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ORIGINAL ARTICLE

Treatment patterns in hormone-sensitive metastatic prostate cancer: data from a referral hospital in Bogota, real-world evidence study

Patrones de tratamiento en cáncer de próstata metastásico hormonosensible: datos de un hospital de referencia de Bogotá, estudio de evidencia del mundo real

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Abstract

Objective: *The objective of the study is to determine through a historical cohort, the characteristics, treatment patterns, and outcomes of a population with hormone-sensitive metastatic cancer at a referral center in Bogota.* **Method:** *This was a historical cohort observational study. All patients with metastatic hormone-sensitive prostate cancer from 2018 to May 2022 who received androgen deprivation therapy with or without treatment intensification were included through convenience sampling. The distribution of the epidemiological variables of interest, treatment of choice, and survival analysis was performed, as well as the distribution by years of the therapies of choice. Statistical significance was set at p < 0.05.* **Results:** *We included 125 hormone-sensitive metastatic prostate cancer (mHSPC) patients with a median age of 73.5 years (confidence interval: 71.48-75.31), a median PSA of 209 ng/mL, and 90% of patients with synchronous mHSPC. The distribution of high-volume mHSPC was 92% and M1b was 91%. The distribution of castration methods over time revealed that 21% of the patients underwent surgical castration and 79% received pharmacological castration. Since 2018, 40% of patients received androgen deprivation therapies (ADT) exclusively, 30% received treatment with taxanes, and 30% received androgen receptor axis-directed therapies. Trends in treatment distribution from 2018 to 2022 indicated a decline in exclusive ADT use from 41% in 2019 to 16% in 2022. 9% of the patients abandoned treatment.* **Conclusion:** *A description of the population of a national reference center for the treatment of hormone-sensitive prostate cancer with demographic characteristics according to global trends was provided.*

Keywords: *Prostate cancer. Androgen deprivation therapy. Combined androgen blockade. Metastatic hormone-sensitive prostate cancer.*

Resumen

Objetivo: *Caracterizar a la población y el tratamiento recibido de pacientes con cáncer metastásico hormonosensible (mHSPC) en un centro de referencia en Bogotá.* **Método:** *Cohorte histórica, observacional. Se incluyeron todos los pacientes con mHSPC que recibieron terapia de supresión androgénica, con o sin intensificación, desde el 2018 hasta mayo del 2022. Muestreo por conveniencia. Se describe la distribución de las variables epidemiológicas de interés, el tratamiento de elección, se realiza un análisis de supervivencia, así como de distribución por años de las terapias de elección. Se consideró significación estadística con un grado de significación (p) < 0,05.* **Resultados:** *Se incluyeron 125 pacientes con mHSPC, con una*

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mediana de edad de 73,5 años (IC: 71,48-75,31), con una mediana de antigeno porstático específico (PSA) de 209 ng/mL, el 90% de los pacientes con mHSPC sincrónicos. La distribución de mHSPC de alto volumen fue del 92%, M1b 91%. La distribución global en el tiempo de castración quirúrgica fue del 21% y farmacológica del 79%. El 40% de los pacientes recibieron desde el 2018 terapia de deprivación de andrógenos (ADT) exclusiva, tratamiento con taxanos el 30% y terapias dirigidas al eje del receptor de andrógenos el 30% de los pacientes. Se describen las tendencias de distribución por años desde 2018 hasta 2022, pasando de ADT exclusiva en un 41% para el 2019 a un 16% para el 2022. El 9% de los pacientes abandonaron el tratamiento. **Conclusión:** *Se realiza una descripción de la población de un centro de referencia nacional en el tratamiento de cáncer de próstata hormonosensible con características demográficas acorde a las tendencias globales.*

Palabras clave: *Cáncer de próstata. Terapia de deprivación androgénica. Bloqueo androgénico combinado. Cáncer de próstata metastásico hormonosensible.*

Introduction

Treatment for hormone-sensitive metastatic prostate cancer (mHSPC) has evolved in recent years with the addition of multiple treatment intensification options associated with androgen deprivation therapies (ADT), which were previously considered the mainstay of treatment, Treatment intensification includes taxane-containing chemotherapy and therapies that target the androgen receptor axis-directed therapies (ARATs)[1].

