Beyond Survival: Economic Analyses of Chemotherapy in Advanced, Inoperable NSCLC

Review Article [1] | February 01, 1998
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Research shows that chemotherapy for inoperable non-small-cell lung cancer (NSCLC) improves survival. The economic implications of this treatment choice may be substantial. This paper reviews studies examining the cost-

Mather et al review economic analyses of chemotherapy in stage IIIB and IV non-small-cell lung cancer (NSCLC) to answer the question, Is chemotherapy more cost-effective than best supportive care for non-small-cell lung cancer? Whether we like it or not, these questions are integral to medical decision-making.[1] The data presented in their review indicate that chemotherapy for non-small-cell lung cancer is probably within the bounds of an effective use of societal resources. As seen in the authors' Table 2, chemotherapy as compared to best supportive care, or slightly more effective chemotherapy compared to slightly less effective chemotherapy, gives cost-effectiveness ratios of less than $20,000 per additional year of life saved. This compares favorably with the treatment of hypertension, lowering of serum cholesterol, screening mammography, and a host of accepted uses of medical resources.[2]

The authors conclude that, based on the available clinical and economic data, patients can be reasonably offered chemotherapy for stage IIIB and IV disease to extend survival, and that this can be done at a cost that society can afford. These conclusions are consistent with clinical practice guidelines published by the American Society of Clinical Oncology[3] and by the Province of Ontario,[4] both of which suggest that the survival benefit is sufficient for patients to receive first-line chemotherapy for non-small-cell lung cancer.

What About Newer, More Expensive Chemotherapy?
Do these conclusions apply to newer chemotherapy that is more expensive than the regimens reviewed by Mather et al? That question cannot be answered as definitively. As part of a project that allowed patients to choose between undergoing chemotherapy or keeping the money that would have been spent on it, we priced the various regimens used at our hospital for non-small cell lung cancer (Table 1). The cost of six cycles of chemotherapy ranged from inexpensive to very expensive. The use of docetaxel (Taxotere) or other expensive agents would increase the cost even more. These regimens, which cost severalfold more than those used in the programs evaluated by Mather et al (with the exception of vinorelbine [Navelbine] plus cisplatin [Platinol]) are almost certain to have much higher cost-effectiveness ratios. The cost of these regimens could well be beyond what society might reasonably be expected to pay, unless their effectiveness is substantially better in phase III trials.

As first-line chemotherapy has become accepted as state-of-the-art care for patients with non-small-cell lung cancer and good performance status, the focus of economic analysis should shift to drug-drug comparison and the use of second-line chemotherapy. Second-line chemotherapy has not been subjected to a cost-effectiveness analysis. Most second-line chemotherapy programs have had dismal results, and have shown no effect on survival, except when compared to historical controls (always subject to bias). Thus, no statement can be made about either the routine use or cost-effectiveness of second-line non-small-cell lung cancer treatment. However, given that its effectiveness is almost certainly severalfold less than that of first-line therapy, second-line treatment would have to be very inexpensive to have an acceptable cost-effectiveness ratio. All of the second-line treatments being evaluated that include paclitaxel (Taxol), docetaxel, and other expensive drugs, would not fit that bill.

What Do Patients Want?
Although cost-effectiveness is clearly important, we are not sure whether it is the right question to be asked, or one that should be asked in a vacuum. A more important question is, what do our patients want? Our patients want to be cured, or at least to live as long as possible, and they want relief of symptoms. They are often convinced that there is some treatment out there that can help
dramatically, and generally are not interested in cost considerations. Mather et al note that patient preferences are important and should be collected on a clinical trial, but we are not aware of any good way to collect them. As Mather et al point out, once patients select a treatment, typically they are convinced of its efficacy and would be highly unlikely to state that they made the wrong choice.

The 1985 survey of Canadian physicians,[5] 85% of whom said that they would not choose chemotherapy for themselves if they had non-small-cell lung cancer, is often cited as an argument against the use of chemotherapy. We find these data to be of little value. In 1985, the medical community was not yet convinced that cisplatin-based therapy provided any survival benefit. This was before the advent of the serotonin antagonist antiemetics—the days when we used to turn our heads while patients smoked pot in the bathroom, and when patients expected to vomit even after beingbombarded with high doses of benzodiazepines or metoclopramide. More effective regimens, such as vinorelbine plus cisplatin, and paclitaxel plus cisplatin or carboplatin (Paraplatin) had not yet emerged.

What Do Patients With Advanced Cancer Want?

