

Patterns of Care and Outcomes for Non-Metastatic Prostate Cancer in the United States: Results of the CancerMPact[®] Survey 2018

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Purpose: We describe patterns of care and treatment outcomes for non-metastatic PCa (nmPCA), either hormone-sensitive or castration-resistant, in the United States of America (USA) in 2018.

Methods: A survey (CancerMPact[®]) recruited physicians nationwide to answer an online questionnaire about how they treated patients with nmPCA. Questions covered aspects of treatment at all disease stages. Board-certified urologists and oncologists with at least five years of clinical practice and who treated at least 30 PCa patients monthly were included.

Results: The survey included responses from ninety-four physicians with an average of 17.5 years of clinical practice, who had treated a combined average of 4415 patients with nmPCA per month in 2018. Approximately 40% of patients in stage I were managed with either active surveillance or observation/no therapy, decreasing to 20%, 8% and 6% in stages II, III and IV(M0), respectively. Intensity-modulated radiotherapy was favored over other radiotherapy modalities, with rates of use ranging between 60% and 69% depending on disease stage. Leuprolide as monotherapy or in combination with enzalutamide, abiraterone or bicalutamide were the most common systemic treatment options for non-metastatic hormone-sensitive PCa (nmHSPC) patients with the first or second recurrence. Only 16.5% of non-metastatic castration-resistant PCa (nmCRPC) patients did not relapse within five years of initial therapy for nmCRPC.

Conclusion: While PCa treatment recommendations are rapidly changing due to advances in treatment, we observed great concordance between their most current versions and real-world data treatment patterns reported by US physicians.

Keywords: real-world evidence, treatment, physician reported, questionnaire

Introduction

Prostate cancer (PCa) is the most common malignancy among men in the United States (USA)¹ and the second-most common worldwide.² Among men living in the USA in 2019, PCa accounted for 20% of the estimated 870,970 new diagnoses of cancer and 10% of the deaths from cancer.¹ More than 90% of PCa cases are detected in the local or locally advanced stages (stages I–IV M0).^{3,4} Advanced age is one of the strongest risk factors, with males having a 0.8% and 8.4% probability of developing PCa by age 55 and 75, respectively.⁵ African American ancestry and family history are also strong risk factors for PCa.⁴

Selection of the best treatment or care option for non-metastatic PCa is not trivial and must be based on risk stratification according to prostate specific antigen (PSA) level,

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clinical stage, digital rectal exam, Gleason score and extent of prostatic and extraprostatic involvement.^{6–10} The importance of shared decision-making, by informing patients about short- and long-term morbidity and side effects for each approach and considering their values and preferences, has been incorporated into most treatment guidelines.⁸ Radical prostatectomy, external beam radiotherapy (EBRT)/brachytherapy with or without androgen deprivation therapy (ADT) or active surveillance for selected patients are all appropriate choices for low-risk cancer. Radiotherapy with or without ADT is the preferred option for patients at intermediate risk (T2b–2c, PSA level between 10 and 20 ng/mL, and Gleason score 7).^{6,8} Radiotherapy with adjuvant ADT is also recommended for unfavorable intermediate-risk or high-risk disease; while the first group usually receives adjuvant ADT for only 6 months, it should last about 24 months in the high-risk group.^{6,8} Finally, observation and watchful waiting have been recommended for men with a life expectancy of five years or less with low or intermediate risk.^{8,10} While luteinizing hormone-releasing hormone (LHRH) agonists represent the standard systemic ADT, there have been a number of approvals in the last few years for both second-generation hormones and drug-based therapy.

Although most men with localized PCa respond to initial treatment, 20% to 50% show a rise in PSA within 10 years.¹¹ Patients are commonly asymptomatic in this stage and do not present clinical evidence of metastases.⁶ At this phase of the disease, systemic ADT is the treatment of choice for patients who are not candidates for salvage prostatectomy or salvage radiotherapy, or who have already been submitted to one of these strategies.¹² After an average time of 19 months, the disease progresses again from a hormone-sensitive to a castration-resistant state.¹³ Non-metastatic castration-resistant PCa (nmCRPC) is generally defined as PSA recurrence while on ADT in the absence of obvious metastasis obtained through conventional imaging.¹⁴

Treatment guidelines for PCa have undergone important changes in recent years, almost keeping pace with the development of new treatment strategies and molecules.^{15,16} Next-generation hormone therapies, such as enzalutamide and abiraterone, first received regulatory approvals for the treatments of relapsed /refractory metastatic CRPC patients, and later expanded their indications to non-metastatic or hormone-sensitive PCa patients. However, real-world studies investigating non-metastatic PCa treatment management are limited. The aim of this study is to describe patterns of care for non-metastatic

PCa, either hormone-sensitive or resistant to castration, in the United States.

