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A Comparison of Preferences of Targeted Therapy for Metastatic Renal Cell Carcinoma between the Patient Group and Health Care Professional Group in South Korea

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A B S T R A C T

Objectives: To evaluate the preferences of health care professional groups and patient groups with respect to efficacy, adverse events, and administration method for targeted agents of metastatic renal cell carcinoma. **Methods:** A total of 485 respondents including cancer patients and health care professionals (medical oncologists, nurses, and pharmacists) were surveyed by using a discrete choice experiment in South Korea. Through a literature review and expert consultation, six attributes—progression-free survival, four adverse events (bone marrow suppression, hand-foot skin reaction, gastrointestinal perforation, and bleeding), and administration—were selected. This study employed the conditional logit regression model. **Results:** The six attributes are statistically significant for the patient group and health care professional group. The two groups, however, present differences in progression-free survival, hand-foot skin reaction, gastrointestinal perforation, and administration. The relative importance of adverse events is greater for the patient group, while that of efficacy and administration is greater for the health professional group. For doctors, the relative importance of efficacy is as high as 31%, compared with 7% for the patient group. If progression-free survival is prolonged by 1 month, the acceptable level of bone marrow suppression is 1.3% for the patient group and 9.6% for doctors and that of hand-foot skin reaction is 1.0% and 11.8%, respectively, for the patient group and doctors. **Conclusions:** This study demonstrates substantial differences in the preference for a targeted drug between the patient group and the health care professional group. Doctors prefer effective and orally administered drugs while patients show more reluctant attitudes about adverse events than do health care professionals.

Keywords: discrete choice experiment, preference, relative importance, renal cell carcinoma, trade-off.

Introduction

Metastatic renal cell carcinoma (mRCC) is resistant to frequently used cytotoxic chemotherapy or radiotherapy [1], and the efficacy of immune therapy for mRCC has also been limited [2]. Therefore, patients suffering from mRCC did not have many choices regarding treatment prior to the development of targeted therapy. As a result of recent studies on the molecular mechanism of renal cell carcinoma, targeted agents for suppressing the angiogenesis of tumor cells have been developed [3] and proven to prolong the progression-free survival (PFS) and the overall survival (OS) of the patient.

There are several targeted agents in the treatment for mRCC, but they differ from each other in terms of efficacy, adverse event profiles, and administration [4]. For instance, sunitinib is different from bevacizumab even though they are both targeted agents that can be regarded as primary standard treatments for mRCC. Sunitinib is more efficacious and is an orally administered drug but has numerous more adverse events while bevacizumab has fewer adverse events but is less effective and is an intravenously administered drug [4–6].

Generally, preference for a drug depends on not only the efficacy of the drug but also various other attributes such as adverse events and the administration method. It can thus be anticipated that the preferences of not only health care professionals but also patients would have an impact on the successful treatment of disease. In the treatment of relatively severe diseases such as cancer, patients usually passively follow the treatment suggested and determined by the medical staff because of information asymmetry relating to their diseases and drugs [7,8]. If, however, the efficacy does not satisfy their expectations or if adverse events that are unexpected or serious or reduce quality of life occur, their compliance and, consequently, the treatment outcome would be negatively affected [9,10]. Good communication between a physician and a patient can lead to the patient's active participation in the treatment decision, which is related to improved outcomes [11–13]. The preferences of medical staff and patients and the gaps between these two groups should hence be carefully examined.

The discrete choice experiment (DCE) evaluates a product's value by considering several of its representative attributes. In the field of health care research, the DCE is used in examining the

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preferences for drugs or treatments as well as the willingness to pay [14–19]. This study, through a DCE survey, aimed to elicit the preferences of medical staff and patients/patients' family members for recently developed targeted agents used in mRCC and to identify the significantly important factors influencing drug preference.

Methods

DCE methodology

A DCE assumes that the utility of a certain product is determined by several product attributes and their levels [20,21]. In a DCE, hypothetical scenario sets with differing levels of attributes are presented to respondents; each respondent combines the information and chooses the most preferable among the alternatives. The value of the product is estimated from the combination of attributes and levels selected [22]. The attributes should have significant impacts on drug selection; the levels should be realistically achievable to the extent that the respondents can carefully consider them in the selection [20].

