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Annals of Urology Research & Practice

Open Access | Research Article

Insights into the Current Treatment of Prostate Cancer in Germany: UNDERSTAND - A Multicenter Healthcare Research Study

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Received: Nov 28, 2023

Accepted: Dec 20, 2023

Published Online: Dec 27, 2023

Journal: Annals of Urology Research & Practice

Publisher: MedDocs Publishers LLC

Online edition: http://meddocsonline.org/

Keywords: Prostate cancer; Treatment pathways; Multidisciplinary collaboration; Real world evidence; Testosterone monitoring; Germany.

Abstract

Background: The UNDERSTAND study aimed to gather insights into the current treatment landscape for Prostate Cancer (PCa) in Germany. The study evaluated multidisciplinary collaborations, treatment pathways, frequency of testosterone level monitoring, perceived differences between available treatments, and the potential impact of the COVID-19 pandemic.

Methods: The study approached 2500 office-based urologists to participate in this healthcare research study by completing a questionnaire. The collected data underwent descriptive statistical evaluation. No statistical hypotheses were formulated.

Results: Out of 2500 contacted urologists, 210 agreed to participate, of which 208 completed the questionnaire. The majority of urologists preferred to collaborate with radiation therapists (92.3%) and urological surgeons (86.5%). However, 19.2% never attended multidisciplinary team meetings. A significant number of patients were diagnosed at the early stages (T1/T2), but a fifth of them presented with advanced disease (N+/M+) at diagnosis, demonstrating the need for interdisciplinary management of PCa.

The most important discriminating factors between products were preparation effort and injection comfort, but participants also perceived differences in effectiveness.

All participants regularly monitored PSA, while only 47.1% regularly monitored testosterone levels. Usually, the initially prescribed ADT was maintained after progression to CRPC.

For 17.5% of patients, repeat injections of depot formulations were received in an interval longer than prescribed in the product information.

Most participants anticipated an increase in the number of patients with more advanced prostate cancer due to the COVID-19 pandemic.

Cite this article: Ohlmann CH, Ruhland S. Insights into the Current Treatment of Prostate Cancer in Germany: UNDERSTAND - A Multicenter Healthcare Research Study. Ann Urol Res. 2023; 1(2): 1002.

Conclusions: Attendance of office-based urologists at multidisciplinary team meetings was sub-optimal, and a considerable gap was identified between guideline-recommended testosterone monitoring and its practical application.

A substantial percentage of patients received their injections late, posing a risk of temporary testosterone surges, especially in patients who recently started with ADT.

Most participants projected that the COVID-19 pandemic would result in an increase in the number of patients with more advanced prostate cancer.

Introduction

Prostate cancer is the second most prevalent cancer in men [1], comprising an estimated 15% of all cancers diagnosed worldwide [2]. After the finding by Huggins and Hodges in the 1940s [3] that prostate cancer is hormone dependent, Androgen Deprivation Therapy (ADT) quickly became the standard therapy for advanced disease [4]. Bilateral orchiectomy and estrogens were subsequently replaced by the newly discovered and well-tolerated GnRH agonists in 1979 as a more acceptable means to reach castration levels.

Due to constraints in the sensitivity of tests for serum testosterone, castration level was initially defined as below 50 ng/dL (1.7 nmol/L) [1]. Modern methods have shown however that surgical castration results in mean serum testosterone levels of 15 ng/dL [5]. Although the historical threshold is still being utilized in registration trials assessing castration in prostate cancer, it has been stated that a target of < 20 ng/dL (0.7 nmol/L) is a more appropriate level [1,6] based on prospective and retrospective studies showing that greater testosterone suppression leads to clinical benefit including a longer time to Castration-Resistant Prostate Cancer (CRPC) or death, Progression-Free Survival (PFS), Cause-Specific Survival (CSS), and Overall Survival (OS). Guidelines recommend periodic measurements of both PSA and testosterone while on hormonal treatment [1].

During the last decade, landmark studies and the availability of new medical therapies have changed the treatment landscape of prostate cancer. Sweeney et al. showed that upfront docetaxel on top of ADT significantly improved OS compared to ADT alone in patients with metastatic, Hormone-Sensitive Prostate Cancer (mHSPC) [7]. Since the confirmation of these results in the STAMPEDE trial [8] guidelines worldwide recommend offering combined ADT and chemotherapy to fit patients presenting with metastatic disease [1]. Similar recommendations followed for other therapies initially reserved for CRPC including abiraterone acetate plus prednisone, apalutamide, and enzalutamide. These drugs are now recommended in combination with ADT based on their OS benefit in patients with mHSPC [1]. With ADT being the backbone in all these studies it remains a crucial part of the standard of care in the treatment of metastatic prostate cancer to date, both in HSPC and CRPC. Along with these changes, the treatment of prostate cancer has become more complex and therefore increasingly multidisciplinary.