Materials and Methods

An internal team of oncology experts at the Health Division of Kantar developed the CancerMPact[®] - Treatment Architecture – United States PCa survey. The survey is conducted annually and assesses the current clinical management of PCa patients by stage for all treatment modalities. To develop the questionnaire, the Kantar team reviewed USA PCa treatment guidelines and approvals of new drugs by the US Food and Drug Association (FDA). The Kantar team also performed a literature review of pivotal trial data from peer-reviewed medical journals and major oncology conferences to determine current practices and potential changes in PCa treatment up to 2018. We acknowledge recent changes post-2018 have occurred in treatment due to trial data and approvals in the nmCRPC setting.

Ninety-four physicians nationwide answered the online PCa survey in September 2018. Only board-certified urologists, medical oncologists, hematology oncologists and medical oncologists/ hematology oncologists with at least 5 years of clinical practice after residency, and who treated at least 30 PCa patients monthly were included in the study.

The survey included questions about the physicians' experience (such as years in practice, practice type, number of patients seen on a monthly basis) and about treatment of their PCa patients within the last six months. Physicians were explicitly asked to disregard their personal opinions and to objectively report how they treated their patients based upon their own clinical practice and experience; definitions such as for stage or castration resistance were not provided. They answered questions about treatment modalities (radiation, surgery, systemic therapy, etc.), systemic therapy regimens used for each clinical situation, and their duration. The survey covered aspects of treatment across all stages of the disease as well as response outcomes.

Another company (Lightspeed) programmed, fielded, and hosted the online questionnaire. The anonymized raw data was securely transferred to the Health Division at Kantar, which performed data analysis and tabulation. No formal statistical treatment was given to the results and data were reported as unweighted average of all responses. This work used secondary data and therefore is exempted from ethic committee approval. In this paper, we report the survey results for non-metastatic PCa only.

Results

Physicians Profile

The detailed profile of the 94 physicians who answered is shown in [Table 1](#). On average, respondents treated 68 PCa patients per month, with the total number of monthly cases reported by physicians as 6389 patients across all stages. Urology was the predominant specialty (43.6%) and private practice was the most common setting (36.7%). According to the physicians, non-metastatic PCa accounted for 69.1% of their cases [21.3%, 16.7%, 13.9%, and 17.2% of patients in stages I, II, III, and IV (M0)], while metastatic PCa [stage IV(M1)] corresponded to 30.9% of their cases. Based on these percentages and on the estimated total of 6389 PCa patients treated by the physicians each month, responding physicians saw approximately 4415 non-metastatic PCa cases per month.

Treatment of Non-Metastatic Hormone-Sensitive Prostate Cancer Initial Therapy

[Table 2](#) presents the utilization of the most common initial therapy modalities for nmHSPC in the USA, as estimated

Table 1 Characteristics of Physicians Surveyed for Prostate Cancer Treatment Patterns and Response Outcomes

Characteristics of Respondents	N/ %
Physicians surveyed (N)	94
Average number of years of practice after residency	17.5
Average number of PCa patients treated by each physician monthly	68
Board-Certified Specialty (%)	
Urology	43.6
Medical oncology	30.9
Medical oncology/hematology oncology	16.0
Hematology oncology	9.6
Practice Settings (%)	
Private practice	36.7
Oncology group practice	17.4
Hospital, general	13.3
Academic medical center	12.1
Cancer center, affiliated with a hospital	12.0
Hospital, affiliated with a medical school	4.6
Cancer center, independent	3.9
Stage of Treated Patients (%)	
I	21.3
II	16.7
III	13.9
IV(M0)	17.2
IV(M1)	30.9

Abbreviations: PCa, prostate cancer; N, number of respondents.

by the responding physicians. Around 40% of the patients in stage I were managed with either active surveillance or observation/ no therapy, with that rate decreasing to 20%, 8% and 6% in stages II, III and IV(M0), respectively. Radiotherapy-only (25.2%) and surgery-only (24.7%) were the most common modalities for stage II patients, while radiotherapy with (28.5%) or without (16.9%) systemic therapy was the main modality for stage III patients. In stage IV(M0), systemic therapy-only (56.7%), which includes hormone therapy, chemotherapy, immunotherapy, radiopharmaceuticals and other targeted therapies, was largely preferred over other treatment modalities.

