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Update on Non-Hodgkin Lymphoma: Alignment of the Current Treatment Landscape and Value-Based Care

TARGET AUDIENCE

This activity was developed for pharmacists and other healthcare professionals practicing in a managed care environment.

LEARNING OBJECTIVES

After completing this activity, the reader should be able to:

- Explain the impact of key clinical data presented at ASH 2010 on payers and providers in the treatment and management of non-Hodgkin lymphoma (NHL)
- Identify patient/disease-associated factors, as well as economic factors that may affect the choice of a therapeutic agent and be able to formulate a management strategy using a risk-adapted approach to the treatment of NHL
- Construct informed treatment decisions for the purpose of improving the long-term outlook for patients with NHL across the lifecycle of the disease
- Identify and discuss the future of NHL treatment and the potential clinical, business, and regulatory changes that could affect the cost-value benefit design

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Payers' Perspectives on Non-Hodgkin Lymphoma: Aligning Current Treatments with Value-Based Patient Care

By Caroline Helwick

At the 2010 annual meeting of the American Society of Hematology (ASH), many presentations focused on current and new therapies for non-Hodgkin lymphoma (NHL), the benefits and risks of these therapies and the associated costs and their impact on health insurance plans and patients. The following article provides updates on key presentations delivered at the 2010 ASH meeting, focusing on value-based care for patients with NHL and the associated cost issues that are of concern for payers and patients. The article highlights concerns relevant to the alignment of best available cancer therapies with the needs of patients, payers, and other healthcare stakeholders involved in the management of this disease.

Early Rituximab Therapy in Asymptomatic Follicular Lymphoma Shows Benefit

An early course of rituximab can help to defer chemotherapy for nearly 3 years for patients with follicular lymphoma (FL), according to a key study presented at ASH 2010.¹

FL is the most common of the indolent lymphomas, accounting for nearly one fourth of the NHL cases in North America. Previous research has shown

little benefit for treating patients with FL who have not developed symptoms; the disease typically presents at an advanced stage, and patients are often asymptomatic.

"Follicular lymphoma is a slow-growing cancer that is usually widespread when it is diagnosed. It is generally considered to be incurable, and patients have an average life expectancy of 10 to 12 years. Many people feel very well when they are first diagnosed and do not have any symptoms. We know from previous studies that there is no benefit in starting treatment early when patients have no symptoms, compared to waiting until symptoms develop," said Kirit M. Ardesna, MD, of University College London Hospitals, United Kingdom.

As a result, most physicians normally defer treatment for NHL and monitor patients closely until the disease progresses, usually at around 2.5 years, although a growing number of American clinicians have already begun early treatment, according to Ardesna. This study supports that practice.¹

Ardesna added that although "watchful waiting" delays the side effects of treatment, it creates anxiety in many patients. Early treatment would be an option for these patients.

Study Details

The study randomized 462 patients into 3 treatment arms:

- Watch and wait (ie, no rituximab; n = 186)
- Rituximab (375 mg/m²) weekly for 4 weeks (rituximab induction; n = 84). This arm was closed midway through the trial, because of slow recruitment and because several other studies were showing a benefit to rituximab maintenance
- Rituximab induction followed by rituximab maintenance (n = 192), which consisted of 1 dose of rituximab given every 2 months for 2 years, starting at month 3 and given until month 25.

The primary end point of the study was time to initiation of new chemotherapy or new radiotherapy at 3 years.

Overall, only 48% of patients in the watch-and-wait arm had not started chemotherapy or radiotherapy, whereas in the rituximab induction arm, 80% of patients were treatment free, and in the rituximab maintenance arm, 91% of patients were free of treatment (Figure 1).¹ Median time to initiation of chemotherapy was not reached at 4 years in the rituximab arms. Progression-free survival (PFS) at 3 years was 81% for the maintenance arm versus 33% for the

observation arm, representing a 79% reduction in risk ($P < .001$; Figure 2), Ardesna reported.

Rituximab was well tolerated, with few adverse events. There were 7 infections (all grade 3 that required intravenous antibiotics); 5 cases of allergic reactions that resulted in bronchospasm in 2 patients; and 4 cases of neutropenia.

"Our study has shown that we can defer chemotherapy by a long time in patients who have asymptomatic follicular lymphoma," Ardesna commented. He predicted that such an approach will prove attractive to patients, because they can defer chemotherapy and avoid the associated side effects for a longer time. "I imagine this will become the standard of care," he said.

The trial answered questions that have been on the minds of hematologists for some time: should asymptomatic patients, or those who have low tumor burden, be watched or treated? Does early treatment offer a clinical benefit to them? asked Nancy Valente, MD, global head of the hematology development at Genentech/Roche. In this study, early treatment was shown to benefit patients who normally would be followed carefully, offering an alternative to the current care standard, Valente said.

Commentary and Concerns

The new data come from “a very high-quality study” and show that there is a clear advantage to starting rituximab therapy early on, even before symptoms arise,¹ said Charles Abrams, MD, of the University of Pennsylvania, Philadelphia, who is Secretary of ASH.

“These data will lead to changes in clinical practice, perhaps not so much in the United States as elsewhere in the world,” Abrams predicted. He explained that in the United States, some clinicians are already taking this approach, whereas in Europe and Canada clinicians treat more conservatively.

The study, or at least the preliminary analysis, also did not address quality-of-life (QOL) issues, which was of concern to some ASH attendees. The study also did not show an overall survival (OS) benefit, with 96% of patients in both arms alive at 3 years.¹ Ardesna stressed that this was a preliminary analysis and that QOL measurements, as well as OS, would be part of the next phase of research.

Other hematologists raised concerns about the cost of treating patients with many more courses of rituximab, and some questioned whether early treatment with rituximab may blunt a patient’s response to immunochemotherapy down the line, when it may be more warranted.

Ardesna said that he believes early treatment will not compromise future response, speculating that it may lead to tumor shrinkage and reduce genetic mutations, thus setting up patients to be even better candidates for therapy.

He also pointed out that some patients—perhaps 1 of 5—will never develop full-blown disease, because their tumor will remain indolent for many years. “At the moment, however, we can’t identify them,” Ardesna said. “We have no way of knowing who will progress and who won’t.”

Future research may refine the patient subgroups that will benefit most from treatment in the asymptomatic state, thus sparing some patients a long and expensive therapy. “We are going to be following these patients, and the study will be ongoing for several years. We are in this for the long term,” he said.

Multiple Studies Confirm Benefit of Maintenance Rituximab in Follicular Lymphoma

For several years, treatment with rituximab for patients who respond to induction therapy has been widely recommended. Studies of patients with FL presented throughout the meeting confirmed the benefit of maintenance therapy with rituximab and offered data on safety and outcomes with long-term use.

Benefit Sustained at 2 Years in PRIMA

In 2009, the Primary Rituximab and Maintenance (PRIMA) trial firmly established the benefit of 2 years of maintenance therapy with rituximab in patients with FL who respond to induction immunochemotherapy.² At ASH 2010, PRIMA investigators reported that after 3 years of follow-up, maintenance therapy sustained these benefits.³

“Rituximab maintenance therapy improved PFS and response rates, with no unexpected toxicities. All patients randomized to maintenance therapy have excellent survival to date,” said Gilles Andre Salles, MD, of the Centre Hospitalier Lyon-Sud, Pierre-Benite, France. “The take-home message is that for patients who need treatment, efficacy can be improved by adding 2 years of maintenance therapy with rituximab. The PRIMA results indicate that rituximab maintenance should be considered in all FL patients who respond to first-line immunochemotherapy.”