During the past 7 years, treatment paradigms have changed dramatically with the incorporation of four treatment lines. Beginning in 2015 and continuing through 2017, docetaxel and abiraterone emerged as viable treatment options for mHSPC based on the results of pivotal trials such as CHAARTED, LATITUDE, and STAMPEDE[2-5]. In 2018, enzalutamide and apalutamide were added into the therapeutic armamentarium following the publication of landmark trials such as ARCHES, ENZAMET, and TITAN[5-7]. Recently, primary radiotherapy has become an additional treatment option for patients with oligometastatic disease, owing to insights from the STAMPEDE trial[8]. Many ongoing trials are testing new androgen axis inhibitors, either as monotherapies or in combination, including pioneering studies involving triplet regimens.

As newer therapies targeting the androgen receptor axis have received regulatory approval relatively recently, there is few real-world data evaluating their utilization in the mHSPC landscape; hence, the purpose of this study was to determine through a historical cohort, the characteristics, treatment patterns, and outcomes of a population with mHSPC in a referral center in Bogotá. To the best of our knowledge, this is the first local study to report these data.

Materials and methods

This was a retrospective, observational study. All patients with mHSPC who were attended at the Hospital Universitario San Ignacio, a referral hospital in Bogota, Colombia, between January 2018 and May 2022 were included in our study using convenience sampling. Our study only included metastatic disease diagnosed through conventional imaging modalities (computed tomography, bone scintigraphy, or magnetic resonance imaging).

Disease volume was defined according to the CHAARTED trial; hence, high-volume disease is when the patient had more than four osseous metastases, with at least one extra-axial, or the presence of visceral metastases, with the remainder being low volume. Metachronous disease was defined when metastatic disease occurred after an initial presentation as a localized disease, having received definitive treatment and metachronous disease was defined when metastatic disease was diagnosed at the time of the initial diagnose of mHSPC.

Standard descriptive statistics were analyzed for all variables. The results are expressed as mean or median with standard deviation or interquartile range for continuous variables, depending on whether they distributed normally, and as a number of patients with percentages for categorical data. Normal distribution was assessed with the Shapiro–Wilk test. Continuous variables were assessed through analysis of variance if normally distributed or with the Kruskal–Wallis test for non-normally distributed data and discrete variables. Categorical variables were analyzed through the chi-square test.

Survival and distribution of outcome measures were estimated using the Kaplan–Meier method. Cox proportional hazard models, stratified according to risk factors, were used to estimate hazard ratios (HR) for the time-to-event endpoints. Stratified log-rank tests were used to compare the distributions of events and times among the different groups.

All statistical calculations were performed in R (Data analysis and statistical software). A $p < 0.05$ was considered significant.

Results

A total of 125 patients with mHSPC were included in this study. The baseline characteristics of our population are described in table 1. Median age was of our cohort was 73.5 years (confidence interval [CI]: 71.48-75.31), the median PSA was 209 ng/mL, and 90% of patients had synchronous mHSPC. The distribution of high-volume mHSPC was 92% and that of M1b was 91%. Of these patients, 21% underwent surgical castration and 79% received pharmacological treatment.

Table 2 and figure 1 show the changes in the percentage of patients within each treatment regimen. In 2018, 41% of patients received ADT exclusively, 30% were treated with taxanes, and 28% received ARATs. Overtime the percentage of patients receiving ADT exclusively decreased going from 41% by 2019 to 15% by 2022.

Analysis of the baseline characteristics of our population through the type of therapy received is shown in table 3. Patients who received ADT exclusively were older and had a lower disease volume. Those receiving ADT and ARAT had a lower median PSA compared to patients receiving taxane intensification therapy.

