ASCO Cage Match: BR vs R-CHOP

I recently attended the ASCO annual meeting in Chicago. It's huge, but remarkably organized and well run. I think it helps that the meeting has been held at the same site for several years, which makes the execution more predictable. What's more, Chicago is fabulous to visit and can handle a meeting of this size easily.

I was asked to discuss several presentations at the lymphoma oral abstract session. The job of the discussant is not to repeat what was just presented, but rather to put what everyone has just heard into some sort of context. Two of the presentations I discussed provided long-term follow-up data from previously published studies. Mathias Rummel presented long-term follow-up data from the StiL trial, which was the first study to suggest that BR is superior to R-CHOP in follicular lymphoma and mantle cell lymphoma. The long-term follow-up focused on the patients with follicular lymphoma. After more than 9 years of follow-up, the StiL data continued to show substantial superiority of BR over R-CHOP, with a median PFS of 69 vs 31 months. This difference translated into a significant benefit in terms of time to next treatment, although no difference in OS was noted. There also was no difference in risk for secondary malignancies.

Ian Flinn presented long-term follow-up data from the BRIGHT study. BRIGHT, which was conducted in North America, compared BR with R-CHOP/R-CVP. Whether a patient received R-CHOP or R-CVP was up to the treating physician. BR was superior to R-CHOP/R-CVP for PFS, although when the patients treated with BR were analyzed against just the patients assigned to R-CHOP, the statistical significance of the difference was lost. In addition, with long-term follow-up, significantly more secondary malignancies developed in the patients treated with BR than in those treated with R-CHOP/R-CVP (42 vs 24). It is always a little disturbing when 2 randomized trials do not yield congruent results. Why should BR beat R-CHOP so handily in the StiL trial when the two regimens are more or less tied in BRIGHT?

In my discussion, I hypothesized that maintenance rituximab might have a differential effect. We know from the PRIMA trial that maintenance rituximab substantially prolongs PFS after R-CHOP. Is it possible that the same benefit is not realized after BR? No maintenance was given in the StiL trial, whereas approximately half of the patients in BRIGHT received maintenance. In the GALLIUM trial, presented at the 2016 ASH meeting, all the patients received maintenance, and individual centers could select their chemotherapy backbone. When BR plus maintenance was analyzed vs R-CHOP plus maintenance, no difference in PFS was found. In other words, maintenance pulls up the PFS curve after R-CHOP but is unable to do the same after BR. Of course, I am just speculating. I have no idea whether this is true or not. It's an important issue to sort out, and Ian Flinn assured me that he and his colleagues would further analyze the data from BRIGHT.

There is also the safety issue to consider. As I mentioned in a previous column, the rate of fatal adverse events in GALLIUM was close to 5% for the patients who received BR followed by maintenance rituximab, whereas it was 2% for the patients who received R-CHOP followed by maintenance. Infections appear to be a significant source of this risk, and it is apparent that bendamustine has a considerably greater effect on T cells than R-CHOP does. Many well-respected lymphoma experts have locked in on this worrisome finding and declared bendamustine unsuitable for frontline use in follicular lymphoma. The "benda-haters" are a growing faction in the lymphoma world.

My own experience with bendamustine for frontline use in follicular lymphoma (and mantle cell lymphoma) has been largely positive. In E2408, a frontline trial of more than 300 patients with follicular lymphoma in which BR plus rituximab maintenance was used in all arms, Andy Evens and I noted that the rate of fatal adverse events was 2.8%—not the 5% seen in GALLIUM.

Toward the conclusion of my discussion, I listed the pros for BR and the pros for R-CHOP. The lists were comparable in length. I continue to use BR as frontline therapy. I do acknowledge that BR is more myelosuppressive and immunosuppressive, but with BR, I like the lack of neuropathy, the lack of corticosteroid use, and the lack of alopecia. I also like the ability to save the anthracycline for another day. In BRIGHT, quality of life was better with BR than with R-CHOP.

I recognize that these are mostly short-term issues, and it will be very important to continue to collect data on infections and secondary malignancies after BR therapy. This story is sure to evolve as we see more long-term follow-up data from all our trials.

Until next month …

Brad S. Kahl, MD