Gynecologic Oncology xxx (2016) xxx–xxx

Contents lists available at ScienceDirect

Gynecologic Oncology

journal homepage: www.elsevier.com/locate/ygyno

Treatment preferences of advanced ovarian cancer patients for adding bevacizumab to first-line therapy

Jung-Yun Lee [a], Kyunghoon Kim [b], Yun Shin Lee [c], Hyo Young Kim [c], Eun Ji Nam [a], Sunghoon Kim [a,*], Sang Wun Kim [a], Jae Weon Kim [d], Young Tae Kim [a,*]

[a] Department of Obstetrics and Gynecology, Institute of Women's Life Medical Science, Yonsei University College of Medicine, Seoul, Republic of Korea
[b] Korea Information Society Development Institute, Chungcheongbuk-do, Republic of Korea
[c] KAIST College of Business, Korea Advanced Institute of Science and Technology, Seoul, Republic of Korea
[d] Department of Obstetrics and Gynecology, Seoul National University College of Medicine, Seoul, Republic of Korea

HIGHLIGHTS

- We explored patients' preferences for adding bevacizumab to first-line therapy.
- A discrete choice experiment and trade-off question were designed and distributed to ovarian cancer patients.
- Patients' preferences for bevacizumab depend primarily on drug costs.

ARTICLE INFO

Article history:
Received 6 June 2016
Received in revised form 13 October 2016
Accepted 14 October 2016
Available online xxxx

Keywords:
Ovarian cancer
Bevacizumab
Treatment preference
Discrete choice experiment
Trade-off question

ABSTRACT

Background. The GOG-218 and ICON-7 studies recently showed that adding bevacizumab to first-line therapy for patients with advanced ovarian cancer increased progression-free survival. However, the high cost and long treatment duration prevents the incorporation of bevacizumab in practice. The aim of this study was to explore and quantify patients' preferences for adding bevacizumab to first-line therapy.

Methods. A discrete choice experiment (DCE) and trade-off question were designed and distributed to 102 ovarian cancer patients. Participants were asked to choose between two hypothetical first-line therapies that differed in terms of effectiveness, safety, and the financial burden. A trade-off technique varying the cost of bevacizumab was used to quantify a willingness-to-pay threshold for selecting bevacizumab.

Results. All attributes of the DCE had a statistically significant impact on respondents' preferences and the financial burden was the most important attribute. The results of the trade-off question showed that more than half of patients would prefer to add bevacizumab to standard chemotherapy when the cost of the drug was reduced to 17% (1/6) of the baseline cost.

Conclusion. Patients' preferences for bevacizumab in the adjuvant treatment of ovarian cancer depend primarily on drug costs. Our results suggest that the current cost of bevacizumab is sufficiently high that the majority of ovarian cancer patients are not willing to pay to accept a small increase in progression-free survival.

1. Introduction

Ovarian cancer is the deadliest gynecologic cancer, and its incidence and mortality are increasing in Korea [1,2]. The current standard care route is surgical cytoreduction followed by platinum-based cytotoxic chemotherapy. Despite good responses, most patients with advanced ovarian cancer will have a recurrence and die of their disease [3,4]. As such, there is an urgent need to improve the outcomes of patients with this aggressive cancer.

The Gynecologic Cancer Intergroup (GCIG) International Collaboration on Ovarian Neoplasms (ICON-7) trial and Gynecologic Oncology Group (GOG) 218 (GOG-218) study recently reported improvements in progression-free survival (PFS) when bevacizumab was added to standard platinum-based chemotherapy [5,6]. The GOG-218 results showed that median PFS increased by 3.8 months when maintenance bevacizumab was added following paclitaxel, carboplatin, and bevacizumab, compared to a control arm without any bevacizumab.

However, there are discrepancies between the evidence of randomized controlled trials and actual practices. The high drug cost, increased

* Corresponding authors at: Department of Obstetrics and Gynecology, Institute of Women's Life Medical Science, Yonsei University College of Medicine, 50–1 Yonsei-ro, Seodaemun-gu, 03722 Seoul, Republic of Korea.
E-mail addresses: shkim70@yuhs.ac (S. Kim), ytkchoi@yuhs.ac (Y.T. Kim).

http://dx.doi.org/10.1016/j.ygyno.2016.10.021
0090-8258/

risk of serious adverse events (bowel perforation, hypertension), and long treatment duration (15 months) prevent the incorporation of bevacizumab in practice. Researchers recently performed a cost-effectiveness analysis and showed that the routine use of bevacizumab is not cost-effective in the front-line management of advanced ovarian cancer [7–10].

Patient preference increasingly plays a role in cancer treatment [11]. It is not yet known whether patients would accept the high cost and complication rate of bevacizumab to benefit from a lower risk of recurrence or whether they would prefer to accept a higher risk of recurrence to avoid the risk of complications and save money. So far, patient preferences for the type of adjuvant treatment received have been underestimated [11,12]. The aim of this study was to explore and quantify patients' preferences for adding bevacizumab based on the best available evidence.