The median follow-up time was 9 months, biochemical recurrence-free survival rate was 78%, and overall survival rate was 86% (Fig. 2). The analysis of progression-free survival and time to castration resistance was significantly influenced by varying follow-up durations between the introduction of different therapies. The average time to castration resistance in patients receiving exclusive ADT was 18 months, with a 95% CI of 13.676-22.324. Calculating the time to castration resistance in other therapies is constrained due to the mean follow-up, resulting in biased estimations.

Table 1. Baseline demographic and clinical characteristics

Sample characteristics (n = 125)			
Variable	**n**	**%**	**p-value**
Age (years) mean = 73.4 SD (10.9) CI (71.489-75.311)			0.56
ECOG			
0-1	66	52.80	0.28
2-4	59	47.20	
PSA (ng/ml) mean = 529.6 CI (349.913-709.287)			0.07
Type of castration			
Pharmacological	95	76.00	0.002
Orchiectomy	27	21.60	
PSA (ng/mL) 3 months mean = 54.7 CI (37.871-71.529)			
PSA (ng/mL) 6 months mean = 23.4 CI (12.882-33.918)			
Grade group gleason (GGG)			
1	8	6.40	0.02
2	9	7.20	
3	0	0.00	
4-5	58	46.40	
cT			
≤ T2	30	24.00	0.86
> T2	70	56.00	
Tx	25	20.00	
cN			
N1	39	31.20	0.07
N0	58	46.40	
cM			
M1a	9	7.20	0.000016
M1b	91	72.80	
M1c	25	20.00	
Disease volume			
Low volume	33	26.40	< 0.00001
High volume	92	73.60	
Therapy			
ADT	50	40.00	0.096
Taxane + ADT	37	29.60	
ARAT + ADT	35	28.00	
Other	1	0.80	
Therapy discontinuation			
Yes	12	9.60	< 0.00001
No	113	90.40	
Local disease treatment			
Radical prostatectomy ± Lymphadenectomy	6	4.80	0.000116
Radiotherapy	10	8.00	
None	109	87.20	
Timing			
Synchronic	85	68.00	0.004
Metachronous	40	32.00	

CI: confidence interval; SD: standard deviation; ARAT: androgen receptor axis-directed therapies; ADT: androgen deprivation therapies.

Discussion

To the best of our knowledge, this is the first local study to publish the treatment patterns of patients with mHSPC and represents real-world evidence on the current treatment approach for patients with this condition.

Our study had several noteworthy findings, such as the increase in the usage of intensification regimens. This upward trend can be attributed to the heightened awareness among physicians regarding the efficacy of these innovative therapeutic approaches. This heightened awareness is, in turn, substantiated by a body of research that has consistently demonstrated superior survival outcomes associated with such regimens, which we could not demonstrate due to a short period of follow-up.

Three studies justify the use of chemotherapy in combination with ADT. All trials compared ADT alone as the standard treatment with ADT combined with immediate

Table 2. Therapy distribution trends

Year	Therapy	n	%
2018	ADT	1	100
	Taxane	0	0
	ARAT	0	0
	Other	0	0
2019	ADT	14	56.00
	Taxane	7	28.00
	ARAT	4	16.00
	Other	0	0.00
2020	ADT	18	43.90
	Taxane	12	29.27
	ARAT	11	26.83
	Other	0	0.00
2021	ADT	16	30.77
	Taxane	17	32.69
	ARAT	18	34.62
	Other	1	1.92
2022	ADT	1	14.29
	Taxane	0	0.00
	ARAT	6	85.71
	Other	0	0.00

ARAT: androgen receptor axis-directed therapies; ADT: androgen deprivation therapies.

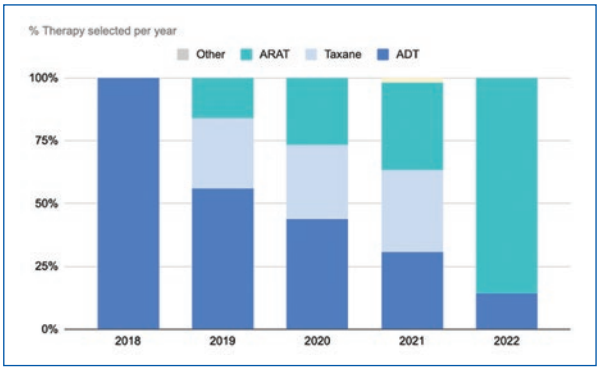

Figure 1. Selected therapy per year.

