature [4,6,7,17,18]. However, this is likely due to several differences in population including that our cohort represents more advanced disease given the median of three prior systemic agents. Additionally, the definition of progression differs between studies, with ours being an increase of 2 ng/mL and 25% above PSA nadir in comparison with the increase of 5 ng/mL [7] and 50% [9,28] above nadir used for many reports in the published literature.

Conclusions

In a retrospectively reviewed cohort of oligoprogressive CRPC patients, MDT appears to have favorable clinical results, prolongs the efficacy of current systemic therapy, and may improve outcomes over treatment with change in systemic therapies alone. Future prospective trials are needed to confirm these results.

Author contributions: Bradley J. Stish had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.
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Analysis and interpretation of data: Deek, Taparra, Phillips, Velho, Gao, Deville, Song, Greco, Carducci, Eisenberger, DeWeese, Denmeade, Pienta, Paller, Antonarakis, Olivier, Park, Tran, Stish.
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Appendix A. Supplementary data

Supplementary material related to this article can be found, in the online version, at doi:https://doi.org/10.1016/j.euo.2020.05.004.

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