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A personalized paradigm in the treatment of platinum-resistant ovarian cancer – A cost utility analysis of genomic-based versus cytotoxic therapy

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HIGHLIGHTS

- Genomic-based targeting therapy for recurrent ovarian cancer is not cost-effective.
- Reducing the cost of targeted therapy improves its cost-effectiveness.
- Reducing the cost of genomic testing also impacts cost-effectiveness.

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ABSTRACT

Objective. To assess the cost-effectiveness of a strategy employing genomic-based tumor testing to guide therapy for platinum-resistant ovarian cancer.

Methods. A decision model was created to compare standard of care (SOC) cytotoxic chemotherapy to a genomic-based treatment strategy. The genomic arm included tumor testing with treatment directed at targets identified. Overall survival was assumed to be similar between strategies; quality of life (QOL) was assumed superior during targeted therapy compared to chemotherapy. Pertinent uncertainties (cost of targeted therapy and genomic testing, response to targeted therapy, probability of a tumor having a targetable alteration, and impact on QOL) were evaluated in a series of one-and two-way sensitivity analyses.

Results. The genomic testing strategy was more expensive ($90,271 vs. $74,926) per patient than SOC. The incremental cost-effectiveness ratio (ICER) of the genomic strategy was $479,303 per quality-adjusted life year saved (QALY). Model results were insensitive to the cost of genomic testing, differences in QOL, and the probability of identifying a targetable alteration. However, the model was sensitive to the cost of targeted therapy. For example, when the cost of targeted therapy was reduced to 56% of its current cost (or $6400/cycle), the genomic strategy became more cost-effective with an ICER of $96,612/QALY.

Conclusions. Genomic-based tumor testing and targeted therapy in patients with platinum-resistant ovarian cancer is not cost-effective compared with SOC. However, reducing the cost of targeted therapy (independently, or in combination with reducing the cost of the genomic test) provides opportunities for improved value in cancer care.

1. Introduction

Ovarian cancer is the fifth most common cause of cancer deaths in women in the United States, with 14,240 women expected to die of the disease in 2016 [1]. The current standard of care for ovarian cancer includes surgical cytoreduction with adjuvant platinum and taxane-based cytotoxic chemotherapy. Despite these interventions, some patients develop recurrence within 6 months of stopping primary treatment, referred to as "platinum-resistance". In these patients, the median progression-free survival is approximately 3 months and the median overall survival is approximately 12 months [2].

Due to the poor survival associated with this clinical scenario, there has been a push to consider novel treatment options. One such option, albeit for patients with at least 3 prior courses of chemotherapy, is to test for a germline *BRCA* 1 or 2 mutation and, for those found to have a germline alteration, to treat with a poly-ADP ribose (PARP) inhibitor [3]. Another approach has been to query the tumor genome for somatic (rather than germline) mutations to guide therapy. The Cancer Genome Atlas (TCGA) researchers analyzed 489 samples of high-grade serous ovarian adenocarcinoma and found a number of mutations and altered

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pathways that may serve as current or future therapeutic targets [4]. There are commercially available genomic profiling tests available to evaluate a patient's tumor for such alterations. For example, the FoundationOne (Foundation Medicine, Inc., Cambridge, MA), at a list price of $5800, analyzes a patient's tumor genome using "next-generation sequencing" and reports genomic alterations, as well as potential therapies (if available) for each alteration. This test has been reported in patients with epithelial ovarian cancer with findings of multiple potentially targetable alterations [5]. Given the poor prognosis and lack of an ideal treatment for patients with recurrent, platinum-resistant ovarian cancer, it is hoped that a genomic-based strategy will be useful in guiding therapy. Such a strategy has the potential to select targeted therapies that, in certain patients, might be more effective and less toxic than standard of care cytotoxic chemotherapy (SOC). However, it is yet unknown whether this approach improves outcomes for such patients, or is cost-effective. The goal of this study was to examine the cost-effectiveness of a strategy that uses genomic-based tumor testing to guide therapy for platinum-resistant ovarian cancer, compared to standard cytotoxic chemotherapy.

2. Methods

We employed a simple decision model (Fig. 1) to evaluate the costs and outcomes of two strategies for the treatment of platinum-resistant, recurrent ovarian cancer—standard-of-care (SOC) cytotoxic chemotherapy and genomic-based targeted therapy. The time horizon was 1 year.

The United States healthcare sector was the setting of this study, and costs of interventions were derived from a payer perspective. The model was populated using published data. Costs were estimated in 2014 US dollars. Effectiveness was measured using quality-adjusted life years (QALY). The primary outcome in this study was the incremental cost-effectiveness ratio (ICER), expressed in dollars per QALY gained.