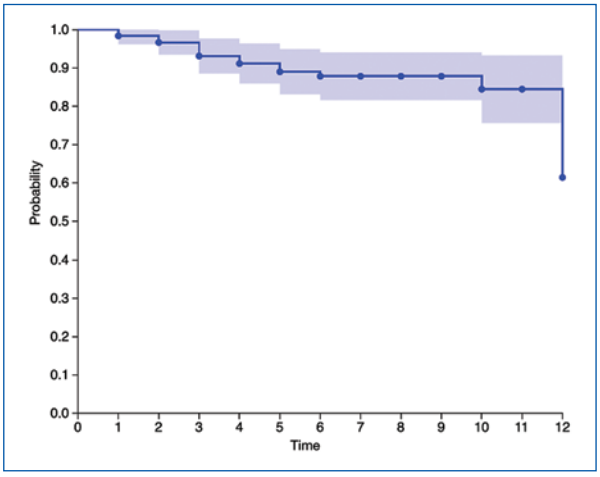

Figure 2. Survival analysis. Kaplan–Meier estimates of OS in all patients.

docetaxel (75 mg/m^2, every 3 weeks within 3 months of starting ADT); the main outcome was overall survival. The follow-up time was between 29 and 50 months. The studies independently demonstrated an improvement in the primary outcome with the addition of docetaxel. The meta-analysis of these studies showed an increase in overall survival by adding chemotherapy to ADT (HR: 0.77; 95% CI: 0.68-0.87; p < 0.0001)[9].

Representative studies on the use of abiraterone and ADT include the STAMPEDE and LATITUDE trials. The regimen was abiraterone acetate (1000 mg daily) plus prednisone (5 mg daily) during ADT in men with mHSPC. The main outcome measure was also overall survival. The two studies demonstrated an impact on overall survival for the combination in a follow-up time between 30 and 40 months[3,4].

There are two large clinical trials on the use of enzalutamide in combination with ADT, ENZAMET, and ARCHES. In ARCHES, the primary endpoint was radiological progression-free survival (rPFS), finding a benefit with an HR of 0.39 (0.3-0.5). In ENZAMET as the primary outcome, overall survival was assessed with a follow-up period of 34 months, revealing a statistically significant difference, with a HR of 0.67 (95% CI: 0.52-0.86)[5,6].

In the TITAN trial, apalutamide was used as an ARAT, with rPFS and overall survival as coprimary outcomes. rPFS with a HR of 0.48 (0.39-0.6) and overall survival at 24 months improved with the combination with a HR of 0.67 (0.51-0.89)[7].

Findings of our study are similar with those of other real-world evidence studies, where there is still a high percentage of patients exclusively receiving ADT, for example, in their study, Karim et al.[10] which carried put his study in Alberta, Canada, with data from January 2016 to 31 December 2020, also found an increase in

