The Too-Typical Clinical Conundrum

In the March issue, I wrote about a patient who had a lot to teach me about life. This month, I am writing about a different patient, for a different reason: I need your help. The patient is a 90-year-old woman who was given a diagnosis of Waldenström macroglobulinemia in 2014. She received treatment with rituximab and cyclophosphamide at that time, with a good response. In 2017, she needed to resume therapy because of anemia and a rising IgM. She started acalabrutinib at 100 mg twice daily. Almost immediately after starting the acalabrutinib, her hemoglobin fell to 6 g/dL. Despite the timing, this drop was likely caused by further progression of the Waldenström macroglobulinemia rather than by the acalabrutinib. The patient was certain that the acalabrutinib was the cause, however, and when her treating physician could not convince her otherwise, she dropped the acalabrutinib to 100 mg daily. Her hemoglobin recovered, and her IgM decreased to 2500 mg/dL over the next several months. Unfortunately, over the next year, her IgM increased to 4000 mg/dL. Her treating oncologist tried to have her resume acalabrutinib at 100 mg twice daily, without success.

After seeking multiple opinions, she settled on my practice, and I was able to convince her to restart the twice-daily dosing of acalabrutinib in order to determine whether the rise in her IgM was due to subtherapeutic dosing of acalabrutinib before switching therapies. Over the next several weeks, her IgM continued to rise and her hemoglobin started to decrease. Although I took this to mean that the Waldenström macroglobulinemia was resistant to the acalabrutinib and recommended alternate therapy, the patient argued it was the twice-daily dosing of the acalabrutinib that had led to the worsening state. She insisted on reducing the acalabrutinib back to daily dosing.

My discussions with her were quite interesting, to say the least. This was an extremely mentally acute octogenarian, whose knowledge of Waldenström macroglobulinemia exceeded that of many of my colleagues who do not specialize in CLL and lymphoma. What ensued over the next few weeks troubled me greatly, however. She became increasingly firm in her belief that the worsening anemia in 2017 and the rise in IgM in 2021 were caused by the twice-daily dosing, not by disease progression. She would return to my office weekly to check her laboratory test results and debate with me the merits of returning to once-daily dosing. I spent hours explaining to her the mechanism of action, the pharmacokinetics, the pharmacodynamics, and the dosing rationale for acalabrutinib. I reviewed the phase 1 data, including the use of up to 400 mg daily without complications or changes in efficacy. I acknowledged that given her small size, once-daily dosing of 100 mg of acalabrutinib was likely to be just as efficacious for her as twice-daily dosing, and my interest in trying the higher dosage had been more related to making sure that issues with absorption would not factor in. I finally convinced her to accept an alternate treatment regimen. Unfortunately, on the day she came in to start, she stated that she had changed her mind and wished to continue with once-daily acalabrutinib. When I resisted, she chose to seek out other opinions regarding the possibility of continuing once-daily acalabrutinib and left my practice.

Although I respect and appreciate the importance of patients seeking additional opinions, and recognize that I may have unwittingly extricated myself from a very difficult situation, I am troubled by my inability to convince this patient of the need to switch therapy. I am often tempted to use the Care Everywhere function in Epic to check up on her and see how she is doing, even without her authorization. I hope she has found a physician able to convince her to accept a new and effective therapy, or even continue acalabrutinib once daily and prove me wrong by eventually having her IgM respond.

I cannot keep from wondering what I could have done differently with her. Was I too permissive, providing her with too much fertile ground for spawning non–data-driven theories on therapeutics? Should I never have engaged in her debate? Am I being too paternalistic in even worrying about her? Might I have lost perspective and become too involved with my patient? What would you have done differently for my patient? I found her mental acuity, knowledge, and advocacy for herself impressive. Unfortunately, in my opinion, those traits did not serve her well in this situation. I continue to wonder how she is doing.

Sincerely,

Richard R. Furman, MD