“For patients with a high tumor burden, the PFS of 79% seen 3 years after randomization has not been seen before in large studies of follicular lymphoma,” he added.

Salles presented data on 1193 patients randomized to induction chemotherapy with R-CHOP (rituximab, cyclophosphamide, doxorubicin hydrochloride, vincristine sulfate, prednisone; n = 805), R-CVP (rituximab, cyclophosphamide, vincristine, prednisone; n = 272), or R-FCM (rituximab, fludarabine, cyclophosphamide, and mitoxantrone; n = 45). Patients in complete remission (CR), unconfirmed CR (CRu), or partial remission (PR) were eligible for randomization to either rituximab maintenance therapy (n = 505) or observation (n = 513). Rituximab was given as 1 infusion of 375 mg/m² every 8 weeks for 2 years. At the time of randomization, the CR rate was 39%, the CRu rate was 31%, and the PR rate was 29%.³

The overall response rate (ORR) to maintenance rituximab was robust: 52% of patients in PR after induction converted to CR/CRu after 2 years of maintenance compared with 30% of the observation arm (P = .0001).

The 3-year PFS was 60.3% in the observation arm and 78.6% in the rituximab maintenance arm (P < .001). The effect of rituximab was consistent across age-groups, sex, Follicular Lymphoma International Prognostic Index score, induction chemotherapy type, and response to induction chemotherapy. At the time of data cut-off, mortality rates were similar between groups: 5% in the rituximab maintenance arm and 6% in the observation arm.

Infection was the most common adverse event, occurring in 39% of patients receiving rituximab maintenance

and in 24% not receiving maintenance rituximab. Grade 3 or 4 adverse events were found in 24% and 17% of patients, respectively, and patients in the maintenance arm experienced more neutropenia (4%) than patients not in the rituximab maintenance arm (1%).

Three Years of Maintenance Delays Progression

A retrospective population-based analysis using the British Canadian Cancer Agency Lymphoma Cancer Database confirmed better outcomes with maintenance rituximab versus observation.⁴

The study included 251 patients receiving R-CVP as induction therapy up to January 2010. Outcomes of responders who received maintenance therapy versus observation were compared.

With a median follow-up of 3 years,

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87% of patients were alive and 13% had died; 11% developed progressive disease while receiving rituximab maintenance, and within this subset of patients, 23% of patients in PR converted to CR/CRu while receiving maintenance therapy, reported Alden A. Moccia, MD.

The 3-year PFS estimate was significantly higher for patients receiving maintenance compared with those observed after having responded to

Figure 1 Time to Initiation of New Therapy

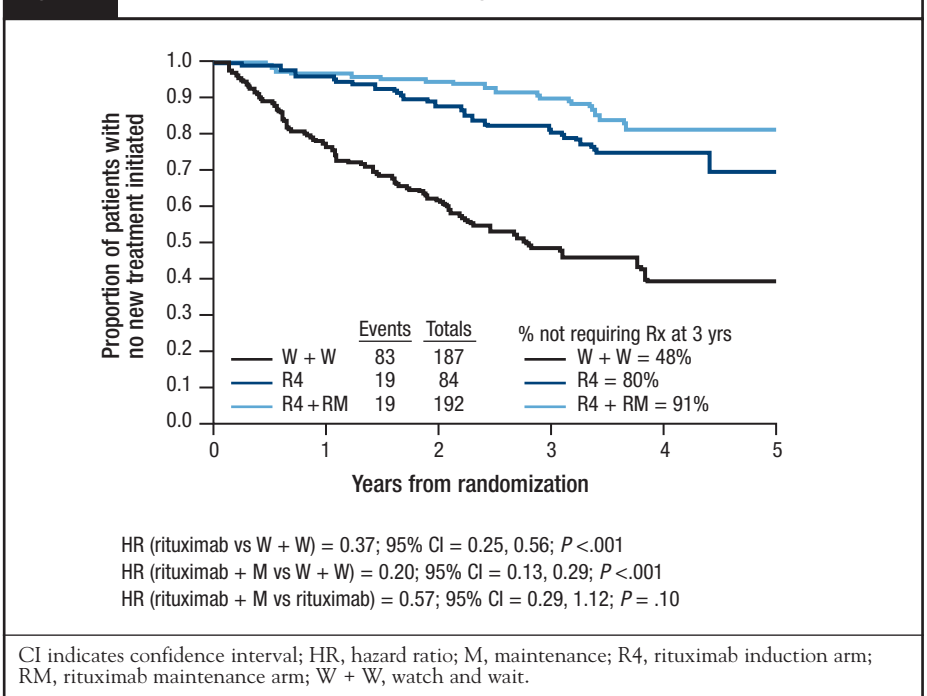
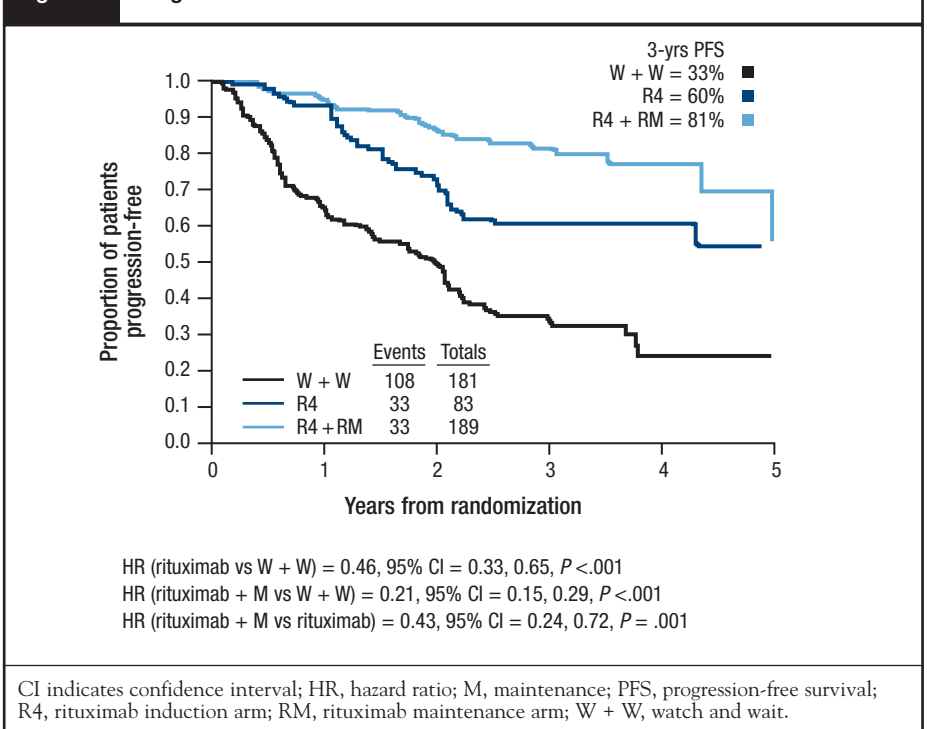


Figure 2 Progression-Free Survival



R-CVP: 83% versus 62%, respectively ($P = .002$). The 3-year OS was similar, at approximately 92%.

"This population-based analysis confirms the benefit of rituximab maintenance following immunochemotherapy in patients with untreated follicular lymphoma," Moccia said. In addition, the R-CVP regimen produced outcomes that compared favorably with more intensive combinations and appeared less toxic. Patients whose disease was refractory to R-CVP had a poor prognosis.