One very important part of patient choice deserves clarification. We do not believe that the preferences of generally healthy individuals can be presumed to be the preferences of those same individuals when they are facing death, as patients with advanced non-small-cell lung cancer are. For insight into the preferences of those with advanced cancer, one must ask them. When seriously ill patients (13% with non-small-cell lung cancer) were asked how much time they would trade in their current health state for 2 weeks of perfect health, 9% were willing to live 2 weeks or less in perfect health rather than 1 year in their current state (utility = 0.04),[6] whereas 35% were unwilling to exchange any time in their current state of health for a shorter life in excellent health (utility = 1.0). The mean utility for this seriously ill group was 0.72, indicating that patients valued 12 months in their current state as much as 8 or 9 months in perfect health. Although the presumed poor quality of life of patients given chemotherapy is another argument made against the use of chemotherapy for non-small-cell lung cancer, the data suggest that most actual patients value quantity over quality of life and are willing to accept toxicity.[6,7] Davies and colleagues have documented the difficulty that glioma patients have in making a rational decision about treatment that balances the poor prognosis, inability of radiation to stabilize symptoms, side effects, and societal expectations for treatment.[8,9] Indeed, there seems to be no justification for using the physician-rated preference of 1 month of survival equaling 2 months spent on chemotherapy, as Kennedy et al did,[10] which partly explains why their cost-utility analysis of the same non-small-cell lung cancer data differs so much from that of Jaakkimainen et al.[11] Ideally, any quality-adjusted survival rates must use the preferences of real cancer patients, not surrogates, as surrogates consistently underestimate the utility to patients of their current health state.

Will Quality of Life Data Help Treatment Decision-Making?

Mather et al are hopeful that quality-of-life analysis will help patients and physicians make better choice about non-small cell chemotherapy choices. Bergman and Aaronson recently reviewed a number of good quality-of-life studies.[12] Our opinion of those data is that the studies complement the clinical trials but, in no case, supplant them. That is, if survival is enhanced, quality-of-life studies results go hand in hand. We are aware of no study with quality-of-life as the major end point that has changed clinical practice in this disease despite 10 years of data collection. To us, a compelling quality-of-life study would be one in which survival was enhanced by chemotherapy but quality of life was poor, such that patients chose the arm with poorer survival; or conversely, a study showing worse survival for a particular chemotherapy but much better quality of life, such that patients chose it and would forego the extra weeks or months of survival. We are not aware of any studies that have reached this sort of meaningful clinical conclusion. This dearth of useful information is not the fault of patients, investigators, researchers, quality-of-life instruments, or study design. Non-small-cell lung cancer is a complicated disease, chemotherapy is only one small component of global quality of life, and patients show remarkable adaptability to adverse circumstances. And, we should not forget that the quality of life of patients with progressive disease is often very poor. Thus, although we support quality-of-life studies, we doubt that they will have a major impact on clinical practice.

How Can We Help Patients Make Decisions?

What then, is to be done to help patients make decisions about such treatment? In our view, the debate over whether chemotherapy prolongs survival in unresectable stage III or stage IV patients with non-small-cell lung cancer is over.[13,14] Debate should now shift to cost-effectiveness, improving quality of life, patient preference considerations, and which regimen can optimize
survival, cost, and quality of life (Table 2). First, we need better ways to explain the results of clinical trials, and to know that patients are giving careful consideration to both best supportive care and chemotherapy.

Second, we need to end the dichotomy between best supportive care without chemotherapy and best supportive care with chemotherapy. This argument is divisive, ignores the substantial gains of chemotherapy in this and other diseases, and polarizes two camps of health-care professionals who should both be interested in helping patients either be cured or adapt to their disease. Third, we need a new careful evaluation of what health-care professionals would do themselves if faced with the disease, we need to differentiate what providers would do in this situation from what actual patients would do. Perhaps a support network of people who have been through chemotherapy could help those who are considering it (if we can find enough survivors and keep them from biasing the argument either for or against treatment).

Fourth, we need to keep the cost of chemotherapy regimens down. Although the treatments reviewed by Maher et al were [cost-effective,] they still cost additional money. Adding a first-line regimen that costs 7 times as much, and then a second-line regimen that costs 10 times as much will cause resources to disappear far too quickly and unwisely. As our expert noted, we can still go broke providing [cost-effective] care.

Finally, we need to incorporate some quick, simple economic analyses into a few of the ongoing clinical trials. If the combination of carboplatin and paclitaxel improves survival by 6% at 1 year, we need to know whether the additional expense is justified, and only a formal cost-effectiveness analysis will answer that question.

What We Know Now

We now know enough about treating this disease to make some recommendations. We know that it would be unethical to conduct another trial of chemotherapy vs [best supportive care] (whatever that is) in non-small-cell lung cancer. We know that vinorelbine prolongs survival over minimally active therapy with fluorouracil and leucovorin.[15] We know that cisplatin-based chemotherapy prolongs survival over supportive care alone.[16] We know that cisplatin plus vinorelbine prolongs survival compared to cisplatin alone, vinorelbine alone, and cisplatin plus vindesine (Eldisine).[17] We know that cisplatin plus vinorelbine and cisplatin plus paclitaxel are sufficiently better than cisplatin plus etoposide (VePesid) to be the recommended treatments.[3]

The perception by many physicians that carboplatin plus paclitaxel has substantial efficacy and less toxicity has earned it a place as one of the major regimens used to treat non-small-cell lung cancer. Fortunately, a direct, randomized comparison of carboplatin plus paclitaxel vs cisplatin plus vinorelbine is underway; unfortunately, it does not include a much-needed economic analysis using real costs.

Patients with good performance status should be offered first-line chemotherapy but must be adequately informed of its modest efficacy, toxicity, and costs. For the patient, chemotherapy is rational; for the physician to intentionally decide not to offer chemotherapy is no longer acceptable in 1997.

References:


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