Overview of Economic Analysis of Le Chevalier Vinorelbine Study

By Bruce E. Hillner, MD and Thomas J. Smith, MD

The costs and relative cost-effectiveness of different treatments for common illnesses are an increasing concern. New treatments for advanced non-small-cell lung cancer are having an impact. However, these treatments vary markedly in their direct financial costs, toxicity, and quality-of-life profiles. Direct comparisons between most combination regimens are not yet completed. Vinorelbine (Navelbine) is the first new agent approved in the United States for the treatment of metastatic non-small-cell lung cancer in more than a decade. We previously reported results of a post-hoc economic analysis that compared the anticipated cost-effectiveness of three regimens used to treat non-small-cell lung cancer (vinorelbine alone versus vinorelbine plus cisplatin [Platinol] versus vindesine plus cisplatin, the assumed standard treatment in Europe). Results showed that vinorelbine plus cisplatin was the most effective regimen. Using vinorelbine alone as a baseline, vinorelbine plus cisplatin added 56 days of life at an additional cost of $2,700, resulting in a cost-effectiveness ratio of $17,700 per year of life gained. Similarly, vindesine plus cisplatin added 19 days of life at a cost of $1,150, or $22,100 per year of life gained. Compared to vindesine plus cisplatin, vinorelbine plus cisplatin added 37 days of life at a cost of $1,570, or $15,500 per year of life gained. We conclude that the incremental cost-effectiveness of the vinorelbine plus cisplatin regimen was less than most commonly accepted medical interventions. If vinorelbine is preferred because of its favorable toxicity profile, the additional effectiveness of cisplatin added substantial efficacy at an acceptable cost.[ONCOLOGY(Suppl 4):14-17, 1998]

The failure to contain health care costs and curtail their growth is a problem common to all nations and a continuing focus of public policy debate. Attempts to control costs cannot be left to administrators and public health officials. As Eisenberg has stated, to suggest that medical decision making can be divorced from consideration of cost denigrates the complexity of patient care.[1] The application of economic principles to medicine does not necessarily mean that less money should or will be spent in total or for a specific condition, but rather, that these resources will be used more efficiently. Oncology services have been a particular focus of attention regarding medical costs. Oncologic costs of care for Medicare patients grew by approximately 17% annually in the late 1980s. Current estimates are that costs for oncologic care account for about 15% to 20% of the health care dollar in the United States. The several reasons for this growth include:

- Demographic changes
- A common reluctance to stop therapy
- Increasing attention to quality-of-life concerns
- Innovations in biotechnology (ie, potentially effective new therapies)
- There is rarely one optimal treatment for an individual’s cancer.

The use of chemotherapy for metastatic non-small-cell lung cancer (NSCLC) is controversial. A common perception has been that chemotherapy has little impact on long-term survival. Two meta-analyses of published clinical trials, however, found a 27% to 34% reduction in risk of early death with treatment at 6 months.[2,3] In addition, recent practice guidelines from the American Society of Clinical Oncology state that chemotherapy, ideally a platinum-based regimen, is appropriate for selected patients who have a good performance status with both unresectable, locally advanced, and metastatic NSCLC.[4] Whether the use of chemotherapy has a beneficial
Overview of Economic Analysis

For these reasons, we performed a post-hoc analysis using financial data from the Medical College of Virginia/Virginia Commonwealth University, representative of large American academic centers of the three arm vinorelbine (Navelbine) trial led by Dr. Le Chevalier. We sought to estimate the cost and cost-effectiveness of vinorelbine alone and vinorelbine plus cisplatin (Platinol) against a regimen commonly used in Europe of vindesine plus cisplatin, using results from the largest randomized trial of vinorelbine. The intent of this analysis was to assess the incremental efficacy (the difference in survival between regimens), incremental costs (the difference in treatment toxicity, monitoring, and drug costs), and incremental cost-effectiveness (the societal resources necessary to gain an additional year of life with each regimen).

Mean survival, preferred to median survival as a measure of benefit for use in cost-effectiveness calculations, was estimated from a clinical trial in which 612 patients were randomly assigned to one of three arms: (1) vinorelbine alone, 30 mg/m² intravenously (IV) weekly; (2) vinorelbine, 30 mg/m² IV weekly, plus cisplatin, 120 mg/m² IV on days 1 and 29, then every 6 weeks; or (3) vindesine, 3 mg/m² IV weekly for 7 weeks, then every 2 weeks, plus cisplatin at the same dose and schedule. Table 1 summarizes clinical results for patients in all three study arms.

