

Lack of Concordance between Real-World Treatment Patterns and Clinical Guideline Recommendations for Metastatic Hormone-Sensitive Prostate Cancer (mHSPC) Patients

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BACKGROUND AND OBJECTIVES

- Prostate cancer (PC) is a leading cause of cancer-related mortality in men.¹
- Androgen deprivation therapy (ADT) using a luteinizing hormone-releasing hormone (LHRH) agonist/antagonist has been the cornerstone of systemic treatment for metastatic hormone sensitive prostate cancer (mHSPC) since the 1940s. Addition of an androgen receptor inhibitor (ARI) (e.g., bicalutamide) to ADT followed, but has remained controversial in terms of clinical utility.²
- Recently updated country-specific and international PC treatment guidelines recommend combining ADT with chemotherapy (docetaxel), or an androgen synthesis inhibitor (ASI) (abiraterone), or a novel androgen receptor inhibitor (nARI) (apalutamide, enzalutamide), as standard of care options for mHSPC.³⁻⁷
- The objective of this study was to evaluate global real-world mHSPC patient characteristics, treatment patterns, and concordance with treatment guidelines.

METHODS

Study Design

- This was a retrospective, real-world data analysis of mHSPC patients using IPSOS Global Oncology Monitor Database (GOMD) from January 2018 to June 2020.
- GOMD is a validated syndicated oncology patient record database composed of physician responses about their patients from periodically-fielded surveys.

Study Population

- 6,198 mHSPC patients from US (N = 3,893), Germany (N = 867), France (N = 513), China (N = 284), and Japan (N = 641) were included.
- 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 is considered hormone refractory/castrate resistant = "No".
- Exclusion criteria**
 - Diagnosis of any other primary cancer during the study period

Statistical Analysis

- Descriptive analysis assessed the treatment patterns and patient characteristics.

RESULTS

Global Patient Sociodemographic and Clinical Characteristics

- The 6,198 mHSPC patients included in the study were predominantly aged 70 years and older (67.0%-80.3%). Within each of the five countries, patients had higher-grade prostate cancer with Gleason scores 8-10 (49.7%-79.3%) and metastatic disease within the bone (69.0%-84.2%). Patients were largely well-functioning with ECOG scores 0-1 (59.2%-90.6%). Hypertension was the most common comorbidity (40.2%-63.1%).

RESULTS (CONTINUED)

Global mHSPC Treatment Patterns

- Among all drug classes, LHRH agonists (78.4%) were most frequently prescribed in Western countries (69.4%-82.6%), while ARIs were most frequently prescribed in Eastern countries (70.8%-74.6%) (Fig. 1).
- Among monotherapies, ADT (20.3%-58.1%) use was highest in all countries except China where ARI (15.5%) use was highest (Fig. 2).
- The most-used combination therapies varied for Western countries (US: abiraterone + ADT (13.7%) and ARI + ADT (13.7%) split, Germany: docetaxel + ADT (11.2%), and France: abiraterone + ADT (17.9%); and was ARI + ADT (54.6-67.2%) for Eastern countries (Fig. 3).

U.S.

- Among all drug classes, LHRH agonists (82.6%) were most frequently prescribed followed by ARIs (15.8%) and ASI (15.5%).
- Among monotherapies, ADT (53.9%) was most-used.
- Among combination therapies, abiraterone + ADT (13.7%) and ARI + ADT (13.7%) were most-used.

Germany

- Among all drug classes, LHRH agonists (69.4%) were most frequently prescribed followed by LHRH antagonists (19.6%).
- Among monotherapies, ADT (58.1%) was most-used both within Germany and as compared to other countries.
- Among combination therapies, docetaxel + ADT (11.2%) was most-used.

France

- Among all drug classes, LHRH agonists (76.6%) were most frequently prescribed followed by ASI (19.5%).
- Among monotherapies, ADT (53.4%) was most-used.
- Among combination therapies, abiraterone + ADT (17.9%) was most-used.

China

- Unlike in Western countries but like in Japan, the most frequently prescribed drug class in China was ARIs (74.6%) followed by LHRH agonists (71.8%).
- Among monotherapies, ARIs (15.5%) were most-used.
- Among combination therapies, ARI + ADT (54.6%) was most-used.

