

How to Treat Hodgkin Lymphoma



Last weekend, I attended the 2017 ASH Meeting on Hematologic Malignancies. This is an incredible 2-day meeting organized around a series of “How I Treat” lectures, which are a spin-off of a *Blood* series by the same name. I find these pieces to be incredibly valuable, which is one of the reasons we added a “How I Treat” column to this month’s issue of *Clinical Advances in Hematology & Oncology*. You are allowed inside the head of an expert who not only knows the data but also manages a large number of patients with a particular disorder. As you know, reading the literature and knowing the data take one only so far.

Every talk delivered was fantastic. One I was particularly eager to hear was Nancy Bartlett’s, “How I Treat Hodgkin Lymphoma.” Nancy, a colleague of mine at Washington University School of Medicine in St. Louis, has probably forgotten more about HL than I will ever know. Since the publication of several landmark studies on HL in the past 2 years, the management has become far more nuanced than it was before.

Nancy separated patients with HL into 3 main groups: advanced-stage (cure rate, 75%), early-stage unfavorable or bulky (cure rate, 80%), and early-stage favorable or nonbulky (cure rate, 90%). I would encourage you to determine which group your new HL patient falls in and then follow Nancy’s approach. In all these scenarios, you can now use interim PET to help you risk-stratify your patient and modify your approach to treatment based on PET results after cycle 2. For advanced-stage patients, she recommends ABVD chemotherapy for 2 cycles followed by interim PET. Based on the RATHL study (*NEJM*, June 23, 2016), it is safe to eliminate bleomycin from cycles 3 through 6 of ABVD in interim PET-negative patients. There are no randomized data to tell us exactly how best to manage interim PET-positive patients. In the RATHL trial and the US Intergroup S0816 trial (*JCO*, June 2016), this group was assigned to receive the escalated BEACOPP regimen, with 3-year PFS rates of 67% and 64%, respectively—better than those of historical controls receiving ABVD.

The management of early-stage patients is more complicated, and a certain amount of individualization will be necessary based on the clinical situation. For example, you may be more motivated to avoid mediastinal radiation in a 22-year-old woman than in a 46-year-old man. The first decision is to select a risk-stratification strategy. The German Hodgkin Study Group and EORTC both have criteria (which vary slightly) for defining favorable vs unfavorable risk, along with a treatment paradigm for each risk group. EORTC recently published

a complicated but informative study, EORTC H10 (*JCO*, June 2017), which used an interim PET risk-adapted approach. A breakdown of this trial would take an entire column; I encourage readers to see Ralph Meyer’s accompanying editorial. The one straightforward conclusion from the EORTC H10 trial is that for the small group of patients who have early-stage disease (both favorable and unfavorable) and are interim PET-positive, outcomes were improved by changing the chemotherapy from ABVD to escalated BEACOPP followed by XRT.

Rather than the somewhat complicated favorable vs unfavorable criteria, both Nancy and I tend to use bulk (defined as a mass ≥ 10 cm) as a simpler way to separate early-stage patients. The UK group and the US Intergroup have adopted this strategy for their trials. Two trials have informed us on how to manage early-stage nonbulky patients. In the UK group’s RAPID trial (*NEJM*, April 23, 2015), a PET-directed strategy showed a small loss of disease control with omission of XRT in the interim PET-negative patients. The loss was so small, however, that omitting XRT for the majority still seemed prudent. The US Intergroup 50604 trial (ASH meeting, 2015) used a similar strategy, in which patients received ABVD $\times 2$ or, if interim PET-negative, ABVD $\times 2$ with no XRT. The 3-year PFS was 92%, which suggests that radiation can be safely eliminated for most early-stage nonbulky patients. Whether XRT can be safely eliminated from the treatment of early-stage bulky patients who are interim PET-negative is less clear, but emerging data sets suggest it can be. Those patients, however, need a full course of chemotherapy. Bulky stage II patients were included in RATHL, so eliminating the bleomycin in the interim PET-negative patients after cycle 2 is safe.

As you can see, the management of HL has become quite sophisticated. What is clear is that the separation of patients into those with advanced-stage, early-stage bulky, or early-stage nonbulky disease defines 3 treatment groups. The treatment strategy in each group can be further tailored according to the results of interim PET after cycle 2. Fortunately for me, I am in clinic with Nancy every Wednesday.

Until next month ...

A handwritten signature in black ink that reads "Brad Kahl".

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