Utilization of EBRT by the surveyed physicians is presented in [Table 3](#). Over two-thirds of stage I–III and over half of stage IV(M0) nmHSPC patients receiving radiotherapy were treated with Intensity Modulated Radiotherapy (IMRT).

The systemic regimens utilized as initial therapy for nmHSPC, with their respective utilization rate and average duration, are presented in [Table 4](#). LHRH analogs were the primary ADT agents used in the USA, with leuprolide as a monotherapy and combination regimens containing leuprolide and/or bicalutamide being the preferred regimens. Regimens containing the second-generation hormone therapies enzalutamide and abiraterone were more commonly used in stage IV(M0) than in earlier stages. This was also true for docetaxel.

[Table 5](#) displays response and recurrence rates by time period after first-line therapy for nmHSPC stratified by stage. Approximately 50% of patients with stage I disease, 40% with stage II disease, and approximately one-quarter of patients in stage III did not relapse within ten years of therapy. That figure was less than 10% among stage IV(M0) patients.

Regarding type of first recurrence, stage I and II patients were most likely to experience a biochemical (PSA) progression only (64.0% and 56.1% of patients, respectively) (data not shown). Metastatic recurrence was considerably more frequent among stage IV(M0) patients (41.2%) as compared to patients in stage I, II or III (13.2%, 16.2% and 24.3%, respectively). Nearly 25% of stage IV(M0) patients developed metastatic CRPC upon recurrence after receiving first-line hormone therapy. Physicians also reported the stage of first recurrence for stage I–III patients with a diagnosed local recurrence. Approximately 65% of stage I, 55% of stage II, and 43% of stage III patients recurred with localized disease within stage I–III and the remainder recurred with stage IV(M0) disease.

Table 2 Rate of Utilization of the Most Common Initial Therapy Modalities for nmHSPC, by Stage

Modality	Stage I	Stage II	Stage III	Stage IV(M0)
	N=68	N=78	N=84	N=91
Active surveillance	30.3%	12.9%	5.4%	2.2%
RT only	22.3%	25.2%	16.9%	6.1%
Surgery only	22.2%	24.7%	11.7%	2.8%
Observation/no therapy	10.0%	6.9%	2.6%	3.5%
RT, systemic therapy ^a	5.7%	12.1%	28.5%	16.1%
Systemic therapy only	3.6%	5.4%	8.3%	56.7%
HIFU only	2.2%	2.6%	2.3%	3.3%
Surgery, systemic therapy	1.4%	2.1%	6.8%	1.9%
Surgery, RT, systemic therapy	1.3%	3.4%	6.2%	4.5%
Surgery, RT	1.0%	4.7%	11.1%	2.4%
Orchiectomy only	0.0%	0.1%	0.1%	0.5%

Note: ^aSystemic therapy includes hormone therapy, chemotherapy, immunotherapy, radiopharmaceuticals, and other targeted therapies.

Abbreviations: HIFU, high-intensity focused ultrasound; N, number of respondents; RT, radiotherapy.

Table 3 Type of External Beam Radiotherapy Used in Treatment of Local and Locally Advanced Prostate Cancer, by Stage

Type of Radiotherapy	Stage I	Stage II	Stage III	Stage IV(M0)
	N=56	N=71	N=81	N=55
Intensity Modulated Radiotherapy	69.4%	68.8%	68.4%	59.8%
Stereotactic Body Radiation Therapy	11.6%	13.0%	12.7%	17.6%
Any other type of EBRT	9.9%	9.0%	9.3%	6.0%
Proton beam radiation therapy	9.2%	9.3%	9.6%	16.6%

Abbreviations: EBRT, external beam radiotherapy; N, number of respondents.

Treatment After First Recurrence

Table 6 presents the overall utilization of the most common treatment modalities for nmHSPC patients who experienced a recurrence after initial treatment, either with a rising level of PSA or a diagnosed local recurrence. At least half of patients with a recurrence received systemic therapy with or without radiotherapy regardless of the initial treatment. Active surveillance accounted for roughly 10% of patients with a recurrence who underwent radiotherapy or surgery as initial treatment.