In view of the above, we aimed to document how prostate cancer is currently treated in routine clinical practice in Germany with this prospective healthcare research study (UNDERSTAND). The survey employed focused on multidisciplinary collaborations, medical training, treatment pathways, the frequency and relevance of monitoring testosterone levels and the perceived differences between the available treatments. Differences regarding handling, storage conditions and efficacy including suppression of testosterone and PSA were evaluated. In addition to that, one set of questions addressed the possible impact of the COVID-19 pandemic on prostate cancer treatment.

Materials and Methods

This was a prospectively planned, multicenter healthcare research study conducted in Germany. Office based urologists (N=2500) geographically distributed across Germany were contacted to participate in this questionnaire-based study. Urologists were asked to complete a numbered, paper questionnaire. The questionnaire contained 82 multiple-choice questions on several topics, including: physician characteristics (14 questions), product characteristics considered to be important for ADT (19 questions), the role of the GP in prostate cancer screening and referral of patients (4 questions), the importance of medical education for the urologists and their employees and the amount of training attended over the last year (6 questions), the use of ADT in castration-resistant prostate cancer (3 questions), organization of follow-up visits and patient adherence to prescribed medication intervals (6 questions), shared decision making in choosing a specific ADT (3 questions), habits of testosterone and PSA monitoring (6 questions), timing and reasons for changing to another form of ADT (10 questions), anticipated post-COVID impact on patient numbers and organization of the practice (3 questions). An English translation of the questionnaire is available as supplementary data.

Some of the questions allowed for more than one answer to be provided in which case the frequency sums up to more than 100%. Since this study collected urologists' views on the treatment of prostate cancer and estimations on the disease characteristics of this population in their clinical practice, no patient data was collected. If individual urologists consulted their hospital database to better answer the questions, the data recorded on the questionnaires was aggregated and cannot be traced to any individual patient. Therefore ethics committee approval was not required. The study started in September 2021 and ended in April 2022.

Physician characteristics

Participating urologists documented data on the multidisciplinary aspects of treating their prostate cancer patients. These included preferred specialties for collaboration, characterization of quality collaboration and participation in multidisciplinary team meetings.

Patient characteristics

Patient population characteristics were documented which included the number of newly diagnosed and currently treated patients, and the distribution over the different disease stages.

Treatment and follow-up

The number of patients currently treated with ADT was recorded along with a percentage distribution by active substance prescribed, the factors influencing the choice for a specific ADT, and events that triggered a change of ADT. Perceived differences in the ability to lower testosterone between products were documented by rating them on a scale of 1-5 (1=very good to 5=poor) or 'not assessable' in case there was no experience with a product.

Brand names of androgen deprivation therapies available on the German market were used in the questionnaire and include: Decapeptyl® N (triptorelin acetate, Ferring), Eligard® (leuprolide, Recordati), Enantone/Trenantone/Sixantone (leuprolide, Takeda), Firmagon® (degarelix, Ferring), Leuprone® HEXAL® (leuprolide, Hexal), Leuprolin-ratiopharm® (leuprolide, ratiopharm), Leupro-Sandoz (leuprolide, Hexal), Lutrate® Depot (leuprolide, HIKMA Pharma), Pamorelin® (triptorelinembonate, Ipsen), Profact® (buserelin, Cheplapharm Arzneimittel), Zoladex® (goserelin, AstraZeneca). Brand names can be different in other countries.

Procedures employed to monitor patients during ADT were recorded along with their timing and frequencies. In addition, participants' views on the importance of profound testosterone reduction were documented together with the frequency of and reasons for changing ADT, and what form of ADT was switched to.

Procedures and the kind of therapies used in patients with castration-resistant prostate cancer (CRPC) were also documented.

Patient compliance and follow-up

Information on patient compliance, views on who is responsible for compliance, and actions taken if patients did not show up for their appointment was recorded as well as information about systems employed to remind oncology patients of their upcoming appointment.

Additionally, participants' views about changes in the post-COVID era were documented.

Statistical analyses

Analyses were performed using a descriptive statistical evaluation only of all collected criteria. For qualitative criteria, the number of cases, the absolute and the relative frequency of each characteristic was calculated. For quantitative criteria calculations included the number of cases as well as the maximum, minimum, 25% quantile, median, 75% quantile, mean, standard error and standard deviation. No statistical hypotheses were formulated.

Answers were checked for plausibility. Questions asking for a division in percentages need to sum to a 100%. In instances where the sum exceeded a 100% the answer was listed as implausible and not included in the analysis. If the sum was less, it was normalized to 100%. For other questions it was allowed to provide more than one answer allowing the sum of percentages listed to exceed a 100%. Missing values were not replaced.