Safety Demonstrated Over 3-Plus Years

The safety of 3 or more years of "prolonged maintenance" was validated in the phase 3 Schweizerische Arbeitsgemeinschaft für Klinische Krebsforschung (SAKK) 35/03 trial, which was led by Swiss investigators.⁵

"We found that rituximab maintenance beyond 2 years is feasible, without evidence of increased toxicity," said Christian Taverna, MD, of Kantonsspital Munsterlingen, although he advised close monitoring of such patients.

All 270 patients (untreated, chemotherapy-resistant, or relapsed) received rituximab induction, and responders were randomized to a short maintenance of 4 doses every 2 months or prolonged maintenance with rituximab given every 2 months for up to 5 years. Safety was assessed after 3.3 years.

During maintenance therapy, 899 adverse events were observed, only 28 of which were grade 3, and 8 were grade 4. Grade 3 neutropenia occurred in 5 patients and grade 4 occurred in 1 patient. Seven grade 3 or 4 infections were reported, primarily pneumonia, appendicitis, and diverticulitis. Five patients developed subsequent cancers.

In the prolonged maintenance arm, 2 patients discontinued treatment because of unacceptable toxicity after 16 and 42 months, respectively, and 1 discontinued treatment because of subsequent breast cancer after 20 months. Of the patients, 63 remain on maintenance for

2 or more years, of which 48 have been treated for at least 3 years. According to Taverna, 2 patients have completed 5 years of maintenance rituximab.

He acknowledged concerns about infections associated with long-term rituximab use, and pointed out that the low incidence of infections observed in the SAKK trial might be attributed to the fact that induction was accomplished with rituximab monotherapy—not in combination with chemotherapy, as in previous studies.

Rituximab Peritransplant Improves Outcomes

Autologous stem cell transplantation (ASCT) significantly improves PFS and OS in patients with relapsed or resistant FL compared with chemotherapy alone, and studies have suggested that rituximab given around the time of transplant further improves survival outcomes. However, in contrast to maintenance rituximab post-chemotherapy in untreated FL, the true benefit and safety of maintenance rituximab after ASCT is unknown.

Studies of patients with FL presented throughout the meeting confirmed the benefit of maintenance therapy with rituximab and offered data on safety and outcomes with long-term use.

Investigators from the United Kingdom evaluated this approach, which is called *in vivo* purging pretransplant with immediate posttransplant maintenance.⁶ They found that rituximab *in vivo* purging and maintenance resulted in superior PFS compared with no rituximab, although OS was not improved, and 80% of patients in both arms were alive at 5 years. The drug did not compromise peripheral blood stem-cell harvesting or engraftment, reported Ruth Pettengell, MD, of St. George's University of London.

The study included 280 rituximab-naïve patients in their first, second, or third remission (80% had 2 prior lines of therapy) who responded to induction chemotherapy and were randomized to rituximab purging (375 mg/m² 4 times weekly) versus no purging. Both were followed by stem cell collection and high-dose therapy, then randomization to maintenance rituximab 375 mg/m² every 3 months for 2 years or to observation.

Transplant was accomplished in 70%

of patients. No graft failures or late neutropenia were reported. Transplant-related mortality was 0.5%. Only 3 infection-related deaths were reported within 5 years, Pettengell said.

Results showed that 5-year PFS was highest when patients received rituximab purging plus maintenance: 62.9% versus 37.6%, for patients receiving no rituximab purging or maintenance, respectively, for a 24% significant reduction in risk ($P = .004$).

Maintenance also provided significant benefits in delaying disease progression. The 5-year PFS in patients on maintenance therapy was 54.9% versus 42.0% without maintenance therapy, respectively, a 35% risk reduction ($P = .01$), although OS was similar at around 81% per arm, Pettengell said.

"Rituximab *in vivo* purging and maintenance resulted in superior PFS compared with no rituximab," she said, "and posttransplant maintenance significantly improved PFS compared with observation. The PFS curve at 6 years suggested that a subset of patients may achieve durable disease control."

Lymphoma: Rituximab Efficacy Shown in Several Treatment Combinations

Rituximab has become an almost universally useful agent in NHL treatment. The biologic agent is designed to be highly specific for its target: cancerous B-cells of the immune system. The targeting is so precise that rituximab is able to approximate, if not surpass, the rates of efficacy for chemotherapeutic agents while having none of the chemotherapy-related toxicities. These qualities make it a very attractive candidate for combination regimens in the setting of NHL. Three such regimens were highlighted at ASH 2010.

GELA: Study of Elderly Patients

A growing number of patients with NHL are elderly, and the Groupe d'Etude Des Lymphomes De L'Adulte (GELA) study evaluated a regimen that may prove effective and less toxic in patients aged ≥ 80 years.⁷

"In Western Europe, an 80-year-old man presently has a remaining 9.5 years of life expectancy," said Frederic Peyrade, MD, of the Centre Antoine Lacassagne, Nice, France. "That means that by 2050, there will be twice as many individuals in this age bracket as there are now, and that will represent greater than 15% of the overall population."

The lymphoma caseload among the elderly will inevitably increase, he concluded, yet little data are available to guide treatment choice or even the decision of whether to treat these patients at all.

To evaluate a tolerable treatment regimen, GELA enrolled 149 treatment-

naïve, diffuse large B-cell lymphoma (DLBCL) patients and treated them with rituximab in combination with a reduced-dose version of CHOP, termed "R-mini-CHOP," given every 21 days for 6 cycles.

After a median follow-up of 20 months, the ORR was an impressive 74%, with 40% of patients having a CR; this success translated into a 2-year survival rate of 59%. Grade 3 and 4 toxicities were uncommon and generally occurred within the first treatment cycle.

Reflecting on the quality of the responses, Peyrade stated, "It means that even with these very old patients, obtaining the best response possible remains crucial in terms of overall survival." In general, he said, these results indicate that even patients aged >80 years should be considered for treatment.

Rituximab/Bendamustine

Mathias J. Rummel, MD, PhD, of Justus-Liebig Universität Giessen, Germany, reported final results of NHL 2-2003 from the Study Group of Indolent Lymphomas.⁸ The trial examined the use of rituximab in combination with bendamustine (R-Bd), an alkylating agent available for years in Europe but not approved in the United States until 2008. NHL 2-2003 compared this combination with a standard regimen of rituximab/fludarabine (R-F). The purpose of the study was a so-called "noninferiority" determination between the 2 therapeutic approaches.

NHL 2-2003 enrolled 219 patients with a variety of lymphomas, mostly FL (47%) and mostly advanced disease for which patients had received prior treatment.

Results for the R-Bd combination were more favorable than those achieved with standard R-F, with ORRs of 82% versus 49%, respectively, and CRs of 39% versus 16%. Event-free survival (EFS) was 30.4% for R-Bd versus 11.2% for R-F. Best responses were observed in the FL subgroup.

Side effects were less common than previously seen with this regimen, said Rummel. Grade 3 and 4 toxicity was uncommon, and most complaints were for nausea and fatigue. Slightly more infectious complications occurred with R-Bd, but the difference was not significant; no dose reductions were required.

OS was similar for the 2 regimens; however, the protocol was amended midstudy to implement the newly established paradigm of 2 years of rituximab maintenance. It is uncertain what effect, if any, this had on the comparisons of eventual outcome for study patients, he said.

