

Pharmacoeconomics of Emerging Therapies for Rheumatoid Arthritis

Based on a presentation by Arthur Kavanaugh, MD

Presentation Summary

Rheumatoid arthritis is a costly disease. Patients with this condition not only utilize substantial medical resources, but also incur high indirect costs in the form of work disability. These indirect costs are generally much greater than the direct costs. Therefore, a new therapy that is able to control this disease more effectively may be cost effective, even if the direct costs of the

therapy itself are high. From a cost-analysis point of view, patients with refractory disease may be good candidates for a new therapy. All costs, direct and indirect, should be considered, and a global, long-term perspective on patient care should be taken. One way to estimate the worth of a therapy based on its ability to improve how patients feel would involve a utility or quality-of-life analysis.

“Rheumatoid arthritis is certainly costly,” said Arthur Kavanaugh, MD, Associate Professor of Medicine, University of Texas Southwestern Medical Center, and Chief of Rheumatology, Dallas Veterans Administration Medical Center. “It’s costly in terms of work disability as well as in terms of what the patients have to pay.” Patients with this condition utilize substantial medical resources, including healthcare provider time and surgical services.

The rationale for considering expensive therapies is that rheumatoid arthritis (RA) is already an expensive disease. Therefore, a therapy that is able to control the disease more effectively than current treatment may have incremental cost effectiveness. The issue at hand is explaining why a newer, more expen-

sive therapy may be indicated in certain cases.

“There are many different answers to even very simple questions when you talk about cost,” Dr. Kavanaugh observed. An obvious consideration is the cost of the medications. “The people who will have to pay for relatively expensive medications will want to know whether they are worth it,” he commented.

Types of Cost Analysis

Cost Benefit. According to Dr. Kavanaugh, the simplest type of analysis involves determining the cost of the medication and the cost of the disease. In a cost-benefit or cost-minimization analysis, both the cost and the outcomes are expressed in dollars. This type of analysis has both strengths and weaknesses, but it is relatively straightforward.

term effects. A question regarding the new agents is whether patients will have increased susceptibility to infection. If so, Dr. Kavanaugh noted, then it is appropriate to consider that as a direct cost. He gave the example of 1 of 1000 patients being hospitalized for pneumonia; that cost needs to be considered as the analyses are done.

Decision-Analysis Model

In 1994, Dr. Kavanaugh's group performed a decision analysis to compare the costs of a hypothetical new biologic agent with traditional disease-modifying antirheumatic drugs.⁵ Based on a survey of local rheumatologists at the time, methotrexate (MTX) was the most common therapy, and intramuscular gold was the second choice. But, most of those rheumatologists would have different drugs of choice if surveyed today. The decision-analysis process is illustrated in Figure 1.

Presence of Side Effects. The first decision is made on the basis of whether patients have side effects. Patients experiencing a major side effect were defined as nonresponders. They would be charged the costs of diagnosing and treating the specific side effects. Patients experiencing a minor side effect could still be defined as responders, but would also incur the costs of having such a side effect.

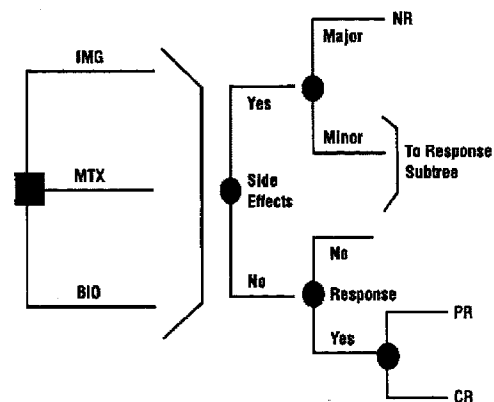
Patient Response. Patients may or may not respond to a treatment. If they do respond, the response would be defined as either partial or complete. The difficulty in this sort of analysis, according to Dr. Kavanaugh, is that looking at studies and determining how many people statistically respond to MTX is easy, but determining how many people on MTX are going to have a complete response is harder. For example, how many patients are going to do so well that they will be able to go back to work full-time and not

incur any work disability? In turn, how many people will have only a partial response?

