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Patient Preferences and Urologist Judgments on Prostate Cancer Therapy in Japan

Masahiko Nakayama[1], Hisanori Kobayashi[1], Masateru Okazaki[1], Keiichiro Imanaka[2], Kazutake Yoshizawa[1], and Jörg Mahlich[3,4]

Abstract

The purpose of the present study is to investigate the concordance of treatment preferences between patients and physicians in prostate cancer (PCa) in Japan. An internet-based discrete choice experiment was conducted. Patients and physicians were asked to select their preferred treatment from a pair of hypothetical treatments consisting of four attributes: quality of life (QOL), treatment effectiveness, side effects, and accessibility of treatment. The data were analyzed using a conditional logistic regression model to calculate coefficients and the relative importance (RI) of each attribute. A total of 103 PCa patients and 127 physicians responded. The study looked at 37 patients considered as advanced PCa and 66 who were non-advanced PCa. All of the physicians were urologists. Advanced PCa patients ranked the attributes as follows: treatment effectiveness (RI: 32%), accessibility of treatment (RI: 26%), QOL (RI: 23%), and side effects (RI: 19%). For physicians, the RI ranking was the same as for advanced PCa patients; treatment effectiveness (RI: 29%), accessibility of treatment (RI: 27%), QOL (RI: 26%), and side effects (RI: 18%). For non-advanced PCa patients, accessibility of treatment ranked the highest RI (27%) and treatment effectiveness ranked as the lowest RI (14%). Our study suggests that the ranking of the attributes was consistent between advanced PCa patients and physicians. The most influential attribute was treatment effectiveness. Treatment preferences also vary by disease stage.

Keywords

Japan, prostate cancer, treatment preferences, discrete choice experiment

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In 2013, the incidence of prostate cancer (PCa) was estimated to be approximately 1.4 million worldwide with a continuous increase (Fitzmaurice et al., 2015). The development and growth of PCa depends on the androgen-signaling pathway. Castration has been the primary treatment for advanced PCa (Parker, Gillessen, Heidenreich, & Horwich, 2015). As understanding of the mechanism of tumor growth increased, a number of new drugs, including docetaxel, abiraterone acetate, and enzalutamide, to target the disease were developed over the past two decades. These new drugs can improve treatment outcomes such as the prolongation of survival and quality of life (QOL) (Basch et al., 2013; de Bono et al., 2011; Kantoff et al., 2010; Scher et al., 2012; Tannock et al., 2004). Several potential treatment options for castration-resistant prostate cancer (CRPC) are now available with different risk and benefit profiles. It is the task of the physician to select and provide the best treatment option for each patient (Kim & Ryan, 2016). This selection of treatment should include patient preferences as the key component of patient-centered care (Institute of Medicine & Committee on Quality of Health Care in America, 2001). A recent study with Japanese PCa patients reported

[1]Medical Affairs Division, Janssen Pharmaceutical K.K., Tokyo, Japan
[2]Research and Development Division, Janssen Pharmaceutical K.K., Tokyo, Japan
[3]Health Economics Division, Janssen Pharmaceutical K.K., Tokyo, Japan
[4]Düsseldorf Institute for Competition Economics (DICE), University of Düsseldorf, Germany

Corresponding Author:
Jörg Mahlich, Health Economics, Janssen Pharmaceutical KK, 5-2, Nishi-kanda 3-chome Chiyoda-ku, Tokyo, 101-0065, Japan.
Email: jmahlich@ITS.JNJ.com

that Japanese patients are as interested in being involved in decision making as are patients in the United States (Schaede et al., 2018).

Patients' and physicians' treatment preferences have been studied in a number of diseases such as skin disease, infections, and cancer using discrete choice experiments (DCEs; Ashcroft, Seston, & Griffiths, 2006; Bolt, Mahlich, Nakamura, & Nakayama, 2018; Jenkins et al., 2013; Mühlbacher, Stoll, Mahlich, & Nübling, 2013; van Dam et al., 2010). DCE is a statistical methodology that was mainly used in economics and later applied to the medical sciences (Ryan & Farrar, 2000). It allows analyzing the RI of multiple factors underlying the selection of any particular option. DCE studies have also been used in several studies to identify patient preference for PCa treatment, focusing on PCa screening or early-stage PCa treatment (Howard, Salkeld, Patel, Mann, & Pignone, 2015; King et al., 2012; Lloyd, Penson, Dewilde, & Kleinman, 2008; Sculpher et al., 2004). These studies mainly focused on the trade-off between life expectancy, the side effects of androgen deprivation therapy (ADT; e.g., loss of libido, hot flushes) caused by luteinizing hormone-releasing hormone (LHRH) agonists, and the cost of treatment.