Rituximab/Bortezomib

Bortezomib, a proteasome inhibitor cur-

FDA Approved Rituximab for Advanced Follicular Lymphoma

On January 28, 2011, the US Food and Drug Administration approved rituximab as a maintenance treatment for patients with advanced FL who responded to initial therapy with this drug plus chemotherapy (ie, induction therapy). This approval echoed the recommendation by the European Commission in October 2010 to approve rituximab for this indication.

rently indicated for use in multiple myeloma and advanced mantle-cell lymphoma, was combined with rituximab (R-Bt) in a large phase 3 trial that enrolled 676 patients with relapsed, rituximab-naïve, or rituximab-sensitive FL.⁹ Results for the combination versus rituximab alone were reported by Bertrand Coiffier, MD, PhD, of the Hospices Civils de Lyon, France.

Because bortezomib had previously shown activity in heavily pretreated patients with indolent lymphoma, and preclinical evidence suggested promise for the R-Bt combination, Coiffier and colleagues predicted a therapeutic response with R-Bt in patients with FL, he explained.

Patients were randomized to rituximab or the R-Bt combination, treated for 25 weeks, and followed for a median of 33.9 months.

As expected, because of advanced disease, discontinuation rates in this study were high (29%); however, response was good in light of considerable pretreatment, Coiffier reported. The ORR was 63% with the combination versus 49% with rituximab alone, and CRs were achieved in 25% and 18%, respectively.

Differences in PFS, however, were slight: PFS was 12.8% for R-Bt versus 11% for rituximab alone. Patients with the worst prognosis at baseline, however, fared significantly better with the combination. "This is important for me," said Coiffier, "that the patients with the higher risk to progress still do better with the combination."

Toxicity for R-Bt was higher than for rituximab alone, but grade 3 and 4 side effects were uncommon and transient. Based on these results, Coiffier said that he hoped that future efficacy could be boosted with a combination of R-Bt-CHOP.

Radioimmunotherapy in NHL

Various novel approaches have been tested in an attempt to improve CR rates and achieve a survival advantage in indolent NHL. A regimen that combines chemotherapy induction (fludarabine and mitoxantrone), consolidation with radioimmunotherapy (90Y-ibritumomab tiuxetan), and maintenance with rituximab produced durable responses without additional toxicity in a small study of 22 patients with FL presented at the meeting by Reem Karmali, MD, of Rush University Medical Center, Chicago.¹⁰

The ORR to induction was 95%, and 19 patients continued to radioimmunotherapy, all of whom responded. Radioimmunotherapy converted 60% of PRs to CRs. During or after maintenance rituximab, the response rate was 80%, and 75% of the responses were CRs. The lower response rate—from 95% to 80% during maintenance—reflects relapses, Karmali reported.¹⁰

At a median follow-up of 49.6 months, median PFS was 47.2 months. Seven patients relapsed, and 2 of these patients died. Of the remaining patients, 24% are stable and 76% are in CR. Approximately 80% are alive at 6 years.

Karmali suggested that, "This regimen is a viable option in the frontline treatment of FL patients with high tumor burden and intermediate-high FL scores."

R-CHOP Plus Radioimmunotherapy Effective

Karmali also led a phase 2 study in 20 patients with DLBCL that evaluated a regimen combining R-CHOP-14 (R-CHOP every 2 weeks for 6-8 cycles) cycles with radioimmunotherapy consolidation with 90Y-ibritumomab tiuxetan given 6 to 8 weeks after immunochemotherapy was completed.¹¹

After R-CHOP-14 induction, the PR rate was 25% and the CR rate was 75% (ie, all patients responded). After radioimmunotherapy, 4 patients converted to CR, for a conversion rate of 80%. At a median follow-up of 44.2 months, the relapse rate was only 15%. "All these patients had high-risk features and received further treatment," he said. "One is now in CR."

Median PFS was 92.6 months, and median OS has not been reached. To date, 17 patients remain alive, all in CR, making the estimated median OS 125 months. Grade 3 or 4 neutropenia developed in 50% of patients, but no patients developed neutropenic fever. There were no cases of myelodysplastic syndrome/acute myeloid leukemia.

"Dose-dense R-CHOP followed by Zevalin [ibritumomab injection] consolidation maintains durable responses with good tolerability," Karmali said. "An 80% conversion rate of PR to CR was achieved after radioimmunotherapy."

Karmali said that he believes both novel regimens his group is studying warrant further investigation in randomized trials.

Progression of FL Is Costly

Disease progression is associated with significantly higher costs and healthcare utilization for patients with FL compared with those with stable disease, and treatment that prevents or delays progression not only improves clinical outcomes but also provides economic benefits in lowering the cost of care, a study from Genentech and US Oncology showed.¹²

"Follicular lymphoma accounts for approximately 70% of indolent lymphomas. We estimated the marginal cost of progression for patients with FL treated in the outpatient community setting," said Sacha-Satram Hoang, PhD, of Genentech, South San Francisco.

Using US Oncology's iKnowMed electronic medical record (EMR), inves-

tigators identified 1002 patients with FL who achieved CR or stable disease. The database captures information from a network of approximately 1200 community-based oncologists who treat patients according to usual clinical practice, with no criteria for therapy selection and no schedule of visits imposed. To estimate outpatient cost of care, the study linked the EMR data to US Oncology's claims data warehouse.

Patients were categorized into 2 cohorts based on whether they experienced disease progression. Costs per patient per month (estimated based on outpatient claims and normalized to 2007 Medicare reimbursement rates) were compared between patients who did and did not progress. Econometric regression analysis was used to compare healthcare costs after adjusting for potential confounders. The study also compared resource utilization as measured by outpatient physician visits, chemotherapy visits, laboratory procedures, and acute care visits.

Of the 1002 patients with FL, 204 progressed and 798 did not. At baseline, patients with disease progression were more likely to have been diagnosed with advanced disease, have 4 or more positive lymph nodes, have worse performance status, and have high lactate dehydrogenase and low hemoglobin levels compared with patients whose disease did not progress.¹²

The mean overall costs per patient per month over the 6-month follow-up period were significantly higher for patients who progressed: \$3612 versus

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\$965, respectively, for a very significant difference of \$2647 ($P < .001$).¹² Differences in cost were significant in all categories (Table 1).

This resulted in a relative cost that was nearly 4 times higher for patients who experienced disease progression. After adjusting for differences in clinical factors, disease progression was associated with a 2-fold increased cost ($P < .001$). The cumulative 6-month total cost for patients who progressed was \$21,496 versus \$5165 for nonprogression,¹² Hoang reported.

Patients with disease progression had significantly higher frequencies of outpatient physician visits and laboratory procedures compared with patients without progression and were significantly more likely to receive chemotherapy and be admitted to the hospital and/or emergency department.

The investigators believe these costs may be underestimated. "We followed patients for a maximum of 6 months, which may have led to an underestimation of reported costs and the rate of treatment failure of progressive disease. Also, costs for radiologic services and inpatient consultation visits may be

NICE Recommends Maintenance Treatment for Follicular NHL

Coinciding with ASH 2010, the United Kingdom's National Institute for Health and Clinical Excellence (NICE) issued preliminary draft guidance recommending the use of rituximab as a first-line maintenance treatment for certain patients with advanced FL, based on evidence that rituximab delays disease progression. The recommendation pertains to patients with advanced FL that have responded to first-line induction therapy with rituximab in combination with chemotherapy.

Peter Littlejohns, Clinical and Public Health Director at NICE, commented, "A maintenance treatment is used to stop a cancer from returning following initial chemotherapy. For FL, no such maintenance treatment has so far been available, and therefore rituximab could be a valuable treatment option. The evidence highlighted that it could keep a patient's cancer in remission after they have had chemotherapy and therefore delay the need for further chemotherapy. This should mean that patients have fewer chemotherapy-associated side effects long-term and so improve their quality of life.

