ORIGINAL ARTICLE

Tumour Characteristics and Real-world Treatment Patterns Among Patients Diagnosed With Metastatic Prostate Cancer in Sarawak - A 8-year Review

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ABSTRACT

Introduction: Numerous novel systemic treatments have emerged for patients with primary metastatic prostate cancer (mPC), addressing both hormone-sensitive (mHSPC) and castration-resistant prostate cancer (mCRPC). However, limited understanding exists in integrating these therapies into clinical practice. This study provides an overview of mPC, presenting baseline disease characteristics, treatment profiles, and outcomes of mPC specifically in Sarawak. **Materials and methods:** Our study focused on registered male patients diagnosed with metastatic prostate cancer at Sarawak General Hospital between 2016 and 2023, aged over 18. Surveys were carried out during routine clinical practice, covering patient demographics, clinical parameters, primary treatments, follow-up, and outcomes. The study described treatment patterns following diagnosis. **Results:** Demographic and tumor profiles of 212 patients with metastatic prostate cancer in Sarawak General Hospital from 2016- 2023 were retrospectively analyzed. Patients with mPC was notably prevalent among individuals of Chinese ethnicity, accounting for 43.4% of cases, with over 50% of patients presenting with high-volume disease irrespective of ethnicity. The primary treatment modality for the majority of mPC patients was androgen deprivation therapy (ADT) alone. Among the cohort, 19.3% (n=41) experienced disease progression to metastatic castration-resistant prostate cancer (mCRPC) since 2016. Novel hormonal therapy (NHT) emerged as the predominant first-line treatment for mCRPC, administered to 53.7% of patients. **Conclusion:** The majority of prostate cancer patients in Sarawak are diagnosed in the metastatic stage and were of high volume at diagnosis. Aggressive treatment was initiated early in an attempt to improve treatment outcomes and overall survival.
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Keywords: Metastatic prostate cancer, Androgen deprivation therapy, Novel hormonal therapy, Castration-resistant, Hormone-sensitive

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INTRODUCTION

Prostate cancer is a significant health concern in Asia, ranking fourth in incidence and eighth in cancer-related mortality (1). Disparities exist in mortality-to-incidence ratios between European and Asian countries. In 2022, Europe had 473,011 cases compared to Asia's 386,424 diagnoses, with Asia experiencing a slightly higher mortality rate of 30.3%. Among Asian nations, Malaysia, Thailand, and the Philippines had mortality-to-incidence ratios more than double those of Japan and South Korea (2). These findings highlight survival rate disparities across countries, particularly concerning metastatic prostate cancer, which carries a low 5-year survival rate of 30% (3).

Prostate cancer ranks as the third most common cancer among Malaysian men, with evidence pointing to a growing incidence. Between 2011 and 2016, there were 4,189 diagnosed cases, a significant increase from the 3,132 cases reported between 2007 and 2011. Staging data for 40.2% of cases showed that 68.6% were detected at advanced stages (III & IV), marking a rise from the previous report where late-stage cases comprised 60% of diagnoses (4).

Sarawak, the largest state in Malaysia, with its economic hub in Kuching, has witnessed a significant population increase from 2010 to 2023, reaching 2,907,500 residents. The Sarawak General Hospital in Kuching serves as the primary referral center for urology cases across the state. Despite the availability of the prostate-specific antigen (PSA) test, over half of prostate cancer cases in Sarawak are diagnosed at advanced stages (III and IV). While novel hormonal therapies (NHT) and chemotherapy have shown efficacy in metastatic prostate

cancer (mPC), their real-world application in the local population lacks contemporary data. The objective of this study was to profile metastatic prostate cancers in Sarawak, aiming to identify tumor characteristics and elucidate contemporary treatment modalities.

