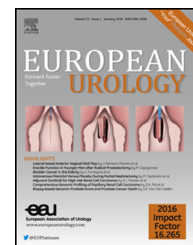


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## Platinum Priority – Brief Correspondence

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# Radical Prostatectomy in Metastatic Castration-resistant Prostate Cancer: Feasibility, Safety, and Quality of Life Outcomes

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## Abstract

Ongoing prospective studies are evaluating treatment of the primary tumor in men with de novo metastatic prostate cancer (PCa). One potential benefit is prevention of morbidity from local progression. Thus, local therapy may be best applied selectively to men with local progression once resistance to first-line therapies has occurred. Here, we gather support for the hypothesis that radical prostatectomy (RP) is safe and preserves quality of life (QOL) when applied in men with metastatic castration-resistant PCa (mCRPC). We analyzed 14 patients who underwent RP in the setting of mCRPC from 2008 to 2016. Median time from mCRPC to RP was 5.1 mo (interquartile range [IQR] 1.4–12.0). Median preoperative and <3 mo postoperative Expanded Prostate Cancer Index Composite urinary function QOL scores were 84 (IQR 70–95) and 78 (IQR 62–81), respectively. There were one Clavien Grade III, three Grade II, and one Grade I complications postoperatively. In these patients with mCRPC, RP was feasible with limited minor complications.

**Patient summary:** We report on a select group of men with metastatic castration-resistant prostate cancer who had prostatectomy. Prostatectomy is highly investigational in this setting and should not be used outside of a clinical trial other than for symptom relief.

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Ongoing clinical trials are testing the effect of local therapy in men with de novo metastatic prostate cancer (PCa). Proposed mechanisms of benefit include elimination of the immunosuppressive effect of the primary tumor, removal of a source of lethal clone reseeding and systemic release, and avoidance of local progression morbidity [1]. Signs and symptoms of local progression can decrease patients' performance status and limit candidacy for systemic therapies, impacting survival. Palliative outlet procedures

or urinary diversion may also be required. While these complications reportedly occur in 36–61% of men with de novo metastatic PCa [2], a large proportion never shows signs or symptoms of local progression. Improved systemic agents might also delay the onset of symptoms from local progression. Thus, local therapy, with its own incumbent toxicities, may be best delayed to later disease stages.

The impact of the disease state and exposure to multiple lines of systemic therapy on patients' ability to undergo

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**Table 1 – Summary of systemic therapies received in addition to LHRH agonist/antagonist prior to RP in the setting of mCRPC, treatment times, rationale for RP, and follow up**

Pt	Systemic therapy in order received prior to RP	Time from treatment start to mCRPC (mo)	Time from mCRPC to RP (mo)	PCWG2 status on restaging imaging prior to surgery <sup>a</sup>	Rationale for RP	Follow-up after RP (mo)	Status at last follow-up
1	Cabozantinib	11.3	0.9	5	NCT02113657 <sup>b</sup>	34	Alive; no significant voiding symptoms
2	None	9.5	1.6	4	NCT02113657 <sup>b</sup> ; obstructive LUTS <sup>c</sup>	36	Dead of disease; no obstruction or renal failure
3	Carboplatin/docetaxel <sup>d</sup>	4.9	6.0	4	NCT02113657 <sup>b</sup> ; urinary retention <sup>e</sup>	37	Alive; no significant voiding symptoms; pad free
4	Cabazitaxel/carboplatin; cisplatin/etoposide	2.9	18.9	5	NCT02113657 <sup>b</sup> ; gross hematuria	7	Dead of disease; no obstruction or renal failure
5	Bicalutamide; sipuleucel-T; abiraterone	16.5	20.4	4	NCT02113657 <sup>b</sup>	48	Alive; nocturia 2–3 times per night
6	Cabazitaxel/carboplatin; abiraterone	7.9	9.7	4	NCT02113657 <sup>b</sup> ; Obstructive LUTS <sup>c</sup>	17	Alive; right ureteral obstruction due to disease progression—JJ stent, 2 pads/d
7	Bicalutamide; docetaxel	17.9	0.7	4	NCT02113657 <sup>b</sup> ; Obstructive LUTS <sup>c</sup>	20	Alive; no significant voiding symptoms
8	Ketoconazole/bicalutamide; cabazitaxel/carboplatin; docetaxel	5.2	9.2	4	NCT02113657 <sup>b</sup> ; Obstructive LUTS <sup>c</sup>	7	Dead of disease; no obstruction or renal failure
9	Bicalutamide; carboplatin/docetaxel	10.0	3.3	4	AVPC <sup>f,g</sup>	70	Alive; nocturia 2 times per night
10	Axitinib	6.1	0.07	3	Multidisciplinary conference consensus <sup>g</sup>	35	Alive; no significant voiding symptoms
11	Bicalutamide; axitinib; abiraterone	7.4	4.1	4	Primary tumor progression <sup>g,h</sup>	36	Dead of disease; no obstruction or renal failure
12	Bicalutamide; ipilimumab	5.6	8.3	4	Bulky primary tumor <sup>g</sup>	25	Alive; 1 pad/d at 3 mo after operation
13	Abiraterone/enzalutamide	5.5	38	4	Long duration of response to systemic therapies <sup>g</sup>	26	Alive; no significant voiding symptoms
14	ketoconazole	2.4	1.9	4	Urinary retention <sup>e</sup>	110	Dead of disease; no obstruction or renal failure

AVPC = aggressive variant prostate cancer; LHRH = luteinizing hormone-releasing hormone; LUTS = lower urinary tract symptoms; mCRPC = metastatic castration-resistant prostate cancer; PCWG2 = Prostate Cancer Working Group 2; PSA = prostate-specific antigen; Pt = patient; RP = radical prostatectomy.

<sup>a</sup> Prostate Cancer Working Group 2 Classification: 1—locally progressing tumors and no metastatic disease; 2—rising PSA and no detectable metastatic disease (rising PSA—castrate); 3—nodal spread and no evident bone or visceral disease; 4—bone disease with or without nodal disease, and no evident visceral spread; 5—visceral metastases with or without spread at other sites.

<sup>b</sup> Consideration for enrollment in clinical trial NCT02113657 requiring successful primary tumor DNA sequencing.

<sup>c</sup> Obstructive LUTS at initial disease presentation persistence until prostatectomy without urinary retention.

<sup>d</sup> Separated by forward slash denotes concomitant treatment, separated by semicolon denotes subsequent treatment.

<sup>e</sup> Urinary retention requiring clean intermittent catheterization or suprapubic tube.

<sup>f</sup> Consolidative therapy in setting of AVPC [5].

<sup>g</sup> Clinical judgment in specific clinical setting noted.

<sup>h</sup> Rapid progression of primary tumor in setting of low-volume distant metastases.

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