"However," he continued, "the evidence submitted by the manufacturer did include some uncertainties, mostly around the extent to which rituximab can extend a patient's life expectancy and the impact of this assumption on its cost-effectiveness. While the committee felt that the drug is likely to be an appropriate use of NHS [National Health Service] resources, it expects that the manufacturer will confirm this by providing further, more specific, information."

The NICE Appraisal Committee is particularly interested in obtaining a revised cost-effectiveness analysis for patients aged 60 to 65 years (the age at which most people are first treated in the United Kingdom) at the start of treatment and in which the duration of clinical benefit from rituximab maintenance treatment is 3 to 4 years. Once all questions have been answered, NICE will issue full guidance on maintenance rituximab.

underestimated since patients may have received these outside the US Oncology Network,” Hoang suggested.

The implications of the findings, according to the researchers, are that therapies that delay disease progression for FL may provide substantial economic benefits in addition to improvements in clinical outcomes.

Rituximab Maintenance Shown Cost-Effective in UK Study

The phase 3 PRIMA study demonstrated that rituximab maintenance therapy after induction immunochemotherapy in patients previously untreated for FL significantly improves PFS, with little additional toxicity.² Using clinical evidence from PRIMA, an economic analysis presented at ASH 2010 evaluated whether rituximab maintenance after a response to rituximab-chemotherapy induction is a cost-effective option compared with observational practices in the United Kingdom’s National Health Service (NHS).¹³ The findings were presented by Konstantinos Papadakis, MD, of Hoffmann-LaRoche, Welwyn Garden City, United Kingdom.

The study used a transition state (Markov) model in which patients with FL and complete or partial response to first-line immunochemotherapy induction were assigned across 4 health states reflecting their disease status—PFS in first-line maintenance, PFS in second-line maintenance, progressive disease, or death.

The model incorporated a 25-year horizon to capture the lifetime of an average patient. Data from key trials and treatment guidelines were used to develop probabilities. It was assumed that the treatment benefit of maintenance was sustained for 72 months. Beyond that point, treated patients have the same probability of progression to second-line maintenance as patients who were only observed.

Costs associated with the average dose of rituximab maintenance, postprogression treatments, and management of grade 3 and 4 adverse events observed in PRIMA were incorporated into the rele-

Rituximab in vivo purging and maintenance resulted in superior PFS compared with no rituximab, although OS was not improved, and 80% of patients in both arms were alive at 5 years.

vant health state. Drug administration, patient monitoring, and pharmacy costs were informed by expert opinion and the NHS schedule of reference costs.

The average OS in the first-line maintenance cohort was projected to be 1.27 years longer on average than with observation (10.31 years vs 9.05 years), and to be associated with an additional 1.17 quality-adjusted life-years (QALYs).

“This is largely due to patients treated with first-line rituximab maintenance spending more time progression-free in the first line (1.17 years),” Papadakis said.

Total costs were £14,129 higher with first-line maintenance than with observation and were driven by the cost of the study drug and its administration. However, this was partially compensated by the lower costs of rituximab therapy in the second line, where the cost-savings were £198, as well as lower costs of supportive care incurred at disease progression, where £906 was saved, he said.

The incremental cost-effectiveness ratio (ICER) for first-line rituximab maintenance was £14,712 per life-year gained and £15,983 per QALY gained, “well below an assumed willingness to pay the threshold of £30,000,” he noted.

Although there is uncertainty associated with the cost of FL progression and relapse treatment, the ICER did not exceed £21,155 per QALY despite a wide variation in each parameter value used in the probabilistic and deterministic sensitivity analyses, he added.

“The cost-effectiveness of rituximab maintenance in follicular lymphoma patients after response to immunochemotherapy is well within the acceptable willingness-to-pay ceiling and remains valid under most plausible sensi-

tivity scenarios,” he said. “This provides adequate reassurance that the superior clinical benefits of first-line maintenance are sufficient to justify the additional costs over observational practice.”

Practice Makes Perfect

Two sessions presented under the “Practice Makes Perfect” banner at ASH 2010 drew attendees concerned about emerging requirements that providers and payers demonstrate “quality care.”

New Models for Payment: Pathways

Pathways take clinical guidelines a step further, not only evaluating treatments for their evidence basis and toxicity but—these factors being equal—also determining (and advocating) treatments that are more cost-effective, said Gerald Robbins, MD, of Florida Cancer Institute, New Port Richey, who presided over a session called “New Models for Payment, Pathways, and Insurers.”

“Many people view pathways as something thrown together,” he said in an interview “but to construct pathways correctly requires a tremendous amount of effort and structure.” Therefore, he added, not all pathways are equal.

Two of the most well-known pathways come from US Oncology and the University of Pittsburgh Medical Center (UPMC). These pathways started within committees that were already established for disease management. The committee members reviewed data; developed, reviewed, and voted on the pathways; had the larger membership vote on the pathways; and had a built-in structured review of the pathways every 3 to 6 months. In other words, the pathways stand up to scrutiny, Robbins emphasized.

“There are practice-changing findings that emerge, and you have to be prepared to alter the pathway on the basis of new data. You need to be fluid; you need to have a process for reevaluation and physician input,” he pointed out.

The Florida Society of Clinical Oncology (FLASCO) has been interested in choosing a pathway program and has evaluated those offered by US Oncology, UPMC, P4 Healthcare, and others. The aim is to find a pathway that will be acceptable to all members and that will mesh well with payers’ needs, noted Robbins, who is President of

FLASCO. “We will be writing a report on various pathway programs and our recommendations, but will not make one single endorsement,” he said. “We are looking at various pilot programs, with the goal of improving quality and controlling costs.”

“We are trying to be very proactive with the payers. Our membership also feels a global responsibility for controlling healthcare costs. Physicians see the same growth in the cost curve and a non-sustainable trend,” Robbins emphasized. “And we are trying to change the typically adversarial relationship with payers to one of more cooperation.”

That change can be seen in several forms—a payer relations committee intended to improve communications with payers, meetings with medical directors, and a “payer’s summit,” to which the medical directors of several companies were invited to meet with FLASCO representatives. “We discussed what is important to payers and to FLASCO members,” he said. For example, FLASCO and its members want to avoid having to use a pathway for one payer, and another for a different payer, he offered. “This would be a nightmare.”

By the same token, Robbins continued, “what if a group decides on a pathway and the carrier responds that it cannot scale up so that each practice uses its own pathway?” The summit laid bare such scenarios and facilitated transparency, he explained.

“For payers and providers to work together you have to have a comfort zone and transparency. We are taking baby steps. Several payers have reciprocated and have shown an interest in working with us on these details. Admittedly, it’s strange territory for doctors to partner with insurance companies, as much as the opposite,” Robbins commented.

The session provided for discussion about how pathways are being developed and used in hematology and allowed an opportunity for some venting, he said. “The attendees were very concerned about the future of outpatient hematology/oncology, and how these pathways will impact their practices. They were interested in learning about them, because they realize they are one of the most important ways of controlling costs,” Robbins pointed out.

Pay-for-Performance and PQRI

Participation in so-called physician quality reporting initiatives (PQRIs) has not been particularly robust and may not be the best way to encourage quality care, according to Steven L. Allen, MD, Assistant Chief of Hematology, North Shore Long Island Jewish Health System, Manhasset, New York.

