

# Maintenance Therapy Gains Ground in Blood Cancers

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Separate studies show that patients with follicular lymphoma or multiple myeloma can benefit from maintenance therapy, treatment given after initial therapy to prolong remission.

Updated results from the PRIMA trial, an international phase 3 study, compared 28 months of Rituxan (rituximab) to the traditional four months in newly diagnosed patients with follicular lymphoma. All patients received chemotherapy and induction therapy of four months of Rituxan, then randomized to either an observation arm or continued therapy for an additional two years of Rituxan. Researchers found that maintenance therapy increased progression-free survival from 66 percent to 82 percent. More patients also had complete remission, 47.7 percent of patients in the observation arm compared with 66.8 percent on maintenance therapy, although differences in overall survival have not yet been reported.

The benefit was seen in patients regardless of age, type of chemotherapy, and whether or not they responded to the initial treatment. Side effects were increased with the longer therapy, particularly infection and decreased white blood cell counts. Researchers remarked that this may become the new standard of care for follicular lymphoma patients.

In multiple myeloma, three studies looking at maintenance therapy showed the approach could change the way myeloma patients are treated, including those who are over 65 and for patients undergoing stem cell transplantation.

In a phase 3 study examining whether Revlimid (lenalidomide) lengthens the time to recurrence in multiple myeloma, maintenance therapy appears to be successful in this disease as well. Some myeloma patients are treated with high-dose chemotherapy and a stem cell transplant, but the disease usually recurs over time. Patients in the study were treated with high-dose chemotherapy and transplant and then given Revlimid for two months to knock the disease into complete remission. More than 600 patients were then randomized to receive either maintenance Revlimid or a placebo until the disease recurred. At three years, patients on maintenance therapy had better disease control, with 68 percent of patients on maintenance therapy experiencing no relapse compared with 35 percent on placebo. Revlimid also stopped the cancer from getting worse in 54 percent of patients. While Thalomid (thalidomide), an older-generation drug, has been shown to delay recurrence in some patients, it has significant side effects, including neuropathy. If the data with Revlimid holds up, it could be a

valuable option for patients in lieu of Thalomid but with better results and little risk of neuropathy. Final results are expected to be announced in December at the American Society of Hematology's annual meeting.

Another study looked at whether maintenance Revlimid given about three months after a stem cell transplantation would prolong the time the disease did not progress. Of the 568 myeloma patients enrolled in the four-year, phase 3 study, 418 patients were evaluated for the interim results released this year. After a follow-up of one year, the number of events, including progression, occurred in far fewer patients on the maintenance drug than placebo (29 compared with 58). This also equates to a 58 percent decrease in the risk of progression with the maintenance therapy compared to placebo. In terms of median time to progression, half of the placebo group experienced disease progression after 25.5 months while half of the maintenance group has not yet had disease progression. After a median one-year follow-up after transplant, there is not yet a difference in overall survival between the two arms. Side effects were more common in the Revlimid arm, including neutropenia and thrombocytopenia.

In the third study, researchers tested an experimental combination in elderly, newly diagnosed myeloma patients. The Italian phase 3 study included 511 patients aged 65 and older who were randomized to receive the standard treatment of Velcade, melphalan, and prednisone or the same combination but with the addition of Thalomid (thalidomide) followed by a maintenance regimen of Velcade and Thalomid. Results of the study showed that patients given the experimental treatment had better complete response rates (38 percent versus 24 percent) and longer progression-free survival. After three years, 54 percent of patients had not progressed on the four-drug combination compared with 40 percent on the standard treatment. Overall survival was similar in both groups after three years, but Antonio Palumbo, MD, who presented the findings, said it may be too early to see a difference. However, he says we may see a median survival of six-years with the combination, which would be very promising in this elderly population. Researchers also noted that when Velcade was given as a weekly infusion, as opposed to twice weekly, the risk of peripheral neuropathy decreased (8 percent versus 5 percent). Peripheral neuropathy is a painful side effect that occurs as a tingling or stinging sensation in the hands and feet. Other side effects included neutropenia and heart complications. This is the first study that shows a four-drug combination followed by maintenance is better than the standard treatment of VMP, which led Palumbo to conclude that the experimental therapy should be adopted for elderly, newly diagnosed myeloma patients.

The common theme with these studies is that prolonged remission does come at a cost of added side effects, and so far, patients do not seem to live longer with maintenance therapy. There may be survival differences with longer follow-up, and factors to select patients for maintenance therapy might further enhance the benefit.