After observation or active surveillance as the initial approach after a first recurrence, 51.1% or 65.9% of patients proceeded to receive treatment, within a mean time of 14.4 or 15.1 months under observation or active surveillance, respectively.

Table 7 displays the most common systemic regimens utilized, along with their average duration, for recurrent nmHSPC. Over 50% of patients received leuprolide with or without enzalutamide or bicalutamide at first recurrence, regardless of disease stage. More stage IV(M0) than stage I–III patients received abiraterone or enzalutamide regimens at first recurrence.

Table 8 presents the type of second recurrence by stage of disease after the first recurrence. Recurrent Stage IV(M0) patients were more likely to develop a metastatic recurrence as a second recurrence than stage I–III patients. Approximately 40% of stage I–III patients experienced a second local recurrence as stage I–III disease. The remainder of patients who had a second local recurrence experienced locally advanced, stage IV(M0) disease.

Table 9 presents the utilization of the most common treatment modalities for nmHSPC patients who had a second recurrence. Approximately 60% of stage I–III and stage IV(M0) patients received systemic therapy for the second recurrence.

The most common systemic regimens and the average duration of treatment for nmHSPC at second local recurrence, by stage, are described in **Table 10**. While many patients received traditional hormone therapies such as bicalutamide plus leuprolide or leuprolide alone, almost 35% of stage IV patients received abiraterone or enzalutamide in combination with leuprolide.

Table 4 Rate of Utilization and Duration of Systemic Therapies for Newly Diagnosed nmHSPC, by Stage

Regimen ^a	Stage I N=23		Stage II N=38		Stage III N=71		Stage IV(M0) N=85	
	Utilization (%)	Duration (Months)	Utilization (%)	Duration (Months)	Utilization (%)	Duration (Months)	Utilization (%)	Duration (Months)
	Leuprolide	39.9	23.0	35.7	20.0	35.8	26.2	22.5
Bicalutamide, leuprolide	7.0	17.8	14.6	16.6	13.8	22.2	15.6	20.2
Flutamide, goserelin	7.0	5.3	3.6	6.0	0.9	9.3	1.3	23.0
Enzalutamide, leuprolide	5.2	18.8	2.8	18.4	7.6	19.8	12.6	22.0
Bicalutamide, goserelin	5.2	7.3	0.3	7.0	2.1	15.4	1.6	24.0
Degarelix	4.1	20.8	1.5	18.8	5.6	15.5	5.1	14.2
Abiraterone, prednisone, leuprolide	3.7	7.3	4.9	8.9	5.0	9.5	9.0	21.4
Goserelin	3.5	16.0	4.2	17.8	2.6	15.6	0.6	21.0
Flutamide, leuprolide, docetaxel	3.5	5.5	0.7	6.0	0.9	5.0	0.4	6.0
Triptorelin	2.8	28.2	0.5	36.7	0.8	23.8	0.4	13.3
Bicalutamide, triptorelin	2.6	9.7	0.2	20.0	0.9	23.3	1.4	15.0
Flutamide, leuprolide	2.4	7.0	3.8	5.4	0.9	5.3	3.3	13.4
Bicalutamide, leuprolide, docetaxel	2.4	6.0	3.5	13.0	4.1	15.7	1.4	7.9
Abiraterone, prednisone, goserelin	2.2	6.0	3.7	6.7	3.2	16.3	3.0	13.0
Flutamide, triptorelin	2.0	5.5	0.7	6.0	2.1	5.3	2.4	9.7
Enzalutamide, goserelin	1.7	3.0	0.8	7.0	—	—	1.4	21.3
Bicalutamide, goserelin, docetaxel	1.1	6.0	0.8	6.3	0.6	6.0	2.7	11.2
Bicalutamide, triptorelin, docetaxel	1.1	5.0	1.2	8.0	—	—	2.3	5.3
Flutamide, goserelin, docetaxel	0.9	5.0	2.1	7.3	0.9	6.5	—	—
Enzalutamide, triptorelin	0.2	36.0	6.3	6.3	1.4	22.0	1.2	15.0
Leuprolide, docetaxel	—	—	3.3	11.0	4.1	11.1	6.1	14.5
Flutamide, triptorelin, docetaxel	—	—	1.4	5.7	0.7	10.5	1.1	21.0
Triptorelin, docetaxel	—	—	1.3	7.0	2.7	5.6	0.9	8.7
Goserelin, docetaxel	—	—	0.2	6.0	2.0	4.5	0.4	24.0

Note: ^aOnly regimens used by at least 1% of patients in one of the subgroups are shown.