Japan

- Like in China, the most frequently prescribed drug class in Japan was ARIs (70.8%) followed by LHRH agonists (69.7%).
- Among monotherapies, ADT (20.3%) was most-used.
- Among combination therapies, ARI + ADT (67.2%) was most-used both within Japan and as compared to other countries.

Figure 1. Guideline-Relevant mHSPC Drug Classes (% Utilization)

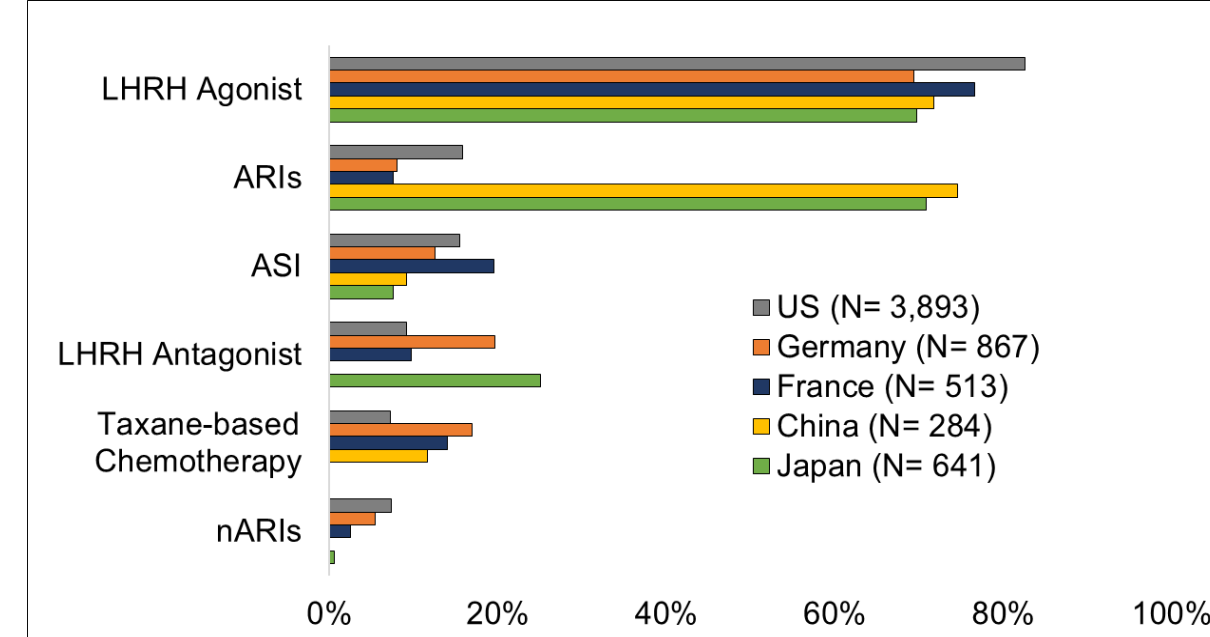


Figure 2. mHSPC Monotherapies (% Utilization)