Because the decision tree was designed to be simple, the analysis was done over a short (6-month) time frame. This time frame was chosen because a patient who is a nonresponder in clinical practice or a patient who has a side effect would not be kept on a medication for more than 6 months.

Cost of Therapy. Based on published information about the cost of RA in terms of work disability, the indirect cost of MTX therapy was calculated to be \$3200; the total cost was \$5400.^{1,2,5} The indirect costs stem from the fact that not everyone who is treated experiences improvement in their arthritis symptoms to the extent that they are able to go back to work full-time.

Figure 1. Decision Tree for the Treatment of Rheumatoid Arthritis



BIO = hypothetical biologic agent; CR = complete response; IMG = intramuscular gold; MTX = methotrexate; NR = no clinical response; PR = partial response. Source: Reference 5.

The total cost of the biologic agent was set at \$5000 for 6 months of administration. At that time there were no biologic agents marketed for treating RA. This cost was derived from the costs for 6 months of treatment with biologic agents available at the time for other indications. As it turns out, that figure was a fairly good estimate for the biologic agents now available for RA. As that figure is considerably higher than the cost of the other medications, it is the main cost driver. The direct costs of an expensive agent in this sort of model outweigh the indirect costs. For a traditional disease-modifying antirheumatic drug such as MTX, the indirect costs are the primary cost drivers.

Sensitivity Analysis of Response. A two-way sensitivity analysis of response for the 6-month time frame is shown in Figure 2. The

researchers varied elements in the decision analysis (eg, the extent of response and the costs of the agents). Above the line of equality, MTX is the preferred treatment from a cost standpoint. Below the line, the biologic agent is preferred. The new agent would need to be very effective (ie, many of the patients having a complete response). Even with two thirds or more of the patients having a complete response to therapy with the biologic agent, total costs for the drug would have to be approximately \$3000 or less for it to be preferred from a cost standpoint.

Limitations of the Model. Several considerations could have important effects on the analysis as it was performed. For example, the response rate to MTX was quite high. If a population of patients who had a lesser response to MTX were assessed, the analysis should be more favorable to a biologic agent that was still effective when used in such a population of patients.

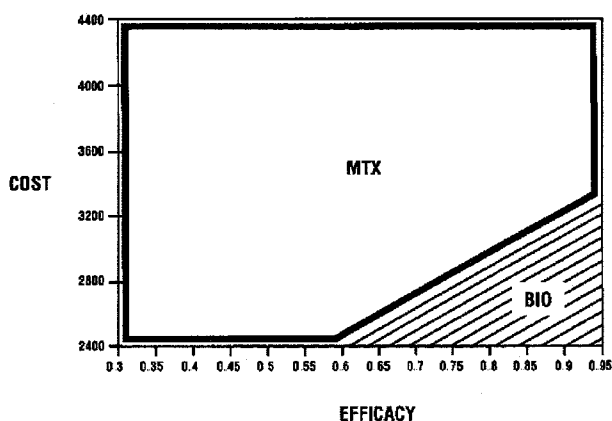
Further, Dr. Kavanaugh commented, a 6-month time frame can't reflect some of the more expensive outcomes of RA. He gave as an example the possibility that a therapy would be so successful that it could prevent or delay total joint replacement, an outcome that could only be captured in a study with a longer time frame. Evaluation of mortality also needs a longer time frame. In addition, failure costs were not included in this analysis.

The indirect costs may have been underestimated, Dr. Kavanaugh said. Only human capital was used, with no real consideration of utility analysis. However, he cautioned, rheumatologists need access to real information if they are going to make a persuasive argument that a new, expensive therapy is worthwhile.

Quality-of-Life Issues

A utility or quality-of-life analysis would be one way to estimate the

Figure 2. Two-Way Sensitivity Analysis Comparing the Total Costs of Therapy With a Hypothetical Biologic Agent or MTX Over 6 Months



All values below the line of equality (hatched area) indicate those estimates of cost and efficacy that make the biologic agent the preferred therapeutic choice. All values above the line of equality (darkened area) indicate that MTX would be the preferred therapeutic choice with regard to total costs of therapy.

BIO = hypothetical biologic agent; MTX = methotrexate. Cost = cost of medications. Efficacy = percent of patients with complete response.

