Patient Versus Physician Valuation of Durable Survival Gains: Implications for Value Framework Assessments

Jason Shafrin, PhD[1],*, Taylor T. Schwartz, MPH[1], Tony Okoro, PharmD[2], John A. Romley, PhD[3]

[1]Precision Health Economics, Los Angeles, CA, USA; [2]Bristol-Myers Squibb, Princeton, NJ, USA; [3]University of Southern California, Los Angeles, CA, USA

ABSTRACT

Background: Previous research indicates that patients value therapies that provide durable or tail-of-the-curve survival gains, but it is unclear whether physicians share these preferences. **Objective:** To compare patient and physician preferences for treatments with a positive probability of durable survival gains relative to those with fixed survival gains. **Methods:** Patients with advanced stage melanoma or lung cancer and the oncologists who treated these patients were surveyed. The primary end point was the share of respondents who selected a therapy with a variable survival profile, with some patients experiencing long-term durable survival and others experiencing much shorter survival, compared to a therapy with a fixed survival duration. Parameter estimation by sequential testing was applied to calculate the length of nonvarying survival that would make respondents indifferent between that survival and therapy with durable survival. **Results:** The sample comprised 165 patients (lung = 84, melanoma = 81) and 98 physicians. For lung cancer, 65.5% of patients preferred the therapy with a variable survival profile, compared with 40.8% of physicians (Δ = 24.7%; P < 0.001). For melanoma, these figures were 63.0% for patients and 29.7% for physicians (Δ = 33.3%; P < 0.001). Patients' indifference point implied that therapies with a variable survival profile are preferred unless the treatment with fixed survival had 13.6 months (melanoma) or 11.6 months (lung) longer mean survival; physicians would prescribe treatments with a fixed survival if the treatment had 7.5 months (melanoma) or 1.0 month (lung) shorter survival than the variable survival profile. **Conclusions:** Patients place a high value on therapies that provide a chance of durable or "tail-of-the-curve" survival, whereas physicians do not. Value frameworks should incorporate measures of tail-of-the-curve survival gains into their methodologies.

Keywords: cancer, preferences, survival, value framework.

Copyright © 2017, International Society for Pharmacoeconomics and Outcomes Research (ISPOR). Published by Elsevier Inc.

Introduction

Prior research indicates that patients place substantial value on a modest chance of a durable survival response, over and above average survival [1]. Almost four-fifths of patients preferred a therapy with a greater chance of durable survival gain, holding constant its effect on average survival. Put differently, patients are willing to risk premature mortality in pursuit of a chance at a durable survival gain.

This research topic is of more than academic interest. Value frameworks for oncology treatments have been developed by a number of organizations, including the American Society of Clinical Oncology, the European Society for Medical Oncology, the Institute for Clinical and Economic Review, the Memorial Sloan Kettering Cancer Center, and the National Comprehensive Cancer Network [2–6]. Most of these frameworks rely on efficacy measures based on improvements in survival for the median patient. A revised version of the American Society of Clinical

Oncology framework [7], however, also takes into account improvements in "tail-of-the-curve" survival.

To better understand attitudes toward durable or tail-of-the-curve survival benefits, this study surveyed cancer patients and physicians and extends previous research in three ways. First, we compared patient treatment preferences against physician preferences for treating patients. Second, we examined preferences for patients with non–small cell lung cancer (NSCLC), a tumor site not studied in previous research on patient valuations for durable survival gains. Third, although many studies have compared patient and physician preferences [8–12], this study specifically assessed whether physicians view a chance of durable survival, independent of mean survival, in the same way that patients do. Thus, this study highlights whether there were differences in patient and physician attitudes toward tail-of-the-curve survival (i.e., durable survival) and how such differences could inform current treatment decision making and value framework development.

Methods

This prospective survey of cancer patients and physicians aimed to determine how each group values therapies that offer a positive probability of durable survival gains. The durable survival therapies had variable survival profiles, wherein some patients' survival after treatment is significantly below mean survival and other patients have durable response to treatment and live much longer than the mean patient.

Durable survival treatments were calibrated based on survival profiles from pivotal trials of nivolumab among patients with advanced NSCLC and ipilimumab among patients with advanced melanoma. Ipilimumab was selected because it had the longest study follow-up time (10 years) of available immuno-oncology therapies [13]. Patient treatment preferences and physician prescribing preferences for therapies with a chance of durable survival were compared with therapies with fixed survival duration. A fixed survival therapy is a hypothetical therapy under which all patients live for a specified period of time and then die immediately afterward.