Results

Of the 2500 urologists contacted, which comprised 78.1% (2500/3200) of all office-based urologists in Germany at the time of this study [9], 210 were willing to participate. Two were excluded for not submitting the questionnaire. Thus, 6.5% (208/3200) of all urologists are represented in this study.

Physician characteristics

At the time of documentation, the participating physicians worked as urologists for a mean of 12.7 ± 8.8 years. Prior to that they worked in a hospital for 9.8 ± 5.0 years (mean±SD). The most preferred physicians to collaborate with were radiation therapists (192/208=92.3%), urological surgeons (86.5%) and oncologists (65, 9%). Participants most often valued a cooperation if it was characterized as being 'trustful' (87.5%), followed by 'regular exchange of information' (75.5%) and 'professional supplementation' (72.1%).

Over half of the participants frequently attended Multidisciplinary Team Meetings (MDTMs) with a frequency of 2-5 times per quarter being most often reported (41.8%), followed by 6-10 times and more than 10 times per quarter (8.2% and 2.9% respectively). The complex disease situation (76.9%) and the presence of several specialists involved in the treatment of the patient (65.4%) were the most frequently documented reasons to attend. Surprisingly, nearly a fifth (19.2%) do not attend MDTMs at all.

Patient characteristics

The mean number of newly diagnosed and currently treated patients with prostate cancer per quarter per urologist was 12.4 ± 15.8 (median: 8.5) and 141.5 ± 128.1 (median: 100) respectively. Newly diagnosed patients mostly presented themselves with T1 (35.4% ± 27.7%, median: 30%) or T2 (42.2% ± 23.3%, median: 40%) prostate cancer while predominant stage in currently treated patients was T2 (45.0% ± 20.3%, median: 45%). Interestingly, more than 20% of cases are already diagnosed at a more advanced disease stage (N+ and M+). This number is higher than initially expected and could represent a possible consequence of the highly anticipated diagnostic gap due to the COVID pandemic. Currently treated patients most frequently had hormone-sensitive prostate cancer, either non-metastatic (36.8%) or metastatic (27.7%). The percentage of patients with a Non-Metastatic Castration-Resistant PCa (nmCRPC) that are currently under treatment (15.6%) is surprisingly high as nmCRPC is rather rare, especially since the introduction of PSMA-PET and normally accounts for 1-2% of PCa cases. The disproportionate amount of documented nmCRPC patients might be a phenomenon observed within urologists due to a possibly rarer use of PSMA-PET in diagnoses. Demographic variables obtained on this patient population are shown in **Figure 1.**

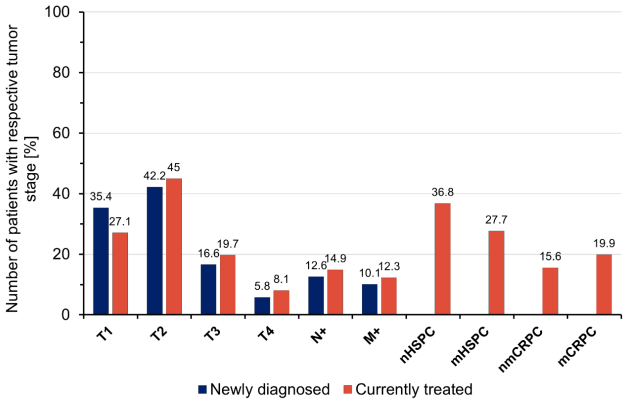

Figure 1: Reported prostate cancer stages of newly diagnosed and currently treated patients. (N = 208).
'T1-T4' and 'n(m)HSPC plus n(m)CRPC' sum up to 100%. mCRPC: Metastatic Castration-Resistant Prostate Cancer; mHSPC: Metastatic Hormone-Sensitive Prostate Cancer; nmCRPC: Non-Metastatic Castration-Resistant Prostate Cancer; nHSPC: Non-Metastatic Hormone-Sensitive Prostate Cancer.

Treatment and follow-up

The mean number of patients currently treated with ADT was 62.7 ± 54.7 patients/HCP/quarter (median: 50 patients) with leuprolide as the most preferred drug (**Figure 2**). The percentage distribution of the different GnRH agonists narrowly

reflects the distribution of these product in the German market and therefore underlines the representativeness of the sample and minimizes a possible selection bias.