Only few studies have included advanced PCa populations (Eliasson, de Freitas, Dearden, Calimlim, & Lloyd, 2017; Lloyd et al., 2008; Uemura et al., 2016). Advanced PCa includes metastatic castration-resistant prostate cancer (mCRPC) and is considered to be an incurable disease for which systemic therapy is recommended (Saad et al., 2015). The most recent study of patients' treatment preferences in advanced PCa in Japan used several attributes and levels which are relevant to treatment with radium (^{223}Ra) chloride, abiraterone acetate, and docetaxel (Uemura et al., 2016). The authors reported that of the side effects especially fatigue was the most important treatment attribute (24.86%) rather than efficacy (23.23%) in those patients. However, the study did not investigate physicians' preferences and, therefore, does not allow drawing conclusions as to whether the degree patient preferences were taken into consideration in the treatment decision. Since studies frequently point out that patients' views and beliefs and those of their physicians are not always in agreement where treatment is concerned (Emberton, 2010), the current study aims to compare patients' and physicians' preferences for treatment of PCa in a Japanese setting. The aim of this study is to look for potentially different treatment preferences in advanced and non-advanced PCa patients.

Materials and Methods

Patients and Physicians

An internet-based survey of both patients and physicians was performed. The survey was conducted by Anterio Inc., a Tokyo-based medical market research company. An invitation to participate in this research was sent by e-mail to patients with PCa listed in the Anterio Inc. registry. A total of 2,622 men were invited to join the survey between August and November 2015. Information on age, residence status, employment status, hospital type and accessibility, prostate-specific antigen (PSA) levels, metastatic status of PCa, Functional Assessment of Cancer Therapy-Prostate (FACT-P) score, and current PCa medication was collected. The Japanese version of the FACT-P questionnaire was validated by Fujimura et al. (2009) and is the PCa subscale of the FACT-G questionnaire used to evaluate health-related QOL in cancer patients. To identify patients with advanced PCa, two selection criteria were applied: (a) patients who self-reported metastases, and (b) patients who self-reported using a drug with an indication or recommendation for CRPC in Japan (i.e., flutamide, abiraterone acetate, enzalutamide, docetaxel, cabazitaxel, dexamethasone, or prednisolone; The Japanese Urological Association, 2012).

Simultaneously, an invitation was sent by e-mail to 44,400 physicians. We applied a filter to preselect physicians with a minimum of 5 years of clinical experience who were treating at least 10 patients with PCa and allocating at least 50% of their time to medical consultation. This way we obtained a sample of 127 physicians. The following data were collected from these physicians: age, gender, hospital type and department, medication use for CRPC, years of clinical experience, and number of PCa patients (total and CRPC).

Development of Discrete Choice Experiment Questionnaire

Development of attribute list. The team of authors including a trained urologist initially selected items for the draft questionnaire based on a literature search (see Lloyd et al., 2008). The draft questionnaire was reviewed and modified by 10 patients and five physicians in a face-to-face meeting. A qualitative pre-study test run was then performed by 25 patients with PCa to check the quality of the draft questionnaire. As a result of the pre-study test run, 24 items were finalized for the quantitative study. In the next step, an internet-based quantitative study was performed with PCa patients who received pharmacotherapy. PCa patients were extracted from the Anterio Inc. database and responses to the selected items were obtained from 150 PCa patients. The responses obtained from the quantitative study were then analyzed by principal component analysis in order to reduce and categorize the number of attributes for the DCE. The principal component analysis resulted in four top level attributes: QOL, treatment effectiveness, side effects, and accessibility of treatment.

Table 1. Sample Choice Set.

