Gynecologic Oncology xxx (2017) xxx–xxx

Contents lists available at ScienceDirect

Gynecologic Oncology

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

Adding bevacizumab to single agent chemotherapy for the treatment of platinum-resistant recurrent ovarian cancer: A cost effectiveness analysis of the AURELIA trial

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HIGHLIGHTS

- ICER of adding bevacizumab to chemotherapy for ovarian cancer is $410,455/QALY.
- Adding bevacizumab is not cost effective at WTP threshold of $100,000/QALY gained.
- Cost of bevacizumab must be reduced to 20% of the cost in 2015 to be cost effective.

ARTICLE INFO

Article history:
Received 16 September 2016
Received in revised form 21 February 2017
Accepted 24 February 2017
Available online xxxx

Keywords:
Cost-effectiveness
Bevacizumab
Aurelia

ABSTRACT

Objective. AURELIA, a randomized phase III trial of adding bevacizumab (B) to single agent chemotherapy (CT) for the treatment of platinum-resistant recurrent ovarian cancer, demonstrated improved progression free survival (PFS) in the B + CT arm compared to CT alone. We aimed to evaluate the cost effectiveness of adding B to CT in the treatment of platinum-resistant recurrent ovarian cancer.

Methods. A decision tree model was constructed to evaluate the cost effectiveness of adding bevacizumab (B) to single agent chemotherapy (CT) based on the arms of the AURELIA trial. Costs, quality-adjusted life years (QALYs), and progression free survival (PFS) were modeled over fifteen months. Model inputs were extracted from published literature and public sources. Incremental cost effectiveness ratios (ICERs) per QALY gained and ICERs per progression free life year saved (PF-LYS) were calculated. One-way sensitivity analyses were performed to evaluate the robustness of results.

Results. The ICER associated with B + CT is $410,455 per QALY gained and $217,080 per PF-LYS. At a willingness to pay (WTP) threshold of $50,000/QALY, adding B to single agent CT is not cost effective for this patient population. Even at a WTP threshold of $100,000/QALY, B + CT is not cost effective. These findings are robust to sensitivity analyses.

Conclusions. Despite gains in QALY and PFS, the addition of B to single agent CT for treatment of platinum-resistant recurrent ovarian cancer is not cost effective. Benefits, risks, and costs associated with treatment should be taken into consideration when prescribing chemotherapy for this patient population.

1. Introduction

Ovarian cancer is the leading cause of death from a gynecologic malignancy in the United States, with 14,180 women expected to die of the disease in 2015 [1]. The current standard of care for treatment of ovarian cancer is surgical cytoreduction followed by platinum-based chemotherapy. Despite this aggressive treatment, the majority of women diagnosed with ovarian cancer will recur. Patients who recur within 6 months following completion of platinum-based chemotherapy are considered platinum-resistant. Subsequent treatment of these patients

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http://dx.doi.org/10.1016/j.ygyno.2017.02.039
0090-8258/

is typically with sequential single agent chemotherapy including paclitaxel, pegylated liposomal doxorubicin, and topotecan [2–6]. However, prognosis remains poor in the platinum-resistant recurrent setting.

Recently, biologic therapies have been introduced in the treatment of ovarian cancer. Bevacizumab, a monoclonal antibody that targets vascular endothelial growth factor (VEGF), has demonstrated activity in platinum-resistant ovarian cancer, both as monotherapy [7,8] and in combination with cytotoxic chemotherapy [9,10]. AURELIA, the first randomized phase III trial of adding bevacizumab to single agent chemotherapy in platinum-resistant recurrent ovarian cancer patients, found a significant improvement in progression free survival (PFS) with the addition of bevacizumab (6.7 months versus 3.4 months with single agent chemotherapy alone, $p < 0.001$) [11].

While bevacizumab demonstrates significant promise in improving PFS in platinum-resistant recurrent ovarian cancer, its use is associated with significantly higher treatment costs. Recently, there has been growing interest in evaluating the costs associated with the addition of biologic therapies to the treatment of patients with ovarian cancer [12–16]. To date, these studies have all evaluated bevacizumab in the upfront treatment of ovarian cancer and have not found this drug to be cost effective in this setting. The goal of this study was to evaluate the cost effectiveness of adding bevacizumab to single agent chemotherapy among patients with recurrent platinum-resistant ovarian cancer.