Source: Reference 5

worth of a therapy based on its ability to improve how people feel. Although determination of quality-adjusted life years is commonly done, it is not the only way to assess quality of life. Dr. Kavanaugh used the Q-TWIST (quality-adjusted time without symptoms and toxicity) analysis as an example.

The questions used to evaluate quality of life vary. People can simply be asked how well they're feeling according to different scales. The questions also can be phrased in terms of a time trade-off (how much time living in an arthritis-free state would a patient trade for living a longer number of years with active arthritis?) or in terms of cost (how much would a patient be willing to pay to not have arthritis?). In addition, he noted that there are questions regarding the reliability and sensitivity of the analyses themselves.

"Obviously," Dr. Kavanaugh said, "if you have a therapy that makes people feel better and increases their number of quality-adjusted life years and that therapy is less costly, then it is a very useful intervention. If it is less effective and more costly, then it is not useful at all."

However, he noted that many therapies will likely fall into an in-between region. Then, judgment calls must be made. For example, he said, is it worth \$25,000 to get one more quality-adjusted life year? Is it worth \$100,000?

How much is a quality-adjusted life year worth? In the United States, the accepted standard is about \$50,000. This amount is based on the cost of hemodialysis per QALY; because the US government pays for hemodialysis treatment, this dollar amount is considered an acceptable amount for one life year. Therapies that cost \$50,000 or less per QALY (eg, joint replacement surgery, treating hypertension) are often deemed worthwhile by that standard.

Who Should Receive the New Biologic Agents?

Dr. Kavanaugh believes that the more severe and refractory the disease, the more cost effective an expensive therapy can be. "People with refractory disease may be the optimal patients from the point of view of cost analysis," he said. If future studies show that patients with early disease who receive the new therapies can have good long-term outcomes (eg, remission or a radical decrease in requirements for medical care), then they, too, will be candidates.

Conclusion

Dr. Kavanaugh said that rheumatologists need to take a global, long-term perspective on patient care. He commented that it can be difficult to convince other people that preventing progression of RA could be cost saving, and that the best argument is to consider all the costs as well as the long-term results of therapies.

Some sort of utility analysis, especially for interventions such as anti-tumor necrosis factor agents, would be valuable as well. "If a therapy makes someone feel so much better," Dr. Kavanaugh concluded, "then that certainly must be worth something."

... DISCUSSION HIGHLIGHTS ...

After Dr. Kavanaugh gave his presentation, he responded to comments from the roundtable participants.

Comment: In 1996, a publication by McIntosh in the *British Journal of Rheumatology* suggested the cost of rheumatoid arthritis in the U.K. was about 1.2 billion pounds [\$1.9 billion] a year. Our Department of Health [in the U.K.] believes that it spends about 100 million pounds [\$160 million] a year. When we put this discrepancy to them, their view was that these very large social service costs were all very well, but that wasn't going to help the health service fund new treatments

because there was no way that one government department was going to transfer money to another. I don't think that showing magnificent savings in work time and all these other issues relating to patients is going to be effective with the payers. We need to take a somewhat emotional view, I think, and convince them of the benefits for patients.

Dr. Kavanaugh: That's an excellent point, but I think it can be a tough sell. I think in the United States people say, how are you going to convince an organization to pay to prevent something that's going to happen 10 years from now if they are not going to be providing care to that patient in 10 years' time? Their scale of thinking may be very different.

Comment: Therapy like this [for RA], if it's effective, should prolong life. And prolonged life will increase costs. This is analogous to the old smoking conundrum that if more people smoke, the cost to the government decreases because the smokers won't live as long. If a therapy is effective, patients will live longer and incur more costs.

Comment: Smoking is a bad paradigm because smokers get sick at the end of their life. But there are certain disease conditions where these rules seem to be completely abrogated. In some situations, cost is not an issue even in the HMO environment.

Dr. Kavanaugh: Political and social concerns are important issues. For example, we as a society are willing to pay for some procedures that may be quite undesirable from a cost-effectiveness point of view, while others that are much more preferable may not be readily reimbursed. My personal opinion is that arthritis patients have a relatively low profile with regard to these issues. As patients become aware of these new therapies, they may become more active and vocal in obtaining access to them.

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