Real-World Treatment Patterns in Metastatic Hormone-Sensitive Prostate Cancer (mHSPC) Patients in the US, Germany, France, China, and Japan

P.J. Goebell¹, R. Shah², R. Raina², S. Rege², S.L. Chen³, J. Partridge³, A.R. Waldeck³

¹Division of Urology, University Hospital Erlangen, Erlangen, Germany, ²OPEN Health Evidence and Access, Bethesda, MD, USA, ³Bayer Healthcare Pharmaceuticals, Whippany, NJ, USA

BACKGROUND AND OBJECTIVES

- Prostate cancer (PC) is the second-most commonly occurring cancer in men and a leading cause of cancer-related mortality.
- Metastatic PC disease which is responsive to surgical or medical castration with luteinizing hormone-releasing hormone (LHRH) agonists/ antagonists, is characterized as metastatic hormonesensitive PC (mHSPC).²
- Other than LHRH agonists/antagonists, first-generation antiandrogens such as bicalutamide have been shown to provide a small survival benefit.³
- · Second-generation androgen receptor inhibitors (SGARIs) are the most recent class of agents rapidly gaining approval and reimbursement, thereby expanding the set of mHSPC treatment options and paving the way for treatment landscape evolution.
- US and international prostate cancer treatment guidelines have recommended various combination therapy regimens using an LHRH agonist/antagonist together with an SGARI, or androgen synthesis inhibitor (ASI), or chemotherapy (docetaxel), as standard of care options for mHSPC treatment. These guidelines are undergoing updates as new treatments and evidence become available.⁴⁻⁷
- The objective of this study was to describe mHSPC patients' current treatment patterns. contextualized by their demographic and clinical characteristics and treating physicians characteristics, under respective healthcare systems in the US, Germany, France, China, and Japan.

METHODS

Study Design

Observational, retrospective, cohort study.

Data Source

- The study is based on IPSOS Global Oncology Monitor Database (GOMD) comprising physicianprovided answers about their patient charts.
- The data is collected through a standard questionnaire fielded by IPSOS on a quarterly basis and compiled to form semi-annual data cross-sections.
- The study included cross-sectional data from January 2018 to June 2020.

Study Population

Inclusion criteria

- Country of origin: US, Germany, France, China, or Japan
- Age ≥ 18 years
- mHSPC disease as determined through a combination of 2 questionnaire fields: 1) Current patient status = "Metastases"; 2) Whether patient considered hormone refractory/castrate resistant = "No".
- Exclusion criteria
- Diagnosis of any other primary cancer during the study period.
- Sample sizes
 - Total N=6,198 mHSPC patients (US, N= 3,893; Germany, N= 867; France, N= 513; China, N= 284; Japan, N=641)

Operational Definitions for Drug Classes

• **Table 1** presents the operational definitions for each drug class.

Statistical Analysis

- Descriptive statistics were used to assess demographic, clinical, and current treatment patterns for mHSPC patients, along with characteristics of their treating physicians
- For categorical variables, frequency and percentage distributions were reported.
- For continuous variables and for ordinal scaled variables, mean, standard deviation, median, and ranges (IQR) were reported.

Table 1. Operational Definitions for Drug Classes

Drug Class	Individual Drugs				
LHRH Agonist	Leuprolide, goserelin, histrelin, triptorelin, buserelin				
FGARIS	Bicalutamide, nilutamide, flutamide				
ASI	Abiraterone				
LHRH Antagonist	Degarelix				
Taxane Chemotherapy	Docetaxel, paclitaxel, cabazitaxel				
Other Chemotherapy	Carboplatin, estramustine, 5-fluorouracil, cisplatin cyclophosphamide, oxaliplatin, etoposide, vincristine liposomal irinotecan, PEG-liposomal doxorubicin, gemcitabine, mitoxantrone, vinorelbine, capecitabine, tegafur + uracil				
SGARIs	Enzalutamide, apalutamide, darolutamide				

RESULTS

Sociodemographic and Clinical Characteristics

- baseline health status.

- unavailable.

Table 2. Demographic and Clinical Characteristics of mHSPC Patients

Age group
Race
Concomitant conditions
ECOG Score category
Metastatic site
Bone symptom status
Gleason Score

category
category

Patient comanagement

Treating physician specialty

^aOther metastatic sites i

• A total of 6,198 mHSPC patients were included in the study (Table 2).

• Within each of the five countries, patients were predominantly aged \geq 70 years (67.0%-80.3%) with Gleason Scores in either the 8-10 or 7 ranges. Within each of the countries, a large majority of patients had metastatic disease within the bone (69.0%-84.2%) that was either asymptomatic or mildly symptomatic.