Key assumptions of the model were: (1) Due to the lack of data on the effect of genomic testing-based therapy on survival in this setting, survival time was assumed to be identical between strategies in our analysis. (2) A patient in the genomic-based targeted therapy arm was assumed to have a 54.2% chance of having a targetable alteration, a 19.2% chance of having a second targetable alteration, and no chance of having >2 targetable alterations (estimates based on per-patient alteration data reported in Ross et al. [5]). Of note, we deemed an alteration "targetable" if it can be targeted by a drug that a) has yielded a response in a phase II or III clinical trial of patients with ovarian cancer and b) is FDA-approved for use in ovarian or other cancer(s). (3) SOC chemotherapy was given in a defined priority sequence based on FDA approval and NCCN guidelines (see Fig. 1 for sequence order). Due to time horizon limitations, not all regimens that are FDA approved and within NCCN guidelines for this scenario could be included. (4) Patients in the genomic arm who did not have a targetable alteration were given SOC therapy in the same sequence as those in the SOC arm. (5) All therapy was given for a minimum of 3 months. If there was no response after the initial 3 months, the patient was considered to have progression of disease and moved on to the next treatment in the sequence. If the patient responded after the first 3 months, treatment would continue for an additional 3 months. At the end of those 6 months, there was a 50% chance of going on to a secondary treatment (with progressive disease) and a 50% chance of staying off treatment (with stable

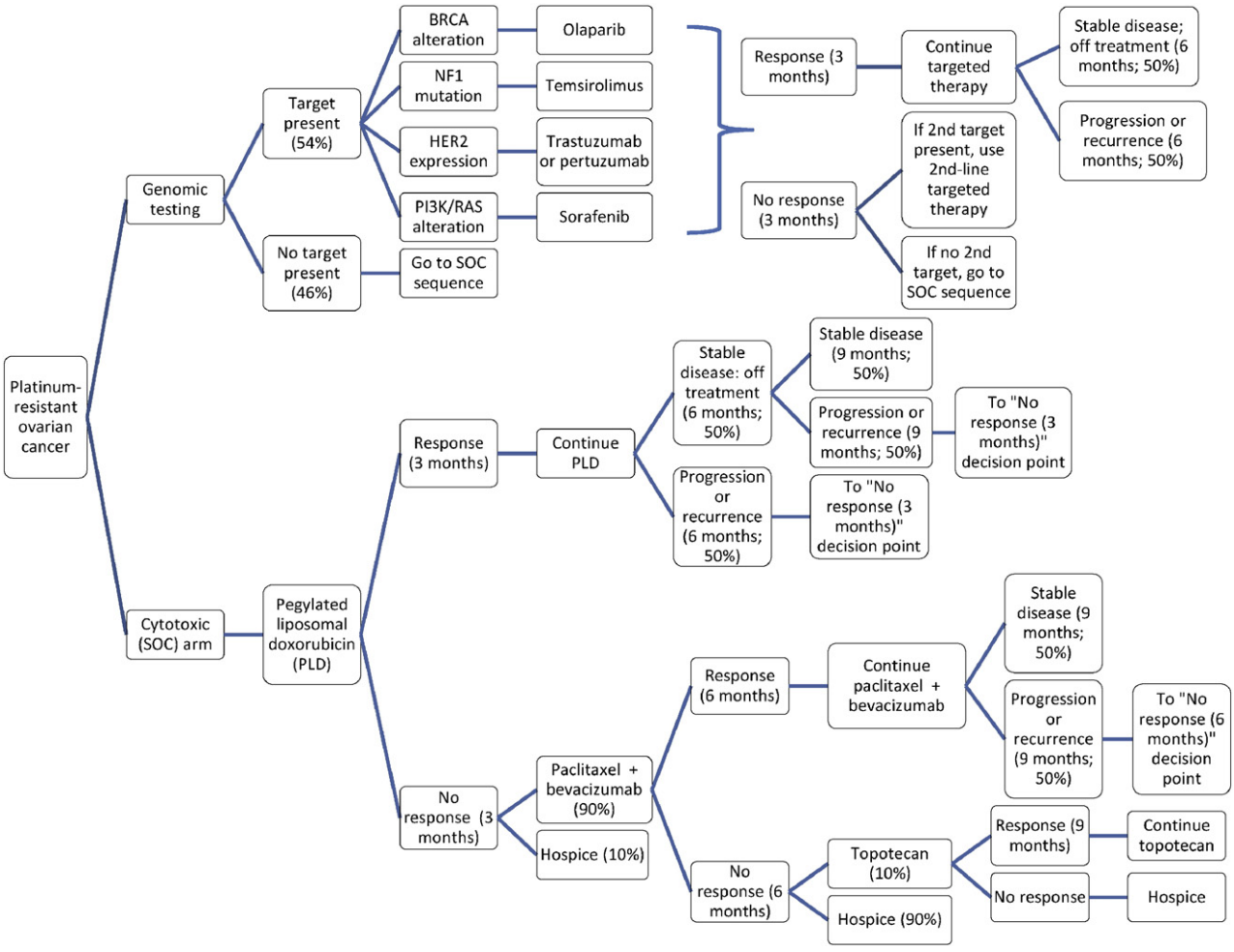

Fig. 1. Decision tree structure used for the cost-utility model of genomic-based vs. cytotoxic therapy for platinum-resistant ovarian cancer.