Allen led a session on pay-for-performance programs and PQRI, noting that

Drug Regimens

R-CHOP: Rituximab, cyclophosphamide, doxorubicin hydrochloride, vincristine sulfate, prednisone

R-CVP: Rituximab, cyclophosphamide, vincristine, prednisone

R-FCM: Rituximab, fludarabine, cyclophosphamide, mitoxantrone

R-Bd: Rituximab, bendamustine

R-F: Rituximab, fludarabine

R-Bt: Rituximab, bortezomib

“Participation has so far been poor in the PQRI program of the CMS [Centers for Medicare & Medicaid Services]. However, for those who have become involved, about 90% successfully complete the 4 measures.”

The metrics, which Allen helped to develop, gauge whether hematologists perform flow cytometry and cytogenetic tests appropriately at diagnosis, prescribe bisphosphonates for multiple myeloma, and screen for iron levels when prescribing erythropoiesis-stimulating agents in patients with myelodysplastic syndrome.

Physicians who successfully complete these measures (ie, appropriately conduct at least 80% of cases submitted to CMS for payment in 2009) receive, as a bonus, 2% of their Medicare Part B billing. This bonus was decreased to 1% in 2011, and will decrease to 0.5% in the following 2 years. After that, not only will any bonus be eliminated, but hematologists will actually be penalized for not participating in PQRI, he said.

There are approximately 150 metrics with PQRI, and clinicians can participate in any of them. The 4 mentioned above were designed to be relevant to hematology practices, Allen noted.

“Attendees at the session were concerned about what they can do to meet the criteria and to receive the incentive payment. They were also concerned about how to properly complete the necessary paperwork,” Allen said.

“Not many hematologists have signed up,” Allen reported. “They are concerned about the time it takes. The learning curve is difficult, and there have been delays in payment, but this past year more doctors got paid.”

Physicians in large groups do not have to participate (and do the work) individually, he noted. “The group can do it as a whole.” The definition of a “group” is changing, so that 2 or more physicians now constitute a group. Allen believes this may ease the burden and encourage more physicians to become involved in PQRI.

It has been more common for institutions, rather than physicians, to get on board. “They want to get ready for the time when PQRI becomes mandatory,” he said. But there is a downside. “It is costing institutions—hospitals and health systems—more to do the paperwork than they are getting back, even at the 2% level. Perhaps with experience and new technology, the cost of doing the paperwork will decrease.”

The bottom line, according to Allen, is that PQRI “is not as good as it sounds,” at least at this point. “Encouraging quality is what we all want—physicians, payers, and the public,” he said. “But shortly we will be penalizing people, and I don’t know that philosophically this is the best way to encourage quality care. All physicians

want to provide quality care; it’s why we go into medicine. But we can encourage this through education. Assistance in understanding the current standards of care, and what is expected of physicians, might be better received and be more successful than this financial incentive model.”

Benefit and Cost-Effectiveness of Growth Factors Examined

The hematopoietic granulocyte colony-stimulating growth factors (G-CSFs) filgrastim and pegfilgrastim accelerate neutrophil engraftment and decrease the number of days of febrile neutropenia after chemotherapy and ASCT. Cancer delivery models are under pressure to become more efficient in an increasingly cost-restrictive environment, and because these agents are expensive, there is a need to establish their true benefit and cost. The following are among a number of studies presented at ASH that looked at these issues.

Pegfilgrastim Cost-Effectiveness Shown

Filgrastim is used daily for up to 2 weeks per chemotherapy cycle, whereas pegfilgrastim is used once per cycle. A single dose of pegfilgrastim, the newer agent, is as effective as many doses of filgrastim in patients with cancer treated with conventional chemotherapy, but there are no convincing comparative studies assessing the efficacy, safety, and economic impact of 1 injection of pegfilgrastim after reinjection of stem cells.

In a French open-label randomized phase 2 trial comparing one 6-mg dose of pegfilgrastim to multiple doses (mean of

7) of filgrastim 5 µg/kg/day in 80 patients with lymphoma who underwent ASCT, outcomes favored pegfilgrastim.¹⁴ The investigators suggested, therefore, that pegfilgrastim be considered “a standard of care” after high-dose chemotherapy and ASCT. The results were reported by Catherine Sébba, MD, of the Centre Leon Bérard, Lyon, France.

“We found that pegfilgrastim after ASCT is at least as efficient as filgrastim on clinical outcomes, especially on duration of febrile neutropenia, and as safe as filgrastim,” Sébba said (Table 2). “In terms of economic outcomes, pegfilgrastim strictly dominates filgrastim, that is, offers better effectiveness and lower costs on the primary end point, febrile neutropenia” (Table 3).

Various novel approaches have been tested in an attempt to improve CR rates and achieve a survival advantage in indolent NHL.

Labor Costs Are Lower with Pegfilgrastim

A cost model of expenses associated with growth factor use found an advantage with pegfilgrastim use compared with filgrastim, according to Douglas Taylor, of

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i3 Innovus, Lakeland, Tennessee.¹⁵

“Little is known regarding the use of practice resources needed to deliver therapy with growth factors. We constructed an empirical model to calculate the human resource time and cost associated with the delivery of filgrastim and pegfilgrastim,” Taylor said.

The study used a practice-level model to detail staff tasks required over 1 month in administering G-CSF. Specific clinic characteristics were included (eg, number of patients receiving G-CSF, number of filgrastim injections per cycle, hourly pay rates for staff). Interviews were conducted with 400 medical professionals at 20 community oncology practices to provide data for the time and personnel required for various tasks (ie, scheduling, front desk, phlebotomy, laboratory, triage, injection, and billing). The costs of the drugs were not included in the model. The base-case scenarios contrasted 1 patient versus 30 patients per month.

The use of prophylactic pegfilgrastim resulted in substantial savings, in a comparison with filgrastim given as either 6 or 11 injections per cycle and in scenarios based on 1 or 30 patients per month. Nursing hours involved in treating 1 patient per month with 6 injections were

Table 1 Six-Month Mean Cost of Care Overall and by Category

Cost feature	No progression, \$ (N = 798)	Disease progression, \$ (N = 204)	C _P – C _{NP} ^a	P
Overall cost	964.61	3611.51	2646.90	<.001
Outpatient visits	39.55	101.66	62.11	<.001
Acute care ^b	2.64	23.85	21.21	<.001
Chemotherapy	731.58	2554.12	1822.54	<.001
Other medication	107.78	714.98	607.20	<.001
Laboratory procedures	12.22	29.03	16.81	<.001
Minor procedures	3.08	9.55	6.47	<.001
Nursing care/hospice	0.43	1.37	0.94	.007
Other	0.69	4.61	3.92	.001
Radiotherapy	25.42	49.38	23.96	<.001
Radiation (nonradiotherapy)	40.23	121.35	81.12	<.001

^aC_P – C_{NP} indicates the cost of progressing minus cost of not progressing.

^bInpatient and emergency department visits.

Table 2 Selected Clinical Outcomes^a

Clinical outcome	Pegfilgrastim	Filgrastim
Days of febrile neutropenia (lymphoma), N	3.49	4.15
Days with fever, N	5.65	7.12
Days to reach absolute neutrophil count ≥ 1.0 G/L, N	10.05	11.99
Days with platelets < 20 G/L, N	3.19	3.61
Days of hospitalization from reinjection, N	15.48	16.64
Days of antibiotics, N	5.42	9.86
Patients without fever, %	6	6
Patients with grade 3-4 adverse events, %	39	40

^aData also reflect outcomes in 71 multiple myeloma patients included in the population.