Abbreviations: nmHSPC, non-metastatic hormone-sensitive prostate cancer; N, number of respondents.

Table 5 Results of Initial Therapy for nmHSPC, by Stage

Response to Therapy	Stage I, % (N=67)	Stage II, % (N=78)	Stage III, % (N=84)	Stage IV(M0), % (N=91)
Patients who did not respond to therapy (refractory)	7.7	6.5	9.0	12.4
Patients who responded but relapsed within one year of therapy	7.1	10.1	17.0	20.7
Patients who responded but relapsed between one and five years of therapy	15.0	21.3	26.6	39.7
Patients who responded but relapsed between five and 10 years of therapy	19.9	23.1	23.7	17.8
Patients who responded and did not relapse within 10 years of therapy	50.3	39.0	23.7	9.4

Abbreviations: nmHSPC, non-metastatic hormone-sensitive prostate cancer; N, number of respondents.

Table 6 Treatment Utilization by Modality Regimen and Stage Among Patients with nmHSPC Prostate Cancer Who Experienced a First Recurrence

Treatment Regimen for First Recurrence ^a	Initial Treatment		
	Definitive Radiotherapy, % (N=88)	Surgery, % (N=81)	Systemic Therapy Only, % (N=73)
Systemic therapy only ^b	53.6	49.0	61.2
RT, systemic therapy	15.2	17.6	11.3
Active Surveillance	10.4	9.7	6.8
Observation/No therapy	5.2	5.0	3.3
Surgery, systemic therapy	5.2	0.0	2.3
HIFU only	3.3	3.8	3.8
Surgery only	3.0	0.0	1.7
Surgery, RT	2.6	0.0	3.4
Surgery, RT, systemic therapy	1.0	0.0	0.2
Orchiectomy only	0.4	1.7	0.2
RT only	0.0	13.2	5.8

Notes: ^aOnly regimens used by at least 1% of patients in one of the subgroups are shown. ^bSystemic therapy includes hormone therapy, chemotherapy, immunotherapy, radiopharmaceuticals, and other targeted therapies.

Abbreviations: nmHSPC, non-metastatic hormone-sensitive prostate cancer; HIFU, high-intensity focused ultrasound; N, number of respondents; RT, radiotherapy.

Treatment of Non-Metastatic Castration-Resistant Prostate Cancer

Utilization of the most common therapy modalities for nmCRPC in the USA is described in Table 11. According to the respondent physicians, approximately 60% of nmCRPC patients received systemic therapy alone, while approximately 12% of patients remained under observation or active surveillance.

Among the patients whose disease recurred as nmCRPC and underwent observation or active surveillance, 41.1% and 56.5% eventually received treatment, respectively; mean duration of observation and active surveillance was 11.4 and 13.4 months, respectively. Physicians also estimated that 35% of their nmCRPC

patients remained untreated until they became metastatic (data not shown).

Systemic Therapy

Table 12 displays the most common regimens utilized as initial systemic therapy for nmCRPC patients in the USA, as well as their respective duration. Over 50% of patients received a second-generation hormone (enzalutamide, apalutamide) as initial therapy for nmCRPC disease.

Treatment Results

Responding physicians report that 15.5% of their patients did not respond to the initial therapy for nmCRPC (Table 13). In addition, 26.6% of patients responded but relapsed within one year of therapy and 41.3% between

Table 7 Rate of Utilization and Duration of Systemic Regimens for Recurrent nmHSPC, Stages I–III (A) and Stage IV(M0) (B)