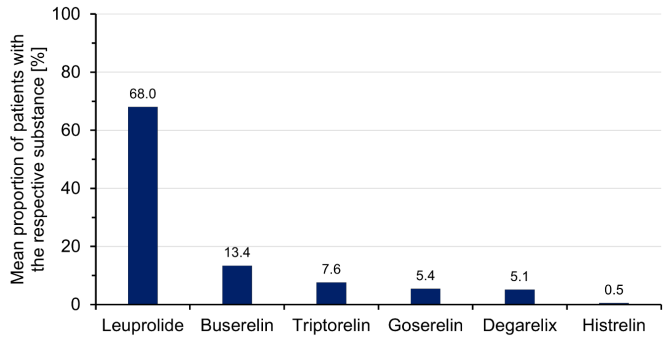

Figure 2: Active substances currently used in ADT, proportion of patients with the respective active substance (mean) [%], (N = 208).

The most important patient characteristic to influence the choice for a specific ADT was the presence of concomitant diseases (148/208=71.2%) followed by the patient's wish for longer intervals, tumor status and patient's mobility reported by 43.3%, 41.8% and 38.9% of the participants, respectively. Participating urologists most frequently reported relevant differences between available products for ADT to be preparation effort (80.8%), injection comfort for the patient (77.4%) and the availability of several depot formulations (52.4%). Products were less often viewed to have relevant differences on aspects of effectiveness (18.8%) and safety/adverse drug reactions (16.8%). Regarding effectiveness, the products most frequently reported by participants as providing a good or very good testosterone reduction were Enantone®/Trenantone®/Sixantone® (91.8%) and Eligard® (90.4%). However, when only very good (value 1) assessment of effectiveness and testosterone reduction is considered, Eligard® was reported most often in both assessments. Very few participants assessed products to provide a deficient testosterone reduction (**Figure 3**). Same holds true for the evaluation of PSA reduction.

For Decapeptyl® N and Lutrate® Depot there was only little data available as those products only play a minor role in the German GnRH agonist market. Therefore, those results might not represent the assessment of physicians outside of Germany.

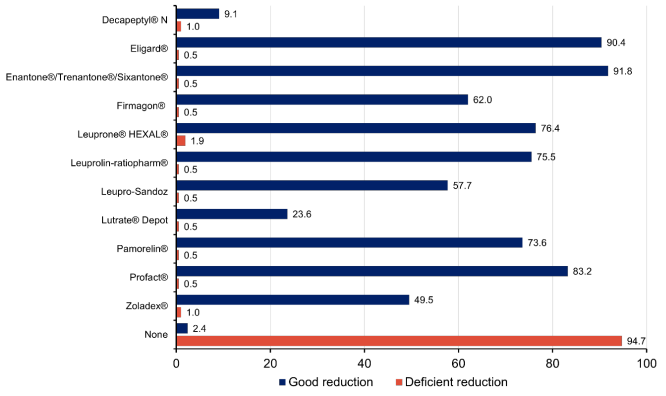

Figure 3: Assessment of degree of testosterone reduction, percentage of participants [%] (N = 208).

Participants' assessment of the degree of testosterone reduction realized by the various products. Reduction was rated on a scale from 1 (= very good) to 5 (= deficient). Ratings were grouped into 'good reduction' (values 1 and 2) and 'deficient reduction' (values 4 and 5). Multiple answers were possible.

When asked what participants find of importance in products providing flexibility in dosing intervals (i.e. testosterone not rising immediately after the recommended dosing interval has elapsed), the majority documented that it provides more confidence in situations were recommended dosing intervals are not adhered to (72.1%) followed by participants stating that they choose a product with such a safety buffer because of the improved treatment safety (36.5%).

Procedures most often used by the participants to monitor ADT in their patients were regular testing of PSA (206/208=99.0%) and testosterone levels (82.7%). Regular check-ups for bone density was employed by a minority (4.3%). PSA levels were checked regularly by most participants with a monitoring frequency of every three months during therapy (96.2%) and a determination before therapy start (79.3%) being most often reported (**Figure 4**). If PSA was monitored regularly additional measurements of testosterone levels were most often performed in situations of rising PSA (81.3%) and/or clarification of CRPC (70.7%).

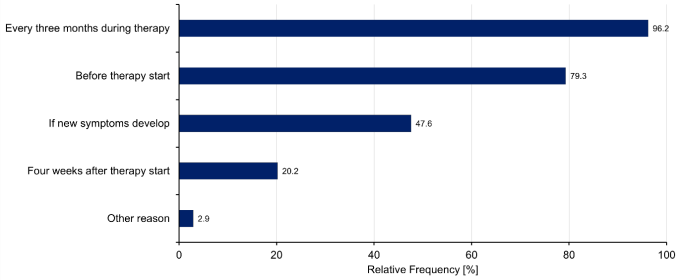

Figure 4: Time or reason for determination of PSA level. Frequency these multiple-choice answers were selected by the participants (N = 208). The frequency sums up to more than 100% because participants were allowed to provide more than one answer.