Table 3 Mean Costs of Primary In-Hospital Care (in 2009 Euros)

Factor	Pegfilgrastim, €	Filgrastim, €
Hospitalization	20,680	22,236
Transfusion	1033	1312
Anti-infection prescription	851	1138
Growth factors	639	762
Total cost	23,204	25,448

9.4 versus 1.5 hours for pegfilgrastim; for 11 injections nursing hours were 17.3 versus 1.5, respectively.¹⁵

When extrapolated to 30 patients per month, this entailed 283 and 519 nursing hours for filgrastim, respectively, compared with 1.5 and 45 total hours for pegfilgrastim, respectively, Taylor reported.

The 30-patient model predicted that monthly opportunity costs (labor needed for filgrastim minus pegfilgrastim) were more favorable for pegfilgrastim compared with 6 and 11 days of filgrastim, respectively. Staff hours would be reduced from 756 to 378, and staff costs would be reduced from \$18,000 to \$9000.¹⁵

On a per-patient basis, the monthly opportunity costs were more favorable for pegfilgrastim: staff hours would be reduced from 25 to 13 hours, and staff costs would be reduced from \$600 to \$300.¹⁵

“The use of pegfilgrastim as compared with filgrastim was associated with substantial savings in time and labor costs,” Taylor said, acknowledging that the model did not include the cost of purchasing the drugs. “We think future medical care delivery models should consider practice resource requirements as a means of increasing efficiency and cost-effectiveness.”

FDG-PET Use Widespread, Despite Little Evidence of Utility

The use of fluorodeoxyglucose-positron emission tomography (FDG-PET) for the initial staging of FL varies by cancer center and is widespread, despite a paucity of evidence supporting its use, most notably in terms of an association with better treatment outcomes.

“We think future medical care delivery models should consider practice resource requirements as a means of increasing efficiency and cost-effectiveness.”

—Douglas Taylor

This was the conclusion of a multicenter study that examined data from the National Comprehensive Cancer Network (NCCN) NHL Outcomes Database, a repository of comprehensive clinical, treatment, and outcomes data for patients treated at 7 participating NCCN centers.¹⁶

“The management of follicular lymphoma can vary according to stage at presentation. The use of FDG-PET for initial staging may result in upstaging and/or changes in treatment strategy,” said Karim E. Abou-Nassar, MD, of the Dana-Farber Cancer Institute, Boston. “In this study, we describe the patterns of use of FDG-PET for the initial staging of patients with newly diagnosed disease and its potential impact on treatment.”

The population included 953 persons diagnosed with low-grade FL between 2001 and 2009. All patients received staging imaging within 6 weeks of diagnosis and were followed for at least 6 months. Baseline characteristics, clinical characteristics, and treatment were compared according to receipt of FDG-PET for initial staging.

The study showed that 56% of patients underwent FDG-PET as part of the initial staging work-up, and the use of this varied significantly across NCCN centers. Among patients undergoing imaging, 82% received early treatment (ie, within 180 days of diagnosis) compared with 61.5% of those who were staged with conventional computed tomography scanning only.

By disease stage, among the 189 patients who had early-stage disease, 63.5% underwent FDG-PET for initial staging, again with the use significantly varying across centers. Of all the early-stage patients, 29.1% were treated with radiotherapy alone, 36% received chemoimmunotherapy alone, 14.8% were treated with combined radiotherapy and chemoimmunotherapy, and 20.1% were observed (ie, no treatment yet).¹⁶

“The choice of the initial treatment strategy for early-stage FL did not vary significantly by the use of FDG-PET,” Abou-Nassar reported.

“Patients who undergo FDG-PET scan for initial staging appear more likely to receive early therapy although this may not be directly attributed to the

FDG-PET results. The management of early-stage follicular lymphoma is surprisingly heterogeneous and varies across NCCN centers, but it is not influenced by the use of FDG-PET scan at staging. Given the widespread use and high cost of FDG-PET, its clinical utility in early-stage disease should be further evaluated,” Abou-Nassar maintained. ●

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Advances and Challenges in Non-Hodgkin Lymphoma: A Payer's Perspective

By John Fox, MD

Associate Vice President, Medical Affairs, Priority Health, Grand Rapids, Michigan

Although rituximab was approved in 1997 as a single agent for patients with relapsed or refractory low-grade or follicular CD20-positive B-cell non-Hodgkin lymphoma (NHL), the number of studies demonstrating its broad potential continues to increase.

As discussed in Ms Helwick's article and presented at the 2010 meeting of the American Society of Hematology, the demonstration that immunoprophylaxis in patients with asymptomatic follicular lymphoma (FL) reduces the risk of progression at 3 years by 79% is yet another example.¹ This begs the question whether this should become the new standard of care. From the payer's perspective, we would advocate a response using the Institute for Healthcare Improvement's Triple AIM goals, which call for improving patient experience with the healthcare system, improving health outcomes meaningful to the patient, and reducing per-capita cost.²

Arguably, such preventive encounters with the health system are likely a better experience for the patient than the treatment of progressive disease. In one study, only 2 patients required treatment for 1 additional person to benefit (ie, number needed to treat, 2.1; absolute risk reduction, 48%).¹ Although one could reasonably argue that improving progression-free survival (PFS) and avoiding chemotherapy would improve quality of life, this measure was not assessed. Most notably, improved overall survival (OS) was not observed.¹ And what about cost? This study begs for a formal cost-effectiveness analysis to assess whether the \$70,000 plus cost of 25 months of chemoprophylaxis reduces overall costs. Regrettably, an intermediate and potentially more cost-effective regimen—induction without maintenance—was not studied.

Findings from the Primary Rituximab and Maintenance (PRIMA) trial also demonstrated PFS benefit, but again no OS benefit, with statistically increased risk of grade 3-4 adverse events and serious infections.^{3,4} Numerous other studies in this continuing education activity cite the benefits of maintenance therapy in patients with NHL,^{1,5,6} and rituximab in combination with chemotherapy followed by rituximab maintenance seems to be the optimal option in patients with relapsed disease.⁷ This, in combination with preliminary statements from the United Kingdom's National Institute for

Several reviews show that in patients receiving myelosuppressive chemotherapy, pegfilgrastim is cost-effective—but not cost-saving—compared with 6 days of filgrastim.

Health and Clinical Excellence (NICE) on maintenance therapy in FL, will almost certainly lead to private payer coverage, even without demonstrated survival benefit.

What about cost? Annual net revenue for rituximab was close to \$5.5 billion in 2008, with that amount likely to increase further given the expanded indications.⁸ Payers would welcome predictive markers identifying patients most likely to benefit from anti-CD20 therapy, yet few potential markers are being studied.^{9,10} Payers may have to wait until patent expiration in 2015 for biosimilars to become available and make therapy more cost-effective or even cost-saving for this patient population.

Similar to red-cell colony-stimulating factors (CSFs), payers are increasingly evaluating the health benefits of granulocyte CSFs (G-CSFs). Previous randomized trials have shown that pegfilgrastim is no more effective than filgrastim for primary prophylaxis in this patient population, although a recent meta-analysis shows pegfilgrastim is more effective at preventing episodes of febrile neutropenia.¹¹ Several reviews show that in patients receiving myelosuppressive chemotherapy, pegfilgrastim is cost-effective—but not cost-saving—compared with 6 days of filgrastim.¹²⁻¹⁴ In contrast, the new study presented at the meeting by Catherine Sébban, MD, showed pegfilgrastim dominating (better outcomes, lower cost) filgrastim post-ASCT (autologous stem cell transplantation) in patients with NHL.¹⁵ Given the extraordinary cost difference between these 2 agents, payers will have to weigh whether the long-term potential savings justify the upfront costs of daily versus biweekly injections. New predictive tools to quantify the risk of febrile neutropenia will stratify patients more consistently than current National Comprehensive Cancer

Network guidelines and will further justify expenditures for G-CSFs.¹⁶

There is no payer in the United States that is not exploring methods of controlling oncology costs. Pathways programs, as pointed out in the main article, are challenging to construct, especially if the aim is to find a pathway acceptable to all oncologists. More challenging still will be maintaining these guidelines and the principles of choosing the most cost-effective therapy, especially given the plethora of new agents gushing from the pipeline.