Regimen ^a	Stage I–III Hormone Sensitive First-Local Recurrence		Stage IV(M0) Hormone Sensitive First-Local Recurrence	
	N=82		N=73	
	Utilization (%)	Duration (Months)	Utilization (%)	Duration (Months)
Leuprolide	29.9%	24.3	19.1%	20.8
Enzalutamide, leuprolide	18.0%	19.8	22.7%	19.0
Bicalutamide, leuprolide	11.9%	18.8	12.6%	17.6
Abiraterone, prednisone, leuprolide	6.8%	18.7	10.6%	16.6
Leuprolide, docetaxel	4.7%	11.0	5.6%	10.4
Enzalutamide, goserelin	3.4%	16.2	2.9%	15.6
Degarelix	3.0%	20.0	1.6%	14.5
Goserelin	2.9%	15.3	0.6%	16.5
Abiraterone, prednisone, goserelin	2.4%	18.3	3.1%	15.7
Bicalutamide, goserelin	2.1%	24.7	4.4%	12.0
Bicalutamide, leuprolide, docetaxel	1.8%	9.1	1.7%	13.6
Flutamide, goserelin	1.7%	3.3	0.9%	4.0
Flutamide, leuprolide, docetaxel	1.6%	7.3	0.5%	7.0
Bicalutamide, triptorelin	1.3%	9.5	1.4%	6.7
Flutamide, leuprolide	1.2%	8.3	2.5%	12.7
Enzalutamide, triptorelin	1.2%	12.5	1.0%	7.7
Nilutamide, leuprolide	1.0%	6.3	0.1%	9.0
Flutamide, goserelin, docetaxel	0.4%	5.0	2.9%	8.7
Triptorelin, docetaxel	0.6%	10.0	1.2%	7.5
Nilutamide, goserelin, docetaxel	0.2%	14.0	1.0%	6.0

Note: ^aOnly regimens used by at least 1% of patients in one of the subgroups are shown.

Abbreviations: nmHSPC, non-metastatic hormone-sensitive prostate cancer; N, number of respondents.

Table 8 Types of Second Recurrence for nmHSPC and Their Respective Rates, by Stage After the First Recurrence

Type of Second Recurrence	Stages I–III, % (N=84)	Stage IV(M0), % (N=75)
Biochemical recurrence only (rising PSA and/or absolute PSA levels)	35.4	22.3
Confirmed radiographic diagnosis of local recurrence but remained hormone sensitive	19.7	18.7
Confirmed radiographic diagnosis of local recurrence and became castrate-resistant	14.1	17.4
Metastatic recurrence but remained hormone sensitive	13.6	16.5
Metastatic recurrence and became castrate-resistant	17.2	25.2

Abbreviations: nmHSPC, non-metastatic hormone-sensitive prostate cancer; N, number of respondents; PSA, prostate-specific antigen.

one and five years of therapy. Only 16.5% of nmCRPC patients did not relapse within five years of initial therapy for nmCRPC. Among patients who recurred, 30.1% developed a local recurrence and 69.9% developed a metastatic recurrence; they remained non-metastatic for a mean of 17.2 months before developing metastatic CRPC.

Discussion

We report the results of a nationwide survey fielded in 2018 with USA physicians who treated non-metastatic PCa in different practice settings. The survey comprised 94 physicians who treated an estimated average of 4415 non-

metastatic patients per month. Through their responses to the survey, these physicians described their treatment patterns and response outcomes among their non-metastatic PCa patients. These data provide an updated overview of the current non-metastatic PCa treatment landscape and outcomes for both hormone-sensitive and castration-resistant patients in the USA.

Non-metastatic patients comprise about 90% of newly diagnosed prostate cancer cases, but only 70% of patients treated by physician respondents in our survey. This is likely due to early-stage patients being less likely to receive treatment upon initial diagnosis. Observation and active

Table 9 Treatment Utilization by Modality Regimen and Stage Among Patients with nmHSPC Prostate Cancer Who Experienced a Second Recurrence

Modality	Stages I–III HSPC Second-Recurrence, % (N=80)	Stage IV(M0) HSPC Second-Recurrence, % (N=66)
Systemic therapy ^a only	62.7	59.4
RT, systemic therapy	10.2	8.2
Surgery, systemic therapy	6.6	8.0
Surgery, RT	4.3	4.3
RT only	3.6	6.0
Active surveillance	3.2	3.0
Observation/no therapy	3.1	2.8
Surgery only	2.7	2.4
HIFU only	1.6	2.2
Surgery, RT, systemic therapy	1.5	3.6
Orchiectomy only	0.5	0.1

Note: ^aSystemic therapy includes hormone therapy, chemotherapy, immunotherapy, radiopharmaceuticals, and other targeted therapies.

Abbreviations: nmHSPC, non-metastatic hormone-sensitive prostate cancer; HIFU, high-intensity focused ultrasound; N, number of respondents; RT, radiotherapy.