In contrast, regular monitoring of testosterone levels was done less often. Only around half the participants (47.1%) reported regularly evaluate testosterone levels during the whole period of ADT. The most frequently reported reason (**Figure 5**) to measure testosterone levels was to check if medical castration was achieved in cases of rising PSA in patients on ADT (60.6%).

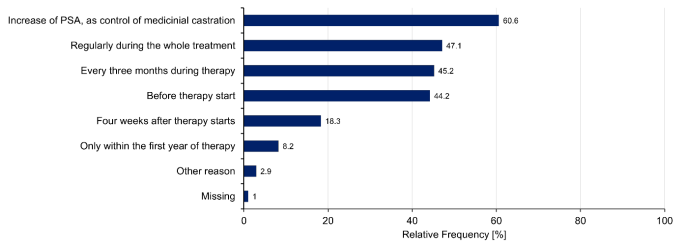

Figure 5: Time or reason for determination of testosterone level during ADT, multiple answers possible (N = 208).

When asked about the relevance of lowering testosterone levels as much as possible most participants (83.2%) stated to follow the EAU guideline. Other documented answers were that a profound reduction of testosterone is associated with a lower risk of disease progression (51.9%), and an association with a lower risk of death (20.7%). Additionally, 82 participants (39.4%) reported that they would change ADT if testosterone values below 20 ng/dL were not obtained.

Regarding changing ADT, half of the participants reported that the substance for ADT is typically not changed during treatment (50.5%) with an additional 42.3% documenting that this

occurs only once during treatment. A change of ADT was nearly always initiated by the physician (99.5%) with 'insufficient effectiveness' (95.2%) and 'insufficient tolerability' (88.9%) being the most frequently reported reasons. From the patients' point of view 'insufficient tolerability' (92.8%) was the most frequently reported reason to trigger a change in ADT (Figure 6), with 'injection reactions' most frequently documented (154/193=79.8%) as the underlying reason.

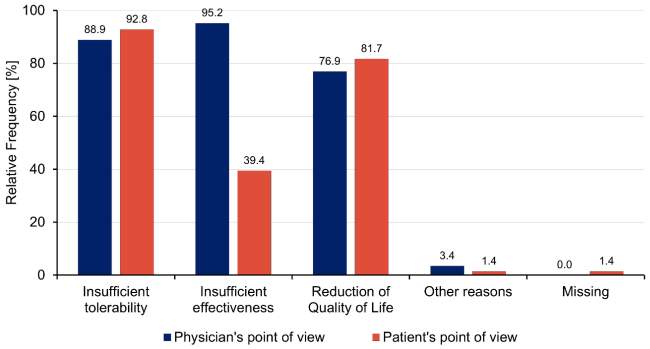

Figure 6: Reasons that trigger a change of ADT from the physician's and the patient's point of view, multiple answers possible (N = 208).

In situations where testosterone levels were increased despite ADT, participants mostly switched to another product (63.9%) which mostly involved a switch from leuprolide to another GnRH agonist (70.7%). Other measures taken were verification of the injection interval, verifying the correct application and a change to CRPC therapy in 60.6%, 53.8% and 39.4% of cases, respectively.

When disease progression on ADT occurred participants most frequently reported checking testosterone levels (87.0%). Other measures -alone or in combination- included requesting new imaging (79.3%) and checking the increase of PSA twice (75.0%). Computed Tomography (CT) scan or bone scintigraphy was the most often requested forms of imaging (both 90.3%).

Additional ADT treatment choices in CRPC

Nearly all participants (198/208=95.2%) also reported treating CRPC, albeit often (49%) in collaboration with an oncologist. In all known cases participants reported continuing ADT in CRPC, ADT and the product prescribed initially is usually maintained (191/206=92.7%). If ADT was changed the most frequently reported reason was the testosterone level (3/11=27.3%).

Regarding the primary treatment option for patients with CRPC, plausible data was available in 147/208 (70.7%) of cases. Abiraterone and enzalutamide were the treatment options most often reported with a frequency of 40.1% (59/147) and 30.6% (45/147) respectively. Apalutamide, docetaxel and darolutamide were documented in 21/147 (14.3%), 19/147 (12.9%) and 3/147 (2.0%) of cases, respectively. Chemotherapy was usually not initiated by the participants, only 76/208 (36.5%) reported administering it in their own practice. The remaining participants (n=132) reported that chemotherapy was most often administered by collaborating oncologists (86/132=65.2%). Local medical care centers, collaborating uro-oncologists and the nearest university clinic were also reported to initiate chemotherapy (**Table 1**).

Table 1: Reported initiators of chemotherapy other than the participants themselves [%] (N = 132).