Factor of treatment characteristics	Positive level	Negative level
Expected QOL	Possible with treatment	Limited—restricted by the treatment
Expected effect of treatment to keep disease stable (treatment effectiveness)	Maximum expected	Minimum expected
Expected side effects of treatment (side effects)	Few side effects impacting activities of daily life	Some side effects impacting activities of daily life
Convenience of treatment (accessibility of treatment)	Minimal influence on, or interference with, everyday life	Significant influence on, or interference with, everyday life

Note. QOL = quality of life.

Discrete choice experiment. The four selected attributes were translated into everyday language so the patients could easily understand them and in order to define positive and negative levels for each attribute (Table 1). Eight discrete choice sets were developed according to an orthogonal array. Each set had a pair of hypothetical treatments. These sets were presented to patients one after the other who were asked to pick one preferable treatment from each choice set on each occasion. Physicians were similarly asked to choose one of two preferable hypothetical treatments in each set for CRPC.

Statistical Analysis

The patients' and physicians' characteristics were summarized by using percentage, mean value including standard deviation (*SD*), or median value including a range of values. The primary focus of the study was each attribute's RI to patients with advanced PCa and to physicians. A conditional logistic regression model was used for calculating the coefficients of each attribute. The method was developed by McFadden (1973) and is now a standard approach in DCEs (Lancsar & Louviere, 2008; Louviere, Flynn, & Carson, 2010). The RI of attributes (percentage) was calculated by dividing the utility range by the sum of all utility ranges for all attributes. The likelihood ratio test was used to evaluate the statistical significance of each attribute. A p-value of .05 was used to define statistically significant results. Coefficients and the RI in patients with non-advanced PCa were calculated as well. All statistical analyses were performed using JMP® version 13.0 (SAS Institute Inc., Cary, NC 27513-2414, USA).

Results

Baseline Demographics and Characteristics

Patient demographics and characteristics are summarized in Table 2. We obtained responses from 103 patients (i.e., response rate of 4%) and 127 physicians (i.e., 0.4% of all screened physicians). Among the patients, 37 (36%) were considered to have advanced PCa. The median age was 68 years (range 53–81), the mean FACT-P score was 99.8 (± 20.4); 35 of 37 patients reported their current PSA level, the mean PSA was 25.8 ± 98.8 ng/ml: 31 patients had metastases, and five patients did not have metastases. One patient did not know his metastatic status. All six patients who either did not report metastases or did not know their metastatic status had prescriptions of drugs that are indicated for CRPC. Therefore, those patients were classified as advanced PCa patients.

For patients with non-advanced disease, the median age was 72 years (range 40–86), the mean FACT-P score was 114.2 (± 14.2); 57 of 66 (86%) patients reported their current PSA level and the mean PSA was 0.7 ± 2.6 ng/ml. All of the 127 physicians responding were male urologists, with a median age of 46 years (range 30–69) and 41 (323 %) of them worked in a general hospital (Table 3).

Regression Results

For the group of advanced PCa patients, the attribute "treatment effectiveness" showed the highest coefficient value, representing 32% of the RI among the attributes. The RI values for the "accessibility of treatment" and "QOL" coefficients were 26% and 23%, respectively. The lowest coefficient was "side effects," with a RI of 19% (Table 4). The group of non-advanced patients was also analyzed. The rank of their coefficients showed a trend that was different from that identified for patients with advanced disease. "Accessibility of treatment" had the highest coefficient value, with 39% of RI among the attributes. The second-highest RI in this group of patients was "QOL," at 27%. Of lowest RI was "treatment effectiveness," with 18% importance

In the analysis of physicians, coefficients achieved the same ranks as for patients with advanced PCa. "Treatment effectiveness" ranked highest, with 29% relative importance, followed by "accessibility of treatment" (27%) and "QOL" (26%). These three attributes shared 82% of the relative importance. The RI of "side effects" was 18% (Table 4).

Discussion

The results of the current study suggest that patients have differing treatment preferences depending on their disease

Table 2. Patient Demographics and Characteristics.