MATERIALS AND METHODS

Study Population and Design

Our study focused on registered male patients diagnosed with metastatic prostate cancer at Sarawak General Hospital between 2016 and 2023, aged over 18. Data collection involved a point-in-time extraction of medical chart data conducted by physicians. Surveys were carried out during routine clinical practice, covering patient demographics (such as ethnicity, age at diagnosis, Eastern Cooperative Oncology Group (ECOG) score, clinical parameters, primary treatments (ADT, chemotherapy, radiotherapy, novel agents, maximal androgen blockage (MAB)), follow-up (concluding at death or 2023-12-31), and outcomes (including PSA level after starting treatment, duration to PSA nadir, progression to CRPC, treatment in CRPC and prostate-specific antigen doubling time, PSADT). Tumor characteristics included initial prostate-specific antigen (iPSA) level at diagnosis, the International Society of Urological Pathology (ISUP) grade group (GG) of cancer, and the volume of metastasis (CHAARTED score). Prospective data was retrieved from the hospital-based patients' case notes collected at the Sarawak General Hospital Prostate Cancer Clinic.

Study treatments

First-line metastatic hormone-sensitive prostate cancer (mHSPC) treatments were described overall and stratified by treatments received in the HSPC settings. Patients were classed as either with no treatment; treated with androgen deprivation therapy only (ADT monotherapy); treated with ADT and chemotherapy (docetaxel); treated with a novel hormonal agent (NHA- abiraterone, apalutamide, or enzalutamide); treated with maximal androgen blockade (MAB – ADT+bicalutamide); or treated with ADT and radiotherapy. Next, for those patients progressed to metastatic castrate-resistance prostate cancer (mCRPC), they are treated either with ADT only; ADT and chemotherapy; or ADT and NHA.

Statistical analysis

Descriptive analysis of the data was performed using IBM SPSS Data Collection Survey Reporter Version 21 (New York, USA). A p-value of ≤0.05 in statistics was defined as significant. The utilization of systemic treatment among patients with mHSPC and those with mCRPC was explained by frequencies and proportions. The analysis was stratified based on the diagnostic period. Continuous variables were presented with median and interquartile range, while categorical variables were reported with frequency and percentage distribution.

Ethnic of the Study

The study will adhere to ethical principles as delineated in the Declaration of Helsinki and the Malaysian Good Clinical Practice Guideline. Before the commencement of any study-related activities, requisite ethical and other relevant approvals. This study is registered with the National Medical Research Registry (NMRR ID-23-00304-FXL) and has been approved by the Medical Research and Ethics Committee (MREC).

RESULTS

Patient demographics and baseline characteristics

A total of 212 patients with mPC cases were recorded between 2016 to 2023 in Sarawak General Hospital. The demographic and clinical characteristics summary is provided in Table I. The median age at diagnosis for mPC patients was 71 years (IQR 67.0-76.8). Only 7.5% of patients are diagnosed at an age below 60 years. Predominantly, the Chinese ethnicity accounted for the highest proportion of cases (43.4%), followed by Sarawak natives (32.1%), Malay (23.1%), and individuals from other races (1.4%). Most patients, regardless of ethnicity, were diagnosed with a performance status (EOCG PS) of 0 or 1. At the point of diagnosis, over half of the patients were diagnosed with a PSA level of ≥100 ng/mL. The average iPSA level across the cohort was 532.44 ng/mL (interquartile range 45.38 - 310.23, median 100 ng/mL). Approximately two-thirds of the patients were categorized within ISUP group 3, 4, and 5. Over the study period, there was a declining trend in the total number of patients diagnosed, dropping from 30.7% to 16.5% (Table I).