Initiator of chemotherapy	N (%)
Collaborating oncologists	86/132 (65.2%)
Local medical care centers	46/132 (34.8%)
Nearest university clinic	32/132 (24.2%)
Collaborating uro-oncologists	41/132 (31.1%)

Patient compliance and follow-up

Most participants (153/208=73.6%) believed both physician and patient are responsible for therapy adherence. Therapy intervals were being followed exactly in approximately three quarters (73.3% ± 26.0%, median: 80%) of cases and appointments were different degrees of late in 17.5% (**Figure 7).**

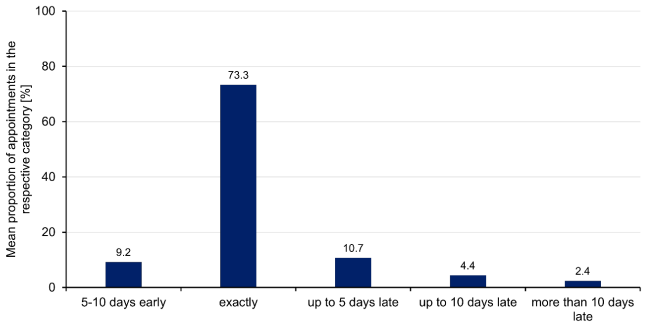

Figure 7: Adherence to therapy intervals, proportion of appointments in the respective category (mean) [%] (N = 208).

Most participants (190/208=91.3%) reported that patients visited the practice only by appointment with a large minority (42.8%) documenting that patients themselves are responsible for compliance with control intervals. A third of the participants (30.3%) employed a system to remind all oncology patients of their upcoming appointment. The most frequently used system was a paper-based reminder (43/63=68.3%) followed by telephone calls (31/63=49.2%), SMS (16/63=25.4%) and a messenger service (4/63=6.3%). Unprompted follow-up visits because of changes were documented by 60/208 (28.8%) of the participants. If patients did not show up for their appointment the participants would either call the patient (84.1%), write a letter (38.9%), inform the family doctor (1.9%), or do nothing (11.5%). On the role of the general practitioner, participants estimated check-ups to be performed by the general practitioner and urologist in 38.8±19.0% and 58.5±19.7% of cases, respectively.

Participants expected several changes in the wake of the COVID-19 pandemic. Most frequently an increase was expected in the number of patients with more advanced prostate cancer (147/208=70.7%) along with an increase in the number of medical check-ups (55.8%) while 15.9% expected a decrease in medical check-ups.

Discussion

The objective of this prospective healthcare research study was to examine how patients with prostate cancer are being currently treated in routine clinical practice in Germany. Topics of special interest were multidisciplinary collaborations, treatment pathways in newly diagnosed and currently treated patients as well as the frequency and relevance of monitoring testosterone levels and the perceived differences between the available treatments.

Although in the top three of preferred specialists to collaborate with, oncologists (137/208=65.9%) were less often listed than radiation therapists (92.3%) and urological surgeons (86.5%). A 2014 study by Beermann et al [10] showed that German urologists more often collaborate with urologists specialized in oncology (59.5%) than with oncologists (35.5%). Of those urologists opposing collaborations, 39.8% felt they could offer all treatments needed by patients with urological tumors. Since then, even more treatment options such as abiraterone and enzalutamide have become available for urologists. At the same time there has been a growing attention for the need for a multidisciplinary approach.

Intriguingly, a fifth (19.2%) of the participants never attended Multidisciplinary Team Meetings (MDTMs). A recent systematic review concluded that although the number of studies evaluating the effect of MDTMs is scarce for prostate cancer, the evidence does suggest that employing MDTMs can have a significant effect on treatment decisions [11]. Available studies showed that on average MDTMs changed 27.1% (range 1.6%-43%) of prostate cancer management plans from the original and although not measured for prostate cancer, there is some evidence that MDTMs improve patient outcomes such as survival for colorectal, lung and breast cancer patients [11]. Additionally, the EAU guideline [1] recommends the practice of MDTMs in the management of PSA-only recurrence after treatment with curative intent, symptomatic metastatic CRPC, and life-prolonging treatments of castrate-resistant disease (strong recommendation).