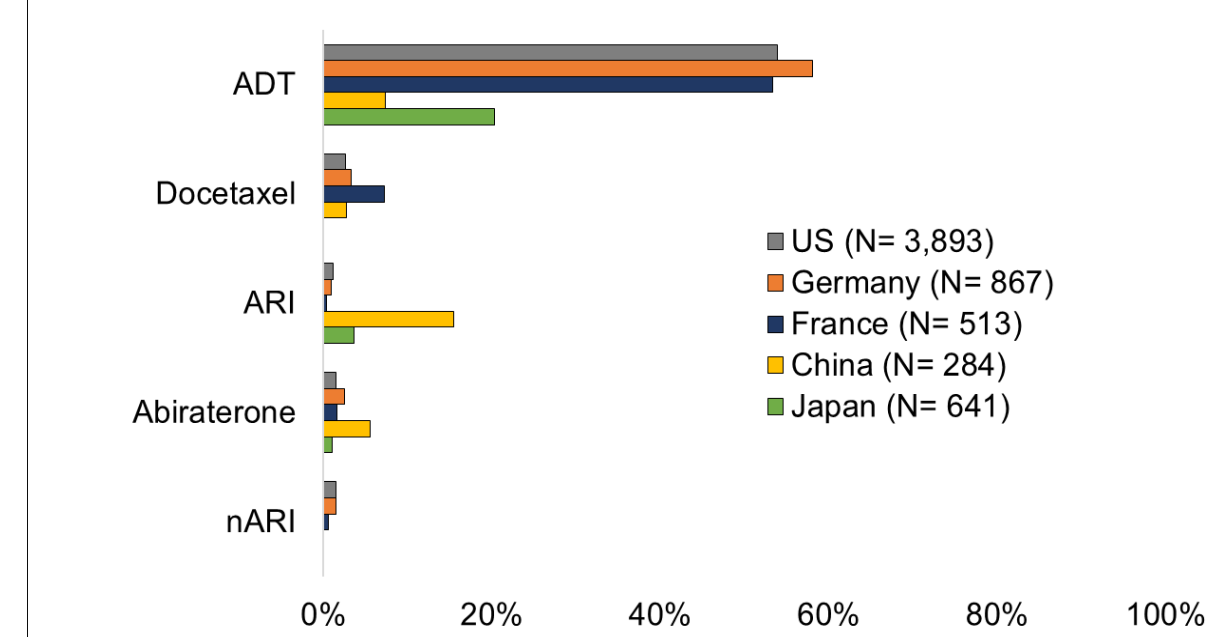
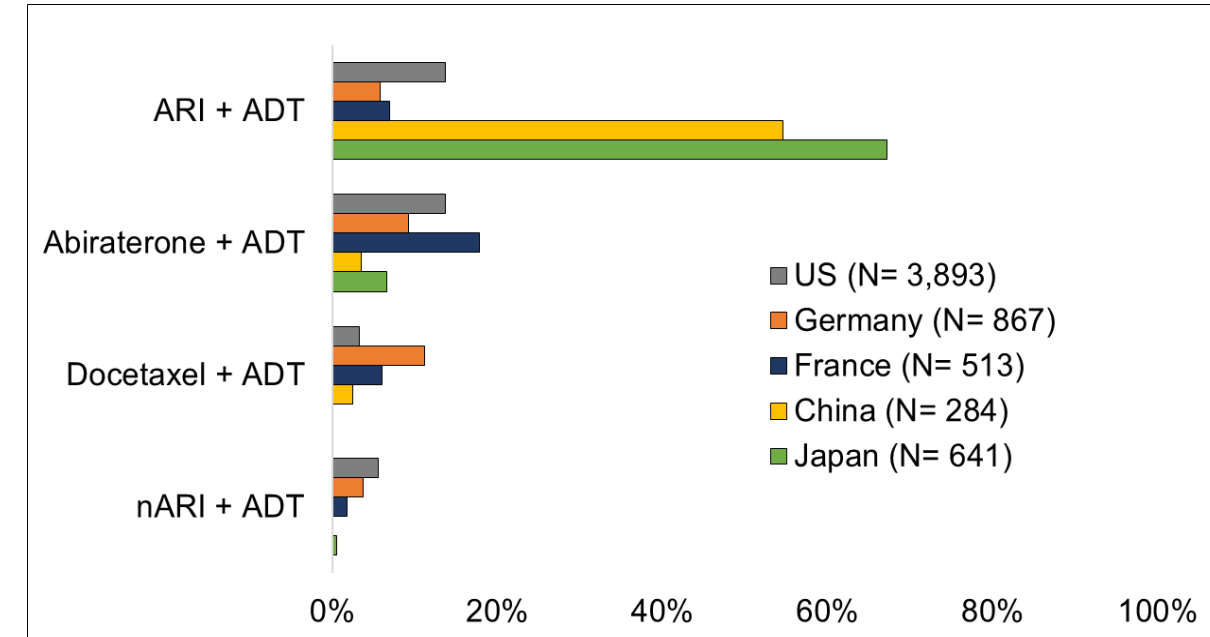


Figure 3. mHSPC Combination Therapies (% Utilization)



ADT: Androgen deprivation therapy; ASI: Androgen synthesis inhibitor; ARI: Androgen receptor inhibitor; LHRH: Luteinizing hormone-releasing hormone; nARI: Novel androgen receptor inhibitor
Note: Abiraterone use with or without prednisone, as monotherapy or combination therapy, was considered. Other monotherapies and other combination therapies (not reported in above figures) constituted small proportions of all therapies used.