Table 10 Rate of Utilization and Duration of Systemic Regimens at Second Local Recurrence for nmHSPC Stages I–III (A) and Stage IV (M0) (B)

Regimen ^a	Stages I–III Hormone Sensitive Second-Local Recurrence N=78		Stage IV(M0) Hormone Sensitive Second-Local Recurrence N=64	
	Utilization (%)	Duration (Months)	Utilization (%)	Duration (Months)
Enzalutamide, leuprolide	28.3%	16.0	30.7%	18.0
Abiraterone, prednisone, leuprolide	13.8%	15.4	13.4%	14.3
Bicalutamide, leuprolide	12.4%	18.6	8.6%	17.9
Leuprolide	12.0%	17.2	9.8%	17.0
Leuprolide, docetaxel	4.6%	8.8	6.5%	9.9
Enzalutamide, triptorelin	3.6%	12.3	1.8%	7.8
Degarelix	2.6%	11.0	2.2%	9.0
Bicalutamide, leuprolide, docetaxel	2.5%	11.0	4.0%	13.7
Abiraterone, prednisone, goserelin	2.1%	8.3	5.9%	7.3
Enzalutamide, goserelin	2.1%	12.3	1.3%	7.5
Bicalutamide, triptorelin	2.0%	4.7	0.7%	9.0
Triptorelin, docetaxel	1.8%	8.4	1.3%	6.0
Bicalutamide, goserelin, docetaxel	1.7%	7.4	2.8%	12.5
Flutamide, leuprolide, docetaxel	1.5%	12.0	—	—
Bicalutamide, goserelin	1.3%	36.0	—	—
Flutamide, goserelin	1.2%	4.0	1.6%	5.7
Enzalutamide	1.1%	24.0	—	—
Abiraterone, prednisone, triptorelin	1.0%	21.0	0.3%	8.0
Goserelin	0.2%	12.0	1.8%	3.8
Nilutamide, goserelin, docetaxel	0.8%	11.5	1.2%	10.0
Flutamide, triptorelin	0.3%	5.0	1.2%	4.0

Note: ^aOnly regimens used by at least 1% of patients in one of the subgroups are shown.

Abbreviations: nmHSPC, non-metastatic hormone-sensitive prostate cancer; N, number of respondents.

surveillance were the main approaches adopted by physicians in the initial management of stage I PCa (40% of patients) and the third-most common choice for the

management of stage II patients. These findings are in agreement with a retrospective analysis of the National Cancer Data Base¹⁷ and a recent nationwide study in the

Table 11 Treatment Utilization by Modality Regimen Among Patients with nmCRPC

Modality	Non-Metastatic CRPC Patients, % (N=82)
Systemic therapy ^a only	59.0
Surgery, systemic therapy	8.7
Active surveillance	7.4
RT, systemic therapy	7.1
RT only	4.8
Observation/no therapy	4.1
Surgery only	2.6
Surgery, RT	2.6
HIFU only	2.2
Surgery, RT, systemic therapy	1.3
Orchiectomy only	0.4

Note: ^aSystemic therapy includes hormone therapy, chemotherapy, immunotherapy, radiopharmaceuticals, and other targeted therapies.

Abbreviations: nmCRPC, non-metastatic castration-resistant prostate cancer; HIFU, high-intensity focused ultrasound; N, number of respondents; RT, radiotherapy.

Table 12 Rate of Utilization and Duration of Systemic Regimens Among Patients with nmCRPC

Regimen	Utilization (N=74)	No. of Months
Enzalutamide	31.1%	14.0
Apalutamide	17.2%	17.8
Abiraterone, prednisone	16.5%	13.7
Bicalutamide	11.8%	11.4
Enzalutamide, prednisone	8.0%	11.2
Investigational drug (clinical trial)	3.0%	—
Docetaxel, prednisone	2.9%	8.3
Ketoconazole, hydrocortisone	2.4%	7.9
Nilutamide	2.4%	6.2
Corticosteroid only	1.6%	7.3
Leuprolide	1.4%	24.0
Ketoconazole	1.3%	7.3

Abbreviations: nmCRPC, non-metastatic castration-resistant prostate cancer; N, number of respondents.