Differences in the extent of testosterone suppression may have clinical relevance since levels < 20 ng/dL have been correlated with improved outcomes compared to the historical castration level of < 50 ng/dL [1,12,13]. Based on a meta-analysis by Seidenfeld et al.[14] the EAU guideline concludes that despite the lack of formal comparisons, GnRH agonists are considered to be equally effective [1]. The results from this study indicate that the participating urologists appear to agree with this conclusion since effectiveness was only mentioned by 18.8% as a perceived relevant difference between available products. Nonetheless, when asked to rate products, Eligard® and Enantone®/Trenantone®/Sixantone® were mentioned most frequently as products giving a good testosterone reduction (188/208=90.4% and 191/208=91.8% of participants respectively) with Eligard® being the most frequently documented product when solely very good assessment is considered. Same holds true for the assessments of effectiveness and PSA reduction. Although the evaluation of all GnRH agonists in these three categories was generally good, rod-shaped leuprolide implants like Leuprone-Hexal® or Leuprolin-ratiopharm® were well behind the suspension formulations. However, in the absence of actual measurements in this study, this should be viewed as a subjective assessment. Regardless, there is a strong body of clinical and real-world evidence corroborating the very good effectiveness, tolerability as well as testosterone and PSA suppression ratings of Eligard® [15–22] . Interestingly, there is almost no data on these matters published for other GnRH agonists.

The EAU guideline states that testosterone monitoring should be considered part of clinical practice in men receiving GnRH therapy. Even though most will reach testosterone levels < 50 ng/dL (1.7 nmol/L), and many will even achieve levels < 20 ng/dL (0.7 nmol/L), a substantial proportion of patients will not achieve this goal (13-38%) or experience temporary testosterone surges (24%) during long-term treatment [1]. Therefore, products with a proven long-lasting testosterone suppression and a low rate of testosterone breakthroughs (< 1%) should be selected for ADT. However, only for a few hormonal agents (Eligard®, Leuprone®, Lutrate® Depot, Firmagon) data is available [15–17 ,22,23]. A monitoring frequency of every 3-6 months has been suggested to ensure achieving and maintaining of castration levels especially (strong recommendation) during the first year of therapy [1]. Additionally, testosterone should be assessed in patients with suspected disease progression (strong recommendation). Anecdotal evidence as well as results from real-world evidence studies [24,25] suggest that these recommendations are often not adhered to in daily practice. This study confirms these earlier results by showing that just about half of the participants regularly determine testosterone levels during ADT (45.2% - 47.1%) or before therapy start (44.2%). More than 60% tested testosterone levels to confirm medical castration in case of rising PSA.

Temporary testosterone surges during long-term treatment may occur due to non-adherence with recommended dosing intervals. Crawford et al. showed a high incidence (> 80%) of patients' non-adherent to recommended dosing intervals in a retrospective analysis of more than 2000 patient records [13]. Additionally, the two leuprolide formulations studied employing different delivery methods showed a different likelihood of testosterone levels above 20 and 50 ng/dL. The formulation using a microsphere delivery (Lupron Depot®) was 1.5 times more likely to exceed these levels than the gel formulation (Eligard®). In the current study the compliance was good in most patients with 73.3% exactly following therapy intervals. Nonetheless, almost a fifth of patients (17,5%) received injections late introducing the risk of temporary testosterone surges, especially in those patients who recently started GnRH agonist therapy. Reasons for non-compliance were not queried so we cannot draw any conclusions on this aspect. A scenario is that these patient visits may not have been scheduled in alignment with recommended dosing intervals or patients. Alternatively, these patients may not have shown up for their appointments although no data was collected on how often this occurred. Most of these patients would be contacted which would make timely rescheduling possible. A notable 11.5% of participants, however, would not contact their patients at all. Here, both patients and participants may clearly benefit from the introduction of a recall system for cancer patients. Interestingly, many participants (72.1%) recorded that flexibility in dosing intervals provided them with more confidence in case of non-adherence to dosing intervals while only 36.5% recorded that they would also choose a product with such a safety buffer.

Furthermore, possible effects of the COVID-19 pandemic on the routine clinical practice of PCa treatment were investigated. Most participants expected an increase in the number of patients with more advanced prostate cancer as well as an increase in the number of medical check-ups post-COVID-19 pandemic. This is indeed a possibility considering the significant cut-down the pandemic had on urology clinics, outpatient consultations, and urological procedures worldwide [26,27]. Given the high percentage of T3 and T4 PCa at diagnosis, the start of this expectation may have been already observed in this study. Alternatively, the backlog caused by the pandemic may also cause routine follow-up appointments to be scaled down compared to pre-COVID-19. A minority of participants reported expecting this. Delays in the diagnosis of patients with forms of cancer urgently needing treatment may result in loss of life-years [28].

It's not possible to generalize the findings from this study to other countries. The collaboration in this study is specific to the German health care system because 90% of patients are being treated by the office-based urologist as opposed to clinic-based urologists, which is not typically the case in most other European countries.

Limitations of this study include the observational character of the study. Additionally, selection and non-response biases cannot be fully excluded. For example, since the urologists were contacted by the sponsor those willing to participate may have had a more positive opinion of both sponsor and its product compared to those who were not willing, thus influencing the results of product-related questions. Another limitation is that the present study only reflects the participants' views and is not based on chart reviews. Recollections may not accurately reflect actual practice. Likewise, physicians' views on what patients find important have often been found to differ from the patients' own views [25].