The clinical trial did not prospectively collect economic or quality-of-life data. We were given access to the primary data. The cost-effectiveness analysis was performed using the final data set that included any additional 12 months of patient follow-up. The analysis assumed that all patients were treated until disease progression, unacceptable toxicity, or patient refusal, or had stable disease for 18 months post-treatment. The post-hoc analysis included all direct treatment costs including toxicities and monitoring. The analysis was performed as if all patients were treated at the Medical College of Virginia. The analysis assumed that all patients received identical supportive care. The efficacy and costs of second-line chemotherapy or other palliative care were not assessed. Costs were estimated from specific institutional cost-to-charge ratios that varied with the type of service, such as drug acquisition, radiology, hospital "hotel" costs, etc. The costs of vinorelbine were based on the projected wholesale price. Patients treated with cisplatin were assumed to receive it as outpatients, reflecting the current US pattern of care.

The findings of the economic analysis are summarized in Table 2 above. The vinorelbine used as monotherapy arm had the lowest costs due to fewer required antiemetic drugs and laboratory monitoring tests. Vinorelbine plus cisplatin had the highest total treatment costs; 64% to 81% of total treatment costs were for chemotherapy, supportive drugs, and laboratory tests, and 41% to 46% of costs were for chemotherapy only.

The incremental costs per patient for these regimens ranged from $1,150 to $2,700, or about $42 to $60 per day of life gained. When multiplied by 365 days to convert these findings to the benchmark of comparison, cost per year of life saved, the incremental costs ranged from $15,500 to $22,100 per life year gained.

Quality of life with each of the treatment strategies was not formally prospectively collected during the clinical trial. Our analysis allowed us to speculate about the effect of relative differences in quality of life between the single-drug arm (vinorelbine) and the cisplatin-containing arms. A sensitivity analysis of the importance of patient utilities for cisplatin-associated toxicity found that if vinorelbine compared with cisplatin treatment was associated with a 0.12 (absolute) greater utility or quality of life, then the vinorelbine alone strategy was the preferred one.

Conclusions

Concerns about the costs of established and new medical therapies will be increasingly scrutinized. Long-term efficacy of chemotherapy for non-small-cell lung cancer is less than desired, but the efficacy and cost effectiveness of new treatment combinations using vinorelbine are comparable to those of other commonly accepted medical therapies. A common assumption that oncology treatments for advanced disease are not effective or cost effective may not be justified if efficacy from clinical trials can be translated to community settings. In addition, once results are available from ongoing head-to-head randomized comparisons of multi-drug regimens, eg, vinorelbine plus cisplatin compared with carboplatin (Paraplatin) plus a taxane, clinical economists will be able to make more direct inferences about the incremental cost effectiveness of these newer interventions.
Discussion

**Question:** Could you elaborate on the difference between cost versus charge information? You said the difference between costs and charges was profits, suggesting that profits (or mark-up) were not a legitimate part of cost. In fact, the reason to pay attention to charges versus cost is that charges are often not paid, and what is paid is the cost.

**Dr. Hillner:** True enough, but it is not clear where you should draw the line as far as what cost is. An economist, as opposed to a clinician, might slice and dice this, but the main point an organization needs to focus on is the bottom-line cost before even a potential profit, by trying to focus on the cost in an interval of time of delivering some type of product, either a physician service, a laboratory test, a radiologic assessment, or a drug, for example.

**Question:** You mentioned the quality-of-life adjustment that you have done using a Q-TWist type of analysis. Because Q-TWist analysis involves a description of the toxic episode and placing a value on that, who did you use to value the toxicities?

**Dr. Hillner:** We did not prospectively collect either provider or patient data on that. We were determining hypothetical results—what we may have found had we collected the data.

**Question:** Did you include in your cost data the numbers of hospitalizations and the causes of hospitalization?

**Dr. Hillner:** Hospitalization was viewed primarily as a failure event. We handled hospitalizations in the following manner: For patients at the beginning of drug therapy, each of the drug interventions was assumed to be delivered as an outpatient. The reasons for hospitalization were only febrile neutropenia or failure due to disease progression. For patients discontinuing therapy due to progression of disease, who were subsequently hospitalized, we assumed that the length of hospitalization was the same regardless of the therapeutic intervention that the patient had previously received. Thus, only the number of hospital days related to treatment-associated toxicities could differ between treatments. Febrile neutropenia was the primary toxicity and a modest number of patients needed intravenous fluids for dehydration.

**Question:** It would be interesting to test that because the assumption of equal cost from time of progression is quite a large assumption.

**Dr. Hillner:** It is not intuitively obvious whether the subsequent pattern of recurrence or failure is different based on having received a different chemotherapy regimen. I think most oncologists would say that there is no reason to expect the rate of central nervous system complications versus chest complications to be different because of the prior chemotherapy.

**References:**


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