Table I: Patient baseline disease characteristics

Characteristics	Frequency distribution, n (%)				
	Overall (N=212)	Malay (n=49)	Chinese (n=92)	Sarawak ethnic group (n=68)	Others (n=3)
Age at diagnosis, year (median, IQR)	71 (67.0-76.8)	70.0 (66.0-76.0)	71.5 (68.0-77.0)	71.5 (67.0-76.0)	72.5 (70.0-75.0)
ECOG performance status at baseline					
0	96 (45.3)	17 (34.7)	47 (51.1)	31 (45.6)	1 (33.3)
1	67 (31.6)	16 (32.7)	30 (32.6)	19 (27.9)	2 (66.7)
2	15 (7.1)	3 (6.1)	8 (8.7)	4 (5.9)	0 (0)
3	12 (5.7)	4 (8.2)	5 (5.4)	3 (4.4)	0 (0)
4	1 (0.5)	0 (0)	0 (0)	1 (1.5)	0 (0)
Unknown	21 (9.8)	9 (18.4)	2 (2.2)	10 (14.7)	0 (0)
iPSA at diagnosis (ng/ml)					
≤20.0	20 (9.4)	2 (4.1)	9 (9.8)	9 (13.2)	0 (0)
21.0-50.0	38 (17.9)	5 (10.2)	20 (21.7)	12 (17.6)	1 (33.3)
51.0-99.0	37 (17.5)	7 (14.3)	19 (20.7)	10 (14.7)	1 (33.3)
100.0-199.0	49 (23.1)	15 (30.6)	18 (19.6)	15 (22.1)	1 (33.3)
200.0-399.0	18 (8.5)	2 (4.1)	6 (6.5)	10 (14.7)	0 (0)

CONTINUE

Table I: Patient baseline disease characteristics. (CONT.)

Character-istics	Frequency distribution, n (%)				
	Overall (N=212)	Malay (n=49)	Chinese (n=92)	Sarawak ethnic group (n=68)	Others (n=3)
iPSA at diagnosis (ng/ml)					
≥400.0	49 (23.1)	18 (36.7)	19 (20.7)	12 (17.6)	0 (0)
Unknown	1 (0.5)	0 (0)	1 (1.1)	0 (0)	0 (0)
ISUP Grade Group					
1	11 (5.2)	2 (4.1)	6 (6.5)	3 (4.4)	0 (0)
2	22 (10.4)	5 (10.2)	5 (5.4)	11 (16.2)	1 (33.3)
3	29 (13.7)	9 (18.4)	10 (10.9)	10 (14.7)	0 (0)
4	53 (25.0)	10 (20.4)	29 (31.5)	12 (17.6)	2 (66.7)
5	72 (34.0)	16 (32.7)	33 (35.9)	23 (33.8)	0 (0)
Unknown	25 (11.7)	7 (14.3)	9 (9.8)	9 (13.2)	0 (0)
Bone Scan					
Yes	162 (76.4)	41 (83.7)	69 (75.0)	49 (72.1)	3 (100)
No	50 (23.6)	8 (16.3)	23 (25.0)	19 (27.9)	0 (0)
CHAARTED Score					
High volume	112 (52.8)	32 (65.3)	48 (52.2)	31 (45.6)	1 (33.3)
Low volume	61 (28.8)	11 (22.4)	29 (31.5)	19 (27.9)	2 (66.7)
Unknown	39 (18.4)	6 (12.2)	15 (16.3)	18 (26.5)	0 (0)
Year of diagnosis					
2016-2017	65 (30.7)	12 (24.5)	27 (29.3)	24 (35.3)	2 (66.7)
2018-2019	57 (26.9)	14 (28.6)	22 (23.9)	21 (30.9)	0 (0)
2020-2021	55 (25.9)	10 (20.4)	30 (32.6)	14 (20.6)	1 (33.3)
2022-2023	35 (16.5)	13 (26.5)	13 (14.1)	9 (13.2)	0 (0)

Treatment outcomes

In the mPC patient cohort, the primary treatment approach was ADT alone, given to 56.6% of patients. A smaller portion received combination therapies, including ADT with EBRT (10.8%), abiraterone (10.4%), bicalutamide (9.9%), and docetaxel (9.0%). Apalutamide and enzalutamide were less commonly prescribed as initial treatment in hormone-sensitive state. A minority, comprising 2.4% of the cohort, opted against treatment altogether (Figure 1). In the CHAARTED dataset, around 53% of men had high-volume disease, while 29% had the low-volume disease; the status of the rest was unknown (Figure 2). About half of both high (54.5%) and low-volume (49.2%) disease patients primarily received ADT alone. Among those with high-volume disease, 18% were on ADT with NHT, mainly abiraterone, followed by ADT with chemotherapy (15%). In the low-volume disease group, 28% were treated with ADT and radiotherapy, while 12% received ADT with MAB. Less than 5% underwent ADT with chemotherapy. For patients with unidentified disease status, 90% received ADT alone, while 10% were treated with ADT and MAB. The study found a median duration to nadir of 9 months (range: 1-45 months) and a median nadir PSA of 0.58 ng/mL (interquartile range: 0.06 – 2.59 ng/mL) (Figure 3).