The relative importance of each attribute for preferences and the trade-offs between attributes can be estimated from the results chosen by respondents by considering different attribute levels [15,16,18].

Attributes and attribute levels

Attributes and their levels were identified by a literature review on sunitinib and bevacizumab and were then finalized after expert consultation [23–26]. In addition to these drugs, there are several other targeted agents used for mRCC that have various adverse events. Because of the DCE methodology, however, we focused on these two representative drugs, which are the most common targeted agents as primary standard treatments for mRCC, and chose a limited number of attributes. On the basis of a comprehensive literature review and expert opinions, we selected two major and typical adverse events for each drug that are extremely severe or have a significant impact on the quality of life for patients and hence should be carefully considered in drug use.

As an efficacy attribute, PFS was selected. For ethical reasons in clinical trials, additional treatment is usually permitted after progression of disease and thus OS cannot be seen as a pure efficacy attribute of the drug while PFS appears to be more specific to an individual drug. Selected as adverse events were hand-foot skin reaction (HFSR), bone marrow suppression (BMS), gastrointestinal (GI) perforation, and bleeding. PFS and the four adverse events were defined according to three levels by extension to a hypothetical range based on clinical literature. Sunitinib is orally administered once a day. Bevacizumab is intravenously injected at the hospital once every 2 weeks but must be administered with interferon-α for mRCC, and thus three-times-per-week subcutaneous self-injection at home was included in the category of administration method (Table 1).

	Drug A	Drug B
Progression-free survival	10 months	11 months
Bone marrow suppression (neutropenia/thrombocytopenia)	1%	9%
Hand-foot skin reaction	0%	5%
Gastrointestinal perforation	1%	2%
Bleeding	4%	0%
Administration	Orally once a day (at home)	Intravenous injection once every 2 weeks (at hospital) and subcutaneous injection three times a week (at home)
Which would you choose between Drug A and Drug B?		

Fig. 1 – Example of choice set.

DCE scenario

The levels of six attributes were 3, 3, 3, 3, 3, and 2, and therefore 486 hypothetical profiles were available (i.e., 35*2). We selected similar structures for the attributes and levels as presented in our study "A Library of Orthogonal Arrays" (N.J.A.Sloan, http://www2.research.att.com/~njas/oadir/) to form 18 arrays and generated scenario sets by the fold-over method. In this case, two treatments always have different levels within the scenario set; the generated scenario sets meet orthogonality and minimum overlapping and achieve equal balance where the same number of levels should be included (Fig. 1).

Asking the patients and patients' family members to answer all the 18 choice sets may disturb rational judgment, and consequently they were randomly divided to create two versions. A total of 10 questions were asked, with one dominant choice set added to the last part of the questionnaire for an irrationality check. A pilot test was carried out with 20 persons to check for any problems. After examining terminology and other factors, the final questionnaires were completed. Prior to answering DCE questions, respondents were asked to rank four adverse events used in the survey to identify their perception on severity.

In the DCE questionnaire, the drug name was not stated to avoid any possible selection bias and hence respondents chose their preference between drug A and drug B in the hypothetical scenario set. In the survey questionnaire, brief explanations of the terminologies used in the questionnaire were provided with simple terms to aid in the respondents' understanding.

Data collection

The survey was carried out separately for the patient group and the health care professional group. The former group included cancer patients and their family members, while the latter group included doctors (medical oncologists), nurses (oncology nurses and general nurses), and pharmacists in South Korea. The survey

Table 1 – Attributes and levels for targeted drugs.

Attributes of first-line therapy	Levels			Coefficients in regression analysis
Progression-free survival: PFS (mo)	10	11	13	β_1
Bone marrow suppression: BMS (%)	1	9	18	β_2
Hand-foot skin reaction: HFSR (%)	0	5	10	β_3
Gastrointestinal (GI) perforation (%)	0	1	2	β_4
Bleeding (%)	0	2	4	β_5
Administration (0 = oral, 1 = injection)	0	1		β_6