Study Population

Survey respondents comprised 1) patients with advanced stage lung cancer; 2) patients with advanced stage melanoma; and 3) oncologists who treated patients with lung cancer or melanoma. Patients had to have a diagnosis of cancer or malignant tumor or advanced stage (i.e., stages III or IV) lung cancer or melanoma, be aged $\geq$ 18 years, be a resident of the United States, and sign an informed consent form.

The physicians surveyed were practicing medical oncologists who treated $\geq$ 5 patients with cancer per month, had a medical degree, were board certified in oncology, regularly prescribed chemotherapy and/or targeted cancer treatment to patients with cancer, and signed an informed consent form.

Data Collection Process

Respondents were recruited, and the survey was hosted through a MedPanel patient and physician database. Patients were recruited using HIPAA-compliant methods through their physician network and professional relationships with patient support and advocacy organizations. Researchers have used the MedPanel database to elicit physician opinions across a variety of conditions, including cardiovascular disease [14], hepatitis C [15], chronic pain [16], diabetes [17], and cancer [18].

After the patients were contacted, their current cancer stage was confirmed through screening questions prior before they were sent a unique link to the survey that could not be sent to other individuals. MedPro identification software was used to check physicians' licenses and verify that inclusion criteria were met. Survey recruitment occurred throughout the United States, covering 42 states. The survey was programmed and hosted using survey building software (Jibinu, Fitchburg, MA).

Before the full data collection began, six patients (three with advanced melanoma and three with lung cancer) and four physicians were selected for pilot study interviews to further hone the survey instrument that collected all data necessary to achieve the research objectives. Patients and physicians who completed the survey and physicians who referred patients received remuneration for their time.

The institutional review board approval process was completed through One Health, LLC.

Survey Design

The analytic approach relied on direct solicitation of respondent preferences across nonvarying survival and varying survival treatments. Economists often call propositions with the chance of both a good and bad outcome "lotteries," and numerous studies have measured risk aversion using respondent preferences over different lotteries [19]. Respondents chose between a treatment with a varying survival profile and one with a fixed survival outcome. This study set the fixed survival value of the first scenario presented to be equal to the mean survival of the durable survival therapy.

The survey calibrated the variable survival profiles based on two immuno-oncology treatments for advanced melanoma and NSCLC. Immuno-oncology agents offer the prospect of durable survival gains for a subset of patients treated. For patients with lung cancer, the survey calibrated the durable survival therapy for a nivolumab clinical trial of patients with NSCLC that included 66 months of follow-up survival data [20]. This study calibrated the durable survival therapy presented to patients with advanced-stage melanoma to the results of an ipilimumab clinical trial of unresectable or metastatic melanoma that reported 120 months of follow-up survival data [13].

Patients were asked which therapy they preferred for their own treatment (Fig. 1). Initially, the value of the fixed survival therapy (Therapy A) was set to equal the mean survival of the therapy with a variable survival profile (Therapy B)—specifically, 48 months for melanoma and 30 months for lung cancer. This approach replicated an earlier study that measured patient (but not physician) preferences for variable survival compared with fixed survival profiles [1].

Next, parameter estimation by sequential testing (PEST) was used to identify the point at which respondents were indifferent between the therapy with fixed and variable survival (i.e., the indifference point) [21]. PEST is an adaptive elicitation technique that determines the stimulus value for each new question via the participant's response to the previous question. Under the PEST algorithm, if a survey respondent (patient or physician) preferred the durable survival therapy, the survival of the fixed survival therapy was increased. This process continued until a respondent who initially preferred the variable survival treatment switched to preferring the fixed survival therapy. If the fixed survival therapy was preferred, the value decreased in subsequent questions until an indifference point was reached. Respondents continued to receive questions until an indifference point was reached or until 10 questions were answered.

The patient survey included an eligibility screener to ensure a sample that met the inclusion/exclusion criteria, a burden of cancer module that provided data about the patient's cancer and treatment, and a demographics and backgrounds module to elicit data for exploratory analysis. The latter two modules were administered after the therapy valuation module.

The physician survey contained three modules. In the treatment preferences (PEST) module, physicians were asked which therapies they would prescribe for their patients. The varying and fixed survival treatments were calibrated identically to those in the patient module, but physicians received both advanced melanoma and lung cancer treatment scenarios. Additional sections included an eligibility screener to ensure a sample that met the inclusion/exclusion criteria and a demographics and backgrounds module to elicit data for exploratory analysis.

Outcomes

There were two primary end points: 1) whether the respondent preferred a durable survival therapy compared with a fixed survival therapy; and 2) the indifference point in terms of certain survival between a durable survival therapy and a fixed survival