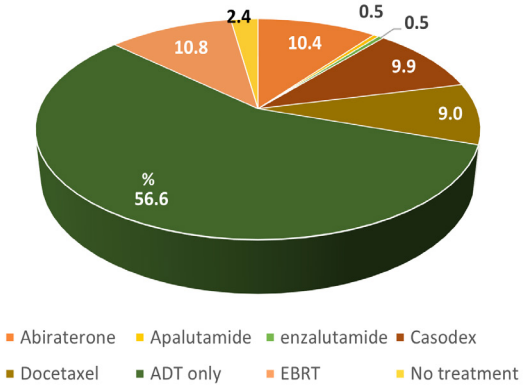

Figure 1: mHSPC treatment patterns among patients in General Hospital Sarawak.

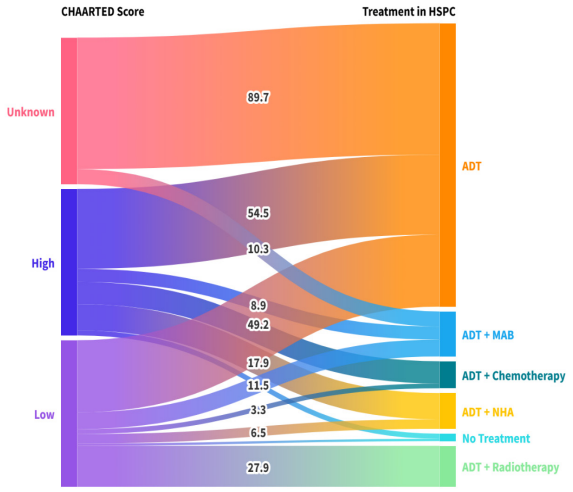

Figure 2. First-line treatment in hormone-sensitive prostate cancer (HSPC).

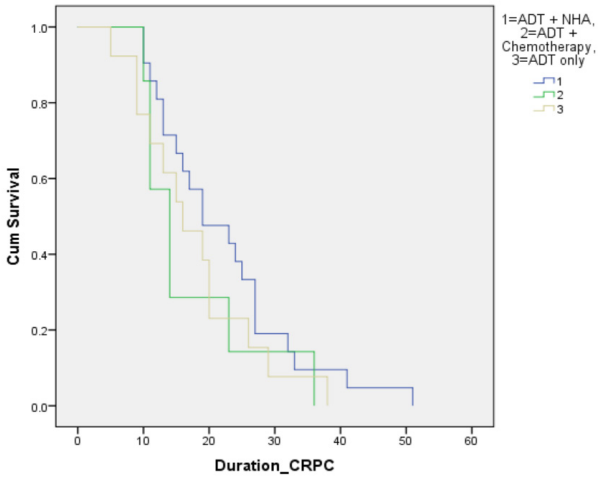

Figure 3. Overall survival with mCRPC stratified by treatment methods.

Progression to CRPC

Among patients diagnosed with mPC, 19.3% experienced disease progression to mCRPC, with a median progression period of 18.0 months. The majority of patients (73.2%) underwent first-line systemic therapy, primarily consisting of life-prolonging therapies like abiraterone, enzalutamide, and docetaxel, while the rest were treated solely with ADT. Notably, in Sarawak, NHT emerged as the predominant first-line treatment for mCRPC (50%), with abiraterone being more commonly used than enzalutamide. A minority (14.3%) received ADT in combination with chemotherapy. The remaining patients opted for ADT monotherapy (35.7%). The PSADT across all patients was 2.9 months. Over an 8-year review, Sarawak General Hospital recorded a mortality rate of about 11.9% among 42 mCRPC patients. Statistical analysis showed no significant difference in duration to mCRPC among the various treatments assessed, indicating comparable survival rates.