The strength of this study is the collection of real-life views of participants on the prostate cancer treatment pathway. To our knowledge, information regarding the collaboration of urologists in multi-disciplinary teams has not been documented before. Similarly, to the best of our knowledge information about continued medical education and adherence to guideline recommended monitoring of PSA and testosterone by German urologists has not been documented before.

Conclusions

The UNDERSTAND study is a prospective healthcare research study that was performed to gain a deeper knowledge on how prostate cancer is currently treated in routine clinical practice in Germany. According to the survey participants most newly diagnosed patients presented themselves with stage T1 or T2 disease while currently treated patients predominantly had stage T2 carcinoma. Despite numerous precaution measures more than a fifth of patients had advanced carcinoma, which underlines the need for interdisciplinary treatment strategies. Interestingly, a significant percentage of urologists never attended multidisciplinary team meetings, which could be significantly improved.

Leuprolide was the predominant active substance prescribed by this group of urologists. Relevant differences between products were mostly viewed to be preparation effort and injection comfort for the patient while nearly all products were assessed almost equally on tolerability and their ability to reduce testosterone. However, differences became more evident when solely "very good" ratings were considered.

While the disease was monitored closely using regular PSA determinations by nearly all participants, there is a clear gap between guideline recommended testosterone monitoring during ADT and its use in daily practice. Testosterone levels were only monitored regularly by half of the participants. However, most of the participants (83.2%) reported following the EAU-Guideline on the topic of the relevance of obtaining the lowest possible testosterone levels. Additionally, ADT was not often changed during therapy and initially prescribed ADT is usually maintained in following progression to CRPC.

Adherence to treatment intervals was strictly followed by most patients but a significant percentage of patients received their injections too late (i.e. outside of the medication interval as prescribed in the product information) introducing the risk of temporary testosterone surges and products providing a certain safety buffer in this respect (e.g. Eligard®) are preferred. A significant percentage of participants (11.5%) would not contact patients not showing up for an appointment.

Most participants expected the COVID-19 pandemic to cause an increase in both the number of medical check-ups and in the number of patients with more advanced prostate cancer.

Supplementary information

The online version contains supplementary material available at [----].

Additional file 1: English translation of the questionnaire employed in this study.

Acknowledgements

Medical writing support, provided by MSc. Peter van Winkel of Polaris Medical, Amsterdam, the Netherlands, and MSc. Michael Gedamke of MSC2, Kiel, Germany, was funded by Recordati Pharma GmbH. This study was funded by Recordati Pharma GmbH, Germany. Data collection and statistical analysis was performed by INPADS GmbH, Bad Dürkheim, Germany. The authors had full access to the data and participated in reviewing and interpreting the data and manuscript. Primary responsibility for opinions, conclusions and interpretation of data lies with the authors. All authors read and approved of the final version of this manuscript.

Authors' contributions

C.-H.O.: Data analysis, manuscript writing/editing. S.R.: Protocol/project development, data collection and management, data analysis, manuscript writing/editing.

Funding

This work was supported by Recordati Pharma GmbH.

Availability of data and materials

Data is available upon reasonable request. The available data consists of the Clinical Study Report as created by the CRO (INPADS GmbH, Bad Dürkheim, Germany) on May 30, 2022. Requests can be sent to Recordati Pharma GmbH, using the email address medicalinformation@recordati.de.

Declarations

Ethics approval and consent to participate

This was a questionnaire-based study. Informed consent was obtained from all the healthcare professionals to participate in the study. All methods were performed in accordance with relevant guidelines and regulations. The data obtained reflect the participating healthcare professionals' views on the treatment of prostate cancer in daily practice in general. No patient data was collected. The data recorded on the questionnaires by the participating healthcare professionals was aggregated and cannot be traced to any individual patient. Within the meaning of Article 2 (2) 2. of the REGULATION (EU) No 536/2014, 'UNDERSTAND' is not a clinical trial but a non-interventional study. Because review by an ethics committee is only required in case of a clinical trial (Section 40 (4) sentence 2 AMG (Arzneimittelgesetz, German Medicinal Products Act) and Art. 4 (2) of the REGULATION (EU) No 536/2014)), ethics committee approval was not required for the UNDERSTAND study.

Consent for publication: Not applicable.

Competing interests

C.-H.O. has received honoraria from Astellas, Astra Zeneca, Bayer, Janssen-Cilag, MSD, Merck, Roche, Recordati, and is on the speaker's bureau for Astellas, Astra Zeneca, Bayer, Janssen-Cilag, MSD, Merck, Roche, Recordati. S.R. is an employee of Recordati Pharma GmbH, Germany.

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