Background	Advanced PCa (*n* = 37)	Non-advanced PCa (*n* = 66)
Median age, years (range)	68 (53–81)	72 (40–86)
Living with family/alone	34/3	63/3
Work status		
Non-working	22	49
Working	15	14
Other	0	3
Hospital type		
Cancer center	4	1
University	10	14
General hospital	21	42
Practitioner	2	9
Perceived access to hospital		
Good	20	25
Acceptable	14	33
Poor	3	8
Mean PSA value, ng/ml (± *SD*)	25.8 (± 98.8) (*n* = 35)	0.7 (± 2.6) (*n* = 57)
Metastatic status		
Positive	31	0
Negative	5	61
Unknown	1	5
Mean FACT-P score (± *SD*)	99.8 (± 20.4)	114.2 (± 14.2)
Medication, *n*		
LHRH agonists	25	42
Bicalutamide	19	45
Dexamethasone	5	
Docetaxel	4	
Flutamide	3	
Abiraterone acetate	2	
Enzalutamide	1	
Prednisolone	1	
Other	1	

Note. FACT-P = Functional Assessment of Cancer Therapy-Prostate; LHRH = luteinizing hormone-releasing hormone; PSA = prostate-specific antigen; PCa = prostate cancer.

stage. Those in the early stages of disease with non-advanced PCa, place less importance on efficacy and emphasize the importance of other attributes such as QOL or the convenience of a treatment. Later stage patients, who are probably aware of their limited life expectancy, place a much higher emphasis on effectiveness which is expressed as a longer life.

These results are consistent with those obtained by Lloyd et al. (2008), who analyzed patient preference in a metastatic PCa setting. Like in our study, efficacy was the most important attribute. On the other hand, Uemura et al. recently reported that side effects, especially fatigue, was the most important attribute rather than efficacy in Japanese CRPC patients (Uemura et al., 2016). Finally, Eliasson et al., who did not include overall survival as an attribute and focused more on side effects, reported that patients indicated a strong preference for treatments that controlled bone pain, had a low risk of fogginess and delayed chemotherapy (Eliasson et al., 2017). For Japan, a recent burden of illness study reported that chemotherapy is associated with a significant increase of both hospital admissions and the number of days spent in hospital (Mahlich, Tsubota, Imanaka, & Enjo, 2018).

The results of the current study further suggest that patients' and physicians' preference for the choice of treatment were similar for advanced PCa patients. "Treatment effectiveness" was most important for both patients and physicians when choosing a treatment.

Concordance between patient and physician preferences cannot be taken for granted. There were many indications with a preference gap indicating a lack of communication between doctors and their patients. Examples of low concordance between physician and patient preferences have been reported for U.S. women

Table 3. Physicians' Background.

Characteristics	(*n* = 127)
Median age, years (range)	46 (30–69)
Gender, *n*	
Male	127
Female	0
Hospital type, *n*	
Government	27
University	33
Private	41
Clinic	20
Advanced cancer care hospital, *n*	
Yes	64
No	63
Median clinical experience after medical internship, years (range)	20 (5–40)
Hospital department, *n*	
Urology	127
Other	0
Average number of PCa patients on treatment (± *SD*)	111 (± 130)
Average number of CRPC patients on treatment (± *SD*)	13 (± 13)
Prescribing experience, *n* (yes/no)	
Enzalutamide	101/26
Abiraterone acetate	83/44
Docetaxel	74/53
Cabazitaxel	32/95

Note. CRPC = castration-resistant prostate cancer; PCa = prostate cancer.

with breast cancer, patients with rectal cancer, or general end of life care (DesHarnais, Carter, Hennessy, Kurent, & Carter, 2007; J. D. Harrison et al., 2008; Janz et al., 2004). A review of 46 studies even concluded that

> most studies reveal a disparity between the preferences of actual patients and those of physicians. For most conditions, physicians underestimated the impact of intervention characteristics on their patients' decision making. Differentiated perceptions may reflect ineffective communication between the provider and the patient (Mühlbacher & Juhnke, 2013)

For PCa, it was reported that treatment decisions were largely based on urologists' recommendations and patient preferences were not sufficiently taken into account (Scherr et al., 2017). The results of the current study, on the other hand, suggest a high concordance between physicians and patients at least for patient population with the advanced PCa. An explanation for this finding would be that patient and physician preferences tend to align as the disease advances. Future research could investigate in a larger cohort of men with non-advanced PCa whether preferences change when they develop advanced PCa.