Netherlands.¹⁸ The former study showed that the use of observation among PCa patients with low-risk disease has consistently increased since 2004, corresponding to roughly 16% of the cases in 2004–2005 and 32% of the cases in 2012–2013, although radical prostatectomy was still the most common approach in this last period. In the Netherlands, 45% to 65% of low-risk PCa patients, depending on the age group, received no active treatment between 2005 and 2015.¹⁸ These results show a reduction in overtreatment and reflect current PCa treatment guidelines.^{8,16,19–21}

Table 13 Results of Initial Therapy for Patients with nmCRPC

Response to Therapy	Non-Metastatic CRPC Patients, % (N=94)
Patients who did not respond to therapy (refractory)	15.5
Patients who responded but relapsed within one year of therapy	26.6
Patients who responded but relapsed between one and five years of therapy	41.3
Patients who responded and did not relapse within five years of therapy	16.5

Abbreviations: nmCRPC, non-metastatic castration-resistant prostate cancer; N, number of respondents.

IMRT was largely favored by physicians over other EBRT modalities. Although IMRT is expensive, it reduces the risk of gastrointestinal toxicities, as well as the rates of salvage therapy.²² Intensity Modulated Radiotherapy is able to deliver high doses of radiation that result in durable responses while minimizing the radiation exposure to adjacent rectal and bladder tissues. Prostate cancer has been the most widely used application of IMRT, particularly because of the damage that other forms of EBRT can inflict on the pelvic region.²³

Recurrence rates and time to recurrence agreed with data obtained in retrospective and prospective studies.^{24–26} We also found that a large proportion of nmHSPC patients with a recurrence (both first and second recurrence) received a second-generation hormone therapy (abiraterone or enzalutamide) combined with leuprolide (data not shown). These second-generation hormone therapies represented the most common systemic treatment options for patients with a second recurrence and were rated among the top four regimens among patients with a first recurrence for all stage subgroups [I, II, III and IV(M0)]. More stage IV(M0) patients received abiraterone or enzalutamide regimens at first local recurrence than stage I–III. Compared to the CancerMPact survey fielded in 2017 (data not shown), there was an increase in the use of enzalutamide over bicalutamide as the combination partner with leuprolide in 2018. Current guidelines do not recommend treatment with ADT and abiraterone or enzalutamide for treatment of nmHSPC.^{8,15,19} Nevertheless, in a randomized study with 1917 men with relapsed PCa not previously treated with hormone therapy, ADT plus

abiraterone and prednisone resulted in significantly higher rates of overall and failure-free survival than ADT alone.²⁷

Regarding nmCRPC, the two most common treatments in 2018 reported by the responding physicians were enzalutamide and apalutamide, in agreement with the most recent guidelines.^{15,19} Interestingly, a study using the 2015–2017 Ipsos Global Oncology Monitor Database found that leuprolide (16%) and triptorelin (10%) were the most commonly used first nmCRPC regimens in the US.²⁸ Together these observations suggest that the real-world treatment landscape for nmCRPC is rapidly changing.

This study was subject to at least three limitations. First, because the survey respondents included only physicians with at least 5 years of clinical practice after residency and who treated at least 30 PCa patients monthly, the results may not reflect treatment practices of physicians with fewer years of practice experience or lower volume of patients. Second, these data could be subject to recall bias; however, we attempted to limit this bias by instructing survey respondents to limit their responses to patients seen in the last six months. Lastly, we did not ask physicians why they made their treatment decisions, which may limit the ability to interpret the results.

Conclusion

Results from this nationwide survey of physicians reporting on their non-metastatic PCa patients provide insights about the evolving treatment landscape for PCa and how new guidelines are incorporated into clinical practice. While PCa treatment recommendations are rapidly changing due to advances in treatment, we observed great concordance between the most recent versions and real-world data treatment patterns reported by USA physicians.

Acknowledgments

The authors would like to very much thank the entire CancerMPact team that made this work possible: Anna Boudoures, Kelly Clapp, Megan Epperson, Christina Fish, Qi Fu, Michael Gaschler, Medina Hasanagic, Sarthak Jain, Leonard Kusdra, Melissa Machado, Bhavna Murali, Knar Nersesyan, Sara Omlid, Michael Ramirez, Fadi Saadeh, Katherine Stockstill, and Cathy Su.

Disclosure

The authors declared following potential conflicts of interest with respect to the research, authorship, and/or publication of this article: All authors are employed by Kantar, a global consultancy company that acts in the healthcare market with

clients from pharmaceutical and biotechnology companies, health insurance companies and hospitals. Otavio Clark is a partner of Kantar Health Brazil, a consultancy company that produces Health Technology Assessment work for pharmaceutical companies. He has also acted as an advisory board member of different pharmaceutical companies. The authors report no other conflicts of interest in this work.

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