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A cost–utility analysis of NRG Oncology/Gynecologic Oncology Group Protocol 218: Incorporating prospectively collected quality-of-life scores in an economic model of treatment of ovarian cancer☆

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HIGHLIGHTS

- Bevacizumab is not cost effective in the adjuvant and maintenance treatment of advanced ovarian cancer.
- Prospective collection of cost and quality of life data is critical to a well-executed cost–utility analysis.

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ABSTRACT

Objective. To estimate quality-of-life (QOL)-adjusted cost–utility with addition of bevacizumab (B) to intravenous paclitaxel/carboplatin (PC) for primary treatment of advanced-stage epithelial ovarian cancer.

Methods. A modified Markov state transition model of 3 regimens evaluated in GOG 218 (PC, PC + concurrent B [PCB], and PCB + maintenance B [PCB + B]) was populated by prospectively collected survival, adverse event, and QOL data from GOG 218. Progression-free survival (PFS) and overall survival (OS) were modeled using primary event data. Costs of grade 4 hypertension, grade 3–5 bowel events, and growth factor support were incorporated. QOL scores were converted to utilities and incorporated into the model. Monte Carlo probabilistic sensitivity analysis was performed to account for uncertainty in estimates.

Results. PC was the least expensive ($4044) and least effective (mean 1.1 quality-adjusted progression-free years [QA-PFY]) regimen. PCB ($43,703 and 1.13 QA-PFY) was dominated by a combination of PC and PCB + B. PCB + B ($122,700 and 1.25 QA-PFY) was the most expensive regimen with an incremental cost–effectiveness ratio of $792,380/QA-PFY compared to PC. In a model not incorporating QOL, the incremental cost–effectiveness ratio (ICER) of PCB + B was $632,571/PFY compared to PC.

Conclusions. In this cost–utility model, incorporation of QOL into an analysis of GOG 218 led to less favorable ICER (by >$150,000/QA-PFY) in regimens containing B compared with those that do not include B. Continued investigation of populations with ovarian cancer in whom the efficacy of treatment with bevacizumab is expected to be increased (or in whom QOL is expected to increase with use) is critical.

Introduction

Ovarian cancer is the most lethal gynecologic cancer, with 14,270 women expected to die from the disease in 2014 [1]. With the current standard of care, patients undergo surgical cytoreduction followed by platinum-based cytotoxic chemotherapy. Despite this aggressive treatment approach, most women diagnosed with advanced ovarian cancer will have a recurrence and die of their disease. Recent advancements

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in the treatment of this disease have included the incorporation of intraperitoneal chemotherapy into the front-line therapy of optimally resected disease. Despite improved survival with this strategy, increased rates of complications compared with intravenous therapy preclude its use in certain patients [2]. Continued investigations of alternative treatment strategies are necessary to maximize survival while minimizing toxicity. In 2011, the Gynecologic Oncology Group (GOG) published the results of a randomized phase III clinical trial investigating the use of bevacizumab with the standard intravenous agents carboplatin and paclitaxel, GOG 218 [3]. The results demonstrated an additional 3.8 months of median progression-free survival (PFS) when maintenance bevacizumab was added following carboplatin, paclitaxel and bevacizumab (14.1 months median PFS), as compared with the control arm without any bevacizumab (10.3 months median PFS). In the quality of life (QOL) analysis of this trial published in 2013, bevacizumab was found to compromise QOL during chemotherapy, as measured by the Trial Outcome Index (TOI) of the Functional Assessment of Cancer Therapy—Ovary (FACT-O) [FACT-O TOI] (before cycle four, there was an approximately three point decrease in QOL with bevacizumab compared to the control arm), but had no impact after chemotherapy was completed [4]. While generally well tolerated, bevacizumab has been associated with an increased risk of serious adverse events such as intestinal perforation, hemorrhage, proteinuria, thrombosis, central nervous system disorders, increased bone marrow suppression, and delayed wound healing. Furthermore, the use of bevacizumab is associated with increased cost, both directly related to the cost of the drug as well as the costs associated with its toxicity. Recently, groups have been interested in the costs associated with novel therapeutics, leading to studies and reviews of the pharmacoeconomics of drugs such as bevacizumab [5]. A previously reported cost–effectiveness model (based on the GOG 218 data presented in abstract form) initiated the discussion of the cost–effectiveness of bevacizumab in treating patients with newly diagnosed ovarian cancer. The authors challenged patients, providers, regulators, and the pharmaceutical industry to begin to think about the responsibility of controlling the escalating cost of healthcare in the United States [6]. However, this prior cost–effectiveness study did not take into account quality of life in different treatment arms. Standard methods for cost–effectiveness include incorporation of quality of life, when available [7]. The incorporation of health related QOL into a cost–effectiveness analysis results in a cost–utility analysis. This methodology considers lower QOL to constitute a decrement in overall effectiveness, and may lead to a substantially different interpretation of cost–effectiveness than without consideration of QOL.