• Patients were largely well-functioning with ECOG score 0-1 (59.2%-90.6%). The top-most common comorbid conditions were consistently hypertension (40.2%-63.1%), followed by either cardiovascular disease (Germany: 33.6%; France: 31.0%; US: 29.9%) or diabetes (China: 32.0%; Japan: 16.8%). Percentage of patients with no comorbidities varied across countries, ranging from 35.1% in Japan to 10.1% in the US, indicating differences in

The US, German, and French cohorts had similarities in age, baseline health and ECOG functioning, disease severity and spread, and generally no to mild bone symptomaticity.

 The Japanese cohort differed in tending to be older, and having fewer concomitant conditions and better functioning, but severer disease based on Gleason scores. The Chinese cohort also had relatively fewer concomitant conditions but simultaneously worse functioning, and greater bone disease symptomaticity.

Patients tended to mostly be treated by urologists (73.9%- 99.4%) except in the US where a slight majority were treated by oncologists (56.3%). Patients were mostly not co-managed in all countries except Japan where data was

	US	Germany	France	China	Japan
	(N = 3893)	(N = 867)	(N = 513)	(N = 284)	(N = 641)
Below 50	0.7%	0.9%	0.2%	1.1%	0.2%
50-69	31.9%	32.1%	23.6%	28.9%	19.5%
70 and above	67.4%	67.0%	76.2%	70.1%	80.3%
Asian	2.4%	0.5%	0.8%	0.0%	100.0%
Black	24.3%	0.2%	3.5%	0.0%	0.0%
Hispanic/ Latino	9.3%	0.2%	0.2%	0.0%	0.0%
Native American	0.8%	0.0%	0.0%	0.0%	0.0%
White	62.8%	86.3%	81.7%	0.0%	0.0%
Other	0.4%	12.8%	13.8%	0.0%	0.0%
Unknown	0.0%	0.0%	0.0%	100.0%	0.0%
Hypertension	63.1%	46.3%	61.8%	54.6%	40.2%
Cardiovascular disease	29.9%	33.6%	31.0%	16.9%	12.8%
Diabetes	25.8%	20.8%	28.8%	32.0%	16.8%
Other	8.4%	18.3%	19.3%	23.6%	5.3%
Pulmonary disorder	13.0%	7.3%	10.1%	12.3%	3.7%
Renal dysfunction	9.3%	8.4%	13.3%	3.5%	5.6%
Obesity	8.4%	15.6%	4.7%	1.4%	0.0%
Depression	5.4%	3.7%	12.3%	0.0%	1.9%
Thyroid disorder	4.9%	3.9%	7.6%	1.1%	0.5%
Dementia	3.0%	3.5%	6.0%	1.1%	6.9%
Liver dysfunction	2.4%	2.5%	2.9%	1.8%	2.3%
Autoimmune disorder	0.7%	0.5%	0.8%	0.4%	0.3%
None	10.1%	14.0%	11.3%	23.2%	35.1%
0-1	84.0%	85.2%	78.6%	59.2%	90.6%
2-3	15.5%	14.6%	21.4%	38.0%	5.6%
3+	0.1%	0.0%	0.0%	2.8%	0.3%
Bone	81.0%	83.9%	83.4%	84.2%	69.0%
Lymph	27.1%	29.4%	55.6%	28.2%	15.9%
Other ^a	7.1%	13.5%	2.5%	0.7%	1.7%
Lung	4.5%	6.9%	2.3%	8.8%	4.4%
Liver	2.2%	2.9%	3.7%	2.1%	0.3%
Brain	0.3%	0.1%	0.0%	0.7%	0.0%
Asymptomatic	47.9%	38.6%	50.9%	39.8%	48.4%
Mildly symptomatic	34.6%	40.8%	24.8%	18.7%	10.1%
Symptomatic	11.3%	12.1%	15.0%	31.7%	8.6%
Missing	6.2%	8.4%	9.4%	9.9%	32.9%
2-6	8.4%	3.3%	10.5%	15.5%	2.8%
7	26.4%	32.4%	39.0%	26.4%	13.7%
8-10	54.2%	59.5%	49.7%	52.8%	79.3%
Missing	7.6%	0.0%	0.0%	1.8%	0.0%
Yes	10.7%	17.1%	29.6%	12.0%	0.0%
No	86.6%	82.9%	70.4%	61.6%	0.0%
Missing	2.7%	0.0%	0.0%	26.4%	100.0%
Urology	42.5%	92.7%	73.9%	80.3%	99.4%
Oncology	56.3%	7.3%	26.1%	15.1%	0.0%
Others	1.2%	0.0%	0.0%	4.6%	0.6%





FGARI: First-generation androgen receptor inhibitor; LHRH: Luteinizing hormone-releasing hormone; SGARI: Second-generation androgen receptor inhibitor; ASI: Androgen synthesis inhibitor; mHSPC: Metastatic hormone- sensitive prostate cancer

RESULTS (CONTINUED)

mHSPC Treatment Patterns

U.S.

