The impact of recent chemotherapy innovation on the longevity of myeloma patients: US and international evidence

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ABSTRACT

The longevity of multiple myeloma patients increased sharply since the late 1990s. This increase coincided with the introduction of several important innovations in chemotherapy for myeloma. In this study, we aim to quantify the impact of recent chemotherapy innovation on the longevity of myeloma patients using both time-series US data and longitudinal data on 38 countries.

We estimate that almost two-thirds (0.99 years) of the 1997–2005 increase in the life expectancy of American myeloma patients was due to an increase in the number of chemotherapy regimens now preferred by specialists. Based on a back-of-the-envelope calculation, this means that the cost per US life-year gained from post-1997 chemotherapy innovation is unlikely to have exceeded $46,000.

We also investigate the impact of chemotherapy innovation on the myeloma mortality rate using longitudinal country-level data on 38 countries during the period 2002–2012. Countries that had larger increases in the number of chemotherapy regimens now preferred by specialists had larger subsequent declines in myeloma mortality rates, controlling for myeloma incidence. The (marginal) effect on the mortality rate of one additional preferred chemotherapy regimen is similar in other countries to its effect in the US. Non-US prices of two of the three new drugs were lower than US prices, so recent myeloma chemotherapy innovation may have been more cost-effective in other countries than it was in the US.

Recent chemotherapy innovation has had a significant positive impact on the longevity of myeloma patients in the countries in which the drugs have been available.

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1. Introduction

Myeloma is a type of bone marrow cancer, where plasma cells found in the bone marrow divide uncontrollably and form tumors that can destroy bones and damage the kidneys (Harrison, 2013). The incidence varies globally from 1 per 100,000 people in China, to about 4 per 100,000 in most developed countries. Thus it is a rare disease, but it is the second most frequent malignancy of the blood in the US, where about 20,000 new cases occur every year. Median age at diagnosis is reported to lie between 61 and 70 years of age, and only 2% of patients are younger than 40 years (Cook, 2008; Raab et al., 2009). About 90% of myeloma patients have multiple myeloma (MM), which is myeloma that affects several different parts of the body.

Fig. 1 shows the age-adjusted multiple myeloma mortality rate per 100,000 inhabitants for the US population for the period 1975–2009.

After rising for about 20 years, the US MM mortality rate has fallen steadily since 1997. In this paper, we investigate the extent to which the recent decline in myeloma mortality was caused by recent innovation in chemotherapy, and whether a similar impact can also be observed in other countries.

First, we will investigate this impact using annual US time-series data during the period 1975–2009. We believe that the sharp discontinuity in the number of available chemotherapy regimens enables us to identify this impact. Second, we will investigate this impact using longitudinal country-level data on 38 countries during the period 2002–2012. In this case, identification is enabled by the fact that some chemotherapy regimens became available later in some countries than in others, or did not become available in some countries by the end of 2010.

In both approaches, the treatment variable is the (current or
Chemotherapy is de facto a date of adoption (FDA) in 1958, 2003, and 2005, respectively (Drugs@FDA, 2012). The NCIt and OncologySTAT lists of myeloma chemotherapy regimens differ in some respects. The NCIt list includes twice as many "old" (pre-1998) regimens as the OncologySTAT list: six as opposed to three. OncologySTAT also distinguishes between regimens designated by specialists as preferred for use in clinical practice and regimens that are not preferred. Preferred status may be interpreted as first-line therapies for certain groups of patients. As shown in Table 1, half of the OncologySTAT regimens are preferred regimens, and all of these are "new" (post-1997) regimens.

Although there are some discrepancies, both sources indicate that there were no innovations in chemotherapy for myeloma patients during the period 1977–1997, but that there have been numerous innovations since 1997. This is illustrated in Fig. 1, which shows annual data on the number of NCIt regimens, OncologySTAT regimens, and preferred OncologySTAT regimens that could have been used to treat myeloma patients in the US during the period 1977–2005 (Fig. 2). Before 1997, treatment options were quite limited, particularly for patients who relapsed. The only real treatment option available besides supportive treatments was stem cell transplantation, which was introduced in the 1980s. However, patients must be fairly young and healthy to withstand the side-effects of transplantation. Many myeloma patients therefore do not qualify for transplantation. Ramesh and Maïke (2013) reports that only about 5% of myeloma patients received stem-cell transplantation in 1994. Thalidomide was the first-in-class immunomodulatory agent with an indication for multiple myeloma (MM). Thalidomide and lenalidomide target both myeloma cells and the bone marrow microenvironment (Raab et al., 2009), whereas bortezomib is a chemotherapeutic agent that induces cancer cell death by inhibiting the proteasome enzyme complex involved in cell cycle control and growth (Harrison, 2013). These agents target the immune system in such a way that patients suffer minimal damage, and normal function of the immune system remains intact (V. Kumar and Chhibber, 2011).

The second source is The Elsevier Guide to Oncology Drugs and Regimens (2012 edition) (also known as OncologySTAT) (Elsevier, 2012). OncologySTAT provides a comprehensive list of more than 290 commonly used single-agent and combination regimens used in the treatment of 26 cancer types. The regimens listed are those most widely used and are in accordance with guideline recommendations of the National Comprehensive Cancer Network, American Society of Clinical Oncology, and National Cancer Institute. They were selected by oncologists at major US cancer centers, including members of the OncologySTAT Advisory Board. (Appendix 2 shows OncologySTAT’s website with the list of chemotherapy regimens used to treat myeloma.)

In Section 2 we will review the related literature. In Section 3 we will analyze the impact of chemotherapy innovation on the longevity of myeloma patients using annual US time-series data.
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