The strengths of the current study are the application of a methodologically sound approach for the development of decision poles and the consideration of a wide range of factors that might affect how treatment decisions are made. Preferences of both advanced PCa and non-advanced PCa patients were evaluated, although this study was not explicitly designed to assess the concordance of patient and physician preferences. Instead of testing the alignment of patient/physician pairs, in this study patients and physicians responded independent from each other and concordance was assessed in terms of the RI of specific treatment attributes. While paired comparisons are an interesting methodological approach, the majority of studies analyzing the concordance of patient and physician preferences still rely on DCEs (M. Harrison, Milbers, Hudson, & Bansback, 2017).

There are some limitations of this study as well. The response rate was low, resulting in a relatively small sample size. The small sample size prevented the authors from utilizing more sophisticated statistical methods such as latent class models that would allow identification of heterogenous preferences across different patient subpopulations. A study by Meropol et al. (2008) in an advanced cancer population showed, for instance, that the preference for QOL versus preference for length of life was associated with older age, male gender, and higher education. Because this study was carried out using an internet-based survey, it only included PCa patients with internet access. This could possibly limit the generalizability of the results. Patient backgrounds were also reported by the patients themselves, which might have influenced the quality of the responses. Patients should respond with their knowledge of the disease status, which is formed by the physician's explanation of the patient's condition. Most of the study patients were aware of their PSA levels. Therefore, it can be assumed that they were well-informed about their disease status. FACT-P scores were also reported to reflect metastatic status. The patients with metastatic PCa had significantly lower scores than those of patients with non-advanced disease (Stone, Murphy, Matar, & Almerie, 2008). In this study, FACT-P scores showed the same trend. Therefore, patient backgrounds would be consistent with the scores. Finally, concordance between physician and patient preferences can be measured more precisely using a study design that builds specific patient/physician dyads and assesses pairwise alignments.

Conclusions

Optimal communication between patient and physician regarding the decision-making process in treatment selection is crucial to patient-centered care. In this study, treatment effectiveness was the most influential attribute during treatment for patients with advanced PCa. When selecting

Table 4. Regression Results.

	Likelihood χ^2	*p*-value	Coefficient	Relative importance
Advanced prostate cancer				
Patients				
QOL	25.651	<.0001	0.352	23%
Efficacy	49.29	<.0001	0.484	32%
Side effects	18.358	<.0001	0.298	19%
Accessibility	33.899	<.0001	0.404	26%
Physicians				
QOL	99.236	<.0001	0.366	26%
Efficacy	124.086	<.0001	0.409	29%
Side effects	48.242	<.0001	0.256	18%
Accessibility	101.898	<.0001	0.371	27%
Non-advanced prostate cancer				
Patients				
QOL	44.676	<.0001	0.340	27%
Efficacy	12.728	.0004	0.182	14%
Side effects	26.526	<.0001	0.262	20%
Accessibility	103.387	<.0001	0.507	39%

Note. QOL = quality of life.

treatment, no striking difference in preferences between patients with advanced PCa and physicians was observed. However, there was a difference between patients with advanced PCa and those with non-advanced disease. It was found that treatment effectiveness was the least influential attribute in non-advanced PCa patients. This suggests that physicians need to adjust their communication with PCa patients to match their patients' status of disease. Our results should improve patient-centered care during treatment for PCa and support the development of a comprehensive understanding of what the optimal communication between patient and physician should look like during the process of selecting treatment. Limitations of the current study include small sample size and self-reported, that is, not validated, responses.

Declaration of Conflicting Interests

The author(s) declared the following potential conflicts of interest with respect to the research, authorship, and/or publication of this article: All authors were employees of Janssen KK at the time the study was conducted.

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Compliance with Ethics Guidelines

This article is based on web-based survey, and does not involve any interventions conducted on human subjects by any of the authors. Informed consent was obtained from all patients to collect their personal information except for individual-specific information capable of identifying individuals

ORCID iDs

Masateru Okazaki https://orcid.org/0000-0001-5455-2909
Jörg Mahlich https://orcid.org/0000-0003-1110-2793

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