Table 3. Epidemiologic factors and associations

Variable	ADT (n = 50)	0 (%)	Taxane (n = 37)	37 (%)	ARAT (n = 35)	35 (%)	p-value	Two groups comparison P value
Age (mean, IC)	78.3 (74.946-81.654)		69.2 (67.00-71.391)		70.7 (67.321-74.079)		0.56	ARAT versus Taxane P = 0.127 ARAT versus ADT P = 0.006 Taxane versus ADT P ≤ 0.00001
ECOG 0-1 2-4	 44 6	 88 12	 33 3	 89 8	 32 3	 91 9	0.23	ARAT versus Taxane P = 0.15 ARAT vs ADT P = 0.15 Taxane versus ADT P = 0.92
PSA (ng/mL)	309 (164.889-453.711)		656 (243.241-1,068.7)		4067 (2,067-10,302)		0.3	
Type of castration Pharmacological Orchiectomy	 39 8	 78 16	 23 11	 62 30	 26 8	 74 23	0.15	
PSA (ng/mL) 3 months	38.8 (19.92-57.676)		80.9 (39.249-122.551)		42.2 (20.866-63.9)		0.12	
PSA (ng/mL) 6 months	15.2 (6.635-23.765)		35.4 (8.374-62.4)		16.5 (3.248-29.7)		0.001	ARAT versus Taxane = 0.00092 ARAT vs ADT P = 0.32 Taxane versus ADT P = 0.01
Grade group Gleason (GGG) mean	4		4		4			
cT ≤ T2 > T2 Tx	 13 26 12	 26 52 24	 23 7 7	 62 19 19	 6 10 19	 17 29 54	0.99	
cN N1 N0	 21 18	 57 49	 14 7	 67 33	 17 10	 63 37	0.49	
cM M1a M1b M1c Brain metastasis Hepatic metastasis Lung metastasis	 4 36 10 0 2 5	 8 72 26 0 4 10	 0 29 8 0 4 7	 0 78 22 0 11 19	 5 24 6 0 2 4	 14 69 17 0 6 11	0.44	
Metastatic disease volume Low volume High volume	 21 29	 42 58	 0 37	 0 100	 12 23	 34 66	0.002	ARAT versus Taxane = 0.013 ARAT versus ADT P = 0.49 Taxane versus ADT P = 0.00093

(Continues)

Table 3. Epidemiologic factors and associations *(continued)*

Variable	ADT (n = 50)	0 (%)	Taxane (n = 37)	37 (%)	ARAT (n = 35)	35 (%)	p-value	Two groups comparison P value
Therapy discontinuation								
Yes	2	4	6	6	3	9	0.53	
No	39	78	28	76	30	86		
Localized disease treatment								
Radical prostatectomy ± Lymphadenectomy	4	8	1	3	1	3	0.39	
RT	5	10	0	0	5	14		
None	45	90	36	97	30	86		
Temporality								
Synchronous	29	58	28	76	26	74	0.89	
Metachronous	4	8	1	3	3	9		
% overall mortality	10	20	5	14	2	6	0.64	
Overall survival (months) OS	40	80	32	86	33	94		

ARAT: androgen receptor axis-directed therapies; ADT: androgen deprivation therapies.

the usage of intensification regimens, that patients who received ADT exclusively were older and had a lower PSA compared to those treated with intensification therapies. Leith et al. who carried out the largest real-world evidence study which included data from seven countries also found an increase in the usage of intensification regimens[11].

It should be noted that there is an important proportion of patient that still receives ADT exclusively as their main therapy; in some patients, this is driven by their physical status, compliance, tolerance to adverse events, and the balance of impact on quality of life versus overall survival, which is an important factor when choosing or not an intensification therapy as showed in other real-world evidence studies. The reasons for exclusive ADT were listed in relation to poor functional status, compliance problems, and probability of adverse events. These results were consistent with those of our cohort[11,12].

Our study has some limitations, first, this is a retrospective study carried out in only one health institution, and second all data was collected from previous medical records, which may not include all of the relevant information or could contain mistakes that could have led to misinterpretation.

Conclusion

A description of the population of a national reference center for the treatment of hormone-sensitive prostate cancer was made included its demographic characteristics according to global trends. This is the first study of its kind in the local context.

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Conflicts of interest

The authors declare no conflicts of interest.

Availability of data and material

The authors declare data transparency.

Ethical disclosures

Protection of human and animal subjects. The authors declare that no experiments were performed on humans or animals for this study.

Confidentiality of data. The authors declare that they have followed the protocols of their work center on the publication of patient data.

Right to privacy and informed consent. The authors have obtained approval from the Ethics Committee for analysis and publication of routinely acquired clinical data and informed consent was not required for this retrospective observational study.

Use of artificial intelligence for generating text. The authors declare that they have not used any type of generative artificial intelligence for the writing of this manuscript nor for the creation of images, graphics, tables, or their corresponding captions.

Ethics

This study is classified as non-risk not necessary to request informed consent; also an institutional review board number was not required due to the observational and retrospective nature of the study.

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