2. Methods

2.1. Model structure

We constructed a decision tree model (Fig. 1) to compare the costs and health outcomes associated with two therapies for patients with platinum-resistant ovarian cancer: (1) standard care, single agent chemotherapy (CT) and (2) single agent chemotherapy plus bevacizumab (B + CT). Assuming a U.S. public payer perspective, we analyzed costs and effectiveness for a hypothetical cohort of 1000 patients. A time horizon of fifteen months was chosen to reflect survival of patients in the AURELIA trial [11]. The cycle length was one month. The main outcomes of interest were costs, quality adjusted life years (QALYs) and progression free survival.

A number of complications are associated with chemotherapy in general, and bevacizumab specifically. The only adverse event modeled was bowel perforation, as this complication has the potential for the most severe implications for outcomes and costs. Because bowel perforation is a complication of bevacizumab only, it does not appear in the CT branches of the model. Costs were assigned to non-fatal and fatal perforations, and it was assumed that the costs of bowel perforation were incurred during one month, during which time no chemotherapy treatment costs were incurred. It was assumed that perforation occurred prior to disease progression in the B + CT arm, as prior data suggests that the median time to progression for patients on bevacizumab was 71 days [17]. Once perforation occurred, we assumed that bevacizumab was discontinued, but that patients continued to incur the cost of chemotherapy alone and experienced utilities congruent with progression free survival.

Patients enter our model in either the CT or B + CT arm. In the B + CT arm, patients either experienced a bowel perforation or not. Those who did experience perforation either recovered or died as a result of the perforation. Those who recovered either experienced progression of disease or remained progression free at the end of the 15-month time horizon. Patients in the B + CT arm who did not experience bowel perforation either experienced disease progression or remained progression free. In the CT arm, patients could not experience bowel perforation, so either experienced disease progression or remained progression free at the end of the 15-month time horizon. We assumed that the benefits of single agent chemotherapy are the same regardless of which single agent drug is selected. Because patients in the AURELIA trial were receiving third-line chemotherapy, we assumed that the number of treatments available to patients with platinum-resistant

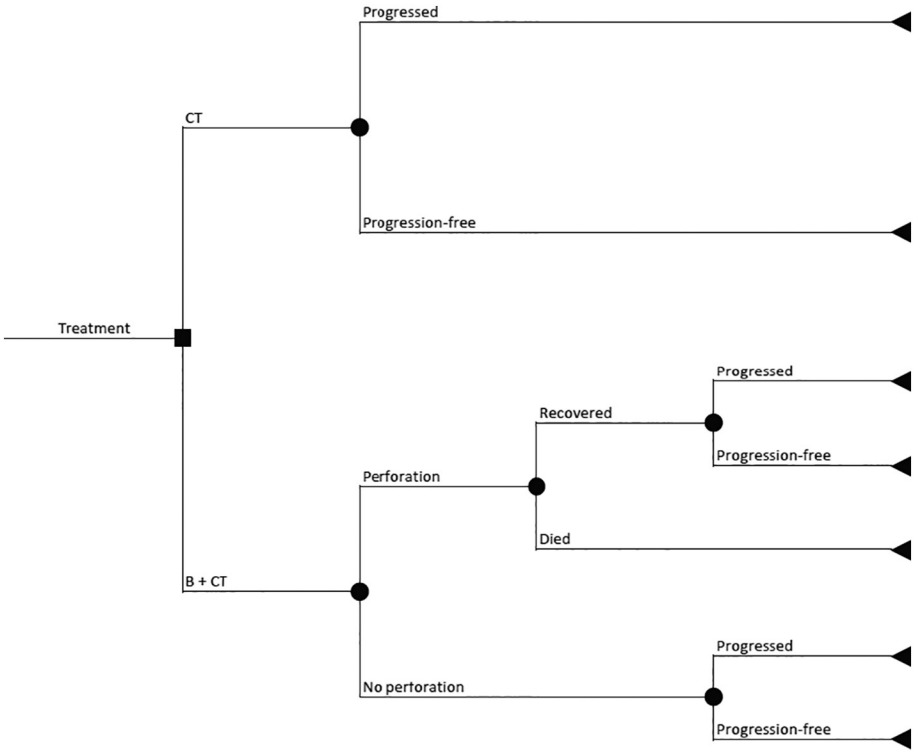

Fig. 1. Decision tree modeling standard treatment for platinum-resistant ovarian cancer versus alternative treatment combining bevacizumab with chemotherapy. CT, single agent chemotherapy; B + CT, single agent chemotherapy plus bevacizumab.

Please cite this article as: W.Z. Wysham, et al., Adding bevacizumab to single agent chemotherapy for the treatment of platinum-resistant recurrent ovarian cancer: A cost effective..., Gynecol Oncol (2017), http://dx.doi.org/10.1016/j.ygyno.2017.02.039