Following the recently released results of the QOL data from GOG 218, we performed a cost–utility analysis of the use of bevacizumab as prescribed in GOG 218, and aimed to determine the impact of bevacizumab on the potential costs associated with the treatment of advanced ovarian cancer.

Methods

Model structure

We constructed a cost–utility model [8] using a modified Markov state transition structure (Fig. 1) to compare the three regimens evaluated in GOG 218: (1) paclitaxel/carboplatin (PC), (2) PC + concurrent bevacizumab (PCB), and (3) PCB + maintenance bevacizumab (PCB + B). A third party payer perspective was employed. The model's time horizon was 60 months; one Markov cycle was set equivalent to three months. Discounting of costs and effectiveness was performed at 3% annually. The model was populated by prospectively collected survival, adverse event, and QOL data (Table 1) as reported in GOG 218 [3,4], including standard deviations and classification of distributions.

Costs

Costs were assigned to treatment regimens, growth factor support, and severe adverse events (assigned within the three-month cycle in which they were incurred), and were discounted accordingly (Table 2 and Supplemental Table 1). All costs were inflated to 2013 US dollars using medical inflation rates (http://www.halfhill.com/inflation.html).

Treatment

Costs of chemotherapy and common support drugs were assigned using Medicare J code reimbursements. Outpatient administration fees were assigned using Medicare reimbursements (www.cms.gov).

Growth factors

We incorporated the costs of erythropoietin and granulocyte colony stimulating factor based on the actual number of cycles in which these drugs were administered in each study arm.

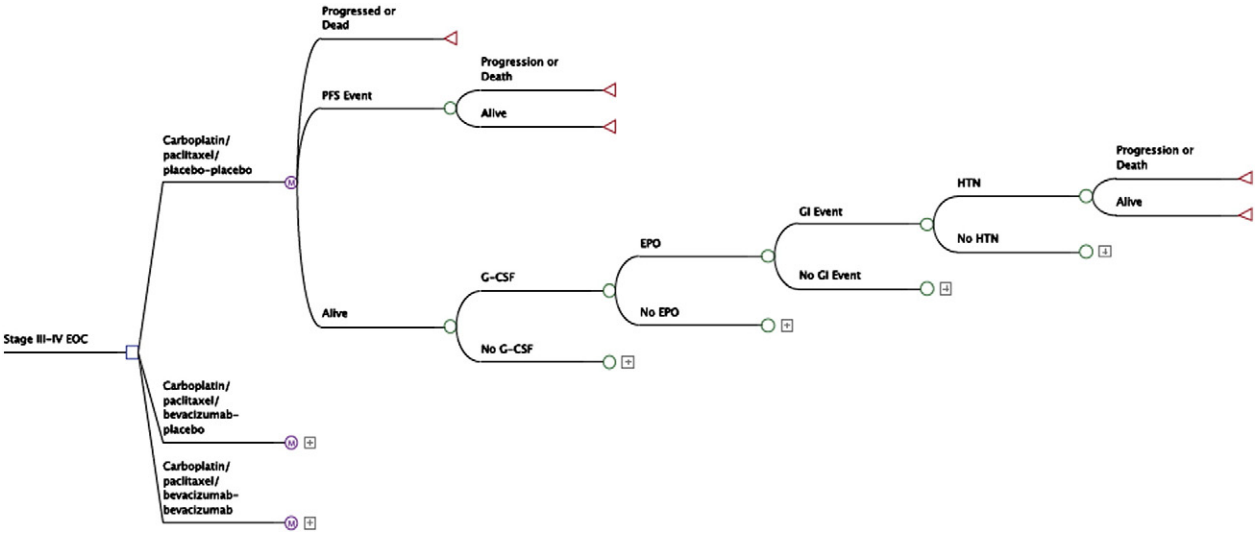

Fig. 1. Decision tree structure for the cost–utility model of GOG 218.