2. Methods

2.1. Study population

Eligible patients included women who were currently and previously candidates to receive bevacizumab as an adjuvant therapy following debulking surgery. We identified patients who had undergone treatment for ovarian cancer at the Women's Cancer Center, Yonsei Cancer Hospital, Korea. Between October 2015 and January 2016, 102 ovarian cancer patients were invited to participate in this study. A discrete choice experiments (DCE) and additional trade-off question were developed and distributed to the study population. Written informed consent was obtained from all patients. The study was approved by the Medical Ethics Committee of Yonsei University College of Medicine.

2.2. Study procedures

Face-to-face interviews were held with each patient to assess preferences and willingness to pay (WTP) for advanced ovarian cancer treatments. Two interviewers were trained and adhered to a strict interview script. The questionnaire was pilot tested (n = 10) to check for any problems with interpretation and face validity. Patients were asked to imagine that they had recently been diagnosed with ovarian cancer and undergone primary debulking surgery. The surgery was successful and the residual tumor was <1 cm. Their clinician then offered them two treatment strategies for adjuvant therapy. We made it clear that the situation was hypothetical and did not refer to their situation.

2.3. Discrete choice experiment (DCE), attributes and levels

DCEs are an attribute-based survey method for measuring preferences. A DCE is carried out by identifying the most important attributes of a cancer treatment and assigning different levels to each attribute [11,13]. Hypothetical scenarios that involve combinations of the different levels of the attributes are created. Patients' preferences for the scenarios are elicited by asking them to choose between selected pairs of scenarios.

The attributes and levels were determined based on a review of the literature and consultation with an expert panel of gynecologic oncologists (EJN, SK, JWK, YTK; n = 4). We identified four attributes: PFS, additional cost, treatment duration, and bowel perforation. Level ranges were obtained from the results of GOG-218 [5], which compared the three arms (paclitaxel plus carboplatin for cycles one through six [PC], PC plus bevacizumab for cycles two through six [PCB], and PCB plus bevacizumab maintenance for cycles two through 22 [PCB + B]).

The attribute "PFS" (effectiveness) was selected and described using two levels: 10 months (PC) and 14 months (PCB + B). The attribute "additional cost from bevacizumab alone" (economic burden) was selected and described by the levels US$60,000 (PCB + B) and US$0 (PC). These costs were obtained from and estimated by the Korean National Health Insurance Service. Drug costs were calculated for a hypothetical woman with a body weight of 60 kg, and the calculated dose for bevacizumab was 15 mg/kg. We did not include administration costs. Costs were expressed in US dollars, and we applied the average exchange rate in 2014. The attribute "treatment duration" was selected and described by every 21 days for five months (PC) and every 21 days for 15 months (PCB + B). Lastly, the attribute "risk of bowel perforation" (safety) was selected and described by the levels 1% (PC) and 3% (PCB + B).

2.4. Bevacizumab DCE questionnaire

The combination of four attributes with two levels each resulted in 16 possible alternatives for the adjuvant treatment of ovarian cancer. In this study, 16 choice sets were constructed. Each choice set included two alternatives describing hypothetical treatments and an opt-out alternative. Fig. 1 gives an example of the choice sets. In these 16

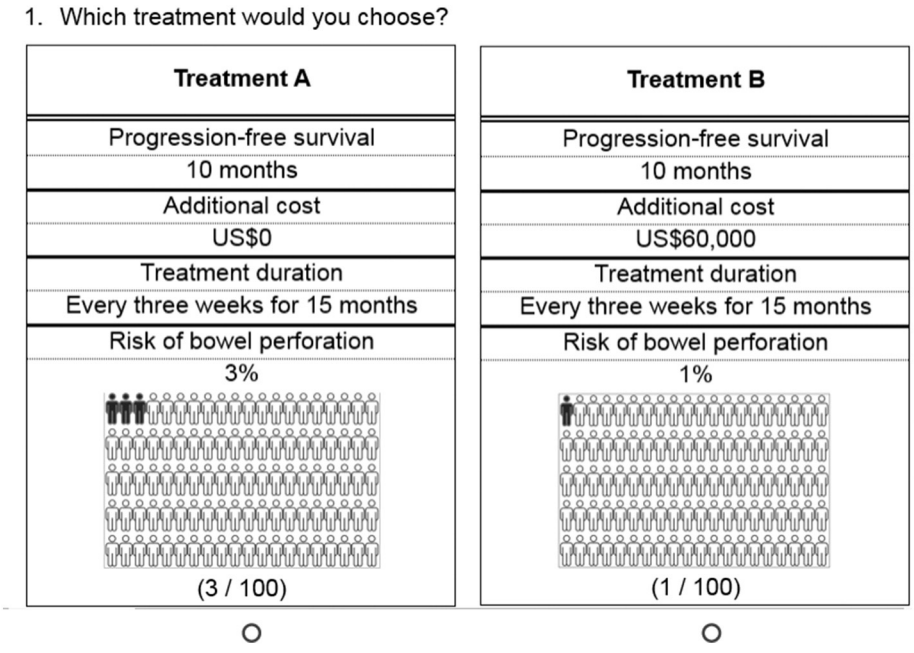

Fig. 1. Example of choice set.

Please cite this article as: J.-Y. Lee, et al., Treatment preferences of advanced ovarian cancer patients for adding bevacizumab to first-line therapy, Gynecol Oncol (2016), http://dx.doi.org/10.1016/j.ygyno.2016.10.021