Inauguration Week

At a dinner party, you should never discuss politics or religion. The same probably holds true for Letters From the Editor. Here I go anyway.

I would like to think that the founding fathers never envisioned how much special interests would come to dominate—and contaminate—the process of good government. Our system, as it currently stands, is fairly broken. However, one of the things we typically do well is transfer power in a peaceful and orderly way. It is perhaps the greatest attribute of our democracy.

As I write this, it is time for the next transition. I did not vote for the winner, and like many, I have a certain amount of anxiety. Before you accuse me of being some "lefty," be advised that I have voted in 8 presidential elections: 4 times elephant and 4 times donkey. (Admittedly, more donkey lately.) Why am I anxious? The campaign rhetoric was disturbing. You know the list: inciting violence at rallies, mocking a reporter with disabilities, the "locker room talk," threatening to lock up one's political opponent, finding scapegoats for our many problems, and more.

I once read a book about leadership (by Kouzes and Posner) that outlined the 5 practices of exemplary leaders: (1) model the way, (2) inspire a shared vision, (3) challenge the process, (4) enable others to act, and (5) encourage the heart. Note number 1. Our leaders should set a tone of decency and civility. Tone matters, and these things tend to trickle down. You might have seen the video showing a school cafeteria full of middle school–aged kids chanting "build a wall" at a few Hispanic kids eating lunch. Although cruelty is hard to watch, I showed it to my kids, hoping it would turn their stomach like it turned mine. Fingers crossed, President Trump will be a better person than candidate Trump. Model the way.

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Back to politically neutral ground. Last month, I started to discuss the GALLIUM study, which was presented at the plenary scientific session of the 2016 ASH meeting. GALLIUM revealed a 34% reduction in the risk of progression of follicular lymphoma when patients received obinutuzumab (O) + chemotherapy vs rituximab (R) + chemotherapy. As I mentioned, the O patients received approximately 36% more monoclonal antibody, making it hard to tell whether O is truly better than R. The other interesting observation was the disparity in death rates among the different chemotherapy regimens. The trial was designed in such a way that each center decided whether to use bendamustine, CHOP, or CVP as the chemotherapy backbone; all patients at a center received that backbone combined with either O or R. Bendamustine (n=686) was used more frequently than CHOP (n=398) or CVP (n=118). Drawing the attention of many was a significant disparity in fatal adverse events (AEs) when analyzed by chemotherapy backbone: 35 with bendamustine (5%), 7 with CHOP (2%), and 2 with CVP (2%). The vast majority of the fatal AEs on bendamustine occurred late, either during maintenance therapy or after the completion of therapy. Causes of death were varied, but infection seemed to be a risk factor.

The PRIMA trial told us that maintenance R after R-CHOP, R-CVP, or F-FCM would improve progression-free survival (PFS). The StiL trial told us that bendamustine/rituximab (BR) was more efficacious and less toxic than R-CHOP. Extrapolating from PRIMA and StiL, many clinicians have routinely utilized R maintenance after a BR induction. Is it possible that maintenance R after BR is harmful? Or perhaps the maintenance is irrelevant, and the fatal AE rate is simply a function of the induction therapy. Or perhaps the data are quirky. I have been using BR with R maintenance for years, and a 5% fatal AE rate seems ridiculously high. Despite the higher fatal AE rate with bendamustine, it performed as well or better than CHOP for PFS, with either monoclonal antibody.

So for me, GALLIUM raised more questions than it answered. Is O better than R? I can't tell. Should I stop using R maintenance after BR induction? I am not sure. For now, I am going to continue with BR and R maintenance, but I will have a low threshold for discontinuation of maintenance should problems arise. These issues need to be sorted out definitively. Perhaps that will be a task for the National Clinical Trials Network. More on that next month . . .

Sincerely,

Brad S. Kahl, MD