These pathways programs are fundamentally flawed; however, they represent the primary mechanism for payment reform.

These pathways programs are fundamentally flawed; however, they represent the primary mechanism for payment reform. We do not pay orthopedic surgeons differentially based on the type of implant they use, nor should we pay oncologists based on the drugs they choose. Programs such as the Physician Quality Reporting Initiative will continue to evolve, and other payment reforms, such as UnitedHealthcare's payment of a management fee and acquisitions costs, will bring oncology care into line with other payment mechanisms in the healthcare system. ●

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Balancing Cost and Efficacy in Non-Hodgkin Lymphoma: A Pharmacist's Perspective

By James T. Kenney, RPh, MBA

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In general, US health plans look for opportunities to guide treatments that balance efficacy and cost-effectiveness in an effort to manage the application of limited financial resources to reimburse providers for their services. The management of patients with cancer in the managed care setting has primarily been left to the discretion of oncologists, regardless of the type and stage of a particular cancer. The potential for new applications of existing treatments and the development of new therapies provide hope for better outcomes and improved survival for patients with different types of cancer. The availability of new therapies also expands the population of patients who will be candidates for these treatments, including patients who were refractory to current options or who previously were not treated because of clinical practice approaches that supported a deferred treatment strategy for the asymptomatic population.

The advent of biotechnology has brought a host of new biologic therapies for the treatment of complex diseases that have led to changes in the therapeutic approaches for a number of diseases. The option to treat patients with non-Hodgkin lymphoma (NHL) earlier in the disease process rather

than withhold treatment until symptoms arise affords physicians the opportunity to offer patients a new option and extend the time before using more traditional and potentially toxic chemotherapeutic alternatives. The efficacy of rituximab in the early treatment of follicular lymphoma (FL) with subsequent deferment of chemotherapy for 3 years can offer clinical benefits to the patients, as well as delay medical and pharmaceutical expenses for the health plan.¹

In Ms Helwick's article, Dr Kirit M. Ardeshta discusses his study that concerns the impact of early treatment on patients with NHL and its effect on future tumor response as an issue for the oncologist who selects a treatment approach for these patients.¹ Dr Ardeshta also suggests that patients may be more appropriate candidates for future treatments when treated earlier in the disease process. These concerns are of interest to health plans from a clinical perspective; however, plans would not attempt to engage in this discussion and would typically opt to allow the treating physician the professional latitude to select the desired treatment pathway for his or her patient.

Dr Ardeshta's comment that does concern managed care health plans is

that 1 of 5 patients who are not exhibiting symptoms of FL will not develop full-blown disease, and the early treatment with rituximab could be a waste of resources.¹ In addition to the cost of therapy, the cost of treating any side effects directly related to the drug therapy must also be covered by the health plans. This gets to a core issue from the payer perspective, which is the desire to identify patients who are appropriate candidates for a particular therapy and in effect more likely to respond to treatment.

Supportive care options with growth factor treatment in the population of patients with NHL are also discussed in this publication. This is an area for which managed care plans actively engage the oncologist in an attempt to best manage this therapeutic area. Plans routinely utilize specialty pharmacies to distribute and often manage these agents.

The discussion in the main article also suggests potential savings with these agents, without factoring in the cost of the medication, which is the key focus from the health plan perspective. Plans need to confirm the savings when the cost of the medication is also factored into the analysis, including any discounts, rebates, or other cost offsets pro-

vided from the specialty pharmacy distribution option. Health plans can often achieve additional savings by simple dose-management approaches or by implementing treatment guidelines with network physicians.

The ideal approach incorporates input from the clinical experts in the field that balances patient, provider, and the health plan needs to achieve optimal patient outcomes, utilizing appropriate resources in the most cost-effective way.

Clearly, many challenges exist for a managed care plan to actively and effectively participate in the oncology management area. A robust development pipeline of medications and diagnostics, patients living longer with cancer, and limited financial resources to cover the cost of care are examples of challenges that must be addressed. A collaborative approach to care will serve our patient populations well in an attempt to achieve an ideal clinical response in our patients. ●

Reference

1. Ardeshta KM, Smith P, Qian W, et al. An intergroup randomised trial of rituximab versus a watch and wait strategy in patients with stage II, III, IV, asymptomatic, non-bulky follicular lymphoma (grades 1, 2, and 3a). A preliminary analysis. Abstract presented at the 52nd American Society of Hematology Annual Meeting; Orlando, FL; December 4-7, 2010. Abstract 6.

Cancer Center Profile

Hallmark Health Hematology and Oncology Center *Continued from cover*

The center also houses an onsite oncology pharmacy. Being positioned on the same floor as the treatment area places the pharmacists right where they need to be. "As in any oncology practice, we are fully available for any kind of consults," Michelle Corrado, PharmD, System Director of Pharmacy Services, told *The Oncology Pharmacist*. "We are regularly requested by patients...if they have any questions about their regimen or side effects, the pharmacist will typically go out to the infusion room and sit and talk with patients and their families, answering any questions they might have."

This ease of communication extends beyond patient consults. Proximity to team members increases the frequency of face-to-face conversations and enhances personalization of cancer care, according to Corrado. "Many interdependencies are needed among physicians, nurses, and pharmacists to get the

right treatment for the right patient; and you really need to know that patient. You need to know that he or she was hospitalized last week. You need to know how his or her labs are trending. You need to know that he or she vomited for 3 days the last time." This degree of information is not always available when pharmacists work remotely. "Sometimes it is just a casual conversation. I really have seen that the level of information you get about the patient increases exponentially by being integrated into the practice," she said.

And this dedication has its rewards. Patients regularly compliment the center, specifically the pharmacy.

Behind the Scenes

What many patients don't know is that their high-quality care stems from a lot of hard work. As in many oncology pharmacies, pharmacists at Hallmark Health head up the Risk Evaluation and

Mitigation Strategies (REMS), including oncology and nononcology REMS programs. For the center, that represents between 6 and 12 programs for such agents as epoetin alfa, darbepoetin alfa, natalizumab, and denosumab, each requiring the verification of lab values and documentation.

Pharmacists also are the point people for the center's computer-based order-entry system (IntelliDose, IntrinsicQ), building any new protocols instituted by the center, including supporting literature, into the system. Add in their use of the existing pharmacy information system (MT Software, MediTech) and the just-implemented electronic health record system (Centricity, GE Healthcare), and the center's pharmacists are coordinating a good amount of high-tech. Plus, they currently are implementing a bar-coding system as an additional source of quality assurance.

Pharmacy also handles pharmaceuti-

cal purchasing and contracting. As the system director, Corrado is responsible for contracting, and Hallmark Health has a buyer. However, "the oncology pharmacy coordinator is responsible for all the inventory [at the center]." The center keeps a very tight inventory margin, which requires close communication with the team. "What patients are coming in. What treatments we need to handle," she explained.

In addition, there is the business plan for the upcoming year. Corrado and the center's oncology pharmacy coordinator will work with the director and the health system's finance and compliance officers to "make sure that we are offering the right therapies for our community, and that goes into the expansion of the nononcology infusions," as the center currently acts as an infusion center for multiple sclerosis treatments, osteoporosis, as well as various neurologic conditions, she said. ●