Hematologists' Preferences for First-line Therapy Characteristics for Multiple Myeloma in Japan: Attribute Rating and Discrete Choice Experiment

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ABSTRACT

Purpose: With the progress being made in the treatment of multiple myeloma and other complex cancers, a variety of clinical research and treatment options are being pursued. This study uses a discrete choice experiment (DCE) to estimate treatment characteristic preferences of hematologists in Japan.

Methods: A 2-stage process was applied within this study. The first stage is an attribute-rating exercise in which each of the full list of 21 attributes is rated on its importance by the clinicians when selecting a first-line therapy. The top 8 rated attributes from a stepwise logistic regression model are then used to develop a DCE to estimate hematologists' willingness to trade-off characteristics of the treatment options in their recommendation of a first-line treatment. A logit model was used to identify the attribute levels that were the strongest determinants of the physicians' treatment preferences.

Findings: From among the potential treatment attributes presented, improved overall survival had the most significant impact on the treatment choice of participating Japanese hematologists. Improvement in the ability to promptly reduce M-protein is also a highly prioritized treatment characteristic, with hematologists willing to sacrifice just over 1 month extra overall survival for this. Additionally, the hematologists' value improved suitability for chromosomal abnormalities with poor prognosis, suitability of the mechanism of action in initial treatment, and promptly improving calcium-renal-anemia-bone symptoms each at roughly 0.9 months extended overall survival. The reduction of adverse events is among the other significant factors in choice of treatment, though it was not found to be as strong a determinant as those mentioned.

Implications: This study reinforces the expectation that clinical research and treatment options should continue to focus on overall survival and are key priorities in multiple myeloma treatment development. However, clinicians are willing to consider and trade off other clinical factors and markers in their choice of treatment. The potential improvements presented were also found to have a greater impact on treatment choice than aversion to the potential worse outcomes presented. (*Clin Ther*. 2018;40:296–308) © 2018 The Authors. Published by Elsevier HS Journals, Inc.

Key words: discrete choice experiment, hematology, Japan, multiple myeloma, oncologists, treatment preferences.

INTRODUCTION

Multiple myeloma (MM) is a cancer of plasma cells and is characterized by increased monoclonal gammopathy in the serum and urine.[1] The precise mechanisms through which the disease is triggered are still unknown; however, it is well known that patients with MM have genetic or chromosomal abnormalities.[2] It has been estimated that MM is responsible for 1% of all cancers and 10% of all hematologic malignancies.[3] According to a recent meta-analysis of MM in Japan, the estimated incidence rate per year is between 1.3 to 5.4 per

100,000 persons, with a 5-year prevalence rate of 9.7 per 100,000 persons.[4] Disease prevalence increases with age, and people aged 60 years or older account for 70% of total MM patients.[5]

The major clinical symptoms of MM include anemia, immunological deterioration, renal problems, hypercalcemia, and bone problems.[2] In particular, destruction of bone tissue remains a major factor in the deteriorating quality of life among patients with MM, despite recent advances in treatment.[6] According to clinical data derived from a study of 2234 patients who were newly diagnosed between January 2001 and December 2012, the median overall survival (OS) was 60.6 months for the cohort. When compared with a median OS of 38.9 months in a study of a 1990–2000 cohort, the 2001–2012 cohort had significantly improved OS.[7] A recent review found that the total medical cost for a patient with relapsed or refractory MM is expected to exceed ¥1,383,000 in Japan.[4]

Treatment Options

Treatment guidelines for plasma cell neoplasms depend on the specifics of the patient's clinical condition. According to guidelines published by the Japanese Society of Hematology, for patients with monoclonal gammopathy of undetermined significance or asymptomatic myeloma, watchful waiting is the primary therapeutic strategy. On the other hand, treatment interventions for MM depend on the suitability of the patient for transplantation, and whether it is recurrent or nonresponsive.[8]

Use of Discrete Choice Experiments

Discrete choice experiments (DCEs) are a set of stated preference, questionnaire-based methods that enable the researchers to statistically estimate how respondents value different aspects of services. This is done by asking study subjects to choose between pairs of hypothetical options with different attributes (characteristics) at specified levels set based on an experimental design. DCEs are characterized by the respondent's trade-offs to maximize utility based on the levels of the attributes of the options presented. To date, patient and physician treatment preferences have been studied in a number of indications, such as dermatology, HIV, and cancer.[9–12]

DCEs are increasingly being used to elicit and measure preferences when addressing a wide range of health-related decisions.[13,14] With regard to treatment attributes of MM therapy, hematologists' and patients' preferences were explored and compared in an attribute-rating exercise and DCE study in Germany.[15] The findings indicated that physicians ranked prolonged life expectancy as the most important treatment attributes. Maintaining further treatment options was the second most important attribute, followed by breaks in therapy and physical quality of life.

Study Objective

The objective of our study was to examine hematologists' preferences in treating MM using a DCE. As far as we know, in Japan, there has been no such DCE study examining physicians' preferences in MM treatment options. The study results should help inform physicians and policy makers in Japan to develop more effective ways of treating patients with MM.

METHODS

As is recognized in the DCE literature and across good practice guidelines, attribute and level selection within a DCE study is a critical step, not just for ensuring inclusion of relevant attributes, but also for selecting levels that will reflect the decision of interest and induce trade-offs among the choice sets for the respondents.[16] Therefore, this study was conducted in 2 steps: (1) an attribute-rating exercise of hematologists' stated preference followed by (2) a DCE building on the results of the rating exercise to determine hematologists' willingness to trade off characteristics of the treatment options. The study was approved by the sponsor's internal approval committee and was in line with ethical and legal guidelines for Japan. The data were collected through a web-based panel and individual identifying information was not obtained. Participating hematologists were informed of the study purpose.

Attribute-rating Exercise

We conducted an online survey asking which attributes hematologists consider most important in a first-line treatment of MM. The attribute-rating exercise was intended to identify key attributes to be included in the actual DCE exercise. The questionnaire was sent to physician between October 28 and November 4, 2016. Respondents were limited to hematologists in Japan who have between 3 and 35