- As compared to other countries, the US reported the highest use of SGARI combination therapy with other agents (5.9%) and was tied with Germany in reporting highest use of SGARI monotherapy (1.5%).
- Taxane chemotherapy and ASI (Abiraterone) were relatively prevalent.

German

- As compared to US, Germany reported a lower use of SGARI combination therapy (3.9%) and was tied with the US in the highest use of SGARI monotherapy (1.5%).
- As compared to other countries, Germany reported the highest use of taxane chemotherapy, with relatively frequent ASI use as well.

France

- SGARI combination therapy use was reported in 1.9% of the patients, while SGARI monotherapy use was reported in 0.6% of the patients
- France reported relatively high use of taxane chemotherapy and ASI.

China

- Differing from US and EU countries but alike to Japan, the majority of patients in China were treated with combination therapy (67.3%).
- No SGARI combination therapy or monotherapy use was reported in China.
- Taxane chemotherapy and ASI chemotherapy use were relatively frequent.

- Like in China and unlike in US and EU countries, the majority of patients were treated with combination therapy (74.6%).
- SGARI combination therapy use was reported in 0.6% of the patients. No SGARI monotherapy use was reported in Japan
- No taxane chemotherapy use was reported in Japan.

DISCUSSION

- The mHSPC treatment landscape is rapidly evolving with recent regulatory approvals and reimbursement, particularly for SGARIs. This is critical context for this retrospective observational study which as such, provides a specific snapshot in time.
- Specifically, the Jan 2018 Jun 2020 study period spans a time during which, in the US, SGARI regulatory approvals and reimbursement have come about. Thus, even for the US where the study found SGARI use to be relatively high among the five markets, utilization patterns may be anticipated to evolve significantly.
- The results of the current analysis are consistent, however, with previous literature, which found a lower utilization of intensified treatments among US patients with mHSPC.^{8,9}
- In the EU, regulatory approvals for SGARIs in mHSPC were granted fairly recently (early 2020 onward) with reimbursement granted subsequently or still under review by market, contributing to the low utilization rates observed in the study.
- In China, regulatory approval for mHSPC has been granted for only one SGARI. timing of which fell outside of the study window (later in 2020), and national reimbursement existed for neither, contributing to the observation of no SGARI
- · In Japan, where SGARIs and chemotherapy currently have different indications, treatment patterns indeed reflect this more unique situation, with no chemotherapy use for mHSPC observed yet within this study.
- Findings of high rates of monotherapy and specific combination regimens show inconsistency with guidelines which recommend combination therapies, including chemotherapy (docetaxel) or an SGARI with an LHRH agonist/antagonist, as standard of care options.⁴⁻⁷ However, in a rapidly evolving treatment landscape, it is not unusual to observe real-world utilization patterns to trail guidelines.
- Future studies are needed to monitor how these real-world treatment patterns evolve over time as market uptake of newer agents increase over time and utilization catches up with guideline recommendations.

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CONCLUSIONS

- This is the first real world study to examine treatment pattern among mHSPC patients, across the US, Germany, France, China, and Japan.
- The US, German, and French cohorts were similar in terms of age, baseline health and ECOG functioning, as well as disease severity and bone symptom status, but differed in terms of treating physician specialty mix and extent of co-management. The Chinese and Japanese cohorts tended to have fewer concomitant conditions and more severe disease, manifesting itself, however, in different ways, and was cared for by different physician specialties
- Despite mHSPC being subject to evolving approvals, reimbursement and treatment guidelines, some general conclusions emerged:
- (1) (Taxane) chemotherapy utilization reflected that it is, and remains, an important component of mHSPC standard of care in the US, Germany, France, and China, with further changes anticipated in Japan.
- (2) Abiraterone (ASI) therapy was also relatively prevalent, and with continued treatment evolution, it will be of interest to understand its potentially evolving place in mHSPC therapy
- (3) SGARI utilization, as of yet, was in the single-digits, but may be anticipated to increase, given strong evidence of the respective clinical trials as well as the recency of regulatory and reimbursement approvals.
- Lastly, our study shows the importance of patient-individualized therapy; a total of 196 different regimens (drug combinations) were observed, including treatment intensification with doublet therapies. While triplet therapy was observed, it was, as of yet, <1% across countries.
- Studies of the SGARI, darolutamide, in mHSPC have yet to read out.

STUDY LIMITATIONS

- mHSPC clinical diagnosis in the IPSOS GOMD data is physician-adjudicated and may therefore not follow a standardized set of diagnostic criteria across countries.
- This study is cross-sectional in nature, and thus cannot assess changes in treatments, for a given cohort, prescribe over time.

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DISCLOSURE

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