RESULTS (CONTINUED)

Global mHSPC Patient Characteristics by Guideline-Relevant Treatment Groups

- The most observable differences were between docetaxel versus non-docetaxel patients where the former were younger, had more advanced disease, but were better-functioning (Table 1).
- Top comorbidities were hypertension, cardiovascular disease, and diabetes across all treatment groups.

Table 1. Global mHSPC Patient Characteristics by Guideline-Relevant Treatment Groups

| Variables | ARI + ADT (N = 1,205) | Abiraterone + ADT (N = 758) | Docetaxel + ADT (N = 264) | nARI + ADT (N = 264) |
|--------------------|-----------------------|-----------------------------|---------------------------|----------------------|
| Age (≥ 70 years) | 888 (73.7%) | 483 (63.7%) | 100 (37.9%) | 161 (61.0%) |
| Bone metastasis | 877 (72.8%) | 657 (86.7%) | 255 (96.6%) | 216 (81.8%) |
| Gleason score 8-10 | 736 (61.1%) | 477 (62.9%) | 206 (78.0%) | 137 (51.9%) |
| ECOG score 0-1 | 1014 (84.1%) | 683 (90.1%) | 244 (92.4%) | 205 (77.7%) |
| Hypertension | 678 (56.3%) | 416 (54.9%) | 155 (58.7%) | 152 (57.6%) |
| CVD | 263 (21.8%) | 201 (26.5%) | 53 (20.1%) | 79 (29.9%) |
| Diabetes | 300 (24.9%) | 177 (23.4%) | 43 (16.3%) | 66 (25.0%) |

CVD: Cardiovascular disease; ECOG: Eastern Cooperative Oncology Group

DISCUSSION

- International and national prostate cancer clinical guidelines are largely aligned in recommending combination therapy using ADT and one among docetaxel, abiraterone, enzalutamide, apalutamide for treatment of mHSPC.⁴⁻⁷
- Findings of high rates of monotherapy and non-standard of care combination therapies reveal discordance between real-world clinical practice and guideline recommendations.
- Study results are consistent with previous literature, mostly for the US, which also found low utilization of standard of care combination therapies despite guideline recommendations.⁸⁻¹²
- Considering nARIs gained regulatory approval in the US relatively recently (late 2019), the currently low utilization rate is likely to increase in the future.
- Similarly, in the EU, nARIs obtained regulatory approval and reimbursement from May 2020 onwards, potentially contributing to the low utilization rates observed.
- In China, no nARI use was observed since their approval (late 2020) and national reimbursement (2021 and beyond) fell outside of our study time period.
- In Japan, no docetaxel use was observed since its approval and reimbursement (2021), fell outside of our study time period.
- As the mHSPC treatment landscape evolves, future studies are needed to track the evolution of real-world treatment patterns and degree of concordance versus guideline recommendations.

STUDY LIMITATIONS

- Within the GOMD, mHSPC diagnosis is physician-adjudicated and may therefore not follow a standardized set off diagnostic criteria across countries.
- Due to limited data availability, there is an imbalance of sample sizes across countries.

CONCLUSIONS

- To our best knowledge, this is the largest and among the first real-world studies to examine treatment patterns among global mHSPC patients across the US, Germany, France, China, and Japan.
- Despite clinical guidelines recommending combination therapy using ADT and one among docetaxel, abiraterone, enzalutamide, or apalutamide as standard of care options for mHSPC treatment, patients were still mostly treated with either ADT monotherapy (US, Germany, France) or ARI + ADT combination therapy (China, Japan) in clinical practice.
- Docetaxel + ADT continues to be an important standard of care option. nARI + ADT is expected to become increasingly used post-approval and reimbursement.
- Our study findings underscore that globally, real-world treatment of mHSPC lags guidelines, specifically, on the need for augmenting proven treatment options, and hence therapeutic outcomes, beyond ADT alone.

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DISCLOSURE

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