DISCUSSION

Prostate cancer stands as one of the most treatable cancers in men if diagnosed and early treatment is received. According to findings from the Prostate Testing for Cancer and Treatment (ProtecT) Trial, over 90% of patients with localized prostate cancer survived for a median of 10 years, regardless of the treatment methods employed (5). Past research indicates that disparities in prostate cancer awareness, understanding of PSA testing, disease prognosis, and treatment options may stem from varying levels of education, socioeconomic status, healthcare accessibility, and media exposure across different populations (6,7). Addressing these gaps in knowledge can lead to more informed decision-making and ultimately improve the overall management of prostate cancer.

This pioneering Sarawak real-world study sheds light on the prevailing patterns of care among patients diagnosed with mPC, marking a significant milestone in understanding the management of this specific population. The 2023 guidelines from the European Association of Urology (EAU), European Society for Medical Oncology (ESMO), and National Comprehensive Cancer Network (NCCN) recommend several treatment options for mHSPC, including docetaxel, abiraterone, enzalutamide, apalutamide, or localized radiation therapy directed at the prostate (8,9,10). However, in this population-based cohort, it was evident that initiation of ADT was notably utilized in the care continuum of Sarawak natives with high and low-volume diseases of mHSPC. ADT is widely used as first-line treatment in Sarawak may due to the lower total lifetime cost (11) compared to docetaxel with ADT and abiraterone plus ADT in mHSPC population, as well as tolerability and efficacy. A study investigating prostate cancer treatment patterns among multi-ethnic Asian men revealed that curative radiotherapy was the most frequently administered treatment for stage III disease. At the same time, primary androgen deprivation therapy was predominantly utilized for stage IV disease (12). It is also crucial to note that the data collection period coincided with the COVID-19 pandemic, during which some patients in this study began their mCRPC treatment in 2020. This might have influenced preferences towards oral therapies that can be self-administered at home, as opposed to treatments necessitating in-person healthcare visits, such as intravenous chemotherapy.

During the COVID-19 pandemic, efforts were made to reduce the number of outpatient visits for patients requiring injections and prostate-specific antigen (PSA) reviews. To achieve this, collaborations were established with the nearest district hospital to administer ADT injections locally, eliminating the need for patients to travel to Kuching for treatment. Patients requiring oncology referrals continued to visit Kuching, but the number of patients per clinic session was reduced. Telemedicine was implemented, allowing healthcare providers to contact patients to ensure compliance with their treatment regimens and follow-up schedules. While this approach may have resulted in fewer new prostate cancer diagnoses, care for existing patients with metastatic disease was maintained and not neglected during the pandemic.

In the year progression to mCRPC, Sarawak recorded more than half of the patients received life-prolonging NHT with abiraterone or enzalutamide, which was the most common first-line treatment in Sarawak. This trend is more marked in the later year starting 2020, compare to 2017 and 2018 where chemotherapy is the more dominant option, likely due to the growth in knowledge and evidence of NHT utilization in this patient cohort. NHT is also more easily available for clinical use in later years. In other countries such as the United States and European studies also show a similar preference for NHT over chemotherapy as the first-line treatment (13,14,15). Furthermore, it's important to acknowledge that additional treatment avenues will emerge in the future, including triple therapies, PARP inhibitors, PTEN loss therapies, immunotherapies, and lutetium PSMA. Consequently, there will be a growing demand for deeper understanding regarding the ideal treatment sequencing for patients diagnosed with mCRPC.

Certain limitations arise when the presentation of data depends on the inclination of patients who visit and adhere to hospital follow-up appointments more frequently. It's important to acknowledge that our study solely involved consulting patients with mPC at the General Hospital Sarawak. Therefore, our findings may not entirely reflect the broader population of mPC patients.

CONCLUSION

The data presented underscores a significant issue in the healthcare landscape concerning the late-stage

presentation of prostate cancer among multi-ethnics in Sarawak. The challenge of late-stage diagnosis highlights the importance of implementing evidence-based and comprehensive cancer control strategies. By prioritizing early detection and prompt intervention, the burden of advanced prostate cancer can be mitigated, leading to improved outcomes and quality of life for affected individuals in the Sarawak context.

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